EXPERIMENTAL OBSERVATIONS IN THE MORITA BAYLIS-HILLMAN REACTION IN METHANOL

A Dissertation

by

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ABSTRACT

Historically, research projects have originated from the literature group meetings and it was at one of these late night Wednesday meetings, nascent in my graduate career, that I presented a theoretical paper over the mechanism of the Morita Baylis-Hillman reaction. Something about it caught my attention and a project was born. The Morita Baylis-Hillman reaction had been heavily studied in the literature in recent years by both experimental and computational means. Some of these computational studies had even defined a complete theoretical mechanistic energy profile for these reactions. This dissertation describes a combination of experimental and theoretical mechanistic probes, including the observation of intermediates, the independent generation and partitioning of intermediates, thermodynamic and kinetic measurements for both the main reaction and interrelated side reactions, isotopic incorporation from solvent, and kinetic isotope effects, to fully define a more realistic picture of the free-energy profile for a Morita Baylis-Hillman reaction in methanol. Although the majority of this dissertation will be about the Morita Baylis-Hillman reaction in methanol, it could not have been fully accomplished without having to study the Morita Baylis-Hillman in DMSO and the Morita Baylis-Hillman utilizing acrylonitrile as well. All of these observations will be discussed.

DEDICATION

To My Parents - “Icing on the cake”

ACKNOWLEDGEMENTS

I would like to thank my advisor, Dr. Singleton, for his guidance, patience, understanding, and support during my years here. I would like to thank my committee members, Dr. Watanabe and Dr. Bergbreiter for their time and direction. I also want to thank Dr. Miguel Mora-Zacarías for getting to know me.

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Last, and most important, I have to thank my entire family. I could not have done this without you. I thank you for the praises and prayers that you have given me through out all these years. Thank you tía Mari for the tamales, praises, and support and tío Alfredo for the grapefruit every winter. I thank the Montalvo family for their generous thoughts and prayers. Gracias grandma Montalvo por sus bendiciones. I thank the Plata family for being there for me and keeping me in your prayers. I extend my thanks to the Agado family and especially Roli for all the trash talking that kept me sane and for cheering me up when I was down. I wish I could name everyone that touched my life during this time. It all added up; I thank you.

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CHAPTER I

INTRODUCTION

Purpose

The Singleton research group has been carrying out broad-based research in the field of Organic Chemistry in order to study a variety of organic, organometallic, and bioorganic reaction mechanisms by utilizing a combination of kinetic isotope effects (KIEs) and theoretical calculations. An invaluable tool that has aided this research has been the ability to determine multiple small kinetic isotope effects in organic reactions at natural abundance.[1] The experimental kinetic isotope effects are then interpreted with the aid of theoretical calculations to define an experimentally-based reaction mechanism. This combination of experiment and theory provides a powerful tool to the field of organic chemistry and has allowed chemists to mechanistically probe aspects of reactions that were previously intractable.[2]

We are a group that studies mechanisms in organic chemistry and we compete with groups that do solely theoretical studies. There are tricks that we use to study mechanisms. Some of these include kinetic isotope effects at natural abundance, solvent isotope effects, kinetic investigations, kinetic modeling, activation parameters, and emulating a step in a reaction. We then pick out these experiments and compare how they do with theory. For complicated experiments, calculations do not tend to do very well, by themselves.

Kinetic Isotope Effects

Experimental chemistry has been the cornerstone of gaining an understanding into mechanisms of organic reactions; and having an understanding means having control. One particularly useful experiment for taking a step into the understanding of a reaction mechanism is the measure of kinetic isotope effects (KIEs). The rate of a reaction is ultimately bounded by the steepest height of the barrier for the reaction. The kinetic isotope effects represent a measurement of the change in rate when isotopes are substituted and allowed to compete through these energy barriers in the reaction. Variations in these competing isotopes are caused by differences in their zero-point energies (Figure 1). Kinetic isotope effects also contain valuable information about the vibrational normal modes of rate-limiting barrier in the same way an IR spectrum does. This allows a glimpse into the geometry of the species that is being studied at hand that can allow a physical organic chemist to paint a picture of a structure that is ultimately in control of the reaction. Isotope effects can be calculated from theoretical structures and frequencies and with the use of theoretical calculations, the KIEs can be predicted and used to compliment experimental KIEs.

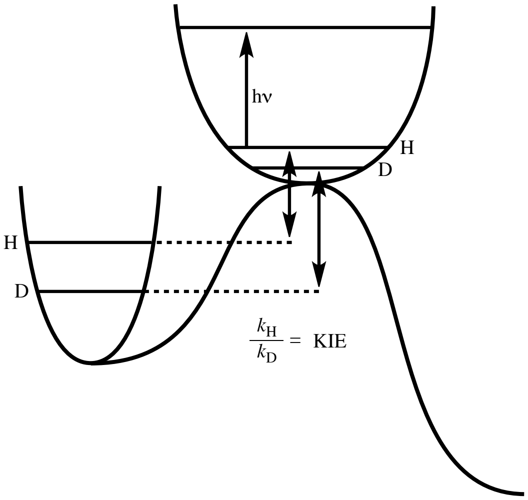


Figure 1. Kinetic isotope effects arise from a difference in zero-point energies of the reacting isotopomers as a reaction proceeds along the path from reactants to the transition state.

Organic compounds contain mixtures of isotopomers; for example, carbon is primarily composed of ^{12}C but it also contains a natural mixture of ^{13}C and ^{14}C as well. During the course of a reaction, products are enhanced in faster reaction isotopomers and reactants in slower reacting isotopomers and if these enhancements can be measured, the isotope effect $k_{\text{light atom}} / k_{\text{heavy atom}}$ at various positions in a compound can be determined. Traditionally, this involved taking a compound and synthetically incorporating a heavy atom at a particular position and then measuring the differences in the rates of reaction of this labeled material versus the unlabeled substrate. This method is exceptionally useful but the abundance of material is going to depend on whether it can be synthesized. The ^{13}C KIEs reported in this dissertation were measured at natural abundance using the Singleton method. This methodology is very effective in determining the rate-limiting step in a chemical reaction and it will be able to help build a glimpse of the geometrical structure that controls the reaction.

Fundamental Origin of Kinetic Isotope Effects

The origin of the kinetic isotope effect is rooted in the differences in the rate that occur when isotopes are substituted for one another. One of the more common and simple substitutions for hydrogen (H) can be deuterium (D); although, substitutions of heavy atoms, i. e., ^{13}C for ^{12}C, can be utilized just as well. Substituting isotopes on a molecular structure generally does not have an effect on the potential energy surface or the electronic structure. The molecular structure and chemical environment remain the same. However, the differences that can be observed, in the isotopologues, is their rate constants, eq 1 and 2. The effect on the rate-constant ratios on the two represent the kinetic isotope effect (KIE) (eq 3).[3]

$$\mathrm{XH} + \mathrm{Y} \overset{k_\mathrm{H}}{\rightarrow} \mathrm{X} + \mathrm{YH} \tag{1}$$

$$\mathrm{XD} + \mathrm{Y} \overset{k_\mathrm{D}}{\rightarrow} \mathrm{X} + \mathrm{YD} \tag{2}$$

$$\mathrm{KIE} = \frac{k_\mathrm{H}}{k_\mathrm{D}} \tag{3}$$

Zero-point energy (ZPE) is one of the major factors that contributes to the kinetic isotope effect; although, other factors are found to play a role as well. The substitution of isotopes brings about changes in zero-point energies; as the reactants of a reaction proceed to the transition state, an isotope effect arises.

As mentioned above, substituting one isotope for another does not alter the potential energy surface. The only thing that does change is the mass. If we contemplate a C-H bond stretch, it manifests itself like a harmonic oscillator. This frequency can be represented in the classical mechanics model of a small mass *m* attached to a larger mass by a spring that has a certain force constant *k*. The vibrational frequency, ν, is then given by eq 4.[4] The force constants, *k*, for the reacting isotopomers, do not change because isotopic substitutions not attribute to any changes in electronic structure of a molecule. The differences that do arise are brought about from the change in mass *m*, and the effect it has on the vibrational frequencies.

$$\upsilon = \frac{1}{2\pi} \sqrt{\frac{k}{\mathrm{m}}} \tag{4}$$

This classical mechanics model can be treated quantum mechanically and the frequencies for the vibrational modes can now be represented by the energy, E, in eq 5.

$$\mathrm{E} = \left(\mathrm{n}+\frac{1}{2}\right) \mathrm{h}\nu \;\; \text{where } \mathrm{n} = 0, 1, 2, \ldots \tag{5}$$

This energy is measured from the lowest point of the potential energy surface of the potential energy well. The molecule will always at least retain some energy. When n = 0, the lowest possible level lies at ½hν above minimum of the potential energy well (eq 6). From this equation, it can be deduced that the zero-point energy is thus proportional to the frequency, ν, and therefore, inversely proportional to the square root of the mass (eq 7). What this translates to is that the zero-point energy of a C-D (heavier isotope) bond is higher than that for a C-H (lighter isotope) bond in the reactants. Something else that should be pointed out is that since the lighter isotope, i. e., C-H molecule, starts out at a higher energy, the barrier that it needs to surpass it is much lower than that for the heavier isotope C-D molecule; which, in turn makes the $k_{\mathrm{H}}/k_{\mathrm{D}}$ be greater than 1.

$$\mathrm{ZPE} = \tfrac{1}{2}\mathrm{h}\nu \qquad (6)$$

$$\mathrm{ZPE} \propto \sqrt{\frac{1}{\mathrm{m}}} \qquad (7)$$

Types of Kinetic Isotope Effects

Kinetic isotope effects are categorized under two main headings, that is, either as primary isotope effects or as secondary isotope effects. One general way to distinguish a primary isotope effect is if in a reaction, there is a bond that either forms or breaks. In the simple case that we have been contemplating as above, a C-H (C-D) bond or atom that has isotopic substitutions that undergoes a σ-bond making or breaking at the rate-limiting step of the reaction, has the effect of a primary isotope effect. The stretching frequency of the reactants is lost to a translation motion over the barrier of interest, and zero-point energy associated with the stretching vibration disappears. These types of primary KIEs have values ranging from 2 to 7 for k_H / k_D and 1.01 to 1.05 for k_{12C} / k_{13C}.

Secondary isotope effects are observed from a bond that has not been broken or formed in reaction where the reactants have undergone isotopic substitution. These secondary effects arise from changes of zero-point energies of ordinary stretching or bending frequencies of the normal modes associated with these atoms. These types of kinetic isotope effects are smaller and may be categorized as *normal* if the lighter isotope reacts faster or *inverse* if the heavier isotope reacts faster. Typical values of these types of secondary isotope effects range from 0.7 to 1.0 for k_H / k_D and 0.99 to 1.00 for k_{12C} / k_{13C}.

The reaction coordinate diagrams below illustrate the secondary isotope effect and the factors that influence its direction and its geometrical interpretation. Figure 2 represents a normal secondary KIE where upon going to the barrier of the reaction, a frequency decrease is observed in any vibrational mode. The isotopically substituted atoms that are attached to the reactive center are undergoing a change in hybridization from sp^3 to sp^2. Figure 3 represents just the opposite of this. The frequency of any vibrational mode increases as the reaction coordinate reaches a maximum and it contributes a factor less than unity. A general rule of thumb in secondary kinetic isotope effects is that deuterium likes to be crowed at the transition state leading to an inverse secondary KIE while an normal secondary KIE can be attributed to an atom that is undergoing a bond weakening in the transition state.

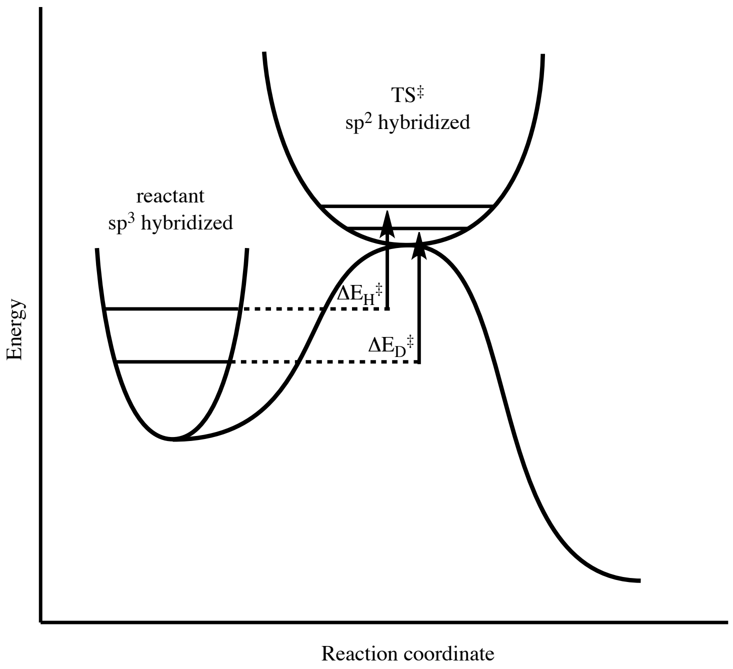


Figure 2. The origin of normal secondary isotope effects.

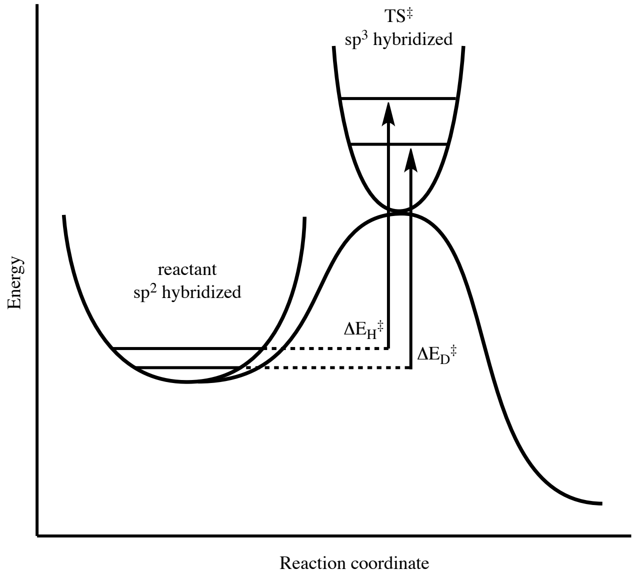


Figure 3. The origin of inverse secondary isotope effects.

Experimental Kinetic Isotope Effects

In most experimental situations, it is assumed that isotopic species will react in identical ways but their rates of reaction will usually react differently. It will also be understood that as the isotopic species progress through the reaction, there will be a change of ratio of these species. Assuming that two isotopic molecules **A** and **B**, with respective concentrations of a and b, will identically and irreversibly proceed to products,[3] then a general rate expression can be written as eq 8 and 9. These expressions may be integrated and thus, a ratio of those rate expressions can be represented in terms of rate constants (eq 10).

$$A_{(1)} + B \xrightarrow{k_1} \text{Product}_{(1)}$$

$$A_{(2)} + B \xrightarrow{k_2} \text{Product}_{(2)}$$

$$-\frac{da_1}{dt} = k_1 a_1 b \tag{8}$$

$$-\frac{da_2}{dt} = k_2 a_2 b \tag{9}$$

$$\frac{k_1}{k_2} = \frac{\log\left(a_1/a_1^0\right)}{\log\left(a_2/a_2^0\right)} \tag{10}$$

A new component is introduced which represents the fractional amount of conversion, F. It is a value that varies from 0 to 1 and it is representative of a conversion of a reaction as it proceeds from start to finish. It can be assumed that the ratio of concentration at some time to the initial concentration can be represented as 1 - F_1, then the above expression becomes eq 11 and when solved for F_2, eq 12 is obtained.

$$\frac{k_1}{k_2} = \frac{\log\left(1-F_1\right)}{\log\left(1-F_2\right)} \tag{11}$$

$$F_2 = 1-\left(1 - F_1\right)^{k_2/k_1} \tag{12}$$

From an experimental analysis, the expression $a_2^0/a_1^0 = R_0$ and $a_2/a_1 = R$ can be formed directly from the ratio of the isotopic molecules. Thus, the substitution of terms from eqs 11 and 12 then gives rise to eqs 13 and 14. The term used for the calculation of the experimental KIE can be represented by eq 15.

$$\frac{k_1}{k_2} = \frac{\log(1 - F_1)}{\log[(1 - F_1)R/R_0]} \tag{13}$$

$$R/R_0 = (1 - F)^{(1/KIE-1)} \tag{14}$$

$$KIE_{calcd} = \frac{\ln(1 - F)}{\ln[(1 - F)R/R_0]} \tag{15}$$

Theoretical Prediction of KIEs

As mentioned earlier, we are a group that studies mechanisms by experimental and theoretical studies and we compete with groups that solely use theoretical studies. The combination of experimental and theoretical studies provides more insight into the understanding of mechanisms in organic chemistry. Theoretical calculations can predict in detail mechanistic models of a chemical reaction. These models can be of reactants, intermediates, transition states, and products. However, the accuracy of these predicted models are only as good as that that can be imagined from reality, i. e., there may be models that exist in reality that could possibly never be imagined. Something to keep in mind when computational studies are obtained is whether the results are accurate depictions of observed experimental data. However, there may be times when experimental data cannot be obtained. The Singleton group uses experimental KIEs and predicted KIEs in combination to gauge the validity of calculations and to help interpret experimental results.

The process of predicting KIEs begins with obtaining a transition state from a density functional theory (DFT) calculation and from that, the scaled vibrational frequencies[5] may be used to predict the isotope effects by applying conventional transition state theory by the method of Bigeleisen and Mayer.[6] Using a tunneling correction of a one-dimentional infinite parabola, the computed KIEs can then be corrected for tunneling.[7]

Conclusion

The Singleton group has effectively utilized a combination of experiment and juxtaposed that with theoretical calculations in order have a better understanding of mechanisms in organic chemistry. This dissertation focuses on applying the theories and methodologies described above in order to better understand what is going on in the transition state for the rate-limiting step of a chemical reaction. The experimental data will be compared to that with calculational data with the hopes that the two will compliment one another.

CHAPTER II

EXPERIMENTAL OBSERVATIONS OF THE MORITA BAYLIS-HILLMAN REACTION IN METHANOL

Introduction

For simple reactions involving only a single kinetic step, the “reaction mechanism” is in general completely defined by the structure of the transition state. This structure can be probed by the many kinetics-based tools of classical experimental chemistry, including the determination of rate-laws, substituent effects, solvent effects, isotope effects, and activation parameters. For a two-step reaction, mechanistic studies are intrinsically less decisive as the reaction now involves two transition states plus an intermediate. For mechanisms involving more steps, the complexities are multiplied. Often only one of the transition states, that for the rate-limiting step, can be scrutinized by kinetic probes, and intermediates along the reaction profile are usually not directly observable. For many important multistep reactions, experimental studies can provide only limited glimpses of the mechanism.

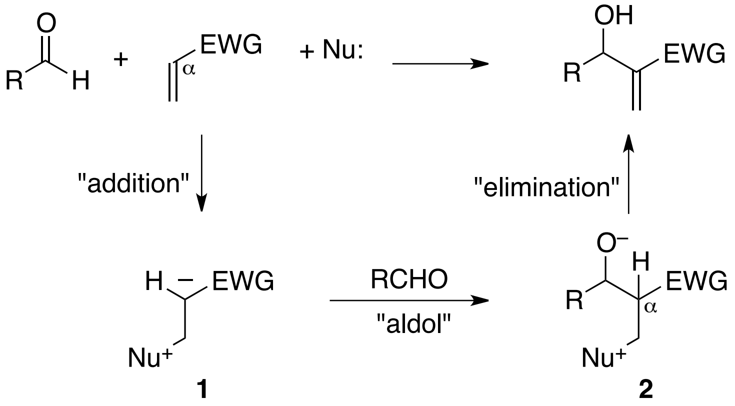
For the understanding of complex reactions, the rise of computational mechanistic chemistry has arguably been the most important advance ever. The combination of reasonably accurate DFT methods and ever increasing computational power has stimulated the application of this technology on a broad front. Few organic reactions, if any, are considered to be too complicated for computational study. Such studies then provide apparently *complete* mechanisms, including the geometries and energies of every intermediate and every transition state along the reaction pathway. This level of detail is beyond the most ambitions dreams of classical experimental mechanistic chemistry.

This impressive accomplishment also constitutes a potential problem. That is, those mechanistic details that cannot be discerned from experimental studies are also not directly confirmable, or falsifiable, by experimental studies. The argument for the accuracy of such studies, if made, is usually an indirect one, most often based on the general accuracy of the potential energy surface for simpler problems or when compared with higher-level calculations. This scientific approach can go wrong on multiple levels. At one level, the accuracy of a theoretical method for some other problem may not imply accuracy for the problem at hand. At a second level, even a perfectly accurate potential energy surface may be quite misleading in comparison to the free energy surface that is a better picture of what controls reactions, and the allowance for entropy may be inaccurate, or else impractical to achieve accurately. At a more human level, calculational studies do not speak to mechanistic possibilities that were not explored, and in a complex reaction, possible mechanisms may easily be missed in the same way that lowest-energy conformations are readily missed in computational conformational analysis. Finally, the paradigms used to interpret computational mechanistic results, particularly statistical rate theories, may not be accurate for a system under study, even for common organic reactions in solution.[8] It should be recognized that the goal of accuracy has been a central feature of computational mechanistic chemistry, and that no small effort has been exerted in this endeavor, but it may also be recognized that the accuracy of many studies is ultimately both uncertain and unexamined.

We describe here a case study of a complex reaction, the alcohol-mediated Morita Baylis-Hillman (MBH) reaction,[9] using a full gamut of experimental mechanistic probes as well as a full computational study using two popular DFT methods augmented by high-level calculations on model reactions. The MBH mechanism in general outline (Scheme 1) is uncontroversial, consisting of the “addition” step by an activating nucleophile to afford the **1**, the carbon-carbon bond forming “aldol” step affording **2**, and a multistep “elimination” to afford the product. (This follows the descriptive terminology used by Hill and Issacs.[10]) However, the multicomponent nature of the MBH reaction and multistep nature of its mechanism provides fodder for many complications that affect experimental observations. We viewed the MBH mechanism as a special opportunity for mechanistic study because the individual steps are amenable with ingenuity to detailed scrutiny using many experimental probes, including the observation of intermediates, the independent generation and conversion of intermediates, thermodynamic and kinetic measurements for both the main reaction and interrelated side reactions, and kinetic isotope effects. The inferences from experimental studies can be compared with computational predictions in a variety of ways, and such comparisons are the focus of the discussion here. The conclusion from our studies is pessimistic from one perspective; it is not clear to us that any accurate information that was not already clear from experiment could have been reliably garnered from calculations, and the computational studies are more misleading than enlightening.

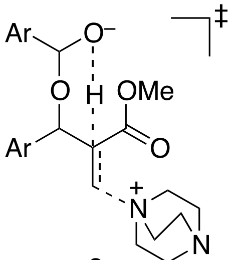
Nonetheless, the computations aid in interpreting experimental observations and the combination of the two details the full mechanistic pathway. Calculations by themselves fail utterly, however, as a replacement for experiment.

Scheme 1



The MBH reaction has been usefully catalyzed or promoted by tertiary amines,[11] phosphines,[12] oxygenated bases,[13,14] Lewis acids,[15] metals,[16] water,[17,18] high pressure,[19] ultrasound,[20] autocatalysis,[21] and even the use of lower temperatures[22] in cases. Some of these reactions are catalyzed but can take weeks to reach any appreciable conversion. Leahy and coworkers describe the reaction of methyl acrylate and acetaldehyde takes 1 week to reach completion at room temperature versus only 8 h at 0 °C. This complexity underscores the importance of mechanistic understanding for the rational control of reactions and development of new reactions. There has thus been considerable interest in the MBH mechanism. In general carbon-carbon bond forming steps tend to have higher barriers than proton transfer steps, so the aldol step might have been expected to be rate-limiting in the mechanism. This idea was supported by Hill and Isaacs for the DABCO-catalyzed reaction of acrylonitrile with acetaldehyde on the basis of third-order kinetics rate = k [MeCHO][acrylonitrile][DABCO], pressure dependence studies, and an H/D kinetic isotope effect (KIE) for the α-position of acrylonitrile of 1.03 ± 0.1.[10] It is interestingly uncertain as to what solvent was utilized in their determination of kinetic isotope effects as it is not mentioned in their study. Their investigations clearly describe the purification and preparation of substrates. Coincidently their synthesis of the α-d-acrylonitrile was formed by equilibrating in d_4-methanol with a catalytic amount of DABCO. A general experimental for the kinetic measurements is provided. It is clear in their kinetics results which solvents were used in the kinetic study; however, it is not certain which of the listed solvents was used for kinetic study of the α-[^{2}H]-acrylonitrile and its ^{1}H analogue. Third-order kinetics was also observed by Bode and Kay for reactions of acrylate esters with pyrindinecarboxaldehydes catalyzed by 3-hydroxyquinuclidine or DABCO.[23]

Much later, McQuade and coworkers stood the simplistic picture of the MBH mechanism on its head by the unexpected finding that the reaction of acrylates with aryl aldehydes in aprotic solvents was overall fourth order.[24] McQuade additionally observed large H/D KIEs for the α-position of acrylates. These observations were inconsistent with a rate-limiting aldol step and they implicate a rate-limiting elimination aided by a second molecule of aldehyde in a hemiacetal intermediate, as in **3**. McQuade suggested that this mechanism was general, even in a case where the α-position H/D KIE dips down to 1.0. McQuade also suggested the mechanism was general with a variety of aldehydes.



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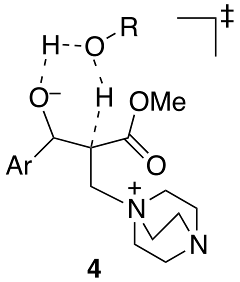


4

The acceleration of the MBH reaction by alcohols and water has long been noted by many groups.[17,10b,23,25] Hill and Issacs proposed that alcohols acted by hydrogen bonding that promoted the aldol step. Aggarwal and Lloyd-Jones[26] observed that the reaction of methyl acrylate (MA) with benzaldehyde exhibited autocatalysis, and they proposed that the product alcohol was acting as a shuttle to transfer a proton from the α-position of **2** to the alkoxide via a six-membered cyclic transition state, as in **4**.

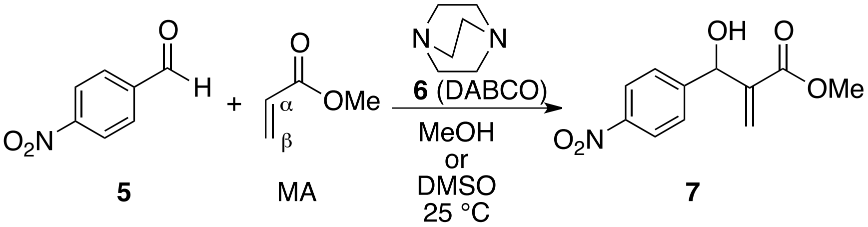
A series of elven papers from multiple groups has studied the MBH mechanism computationally. Every paper that examined the issue, a total of seven, supported the Aggarwal / Lloyd-Jones proton shuttle depicted in **4**, and this prediction was the highlight of most of these papers. None appear to have considered any alternative mechanism for catalysis by water or alcohols. Large computational errors are evident in some of these papers but several of the group undertook substantial and respected approaches to minimizing error. One initial mechanistic paper was reported by Xu in 2006, where the B3LYP/6-311+G*/PCM study of a phosphine-catalyzed model reaction concluded that a 1,3-proton transfer in **2** was rate limiting.[27] The computational results were described as "in good agreement with the previous experimental results" though the calculated free-energy barrier of 63.2 kcal/mol would lead to rates that are roughly 10^{30} lower than experimentally observed rates. Fan and coworkers B3LYP/6-311+G**/CPCM study of a trimethylamine / acrolein / formaldehyde /methanol model reaction supports the Aggarwal / Harvey proton-shuttle mechanism.[28] The calculated $\Delta G^{\ddagger}$ of 50 kcal/mol would lead to rates that are 20 orders of magnitude lower than experimentally observed rates. Li and Jiang did a B3LYP/6-31+G**/CPCM study of a trimethylamine / acrolein / formaldehyde / methanol model reaction that supports the proton-shuttle mechanism, and concluded that "the calculated overall reaction barrier is in agreement with experimental observations."[29] However, the calculated "free energy" barriers did not include any allowance for solute entropy. This is a common error in the literature.[30] The typical error is 12 kcal/mol for bimolecular equilibria and 24 kcal/mol for trimolecular equilibria. If the full calculated solute entropy were included, the barrier would be >50kcal/mol. Sunoj and coworkers chose their DFT method (MPW1K) based on comparison with high-level CBS-4M calculations in computational models.[31] Aggarwal and Harvey employed G3MP2 calculations on a model system to calibrate their B3LYP results.[32] Harvey later studied in detail the ability of diverse computational methods to predict the barrier for an MBH reaction, and he recognized explicitly the difficulty of predicting rate constants quantitatively.[33] Cantillo and Kappe chose M06-2X calculations for their study based on detailed experimental thermodynamics.

Aggarwal and Harvey performed a careful computational study of the mechanism of the amine-catalyzed MBH reaction of benzaldehyde with MA, and they considered in detail how the mechanism occurred in both the presence and absence of a promoting alcohol.[32] Their central conclusion was to support the transition states depicted in **3** and **4**, but the computations provide complete mechanistic pathways for the uncatalyzed and alcohol-catalyzed reactions. These pathways are considered in detail below versus experimental observations.

The approaches to error minimization employed in these works are typical of the better computational mechanistic studies. They are clearly the results of recognition of the potential for computational error. However, the actual errors in the theoretical mechanisms and energies along the reaction pathway were unknown at the start of this work. This was most decidedly the case for free energies. The free energy surface ultimately governs mechanisms, rates, and other experimental observations but the accuracy of computed free energies with regard to actual complex mechanisms in solution in exceedingly difficult to assess. Our studies were initiated with the goal of remedying this ignorance for a specific example of an MBH reaction, and is this way we sought to gain insight into error in the broader perspective of computational mechanistic studies.

Results and Discussion

Most of the observations to be discussed involve the prototypical MBH reaction of *p*-nitrobenzaldehyde (**5**) with MA catalyzed by DABCO (**6**). This reaction cleanly affords the product **7** in both methanol and DMSO at 25 °C, with the DMSO reaction requiring extended reaction times for high conversion. As noted above, the kinetics for this reaction as well as its α-position and aldehydic H/D KIEs had previously been studied carefully by McQuade and coworkers, and the DMSO reaction conditions here were patterned off of those employed by McQuade and coworkers. In cases we observe analogs of this reaction to take advantage of differences in kinetics or thermodynamics for comparison with calculations.



The Addition Step: Shunt Processes and Thermodynamics. The goal in this section is to establish the thermodynamics and kinetics of the addition step of the MBH mechanism as well as the reversible side reactions of the intermediate adduct.

This was not always the case. If transition state **4** were indeed the transition state, as observed by Aggarwal and Harvey, then a solvent isotope effect should be observed. An experiment was devised in order to aid us in the understanding of this hypothesis. Side-by-side reactions using methanol and d_4-methanol were run in order to determine the k_H / k_D from absolute kinetics. Quenched aliquots were taken from the reaction mixture and analyzed by HPLC and ^{1}H NMR for conversion versus time. The date was fit from the assumed rate law: rate = k [**5**][MA][DABCO]. It was also assumed that the concentration of DABCO did not change over time. Figure 4 on page 22 shows the results of the solvent involvement in the rate-determining step. At first glance, it seemed evident that there was a solvent isotope effect; however, the simulation for the deutero data (Figure 4 red line) did not quite fit very well with the experiment data

(Figure 4 blue line). In the deutero kinetics, the reaction started out faster than the simulated kinetics and as time went on, the reaction slowed down, in comparison with the best-fit simulated data. This experiment was repeated two more times in the chance that maybe there was just a random error for the improper fit. KIEs determined for the three sets of data from Figure 4: $k_H / k_D = 2.4, 2.4$, and 2.3. The average of these three sets is 2.4 ± 0.1. At the time, it looked as though the solvent was playing a role in the rate-limiting step as indicated by the solvent isotope effects. As mentioned above, these side-by-side reactions were followed by HPLC. However, NMR spectroscopy was used to follow the third set of data in Figure 4. It was not until then that it revealed the culprit of why the simulation did not have a perfect fit. Deuterium was being substituted into the α-position of methyl acrylate. This warranted another experiment to determine how much deuterium was being incorporated. As of now, it was still looking like there was a solvent isotope effect, but it would then turn out to be something else that was happening in the reaction mixture.

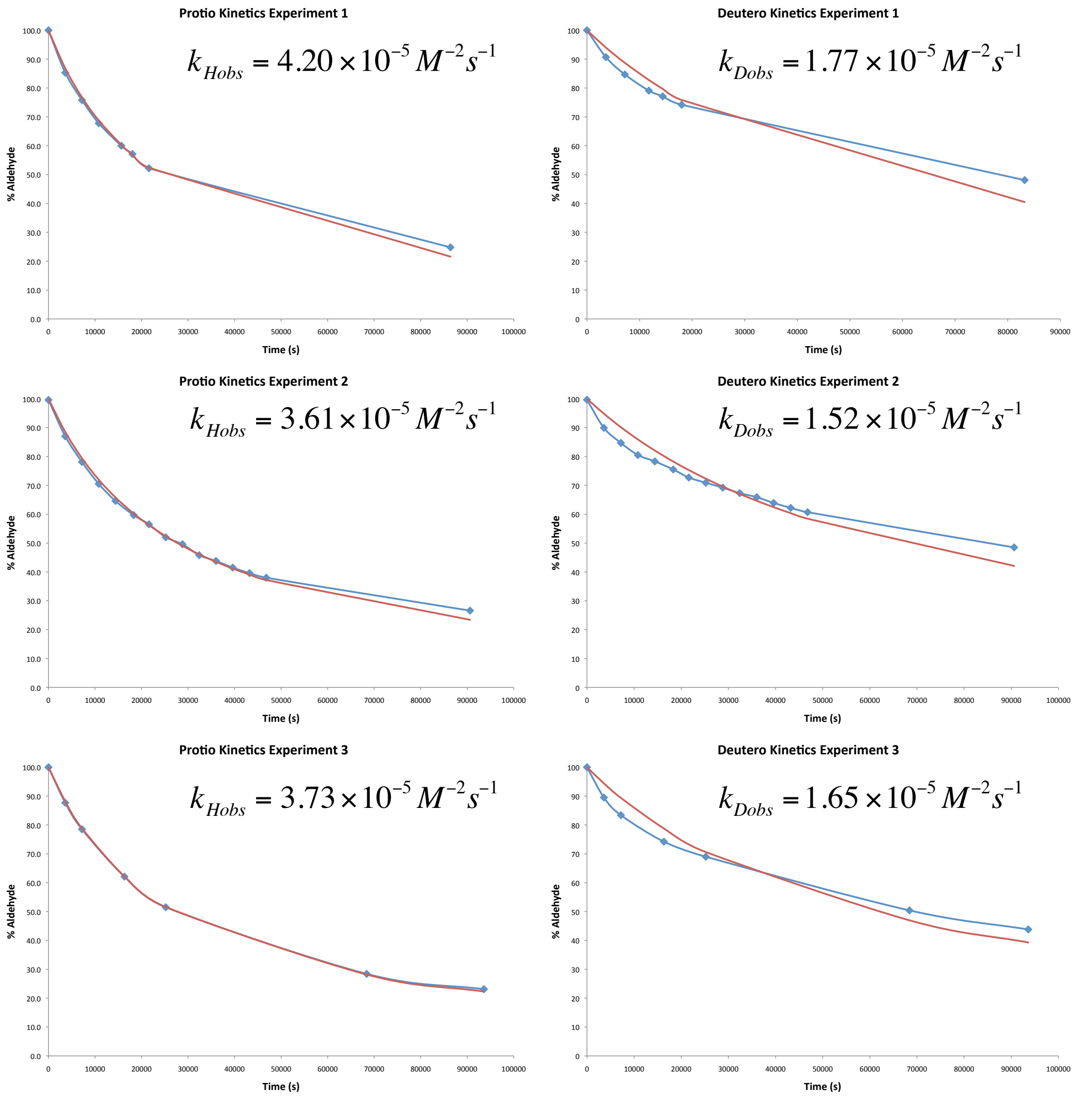


Figure 4. Three independent sets of solvent isotope experiments. The experimental data is in blue and the simulated data (by the assumed rate law: rate = *k* [**5**][MA][DABCO]) is in red. Microsoft excel was used for the simulation.

It was then decided to run an experiment where, aside from following the conversion versus time, we followed the amount of deuterium that was being incorporated into the α-position of MA. Three side-by-side experiments were run; 1) in protio methanol, 2) in deutero methanol, and 3) where the methyl acrylate was allowed to sit overnight in d_4-methanol to allow for complete isotopic exchange (see Figure 5.). The reactions were made as identical as possible to reduce the amount of random error. The results were surprising in the sense that it showed; the solvent isotope effect (k_H / k_D) was equal to 1, and the rate-limiting step was deprotonation. The experiment from Figure 5 was the first line of evidence that would show that the transition state **4** could not be plausible. Early on, we then asked the question; what was doing the deprotonation? This question was the beginning that would lead us to more experiments to better understand the underlying fact that something was not adding up.

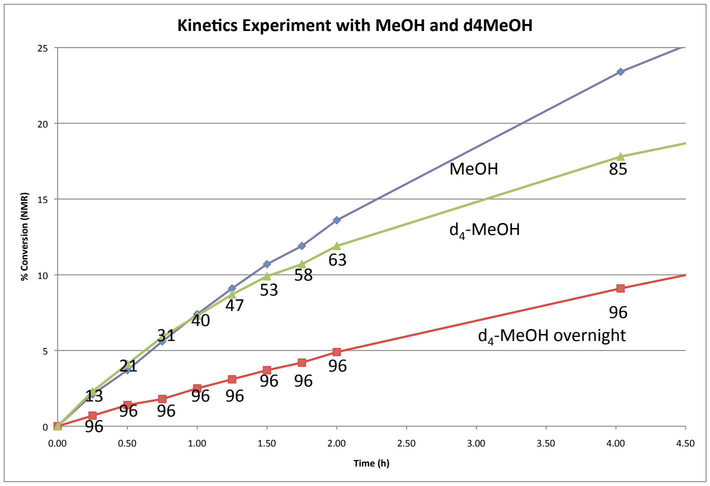
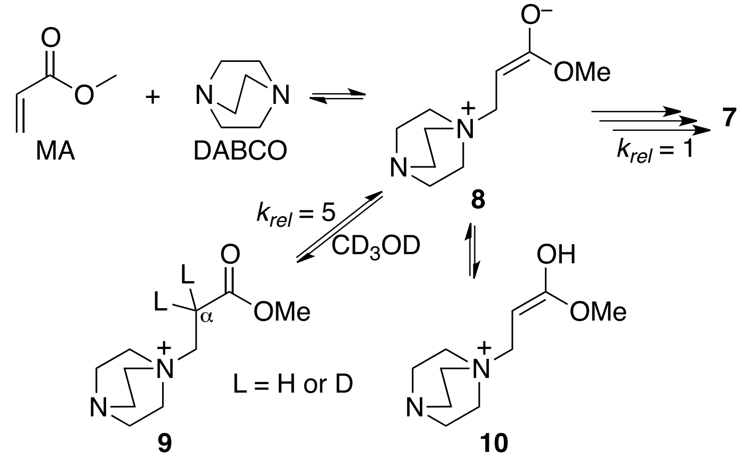


Figure 5. Careful side-by-side experiments of the Morita Baylis-Hillman reaction in methanol and d_4-methanol. Top blue line is reaction in protio methanol. Middle green line is reaction in deutero methanol. Bottom red line is reaction in deutero methanol where the MA was allowed to sit overnight to fully incorporate deuterium into the α-position. The number listed in black, below the green and red lines, are the amount (percentage) of deuterium present in the α-position at that particular instance. ^{1}H NMR was utilized to determine the amount of proton present at the α-position and that value subtracted from the 100% resulted in percent deuterium incorporation.

The addition step of the MBH mechanism is normally depicted simplistically as in Scheme 1, but a complication is that the zwitterionic **1**, or more specifically **8**, could be protonated in the presence of alcohols or water. The protonic equilibrium with methanol forming **10** involves proton transfers between heteroatoms and should be rapidly reversible, but this O-protonation is hidden from experimental detection. The more interesting and experimentally tractable process is the C-protonation affording **9**.



To probe the formation of **9** under the reaction conditions, we followed the reaction in d_4-methanol by ^1H NMR. Deuterium incorporation into the unreacted MA was extensive; by the time that the formation of **7** was 18% complete, 85% of the MA was deuterated. This shows that the C-protonation of **8** is faster than product formation. At a series of points early in the reaction (Figure 6), the deuterium incorporation was consistently an approximate factor of 5 greater than the formation of **7**. If it is assumed that molecules of **9** with one D and one H most often lose H in returning to **8**, then the factor of 5 represents an approximate relative rate for the C-protonation of **8** relative to the *rate-limiting step* for product formation. Since the subsequent aldol and elimination steps should be normal, barriered processes, this observation suggests that the C-protonation of **8** also has a substantial barrier. This point will be significant later. It should be noted that the rate of aldol mechanistic step reacting **8** with the aldehyde is not relevant to the factor of 5 ratio unless the aldol step is the rate-limiting step, but the aldol step cannot possibly proceed more slowly than this factor slower than protonation.

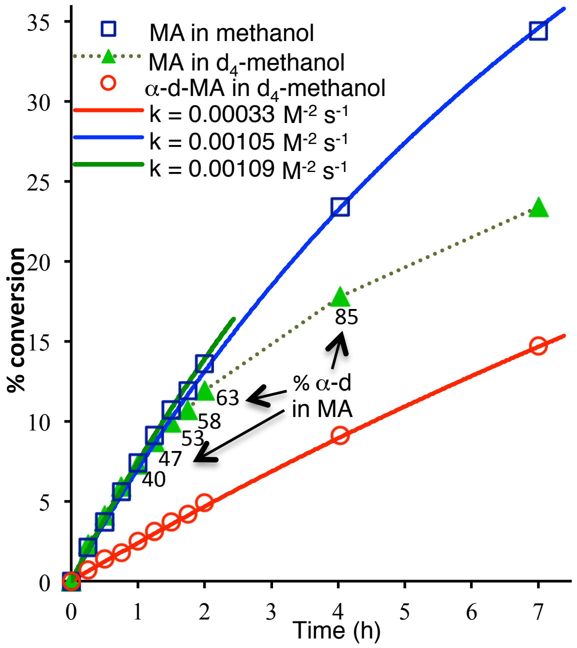
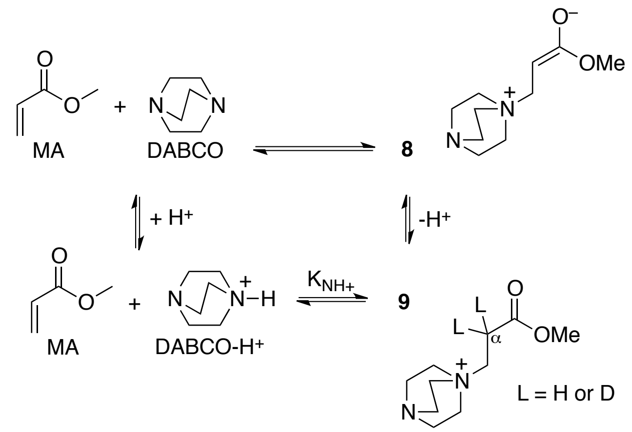


Figure 6. Example kinetics runs, showing reactions of **5** with MA or α-d-MA in methanol or d_4-methanol. The marked points are for experimental observations. The solid lines are theoretical curves based on the rate law rate = *k* [**5**][MA][DABCO], with *k* being the value listed, derived by fitting to the experimental points. The green solid lines represents a fit to the initial four points of the reaction of MA in d_4-methanol; later points fall off the curve due to extensive incorporation of deuterium in the α-position of the MA.

In addition of amines to carbonyl compounds, it sometimes happens that the initial adduct is so unstable that it reverts to the starting materials unless another molecule is *preassociated* to allow immediate trapping of the adduct.[34] We considered that it might be possible in the current case for the aldehyde to facilitate the addition step by preassociation and trapping of **8**. However, the rate of incorporation of deuterium into MA was unchanged in the absence of the aldehyde. This rules out a role for the aldehyde in assisting the addition process.

Since **8** is too unstable to observe, the equilibrium constant for its formation and the associated thermodynamics cannot be measured directly. However, the cationic adduct **9** is readily observable in the reaction of the hydrochloride salt of DABCO with MA (catalyzed by DABCO free base), and this provides the opportunity to assess the stability of **8** using the thermodynamic cycle of Scheme 2. In this cycle, the unobservable equilibrium of MA and DABCO with **8** is related to the observable equilibrium of MA and DABCO-H$^+$ simply by the difference in the acidity of **9** versus DABCO-H$^+$. The acidity of **9** is not known or directly observable (since **8** cannot be observed), but it may assessed in indirect ways.

Scheme 2. Thermodynamic cycle for determining the stability of **8**.

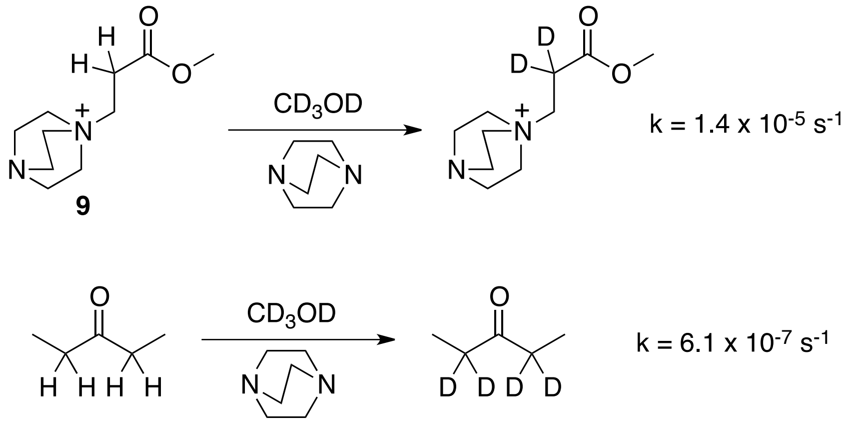


Equilibrium constants K_{NH+} for the conversion of MA / DABCO-H$^+$ to **9** in d_4-methanol were determined at a series of temperatures by NMR observation of equilibrated samples. A complication in this observation was that the equilibration was too slow to practically carry out within the spectrometer. Instead, samples were rapidly warmed or cooled to ambient temperature and a series of spectra were taken to allow extrapolation of the concentrations back to the original mixture. At temperature of 0, 22, 40, and 60 °C, the K_{NH+} values were 1170, 260, 94, and 34.3 M^{-1}, respectively. A plot of ln K_{NH+} versus 1/T gave $\Delta H° = -10.6$ kcal/mol and $\Delta S° = -24.9$ e.u..

The calculation of the thermodynamics of formation of **8** now requires an estimate of the difference in pKa of DABCO-H$^+$ versus **9**. This difference was assessed from the kinetic acidity of **9** when deprotonated by DABCO. Based on deuterium exchange into **9** in d_4-methanol, ignoring any secondary isotope effect or internal return, and allowing for the two exchangeable hydrogens in **9** and the two nitrogens in DABCO, the rate constant for deprotonation of **9** by DABCO was 7 × 10^{-4} M^{-1} s^{-1}. To translate this rate constant into an equilibrium constant using Marcus theory, we used the Guthrie equation[35] log k = 10 - b[1-((log K)/4b)]^2 with the parameter b set as 8.3 based on Bernasconi's observation of an intrinsic rate constant of $10^{1.7}$ for the very similar deprotonation of cationic ketone, 2-acetyl-1-methylpyridinium ion, by amines in 50% DMSO-H_2O.[36] This leads to a log K (for deprotonation of **9** by DABCO) of -8.6. The pKa of DABCO is 8.8 in water,[37] and it changes little with solvent (9.06 in DMSO[38]) as is normal for cationic acids. This leads to a pKa of **9** of ≈17.4. This value seems reasonable when it is considered that the nearby cationic charge in 2-acetyl-1-methylpyridinium ion lowers the pKa of a ketone by approximately 8.3 pKa units[36] and that the pKa of 17.4 is 7.6 less than the normal ester pKa of approximately 25. An upper limit on log K for deprotonation of **9** by DABCO can be set by taking the reverse reaction as being diffusion controlled with a rate constant of approximately 10^{10} M^{-1} s^{-1}. This would place log K at no more than -13.2, so the pKa of **9** can be no more than about 22. Since the protonation of the neutral **8** by DABCO-H^+ involves considerable reorganization, it is likely to occur at a rate that is far less than diffusion controlled, bringing the pKa of **9** toward the first estimate. In support of this, it was noted above that the C-protonation of **8** under MBH conditions must have a substantial barrier to account for the similar rates of deuterium incorporation and MBH product formation. Another approach to assessing the acidity of **9** is by comparing the rate of deuterium exchange into **9** to the rate of deuterium exchange into 3-pentanone under identical conditions. The rate constant for exchange into 3-pentanone was 180 times slower

(Scheme 3). The intrinsic barrier for deprotonation of simple ketones is significantly lower than that for cationic ketones, so the difference in kinetic acidities suggests that **9** is several pKa units more acidic than 3-pentanone. The pKa of 3-pentanone in water is 19.9;[37] it would be somewhat higher in methanol, but the pKa of the cationic **9** should be relatively solvent-independent. Overall, we will take the log K for deprotonation of **9** by DABCO as -8.6, but allow that there is a large uncertainty in this number of perhaps ±2. From this log K and the observed ΔG° for formation of **9**, ΔG° for formation of **8** is approximately +8.6 kcal/mol.

Scheme 3. Estimating pK_A from Kinetic Acidity.



Based on the rate constant for deuteration of methyl acrylate under MBH reaction conditions in d_4-methanol (8.2×10^{-4} M^{-1} s^{-1} at 25°C, based on a k_{obs} of 1.4×10^{-4} s^{-1} with 0.17 M DABCO and treating the reaction as unimolecular in methyl acrylate and DABCO), the barrier for the formation of **9** is 21.7 kcal/mol. Unfortunately this barrier does not reflect the barrier for formation of **8**, as the rate-limiting step in the formation of **9** is protonation of **8**. This is known because DABCO-H$^+$ catalyzed the formation of **9**; the rate of formation of **9** in the presence of 0.667 M DABCO-H$^+$ is approximately 100-fold faster than the rate of deuterium incorporation into MA, which requires the intermediacy of **9**, in the absence of DABCO-H$^+$.

A summary of the approximate free-energy profile for the addition step of the MBH mechanism as derived from these observations is shown in Figure 7. In this profile, the standard state for methanol is considered to be neat methanol (that is, the concentration of methanol is not considered as being in the rate law) while the standard state for all other compounds is 1 M. The free-energy barrier for formation of **8** remains unknown, though the thermodynamic for formation of **8** and the barrier for formation of **9** provide lower and upper bounds for this barrier.

A comparison of the experimental profile with computational predictions highlights some severe limitations of the computations. We first considered the energetics for the formation of **9**. Using B3LYP/6-311+G** calculations employed by Aggarwal and Harvey, along with full optimization using a PCM solvent model for methanol, the predicted ΔH° is -5.3 kcal/mol and ΔS° (adjusted to a 1 M standard state) is -33.1 e.u..

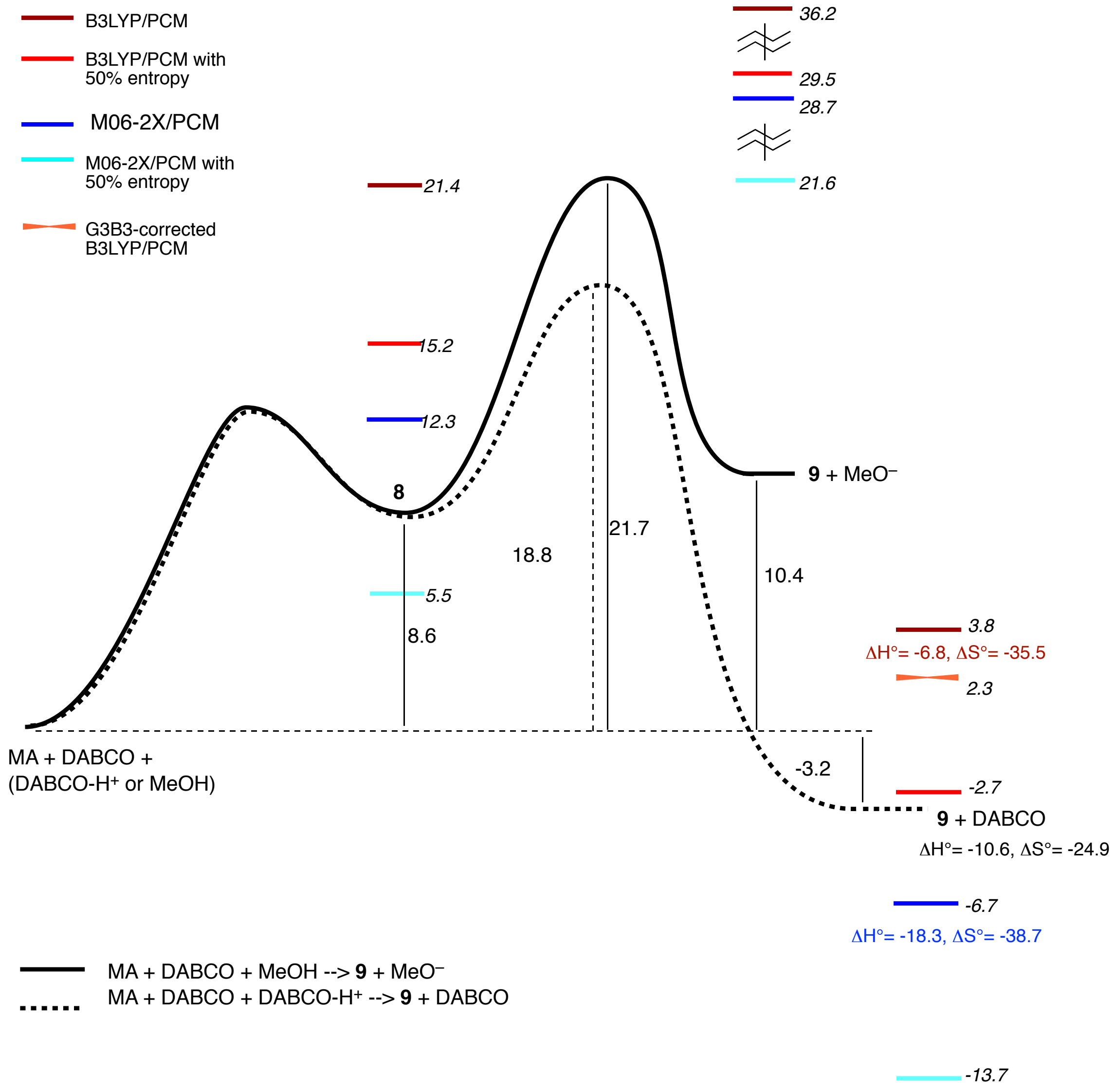


Figure 7. Experimental and calculated energetics for the addition step of the MBH mechanism. Unlabeled numbers are experimental free energies. All free energies are in kcal/mol and use 1 M as a standard state unless otherwise noted.

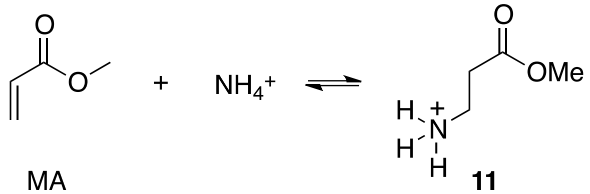
The relatively modest error in the entropy calculation of 8.2 e.u. is most likely the result of the assumption in the calculation that the translational and rotational degrees of freedom are fully free, while in solution these are best understood as being represented by very low-energy vibrations.

The potential for gas-phase calculations to err in their calculation of solution-phase entropies for bimolecular and termolecular reactions has often been noted,[39] and diverse tactics have arisen for dealing with the entropy problem. It is common for calculational papers to use the full gas-phase entropy, but some reduce the entropy by R ln 1354 (the ratio of 55 M to 1 atm),[40] some cut the entropy by 50%,[41] many ignore entropy entirely, some mix methods,[42] and some take the range between ignoring entropy and the full gas phase entropy as an uncertainty in the calculation. The effect of this range of possibilities is to provide a billion-fold range of choices for "predicted" equilibrium or rate constants for bimolecular reactions, and a 10^{18}-fold range of choices for termolecular reactions.

The existence of this entropy error has often been asserted in computational studies, often in response to obvious errors in computational predictions, and it has become common to apply one of several seemingly arbitrary corrections to the entropy or else ignore it completely. The result here, along with other comparisons of experimental and calculated entropy changes or solution versus gas-phase entropy changes, suggests that the error in calculated entropies for solution reactions may often be overstated.

The enthalpy error of 5.3 kcal/mol is more substantial, and the combination of the enthalpy error and the entropy error leads to a predicted equilibrium constant that is too low by about 10^6. This error may in part the result of an intrinsic bias in B3LYP calculations that disfavors σ bonds relative to π bonds.[43] However, M06-2X/6-31+G**/PCM calculations do not fair better; the predicted ΔH° for the M06-2X calculations is -18.3 kcal/mol, off in the opposite direction from the B3LYP calculations. Due to a fortuitous cancellation of the enthalpy error and a now 15 e.u. entropy error, the calculated ΔG° in the M06-2X is only off by 3.1 kcal/mol, but any adjustment for the expected error in the entropy calculation would end up making the prediction worse. Together, the popular B3LYP and M06-2X computational methods provide enthalpy predictions that would lead to a span of nearly ten orders of magnitude in equilibrium constants. The range of entropy calculations / estimates commonly employed in the literature would broaden the possibilities for predicted equilibrium constants by several more orders of magnitude, without ever actually encompassing the experimental value.

The error in the computed energetics for the formation of **9** might have been decreased by a computational approach employing high-level calculations on a model system. The model of addition of NH_4^+ to methyl acrylate to afford **11** was studied using B3LYP/6-311+G** and G3B3 calculations, and the G3B3 enthalpy of reaction was more exothermic by 3.0 kcal/mol (-34.0 kcal/mol versus -31.0). Applying a 3 kcal/mol correction factor to the B3LYP results with MA / DABCO-H^+ versus **9** would bring the enthalpy error down to only 2.3 kcal/mol. It should be noted that this computational tactic cannot be applied to the energetics of **8** due to the instability of model structure corresponding to **8**.

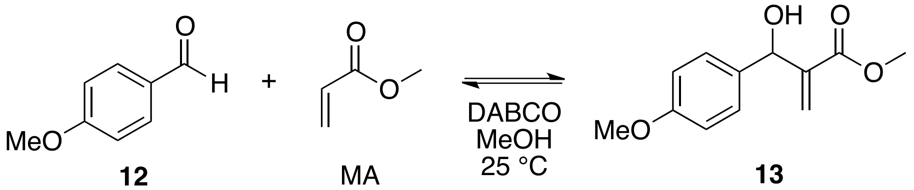


MA **11**

The calculated ΔG° for formation of **8** in the B3LYP/6-311+G**/PCM calculations, adjusted to a 1 M standard state, is 23.1 kcal/mol. These calculations would err in the prediction of the equilibrium constant by a factor of approximately 10^{10}. Some portion of this error is likely due to an overestimate of the loss of entropy, calculated to be -35.1 e.u. at a 1 M standard state. If the error is the same amount as it was in the formation of **9**, allowance for this would bring the error in the equilibrium constant down but it would still be a factor of about 10^8. The error in the calculated entropy could be much larger, as it is well known that entropy changes for polar reactions in polar solution are difficult to predict due to the role of solvent organization. If entropy is thrown out entirely, as is sometimes done in computational studies, the error in the equilibrium constant would go down to about a factor of only 100. However, in the absence of the experimental observation it might just as well have been postulated that the calculation would underestimate the entropy loss on formation of 8 (if it were supposed that solvent organizes about the zwitterion) as overestimate the entropy loss. M06-2X/6-31+G**/PCM calculations fare much better in predicting the ΔG° for formation of **8**, with a value of 13.3 kcal/mol. If the entropy error is the same as it was in **9**, and this were allowed for, the M06-2X ΔG° would be 10.9 kcal/mol, within the uncertainty of the estimate of the experimental value. This might be regarded as a success, but an alternative description might be to say that the selective adjustment of a calculation by the error versus experiment in another calculation can occasionally be used to bring a calculation in line with experiment, provided that the experimental values are already known in order to guide the process. All of the calculations err drastically in the free energy of **9** + MeO^- formed under the MBH reaction conditions. This normal observation illustrates the common computational intractability of acid-base chemistry, as will be important below.

MBH Thermodynamics. Previous workers have noted the reversibility of the MBH reaction,[44] and this reversibility ultimately enforces substantial limitations on the reaction scope. In this section we consider the overall thermodynamics for the MBH reaction and the accuracy of computations in predicting the equilibrium.

The MBH reaction of **5** with MA readily shows signs of reversibility; a dilute (0.014 M) sample of purified **7** and 30 mol % DABCO in d_4-methanol after two weeks exhibited traces (≈0.5%) of MA and **5** by NMR analysis. However, the equilibrium strongly favors **7**, and the amount of MA and **5** present was sufficiently low that an accurate quantitation of the equilibrium constant could not be obtained. To study the equilibrium more accurately, the corresponding reaction of anisaldehyde (**12**) with MA to afford MBH adduct **13** was chosen for the study. The idea of using anisaldehyde instead of **5** is that the greater donation of the electron-rich aromatic into the aldehydic carbonyl would favor the starting materials and facilitate their quantitation. In the event, the equilibrium is very slow, requiring several weeks at 25 °C, but it could be approached from both the starting material and product sides, and an equilibrium constant of 0.7 M^{-1} was observed. This corresponds to a $\Delta G°$ of +0.2 kcal/mol. The product is disfavored despite the unhindered nature of the reactants. The general difficulty of achieving more hindered MBH reactions is hardly surprising in this light.

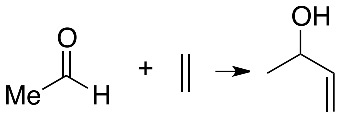


experimental	B3LYP/6-311+G**/PCM	G3B3 model-corrected B3LYP/6-311+G**/PCM
$K = 0.7\ M^{-1}$	$K = 9 \times 10^{-12}\ M^{-1}$	$K = 3 \times 10^{-7}\ M^{-1}$
$\Delta G° = 0.2$ kcal/mol	$\Delta G° = 15.1$ kcal/mol	$\Delta G° = 9.0$ kcal/mol

While our work was in progress, Cantillo and Kappe reported their careful study of the equilibrium of **5** / MA with **7** in methanol.[45] Over the wide temperature range from 19 to 90 °C, their data fit with $\Delta H° = -19$ kcal/mol and $\Delta S° = -50$ e.u., putting the $\Delta G° = -4.1$ kcal/mol at 25 °C. An unrecognized complications in this reaction is that 5 in methanol is in rapid equilibrium with its hemiacetal (*p*-$O_2NC_6H_4CH(OH)(OMe)$, **12**, present at 79% at 25 °C). We have reanalyzed their data allowing for this equilibrium. Over the wide temperature range from 19 to 90°C, the revised data fit with $\Delta H° = -24.4$ kcal/mol and $\Delta S° = -59$ e.u., putting the $\Delta G° = -4.9$ kcal/mol at 25°C.

As discussed by Cantillo and Kappe,[45] B3LYP calculations perform poorly in predicting this equilibrium while M06-2X calculations perform much better and this remains correct despite the revised numbers. The computational entropies in their paper are reported with a standard state of 1 atm versus 1 M for the experimental entropies. This error and enthalpy predictions appear much better than they are. Our purpose in this section is to examine the ability of corrections based on high-level calculations to improve the equilibrium prediction and to examine the accuracy of computational entropy predictions.

Calculations perform poorly in predicting this equilibrium. B3LYP/6-31+G**/PCM(methanol) calculations underpredict the equilibrium constant for the formation of **7** from **5** and MA by about 10 orders of magnitude, placing ΔG° at +9.1 kcal/mol with a 1 M standard state. The enthalpy error itself is 17 kcal/mol, making for over 12 orders of magnitude error in the equilibrium constant at 25 °C in the absence of computational entropy error. B3LYP/6-311+G**/PCM(methanol) calculations place the free energy of reaction, with a 1 M standard state, at 15.1 kcal/mol, leading to a predicted equilibrium constant that is off by about eleven order of magnitude. As previously noted, B3LYP calculations tend to underestimate the stability of σ bonds relative to π bonds, so the error could have been anticipated. A normal approach to avoiding such an error would be to take the tact used above of employing high-level calculations on a model system to correct the B3LYP energetics. Toward that end, the hypothetical reaction of ethylene with acetaldehyde to afford 3-buten-2-ol was examined in both B3LYP/6-311+G** and G3B3 calculations. The reaction is more favorable in the G3B3 calculations by 6.1 kcal/mol, and if this number is used to correct the energetics of the reaction of **12** with MA then the error in the calculated equilibrium constant drops considerably. However, the equilibrium constant is sill off by more than six orders of magnitude. M06-2X/6-31+G**/PCM calculations appear to perform well for the reaction of **12** with MA as they predict a free energy of reaction of 2.0 kcal/mol. Interestingly, correction of the M06-2X energetics by their difference versus the G3B3 energetics in the model reaction would add 2.0 kcal/mol to the predicted ΔG°, making the predicted equilibrium constant much worse in this case. If the equilibrium constant were known ahead of time then this error-worsening correction could naturally be avoided.



13

ΔH° = -13.1 (G3B3)
ΔH° = -6.3 (B3LYP/6-31+G**)
ΔH° = -15.1 (M06-2X/6-31+G**)
ΔG° = -4.1 (G3B3)
ΔG° = 2.0 (B3LYP/6-311+G**/PCM)

In the absence of the experimental measurement of the entropy of reaction for formation of **7**, it would be tempting to ascribe the remaining errors in either the M06-2X free energy or the G3B3-corrected M06-2X free energy to errors in the entropy calculation. It might then be envisioned that an entropy-correction process could bring the predictions in line with experiment. The same 13.8 e.u. entropy correction that worked so well with **8** would bring the G3B3-corrected M06-2X ΔG° to -5.4 kcal/mol, in great agreement with experiment. Any enthusiasm for such a correction scheme might be tempered by the observation that the same correction would worsen the predicted equilibrium constants for formation of **9** by three orders of magnitude. The real fallacy of such a correction scheme becomes obvious however when it is known that the experimental entropy of -59 e.u. is much more negative than the calculated values of -35.5 e.u.. The normal direction of entropy corrections thus takes the entropy predictions further from experiment, and the literature 50% entropy correction misjudges the effect of entropy on the equilibrium by nine orders of magnitude.

MBH Kinetics, H/D Isotope Effects, and Activation Parameters. The progress of a series of MBH reactions of **5** with MA in methanol was followed by analysis of worked-up aliquots by NMR or HPLC. The resulting conversion observations were then modeled differentially using an Excel^{TM} spreadsheet, and these fit well with a kinetic model that was first order in **5** and first order in MA (see Figure 6 on page 25). All relative rates were obtained from side-by-side reactions conducted as identically as possible. No discernable exotherm occurs in these reactions.

The order of methyl acrylate (MA) was studied. A reaction that halved the normal concentration of MA was slower by a factor of 1.9, while a reaction that doubled the normal concentration of acrylonitrile went faster by a factor of 1.9, indicating that the reaction was first order in MA (Table 1).

Table 1. A Comparison of Rates for Reaction of **5** and DABCO with Half, Normal, and Double Concentration of Methyl Acrylate in Methanol at 25 °C.

Rxn.	[PNB] (M)	[MA] (M)	[DABCO] (M)	*k* (M^{-2} s^{-1})	Rate (s^{-1})	Factor
half	0.901	0.451	0.27	0.00032 ± 0.00002	$3.9 \pm 0.2 \times 10^{-5}$	
normal	0.901	0.901	0.27	0.00030 ± 0.00002	$7.3 \pm 0.5 \times 10^{-5}$	1.9
double	0.901	1.802	0.27	0.00029 ± 0.00001	$14.1 \pm 0.5 \times 10^{-5}$	1.9

[PNB] = *p*-nitrobenzaldehyde; [MA] = Methyl Acrylate. Data based on the rate law rate = *k* [PNB][MA][DABCO], with *k* being the value lised, derived by fitting to experimental points. All the reactions were run under general kinetic conditions (see the Experimental Methods section).

The rate law was treated as being rate = *k* [**5**][MA][DABCO], and the average *k* from a series of reactions at 25 °C was $3.0 \pm 0.3 \times 10^{-4}$ M^{-2} s^{-1}. This corresponds to a free energy of activation of 22.3 kcal/mol, considering the standard state to be 1 M. Plotting the rates of the reaction versus the various concentrations of MA and applying a least squares fit reveals an exponent of 0.93 for the order of MA (Figure 8). It should be noted that the although the reactions were done identically as possible to reduce the amount of error, one item that should be pointed out is the progression of the reactions versus time. The reaction that halved the amount of MA progressed to ≈23% conversion while the reaction that doubled that amount of MA, at the exact time progressed to ≈64% conversion. The data that was fitted for the reaction that halved the normal concentration of MA represents the reaction profile earlier in the reaction, as opposed to the data of the reaction that doubled the normal amount of MA is represented by later points in the reaction.

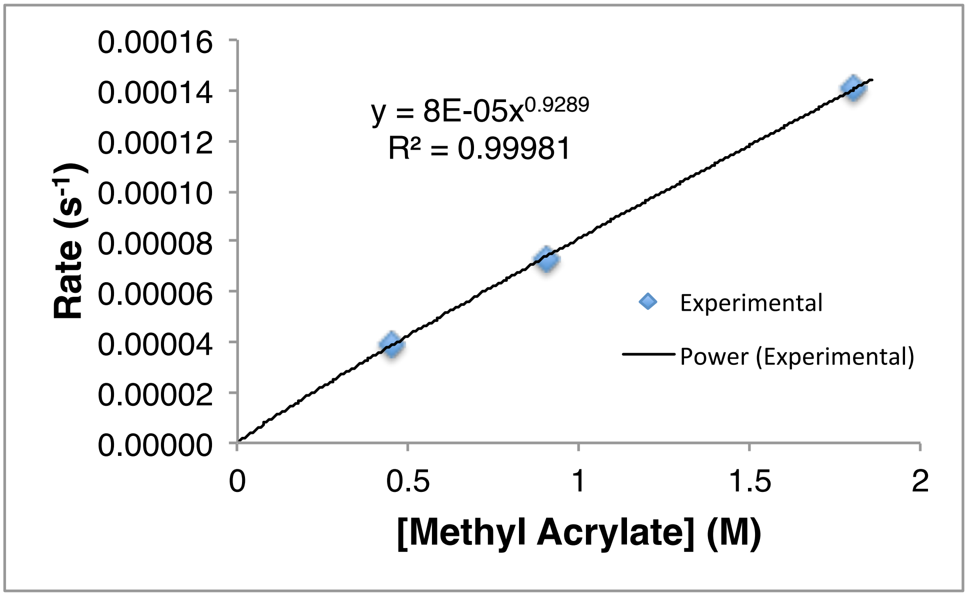


Figure 8. Order plot for the reaction of 5, MA, and DABCO in methanol. Rate as a function of MA. The marked points are for experimental observations. The solid black line represents a fit to the three rates for reaction described above.

A reaction that halved the normal concentration of DABCO was slower by a factor of 2.0 ± 0.1, while a reaction that doubled the normal concentration of DABCO went faster by a factor of 1.9 ± 0.1, indicating that the reaction is first order in DABCO. Addition of 30 mol % of the hydrochloride salt of DABCO had the effect of slowing the reaction by 30 ± 8% while adding 60 mol % slowed the reaction by 59 ± 8%. This result is as would be expected if most of the DABCO-H$^+$ were rapidly converted to the less reactive **9** but otherwise the addition of the buffer DABCO-H$^+$ had no effect of the rate. The rate was also unchanged in the presence of 30 mol % of proton sponge. These observations indicate that the number of protons in the rate-limiting transition state is the same as that in the starting materials. In other words, the total charge on all the molecules involved in the rate-limiting transition state is neutral. All of our observations fit with rate = *k* [**5**][MA][DABCO]. The kinetics do not discern whether additional solvent molecules are specifically involved. The choice of neat methanol as its standard state avoids the need to adjust activation parameters for mechanisms involving additional methanol molecules.

A series of kinetics measurements were conducted with careful temperature control at temperatures ranging from -21.3 °C to 63.7 °C. A striking feature of these results is that the rate constant reaches a maximum near room temperature. An Erying plot of the results (Figure 9 on page 42) is decidedly and reproducibly non-linear. As still be supported by later observations, the curvature in the Eyring plot is consistent with a reaction involving competitive rate-limiting steps having significantly different $\Delta S^{\ddagger}$'s. In such a case, the step with the more favorable (less negative) $\Delta S^{\ddagger}$ and higher $\Delta H^{\ddagger}$

would dominate the barrier at low temperatures while the step with the less favorable (more negative) $\Delta S^\ddagger$ and lower (negative in this case) $\Delta H^\ddagger$ would dominate the reaction at high temperatures, in accord with what is observed. If the reaction involved two separate mechanisms with different $\Delta S^\ddagger$, the curvature of the Eyring plot would be in the opposite direction!

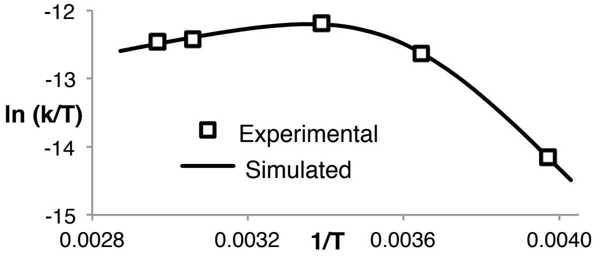


Figure 9. Example Erying plot based on kinetics runs from -21.3 °C to 63.7 °C. The solid line is simulated based on eq 1.

When two sequential steps are competitively rate-limiting and the steady-state approximation applies, it can be readily shown that the observed rate constant is governed by eq 16, where $\Delta G_1^\ddagger$ and $\Delta G_2^\ddagger$ are the total barriers versus starting materials for the two steps. The observed Erying plot could then be simulated well with $\Delta H_1^\ddagger = 12 \pm 2$ kcal/mol, $\Delta S_1^\ddagger = -27 \pm 9$ e.u., $\Delta H_2^\ddagger = -2.3 \pm 1.3$ kcal/mol, and $\Delta S_2^\ddagger = -79 \pm 5$ e.u.. Simulation of independent data gave similar results. The errors in the fit $\Delta H^\ddagger$'s and $\Delta S^\ddagger$'s are notably not independent and the $\Delta G^\ddagger$'s are more precise. The $\Delta G_1^\ddagger$ and $\Delta G_2^\ddagger$ at 25 °C would be 20.2 ± 0.3 and 21.2 ± 0.2 kcal/mol, respectively.

$$k = \frac{k_B T}{h} \frac{e^{-\Delta G_1^{\ddagger}/RT} e^{-\Delta G_2^{\ddagger}/RT}}{e^{-\Delta G_1^{\ddagger}/RT} + e^{-\Delta G_2^{\ddagger}/RT}} \tag{16}$$

From the observations above, the rate law was treated as being rate = k [**5**][MA][DABCO], and the average k from a series of reactions at 25 °C was 3×10^{-4} M^{-2} s^{-1}. This corresponds to a free energy of activation of 22.3 kcal/mol, considering the standard state to be 1 M. It is not possible to discern from the kinetics whether additional solvent molecules are specifically involved in the rate-limiting transition state. By considering the standard state for methanol as neat methanol, the free energy of activation does not need to be adjusted for mechanistic scenarios involving additional methanol molecules.

When the reaction is conducted in d_4-methanol, the kinetics depend on the details of how the reaction is conducted. If the reaction is initiated by adding the DABCO last, the earliest part of the reaction involves unlabeled MA and the initial rate is nearly equal to that of the reaction in unlabeled methanol (Figure 6 on page 25), with the observed solvent $k_H/k_D = 0.96 \pm 0.1$. The observation that the solvent isotope effect is nearly unity indicates that there is no proton transfer of hydroxylic protons in the rate-limiting step. Qualitatively, this would appear to rule out the transition state of the type proposed by Aggarwal and Lloyd-Jones, as depicted in **4**, and it would confute the calculational support for such a structure seen by Aggarwal and Harvey. This interpretation will be considered in more detail below in the light of more direct studies of the elimination reaction.

As the reaction in d_4-methanol proceeds, it slows down as deuterium is incorporated into the α-position of MA. To determine the H/D KIE for the α-position of MA, the MA was first equilibrated with excess d_4-methanol using DABCO in the absence of **5**, then the reaction was initiated by adding **5**. The resulting rate constant was 7.0×10^{-5} M^{-2} s^{-1}, compared to a *k* of 2.2×10^{-4} M^{-2} s^{-1} for a side-by-side reaction in unlabeled methanol. This gives a k_H/k_D of 3.1, which provides strong support for removal of an H / D from the α-position in the rate-limiting step.

From this last observation, we will proceed forward with the working hypothesis that $\Delta G_2^\ddagger$ corresponds to the proton transfer of the elimination step while $\Delta G_1^\ddagger$ corresponds to the aldol step. It will be seen that diverse evidence supports this.

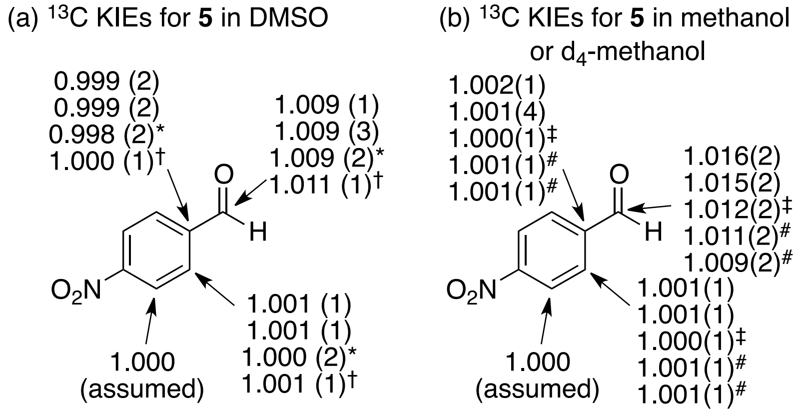
^{13}C Kinetic Isotope Effects. ^{13}C KIEs have some advantage over H/D KIEs in mechanistic studies because their values are in general more accurately predictable from a computational mechanism, if the mechanism is correct. This allows the combination of KIEs and computational studies to provide a detailed picture of the mechanism. We applied the determination of the ^{13}C KIEs to the MBH mechanism with the goal of establishing further details about the mechanism in DMSO and providing more general information about the mechanism in methanol. As it turned out, a surprising observation in the isotope effects aided greatly our goal of learning about each step in the mechanism.

The ^{13}C KIEs for the reaction of **5** with MA were determined at natural abundance by NMR methodology.[1] Duplicate independent reactions in both DMSO and methanol were taken to 77 to 80% conversion of **5**, and the isotopic compositions of samples of the reisolated aldehyde were analyzed by ^{13}C NMR in comparison with sample of the original aldehyde that had not been subjected to the reaction conditions. the carbons meta to the aldehyde on the aromatic ring were treated as an internal standard with the assumption that their isotopic composition did not change over the course of the reaction. From the reaction conversions and the changes in the isotopic composition, the ^{13}C KIEs were calculated as previously described.[1] Due to a long relaxation time and the sharpness of its ^{13}C peak, the *para* position in **5** could not practically be quantitated reliably.

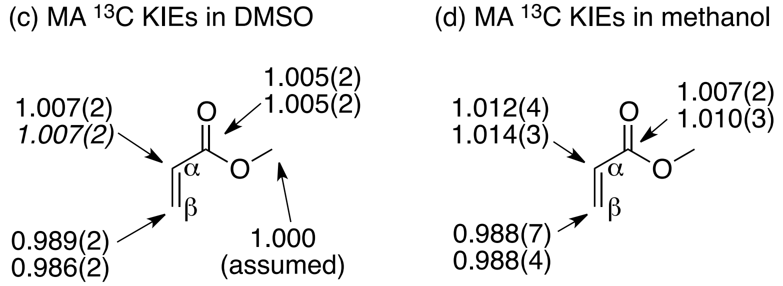
The KIEs for **5** in DMSO and in methanol or d_4-methanol are summarized in Figures 10a and 10b on page 47. In each case a significant but modest ^{13}C KIE was observed for the aldehydic carbon. The remaining ^{13}C KIEs observed were approximately unity, as would be expected for centers unchanged by the reaction. At 1.009, the carbonyl carbon KIE in DMSO is smaller than normally associated with a primary ^{13}C KIE, and the qualitative interpretation of this KIE is that the carbonyl carbon has undergone some process that has modified this center, but that no bond is being made or broken at this center at the transition state for the rate-limiting step. This is as would be expected for the McQuade mechanism. Because of some concern over the effect of water or other hydroxylic impurities (including the product) on the reaction, two additional experiments were conducted in DMSO, one taking careful precautions to minimize the presence of water and a second with 1 % water added to the reaction. The former had no impact on the KIEs while the latter led to a very slight increase in the KIE at the aldehydic carbon.

The KIEs in methanol and d_4-methanol were more interesting. In methanol, the aldehydic carbon ^{13}C KIE of 1.015-1.016 was significantly larger than it was in DMSO. However, it is still qualitatively smaller than the large primary ^{13}C KIE that would be expected if the addition to the aldehyde became rate limiting. (See below for quantitative predictions.) If both the DMSO and the methanol MBH reactions have purely elimination processes as their rate-limiting step, then there is no obvious explanation as to why the isotope effects would differ.

This line of reasoning suggested the possibility that the methanol reaction might be subject to kinetic complexity, that is, competitive rate-limiting steps. When one of the possible competitive rate-limiting steps involves proton transfer, a rigorous test for kinetic complexity involves carrying out the reaction with a deuteron transferred instead of a proton, looking for a change in a carbon KIE.[46] The idea behind such a study is that the primary H/D KIE leads to a change in the relative importance of the mixed rate-limiting steps, resulting in a change in the carbon KIE. In the event, this test was performed initially by simply carrying out the reaction in d_4-methanol, and the aldehydic carbon ^{13}C KIE decreased to 1.012. A flaw in this experiment was that a significant portion of the reaction occurred before high incorporation of deuterium into the MA. When the reaction was carried out with a preequilibrium of MA with d_4-methanol in the presence of DABCO but absence of **5**, the ^{13}C KIE decreased to 1.009-1.011, which is indistinguishable from the DMSO KIEs. These observations strongly support the involvement of competitive rate-limiting steps in the reaction in unlabeled methanol.


(a) ^{13}C KIEs for **5** in DMSO

(b) ^{13}C KIEs for **5** in methanol or d_4-methanol


(c) MA ^{13}C KIEs in DMSO

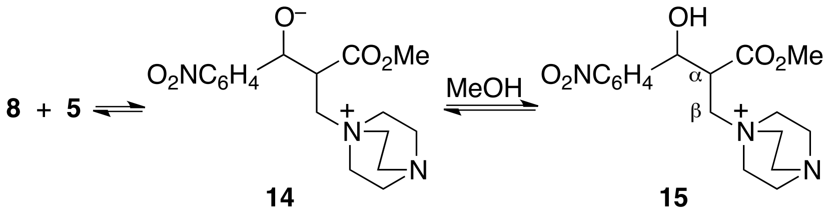
(d) MA ^{13}C KIEs in methanol

Figure 10. ^{13}C KIEs for the DABCO-catalyzed MBH reaction of 5 with MA at 25 °C. KIEs marked with the * are for a reaction with precautions taken to minimize water while KIEs marked with † are for a reaction with 1% water in DMSO used as solvent. KIEs marked with ‡ and # were measured in d_4-methanol, and the # signifies that the MA was prequilibrated with the d_4-methanol before adding DABCO.

The ^{13}C KIEs were also determined for the MA component of the reactions. The KIE measurement was straightforward for the DMSO reactions; reactions taken to ≈80% conversion were quenched by the addition of benzoic acid, and the recovered unreacted MA was analyzed by NMR in comparison with the original methyl acrylate, using the methyl carbon as the internal standard for quantitation. This process did not work for reactions in methanol due to problems with transesterification and recovery of the methyl acrylate. As an alternative strategy, samples of the product **7** from reactions taken to low conversion were analyzed versus samples taken to 100% conversion of the MA. Due to transesterification, the methyl carbon could not be used for quantitation but the negligible KIE in the aromatic carbons of **5** made the aromatic carbons of **7** suitable for the use as internal standards. Due to NMR complications associated with incorporation of deuterium, we unfortunately could not obtain MA KIEs in d_4-methanol.

The MA KIEs are summarized in Figures 10c and 10d. The β-carbon KIE is significantly inverse in each case. ^{13}C KIEs of this magnitude would be associated with a pre-equilibrium converting the carbon to the more constraining potential energy well associated with sp^3 hydridization, followed by a rate-limiting step that is unrelated to this carbon. If the elimination process is rate limiting, the inverse β-carbon KIE appears to qualitatively exclude the concerted (E2) mechanism depicted in **3**. Rather, the elimination would have to occur by a rate-limiting proton transfer followed by a faster loss of DABCO as a separate step in an overall E1cb(irr) process. The α-carbon KIE follows the pattern seen for the aldehydic carbon of **5**: small in DMSO, and larger though still relatively small in methanol. These low KIEs are initially surprising since most reasonable mechanisms involve some bonding change at the α-carbon in the rate-limiting step, but some insight into these KIEs will be obtained with the aid of calculations below.

The Aldol Step: Transition Structures, Predicted ^{13}C KIEs, and Experimental Energetics. For the aldol step in the MBH reaction of MA with **5**, neither the starting material **8** nor the product **14** or its protonated form **15** could be observed, and this precludes direct experimental information about the step. The barrier for the aldol step will ultimately be estimable indirectly from experimental observations, but the path to this estimate first requires consideration of the computational results and predicted KIEs.



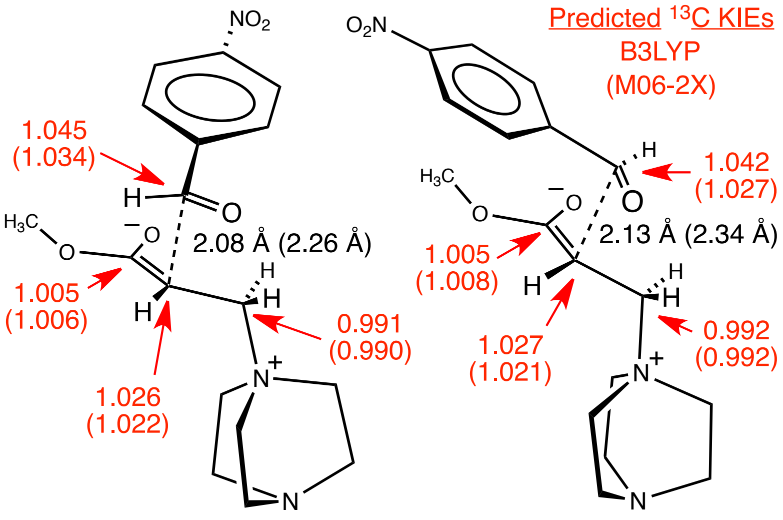
A series of twelve transition structures with relatively low energies were located for the reaction of **8** with **5** in each of B3LYP/6-31+G** and M06-2X/6-31+G** calculations including PCM models for each of methanol and DMSO. The twelve possibilities within each calculational series arise from three rotational orientations of the aldehyde, attack on either the *re* or *si* face of the aldehyde, and the reaction of *Z* versus *E* isomers of **8**. Some additional transition structures involving alternative orientations of the DABCO relative to the aldehyde were observed but these were much higher in energy and not explored systematically. The two lowest-energy transition structures, **16** and **17** (Figure 11 on page 52), orient the aldehydic oxygen *anti* to the enolate double bond and place the DABCO moiety *cis* to the enolate oxygen and anti to the aldehyde. The geometries of the remaining structures, a total of 48, are given in the Appendix.

Considering the error in the B3LYP energetics of **8** discussed above, it should not be surprising that the calculated barriers for the aldol step versus the separate MA / DABCO / **5** starting materials are unrealistic. B3LYP/6-31+G**/PCM calculations would place the free energy barrier for **16** at 36.6 kcal/mol. From experimental date below, we will arrive at a free-energy barrier versus separate starting materials of approximately 21.5 kcal/mol, so the calculated barrier is 15 kcal/mol too high versus experiment, corresponding to an error in the rate constant of about eleven orders of magnitude. The M06-2X calculations fair more acceptably, predicting a free-energy barrier of 17.8 kcal/mol. However, both the B3LYP and M06-2X free-energy barriers include a substantial, and likely greatly overestimated, entropic barrier of approximately -74 e.u.. The literature entropy adjustment of throwing away half of the entropy would increase the predicted rates by 10^8, taking the M06-2X prediction to over ten orders of magnitude too high while bringing the B3LYP-predicted rate to only three orders of magnitude too low.

An alternative approach is to use the calculated barrier relative to **8** in combination with the experimentally estimated energy of **8**. When this is done, the overall barrier associated with **16** in the B3LYP calculations is reasonable 22.8 kcal/mol. The M06-2X calculations appear to fair well in the calculation versus separate starting materials, predicting a free-energy barrier of 17.8 kcal/mol. However, any of the adjustments in the entropy common in the literature would take this number away from experiment to a substantial degree. Worse, the combination of the calculated barrier relative to **8** and the experimental energy of **8** leads to an overall free-energy barrier of only 14.1 kcal/mol, far from the experimental value (and further still in any part of the entropy change were to be discounted).

Despite the dubious barriers, the transition structures define the ^{13}C KIEs that would be associated with a rate-limiting aldol step. The ^{13}C KIEs predicted from conventional TST for the transition structures **16** and **17** were calculated from the scaled theoretical vibrational frequencies[5] by the method of Bigeleisen and Mayer.[6] Tunneling corrections were applied using the one-dimensional infinite parabolic barrier model.[7] Such KIE predictions including a one-dimensional tunneling correction have proven highly accurate in reactions not involving hydrogen transfer, so long as the calculation accurately depicts the mechanism and transition state geometry.[47]

The predicted KIEs for the aldol transition structures are most straightforwardly recognizable as being far from the experimental values. If the aldol step were fully rate limiting, large ^{13}C KIEs would be expected at both the aldehydic carbon of **5** and the α-carbon of MA, in agreement with qualitative expectations. Such large KIEs are not observed, and this is compelling evidence that the aldol step is not rate-limiting, or not majorly so once the possibility of kinetic complexity is considered. McQuade's results had already established this for the DMSO reaction.



16 **17**

Figure 11. The two lowest-energy transition structures for the reaction of 8 with 5. The distances in Å are for the B3LYP/6-31+G**/PCM(methanol) structures, with MO6-2X/6-31+G**/PCM(DMSO) distances shown in parenthesis.

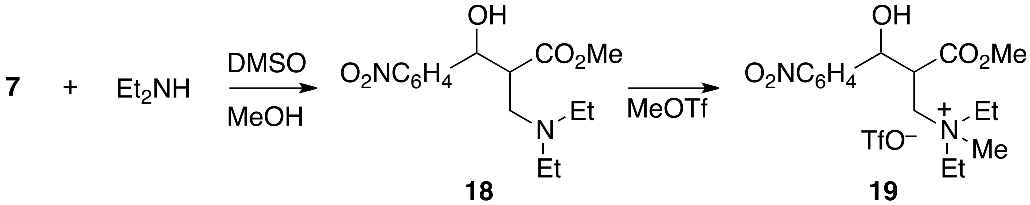
We now consider quantitatively whether the ^{13}C KIEs fit with the elimination step (actually the deprotonation step of the E1cb(irr) process) being mainly rate limiting with the aldol step being minorly rate limiting.

The evidence in a previous section strongly supported competitive rate-limiting steps in the methanol reaction. We consider here the possibility that the elimination step, its nature to be determined, is mainly rate limiting and that the adol step is partially, in a minor way, rate limiting. When a reaction involves competitive rate-limiting steps, the observed KIE depends on the KIE for the individual steps and the relative heights of the barriers involved. For the kinetic scheme of eq 17, the two forward steps involve isotope effects KIE_1 and KIE_2, and the intermediate is partitioned between a product-forming process occurring at rate *rate*$_2$ and a reverse process affording the starting materials occurring at rate *rate*$_{-1}$. It can be readily shown that the observed isotope effect KIE_{obs} will be determined by eq 18, where the commitment factor C_f is the ratio of *rate*$_2$ to *rate*$_{-1}$. For the quantitative analysis of the methanol KIEs here, we will assume that KIE_1, the isotope effect if the aldol step were rate limiting, is approximately the B3LYP-predicted 1.042. We also assume that KIE2, the isotope effect if the elimination were fully rate limiting, has the approximate value of 1.009 as observed for the DMSO reaction. The observed KIE would then be equal to the average experimental value of 1.0155 in unlabeled methanol when $C_f = 0.245$, i. e. when the second step is slower than the first step by a factor of about 4.1. The observed H/D KIE for methanol versus d_4-methanol is 3.1. The observed H/D KIE of 3.1 would itself be a moderately suppressed value relative to the intrinsic H/D KIE for the elimination step. From eq 18, the intrinsic H/D KIE would be 3.6. This makes no difference in the analysis. Assuming that the rate of the aldol step would not change significantly in d_4-methanol, the C_f for the d_4-methanol reaction would to 0.08 and the expected KIE_{obs} for the aldehydic carbon would be 1.011. This is in striking agreement with the experimental ^{13}C KIE in d_4-methanol. This agreement supports the interpretation of the KIEs in methanol as resulting from competitive aldol and elimination steps, with the latter being slower by a factor of roughly four. The rate difference defines the height of the barrier for the aldol step; it would be about 0.8 kcal/mol below that for the overall reaction, or 21.5 kcal/mol. Depending on the choice of assumed value of KIE_1, this value varies by 0.5 kcal/mol, but the observed isotope effects continue to fit well with competitive rate-limiting steps.

$$\text{starting materials} \underset{rate_{-1}}{\overset{KIE_1}{\rightleftharpoons}} \text{intermediate(s)} \xrightarrow[rate_2]{KIE_2} \text{product} \qquad (17)$$

$$KIE_{obs} = \frac{KIE_2 + KIE_1 \cdot C_f}{1 + C_f} \qquad \text{where } C_f = \frac{rate_2}{rate_{-1}} \qquad (18)$$

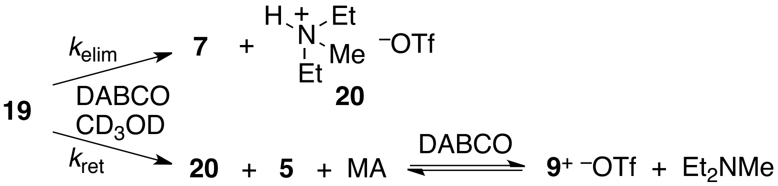
The Elimination Step: Eliminations in Synthesized Intermediates. To learn about the elimination step in the MBH mechanism, we adopted the approach of independently generating an intermediate and studying its conversion under the reactions conditions. No practical synthesis of **15** itself was apparent, but the close analog **19** was readily generated by methylation of **18**, the adduct of MBH product **7** and diethylamine, with methyl triflate. The salt **19** was a 2.5 : 1 mixture of diastereomers and was sufficiently stable to be chromatographed on silica gel using methanol / chloroform as eluent. However, it could not be isolate in analytically pure form due to a slow decomposition into MA, **5**, **7**, and diethylmethylammonium triflate (**20**). The mixture of diastereomers exhibited characteristic peaks in the ^{1}H NMR in d_4-methanol at 5.05 (5.23), 3.98 (3.77) 3.59 (3.72), and 2.85 (2.91) ppm, major and minor (in parentheses) diastereomers, respectively.



18 **19**

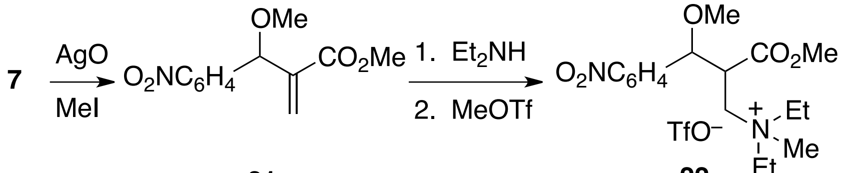
The reaction of **19** under MBH conditions using 30 mol % DABCO in d_4-methanol leads to a mixture of the elimination process affording MBH product **7** plus the ammonium salt **20** and the retro-aldol process affording MBH starting materials **5** and

MA along with **20**. The formation of these products closely follows first-order kinetics; this is surprising at first glance since the formation of **20** would decrease the basicity of the solution (see the example below where this effect comes into play) but the acidity of **20** is effectively buffered by the formation of **9**, which takes up a proton. Kinetic modeling of the product concentrations versus time gave a best-fit ratio of the elimination rate constant k_{elim} to the retro-aldol rate constant k_{ret} of 0.22 : 1. (This ratio was assumed to be the same for both diastereomers of **19** in order to minimize the parameters fit to experiment in the model.) Considering the differences in structure, the similarity of this ratio to the C_f of 0.245 inferred from KIEs above is striking, and the two analyses are mutually supportive.



To approximate absolute values for k_{elim}, the rate law was taken as rate = (k_{elim} + k_{ret}) [**19**][MeO^{-}] (see below) and the concentration of methoxide was inferred from the pK$_a$'s of DABCO-H^{+} and **20**, a self-ionization constant for methanol of 10^{-19}, and the initially measured concentrations of ammonium salts. With these assumptions, the best-fit k_{elim} values for the major and minor diastereomers were 1.3×10^{4} M^{-1} s^{-1} and 3.2×10^{4} M^{-1} s^{-1} , respectively. Due to potential inaccuracy in the concentration of methoxide, these k_{elim} values have a relatively high potential inaccuracy, but the importance of their value will bin in comparison with rate constants below derived from the same assumptions.

In the previous computational study of the MBH reaction by Aggarwal and Harvey, the arguably most interesting conclusion was the role of transition structures resembling **4** in the elimination step. Such structures require a free hydroxyl / alkoxide group in the pre-elimination adduct. Considering the absence of a solvent H/D isotope effects in the MBH reaction of MA with **5** discussed above, the role of the hydroxyl group in the elimination step was studied in more detail. Ammonium salt **22**, the methoxy analog of **19**, was synthesized as a 3.1 : 1 mixture of diastereomers from **7** by O-methylation with AgO / MeI to afford **21** followed by addition of diethylamine, and N-methylation with methyl triflate. Like **19**, **22** could not be isolated in analytically pure form due to a slow decomposition forming **21**, but it could be chromatographed and characterized in the ^{1}H NMR by its peaks at 4.77 (4.55), 3.79 (3.96), 3.73 (3.48), 3.28 (3.26), and 2.88 (2.90) ppm, major and minor (in parentheses) diastereomers, respectively.



21 **22**

Under MBH conditions with DABCO in d$_4$-methanol, **22** affords only **21** and **20**. Unlike with **19**, in this case there is no buffering addition reaction and the pH drops as the reaction proceeds. Accordingly, the reaction does not follow first-order kinetics, but the conversion versus time fits well with the rate law k_{elim} [**19**][MeO-]. The concentration of methoxide ion as the reaction proceeded was kinetically modeled from the concentration of ammonium salts and the same assumptions for pK$_a$'s and the methanol self-ionization constant as used above for **19**. With these assumptions, the best-fit k_{elim} values for the major and minor diastereomers were 3.9×10^{4} M^{-1} s^{-1} and 1.0×10^{4} M^{-1} s^{-1} , respectively.

$$\mathbf{22} \xrightarrow[\text{DABCO, CD}_3\text{OD}]{k_{\text{elim}}} \mathbf{20} + \mathbf{21}$$

The striking result here is that the elimination occurs at nearly identical rates for the hydroxyl compound **19** and methoxy analog **22**. The strong implication of this result, in combination with the absence of an H / D solvent isotope effect in the MBH reaction, is that the hydroxyl group plays no role in accelerating the elimination step. There is no reason for a mechanism to proceed through an unusual mechanistic pathway if the pathway provides no acceleration. In other words, the data argues that calculated structure **4** has no physical relevance.

It is of interest to consider in more general terms whether or not a proton-shuttle pathway of the type depicted in **4** would be expected to be a preferred pathway for the elimination. A proton-shuttle pathway might be considered to be the simplest of potential mechanisms, as it allows the direct conversion of the intermediate **14** into products with the aid of a single molecule of solvent. The beguiling simplicity of such mechanism also makes them computationally tractable, and proton-shuttle pathways have been a popular observation in computational studies in recent years. There is usually however a two-step alternative to proton-shuttle mechanisms involving proton transfer from solvent followed by proton transfer to solvent (or vice versa). This mundane conventional mechanism is often unexplored, perhaps because the acid-base chemistry involved in such steps is not so readily tractable in computational studies. The viability of acid-base mechanisms also have the advantage of having considerable experimental support. For example, while computational studies have at times proposed proton-shuttle mechanisms for keto-enol tautomerisms, experiments have strongly supported a conventional acid-base mechanism. The two-step acid-base mechanism for elimination in the MBH mechanism would involve protonation of **14** by methanol to afford **15** followed by a methoxide-mediated deprotonation at the alpha position to effect the elimination of the DABCO.

It should be recognized that the protonic equilibrium of **14** with the solvent methanol to afford **15** involves an approximately thermoneutral[48] proton transfer between heteroatoms. Such proton transfers occur at near diffusion-controlled rates, and in methanol solvent this should occur order of magnitude faster than any process abstracting a proton from a C-H bond. This makes **15** an obligatory intermediate in methanol after the aldol step, and the apparent simplicity of short-circuiting **15** by direct reaction of **14** is illusory. Rather, the elimination mechanism will proceed from **15** back through **14** only if there is some energetic advantage for such a pathway over the direct abstraction of a proton from **15**. There is no obvious reason why this should be the case, so the evidence against such a mechanism provided by the observations with **19** and **22** should not be surprising.

The Elimination Step: Transition Structures and Predicted KIEs. By either the proton-shuttle or acid-base pathways, the actual reaction in solution would involve an ensemble of transition states and solvation shells. No single model is likely to adequately represent either mechanism. Our computational approach to the consideration of these pathways was to obtain a variety of transition structures, a total of 24, by varying both the involvement of explicit methanol molecules and the involvement of the alkoxide / alcohol group of **14** / **15**, as well as using both B3LYP and M06-2X DFT methods. There is no clear way to judge from computational considerations alone which of the various resulting computational models should best represent the solution reaction; due to the unavoidably incomplete modeling of the solvation the calculated energies are of questionable value even when comparing closely analogous structures. In the place of a purely computational evaluation of the calculated transition structures, we use a comparison of the experimental KIEs with those predicted for the various structures. In this way, the observed KIEs can establish some features of the experimental reaction, even in the absence of a clear choice of computational model or reliable energetics.

The combination of "functional shopping" and "computational model shopping" leads to greatly varying transition structures and predicted KIEs. The range of structures and the general trends are summarized in Figure 12. The transition structures can be described as falling on a spectrum ranging from "early" to "late". Deprotonation of the α C-H bond by a "naked" methoxide anion (i.e., on that lacks explicit hydrogen bonding but is stabilized by the PCM implicit solvent model) is relatively exothermic, and this results in early transition structures with α C-H distances less than 1.3 Å. The predicted C-α KIEs for such structures are 1.006 or less, far from experimental value of $\approx$1.013. It should be recalled that the experimental KIE is a composite arising from a mainly rate-limiting elimination step and a minorly rate-limiting aldol step. This combination was allowed for in the prediction of the isotope effects using eq 17, the predicted KIEs from Figure 5 on page 23, and a C_f value of 0.245 as inferred above. No reasonable change in either the predicted KIEs for the aldol step or the assumed C_f can bring the composite KIE predictions into reasonable agreement with experiment. This disagreement suggests that the naked methoxide / PCM implicit solvent approach is an inadequate model for the transition state.

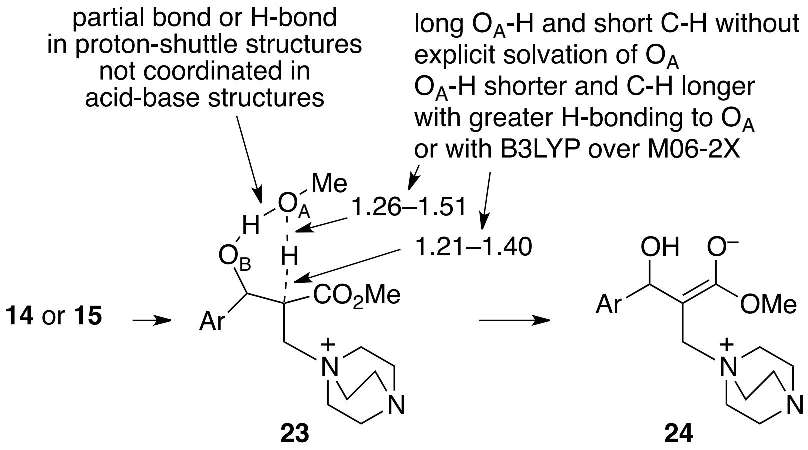


Figure 12. A summary of transition structures for the rate-limiting α C-H deprotonation step.

The methoxide ion carrying out the α C-H deprotonation may be hydrogen bonded to additional solvent molecules in the acid-base transition structures or be hydrogen bonded to the intramolecular hydroxyl group as in the proton-shuttle transition structures. In either case the hydrogen bonding leads to later transition structures. In the

M06-2X transition structures the effect is small, and a single hydrogen bond to the basic oxygen (O_A in **23** and **24**) leaves the transition structure relatively early (α C-H distance of 1.29-1.30 Å). The predicted C-α KIEs for such structures, including three simple M06-2X proton shuttle transition structures, are 1.006-1.008, and this disagreement with the experimental C-α KIE weighs against the accuracy of the transition structures. As an exception to this generalization, a proton-shuttle transition structure that included two methanol molecules hydrogen bonded to O_B of **23** let to a predicted C-α KIE of 1.016. This is within the uncertainty of the experimental measurements. However, the predicted solvent H/D KIE for this structure was 1.59, which is inconsistent with the negligible or slightly inverse experimental solvent KIE.

At the opposite extreme, late transition structures with α C-H distances of 1.38-1.40 Å were obtained in B3LYP calculations that included two hydrogen bonds to O_A. The predicted C-α KIE for such structures was in the range of 1.029-1.034. This is far too high versus experiment.

In both the B3LYP and M06-2X calculations, there is a range of structures that lead to reasonable accurate predictions of the experimental KIEs. In the M06-2X calculations, structures that included *two* hydrogen bonds to O_A lead to C-α KIEs of 1.012 - 1.016, C-β KIEs of 0.998 to 0.990, and acrylate carbonyl carbon KIEs of 1.009-1.012. In the B3LYP calculations, structures that include a *single* hydrogen bond to O_A lead to somewhat less accurate but still reasonable KIE predictions: C-α KIEs of 1.015-1.017, Cβ KIEs of 0.992 to 0.993, and acrylate carbonyl carbon KIEs of 1.007-1.009.

The solvent H/D KIE predicted for all of these structures is in the range of 1.00 to 1.12; considering the general difficulties in predicting solvent KIEs, this agreement is fine.

It is somewhat disconcerting that the models leading to reasonable KIE predictions for the two DFT methods involve different levels of solvation and can involve either proton-shuttle or acid-base pathways. In this way even the limited set of transition structures that are consistent with the experimental KIEs is indecisive about aspects of the mechanism. One the other hand, there is an important commonality among the seven structures giving good KIE predictions in that they all have α C-H distance of 1.33-1.36 Å and O_A-H distances of 1.29-1.32 Å. In previous work we have shown that predicted KIEs can reflect transition state interatomic distances in a way that is independent of both the choice of theoretical method and the detailed choice of the computational model. In this way, series of calculations can be used to delimit transition state distances from experimental KIEs. The α C-H distance of 1.33-1.36 Å and O_A-H distance of 1.29-1.32 Å could then be considered a new example of the experimental measurement of a transition state geometry using KIEs. Although tunneling greatly complicates the interpretation of H/D KIEs for proton transfer reactions, the results here interestingly suggest that heavy-atom KIEs may be used to report on transition state distance for protons being transferred.

The Experimental Free-Energy Profile. The data discussed above along with some additional inferences can be used to define an experimental standard-state free-energy profile for the mechanism of the MBH reaction of MA with **5** in methanol catalyzed by DABCO. This profile is shown in Figure 13 on page 65. It should be recognized that there are significant uncertainties associated with some of the energy values due to the nature of the estimates involved. Nonetheless, the complete free-energy profile is rooted in experimental observations.

In Figure 13 on page 65, the basis for assigning the energies of the transition states for the aldol and elimination steps lies in the Eyring study of the reaction, the partitioning of **19**, and the KIE evidence indicative of mixed rate-limiting steps. The free energy of **8** is based on the observable stability of **9** along with the kinetic acidity of **9**. To get the energy of **15**, we first assume that the rate constant for elimination of **15** mediated by methoxide is approximately the same as it is for the elimination in **19**. This assumption seems reasonable since departure of the differing amines in the two eliminations does not occur during the rate-limiting proton abstraction. With a rate constant of $\approx 2 \times 10^4$ M^{-1} s^{-1} for elimination in **19**, the free-energy barrier for the elimination is ≈11.5 kcal/mol. Some uncertainty in this value arises from the uncertain concentration of methoxide during the elimination reaction of **19**, which in turn arises from uncertainty in the pK_a's of DABCO-H^+ and **20** in methanol. As a check on the reasonableness of the 11.5 kcal/mol value, it may be noted that there is a nearly identical barrier, 11.3 kcal/mol, for the deprotonation of **9** by methoxide (Figure 7 on page 31). This supports the assumption that the difference in the ammonium salts between **15** and **19** makes little difference in the barrier for deprotonation. If the barrier for the elimination reaction of **15** is 11.5 kcal/mol then **15** is 9.7 kcal/mol above the starting materials.

The energy of **14** is based on the assumption that the pKa of the alcohol group of **15** is similar to that of methanol.[48] The lowest-energy conformations of **14** places the ammonium anti to the alkoxide. With this assumption, the free energies of **14** and **15** differ by RT ln [methanol] due to the differing standard state concentrations for **15** versus methanol. Despite the similar standard-state free energies of **14** and **15**, little **14** would be present relative to **15** because the concentration of methoxide anion would be many orders of magnitude below 1 M.

The energy of **24** was estimated from the similarity of the protonation of **24** by methanol to form **15** and the protonation of **8** by methanol to form **9** plus methoxide anion. The barrier in Figure 7 (see page 31) for the formation of **9** + methoxide is known under MBH conditions from the rate of incorporation of deuterium into MA, and it is 13.1 kcal/mol above **8**. If the barrier for the protonation of **24** by methanol is the same as that for protonation of **8**, then **24** would be 8.1 kcal/mol (21.2 - 13.1) above the starting materials. The barriers for formation of **8** and fragmentation of **24** are unknown.

Comparisons with Calculated Energetics. Figure 13 shows how series of computational free energies for the MBH mechanism compare to the experimental free-energy profile. The choice of calculated structures for comparison with experiment requires discussion. We particularly eschewed all supramolecular structures including extra explicit solvent models. All of the intermediates and transition states along the mechanism are strongly solvated, unlike the starting materials and products, and the additional of explicit methanol molecules would tend to lower energies across the board.

In exploratory studies, the worst errors, those for **15** + MeO⁻, were greatly decreased by explicit solvation, while other errors, most notably those for the M06-2X free energies for **16** and **23**, were significantly increased. All of the entropy barriers for **16**/**17** and **23** are taken substantially further from experiment by the addition of explicit solvent. The absence of a clear and tractable way to realistically account for entropy is a central reason for avoiding the supramolcular approach.

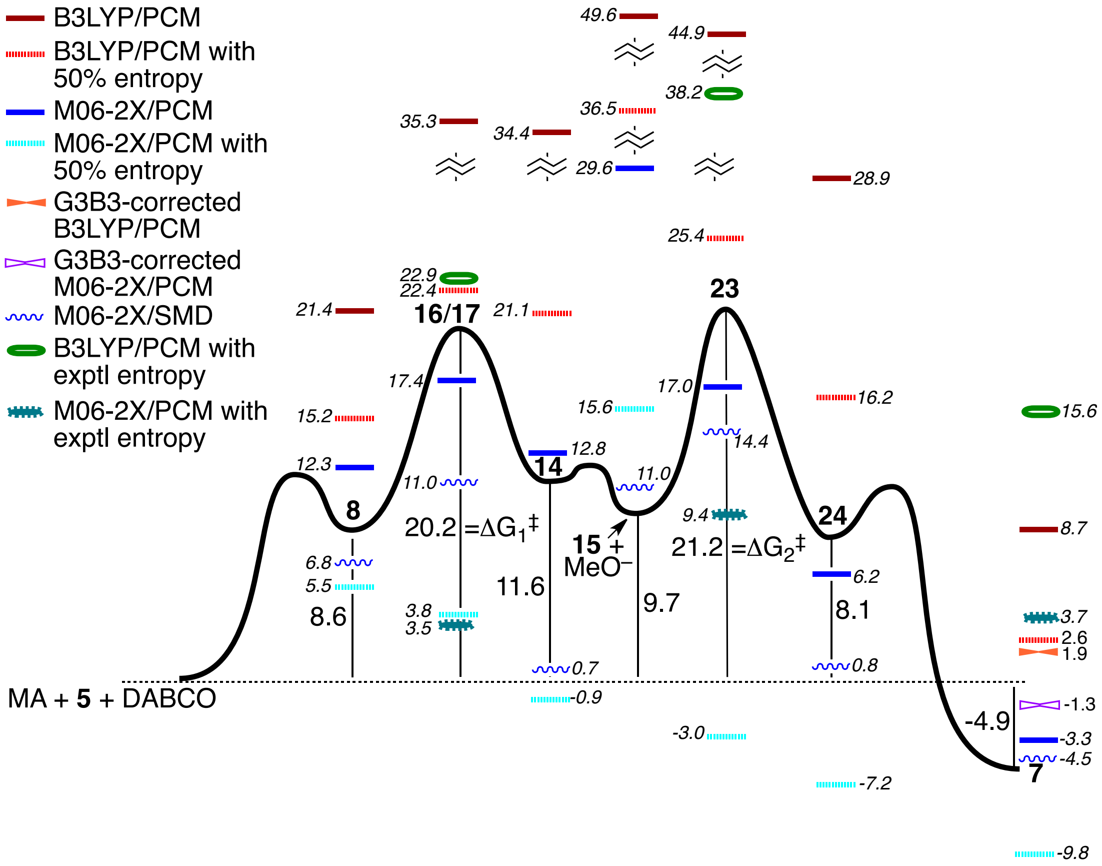


Figure 13. Experimental and computational free energies along the MBH reaction coordinate. The black continuous line is experimental. All of the B3LYP and M06-2X calculations include full optimization with a PCM solvent model for methanol.

However, error in the predicted free energies for **15** + MeO$^-$ (and **9** + MeO$^-$) should be largely discounted as a straw man due to the recognizable inadequacy of the implicit solvation model for MeO$^-$. The preclusion of explicit solvation excludes most variants of structure **23**, and the lowest-energy remaining structures are the simple proton-shuttle structures proceeding directly from **14** to **24**. These structures were used for comparison with the experimental barrier despite their not being consistent with our experimental observations. There are two arguments supporting the value of this comparison with an incorrect calculated mechanism. A qualitative argument is that the proton-shuttle transition states are likely to crudely resemble the actual transition state, at least to the degree that both involve an α C-H deprotonation by a hydrogen-bonded alkoxide oxygen. A more subtle but quantitative argument is that the free energies of the proton-shuttle transition structures should represent upper bounds on the computational free energies of the actual mechanism, calculated by some (unknown) process that would correctly incorporate entropy. The upper-bound limitation arises because reactions must occur by the lowest-energy mechanism so any incorrect mechanism must in reality be higher in energy. The argument here assumes that the computational methods employed would be capable of correctly identifying the mechanism if there existed some method for correctly incorporating the entropy. This assumption is questionable, but if it is not correct for a particular reaction then the computational method is simply not capable of predicting the correct mechanism for that reaction.

Figure 13 on page 65 exhibits most obviously the exceptional error of B3LYP calculations including the full harmonic entropy and M06-2X calculations including

50% of the entropy. Considering the known problems of B3LYP with the energies of σ bonds relative to π bonds,[43d] the B3LYP energetics might be considered to be a straw man, despite their use in many of the MBH mechanistic studies. However, the large errors in the B3LYP energies are not solely the result of an expected σ / π energy error. For the proton-shuttle transition state found by Aggarwal and Harvey, the G3MP2 correction to the energy was only 8.5 kcal/mol. Applying this correction to the 44.9 kcal/mol B3LYP barrier would leave it 15.2 kcal/mol too high, still underestimating the rate by eleven orders of magnitude. A large portion of the remaining error may be ascribed to the entropy problem; the B3LYP $\Delta S^{\ddagger}$ is -101 e.u. compared to the experimental $\Delta S^{\ddagger}$ of approximately -79 e.u.. The extraordinary errors in the B3LYP calculations arise because the two sources of error reinforce each other.

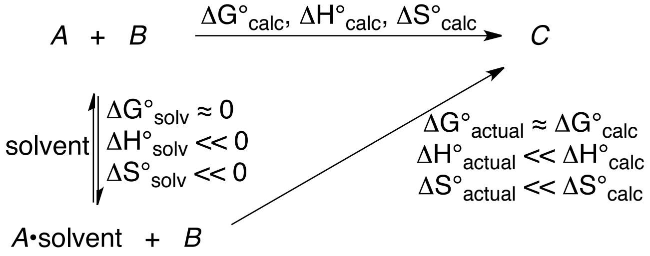
The spectacular failure of M06-2X calculations with a 50% entropy correction would seem less easily anticipated. The M06-2X method would be expected to provide fairly accurate energetics, the expectation of a large entropy error is both widespread and experimentally supported, and a similar entropy correction was employed by Aggarwal and Harvey. In the absence of experimental observations for the reaction at hand, there would be no compelling reason to discount the computational results, but any free-energy profile predicting that the formation of **8** is that rate-limiting step is clearly providing no useful information. The 50% entropy correction is too large, as it predicts the entropic barrier for the proton-shuttle step to be -37.6 e.u. instead of the observed value (with the correct mechanism) of approximately -79 e.u.. However, if the correct entropy is used in place of the 50% entropy correction, the M06-2X calculation on the proton-shuttle transition structure would still underestimate the experimental barrier by 11.8 kcal/mol, overestimating the rate by nine orders of magnitude.

In comparison with the exceptional error of the methods above, the error in the M06-2X calculations including the full harmonic entropy in the M06-2X calculations including the full harmonic entropy and the B3LYP calculations including 50% of the entropy appear small. On an absolute scale, however, the errors in predicted equilibrium or rate constants range up to eight orders of magnitude. The errors are also inconsistent; the B3LYP / 50% entropy calculations have errors versus experiment that range from +2.2 to +8.5 kcal/mol while the M06-2X calculations have erros that range from +3.7 to -4.2 kcal/mol (ignoring **15** + MeO$^-$). This inconsistency is vexing. On a detailed level, it leads to a number of strange predictions. One example is that **8** and **24** are structurally rather similar, yet the M06-2X calculations err in their relative free energies by 5.6 kcal/mol. Another example is that aldol reaction of **8** with **5**, with an M06-2X-predicted $\Delta G^{\ddagger}$ of 5.1 kcal/mol, would be expected to occur at a nearly diffusion-controlled rate when its actual rate constant is only 10^4 M^{-1} s^{-1}. On a general level, inconsistent errors can readily lead to qualitative errors in the prediction of a mechanism. In the MBH reaction, the M06-2X calculations do not predict the correct rate-limiting step and the B3LYP / 50% entropy calculations do not predict that the reaction would succeed at all.

Moreover, the relative success of these calculations appears to result from immense cancellation of errors in enthalpy versus entropy. M06-2X errs in the enthalpies of the aldol and elimination barriers by 16.7 and 11.8 kcal/mol, respectively. Put another way, if the entropy barriers had been calculated perfectly (to match the experimental barriers), the M06-2X calculations would overestimate that rates of the aldol and elimination steps by twelve and nine orders of magnitude, respectively. The B3LYP / 50% entropy calculation errs in the elimination barrier by only 4.2 kcal/mol, but the entropic barrier in this calculation is only -36 e.u.. With a correct barrier, the B3LYP calculations would underestimate the rate by twelve orders of magnitude.

Enthalpy-Entropy Compensation. Caveats on Entropy Corrections and Enthalpy Calculations. We consider here the possibility that the elephantine cancellation of entropy and enthalpy errors in the M06-2X calculations may not be accidental. If so, the relative if crude accuracy of the predicted free energies could reflect an underlying and resiliently useful accuracy in the calculations. This could occur due to the phenomenon of enthalpy-entropy compensation.[49] We use the term "enthalpy-entropy compensation" here in its weak form, which is just the non-profound statement that for weak molecular interactions changes in enthalpy and entropy tend to have the same sign. A stronger from of enthalpy-entropy compensation has been the venerable observation that the two tend to vary in a linear fashion, but the significance of this observation has been questioned.[49]

The general idea of enthalpy-entropy compensation is that enthalpically favorable interactions between molecules are accompanied by entropically disfavored restrictions on their motion. The effects work in opposite directions so the free energy change is smaller. The potential role of enthalpy-entropy compensation in the computation of thermodynamic parameters can be readily understood with reference to a simplified hypothetical association of *A* with *B* to form *C*, where *A* is involved in some specific coordination by solvent that must be released for *C* to be formed. We will assume that the calculated thermodynamics (ΔG°_{calc}, ΔH°_{calc}, ΔS°_{calc},) would be perfectly accurate were it not for this unconsidered coordination, and we sill make the initial assumption that the overall ΔG° for the specific coordination, ΔG°_{solv}, is approximately 0. With a normal solvent concentration greater than unity, most *A* would be coordinated and experimental observations would reflect the conversion of *A*•solvent plus *B* to *C*. The experimentally observed free energy change on formation of *C*, ΔG°_{actual}, would be little changed and the calculated free energy for formation of *C* ΔG°_{calc}, would remain accurate. However, the enthalpy and entropy change associated with coordination would be substantial; the entropy loss in a typical bimolecular association is -30 to -40 e.u. and ΔH°_{solv} approximately -9 to -12 kcal/mol. As a result, despite the accuracy ΔG°_{calc} versus ΔG°_{actual}, the experimentally observed enthalpy and entropy (ΔH°_{actual} and ΔS°_{actual}) would depart substantially from the calculated values.



Stronger coordination of *A* to solvent, making $\Delta G^\circ_{solv} < 0$, would tend to make both ΔH°_{solv} and ΔS°_{solv} more negative while changing ΔG°_{solv} to a lesser extent. This means that the accuracy advantage of ΔG°_{calc} over ΔH°_{calc} should be maintained in the limit of very strong coordination by solvent. It may be recognized that more complex circumstances will not change the story seen in this model example. Any differing solvent coordination of starting materials versus products would cause large but compensating errors in enthalpy and entropy while maintaining *relatively* accurate free energy predictions. The observation of greater accuracy in free-energy calculations relative to enthalpy or entropy calculations appears common in the literature if rarely explicitly recognized; a recent example can be seen in the equilibrium of carbens with halid ions.[50]

The significance of enthalpy-entropy compensation toward the accuracy of computational mechanistic studies has been largely ignored.[51] As noted in an earlier section, experimental activation entropies or entropies of reaction for bimolecular associations are often substantially less negative than calculated values, and this observation has been the core argument for the use of adjusted entropies in the computational of free energies. This argument is severely compromised by the potential role of enthalpy-entropy compensation in the computational error, because it considers only the error in the entropy and does not consider the corresponding and compensating error in the enthalpy. In this light, the use of wholesale entropy correction schemes in mechanistic free-energy calculations would seem insufficiently justified. The exceptional error in the M06-2X / 50% entropy calculations for the MBH reaction suggests that the use of such schemes should be discontinued, at least in the absence of deeper analyses of the particular problem at hand.

A second implication of enthalpy-entropy compensation is subtler but is potentially of broader importance. A widespread practice in computational mechanistic studies is to sidestep the large potential error in entropy calculations by focusing solely on enthalpy. However, enthalpy-entropy compensation has mathematically equivalent effects on entropy and enthalpy predictions. To the extent that enthalpy-entropy compensation plays a role in entropy errors, it will play an equal role in enthalpy errors. As a result, there is no compelling reason to expect that predictions of enthalpies in computational mechanistic studies of reactions in solution will be any more accurate than predictions of free energies, and the discussion above would argue in favor of the opposite conclusion. The extraordinary error in the M06-2X enthalpic barriers for the MBH reaction supports this idea.

The discussion here has necessarily been qualitative and speculative, as there is no simple way to quantitate or even firmly recognize the influence of enthalpy-entropy compensation from the experimental study of a single MBH reaction. Ultimately, we simply do not know how much the coarse accuracy of the M06-2X free energies in the MBH mechanism results from enthalpy-entropy compensation, as opposed to simple fortuity.

Additional Discussion. The MBH reaction in methanol is some ways a challenging system for computational mechanistic chemistry. Each intermediate is either zwitterionic or charged, the effect of the polar solvent in stabilizing the charge is less, and the error inherent to any implicit solvent model in estimating the charge stabilization by solvent would be expected to be substantial. In addition, the bimolecular and trimolecular nature of most of the intermediates and transition states along with the minimally tetramolecular nature of the rate-limiting step inflates the role of entropy in the relative free energies along the mechanistic pathway, and this maximized the potential error due to the misreckoning of entropy. Error in the MBH mechanism should not be a good exemplar for error in some simpler reactions, such as non-polar unimolecular pericyclic rearrangements. On the other hand, all of the intermediates and transition states are closed shell species without low-lying excited states and there is no reason to expect that electronic structure methods should intrinsically lead to sizable errors in the MBH reaction. Overall, the challenges imposed by the MBH mechanism would not appear to be greater than those seen in a large portion of computational studies of reactions in solution.

There is no practical limit to the number of alternative computational method, basis set, entropy-calculation, and solvent model combinations that could be applied to the MBH mechanism. It is inevitable that some subset of the possible computational approaches will provide a more accurate prediction of the free energy surface for the MBH reaction, but such accuracy is meaningless unless the computational approach would reliably and foreseeable make accurate predictions. While any popular computational approach has its virtues, none are used more often in recent literature that those applied here a few would provide a cogent reason to expect more accurate results for the MBH reaction. We explored one additional attractive possibility in the use of the SMD solvent model[52] in place of the PCM solvent model [calculated as M06-2X/SMD//M06-2X/PCM]. However the SMD solvent model did not perform as well, coming closer to experiment in the free energy of **7**, **8**, and **15** but further from experiment, often much further, for every other structure (see Figure 13 on page 65).

M06-2X/SMD perversely predicts high stability for **14** and **24**, and it errs on the enthalpy barrier for the aldol step by over 23 kcal/mol! The combination of the M06-2X/SMD calculations and a 50% entropy correction (dubious considering the nature of the SMD model) leads to free-energy predictions that are too poor to warrant presentation, outside of the interesting if perplexing prediction that **24** would be more stable than **7**.

Additionally, each structure in Figure 13 (see page 65) was reoptimized with the larger 6-311+G** basis set. The mean absolute deviation from experiment increased by 1.9 and 0.1 kcal/mol for the B3LYP and M06-2X functionals, respectively.

Computational methods are simply scientific models. Any model makes some inaccurate predictions but models can retain utility despite significant propensities for inaccuracy. Inaccurate predictions aid the choice of models for future predictions. Because of this, the central scientific problem in the computational study of the MBH mechanism is not the inaccuracy of the predictions. Rather, it is the absence of any particular prediction at all. Fully-defined computational methods (including the choice of basis set, entropy calculations, and solvent model) of course make quite specific predictions. However, there is no consensus about the best choice of method; there is not even a common view on the right way to choose a computational method. In the case of the MBH reaction, defensible and expectantly publishable choices of computational approaches lead to predictions of the facility of the proton-shuttle process that vary by 35 orders of magnitude, while also diverging in the geometry and preferred stereochemistry of transition states. This variance is in practical terms indistinguishable from making no prediction. In addition, studies of the MBH mechanism have not been considered falsified by extreme inaccuracies in predictions. In the terminology of Pauli, computational mechanistic chemistry is "not even wrong" about the MBH mechanism.

A less bleak view of the utility of computations in the study of the MBH mechanism can be built around the argument that the experimental observations for a reaction can and should be used in the choice of theoretical methods used in the study of that reaction. Even a single comparison with experiment is very helpful; the poor predictions of the over-all barrier for the MBH reaction (which is easily estimated without any detailed kinetic study) would allow one to exclude the otherwise defensible B3LYP / full entropy and M06-2X / 50% entropy calculations. If one simply requires consistency with a second experimental observations, i.e., that the reaction of MA with 5 proceeds, then the M06-2X / full entropy calculations would be chosen. This is a tremendous advance over the incredible range of predictions that might be obtained in the absence of consideration of experimental observations, in part because the M06-2X / full entropy calculations provide the best overall prediction of the free energy profile but more importantly because the delineation of a specific method leads to specific and testable predictions. However, the M06-2X / full entropy calculations qualitatively mispredict the rate-limiting step, quantitatively mispredict the enthalpies of the key transition states so this process certainly does not preclude incorrect predictions.

Conclusions

Our experimental observations define a nearly complete free-energy profile for the mechanism of an MBH reaction. The particular reaction studied here involves competitive rate-limiting steps, as is supported by the magnitude of the aldehydic carbon ^{13}C KIE, by the observation of a decrease in this KIE in d_4-methanol, by the partitioning of **19** the reaction conditions, and by the observation of a non-linear Erying plot. The mixed rate-limiting steps allow both barriers to be determined. The observation of shunt product **9**, the thermodynamics for its formation, and the rate of deuterium exchange into **9** delimits energy of intermediate **8**. The rate of product formation from **19** provides the free energy of intermediate **15**, and this in turn provides the energy of **14** from general acidity considerations. The ^{13}C KIE for the β-carbon of MA strongly supports a two-step E1cb(irr) process for the elimination. The energy of the intermediate **24** in the elimination was assigned making use of the similarity of the eliminations of **15** and **9** and the rate of deuterium incorporation into MA via **9**.

A key feature of the mechanism is that the initial aldol adduct **14** is protonated by solvent to afford **15** prior to the α-deprotonation that initiates the elimination. The absence of a proton-shuttle mechanism is supported by a 0.96 ± 0.1 solvent H/D KIE, and it is strongly supported by the nearly identical rates for elimination of **19** and **22**. This conclusion is in contrast to the seven computational mechanistic studies that had previously considered this issue, though the mundane two-step proton transfer mechanism had in fact not been computationally considered. The preferred consideration of computationally tractable mechanisms over less tractable alternatives is common, and the results here underscore that there is no scientific basis for this preference.

The general outline of the MBH mechanism as an addition / aldol / elimination sequence was understood from experimental observations before any computational mechanistic studies. The McQuade mechanism employing a second molecule of aldehyde to facilitate the elimination arose from experimental studies. The suggestion by Aggarwal and Lloyd-Jones that hydroxylic compounds accelerated MBH reactions in a similar way, though not supported here in its details, arose from experimental observations. Though never emphasized, computational studies successfully recognized the E1cb nature of the elimination step. This conclusion however would have been clearly anticipated from experimental studies.[53] The more primordial currency of information provided by computational studies consists of the geometries and energies of intermediates and transition states along the mechanism. Except for the ultimately irrelevant proton-shuttle and direct 1,3-proton transfer transition states, the various geometries received little discussion in the published computational studies. The results here with **23** and **16** / **17** highlight the large variations in geometries and changes in the preferred diastereomer that occur with changes in the theoretical model and computational method. We have sufficiently discussed the problems with the computed energies. Overall, it is not clear to us that any significant accurate information that was not already apparent from experiment either has been, or could have been, reliably garnered purely from computations. In the absence of any consideration of experimental observations in the MBH reaction, defensible computational studies could have made an exceptional diversity of predictions, many of which would have been absurd. In the actual MBH case where much was known experimentally, computational predictions that were consistent with experiment were emphasized while those inconsistent with experiment, such as the B3LYP findings of astronomical barriers and that the product was less stable than the reactants, were ignored. The computational studies then highlighted one essentially pure prediction - that of the proton-shuttle process - and that prediction was incorrect.

From a more positive perspective, computations aided significantly in the mechanistic interpretation of the experimental ^{13}C KIEs in terms of a commitment factor and the mixture of rate-limiting steps involved. Computations intriguingly also provide a detailed, model-independent geometrical interpretation of the ^{13}C KIEs in terms of interatomic distances in the elimination transition state. Regardless of the associated uncertainty, computations remain the only available handle on the transition states for formation of **8** and fragmentation of **24**. Overall, the combination of experimental and computational studies provides a full mechanistic pathway for the MBH reaction including details that would be impossible to discern from either alone.

The scientific approach taken here has been that of a *case study*, and as such it suffers from the general limitations of case studies. The most important of these is the problem of generalization of the results to a broader swath of cases. The problems in the computational study of mechanisms encountered in the MBH reaction certainly cannot be used to paint all computational mechanistic studies. Many, either by simplicity or carefully designed use of the computations, would not be susceptible to the difficulties encountered here. At least, however, it would seem that the study of complex multimolecular polar reactions in solution should be approached with great care and no small amount of skepticism. The strength of a case study is that it identifies problems for consideration in other cases, and the results here suggest a variety of issues that should be carefully considered in the execution and interpretation of computational mechanistic studies.

Experimental Section

k_H/k_D Measurements, Solvent KIEs, and Kinetics of MBH Reaction in Methanol and d_4-Methanol. A mixture of 1.0 g (6.6 mmol) of *p*-nitrobenzaldehyde, 0.60 mL (0.63 g, 6.2 mmol) of methyl acrylate, and 0.223 g (2.0 mmol) of DABCO in 10 mL of methanol, was stirred at 25 °C. Aliquots were drawn from each reaction at different time points during the reaction and were diluted with 1.5 mL of $CDCl_3$, washed with one 1-mL portion of water, dried ($MgSO_4$) and filtered. The samples were analyzed by ^1H NMR.

A similar reaction with the modified procedure that the mixture of MA and DABCO in d_4-methanol was allowed to stand overnight where deuterium equilibrated into α-position of MA. Before the reaction was started, ^1H NMR showed 96% deuterium incorporation into the α-position of MA. The reaction was started with addition of *p*-nitrobenzaldehyde.

A similar reaction with the modified procedure that the reaction was run in 10 mL of d_4-methanol instead of non-deuterated methanol. The amount of deuterium incorporated into the α-position of MA was monitored by ^1H NMR.

Kinetics Experiment with MA and DABCO in Absence of Aldehyde. Example Procedure. Reactions were carried out with methyl acrylate and DABCO at concentrations of 0.33 and 0.10 M, respectively, in d_4-methanol. The amount of deuterium incorporation into the α-position of methyl acrylate was measured by ^{1}H NMR over a 4 h time span. The geminal β-protons were used as internal standards as deuterium was not incorporated into these positions over time. The experimental data was simulated and rate constants determined.

Preparation of DABCO Mono-Hydrochloride Salt. To a cold solution of 3.3 mL (40 mmol) of concentrated hydrochloric acid was added 5.0 g (45 mmol) of DABCO dissolved in a minimum amount of absolute ethanol (6 mL). Upon addition, deliquescent needles formed. The solution was allowed to warm to room temperature and the solution turned clear. It was then concentrated on a rotary evaporator and dried by azeotrope with *iso*-propyl alcohol. The impure crystals were purified by recrystalization using ethanol as the recrystalizing solvent. The crystals were filtered through a Schlenk filter under N_2 and allowed to dry *in vacuo* to yield 3.9 g of DABCO-H^+. The dried crystals were stored under dessicant conditions.

Kinetics Experiments and Equilibrium Constant Measurements of Methyl Acrylate and Excess DABCO-H^+. To a 5-mm NMR tube was added 10 uL (9.6 mg, 0.12 mmol) of methyl acrylate, 35 mg (0.23 mmol) of DABCO-H^+, and 1 mg (0.01 mmol) of DABCO in 1.04 mL of d_4-methanol. The rate of deuterium exchange into the α-position of species **9** was followed by ^{1}H NMR, using the geminal β-protons as an internal standard. The spectra was referenced to the residual methyl peaks in d_4-methanol at 3.3 ppm. Integrations included the β-protons of **9** (δ 3.61 ppm, doublet, 2H), and α-protons of **9** (δ 2.97 ppm, triplet, 1H). From the integrations, a $t_{1/2}$ was obtained of approximately 50,000 s, which translates to a rate constant of k = 0.000014 s^{-1}.

Equilibrium constants were determined at temperatures of 0, 22, 40, and 60 °C and the K_{NH+} values were 1170, 260, 94, and 34.3 M^{-1}, respectively. All spectra were reference to residual methyl peak of d_4-methanol at 3.3 ppm. The spectra were phased and leveled so that integral was flat in between the olefinic peaks (δ 5.88-6.35 ppm.) of MA. Integration was determined by integrating β-protons of **9** (δ 3.61 ppm) with the β-protons of α-d-MA (δ 5.88 and 6.35 ppm). The kinetics of deuterium washing into **9** and the determination of equilibrium constant were done in this same NMR tube. At this point, MA and **9** have deuterium washed into them; so the peaks listed above are those protons of the deuterated species. As the mixture approached equilibrium, smaller and smaller amounts of MA were appearing in the NMR spectrum. In those cases, up to 128 scans were used in order to see, clearly, and integrate the peaks of MA. At higher temperature, as few as 32 scans were utilized. Chemical shifts of α-d_2-**9** in reaction mixture are as follows: ^1H NMR (500 MHz, CD_3OD, 22 °C) δ/ppm: 3.73 (s), 3.60 (s, 2H), 3.42 (m, 6H), 3.20 (m, 6H). Chemical shifts of α-d-methyl acrylate in reaction mixture are as follows: ^1H NMR (500 MHz, CD_3OD, 22 °C) δ/ppm: 6.36 (1H, J_{HH} = 1.5 Hz, J_{HD} =2.7 Hz), 5.88 (1H, J_{HH} = 1.5 Hz, J_{HD} = 3.0 Hz).

Kinetics Experiment with 3-Pentanone. A mixture of 100 μL (81 mg, 0.94 mmol) of 3-pentanone, 11 mg (0.09 mmol) of DABCO, and 14 mg (0.09 mmol) of DABCO-H^+ in 1.02 mL of d_4-methanol. The reaction was left to sit at 22 °C where deuterium exchange was monitored over a week. The β-protons (δ 1.00 ppm) were used as an internal standard to determine the amount of deuterium in the α-position (δ 2.46 ppm). Rate constants for deuterium exchange were calculated. The spectra were referenced to the residual methyl peak of d_4-methanol at 3.3 ppm. Four different time points were gathered and the rate constants were 7.1×10^{-7}, 6.0×10^{-7}, 5.5×10^{-7}, and 5.7×10^{-7} s^{-1}, respectively. The average of these four rate constants was determined to be 6.1×10^{-7} s^{-1}.

Reversibility of the MBH Reaction. To a 5-mm NMR tube was added 3 mg (0.0126 mmol) of MBH product **7** and 0.4 mg (0.0013 mmol) of DABCO in 1 mL of d_4-methanol. The reaction mixture was let to sit for up 17 days where it exhibited traces of MA and **5** by ^{1}H NMR analysis. The mixture was spiked with minute amounts of *p*-nitrobenzaldehyde (**5**), from the bottle, to confirm the presence of **5**. Enough was added to positively distinguish species and identify their appropriate chemical shifts. The spectrum was referenced to the residual methyl peak of d_4-methanol at 3.3 ppm. One of the β-protons exhibited a particular quartet that consisted of a coupling with the geminal β-proton and the vicinal α-deuteron, at 5.86 ppm with a coupling constant of J = 1.5 Hz. One of the α-d-methyl acrylate beta protons was at δ = 5.86 ppm. To get a rough conversion, this peak, along with a nearby peak from the product at 6.08 ppm, was integrated. The other beta peak from α-d-methyl acrylate would be buried under a product peak at δ = 6.36 ppm. The aldehyde peak was seen clearly at 10.13 ppm. With fair certainty, the peak at 8.41 ppm corresponds to one pair of aromatic protons. Although it was not utilized in this experiment, one of the aromatic hemiacetal

($NO_2C_6H_4(OH)H(OMe)$) peaks was at 7.71 ppm and the other chemical shift of the hemiacetal ($NO_2C_6H_4(OH)H(OMe)$) peak was at 5.59 ppm.

Kinetics Experiment to Determine Order in DABCO. Kinetic measurements were obtained by running three side-by-side experiments with MA and *p*-nitrobenzaldehyde (**5**) at concentrations of 0.58 and 0.58 M, respectively, and held constant throughout the three reactions. The concentrations of DABCO of each of the three mixtures were 0.09, 0.17, and 0.35 M, respectively. Reactions commenced with the addition of 0.60 mL (0.63 g, 6.6 mmol) of methyl acrylate to a stirred solution of 1.0 g (6.6 mmol) of **5**, DABCO, and methanol as solvent. The reactions were monitored by taking aliquots of the reaction mixtures, diluting with chloroform, and quenching with water. The organic layer was dried ($MgSO_4$) and concentrated on a rotary evaporator. This was then subject to NMR analysis and subsequently, rate constants simulated. The percent conversion was determined by integrating the pair of aromatic protons of the product **7** at 7.57 ppm to one pair of aromatic protons from the starting material **5** at 8.07 ppm. The rate constants were then simulated using the rate law, rate = *k* [**5**][MA][DABCO]. The rate constants for the 0.5, 1, and 2 equivalents DABCO were determined to be 2.5×10^{-4} M^{-2} s^{-1}, 2.5×10^{-4} M^{-2} s^{-1}, and 2.4×10^{-4} M^{-2} s^{-1}, respectively. The rates were then calculated and they were 1.2×10^{-5} s^{-1}, 2.4×10^{-5} s^{-1}, and 4.6×10^{-5} s^{-1}, respectively. A graph of rate versus concentration of DABCO is fitted with a trend line to give an order of DABCO of 0.97. The rate constants and rates listed above have not been corrected for the actual amount of aldehyde. If a correction were needed, the rates and rate constants can be multiplied by a factor of 4.8 for a temperature of 22 °C.

Kinetics Experiments to Determine Order in MA. Kinetic measurements were obtained by running three side-by-side experiments with DABCO and *p*-nitrobenzaldehyde (**5**) at concentrations of 0.901 and 0.270 M, respectively. The concentrations of MA for each of the three mixtures were 0.451, 0.901, and 1.802 M, respectively. Reactions commenced with the addition of 0.60 mL (0.6 g, 6.62 mmol) of methyl acrylate (MA) to a stirred solution of 1.0 g (6.62 mmol) of *p*-nitrobenzaldehyde (**5**) and 223 mg (1.99 mmol) of DABCO (**6**) in 5.53 mL of methanol. The reactions were monitored by taking aliquots of the reaction mixtures, diluting with chloroform, and quenching with saturated aqueous ammonium sulfate. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. This was then subject to NMR analysis and subsequently, rate constants simulated. The worked-up, dried, samples were diluted in $CDCl_3$. The spectra were referenced to the residual chloroform at 7.26 ppm. Percent conversions were determined by integrating one pair of aromatic product **7** peaks at 7.58 ppm with a pair of aromatic starting material (**5**) peaks at 8.08 ppm. The rate constants for the three reactions were $3.2 \pm 0.2 \times 10^{-4}$ M^{-2} s^{-1}, $3.0 \pm 0.2 \times 10^{-4}$ M^{-2} s^{-1}, and $2.9 \pm 0.1 \times 10^{-4}$ M^{-2} s^{-2}, respectively. The rates for these reactions are $3.9 \pm 0.2 \times 10^{-5}$ s^{-1}, $7.3 \pm 0.5 \times 10^{-5}$ s^{-1}, $14.1 \pm 0.5 \times 10^{-5}$ s^{-1}, respectively. The order in MA was determined to be 0.93.

Kinetics of MBH Reaction with 0, 30, and 60 mol% Hydrochloride Salt of DABCO (DABCO-H$^+$). Example Procedure. Three side-by-side reactions were run. Methanol was used as solvent and adjusted to compensate for the amount of salt added. A mixture of 1g (6.6 mmol) of *p*-nitrobenzaldehyde (**5**), 0.60 mL (0.57 g, 6.6 mmol) of methyl acrylate (MA), and 223 mg (2.0 mmol) of DABCO (**6**) in 10 mL of methanol was stirred at 25 °C. Aliquots were removed periodically over a time span of 67 h and analyzed by ^{1}H NMR. The reactions were followed by taking quenched aliquots at periodic time points. The partitioned organic layer was filtered ($MgSO_4$), concentrated on the rotary evaporator and subjected to NMR analysis. The worked-up, dried, samples were diluted in deuterated chloroform ($CDCl_3$), and the spectrum was referenced to the residual chloroform peak at 7.26 ppm. The percent conversion of the reaction was determined by integrating one pair of aromatic protons from the MBH product **7** at δ = 7.58 ppm versus the same pair of aromatic protons for the starting material **5** at δ = 8.08 ppm. The rate constant for the reaction with no DABCO-H^+ was $k = 2.7 \times 10^{-4}\ M^{-2}\ s^{-1}$, the rate constant with 30 mole% DABCO-H^+ was $k = 1.9 \times 10^{-4}\ M^{-2}\ s^{-1}$, and finally the rate constant with 60 mole% DABCO-H^+ was $k = 1.1 \times 10^{-4}\ M^{-2}\ s^{-1}$. These rate constants were simulated from the rate law, rate = *k* [**5**][MA][DABCO].

The closely analogous 30 mol% reaction used 295 mg (2.0 mmol) of hydrochloride salt of DABCO (DABCO-H^+) in 9.72 mL of methanol.

The closely analogous 60 mol% reaction used 590 mg (4.0 mmol) of hydrochloride salt of DABCO in 9.44 mL of methanol.

Kinetic of MBH Reaction With and Without Proton Sponge. Example Procedure. A mixture of 500 mg (3.3 mmol) *p*-nitrobenzaldehyde (**5**), 0.3 mL (0.29 mg, 3.3 mmol) of methyl acrylate (MA), 111 mg (0.99 mmol) of DABCO (**6**), and 213 mg (0.99 mmol) of Proton Sponge (N,N,N’,N’-tetramethyl,1-8,naphthalenediamine, Aldrich 99%) in 2.55 mL of methanol was stirred at 25 °C. Quenched aliquots at appropriate time intervals were analyzed by ^{1}H NMR and rate constants were simulated. Samples were dissolved in $CDCl_3$ and referenced to δ 7.26 ppm of residual chloroform. The percent conversions were determined from integration of one pair aromatic peaks from the MBH product **7** at 7.58 ppm against an equivalent pair from the starting material **5** at 8.08 ppm. The rate constants for the reaction without the proton sponge was 3.0×10^{-4} M^{-2} s^{-1} and with proton sponge was 2.9×10^{-4} M^{-2} s^{-1}.

A closely analogous, side-by-side, reaction was run with the exception being Proton Sponge (N,N,N',N'-tetramethyl,1-8,naphthalenediamine, Aldrich 99%) was excluded from the reaction mixture and the amount of solvent used was 2.76 mL of methanol.

Preparation of 12. Example Procedure[54]. The MBH product 12 was prepared according to a previously reported procedure. A neat mixture of 1 g (7.3 mmol) of anisaldehyde, 0.66 mL (0.63 g, 7.3 mmol) of methyl acrylate (MA), and 824 mg (7.3 mmol) of DABCO (**6**) was stirred at 25 °C for 5 days where it reached 42 ± 2.3% conversion. The neat mixture was flash chromatographed using 5% acetone in dichloromethane to afford 680 mg of **12**. ^{1}H-NMR (500 MHz, CD_3OD, 25 °C) δ/ppm: 7.24 (m, 2H), 6.85 (m, 2H), 6.27 (m, 1H), 5.98 (m, 1H), 5.50 (s, 1H), 3.76 (s, 1H), 3.64 (s, 3H).

Equilibration of the MBH Reaction. Going Forward From 0% Conversion. A mixture of 268 μL (300 mg, 2.2 mmol) of **12**, 198 μL (189 mg, 2.2 mmol) of MA, and 74 mg (0.66 mmol) of DABCO in 352 μL of d_4-methanol was added to a NMR tube and sealed under N_2. The reaction was followed for a span of 38 days where it reached 43.9

± 2.3% conversion. The percent conversions were determined by integrating a pair of MBH aromatic product (**12**) peaks at δ = 6.76 ppm to that with an equivalent starting material anisaldehyde peak at δ = 7.21 ppm. Another set of peaks that were used to determine the percent conversions was a MBH product **12** peak at δ = 5.06 ppm to the starting material methyl acrylate (MA) peak at δ = 5.19 ppm. Two different percent conversion were obtained and the final percent conversion of the reaction mixture was the average of the two readings.

Equilibration of the MBH Reaction. Going Forward From 30% Conversion. To a glass vial was added 20 mg (0.090 mmol) of **13**, 19 μL (18 mg, 0.207 mmol) of MA, 25 μL (28 mg, 0.207 mmol) of **12**, and 3 mg (0.027 mmol) of DABCO in 8 μL of methanol. This mixture was then transferred to a glass capillary and sealed under N_2. The capillary, with reaction mixture, was inserted into a 5-mm NMR tube and d_4-methanol was added. The reaction progressed forward for 7 days where it reached 42.5 ± 2.3% conversion. The percent conversions were obtained in a similar manner used in the going forward reaction from zero percent conversion.

Equilibration of the MBH Reaction. Going Backward From 50% Conversion. A similar reaction, using 20 mg (0.090 mmol) of 13, 8 μL (8 mg, 0.090 mmol) of MA, 11 μL (12 mg, 0.090 mmol) of **12**, and 3 mg (0.027 mmol) of DABCO in 33 μL of methanol, progressed backwards for 7 days where it reached 47.6 ± 2.4% conversion. The percent conversions were obtained in a similar manner used in the going forward reaction from zero percent conversion.

Determination of Activation Parameters. General Procedure. A mixture of 1.0 g (6.6 mmol) of *p*-nitrobenzaldehyde (**5**), 0.60 mL (0.57 g, 6.6 mmol) of MA, and 223 mg (2.0 mmol) of DABCO (**6**) in 5.53 mL of methanol was stirred at 22 °C. Aliquots were removed periodically and analyzed by ^{1}H NMR. Samples were dissolved in $CDCl_3$, spectra were referenced to 7.26 ppm of residual chloroform. The conversions were determined by integrating a pair of aromatic hydrogens of the product at 7.58 ppm with those against a similar pair in the starting material at 8.08 ppm. Rate constants were simulated using the rate law, rate = *k* [**5**][MA][DABCO]. The *k* for this temperature was 2.96×10^{-4} M^{-2} s^{-1}. The rate constants were corrected to allow for the actual concentration of aldehyde at this temperature. The corrected rate constant for 22 °C is 1.421×10^{-3} M^{-2} s^{-1}.

A closely analogous reaction was stirred at 22 °C. The rate constant and corrected rate constants are 3.12×10^{-4} M^{-2} s^{-1} and 1.498×10^{-3} M^{-2} s^{-1}, respectively.

A closely analogous reaction was stirred at 1.2 °C. The rate constant and corrected rate constants are 1.13×10^{-4} M^{-2} s^{-1} and 9.176×10^{-4} M^{-2} s^{-1}, respectively.

A closely analogous reaction was stirred at 0.2 °C. The rate constant and corrected rate constants are 1.11×10^{-4} M^{-2} s^{-1} and 9.013×10^{-4} M^{-2} s^{-1}, respectively.

A closely analogous reaction was stirred at 53.8 °C. The rate constant and corrected rate constants are 5.18×10^{-4} M^{-2} s^{-1} and 1.301×10^{-3} M^{-2} s^{-1}, respectively.

A closely analogous reaction was stirred at 50.5 °C. The rate constant and corrected rate constants are 5.14×10^{-4} M^{-2} s^{-1} and 1.312×10^{-3} M^{-2} s^{-1}, respectively.

A closely analogous reaction was stirred at -21.3 °C. The rate constant and corrected rate constants are 1.45×10^{-5} M^{-2} s^{-1} and 1.798×10^{-4} M^{-2} s^{-1}, respectively.

A closely analogous reaction was stirred at 63.7 °C. The rate constant and corrected rate constants are 5.98×10^{-4} M^{-2} s^{-1} and 1.304×10^{-3} M^{-2} s^{-1}, respectively.

***p*-Nitrobenzaldehyde (5) KIEs in DMSO. Example Procedure.** A mixture of 8.0 g (52.9 mmol) of *p*-nitrobenzaldehyde (**5**), 594 mg (5.3 mmol) of DABCO (**6**) and 4.8 mL (4.6 g, 52.9 mmol) of methyl acrylate (MA) in 66 mL of DMSO was stirred at 25 °C. Aliquots were removed periodically and analyzed by ^{1}H NMR after an aqueous workup, and after 16 h the conversion was 77.6 ± 1.7%. The reaction was then partitioned between 150 mL of ethyl acetate and 100 mL water, and the organic layer was washed with two 50-mL portions of water and two 50-mL portions of saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% ethyl acetate in hexanes to afford 800 mg of *p*-nitrobenzaldehyde (**5**) with no observable impurities by ^{1}H NMR.

A closely analogous reaction was taken to 79.3 ± 1.6 conversion. Another reaction using freshly dried DMSO and airless precautions was taken to 81.3 ± 1.5% conversion. A fourth reaction with 1% water (v / v, versus the DMSO) was taken to 86.1 ± 1.2% conversion.

Methyl Acrylate (MA) KIEs in DMSO. Example Procedure. A mixture of 25.0 g (165.4 mmol) of *p*-nitrobenzaldehyde (**5**), 5.6 g (49.6 mmol) of DABCO (**6**) and 14.9 mL (14.2 g, 165.4 mmol) of methyl acrylate (MA) in 180 mL of DMSO was stirred at 25 °C. Aliquots were removed periodically and analyzed by ^{1}H NMR, and after 5 h the conversion was 82.9 ± 1.4%. The reaction was quenched by the addition of 16 g benzoic acid. The reaction vessel was connected to a vacuum pump, fitted with a cold trap, and approximately 3 mL of reaction mixture was vacuum-distilled (ambient temperature). The crude distillate was then washed with four-1 mL portions of water. The organic layer was dried ($MgSO_4$) and filtered to afford 825 mg of recovered starting material methyl acrylate with no observable impurities by ^{1}H NMR.

An analogous reaction was taken to 83.8 ± 1.3% conversion.

***p*-Nitrobenzaldehyde KIEs in Methanol. Example Procedure.** A mixture of 8.0 g (52.9 mmol) of *p*-nitrobenzaldehyde, 1.8 g (15.9 mmol) of DABCO and 4.8 mL (4.6 g, 52.9 mmol) of methyl acrylate in 12 mL of MeOH was stirred at 25 °C. Aliquots were removed periodically and analyzed by ^{1}H NMR after an aqueous workup, and after 2 h the conversion was 78.8 ± 1.6%. The reaction was then partitioned between 150 mL of ethyl acetate and 100 mL water, and the organic layer was washed with two 50-mL portions of water and two-50 mL portions of saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% ethyl acetate in hexanes to afford 1.2 g of *p*-nitrobenzaldehyde with no observable impurities by ^{1}H NMR.

An analogous reaction was taken to 79.1 ± 1.6% conversion.

Methyl Acrylate (MA) KIEs in Methanol. Example Procedure. A mixture of 10 g (66 mol) of *p*-nitrobenzaldeyde, 5.96 mL (5.7 g, 66 mmol) of MA, and 2.2 g (20 mmol) of DABCO in 80 mL of methanol was stirred at 25 °C. Aliquots were removed periodically and analyzed by ^{1}H NMR, and after 2 h the conversion was 22.9 ± 1.6%. The reaction was then partitioned between 150 mL of ethyl acetate and 100 mL of water, and the organic layer was washed with two 50-mL portions of water and two 50-mL portions of saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% ethyl acetate in hexanes to afford 1.45 g of product (**7**) with no observable impurities by ^{1}H NMR.

A closely analogous reaction was taken to 23.5 ± 1.7 % conversion.

The procedure for the standard for MA KIEs in methanol is as follows. A mixture of 8 g (53 mmol) of *p*-nitrobenzaldehyde, 0.95 mL (0.91 g, 11 mmol) of MA, and 1.8 g (16 mmol) of DABCO in 17 mL of DMSO was stirred at 25 °C. The reaction was stirred until complete disappearance of MA. The reaction was then partitioned between 150 mL of ethyl acetate and 100 mL of water, and the organic layer was washed with two 50-mL portions of water and two 50-mL portions of saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% ethyl acetate in hexanes to afford 700 mg of product (**7**) with no observable impurities by ^{1}H NMR.

***p*-Nitrobenzaldehyde KIEs in d_4-Methanol. Example Procedure.** A mixture of 3.5 g (23 mol) of *p*-nitrobenzaldeyde, 2.09 mL (2.0 g, 23 mmol) of MA, and 0.8 g (7.0 mmol) of DABCO in 5.3 mL of d_4-methanol was stirred at 25 °C. Aliquots were removed periodically and analyzed by ^{1}H NMR, and after 4 h the conversion was 81.0 ± 1.5%. The reaction was then partitioned between 150 mL of ethyl acetate and 100 mL of water, and the organic layer was washed with two 50-mL portions of water and two 50-mL portions of saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% ethyl acetate in hexanes to afford 651 mg of product with no observable impurities by ^1H NMR.

A mixture of 2.09 mL (2.0 g, 23 mmol) of MA and 779 mg (7 mmol) of DABCO in 5.30 mL of d_4-methanol was stirred at 25 °C. Aliquots were removed periodically and analyzed by ^1H NMR, and after 6 h the conversion to α-d_1-methyl acrylate was 80.7 ± 1.5%. The reaction was then started with the addition of 3.5 mg (23 mmol) of *p*-nitrobenzaldehyde followed by a rinse of 5 mL of d_4-methanol. Aliquots were removed periodically and analyzed by ^1H NMR after an aqueous workup, and after 28 h the conversion was 81.1 ± 1.5%. The reaction was then partitioned between 150 mL of ethyl acetate and 100 mL of water, and the organic layer was washed with two 50-mL portions of water and two 50-mL portions of saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% ethyl acetate in hexanes to afford 730 mg of *p*-nitrobenzaldehyde with no observable impurities by ^1H NMR.

A closely analogous reaction was taken to 86.9 ± 1.1 % conversion.

NMR Measurements. All samples were prepared using a constant amount of analyte (200 mg for samples of *p*-nitrobenzaldehyde, 300 mg for samples of methyl acrylate, 400 mg for samples of product) in 5 mm NMR tubes filled with d_6-DMSO or $CDCl_3$ to a constant height of 5.0 cm. The ^{13}C spectra were recorded at 125.70 MHz with inverse gated decoupling. A T_1 measurement was performed on each sample to ensure that the relaxation rates did not change from sample to sample. Integrations were determined numerically using a constant integration region for each peak of 10 times the width at half-height. A zeroth order baseline correction was generally applied, but in no case was a first order (tilt) correction applied.

The ^{13}C spectra of *p*-nitrobenzaldehyde were taken at a controlled temperature of 40 °C (due to solubility issues with p-nitrobenzaldehyde), using 84-s delays between calibrated 90° pulses, a 6.000-s acquisition time, and collecting 304 576 points. Six spectra were obtained for each sample of recovered *p*-nitrobenzaldehyde along with corresponding samples of *p*-nitrobenzaldehyde that were not subjected to the reaction conditions. The resulting ^{13}C integrations for these spectra are given in the Supporting Information. From the ^{13}C integrations the KIEs and uncertainties were calculated as previously described.

The ^{13}C spectra of methyl acrylate were taken at a controlled temperature of 24 °C, using 187-s delays between calibrated 90° pulses, a 15.000-s acquisition time, and collecting 614 756 points.

The ^{13}C spectra of product were taken at a controlled temperature of 24 °C, using 21-s delays between calibrated 90° pulses, a 7.000-s acquisition time, and collecting 343 136 points.

Calculations and Results for All Isotope Effects for MBH Reactions. The fractional conversion, raw integrations, R/R_0's, and KIEs and all their respective standard deviations and errors are shown in the following series of tables (Table 2 to Table 14).

Due to a long relaxation time and the sharpness of its ^{13}C peak, the *para* position in *p*-nitrobenzaldehyde could not practically be quantitated reliably. Therefore, the integrations for the relevant peaks in *p*-nitrobenzaldehyde were set to relative integrations of 2000 for the meta carbon, and the averaged results from six spectra for each sample are shown below. The relative changes in isotope composition (R/R_0) at each position in *p*-nitrobenzaldehyde were calculated as the ratio of average integrations relative to the standard. The standard deviations Δ (R/R_0) were calculated from eq 19. In this equation *Average Sample* is the average integration for each carbon in the sample, *Average Standard* is the average integration for each carbon in the standard, and *Std.Dev.Sample* and *Std.Dev.Standard* are the standard deviations in the integrations for the sample and standard, respectively.

$$\Delta(R/R_0) = R/R_0 \times \sqrt{\left(\frac{\text{Std.Dev.Sample}}{\text{Average Sample}}\right)^2 + \left(\frac{\text{Std. Dev. Standard}}{\text{Average Standard}}\right)^2} \qquad (19)$$

The KIEs for *p*-nitrobenzaldehyde were then calculated from eq 20, with the standard deviations calculated from equations 21, 22, and 23. For this purpose, F is the fractional amount of conversion, or fraction of reaction, and it varies from 0 to 1.

$$\text{KIE} = \frac{\ln(1 - F)}{\ln[(1 - F)R/R_0]} \qquad (20)$$

$$\Delta\text{KIE}_F = \frac{\partial \text{KIE}}{\partial F}\Delta F = \frac{-\ln(R/R_0)}{(1-F)\ln^2[(1-F)R/R_0]}\Delta F \qquad (21)$$

$$\Delta\mathrm{KIE_R} = \frac{\partial \mathrm{KIE}}{\partial(\mathrm{R/R_0})}\Delta(\mathrm{R/R_0}) = \frac{-\ln(1\text{-}\mathrm{F})}{(\mathrm{R/R_0})\ln^2\left[(1\text{-}\mathrm{F})\mathrm{R/R_0}\right]}\Delta(\mathrm{R/R_0}) \tag{22}$$

$$\Delta\mathrm{KIE} = \mathrm{KIE} \times \sqrt{\left(\frac{\Delta\mathrm{KIE_R}}{\mathrm{KIE}}\right)^2 + \left(\frac{\Delta\mathrm{KIE_F}}{\mathrm{KIE}}\right)^2} \tag{23}$$

Table 2. Set 1. Fractional conversion, raw ^{13}C integrations, R/R$_0$'s, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in DMSO.

EP-1-13 Intermolecular recovered starting material KIEs

F	0.776
1-F	0.224
ΔF	0.017

Reisolated Starting Material EP-1-13-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	891.181	891.186	892.342	894.975	893.283	894.370	892.890	1.601
2) para	980.204	990.667	986.366	976.645	980.623	981.780	982.714	4.999
3) ipso	993.785	994.142	989.872	994.328	992.551	993.835	993.086	1.693
4) ortho	2004.940	2012.110	2006.720	2006.840	2011.780	2005.620	2008.002	3.137
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-1-13-KIE-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	879.824	881.222	880.758	881.703	881.875	882.114	881.249	0.851
2) para	989.101	990.399	996.603	993.443	994.883	998.217	993.774	3.530
3) ipso	993.005	992.018	996.014	993.302	997.873	994.453	994.444	2.167
4) ortho	2002.860	2001.640	2002.910	2007.770	2002.970	2004.640	2003.798	2.168
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE$_F$	R/R$_0$	Δ(R/R$_0$)	ΔKIE$_R$	ΔKIE
1) carbonyl	1.009	-0.0005	1.013	0.002	0.001	0.001
2) para	0.993	0.0004	0.989	0.006	0.004	0.004
3) ipso	0.999	0.0000	0.999	0.003	0.002	0.002
4) ortho	1.001	-0.0001	1.002	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 3. Set 2. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in DMSO.

EP-1-18 Intermolecular recovered starting material KIEs

F	0.793
1-F	0.207
ΔF	0.016

Reisolated Starting Material EP-1-18-KIE-TWO-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1025.1	1030.01	1025.9	1021.55	1023.3	1025.7	1025.275	2.854
2) para	1009.3	1004.61	1008.5	1003.27	1003.8	1010.4	1006.642	3.088
3) ipso	1008.3	1004.48	1005.5	1001.21	1002.5	1004.9	1004.467	2.467
4) ortho	2007.3	2004.89	2004.8	2002.56	2002.9	2006.3	2004.785	1.851
5) meta	2000	2000	2000	2000	2000	2000	2000.000	0.000

Starting Material EP-1-18-KIE-TWO-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1015.3	1014.18	1010.7	1007.56	1012.2	1008.6	1011.440	3.051
2) para	1008.4	1015.68	1011.8	1009.28	1015.9	1001.9	1010.490	5.244
3) ipso	1003.9	1006.08	1006.6	1007.02	1006.9	1004.1	1005.762	1.393
4) ortho	2006.7	2005.51	1998.6	2001.32	2003.5	2001.4	2002.835	3.000
5) meta	2000	2000	2000	2000	2000	2000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.009	-0.0004	1.014	0.004	0.003	0.003
2) para	0.998	0.0001	0.996	0.006	0.004	0.004
3) ipso	0.999	0.0000	0.999	0.003	0.002	0.002
4) ortho	1.001	0.0000	1.001	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 4. Set 3. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in DMSO dried over 3 Å molecular sieves.

EP-1-176 Intermolecular recovered starting material (PNB) KIEs

F	0.813
1-F	0.187
ΔF	0.015

Reisolated Starting Material EP-1-176-KIE-PNB-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1044.350	1037.930	1042.980	1042.340	1039.650	1044.540	1041.965	2.651
2) para	1032.160	1031.690	1013.340	1020.900	1022.980	1021.800	1023.812	7.136
3) ipso	1003.450	1002.080	1002.430	1004.140	1002.550	1001.890	1002.757	0.866
4) ortho	2034.070	2024.060	2026.090	2023.610	2026.110	2028.370	2027.052	3.837
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-1-176-KIE-PNB-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1023.180	1025.590	1025.750	1030.180	1022.930	1026.990	1025.770	2.674
2) para	1022.270	1014.530	1033.420	1023.490	1023.560	1026.950	1024.037	6.173
3) ipso	1005.240	998.496	1002.980	1002.910	998.926	1003.280	1001.972	2.670
4) ortho	2025.810	2024.830	2024.660	2024.900	2028.160	2035.550	2027.318	4.239
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.009	-0.0005	1.016	0.004	0.002	0.002
2) para	1.000	0.0000	1.000	0.009	0.005	0.005
3) ipso	1.000	0.0000	1.001	0.003	0.002	0.002
4) ortho	1.000	0.0000	1.000	0.003	0.002	0.002
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 5. Set 4. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in DMSO dried over 3 Å molecular sieves with the addition of 1% water.

EP-1-180 Intermolecular recovered starting material (PNB) KIEs

F	0.861
1-F	0.139
ΔF	0.012

Reisolated Starting Material EP-1-180-KIE-SAMPLE-TWO

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1025.380	1023.540	1022.570	1021.060	1021.970	1023.600	1023.020	1.505
2) para	1004.300	1004.200	1001.910	1000.850	994.607	998.932	1000.800	3.658
3) ipso	995.613	993.048	992.736	994.545	994.650	996.117	994.452	1.348
4) ortho	2007.880	2004.590	2001.890	2011.120	2003.840	2007.610	2006.155	3.339
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-1-176-KIE-STANDARD-TWO

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1000.370	1002.260	1001.590	999.284	1002.660	1002.140	1001.384	1.300
2) para	998.815	1000.120	1000.540	993.042	996.834	1002.030	998.564	3.221
3) ipso	995.330	995.266	996.006	994.232	991.199	993.861	994.316	1.716
4) ortho	2004.300	2005.020	2003.340	2002.780	1999.600	1999.640	2002.447	2.322
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.011	-0.0005	1.022	0.002	0.001	0.001
2) para	1.001	0.0000	1.002	0.005	0.002	0.002
3) ipso	1.000	0.0000	1.000	0.002	0.001	0.001
4) ortho	1.001	0.0000	1.002	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 6. Set 1. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in methanol.

EP-1-23 Intermolecular recovered starting material (PNB) KIEs

F	0.788
1-F	0.212
ΔF	0.016

Reisolated Starting Material EP-1-23-KIE-SAMPLE-THREE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1020.760	1019.890	1021.690	1023.790	1025.750	1022.060	1022.323	2.132
2) para	1001.770	1005.390	994.133	1003.520	1001.210	1000.020	1001.007	3.857
3) ipso	996.159	991.619	993.671	995.155	995.295	993.408	994.218	1.644
4) ortho	2004.950	2004.950	2001.630	2005.200	2007.380	2006.020	2005.022	1.903
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-1-23-KIE-STANDARD-THREE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	996.943	995.037	997.259	998.269	996.694	1000.930	997.522	1.972
2) para	996.140	1001.890	997.087	993.260	995.871	999.695	997.324	3.051
3) ipso	990.990	991.939	990.489	990.985	993.193	991.554	991.525	0.960
4) ortho	2002.620	2003.820	2003.750	2003.760	2000.690	2003.700	2003.057	1.246
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.016	-0.0008	1.025	0.003	0.002	0.002
2) para	1.002	-0.0001	1.004	0.005	0.003	0.003
3) ipso	1.002	-0.0001	1.003	0.002	0.001	0.001
4) ortho	1.001	0.0000	1.001	0.001	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 7. Set 2. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in methanol.

EP-1-105 Intermolecular recovered starting material (PNB) KIEs

F	0.791
1-F	0.209
ΔF	0.016

Reisolated Starting Material EP-1-105-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1031.860	1032.230	1031.790	1033.520	1026.720	1027.180	1030.550	2.861
2) para	998.805	998.962	1003.120	995.377	999.118	999.765	999.191	2.471
3) ipso	1003.380	1008.310	1009.320	1017.920	1005.920	1009.240	1009.015	4.925
4) ortho	2008.940	2006.630	2006.410	2010.350	2006.340	2009.810	2008.080	1.833
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-1-105-KIE-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1006.170	1006.220	1005.390	1009.620	1009.940	1005.190	1007.088	2.127
2) para	1013.230	1014.340	1008.170	1007.210	1009.690	1000.250	1008.815	5.043
3) ipso	1009.890	1009.880	1002.550	1006.550	1008.020	1006.980	1007.312	2.724
4) ortho	2004.390	2004.890	2006.170	2003.880	2008.260	1999.690	2004.547	2.849
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.015	-0.0007	1.023	0.004	0.002	0.002
2) para	0.994	0.0003	0.990	0.006	0.004	0.004
3) ipso	1.001	-0.0001	1.002	0.006	0.004	0.004
4) ortho	1.001	-0.0001	1.002	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 8. Set 3. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in d_4-methanol.

EP-1-274 Intermolecular recovered starting material (PNB) KIEs

F	0.81
1-F	0.19
ΔF	0.015

Reisolated Starting Material EP-1-274-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1025.880	1023.490	1026.890	1029.030	1026.390	1026.220	1026.317	1.782
2) para	1009.980	1010.020	1011.990	1009.150	1011.850	1011.710	1010.783	1.212
3) ipso	1001.220	1000.260	1000.780	1000.950	1001.160	1000.840	1000.868	0.345
4) ortho	2015.350	2012.520	2014.900	2016.640	2013.990	2013.810	2014.535	1.422
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-1-274-KIE-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1004.740	1008.030	1002.260	1005.680	1003.930	1008.800	1005.573	2.483
2) para	1006.000	1006.090	1002.200	1004.510	1003.830	1003.450	1004.347	1.515
3) ipso	1000.820	1001.200	1000.710	1002.410	1000.470	1003.160	1001.462	1.078
4) ortho	2011.180	2016.940	2010.030	2015.710	2011.430	2015.710	2013.500	2.943
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.012	-0.0006	1.021	0.003	0.002	0.002
2) para	1.004	-0.0002	1.006	0.002	0.001	0.001
3) ipso	1.000	0.0000	0.999	0.001	0.001	0.001
4) ortho	1.000	0.0000	1.001	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 9. Set 4. Fractional conversion, raw ^{13}C integrations, R/R$_0$'s, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in d$_4$-methanol where the methyl acrylate (MA) was preequilibrated with the d$_4$-methanol before adding DABCO.

EP-2-210 Intermolecular recovered starting material (PNB) KIEs

F	0.811
1-F	0.189
ΔF	0.015

Reisolated Starting Material EP-2-210-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1024.870	1024.980	1025.660	1020.830	1026.860	1023.390	1024.432	2.095
2) para	990.410	993.155	994.383	993.466	990.078	991.543	992.173	1.756
3) ipso	994.890	994.869	992.893	992.300	994.319	992.176	993.575	1.265
4) ortho	2007.930	2005.680	2003.150	2003.340	2003.830	2002.680	2004.435	2.003
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-2-210-KIE-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1008.160	1005.820	1010.070	1006.810	1013.360	1009.230	1008.908	2.675
2) para	993.189	994.340	995.640	994.871	994.139	988.336	993.419	2.619
3) ipso	994.163	990.718	991.368	993.360	992.815	992.793	992.536	1.276
4) ortho	2005.010	1998.200	1998.670	2002.300	2005.540	2000.610	2001.722	3.120
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.009	-0.0004	1.015	0.003	0.002	0.002
2) para	0.999	0.0000	0.999	0.003	0.002	0.002
3) ipso	1.001	0.0000	1.001	0.002	0.001	0.001
4) ortho	1.001	0.0000	1.001	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 10. Set 5. Fractional conversion, raw ^{13}C integrations, R/R$_0$'s, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in d$_4$-methanol where the methyl acrylate (MA) was preequilibrated with the d$_4$-methanol before adding DABCO.

EP-2-212 Intermolecular recovered starting material (PNB) KIEs

F	0.869
1-F	0.131
ΔF	0.011

Reisolated Starting Material EP-2-212-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1031.510	1030.090	1031.950	1030.690	1028.760	1032.420	1030.903	1.346
2) para	997.151	1001.110	1002.880	999.728	994.132	999.280	999.047	3.073
3) ipso	994.225	996.386	994.334	994.617	993.824	998.204	995.265	1.693
4) ortho	2007.660	2006.630	2006.270	2006.130	2004.250	2008.050	2006.498	1.343
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-2-212-KIE-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1008.160	1005.820	1010.070	1006.810	1013.360	1009.230	1008.908	2.675
2) para	1001.240	1001.800	1002.720	1003.640	1002.040	996.220	1001.277	2.611
3) ipso	994.163	990.718	991.368	993.360	992.815	992.793	992.536	1.276
4) ortho	2005.010	1998.200	1998.670	2002.300	2005.540	2000.610	2001.722	3.120
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.011	-0.0004	1.022	0.003	0.001	0.002
2) para	0.999	0.0000	0.998	0.004	0.002	0.002
3) ipso	1.001	-0.0001	1.003	0.002	0.001	0.001
4) ortho	1.001	0.0000	1.002	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

The integrations for the relevant peaks in methyl acrylate were set to relative integrations of 1000 for the methoxy carbon. The averaged results from six spectra for each sample are shown below.

Table 11. Set 1. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for methyl acrylate (MA) in DMSO.

EP-2-25 Intermolecular recovered starting material (Methyl Acrylate) KIEs

F	0.829
1-F	0.171
ΔF	0.014

Reisolated Starting Material EP-2-25-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1027.010	1029.120	1028.660	1027.650	1029.270	1027.530	1028.207	0.935
2) beta	1002.330	1006.460	1005.990	1006.090	1007.150	1003.870	1005.315	1.829
3) alpha	1027.250	1034.880	1031.480	1031.060	1032.490	1028.450	1030.935	2.759
4) methyl	1000.000	1000.000	1000.000	1000.000	1000.000	1000.000	1000.000	0.000

Starting Material EP-2-25-KIE-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1019.650	1019.810	1017.650	1019.910	1023.790	1015.330	1019.357	2.806
2) beta	1027.670	1026.780	1024.570	1025.670	1028.460	1022.240	1025.898	2.266
3) alpha	1018.310	1018.670	1020.390	1018.050	1022.170	1012.890	1018.413	3.122
4) methyl	1000.000	1000.000	1000.000	1000.000	1000.000	1000.000	1000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.005	-0.0002	1.009	0.003	0.002	0.002
2) beta	0.989	0.0005	0.980	0.003	0.002	0.002
3) alpha	1.007	-0.0003	1.012	0.004	0.002	0.002
4) methyl	1.000	0.0000	1.000	0.000	0.000	0.000

Table 12. Set 2. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for methyl acrylate (MA) in DMSO.

EP-2-29 Intermolecular recovered starting material (Methyl Acrylate) KIEs

F	0.838
1-F	0.162
ΔF	0.013

Reisolated Starting Material EP-2-29-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1032.150	1030.210	1030.590	1028.850	1026.140	1023.730	1028.612	3.130
2) beta	1003.220	998.945	1002.150	996.298	997.669	992.389	998.445	3.966
3) alpha	1029.450	1033.190	1031.660	1032.360	1029.170	1027.860	1030.615	2.088
4) methyl	1000.000	1000.000	1000.000	1000.000	1000.000	1000.000	1000.000	0.000

Starting Material EP-2-29-KIE-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1024.580	1014.950	1021.200	1019.380	1019.310	1020.380	1019.967	3.128
2) beta	1022.500	1024.880	1024.640	1023.730	1026.530	1027.250	1024.922	1.753
3) alpha	1024.340	1015.280	1016.380	1017.520	1016.260	1020.130	1018.318	3.388
4) methyl	1000.000	1000.000	1000.000	1000.000	1000.000	1000.000	1000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.005	-0.0002	1.008	0.004	0.002	0.002
2) beta	0.986	0.0006	0.974	0.004	0.002	0.002
3) alpha	1.007	-0.0003	1.012	0.004	0.002	0.002
4) methyl	1.000	0.0000	1.000	0.000	0.000	0.000

Under MBH conditions in methanol, the carbon of the methoxy group in methyl acrylate could not be used because the methoxy group can exchange with the solvent due to transesterification. The integrations for the relevant peaks in methyl acrylate (MA) were set to relative integrations of 2000 for the aromatic carbons of the product (**7**).

The KIEs for the product were then calculated from eq 24, with the standard deviations calculated from equations 25, and 26. For this purpose, F is the fractional amount of conversion, or fraction of reaction, and it varies from 0 to 1. In the following, R_p/R_0 is the ratio between the molar activities of the product mixture of isotopic molecules and the corresponding reactant mixture.

$$KIE = \frac{log(1-F)}{log[1-(FR_p/R_0)]} \qquad (24)$$

$$\frac{\partial\left(KIE_R\right)}{\partial\left(R_p/R_0\right)}=\frac{F}{1-\left(FR_p/R_0\right)}\times\frac{\ln\left(1-F\right)}{\ln^2\left[1-\left(FR_p/R_0\right)\right]} \tag{25}$$

$$\frac{\partial KIE_F}{\partial F}=\frac{\frac{R_p/R_0}{1-\left(FR_p/R_0\right)}ln(1-F)-\frac{1}{1-F}ln\left[1-\left(FR_p/R_0\right)\right]}{ln^2\left[1-\left(FR_p/R_0\right)\right]} \tag{26}$$

Table 13. Set 1. Fractional conversion, raw ^{13}C integrations, R_p/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for methyl acrylate (MA) in methanol.

EP-2-194 Acrlate Product KIE

F	0.229
ΔF	0.016

EP-2-194-KIE-STANDARD.fid

100% reaction EP-2-17 High conversion reaction limting in acrylate

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) Carbonyl	1012.110	1011.890	1012.100	1014.130	1010.160	1011.250	1011.940	1.304
2) Quaternary Para	1002.110	1005.480	1001.260	1004.060	1002.110	1001.030	1002.675	1.740
3) Quaternary Ipso	1003.620	1001.740	1001.520	1002.610	1001.170	1000.910	1001.928	1.014
4) alpha-Carbon	1001.530	1000.390	997.329	1000.850	997.227	998.190	999.253	1.895
5) Ortho	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000
6) beta-Carbon	1005.930	998.365	995.764	1002.560	997.846	995.081	999.258	4.192
7) Meta	1999.200	1998.530	1995.120	2001.040	1992.440	1990.660	1996.165	4.095
8) sec-OH Carbon	977.481	979.063	977.684	980.146	978.369	977.182	978.321	1.122
9) Methyl-Carbon	987.524	988.238	986.289	987.894	985.202	987.694	987.140	1.158

EP-2-194-KIE-SAMPLE.fid

low conversion reaction set I

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) Carbonyl	1006.970	1005.330	1009.030	1005.480	1004.210	1006.160	1006.197	1.664
2) Quaternary Para	1000.830	998.510	999.186	1000.050	997.274	1001.800	999.608	1.632
3) Quaternary Ipso	1003.220	1004.160	1005.020	1004.620	1001.950	1002.610	1003.597	1.201
4) alpha-Carbon	989.378	987.602	990.553	991.814	985.158	990.317	989.137	2.400
5) Ortho	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000
6) beta-Carbon	1013.840	1007.210	1016.980	1009.870	1004.210	1004.860	1009.495	5.093
7) Meta	1999.610	1993.690	1999.930	1994.930	1989.830	1996.000	1995.665	3.804
8) sec-OH Carbon	974.714	970.145	974.835	970.106	969.807	973.107	972.119	2.382
9) Methyl-Carbon	996.906	992.025	997.594	997.958	990.930	996.793	995.368	3.064

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R_p/R_0	$\Delta(R_p/R_0)$	ΔKIE_R	ΔKIE
1) Carbonyl	1.007	0.0001	0.994	0.002	-0.002	0.002
2) Quaternary Para	1.004	0.0000	0.997	0.002	-0.003	0.003
3) Quaternary Ipso	0.998	0.0000	1.002	0.002	-0.002	0.002
4) alpha-Carbon	1.012	0.0001	0.990	0.003	-0.004	0.004
5) Ortho	1.000	0.0000	1.000	0.000	0.000	0.000
6) beta-Carbon	0.988	-0.0001	1.010	0.007	-0.007	0.007
7) Meta	1.000	0.0000	1.000	0.003	-0.003	0.003
8) sec-OH Carbon	1.007	0.0001	0.994	0.003	-0.003	0.003
9) Methyl-Carbon	0.991	-0.0001	1.008	0.003	-0.004	0.004

Table 14. Set 2. Fractional conversion, raw ^{13}C integrations, R_p/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for methyl acrylate (MA) in methanol.

EP-2-195 Acrlate Product KIE

F	0.235
ΔF	0.017

EP-2-196-KIE-STANDARD.fid

100% reaction High conversion reaction limting in acrylate

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) Carbonyl	1013.990	1014.760	1013.620	1015.890	1017.400	1016.190	1015.308	1.441
2) Quaternary Para	1005.620	1004.750	1006.190	1004.860	1007.870	1002.800	1005.348	1.687
3) Quaternary Ipso	1002.180	1006.810	1006.230	1003.210	1003.230	1004.590	1004.375	1.839
4) alpha-Carbon	997.968	1000.290	1000.640	1001.610	1002.850	1000.100	1000.576	1.634
5) Ortho	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000
6) beta-Carbon	1004.010	1007.280	1007.260	1000.230	1001.240	1006.320	1004.390	3.088
7) Meta	1998.370	1999.420	1996.320	1999.270	2004.260	1998.170	1999.302	2.670
8) sec-OH Carbon	978.653	979.376	979.558	980.764	981.393	977.096	979.473	1.529
9) Methyl-Carbon	988.791	989.291	989.784	985.380	990.781	987.367	988.566	1.926

EP-2-195-KIE-SAMPLE.fid

low conversion reaction set II

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) Carbonyl	1006.090	1005.180	1007.920	1009.310	1005.870	1004.900	1006.545	1.719
2) Quaternary Para	999.527	1002.610	1000.370	998.312	997.705	996.238	999.127	2.230
3) Quaternary Ipso	1004.820	1004.830	1006.900	1002.550	1001.980	1001.120	1003.700	2.178
4) alpha-Carbon	989.259	989.853	987.296	989.275	986.487	986.491	988.110	1.525
5) Ortho	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000
6) beta-Carbon	1018.110	1017.970	1011.650	1013.950	1014.300	1014.450	1015.072	2.513
7) Meta	2013.180	2014.020	2013.280	2006.540	2007.680	2008.110	2010.468	3.366
8) sec-OH Carbon	973.244	974.021	973.264	971.836	973.152	968.621	972.356	1.962
9) Methyl-Carbon	995.737	996.914	996.771	993.488	992.988	996.582	995.413	1.741

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R_p/R_0	$\Delta(R_p/R_0)$	ΔKIE_R	ΔKIE
1) Carbonyl	1.010	0.0001	0.991	0.002	-0.003	0.003
2) Quaternary Para	1.007	0.0001	0.994	0.003	-0.003	0.003
3) Quaternary Ipso	1.001	0.0000	0.999	0.003	-0.003	0.003
4) alpha-Carbon	1.014	0.0002	0.988	0.002	-0.003	0.003
5) Ortho	1.000	0.0000	1.000	0.000	0.000	0.000
6) beta-Carbon	0.988	-0.0001	1.011	0.004	-0.004	0.004
7) Meta	0.994	-0.0001	1.006	0.002	-0.002	0.002
8) sec-OH Carbon	1.008	0.0001	0.993	0.003	-0.003	0.003
9) Methyl-Carbon	0.992	-0.0001	1.007	0.003	-0.003	0.003

Preparation of Hydroxy MBH Adduct. Example Procedure. A mixture of 1.91 g (8.4 mmol) of MBH product, 4.4 mL (3.1 g, 42.4 mmol), and 0.4 mL (0.3 g, 9.3 mmol) of MeOH in 1 mL of DMSO was stirred at 25 °C overnight. The reaction was then partitioned between 50 mL of dichloromethane and 50 mL water, and the organic layer was washed with two 25-mL portions of water and two 25-mL portions of saturated aqueous NaCl. The organic layer was dried (Na_2SO_4) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% methanol in dichloromethane to afford 1.6 g of adduct. The compound exists as a diastereomeric mixture and the chemical shift values are those of the major component. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.18 (d, 2H, J = 8.8 Hz), 7.54 (d, 2H, J = 8.7 Hz), 5.10 (d, 1H, J = 9.1 Hz), 3.41 (s, 3H), 3.20 (m, 1H), 2.80 (m), 2.67 (m), 2.53 (m), 1.04 (t, 3H, J = 7.1 Hz).

Preparation of Methylated Hydroxy MBH Adduct. Example Procedure. A mixture of 250 mg (0.806 mmol) of Hydroxy MBH Adduct, 100 μL (145 mg, 0.886 mmol) in 1 mL hexanes was stirred at 25 °C for 10 minutes. The reaction was slightly exothermic. After 20 minutes, the hexane layer was decanted and the residue was flash chromatographed using 20% methanol in dichloromethane to afford 161 mg of Methylated Hydroxy MBH adduct. The compound exists as a diastereomeric mixture and the chemical shift values are those of the major component. ^{1}H NMR (500 MHz, CD_3OD) δ 8.26 (d, 2H, J = 8.9 Hz), 7.71 (d, 2H, J = 8.4 Hz), 5.05 (d, 1H, J = 6.8 Hz), 3.98 (dd, 1H, J = 8.6, 14.1 Hz), 3.59 (s, 3H), 2.85 (s, 3H).

Preparation of Methoxy MBH Product. Example Procedure. A mixture of 2.0 g (8.4 mmol) of MBH product, 1.6 mL (3.6 g, 25.3 mmol) of iodomethane, and 2.9 mg (12.6 mmol) of silver (I) oxide, in 20.1 mL of dichloromethane was stirred at 37 °C overnight. An additional 1.6 mL (3.6 g, 25.3 mmol) of iodomethane was added at this time and allowed to sit for an additional 24 hours. Before workup, the conversion was

67.0 ± 2.1% conversion. The reaction was then filtered (celite) and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 100% DCM to afford 1.5 g of Methoxy MBH product with no observable impurities by ^{1}H NMR. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, 2H, J = 8.7 Hz), 7.55 (d, 2H, J = 8.8 Hz), 6.40 (m, 1H), 6.02 (m, 1H), 5.21 (s, 1H), 3.71 (s, 3H), 3.35 (s, 3H).

Preparation of Methoxy MBH Adduct. Example Procedure. A mixture of 1.0 g (3.98 mmol) of Methoxy MBH product, 2.1 mL (1.5 g, 19.90 mmol), 0.2 mL (0.16 g, 4.38 mmol) of methanol in 1 mL DMSO was stirred at 25 °C overnight. The reaction was then partitioned between 50 mL of dichloromethane and 50 mL water, and the organic layer was washed with two 25-mL portions of water and two 25-mL portions of saturated aqueous NaCl. The organic layer was dried (Na_2SO_4) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% methanol in dichloromethane to afford 1.1 g of adduct. ^{1}H-NMR (500 MHz, $CDCl_3$, 25 °C) δ/ppm: 8.21 (d, 2H, J = 8.8 Hz), 7.47 (d, 2H, J = 8.7 Hz), 4.39 (d, 1H, J = 8.8 Hz), 3.69 (s, 3H), 3.14 (s, 3H), 2.91 (ddd, 1H, J = 5.1, 8.9, 10.3 Hz), 2.65 (dd, 1H, J = 10.4, 12.8 Hz), 2.39 (dq, 2H, J = 7.2, 13.0 Hz), 2.26 (dq, 2H, J = 6.9, 13.0 Hz), 2.01 (dd, 1H, J = 5.2, 12.8 Hz), 0.82 (t, 6H, J = 7.1 Hz). ^{13}C-NMR (125 MHz, $CDCl_3$, 30 °C) δ/ppm: 173.4, 147.8, 147.2, 128.1, 123.6, 82.7, 57.1, 52.1, 51.9, 51.5, 47.0, 11.7. ESI-MS: m/z 325.1480 $[M\text{-}C_{16}H_{24}N_2O_5]^+$.

Methylation of Methoxy MBH Adduct. Example Procedure. A mixture of 250 mg (0.77 mmol) of Methoxy MBH Adduct and 96 µL (139 mg, 0.85 mmol) of methyl triflate in 2.5 mL of hexane. The addition was slightly exothermic upon addition of methyl triflate. After 20 minutes, the hexane layer was decanted and the residue was flash chromatographed using 10% methanol in dichloromethane to afford 270 mg of Methylated Methoxy MBH adduct. The compound exists as a diastereomeric mixture and the chemical shift values are those of the major component. ^{1}H-NMR (500 MHz, CD_3Cl), 25 °C) δ/ppm: 8.22 (d, 2H, J = 9.5 Hz), 7.55 (d, 2H, J = 9.5), 4.78 (d, 1H, J = 6.1 Hz), 3.79 (dd, 1H, J = 9.6, 14.1 Hz), 3.67 (s, 3H), 3.26 (s, 3H), 2.91 (s, 3H), 1.24 (m, 6H). ^{1}H-NMR (500 MHz, CD_3OD, 25 °C) δ/ppm: 8.26 (d, 2H, J = 8.9 Hz), 7.36 (d, 2H, J = 8.7 Hz), 4.77 (d, 1H, J = 6.6 Hz), 3.79 (dd, 1H, J = 9.1, 14.0 Hz), 3.73 (s, 3H), 3.28 (s, 3H), 2.88, (s, 3H), 1.22 (m,6H). ^{13}C-NMR (125 MHz, $CDCl_3$, 30 °C) δ/ppm: ESI-MS: m/z 339.1527 $[C_{17}H_{27}N_2O_5]^+$.

Kinetics of Elimination of Methylated Hydroxy MBH Adduct. Example Procedure. A mixture of 161 mg (0.34 mmol) of Methylated Hydroxy MBH Adduct, 11 mg (0.10 mmol) of DABCO, and 41 mg (0.34 mmol) of mesitylene in 0.62 mL of d_4-methanol was monitored periodically by ^{1}H NMR over a span of 10 minutes to 6 hours at 25 °C.

Kinetics of Elimination of Methylated Methoxy MBH Adduct. Example Procedure. A mixture of 269.8 mg (0.55 mmol) of Methylated Methoxy MBH Adduct, 19 mg (0.17 mmol) of DABCO, and 66 mg (0.55 mmol) of mesitylene in 1 mL of d_4-methanol monitored periodically by ^{1}H NMR over a span of 22 hours at 25 °C.

CHAPTER III

THE MECHANISM OF THE MORITA BAYLIS-HILLMAN REACTION WITH ACRYLONITRILE

Introduction

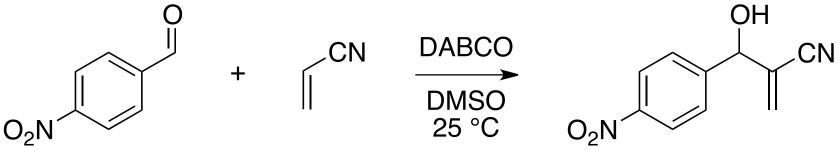
The Morita Baylis-Hillman reaction with the use of acrylonitrile appeared to be another reaction that caught our interest. For some time, there had been a contradictory consensus in the mechanism of the MBH reaction whether the rate-limiting step was either the carbon-carbon (aldol) bond formation or the hemiacetal (elimination) deprotonation step. Early in my graduate career, we had obtained the ^{13}C KIEs for the MBH reactions in DMSO and in methanol. Early on, it could still not be discerned exactly what was going in the reaction. We knew that we had two very distinct isotope effects. The previous work by McQuade had, in some sense, elucidated what the KIEs in DMSO meant. The somewhat larger KIEs in methanol were definitely different from those in the DMSO reaction but there was something about them that left us with the notion of asking ourselves more questions. If the ^{13}C KIEs in methanol had been augmented by just a few percentages, we would have been more comfortable saying that the rate-limiting step in methanol was the carbon-carbon bond formation step; but, the aldehydic ^{13}C KIEs were not that large (1.015 - 1.016). They were however, large enough to imply that there was some component of the carbon-carbon bond formation in the rate-limiting step.

One question that I had pondered for the longest time was why were the results from Hill and Isaacs and the work from McQuade so different. I sought to look for the supporting information from the original Hill and Isaacs paper to see what solvent they had used. Had they used an aprotic solvent such as DMSO, or had they used a protic solvent such as methanol? Or had they used some other solvent? I also questioned what reagents they used. It turns out they had used acetaldehyde. I had also wondered, if when they did the H/D kinetic isotope effects, did they use the alpha deuterated acrylonitrile in the protic methanol and unmistakenly not know that protons would wash into the alpha position of acrylonitrile so quickly that of course their H/D isotope effects would be near unity. I also thought they maybe they would have known that. What I did not know at the time either was did deuterium wash into the alpha-position of acrylonitrile as fast as it incorporates into the alpha-position of methyl acrylate. I scoured the manuscript and incessantly looked to find supporting information to find what solvent was used but I could not locate it. The study by Hill and Isaacs did show they had run kinetics in protic solvents; which was the complete opposite from the McQuade investigations with aprotic solvents.

This prompted me to study the MBH reaction with acrylonitrile in DMSO and in methanol. I would later study the rate of deuterium incorporation as how it was studied in the previous chapter. Described here is a mechanistic study of the Morita Baylis-Hillman reaction using acrylonitrile. The results suggest that the rate-limiting step of the MBH reaction with acrylonitrile in aprotic solvent DMSO is the carbon-carbon (aldol) step.

Results and Discussion

The prototypical MBH reaction of *p*-nitrobenzaldehyde with acrylonitrile catalyzed by DABCO was chosen for the study. This reaction cleanly affords the product in DMSO at 25 °C. As noted above, the kinetics for this reaction as well as its α-position KIEs had previously been studied carefully by Hill and Isaacs, and the DMSO reaction conditions here were patterned off of those employed by McQuade.



^{13}C Kinetic Isotope Effects. As mentioned before, heavy atom KIEs have some advantage over light KIEs in studying mechanisms because their values are in general more accurately predictable from a computational mechanism, if the mechanism is correct.

The ^{13}C KIEs for the reaction of *p*-nitrobenzaldehyde with acrylonitrile were determined at natural abundance by NMR methodology. Duplicate independent reactions in DMSO were taken to 76 to 78% conversion of *p*-nitrobenzaldehyde, and the isotopic compositions of samples of the reisolated aldehyde were analyzed by ^{13}C NMR in comparison with sample of the original aldehyde that had not been subject to the reaction conditions. The carbons meta to the aldehyde on the aromatic ring were treated as an internal standard with the assumption that their isotopic composition did not change over the course of the reaction. From the reaction conditions and changes in the isotopic composition the ^{13}C KIEs were calculated as previously described. Due to a long relaxation time and the broadness of its ^{13}C peak, the *para* position in *p*-nitrobenzaldehyde could not be quantitated reliably.

The KIEs for **5** in DMSO are summarized in Figure 14. An interesting and significant ^{13}C KIE was observed for the aldehydic proton. The remaining ^{13}C KIEs observed were approximately unity, as would be expected for centers unchanged by the reaction. At 1.018-1.021, the carbonyl carbon KIE in DMSO is normally associated with a primary ^{13}C KIE, and the qualitative interpretation of this KIE is that the carbonyl carbon has undergone some process that has modified this center, that is, a bond is being made or broken at this center at the transition state for the rate-limiting step. This is as would not be expected for the McQuade mechanism. If the MBH reaction with acrylonitrile in DMSO has purely elimination processes as their rate-limiting step, then there is no obvious explanation as to why the isotope effects deviated from the MBH reaction with methyl acrylate in DMSO. This line of reasoning suggested the possibility that the acrylonitrile reaction in DMSO might be subject to kinetic complexity as investigated in previous chapters, that is, competitive rate-limiting steps.

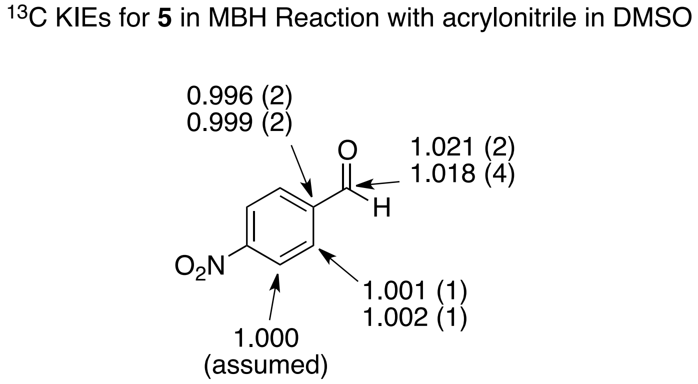


Figure 14. ^{13}C KIEs for 5 in the MBH reaction with acrylonitrile in DMSO at 25 °C.

MBH Kinetics and Activation Parameters. The progress of a series of MBH reactions of PNB with ACR in DMSO was followed by analysis of worked-up aliquots by ^{1}H NMR. The resulting conversion observations were then modeled differentially using an Excel^{TM} spreadsheet, and these fit well with a kinetic model that was first order in PNB and first order in ACR. All relative rates were obtained from side-by-side reactions conducted as identically as possible. No discernable exotherm occurs in these reactions.

The order of acrylonitrile was studied. A reaction that halved the normal concentration of acrylonitrile was slower by a factor of 1.9 ± 0.2, while a reaction that doubled the normal concentration of acrylonitrile went faster by a factor of 2.1 ± 0.2, indicating that the reaction was first order in acrylonitrile.

Table 15. A Comparison of Rates for Reaction of PNB and DABCO with Half, Normal, and Double Concentration of Acrylonitrile in DMSO at 25 °C.

Rxn.	[PNB] (M)	[ACR] (M)	[DABCO] (M)	*k* (M^{-2} s^{-1})	Rate (s^{-1})	Factor
half	0.45	0.23	0.14	0.0054 ± 0.0006	$1.7 \pm 0.2 \times 10^{-4}$	
normal	0.45	0.45	0.14	0.0053 ± 0.0002	$3.3 \pm 0.1 \times 10^{-4}$	1.9 ± 0.2
double	0.45	0.91	0.14	0.0055 ± 0.0006	$7.0 \pm 0.8 \times 10^{-4}$	2.1 ± 0.2

[PNB] = *p*-nitrobenzaldehyde; [ACR] = acrylonitrile. Data based on the rate law rate = *k* [PNB][ACR][DABCO], with *k* being the value lised, derived by fitting to experimental points. All the reactions were run under general kinetic conditions (see the Experimental Methods section).

The rate law was treated as being rate = *k* [PNB][ACR][DABCO], and the average *k* from a series of reactions at 25 °C was $5.4 \pm 0.9 \times 10^{-3}$ M^{-2} s^{-1}, see Table 15. This corresponds to a free energy of activation of 20.5 kcal/mol, considering the standard state to be 1 M. See Figure 15 for order plot.

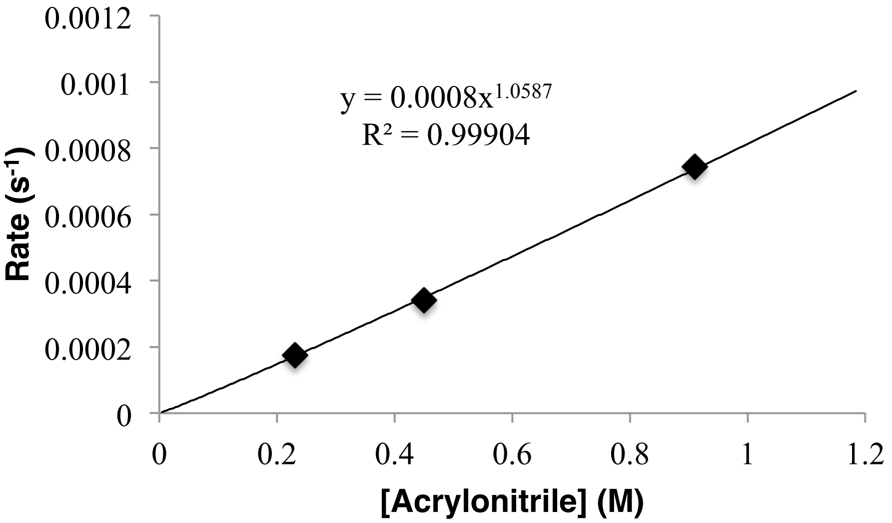


Figure 15. Order plot for the reaction of PNB, acrylonitrile, and DABCO in DMSO. Rate as a function of acrylonitrile. The marked points are for experimental observations. The solid black line represents a fit to the three rates for reaction described above.

Conclusion

The results here suggest Morita Baylis-Hillman reaction of acrylonitrile in DMSO is consistent with a rate-limiting step that is focused on the carbon-carbon step of the reaction. The ^{13}C KIEs are consistent with a bond breaking or bond forming step in the first irreversible step.

Experimental Section

***p*-Nitrobenzaldehyde KIEs in DMSO. Example Procedure.** A mixture of 15.0 g (99 mmol) of p-nitrobenzaldehyde, 3.3 g (30 mmol) of DABCO and 6.9 mL (5.6 g, 99 mmol) of acrylonitrile in 200 mL of DMSO was stirred at 25 °C. Aliquots were removed periodically and analyzed by 1H NMR after an aqueous workup, and after 1 h 15 min the conversion was 77.8 ± 1.7%. The reaction was then partitioned between 300 mL of ethyl acetate and 200 mL of water, and the organic layer was washed with two 100-mL portions of water and two 100-mL portions of saturated aqueous NaCl. The organic layer was dried (MgSO4) and filtered, and the solvent was removed on a rotary evaporator. The residue was flash chromatographed using 10% ethyl acetate in hexanes to afford 1.5 g of p-nitrobenzaldehyde with no observable impurities by 1H NMR.

A closely analogous reaction was taken to 79.3 ± 1.6% conversion.

NMR Measurments. All samples were prepared using a constant amount of anylte (200 mg for samples of *p*-nitrobenzaldehyde, in 5 mm NMR tubes filled with d_6-DMSO to a constant height of 5.0 cm. The ^{13}C spectra were recorded at 125.70 MHz with inverse gated decoupling. A T1 measurement was performed on each sample to ensure that the relaxation rates did not change from sample to sample. Integrations were determined numerically using a constant integration for each peak of 10 times the width at half-height. A zeroth order baseline correction was generally applied, but in no case was a first order (tilt) correction applied.

The ^{13}C spectra of *p*-nitrobenzaldehyde were taken at a controlled temperature of 40 °C, using 73.600-s delays between calibrated 90° pulses, a 5.000-s acquisition time, and collecting 297 618 points. Six spectra were obtained for each sample of recovered *p*-nitrobenzaldehyde along with corresponding sample of *p*-nitrobenzaldehyde that were not subjected to the reaction conditions. The resulting ^{13}C integrations for these spectra are given below, along with sample spectra. From the ^{13}C integrations the KIEs and uncertainties were calculated as previously described.

Calculations and Results for All Isotope Effects for MBH Reactions. The fractional conversion, raw integrations, R/R_0's, and KIEs and all their respective standard deviations and errors are shown in the following tables 16 and 17.

Due to a long relaxation time and the broadness of its ^{13}C peak, the *para* position in *p*-nitrobenzaldehyde could not practically be quantitated reliably. This broadness could be attributed due to quadrupole moment created by the ^{14}N of the nitro group. Therefore, the integrations for the relevant peaks in *p*-nitrobenzaldehyde were set to relative integrations of 2000 for the *meta* carbon, and the averaged results from six spectra for each sample are shown below. The relative changes in isotope composition (R/R_0) at each position in *p*-nitrobenzaldehyde were calculated as the ratio of average integrations relative to the standard. The standard deviations Δ (R/R_0) were calculated from eq 1. In this equation *Average Sample* is the average integration for each carbon in the sample, *Average Standard* is the average integration for each carbon in the standard, and *Std.Dev.Sample* and *Std.Dev.Standard* are the standard deviations in the integrations for the sample and standard, respectively.

Table 16. Set 1. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in the MBH reaction with acrylonitrile in DMSO at 25 °C.

EP-2-152 Intermolecular recovered starting material (PNB) KIEs

F	0.778
1-F	0.222
ΔF	0.017

Reisolated Starting Material 2011-03-03-EP-2-152-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1012.820	1011.250	1012.490	1013.960	1012.280	1013.640	1012.740	0.980
2) para	1009.910	1005.560	1008.690	1009.150	1007.280	1005.680	1007.712	1.833
3) ipso	1007.570	1010.320	1010.960	1011.270	1006.660	1006.120	1008.817	2.296
4) ortho	2012.760	2007.280	2012.640	2008.630	2008.640	2008.640	2009.765	2.334
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material 2011-03-07-KIE-recrysSTANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	980.851	984.268	983.661	977.306	980.603	983.885	981.762	2.699
2) para	1017.160	1011.560	1011.610	1013.820	1010.720	1008.360	1012.205	2.997
3) ipso	1012.270	1013.820	1015.670	1012.270	1016.960	1016.890	1014.647	2.164
4) ortho	2004.860	2012.780	2010.030	2002.750	2006.630	2009.620	2007.778	3.704
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.021	-0.0011	1.032	0.003	0.002	0.002
2) para	0.997	0.0001	0.996	0.003	0.002	0.002
3) ipso	0.996	0.0002	0.994	0.003	0.002	0.002
4) ortho	1.001	0.0000	1.001	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Table 17. Set 2. Fractional conversion, raw ^{13}C integrations, R/R_0's, and ^{13}C KIEs and all their respective standard deviations and errors for *p*-nitrobenzaldehyde in the MBH reaction with acrylonitrile in DMSO at 25 °C.

EP-2-161 Intermolecular recovered starting material (PNB) KIEs

F	0.766
1-F	0.234
ΔF	0.018

Reisolated Starting Material EP-2-161-KIE-SAMPLE

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	1013.560	1020.250	1023.220	1024.750	1021.830	1023.360	1021.162	4.025
2) para	1001.570	1001.480	1001.240	1005.920	1001.360	1000.360	1001.988	1.975
3) ipso	996.860	999.817	1000.020	999.837	996.935	999.054	998.754	1.476
4) ortho	2010.490	2007.250	2012.160	2013.320	2007.980	2013.260	2010.743	2.641
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Starting Material EP-2-161-KIE-STANDARD

Peak	FID 1	FID 2	FID 3	FID 4	FID 5	FID 6	Average	Std. Dev.
1) carbonyl	991.409	998.535	995.417	995.376	998.394	992.220	995.225	2.988
2) para	1015.080	1017.470	1016.080	1016.030	1008.220	1017.700	1015.097	3.508
3) ipso	999.552	1001.120	1004.940	999.075	998.305	999.006	1000.333	2.446
4) ortho	2007.170	2008.390	2006.300	2003.830	2006.460	2003.390	2005.923	1.943
5) meta	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	2000.000	0.000

Calculated KIEs and Uncertainties

Peak	KIE	ΔKIE_F	R/R_0	$\Delta(R/R_0)$	ΔKIE_R	ΔKIE
1) carbonyl	1.018	-0.0010	1.026	0.005	0.004	0.004
2) para	0.991	0.0005	0.987	0.004	0.003	0.003
3) ipso	0.999	0.0001	0.998	0.003	0.002	0.002
4) ortho	1.002	-0.0001	1.002	0.002	0.001	0.001
5) meta	1.000	0.0000	1.000	0.000	0.000	0.000

Kinetics Experiment to Determine Order in Acrylonitrile. Kinetic measurements were obtained by running three side-by-side experiments with *p*-nitrobenzaldehyde and DABCO at concentrations of 0.45 and 0.14 M, respectively, and held constant throughout the three reactions. The concentrations of acrylonitrile of each of the three mixtures were 0.45, 0.23, and 0.91 M, respectively. Reactions commenced with the addition of commenced with the addition of 0.23 mL (0.2 g, 3.3 mmol) of acrylonitrile to a stirred solution of 111 mg, (1.0 mmol) of DABCO, and 500 mg (3.3 mmol) of *p*-nitrobenzaldehyde in DMSO at 25 °C. The reactions were monitored by taking aliquots of the reaction mixtures, diluting with chloroform, and quenching with water. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. This was then subject to NMR analysis and subsequently, rate constants simulated.

Kinetics Experiment to Determine Order in *p*-Nitrobenzaldehyde. Kinetic measurements were obtained by running three side-by-side experiments with acrylonitrile and DABCO at concentrations of 0.44 and 0.13 M, respectively, and held constant throughout the three reactions. The concentrations of *p*-nitrobenzaldehyde of each of the three mixtures were 0.22, 0.44, and 0.86 M, respectively. Reactions commenced with the addition of 0.23 mL (0.2 g, 3.3 mmol) of acrylonitrile to a stirred solution of 111 mg (1.0 mmol) of DABCO, and 500 mg (3.3 mmol) of *p*-nitrobenzaldehyde in DMSO at 25 °C. The reactions were monitored by taking aliquots of the reaction mixtures, diluting with chloroform, and quenching with water. The organic layer was dried ($MgSO_4$) and concentrated in vacuo. This was then subject to NMR analysis and subsequently, rate constants simulated.

Theoretical structures and energies were computed using standard procedures in Gaussian09. Vibrational frequency analyses were carried out on all stationary points. B3LYP and M06-2X methods implemented in Gaussian with 6-31+G** basis set were the standard approach taken for initial optimization of structures.

CHAPTER IV

CONCLUSIONS

The research projects from the Singleton group have traditionally come from literature group meetings. It was from these meetings that the investigations of the Morita Baylis-Hillman reaction ensued. The Morita Baylis-Hillman reaction had been previously studied both experimentally and theoretically and the consensus mechanism had already been established. We viewed the MBH mechanism as a special opportunity for mechanistic study because the individual steps were amenable with ingenuity to detailed scrutiny using many experimental probes, including the observations of intermediates, the independent generation and conversion of intermediates, thermodynamic and kinetic measurements for both the main reaction and interrelated side reactions, and kinetic isotope effects. Density functional calculations greatly complimented our experimental data. It was not clear to us that any accurate information that was not already clear from experiment could have been reliably garnered from calculations, and the computational studies were more misleading than enlightening. Nonetheless, the computations aided in interpreting experimental observations and the combination of the two detailed the full mechanistic pathway. This dissertation highlighted the Morita Baylis-Hillman reaction where the determination of kinetic isotope effects alone did not paint a picture of the reactions rate-limiting step or of its kinetic complexity.

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APPENDIX

Geometries and energies of calculated structures

Table of Contents

All structures and energies were obtained using standard procedure in Gaussian09.

Methanol

B3LYP/6-31+G Gas Phase*

```
methanol-Becke-631Gd-GAS
E(RB3LYP) = -115.725193197

 Zero-point correction=                           0.051291 (Hartree/Particle)
 Thermal correction to Energy=                    0.054607
 Thermal correction to Enthalpy=                  0.055551
 Thermal correction to Gibbs Free Energy=         0.028542
 Sum of electronic and zero-point Energies=        -115.673903
 Sum of electronic and thermal Energies=           -115.670586
 Sum of electronic and thermal Enthalpies=         -115.669642
 Sum of electronic and thermal Free Energies=      -115.696651
```

```
                E (Thermal)           CV               S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total               34.266           8.757            56.845
```

```
 O,0,0.0176584407,0.,-0.0202893877
 C,0,-0.017088087,0.,1.405122776
 H,0,1.0236561756,0.,1.7377499801
 H,0,-0.5133644911,0.8962184017,1.804815958
 H,0,-0.5133644911,-0.8962184017,1.804815958
 H,0,-0.8903355471,0.,-0.3588862843
```

B3LYP/6-31+G** Gas Phase

methanol-Becke-631Gdp-GAS
E(RB3LYP) = -115.734872184

```
 Zero-point correction=                           0.051221 (Hartree/Particle)
 Thermal correction to Energy=                    0.054562
 Thermal correction to Enthalpy=                  0.055507
 Thermal correction to Gibbs Free Energy=         0.028450
 Sum of electronic and zero-point Energies=          -115.683652
 Sum of electronic and thermal Energies=             -115.680310
 Sum of electronic and thermal Enthalpies=           -115.679366
 Sum of electronic and thermal Free Energies=        -115.706422
```

```
                E (Thermal)           CV               S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total               34.238           8.824            56.945
```

```
 O,0,0.0157125004,0.,-0.0213634125
 C,0,-0.0173430446,0.,1.4036951437
 H,0,1.0221411626,0.,1.7384540269
 H,0,-0.512479013,0.8948999197,1.8053905816
 H,0,-0.512479013,-0.8948999197,1.8053905816
 H,0,-0.8883905923,0.,-0.3582379214
```

M06-2X/6-31+G** Gas Phase

methanol-M06-GAS
E(RM062X) = -115.671568977

```
Zero-point correction=                           0.051810 (Hartree/Particle)
Thermal correction to Energy=                    0.055180
Thermal correction to Enthalpy=                  0.056124
Thermal correction to Gibbs Free Energy=         0.029016
Sum of electronic and zero-point Energies=          -115.619759
Sum of electronic and thermal Energies=             -115.616389
Sum of electronic and thermal Enthalpies=           -115.615445
Sum of electronic and thermal Free Energies=        -115.642553

                E (Thermal)            CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              34.626            8.815            57.053
```

```
O,0,0.0138519772,0.,-0.0138126559
C,0,-0.0172971985,0.,1.4009527541
H,0,1.0201597417,0.,1.7371934802
H,0,-0.5117351972,0.8935315291,1.8007477283
H,0,-0.5117351972,-0.8935315291,1.8007477283
H,0,-0.8860821262,0.,-0.352500035
```

*B3LYP/6-311+G** Gas Phase*

methanol-Becke-6311Gdp-GAS
E(RB3LYP) = -115.764943658

```
Zero-point correction=                           0.051037 (Hartree/Particle)
Thermal correction to Energy=                    0.054398
Thermal correction to Enthalpy=                  0.055343
Thermal correction to Gibbs Free Energy=         0.028251
Sum of electronic and zero-point Energies=          -115.713906
Sum of electronic and thermal Energies=             -115.710545
Sum of electronic and thermal Enthalpies=           -115.709601
Sum of electronic and thermal Free Energies=        -115.736692

                E (Thermal)            CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              34.135            8.863            57.018
```

```
O,0,0.0153887973,0.,-0.0216029512
C,0,-0.017159578,0.,1.4018458173
H,0,1.0195696602,0.,1.7389975092
H,0,-0.5118187678,0.8929478783,1.8033787502
H,0,-0.5118187678,-0.8929478783,1.8033787502
```

```
 H,0,-0.8869993438,0.,-0.3526688756
```

B3LYP/6-31+G PCM solvent model in methanol*

methanol-Becke-631Gd-PCM-methanol
E(RB3LYP) = -115.731353131

```
 Zero-point correction=                         0.051247 (Hartree/Particle)
 Thermal correction to Energy=                  0.054582
 Thermal correction to Enthalpy=                0.055526
 Thermal correction to Gibbs Free Energy=       0.028475
 Sum of electronic and zero-point Energies=          -115.680106
 Sum of electronic and thermal Energies=             -115.676771
 Sum of electronic and thermal Enthalpies=           -115.675827
 Sum of electronic and thermal Free Energies=        -115.702878

                    E (Thermal)          CV                S
                     KCal/Mol      Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                 34.251              8.811            56.934

 O,0,0.0183199278,0.,-0.0242521867
 C,0,-0.0139201787,0.,1.4077613209
 H,0,1.0256769231,0.,1.7435345935
 H,0,-0.5143184182,0.8948272298,1.7998201387
 H,0,-0.5143184182,-0.8948272298,1.7998201387
 H,0,-0.8942798358,0.,-0.3533550052
```

*B3LYP/6-31+G** PCM solvent model in methanol*

methanol-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -115.740834125

```
 Zero-point correction=                          0.051173 (Hartree/Particle)
 Thermal correction to Energy=                   0.054524
 Thermal correction to Enthalpy=                 0.055468
 Thermal correction to Gibbs Free Energy=   0.028389
 Sum of electronic and zero-point Energies=          -115.689661
 Sum of electronic and thermal Energies=             -115.686310
 Sum of electronic and thermal Enthalpies=           -115.685366
 Sum of electronic and thermal Free Energies=        -115.712445

                    E (Thermal)          CV                S
```

```
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total               34.214             8.860             56.993
```

```
O,0,0.0166125024,0.,-0.0253988143
C,0,-0.0140543189,0.,1.4064809687
H,0,1.0243396501,0.,1.744308083
H,0,-0.5135323846,0.8936054716,1.800316683
H,0,-0.5135323846,-0.8936054716,1.800316683
H,0,-0.8926730643,0.,-0.3526946034
```

*M06-2X/6-31+G** PCM solvent model in methanol*

methanol-M06-PCM-meoh
E(RM062X) = -115.677603546

```
 Zero-point correction=                           0.051707 (Hartree/Particle)
 Thermal correction to Energy=                    0.055093
 Thermal correction to Enthalpy=                  0.056037
 Thermal correction to Gibbs Free Energy=         0.028889
 Sum of electronic and zero-point Energies=           -115.625896
 Sum of electronic and thermal Energies=              -115.622511
 Sum of electronic and thermal Enthalpies=            -115.621567
 Sum of electronic and thermal Free Energies=         -115.648714
```

```
                E (Thermal)             CV                S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total               34.571             8.856             57.137
```

```
O,0,0.0152903369,0.,-0.0179824607
C,0,-0.0142230751,0.,1.4035543265
H,0,1.0223313908,0.,1.7426596199
H,0,-0.5129131084,0.8924262974,1.7959669878
H,0,-0.5129131084,-0.8924262974,1.7959669878
H,0,-0.8904104358,0.,-0.3468364612
```

*B3LYP/6-311+G** PCM solvent model in methanol*

methanol-Becke-6311Gdp-PCM-methanol
E(RB3LYP) = -115.770766234

```
 Zero-point correction=                           0.050981 (Hartree/Particle)
 Thermal correction to Energy=                    0.054348
```

```
 Thermal correction to Enthalpy=                0.055292
 Thermal correction to Gibbs Free Energy=        0.028184
 Sum of electronic and zero-point Energies=          -115.719785
 Sum of electronic and thermal Energies=             -115.716419
 Sum of electronic and thermal Enthalpies=           -115.715474
 Sum of electronic and thermal Free Energies=        -115.742582

                E (Thermal)         CV              S
                 KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
 Total              34.104           8.895          57.054
```

```
O,0,0.015923205,0.,-0.025441943
C,0,-0.0141033652,0.,1.405328748
H,0,1.0219578438,0.,1.7443142991
H,0,-0.5127870388,0.8919618029,1.798913055
H,0,-0.5127870388,-0.8919618029,1.798913055
H,0,-0.891043606,0.,-0.3486982141
```

B3LYP/6-31+G PCM solvent model in DMSO*

methanol-Becke-631Gd-PCM-dmso
E(RB3LYP) = -115.731450950

```
 Zero-point correction=                       0.051245 (Hartree/Particle)
 Thermal correction to Energy=                  0.054581
 Thermal correction to Enthalpy=                0.055525
 Thermal correction to Gibbs Free Energy=        0.028473
 Sum of electronic and zero-point Energies=          -115.680206
 Sum of electronic and thermal Energies=             -115.676870
 Sum of electronic and thermal Enthalpies=           -115.675926
 Sum of electronic and thermal Free Energies=        -115.702978

                E (Thermal)         CV              S
                 KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
 Total              34.250           8.811          56.935
```

```
O,0,0.018332829,0.,-0.0243169346
C,0,-0.0138649391,0.,1.4078130891
H,0,1.025722481,0.,1.7436216193
H,0,-0.5143419067,0.8948026515,1.7997409787
H,0,-0.5143419067,-0.8948026515,1.7997409787
H,0,-0.8943465575,0.,-0.3532707313
```

*B3LYP/6-31+G** PCM solvent model in DMSO*

methanol-Becke-631Gdp-PCM-dmso
E(RB3LYP) = -115.740928863

```
 Zero-point correction=                           0.051172 (Hartree/Particle)
 Thermal correction to Energy=                    0.054522
 Thermal correction to Enthalpy=                  0.055467
 Thermal correction to Gibbs Free Energy=         0.028387
 Sum of electronic and zero-point Energies=          -115.689757
 Sum of electronic and thermal Energies=             -115.686406
 Sum of electronic and thermal Enthalpies=           -115.685462
 Sum of electronic and thermal Free Energies=        -115.712542

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  34.213               8.861             56.994
```

```
 O,0,0.0166266797,0.,-0.0254636337
 C,0,-0.0139994047,0.,1.4065319661
 H,0,1.0243845579,0.,1.7443933221
 H,0,-0.5135562192,0.8935812063,1.8002390593
 H,0,-0.5135562192,-0.8935812063,1.8002390593
 H,0,-0.8927393944,0.,-0.352610773
```

*B3LYP/6-311+G** PCM solvent model in DMSO*

methanol-Becke-6311Gdp-PCM-dmso
E(RB3LYP) = -115.770858897

```
 Zero-point correction=                           0.050979 (Hartree/Particle)
 Thermal correction to Energy=                    0.054346
 Thermal correction to Enthalpy=                  0.055290
 Thermal correction to Gibbs Free Energy=         0.028182
 Sum of electronic and zero-point Energies=          -115.719880
 Sum of electronic and thermal Energies=             -115.716513
 Sum of electronic and thermal Enthalpies=           -115.715569
 Sum of electronic and thermal Free Energies=        -115.742677

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  34.103               8.896             57.054
```

```
O,0,0.0159331422,0.,-0.0255040433
C,0,-0.0140499957,0.,1.4053839054
H,0,1.022004777,0.,1.7443951203
H,0,-0.5128101207,0.8919374114,1.7988427788
H,0,-0.5128101207,-0.8919374114,1.7988427788
H,0,-0.8911076822,0.,-0.3486315399
```

Methanol in methanol

*B3LYP/6-31+G** PCM solvent model in methanol*

methanolInMethanolB3LYPPCM
E(RB3LYP) = -115.740829866

```
 Zero-point correction=                           0.051199 (Hartree/Particle)
 Thermal correction to Energy=                    0.054539
 Thermal correction to Enthalpy=                  0.055483
 Thermal correction to Gibbs Free Energy=         0.028426
 Sum of electronic and zero-point Energies=          -115.689631
 Sum of electronic and thermal Energies=             -115.686291
 Sum of electronic and thermal Enthalpies=           -115.685347
 Sum of electronic and thermal Free Energies=        -115.712404

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  34.224              8.841             56.946
```

```
C,0,0.0054433935,-0.0094281043,-0.0110953162
H,0,-0.0084416079,0.0146193053,1.0805210608
H,0,1.048232983,-0.0283278288,-0.3506778878
H,0,-0.4995832139,-0.9219598963,-0.350679591
O,0,-0.6746813778,1.1685834643,-0.4594985313
H,0,-0.6775417665,1.1735382967,-1.4258997345
```

*M06-2X/6-31+G** PCM solvent model in methanol*

methanolInMethanolM06PCM
E(RM062X) = -115.677628172

```
 Zero-point correction=                           0.052015 (Hartree/Particle)
 Thermal correction to Energy=                    0.055274
 Thermal correction to Enthalpy=                  0.056218
```

```
 Thermal correction to Gibbs Free Energy=         0.029326
 Sum of electronic and zero-point Energies=          -115.625613
 Sum of electronic and thermal Energies=             -115.622354
 Sum of electronic and thermal Enthalpies=           -115.621410
 Sum of electronic and thermal Free Energies=        -115.648302

                E (Thermal)             CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total             34.685             8.623            56.599

 C,0,0.003616905,-0.0062644484,-0.0126474689
 H,0,-0.0089512846,0.0155019896,1.0780720259
 H,0,1.0451310664,-0.0256289879,-0.3515878175
 H,0,-0.500369522,-0.917923978,-0.3515896967
 O,0,-0.6708554887,1.1619571739,-0.457944846
 H,0,-0.6751432536,1.1693834946,-1.4216321968
```

Dimeric Methanol

*B3LYP/6-31+G** PCM solvent model in methanol*

```
methanolDimerInMethanolB3LYPPCM
E(RB3LYP) = -231.488960412

 Zero-point correction=                           0.104461 (Hartree/Particle)
 Thermal correction to Energy=                    0.112423
 Thermal correction to Enthalpy=                  0.113367
 Thermal correction to Gibbs Free Energy=         0.070917
 Sum of electronic and zero-point Energies=          -231.384500
 Sum of electronic and thermal Energies=             -231.376538
 Sum of electronic and thermal Enthalpies=           -231.375594
 Sum of electronic and thermal Free Energies=        -231.418044

                E (Thermal)             CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total             70.546            22.322            89.344

 C,0,0.2730940269,0.0994145463,-0.186114058
 H,0,1.1717908477,0.3656669119,0.3724443954
 H,0,0.5468916304,-0.1227872589,-1.2232253444
 H,0,-0.1840186089,-0.7847615156,0.2703728096
 O,0,-0.610304031,1.2310405892,-0.1096893146
 H,0,-1.4216892332,1.0308878097,-0.5960591625
 H,0,0.0789067336,2.8864364935,-0.4871191788
```

O,0,0.4470886553,3.7730045997,-0.6783135044
C,0,0.3827788711,4.5594101078,0.5095801644
H,0,0.7945549047,5.5444984313,0.274737936
H,0,-0.6504541436,4.689777658,0.8588829973
H,0,0.9758983471,4.1208696271,1.3235052599

*M06-2X/6-31+G** PCM solvent model in methanol*

methanolDimerInMethanolM062XPCM
E(RM062X) = -231.364160243

```
 Zero-point correction=                           0.105937 (Hartree/Particle)
 Thermal correction to Energy=                    0.113684
 Thermal correction to Enthalpy=                  0.114628
 Thermal correction to Gibbs Free Energy=         0.073671
 Sum of electronic and zero-point Energies=           -231.258223
 Sum of electronic and thermal Energies=              -231.250477
 Sum of electronic and thermal Enthalpies=            -231.249532
 Sum of electronic and thermal Free Energies=         -231.290490

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  71.338             22.191             86.202
```

C,0,0.2891322567,0.3422173085,-0.0717433481
H,0,1.0917912857,0.8370083781,0.4766601915
H,0,0.6800013493,-0.0168002673,-1.0283234622
H,0,-0.0750716875,-0.5047499945,0.5163949035
O,0,-0.7389004652,1.3122130893,-0.2621822073
H,0,-1.4637148719,0.9174540866,-0.7611595118
H,0,-0.1162287237,2.9589761606,-0.7761130096
O,0,0.2867895163,3.8438118291,-0.8256644899
C,0,0.428597413,4.3187179807,0.5014487588
H,0,0.8695077035,5.3166008046,0.4520085963
H,0,-0.5388510592,4.3914623203,1.0128739473
H,0,1.091485283,3.6765463039,1.0948026316

Trimeric Methanol

*B3LYP/6-31+G** PCM solvent model in methanol*

methanolTrimerInMethanolB3LYPPCM
E(RB3LYP) = -347.238328965

```
 Zero-point correction=                           0.157798 (Hartree/Particle)
 Thermal correction to Energy=                    0.170335
 Thermal correction to Enthalpy=                  0.171279
 Thermal correction to Gibbs Free Energy=         0.114758
 Sum of electronic and zero-point Energies=          -347.080531
 Sum of electronic and thermal Energies=             -347.067994
 Sum of electronic and thermal Enthalpies=           -347.067050
 Sum of electronic and thermal Free Energies=        -347.123571

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  106.887             35.535            118.958

 C,0,0.8953478433,0.3044007324,-1.1196128081
 H,0,1.5666170966,1.1270665948,-1.3703542556
 H,0,0.1104261065,0.234693377,-1.880182351
 H,0,1.4660630841,-0.6293345326,-1.0925463065
 O,0,0.3430476841,0.6029482572,0.1747053438
 H,0,-0.2504783675,-0.1135633059,0.4386583795
 H,0,-0.3589275351,2.2230999762,0.43054275
 O,0,-0.7349293066,3.1196033185,0.5754361293
 C,0,0.0819284682,3.8250240399,1.5152081257
 H,0,-0.3570228738,4.8159362341,1.6515258105
 H,0,0.1116295128,3.3152399609,2.4860062466
 H,0,1.1054206644,3.9420300262,1.139895468
 H,0,-2.4975665176,3.0972849395,0.8974384449
 O,0,-3.4643891155,3.0886151433,1.0718060101
 C,0,-4.1205609667,3.8223329738,0.0414752844
 H,0,-5.193187008,3.8044880756,0.2532523324
 H,0,-3.791793533,4.8702893888,0.0109246689
 H,0,-3.9563672363,3.3755028005,-0.9488432729
```

*M06-2X/6-31+G** PCM solvent model in methanol*

```
methanolTrimerInMethanolM062XPCM
E(RM062X) = -347.051721172

 Zero-point correction=                           0.159449 (Hartree/Particle)
 Thermal correction to Energy=                    0.172079
 Thermal correction to Enthalpy=                  0.173024
 Thermal correction to Gibbs Free Energy=         0.116224
 Sum of electronic and zero-point Energies=          -346.892272
 Sum of electronic and thermal Energies=             -346.879642
 Sum of electronic and thermal Enthalpies=           -346.878698
```

```
Sum of electronic and thermal Free Energies=         -346.935497

                  E (Thermal)            CV               S
                   KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total               107.981            35.515          119.545

C,0,1.4749558742,0.5408515661,-0.7077825619
H,0,1.9329683816,1.2499381839,-0.0171865805
H,0,1.5201016111,0.9475395464,-1.7222088916
H,0,2.0241328283,-0.4034245371,-0.6650565121
O,0,0.1241837738,0.3635902014,-0.2809599878
H,0,-0.3085697049,-0.2822003809,-0.852312952
H,0,-0.7886693365,1.8802056916,-0.0555139376
O,0,-1.1607598147,2.7476530515,0.2000940716
C,0,-0.2845680316,3.3421550262,1.1489689501
H,0,-0.7927140034,4.2115870216,1.5717436599
H,0,-0.0445196614,2.6467801683,1.9606395087
H,0,0.6445319238,3.6762432397,0.6743031655
H,0,-2.8624033863,2.8051211339,0.7431450537
O,0,-3.7720699421,3.0262598424,1.0225140731
C,0,-4.1085623277,4.2666474062,0.4284964354
H,0,-5.1139404067,4.5354715282,0.7598547189
H,0,-3.4193561911,5.0643580356,0.7336175352
H,0,-4.1094835864,4.2068822751,-0.6670197489
```

Tetrameric Methanol

*B3LYP/6-31+G** PCM solvent model in methanol*

```
doc-methanolTetramerInMethanolB3PCM
E(RB3LYP) = -462.987820550

 Zero-point correction=                           0.211045 (Hartree/Particle)
 Thermal correction to Energy=                    0.228143
 Thermal correction to Enthalpy=                  0.229087
 Thermal correction to Gibbs Free Energy=         0.159962
 Sum of electronic and zero-point Energies=          -462.776775
 Sum of electronic and thermal Energies=             -462.759678
 Sum of electronic and thermal Enthalpies=           -462.758734
 Sum of electronic and thermal Free Energies=        -462.827858

                  E (Thermal)            CV               S
                   KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total               143.162            48.794          145.486
```

```
C,0,1.3992594544,0.5761051414,-1.4362277972
H,0,0.569665592,0.0585479334,-0.9524578083
H,0,2.2306981404,0.6658320147,-0.7292134693
H,0,1.7200215263,0.0015741812,-2.3110562493
O,0,0.9056105743,1.869083322,-1.8283452345
H,0,1.6148447401,2.361862281,-2.2633205535
H,0,-0.0859808016,2.8115547227,-0.6969321771
O,0,-0.6697013931,3.3266956511,-0.0960360377
C,0,0.1125019915,3.8670828487,0.974758385
H,0,-0.5617905202,4.437562435,1.6170535187
H,0,0.5822534923,3.0745917828,1.5695727365
H,0,0.8892143592,4.5398588299,0.5931353326
H,0,-2.143383188,2.5046512985,0.326595306
O,0,-2.986555617,2.0484663399,0.5634060566
C,0,-4.0906654415,2.845548655,0.1277413782
H,0,-5.0072880847,2.318052077,0.4022452493
H,0,-4.0934838498,3.8307775737,0.6106633379
H,0,-4.0762515212,2.9813033804,-0.9604449128
H,0,-3.0347801863,1.4359739313,2.2361928539
O,0,-3.0675997042,1.0853215148,3.1542446358
C,0,-3.203997863,-0.331574491,3.0961784267
H,0,-3.2362780628,-0.7045666583,4.1236602587
H,0,-4.1309260442,-0.6344056078,2.5896894646
H,0,-2.3552625928,-0.8050571575,2.5834572992
```

*M06-2X/6-31+G** PCM solvent model in methanol*

doc-methanolTetramerInMethanolM062XPCM
E(RM062X) = -462.741811520

```
 Zero-point correction=                           0.214630 (Hartree/Particle)
 Thermal correction to Energy=                    0.230764
 Thermal correction to Enthalpy=                  0.231709
 Thermal correction to Gibbs Free Energy=         0.169195
 Sum of electronic and zero-point Energies=           -462.527182
 Sum of electronic and thermal Energies=              -462.511047
 Sum of electronic and thermal Enthalpies=            -462.510103
 Sum of electronic and thermal Free Energies=         -462.572616

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  144.807             48.121            131.570
```

```
C,0,0.3891914264,0.2689242114,-0.4360626716
H,0,-0.6831999329,0.3258451877,-0.2343736063
H,0,0.9424741211,0.4662200797,0.4876736849
H,0,0.6278987212,-0.7346411328,-0.7987826855
O,0,0.679816222,1.2513422585,-1.4315920962
H,0,1.629039794,1.2712986664,-1.6012928964
H,0,-0.2218240004,2.7231167975,-1.0832141712
O,0,-0.7459193928,3.4271698457,-0.6476590917
C,0,-0.1342623376,3.6974800132,0.6093478604
H,0,-0.6431908418,4.5573800634,1.0484191248
H,0,-0.2293455833,2.8425361892,1.2911374489
H,0,0.926164425,3.9385009584,0.4870514215
H,0,-2.3295389954,2.7815030943,-0.3397434414
O,0,-3.1898183766,2.4291139511,-0.019634556
C,0,-3.6440477506,3.2560629269,1.0437466436
H,0,-4.6223047947,2.8867580278,1.357833849
H,0,-2.9623493004,3.2182037122,1.9023704106
H,0,-3.748848482,4.2964568791,0.7176988865
H,0,-3.08293499,0.7124239905,0.4569897301
O,0,-2.8930216986,-0.1485271724,0.8803617966
C,0,-2.317116658,0.128757639,2.1429852044
H,0,-1.9684778138,-0.8140518203,2.5702893245
H,0,-1.4559477658,0.8061020622,2.0566760815
H,0,-3.0423099951,0.5768645713,2.8343327489
```

DABCO

B3LYP/6-31+G Gas Phase*

dabco-Becke631Gp
E(RB3LYP) = -345.339409582

```
 Zero-point correction=                           0.183984 (Hartree/Particle)
 Thermal correction to Energy=                    0.190301
 Thermal correction to Enthalpy=                  0.191246
 Thermal correction to Gibbs Free Energy=         0.153583
 Sum of electronic and zero-point Energies=          -345.155426
 Sum of electronic and thermal Energies=             -345.149108
 Sum of electronic and thermal Enthalpies=           -345.148164
 Sum of electronic and thermal Free Energies=        -345.185826

                     E (Thermal)             CV                S
```

```
                KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
 Total            119.416          26.118           79.267
```

```
N,0,-0.039079,0.067693,-0.02756
C,0,-0.031276,0.054838,1.448668
C,0,1.355325,0.054755,-0.512245
C,0,-0.724079,-1.146932,-0.512071
H,0,1.334582,0.09155,-1.608009
H,0,1.84366,0.973751,-0.166759
C,0,2.092154,-1.221425,0.008552
H,0,-1.071232,0.091723,1.794383
C,0,0.705335,-1.221476,1.969784
H,0,0.457522,0.9738,1.793626
H,0,-0.745244,-1.110518,-1.607807
C,0,0.012545,-2.42251,0.008737
H,0,-1.764132,-1.110829,-0.166537
H,0,2.452691,-1.846122,-0.817487
H,0,2.963022,-0.963655,0.623007
H,0,1.575092,-0.963714,2.585829
H,0,0.046686,-1.846198,2.584881
N,0,1.176099,-2.035106,0.83168
H,0,-0.645127,-3.047143,0.624793
H,0,0.374172,-3.047329,-0.816533
```

*B3LYP/6-31+G** Gas Phase*

dabcoBeckeGAS
E(RB3LYP) = -345.354317689

```
 Zero-point correction=                           0.183144 (Hartree/Particle)
 Thermal correction to Energy=                    0.189458
 Thermal correction to Enthalpy=                  0.190402
 Thermal correction to Gibbs Free Energy=         0.152824
 Sum of electronic and zero-point Energies=          -345.171173
 Sum of electronic and thermal Energies=             -345.164859
 Sum of electronic and thermal Enthalpies=           -345.163915
 Sum of electronic and thermal Free Energies=        -345.201494

                E (Thermal)          CV               S
                KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
 Total            118.887          26.242           79.090
```

```
N,0,-0.0390794619,0.0676933968,-0.0275599116
```

C,0,-0.0312758489,0.0548380441,1.4486675089
C,0,1.3553250537,0.0547550416,-0.5122451563
C,0,-0.7240789717,-1.1469322178,-0.5120706542
H,0,1.3345819924,0.0915503881,-1.608009322
H,0,1.8436601723,0.9737514337,-0.1667594625
C,0,2.0921535611,-1.22142535,0.0085520945
H,0,-1.0712316988,0.0917229086,1.7943828828
C,0,0.7053346427,-1.2214756753,1.9697837803
H,0,0.457522131,0.9737995126,1.7936255578
H,0,-0.7452438011,-1.1105177056,-1.6078072094
C,0,0.0125450384,-2.4225098574,0.0087374832
H,0,-1.764131719,-1.110829182,-0.1665369344
H,0,2.4526907102,-1.846121503,-0.8174869303
H,0,2.9630223098,-0.963655114,0.6230071435
H,0,1.5750920485,-0.9637144831,2.5858289034
H,0,0.0466855299,-1.8461980103,2.5848812766
N,0,1.1760985849,-2.0351060981,0.8316797998
H,0,-0.6451272839,-3.0471433902,0.6247933115
H,0,0.3741720106,-3.0473291387,-0.8165331614

*M06-2X/6-31+G** Gas Phase*

dabco-M06-GAS
E(RM062X) = -345.193218254

```
 Zero-point correction=                           0.185108 (Hartree/Particle)
 Thermal correction to Energy=                    0.191483
 Thermal correction to Enthalpy=                  0.192427
 Thermal correction to Gibbs Free Energy=         0.153268
 Sum of electronic and zero-point Energies=           -345.008110
 Sum of electronic and thermal Energies=              -345.001736
 Sum of electronic and thermal Enthalpies=            -345.000791
 Sum of electronic and thermal Free Energies=         -345.039950

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  120.157             25.761             82.417
```

N,0,-0.0366577136,0.0634819296,-0.0260062648
C,0,-0.0290097024,0.0506345652,1.4412014616
C,0,1.3493287685,0.0509839958,-0.5075131665
C,0,-0.7178026505,-1.1436249808,-0.5077809718
H,0,1.3281577717,0.0851321642,-1.6022780245

H,0,1.8368717326,0.9679259907,-0.1587548529
C,0,2.0845116638,-1.2224289877,0.0119730093
H,0,-1.0685419044,0.083363256,1.7856703571
C,0,0.7067909007,-1.2219797371,1.9611037136
H,0,0.4608077869,0.968151921,1.7852510632
H,0,-0.7351431666,-1.1081772701,-1.6025445628
C,0,0.0168579258,-2.4160900354,0.0124402602
H,0,-1.7562940672,-1.1079271312,-0.1605111323
H,0,2.4421555274,-1.8461103305,-0.8146156546
H,0,2.9522540815,-0.9632307241,0.6283898354
H,0,1.5774202678,-0.9622960027,2.5732443434
H,0,0.0472947471,-1.8456775224,2.5746449869
N,0,1.1732662753,-2.0312299765,0.8295758797
H,0,-0.6417976373,-3.0375537163,0.6291166947
H,0,0.3782433927,-3.0381944079,-0.813675975

*B3LYP/6-311+G** Gas Phase*

dabco-Becke6311Gpd
E(RB3LYP) = -345.421051579

```
 Zero-point correction=                           0.182247 (Hartree/Particle)
 Thermal correction to Energy=                    0.188508
 Thermal correction to Enthalpy=                  0.189452
 Thermal correction to Gibbs Free Energy=         0.152118
 Sum of electronic and zero-point Energies=           -345.238805
 Sum of electronic and thermal Energies=              -345.232544
 Sum of electronic and thermal Enthalpies=            -345.231600
 Sum of electronic and thermal Free Energies=          -345.268934

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  118.290             26.241             78.576
```

N,0,-0.039079,0.067693,-0.02756
C,0,-0.031276,0.054838,1.448668
C,0,1.355325,0.054755,-0.512245
C,0,-0.724079,-1.146932,-0.512071
H,0,1.334582,0.09155,-1.608009
H,0,1.84366,0.973751,-0.166759
C,0,2.092154,-1.221425,0.008552
H,0,-1.071232,0.091723,1.794383
C,0,0.705335,-1.221476,1.969784

```
H,0,0.457522,0.9738,1.793626
H,0,-0.745244,-1.110518,-1.607807
C,0,0.012545,-2.42251,0.008737
H,0,-1.764132,-1.110829,-0.166537
H,0,2.452691,-1.846122,-0.817487
H,0,2.963022,-0.963655,0.623007
H,0,1.575092,-0.963714,2.585829
H,0,0.046686,-1.846198,2.584881
N,0,1.176099,-2.035106,0.83168
H,0,-0.645127,-3.047143,0.624793
H,0,0.374172,-3.047329,-0.816533
```

*B3LYP/6-31+G** PCM solvent model in methanol*

dabcoPCMmethanol
E(RB3LYP) = -345.360384187

```
 Zero-point correction=                           0.183199 (Hartree/Particle)
 Thermal correction to Energy=                    0.189551
 Thermal correction to Enthalpy=                  0.190495
 Thermal correction to Gibbs Free Energy=         0.152770
 Sum of electronic and zero-point Energies=           -345.177185
 Sum of electronic and thermal Energies=              -345.170833
 Sum of electronic and thermal Enthalpies=            -345.169889
 Sum of electronic and thermal Free Energies=         -345.207614

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                 118.945             26.285             79.398
```

```
N,0,-0.0401364028,0.06889438,-0.0283775552
C,0,-0.0310924766,0.0550148777,1.4509778976
C,0,1.3575854926,0.0550583025,-0.5130396051
C,0,-0.7253389162,-1.1492593673,-0.5128278396
H,0,1.3392410025,0.088478938,-1.6082928911
H,0,1.8480931845,0.970933757,-0.1641284814
C,0,2.0936448727,-1.2201293616,0.0071665208
H,0,-1.0699074417,0.0883218203,1.7987320616
C,0,0.7047455941,-1.2201118411,1.9715520941
H,0,0.4612441683,0.9709061455,1.7970677561
H,0,-0.74395828,-1.1167657177,-1.6081821677
C,0,0.0102664461,-2.4234115918,0.0074428475
H,0,-1.7643797799,-1.1165072428,-0.1657594939
```

```
H,0,2.4524512257,-1.8415660223,-0.8211986318
H,0,2.9623974373,-0.9580659948,0.6217817084
H,0,1.5737648286,-0.9581763088,2.5857289825
H,0,0.0433204295,-1.8416059489,2.5860094903
N,0,1.1765734827,-2.0366927978,0.8319721657
H,0,-0.6500392349,-3.0451740759,0.622575477
H,0,0.3702393674,-3.0449889502,-0.8202693358
```

*M06-2X/6-31+G** PCM solvent in methanol*

doc-DABCOM06PCM
E(RM062X) = -345.199587853

```
 Zero-point correction=                           0.185333 (Hartree/Particle)
 Thermal correction to Energy=                    0.191598
 Thermal correction to Enthalpy=                  0.192542
 Thermal correction to Gibbs Free Energy=         0.154863
 Sum of electronic and zero-point Energies=           -345.014255
 Sum of electronic and thermal Energies=              -345.007990
 Sum of electronic and thermal Enthalpies=            -345.007046
 Sum of electronic and thermal Free Energies=         -345.044724

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  120.230             25.740            79.302
```

```
N,0,1.6197737162,0.2507984192,-0.6452404575
C,0,1.0446140894,-0.3144871299,-1.8754736425
C,0,2.1735209352,1.5787145041,-0.9501558279
C,0,2.7113992088,-0.6231005181,-0.1895260724
C,0,3.7652868692,-0.7979856669,-1.3218554717
C,0,2.1210051231,-0.3538659492,-2.9992840149
C,0,3.3216759958,1.4525193367,-1.9938264156
N,0,3.4259603923,0.0630067093,-2.4644362318
H,0,3.1568447081,-0.1678080814,0.701345748
H,0,2.2808980947,-1.5854795598,0.1062144524
H,0,2.5320050189,2.0253447963,-0.0169475504
H,0,1.3585273754,2.2044859131,-1.3292193726
H,0,0.1856339512,0.2985360648,-2.1672409767
H,0,0.6747963054,-1.3188593848,-1.6434713007
H,0,3.14426771,2.0975745459,-2.8605967233
H,0,4.286925035,1.7335351888,-1.5595692228
H,0,2.2240971896,-1.3614895465,-3.4155951351
H,0,1.862633398,0.3229466081,-3.8207341599
```

```
H,0,4.7694445987,-0.5317836975,-0.9761369605
H,0,3.7977372852,-1.8326655524,-1.6785136641
```

B3LYP/6-31+G PCM solvent model in DMSO*

dabco-Becke-631Gd-PCM-dmso
E(RB3LYP) = -345.345675246

```
 Zero-point correction=                           0.183974 (Hartree/Particle)
 Thermal correction to Energy=                    0.190310
 Thermal correction to Enthalpy=                  0.191254
 Thermal correction to Gibbs Free Energy=         0.153539
 Sum of electronic and zero-point Energies=          -345.161701
 Sum of electronic and thermal Energies=             -345.155366
 Sum of electronic and thermal Enthalpies=           -345.154421
 Sum of electronic and thermal Free Energies=        -345.192136

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  119.421             26.133            79.377
```

```
N,0,-0.0405790864,0.0697881468,-0.0286717523
C,0,-0.0314403903,0.0552180411,1.4496676693
C,0,1.3561869763,0.0550816658,-0.5130287623
C,0,-0.7255845643,-1.1473737208,-0.5128341253
H,0,1.3367202248,0.0855700035,-1.6088263208
H,0,1.8469612343,0.9708548322,-0.162783881
C,0,2.0936559416,-1.2211914526,0.0086379315
H,0,-1.0711040549,0.085908199,1.7966295618
C,0,0.7058922697,-1.2212147969,1.9710585817
H,0,0.4624910743,0.9709264881,1.7954260132
H,0,-0.7421850898,-1.1149991656,-1.6086878447
C,0,0.0115954434,-2.4232554676,0.0081516016
H,0,-1.7643130157,-1.1150465072,-0.1633119613
H,0,2.4514134266,-1.8429502729,-0.8205073251
H,0,2.9607337094,-0.957092784,0.6255702247
H,0,1.5765154547,-0.9573724299,2.5829957338
H,0,0.043207091,-1.8429869632,2.5846129367
N,0,1.176859077,-2.0379046504,0.8321714765
H,0,-0.6501714488,-3.0436389039,0.6240532651
H,0,0.3718597271,-3.0431672614,-0.8213920232
```

*B3LYP/6-31+G** PCM solvent model in DMSO*

dabcoBeckePCMdmso
E(RB3LYP) = -345.360492087

```
 Zero-point correction=                           0.183217 (Hartree/Particle)
 Thermal correction to Energy=                    0.189566
 Thermal correction to Enthalpy=                  0.190510
 Thermal correction to Gibbs Free Energy=         0.152788
 Sum of electronic and zero-point Energies=          -345.177275
 Sum of electronic and thermal Energies=             -345.170926
 Sum of electronic and thermal Enthalpies=           -345.169982
 Sum of electronic and thermal Free Energies=        -345.207704

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  118.954             26.277             79.392
```

```
 N,0,-0.0401305325,0.0689311741,-0.0283715013
 C,0,-0.0310912604,0.0550009769,1.4510380324
 C,0,1.3576334642,0.0550369193,-0.5130740418
 C,0,-0.7253686209,-1.1492756626,-0.5128319821
 H,0,1.3393054538,0.0883277807,-1.6083218108
 H,0,1.8482297629,0.9708770767,-0.1642185335
 C,0,2.0936801406,-1.2201064683,0.0071238466
 H,0,-1.0699032194,0.0881632747,1.7988027252
 C,0,0.7047373199,-1.2200812397,1.9716040469
 H,0,0.4612046253,0.9708596108,1.7972337632
 H,0,-0.7438588103,-1.1168641724,-1.6081793525
 C,0,0.0102322109,-2.4234048338,0.0074410197
 H,0,-1.7643868694,-1.1165941827,-0.1657245888
 H,0,2.4523938378,-1.8414860269,-0.8213081928
 H,0,2.9624660978,-0.9579727603,0.6216533977
 H,0,1.5736760449,-0.9580872502,2.5858544333
 H,0,0.0432084341,-1.84152473,2.5859928653
 N,0,1.1766146719,-2.0367008874,0.8320016495
 H,0,-0.6501361436,-3.0450884367,0.6225623196
 H,0,0.3702083925,-3.044857162,-0.8203470958
```

*B3LYP/6-311+G** PCM solvent model in DMSO*

dabco-Becke-6311Gdp-PCM-dmso
E(RB3LYP) = -345.427216599

```
Zero-point correction=                           0.182631 (Hartree/Particle)
Thermal correction to Energy=                      0.188995
Thermal correction to Enthalpy=                    0.189939
Thermal correction to Gibbs Free Energy=           0.152267
Sum of electronic and zero-point Energies=           -345.244585
Sum of electronic and thermal Energies=              -345.238222
Sum of electronic and thermal Enthalpies=            -345.237278
Sum of electronic and thermal Free Energies=         -345.274950

                E (Thermal)            CV                S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              118.596           26.414            79.287
```

```
N,0,-0.0392809221,0.0675314992,-0.0275482476
C,0,-0.0308262477,0.054899275,1.449265189
C,0,1.3554209389,0.0549272015,-0.5131480603
C,0,-0.7249057925,-1.1470343695,-0.5125785431
H,0,1.3371922207,0.0834927689,-1.6060000795
H,0,1.8466425733,0.9674613917,-0.1648683057
C,0,2.0930282905,-1.2207211928,0.0088897839
H,0,-1.0668608904,0.0849801347,1.7972297906
C,0,0.7055905326,-1.2218078682,1.9705314313
H,0,0.4630190549,0.9667499494,1.7957517964
H,0,-0.7410116309,-1.1167920555,-1.6053872691
C,0,0.012327361,-2.4228236391,0.0085080805
H,0,-1.7607853971,-1.1168078072,-0.1640324528
H,0,2.4501403997,-1.8391125465,-0.81903803
H,0,2.9577894242,-0.9554199227,0.6229979854
H,0,1.5720839981,-0.9577680321,2.5828276407
H,0,0.0428863604,-1.8403848772,2.5817257722
N,0,1.1758978556,-2.0353823366,0.8311433568
H,0,-0.649281741,-3.0400083361,0.6222974017
H,0,0.3696476119,-3.0408262369,-0.8196362405
```

DABCO-H^+

B3LYP/6-31+G Gas Phase*

```
DABCO-H-Becke-631Gd-GAS
E(RB3LYP) = -345.719192606
```

```
Zero-point correction=                           0.199632 (Hartree/Particle)
```

```
 Thermal correction to Energy=                    0.206096
 Thermal correction to Enthalpy=                  0.207040
 Thermal correction to Gibbs Free Energy=         0.169008
 Sum of electronic and zero-point Energies=          -345.519560
 Sum of electronic and thermal Energies=             -345.513096
 Sum of electronic and thermal Enthalpies=           -345.512152
 Sum of electronic and thermal Free Energies=        -345.550184

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  129.327             26.680            80.045
```

```
N,0,-0.0237712972,0.0412253507,-0.0168448916
C,0,-0.0340552306,0.0600874887,1.448991991
C,0,1.3547324436,0.0591653141,-0.5152155788
C,0,-0.7282045478,-1.143971265,-0.5142884335
H,0,1.3351590715,0.0888176651,-1.6077918954
H,0,1.8440933226,0.972747887,-0.1673920859
C,0,2.1336767521,-1.1992473637,-0.018010921
H,0,-1.070804229,0.091119876,1.7944187824
C,0,0.6926248559,-1.1987964601,2.0186382109
H,0,0.4578817037,0.9732770862,1.7940077275
H,0,-0.7448143604,-1.1118997685,-1.6068803323
C,0,-0.0271529268,-2.447199706,-0.0183963338
H,0,-1.7638794734,-1.1114249884,-0.1659224107
H,0,2.474994751,-1.8479728987,-0.828571683
H,0,2.9859344237,-0.9582998198,0.622316535
H,0,1.5798460104,-0.9585334657,2.6097502161
H,0,0.0408719662,-1.8470183503,2.6098183109
N,0,1.1625993112,-2.01292834,0.8231383283
H,0,-0.661365196,-3.0662130421,0.6211118756
H,0,0.3649248092,-3.0657937753,-0.8295765707
H,0,1.6450478401,-2.8483614242,1.164708159
```

*B3LYP/6-31+G** Gas Phase*

DABCO-H-Becke-631Gdp-GAS
E(RB3LYP) = -345.736924747

```
 Zero-point correction=                           0.198820 (Hartree/Particle)
 Thermal correction to Energy=                    0.205304
 Thermal correction to Enthalpy=                  0.206249
 Thermal correction to Gibbs Free Energy=         0.168216
 Sum of electronic and zero-point Energies=          -345.538105
```

```
 Sum of electronic and thermal Energies=             -345.531620
 Sum of electronic and thermal Enthalpies=           -345.530676
 Sum of electronic and thermal Free Energies=        -345.568708

                E (Thermal)           CV               S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total              128.830           26.854            80.045
```

```
N,0,-0.023527875,0.0406743543,-0.0170989365
C,0,-0.0342180975,0.0601079734,1.4489332162
C,0,1.3551882689,0.0596512181,-0.5148475842
C,0,-0.7281363461,-1.1444249123,-0.5149198546
H,0,1.3370123012,0.0906836088,-1.6068012683
H,0,1.8447043275,0.9719461383,-0.1658960772
C,0,2.133660351,-1.1994796079,-0.0185283414
H,0,-1.070122063,0.0907169586,1.7948481044
C,0,0.6927196845,-1.1988507865,2.018674871
H,0,0.4573700178,0.9725253927,1.794658667
H,0,-0.7451080118,-1.1134657507,-1.6068817761
C,0,-0.0270625322,-2.447644572,-0.0179708935
H,0,-1.763143284,-1.1125840838,-0.1667090379
H,0,2.4740200773,-1.8472888156,-0.8294790808
H,0,2.9859952846,-0.9585036371,0.6207070062
H,0,1.5791193003,-0.9576874507,2.6097148341
H,0,0.0409364954,-1.8462731958,2.6096357033
N,0,1.1626046669,-2.0126066548,0.8228644037
H,0,-0.6617529288,-3.0649028492,0.6217159422
H,0,0.363603409,-3.0668343319,-0.8286326001
H,0,1.6444769539,-2.8469789957,1.1640217027
```

*B3LYP/6-311+G** Gas Phase*

DABCO-H-Becke-6311Gdp-GAS
E(RB3LYP) = -345.802721524

```
 Zero-point correction=                       0.198074 (Hartree/Particle)
 Thermal correction to Energy=                   0.204623
 Thermal correction to Enthalpy=                 0.205567
 Thermal correction to Gibbs Free Energy=        0.167246
 Sum of electronic and zero-point Energies=          -345.604648
 Sum of electronic and thermal Energies=             -345.598099
 Sum of electronic and thermal Enthalpies=           -345.597154
 Sum of electronic and thermal Free Energies=        -345.635475
```

```
                E (Thermal)           CV                S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total              128.403             26.977             80.653
```

```
N,0,-0.0227215613,0.0391913169,-0.0162214932
C,0,-0.0338193862,0.059079648,1.4483383299
C,0,1.3544560977,0.0585363437,-0.5139643551
C,0,-0.7269590734,-1.1442899741,-0.5141869732
H,0,1.3368447838,0.089014254,-1.6038607254
H,0,1.8439250586,0.9689198549,-0.1664749013
C,0,2.131794213,-1.1998470338,-0.0176839325
H,0,-1.0674916323,0.0895483987,1.7944097224
C,0,0.6929548832,-1.199054348,2.0169593279
H,0,0.4565646007,0.9696526638,1.7940307141
H,0,-0.7434042012,-1.1138418667,-1.6040882364
C,0,-0.0260722008,-2.446200638,-0.0171634704
H,0,-1.760356509,-1.1132515477,-0.1675897401
H,0,2.4713158963,-1.8454493031,-0.8280719451
H,0,2.9831160478,-0.9582831931,0.619253435
H,0,1.5774062866,-0.9571974804,2.6069073695
H,0,0.0420494609,-1.8441952748,2.6076996812
N,0,1.1625035935,-2.0126913532,0.8230913751
H,0,-0.6607501497,-3.0623242054,0.6202686742
H,0,0.3636845088,-3.0632755171,-0.8271313042
H,0,1.6432992828,-2.8452607446,1.1634874476
```

*B3LYP/6-31+G** PCM solvent model in methanol*

dabco-H-Becke-PCM-methanol-use-this-one
E(RB3LYP) = -345.819928070

```
 Zero-point correction=                           0.199574 (Hartree/Particle)
 Thermal correction to Energy=                    0.205970
 Thermal correction to Enthalpy=                  0.206914
 Thermal correction to Gibbs Free Energy=         0.169137
 Sum of electronic and zero-point Energies=           -345.620354
 Sum of electronic and thermal Energies=              -345.613958
 Sum of electronic and thermal Enthalpies=            -345.613014
 Sum of electronic and thermal Free Energies=         -345.650791
```

```
                E (Thermal)           CV                S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
```

```
 Total                129.248             26.581             79.509
```

```
N,0,-1.2248836007,-0.0042532902,0.0036754554
C,0,-0.7442439736,1.4169298614,-0.210150056
C,0,-0.7330381172,-0.5294503928,1.3371197015
C,0,-0.7389572629,-0.895526801,-1.1209857684
C,0,0.8156325004,-0.8142356169,-1.126127045
C,0,0.8106730626,1.3846324951,-0.1476857947
C,0,0.8217411697,-0.5621871178,1.2672275952
N,0,1.3008564442,0.0045860351,-0.003668474
H,0,-1.1144406684,-1.8990126148,-0.9157692183
H,0,-1.192400529,-0.5275864366,-2.0420166787
H,0,-1.1781516929,-1.5148427531,1.4786475914
H,0,-1.113831147,0.1458536051,2.1045220648
H,0,-1.1931780337,2.0304060827,0.5718727249
H,0,-1.1277135412,1.7396636398,-1.179035042
H,0,1.2473574642,0.0124320393,2.09289378
H,0,1.1841234907,-1.5895402412,1.3474957974
H,0,1.232270475,1.8155063219,-1.0585716174
H,0,1.1690847412,1.9711250688,0.7013576447
H,0,1.2443399427,-1.8154198528,-1.0432119054
H,0,1.1700610134,-0.3699245156,-2.0590108555
H,0,-2.2466617375,-0.0068805165,0.0074191003
```

*M06-2X/6-31+G** PCM solvent model in methanol*

DABCOH+M06PCMmeoh
E(RM062X) = -345.655480727

```
 Zero-point correction=                           0.200989 (Hartree/Particle)
 Thermal correction to Energy=                    0.207388
 Thermal correction to Enthalpy=                  0.208332
 Thermal correction to Gibbs Free Energy=         0.170244
 Sum of electronic and zero-point Energies=          -345.454492
 Sum of electronic and thermal Energies=             -345.448093
 Sum of electronic and thermal Enthalpies=           -345.447149
 Sum of electronic and thermal Free Energies=        -345.485236

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                130.138             26.187             80.162

     1          7           0       -1.220978   -0.003847    0.003733
     2          6           0       -0.737402    1.396938   -0.262526
```

3	6	0	-0.726037	-0.473425	1.345176
4	6	0	-0.731792	-0.931038	-1.077054
5	6	0	0.807566	-0.764336	-1.150460
6	6	0	0.802923	1.380704	-0.091994
7	6	0	0.814170	-0.608315	1.235760
8	7	0	1.298348	0.004696	-0.003817
9	1	0	-1.036715	-1.938141	-0.789558
10	1	0	-1.236528	-0.652610	-2.002561
11	1	0	-1.223342	-1.418282	1.565814
12	1	0	-1.036757	0.274973	2.075608
13	1	0	-1.238121	2.057718	0.445583
14	1	0	-1.051642	1.651623	-1.275719
15	1	0	1.290622	-0.120496	2.088432
16	1	0	1.108485	-1.660173	1.236128
17	1	0	1.275462	1.878897	-0.940863
18	1	0	1.093281	1.909531	0.818692
19	1	0	1.286473	-1.745638	-1.156344
20	1	0	1.094037	-0.239378	-2.064604
21	1	0	-2.243413	-0.007126	0.006573

Methyl Acrylate

*B3LYP/6-31+G** PCM solvent model in methanol*

methylacrylate-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -306.497704019

Zero-point correction= 0.095044 (Hartree/Particle)
Thermal correction to Energy= 0.101705
Thermal correction to Enthalpy= 0.102649
Thermal correction to Gibbs Free Energy= 0.064593
Sum of electronic and zero-point Energies= -306.402660
Sum of electronic and thermal Energies= -306.395999
Sum of electronic and thermal Enthalpies= -306.395055
Sum of electronic and thermal Free Energies= -306.433111

	E (Thermal) KCal/Mol	CV Cal/Mol-Kelvin	S Cal/Mol-Kelvin
Total	63.821	22.217	80.095

C,0,-0.0468643511,0.,0.2066900194
O,0,-0.0422410855,0.,1.4295545127
O,0,1.0784829526,0.,-0.5366141278
C,0,-1.2521496509,0.,-0.6577886196

```
 C,0,2.3311783363,0.,0.1824935676
 H,0,3.1044350107,0.,-0.5839887456
 H,0,2.4086772004,0.893080555,0.8060842983
 H,0,2.4086772004,-0.893080555,0.8060842983
 C,0,-2.4851629656,0.,-0.1394060505
 H,0,-1.0806655445,0.,-1.7296186701
 H,0,-3.3627052629,0.,-0.777510429
 H,0,-2.6414518405,0.,0.9353959425
```

*M06-2X/6-31+G** PCM solvent model in methanol*

methylacrylate-M062X-631Gdp-PCM-methanol
E(RM062X) = -306.355617855

```
 Zero-point correction=                           0.096231 (Hartree/Particle)
 Thermal correction to Energy=                    0.102823
 Thermal correction to Enthalpy=                  0.103767
 Thermal correction to Gibbs Free Energy=         0.065844
 Sum of electronic and zero-point Energies=          -306.259387
 Sum of electronic and thermal Energies=             -306.252795
 Sum of electronic and thermal Enthalpies=           -306.251851
 Sum of electronic and thermal Free Energies=        -306.289774

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  64.522             21.907            79.815

 C,0,-0.0389861994,0.,0.1854245092
 O,0,-0.0397450517,0.,1.4002517366
 O,0,1.0811322597,0.,-0.5467076928
 C,0,-1.248731942,0.,-0.6765680989
 C,0,2.3112666445,0.,0.1882903495
 H,0,3.1008695449,0.,-0.5596377138
 H,0,2.3741710534,0.8919385876,0.8142452547
 H,0,2.3741710534,-0.8919385876,0.8142452547
 C,0,-2.4642311135,0.,-0.1312367955
 H,0,-1.0878762866,0.,-1.7495115621
 H,0,-3.3576857516,0.,-0.7457992145
 H,0,-2.584144211,0.,0.9483799743
```

Int1 Addition of DABCO to MA

*B3LYP/6-31+G** PCM solvent model in methanol*

Int1-E-Becke-631Gdp-PCM-methanol

E(RB3LYP) = -651.843309770

```
 Zero-point correction=                           0.282500 (Hartree/Particle)
 Thermal correction to Energy=                    0.296217
 Thermal correction to Enthalpy=                  0.297161
 Thermal correction to Gibbs Free Energy=         0.240998
 Sum of electronic and zero-point Energies=           -651.560810
 Sum of electronic and thermal Energies=              -651.547093
 Sum of electronic and thermal Enthalpies=            -651.546149
 Sum of electronic and thermal Free Energies=         -651.602312

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  185.879             52.487            118.206
```

```
C,0,-2.7571357068,-2.2571510033,0.207020535
O,0,-2.0306853913,-1.0298080165,0.1210025803
C,0,-0.6349566464,-1.1336403643,0.0632234182
O,0,-0.1107086824,-2.2733376492,0.0676380622
C,0,-0.0050927424,0.1191754684,0.0178849127
C,0,1.4413660307,0.2353544533,0.0292169293
N,0,2.1633391045,0.387691798,-1.4372097409
C,0,1.6569182949,1.6219524325,-2.1311256683
C,0,1.8679817134,-0.8154540292,-2.2907273339
C,0,3.6520637789,0.5034868386,-1.2610428043
H,0,-0.6184516814,1.0126518267,0.0427492879
H,0,-3.8113633757,-1.9753995973,0.2399567565
H,0,-2.5740248457,-2.8953288354,-0.6631816424
H,0,-2.4976839304,-2.8149681393,1.1124328194
H,0,1.8171857528,1.1337641838,0.5258529023
H,0,1.9444117462,-0.652202026,0.4201683732
H,0,2.2301906448,-1.6880283368,-1.7453408104
H,0,0.7825214985,-0.8852614564,-2.3648714171
C,0,2.5681619016,-0.6378416848,-3.6697154881
H,0,3.986386148,-0.3982002015,-0.7435954025
C,0,4.314868443,0.6619579749,-2.6637171625
H,0,3.837687689,1.3638252813,-0.6143944137
C,0,2.3528599994,1.7414467241,-3.5191112908
H,0,0.5734907149,1.5169491455,-2.2053034216
H,0,1.8803446487,2.4700503308,-1.4800722164
H,0,1.6105724063,1.7191461845,-4.3211981347
H,0,2.8960892578,2.6873065737,-3.5904938018
```

```
H,0,4.8595851506,1.6077717018,-2.7221778559
H,0,5.0273698155,-0.1480085883,-2.8397492484
N,0,3.3021199592,0.6369091915,-3.7313041848
H,0,3.273312081,-1.4544162256,-3.8451192544
H,0,1.8314302226,-0.6517669557,-4.4773262844
```

*M06-2X/6-31+G** PCM solvent model in methanol*

Int1-E-M062X-631Gdp-PCM-methanol
E(RM062X) = -651.557132277

```
 Zero-point correction=                           0.286459 (Hartree/Particle)
 Thermal correction to Energy=                    0.299507
 Thermal correction to Enthalpy=                  0.300451
 Thermal correction to Gibbs Free Energy=         0.246640
 Sum of electronic and zero-point Energies=          -651.270673
 Sum of electronic and thermal Energies=             -651.257626
 Sum of electronic and thermal Enthalpies=           -651.256681
 Sum of electronic and thermal Free Energies=        -651.310492

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  187.943             50.993            113.255
```

```
C,0,-4.6093397333,0.8115758458,0.2467934153
 O,0,-3.6052274225,-0.0834948795,0.6981238356
 C,0,-2.5022953208,-0.2304498237,-0.1339094135
 O,0,-2.4670795089,0.4150049816,-1.2051631633
 C,0,-1.5503783791,-1.1186403039,0.3676002994
 C,0,-0.3701998962,-1.4389605786,-0.4299776002
 N,0,0.8977884688,-0.5413248289,-0.1561966672
 C,0,1.3691864529,-0.7240901688,1.2517927697
 C,0,0.5692057256,0.9063613869,-0.3722649757
 C,0,2.0043415189,-0.9234390149,-1.0893712593
 H,0,-1.7272291754,-1.6163065898,1.3125898032
 H,0,-5.3799848579,0.8119476146,1.0188358601
 H,0,-4.2136384174,1.8231984101,0.1190750762
 H,0,-5.039444329,0.4812512676,-0.7030270155
 H,0,0.019547588,-2.447030159,-0.2563677534
 H,0,-0.5357855123,-1.2858740505,-1.5016145755
 H,0,0.0744626795,0.9831699598,-1.3420991409
 H,0,-0.1564732739,1.1727225694,0.3981876807
 C,0,1.8820908784,1.7215721025,-0.2830976881
 H,0,1.673477285,-0.6564954622,-2.0961084767
```

```
C,0,3.2875932347,-0.1633212572,-0.6681919666
H,0,2.1242330239,-2.0077823112,-1.0343061814
C,0,2.4940149703,0.3032305751,1.5302381761
H,0,0.4984372657,-0.5867996709,1.8957181741
H,0,1.7163805228,-1.7573490574,1.3363692887
H,0,2.1333424747,1.103788388,2.1812011872
H,0,3.3323470026,-0.1878787578,2.0296649321
H,0,3.9982505866,-0.8423132743,-0.1899776985
H,0,3.7705534035,0.2687122627,-1.5476839058
N,0,2.964184337,0.9069656259,0.2793436241
H,0,2.1929286968,2.0638204762,-1.2737838292
H,0,1.7335760731,2.6021046198,0.3468313138
```

Adduct of MA and DABCO-H$^+$

*B3LYP/6-31+G** PCM solvent model in methanol*

adduct-A-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -652.331616251

```
 Zero-point correction=                           0.298362 (Hartree/Particle)
 Thermal correction to Energy=                    0.311777
 Thermal correction to Enthalpy=                  0.312721
 Thermal correction to Gibbs Free Energy=         0.257525
 Sum of electronic and zero-point Energies=          -652.033254
 Sum of electronic and thermal Energies=             -652.019840
 Sum of electronic and thermal Enthalpies=           -652.018896
 Sum of electronic and thermal Free Energies=        -652.074091

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  195.643             51.976            116.170
```

```
N,0,2.9483535366,0.976057122,0.1212892588
C,0,1.7843210543,1.7598786823,-0.3118123377
C,0,0.4913673063,0.8934430182,-0.3092060972
N,0,0.8808946622,-0.5562782621,-0.0657287659
C,0,1.9348141255,-0.9430208635,-1.0982650554
C,0,3.2087401553,-0.0845019528,-0.8614826495
C,0,2.6630646325,0.3650656297,1.4262988643
C,0,1.5075404934,-0.6709587701,1.3163853683
C,0,-0.296775452,-1.5101145014,-0.2186584031
C,0,-1.5519306402,-1.1728631716,0.5834725163
C,0,-2.5368096746,-0.26748292,-0.1383392753
```

O,0,-2.5129524895,-0.0206825329,-1.3318442502
O,0,-3.4651355457,0.1963884775,0.7058460505
C,0,-4.5143668378,1.0190097208,0.1366474379
H,0,-2.0813969851,-2.1174195617,0.7577128918
H,0,-5.1527179056,1.2879278482,0.9759987471
H,0,-4.0833009196,1.9104314481,-0.3221824784
H,0,-5.0737488912,0.4489365605,-0.6072517044
H,0,0.0862366623,-2.4876619819,0.0756106891
H,0,-0.534355189,-1.5341707195,-1.2833752112
H,0,-0.0453491379,0.9278949105,-1.256945446
H,0,-0.1859277692,1.1810552294,0.4952014589
H,0,1.4860021007,-0.7658667144,-2.0769136041
H,0,2.1191711665,-2.012267246,-0.9843832436
H,0,0.7250564261,-0.4936244709,2.0531434253
H,0,1.8557395597,-1.7003370002,1.4149346581
H,0,4.0277988401,-0.7070040821,-0.4938882105
H,0,3.5263351561,0.3687748894,-1.8033699762
H,0,1.9796791962,2.1477945477,-1.3141872834
H,0,1.6562369696,2.6114989155,0.3602862487
H,0,2.398537794,1.1573597765,2.1304875762
H,0,3.5643008008,-0.1289173647,1.7967834146
H,0,-1.3471562008,-0.7754166605,1.580123386

*M06-2X/6-31+G** PCM solvent model in methanol*

adduct-A-M062X-631Gdp-PCM-methanol
E(RM062X) = -652.043652670

```
 Zero-point correction=                           0.301610 (Hartree/Particle)
 Thermal correction to Energy=                    0.314585
 Thermal correction to Enthalpy=                  0.315529
 Thermal correction to Gibbs Free Energy=         0.261654
 Sum of electronic and zero-point Energies=          -651.742043
 Sum of electronic and thermal Energies=             -651.729068
 Sum of electronic and thermal Enthalpies=           -651.728124
 Sum of electronic and thermal Free Energies=        -651.781999

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  197.405             50.914            113.390
```

N,0,2.8768953129,1.0010196673,0.1238803452
C,0,1.7066204814,1.7328175369,-0.3627388094
C,0,0.4347680851,0.8526642601,-0.2755843595

```
N,0,0.8666835828,-0.5795884009,-0.0717016462
C,0,1.9097514153,-0.9045554517,-1.1191686871
C,0,3.1830604159,-0.0817477068,-0.8121769076
C,0,2.5641170758,0.4218368759,1.430993444
C,0,1.5145422547,-0.7060205804,1.2874622311
C,0,-0.2790425894,-1.5499222291,-0.2254470632
C,0,-1.5246450692,-1.2189027327,0.5821449414
C,0,-2.476657591,-0.2746564468,-0.1226002564
O,0,-2.4528160898,-0.0269394138,-1.3090189228
O,0,-3.3727914141,0.2242084514,0.7232115494
C,0,-4.3746959688,1.0817386499,0.1508759416
H,0,-2.0768620643,-2.1546907146,0.7237073427
H,0,-5.008524143,1.3819290246,0.9815029462
H,0,-3.9015139908,1.9508312054,-0.3084988611
H,0,-4.9496963526,0.5336262797,-0.5968748933
H,0,0.1182055925,-2.522870616,0.0679398854
H,0,-0.523849139,-1.5721058554,-1.2900459028
H,0,-0.1661045424,0.8849635132,-1.1850495521
H,0,-0.1889421183,1.1212711818,0.5803061753
H,0,1.4660387723,-0.6454306649,-2.0827595787
H,0,2.0837859743,-1.9814620793,-1.0850360331
H,0,0.7341294538,-0.6407209894,2.0454893349
H,0,1.9612740723,-1.7019555952,1.3237821568
H,0,3.9544982486,-0.715126632,-0.3680686333
H,0,3.5788196822,0.3373109637,-1.7394449934
H,0,1.891730581,2.0339661778,-1.396566033
H,0,1.567303091,2.636195806,0.2345614606
H,0,2.1897339453,1.2163452845,2.0806039159
H,0,3.4741190404,0.0166684447,1.878329148
H,0,-1.3176700053,-0.8477682135,1.5883763145
```

***p*-Nitrobenzaldehyde**

*B3LYP/6-31+G** PCM solvent model in methanol*

```
paraNitrobenzaldehydeBeckePCMmethanol
E(RB3LYP) = -550.114859650

 Zero-point correction=                           0.111997 (Hartree/Particle)
 Thermal correction to Energy=                    0.120895
 Thermal correction to Enthalpy=                  0.121840
 Thermal correction to Gibbs Free Energy=         0.076880
 Sum of electronic and zero-point Energies=          -550.002863
 Sum of electronic and thermal Energies=             -549.993964
```

```
 Sum of electronic and thermal Enthalpies=           -549.993020
 Sum of electronic and thermal Free Energies=        -550.037980

                E (Thermal)          CV               S
                 KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
 Total              75.863           32.655           94.626

 C,0,0.0195156787,0.,-0.0167426393
 C,0,0.0054618626,0.,1.3860969726
 C,0,1.2009344339,0.,2.1014403882
 C,0,2.3976528882,0.,1.3845480946
 C,0,2.44149591,0.,-0.0133900479
 C,0,1.24045375,0.,-0.7124089098
 H,0,-0.9399760148,0.,1.920109862
 H,0,1.2111979374,0.,3.1835073246
 N,0,3.6665737379,0.,2.1306017339
 H,0,3.3933529398,0.,-0.5284020126
 H,0,1.2361590347,0.,-1.796840409
 C,0,-1.2715799877,0.,-0.748111655
 O,0,-1.3702703432,0.,-1.9659021062
 H,0,-2.1753873469,0.,-0.1102671485
 O,0,4.720039587,0.,1.4881325237
 O,0,3.6178819324,0.,3.3635860286
```

*M06-2X/6-31+G** PCM solvent model in methanol*

```
Nitrobenzaldehyde-M062X-631Gdp-PCM-methanol
E(RM062X) = -549.880774330

 Zero-point correction=                           0.113879 (Hartree/Particle)
 Thermal correction to Energy=                    0.122682
 Thermal correction to Enthalpy=                  0.123626
 Thermal correction to Gibbs Free Energy=         0.078875
 Sum of electronic and zero-point Energies=           -549.766895
 Sum of electronic and thermal Energies=              -549.758093
 Sum of electronic and thermal Enthalpies=            -549.757149
 Sum of electronic and thermal Free Energies=         -549.801899

                E (Thermal)          CV               S
                 KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
 Total              76.984           32.247           94.186

 C,0,0.0078377496,0.,0.0261140861
```

```
C,0,0.0069920031,0.,1.4249673674
C,0,1.2093173887,0.,2.1174374029
C,0,2.3902196845,0.,1.3787941327
C,0,2.4228338934,0.,-0.0096891479
C,0,1.2080258292,0.,-0.6880558835
H,0,-0.9381849542,0.,1.9571441247
H,0,1.2429816462,0.,3.1997320696
N,0,3.6704167661,0.,2.1084485182
H,0,3.3691346086,0.,-0.5355342849
H,0,1.1959546417,0.,-1.7741721044
C,0,-1.2788283893,0.,-0.721219937
O,0,-2.3645466868,0.,-0.1811066395
H,0,-1.1934263447,0.,-1.8227301216
O,0,4.699889609,0.,1.4554596676
O,0,3.6314395549,0.,3.3268657498
```

Anisaldehyde

*B3LYP/6-31+G** PCM solvent model in methanol*

anisaldehye-A-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -460.139425391

```
 Zero-point correction=                           0.142215 (Hartree/Particle)
 Thermal correction to Energy=                    0.151126
 Thermal correction to Enthalpy=                  0.152070
 Thermal correction to Gibbs Free Energy=         0.108162
 Sum of electronic and zero-point Energies=          -459.997211
 Sum of electronic and thermal Energies=             -459.988299
 Sum of electronic and thermal Enthalpies=           -459.987355
 Sum of electronic and thermal Free Energies=        -460.031264

                E (Thermal)             CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total              94.833             33.243             92.413

 C,0,-0.045901843,0.,-0.0798168856
 C,0,-0.1160527226,0.,1.3220122515
 C,0,1.0377543561,0.,2.1041637334
 C,0,2.2920872285,0.,1.4716622056
 C,0,2.3759213183,0.,0.0619515159
 C,0,1.2222659938,0.,-0.7004818983
 H,0,-1.0877437681,0.,1.8094767551
```

```
H,0,0.9542500663,0.,3.1835711087
H,0,3.3575115944,0.,-0.4006783577
H,0,1.2820172099,0.,-1.7842073323
C,0,-1.2858957103,0.,-0.8589971345
O,0,-1.3558956474,0.,-2.0865557036
H,0,-2.2152524184,0.,-0.2554103662
O,0,3.4779805976,0.,2.1265894222
C,0,3.4836570264,0.,3.5607478306
H,0,4.534229434,0.,3.8487557751
H,0,2.9937956423,0.8968134304,3.9534525401
H,0,2.9937956423,-0.8968134304,3.9534525401
```

*M06-2X/6-31+G** PCM solvent model in methanol*

anisaldehyde-A-M06-PCM-methanol
E(RM062X) = -459.933705081

```
Zero-point correction=                           0.144037 (Hartree/Particle)
Thermal correction to Energy=                    0.152807
Thermal correction to Enthalpy=                  0.153752
Thermal correction to Gibbs Free Energy=         0.110188
Sum of electronic and zero-point Energies=          -459.789668
Sum of electronic and thermal Energies=             -459.780898
Sum of electronic and thermal Enthalpies=           -459.779954
Sum of electronic and thermal Free Energies=        -459.823517

                E (Thermal)             CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total               95.888             32.840             91.686
```

```
C,0,-0.0348981048,0.,-0.0648283802
C,0,-0.1046928789,0.,1.3289050047
C,0,1.0505495833,0.,2.106980773
C,0,2.2964877678,0.,1.4688269365
C,0,2.3767229824,0.,0.0631614169
C,0,1.2223098325,0.,-0.6934089642
H,0,-1.0759992028,0.,1.8176856836
H,0,0.9714786729,0.,3.1868077288
H,0,3.358319457,0.,-0.3987784676
H,0,1.2725277807,0.,-1.778136978
C,0,-1.2787135649,0.,-0.8482686268
O,0,-1.3304468718,0.,-2.0659961607
H,0,-2.2115678466,0.,-0.2523432322
O,0,3.4792719915,0.,2.1184211219
```

```
C,0,3.4648961208,0.,3.5417650778
H,0,4.5086313262,0.,3.8496926013
H,0,2.9668229774,0.8960248778,3.9246022325
H,0,2.9668229774,-0.8960248778,3.9246022325
```

Aldol Transition States re face, cis, A

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-cis-A-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95603990

```
Zero-point correction=                          0.397664 (Hartree/Particle)
Thermal correction to Energy=                   0.420584
Thermal correction to Enthalpy=                 0.421529
Thermal correction to Gibbs Free Energy=        0.341690
Sum of electronic and zero-point Energies=      -1201.558376
Sum of electronic and thermal Energies=         -1201.535456
Sum of electronic and thermal Enthalpies=       -1201.534511
Sum of electronic and thermal Free Energies=    -1201.614350

               E (Thermal)        CV                S
                KCal/Mol    Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total            263.921         87.005          168.034
```

```
C,0,4.4544604826,-0.4676856295,-0.2035063226
C,0,3.6587003572,-1.5924628943,-0.4572852722
C,0,2.4331149129,-1.7029716365,0.1870026981
C,0,1.9874194042,-0.7001954459,1.0660048335
C,0,2.811831219,0.4112482091,1.3073767854
C,0,4.0456289698,0.5382029095,0.678484333
C,0,0.6815335712,-0.8501922038,1.7981312114
O,0,0.2006232542,-2.0068448889,2.0037274866
N,0,5.7440715578,-0.3464891645,-0.868039287
O,0,6.4403796121,0.6506720635,-0.6327461312
O,0,6.0955006296,-1.2443281089,-1.6458024437
C,0,-0.6002798871,0.1272981313,0.4121577574
C,0,-1.8782191099,-0.2781098614,1.0529131862
N,0,-3.1511126188,-0.2844203971,0.1642534716
C,0,-3.0395147765,-1.3130067415,-0.9426493658
C,0,-4.3273082527,-1.2524049792,-1.8147775055
C,0,-0.2681503373,1.5362662177,0.4038435876
O,0,0.6019051865,1.8651062997,-0.5985275908
```

```
C,0,1.0634864637,3.2270843955,-0.629606687
O,0,-0.6491789805,2.3818409684,1.2232505218
C,0,-4.3387474124,-0.6484848544,1.0359055837
C,0,-5.609240418,-0.7545690893,0.1456214335
C,0,-3.4095099247,1.0725422983,-0.4563493671
C,0,-4.7666712815,1.0261170116,-1.2168038063
H,0,-2.1235640994,0.3908752874,1.8806918102
H,0,1.742753913,3.2850161114,-1.4799888184
H,0,0.2265828,3.9162877445,-0.767975027
H,0,1.5916688037,3.4804719501,0.2926890007
H,0,-1.8011701073,-1.3047486921,1.4265297448
H,0,-0.2944534885,-0.4196269603,-0.4743894556
H,0,0.536188434,-0.0621105637,2.5601615709
H,0,2.4861711984,1.1812127186,2.0010265276
H,0,4.6863294648,1.3910091437,0.8642610988
H,0,4.0057110221,-2.3581869005,-1.1397797184
H,0,1.8063465414,-2.5728485269,0.0221025029
H,0,-2.1422836688,-1.079580236,-1.5149486677
H,0,-2.9049323271,-2.2814835953,-0.4577926534
H,0,-3.4019007649,1.8024246345,0.3539278545
H,0,-2.5699322506,1.2788805912,-1.1200185196
H,0,-4.0949913654,-1.5890047371,1.5325122848
H,0,-4.4231488024,0.1345315994,1.7915024631
N,0,-5.3195077733,-0.336386755,-1.2338427183
H,0,-4.08689996,-0.9075164106,-2.8233976885
H,0,-4.7691753295,-2.2485501023,-1.8955548554
H,0,-5.9774082708,-1.7831419512,0.1259500263
H,0,-6.4020564057,-0.1203401603,0.5496481624
H,0,-5.4933150416,1.6884189931,-0.7398906731
H,0,-4.6282771435,1.3641912081,-2.2466863622
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-cis-A-M062X-631Gdp-PCM-methanol
E(RM062X) = -1201.44748416

```
 Zero-point correction=                           0.402238 (Hartree/Particle)
 Thermal correction to Energy=                    0.424695
 Thermal correction to Enthalpy=                  0.425639
 Thermal correction to Gibbs Free Energy=         0.347888
 Sum of electronic and zero-point Energies=          -1201.045246
 Sum of electronic and thermal Energies=             -1201.022790
 Sum of electronic and thermal Enthalpies=           -1201.021845
 Sum of electronic and thermal Free Energies=        -1201.099596
```

```
              E (Thermal)          CV              S
               KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
Total             266.500          85.990          163.640
```

```
C,0,4.3529246072,-0.1390015846,-0.1020143089
C,0,3.7576692939,-1.3748510256,-0.3521119293
C,0,2.5720118198,-1.6779845842,0.3010547898
C,0,1.9888765461,-0.7518536714,1.1731140024
C,0,2.616611491,0.4736172564,1.4142287517
C,0,3.8085413278,0.7929024063,0.7759871195
C,0,0.7093682215,-1.0794933464,1.8741814898
O,0,0.3046929038,-2.2425143048,1.9947018445
N,0,5.6037591337,0.1899871623,-0.7873842757
O,0,6.1165261324,1.2766665306,-0.5648216501
O,0,6.0767911932,-0.6364398122,-1.5532627829
C,0,-0.6170069341,-0.130374296,0.1963592435
C,0,-1.8484384963,-0.4521939351,0.9342036166
N,0,-3.1701578689,-0.3254200308,0.142445463
C,0,-3.2394422713,-1.3526815626,-0.9497587234
C,0,-4.4912071033,-1.0604301207,-1.8132338104
C,0,-0.168751085,1.2151201653,0.1508580021
O,0,0.7933798573,1.4255009602,-0.7991142768
C,0,1.3574323764,2.7324189973,-0.8373553753
O,0,-0.5188915994,2.140087351,0.8987321319
C,0,-4.3288676801,-0.5427609852,1.0748360905
C,0,-5.6263675235,-0.6295732352,0.2351080541
C,0,-3.3035297984,1.0393328977,-0.4736463602
C,0,-4.7389450346,1.1790786087,-1.034912171
H,0,-1.9838787158,0.2250986247,1.7842757241
H,0,2.1235999928,2.7034245416,-1.6121771784
H,0,0.5969841994,3.4766983118,-1.0876915532
H,0,1.8084494426,2.9940994247,0.1234097743
H,0,-1.8488757691,-1.4892495036,1.2902607027
H,0,-0.2601166944,-0.8055447117,-0.573348503
H,0,0.3457364231,-0.2783058397,2.5437534991
H,0,2.1607405227,1.1881509134,2.0955391304
H,0,4.3066515822,1.739897064,0.9452030748
H,0,4.2205100034,-2.0720628719,-1.0396876044
H,0,2.0788336373,-2.6302449101,0.134942797
H,0,-2.3130369334,-1.2842683539,-1.5213797812
H,0,-3.2857121715,-2.3278399463,-0.458718299
H,0,-3.0674184633,1.7710267211,0.3015497301
H,0,-2.5411356724,1.1025240332,-1.2523917114
```

```
H,0,-4.1296737363,-1.4572114374,1.6371422424
H,0,-4.3346913696,0.3033691579,1.7660315916
N,0,-5.3903443612,-0.1317331081,-1.1225255286
H,0,-4.204231972,-0.6131037141,-2.7684260324
H,0,-5.022557541,-1.9918059865,-2.0211890923
H,0,-5.9739870441,-1.6635861569,0.1672834234
H,0,-6.4126866685,-0.0365603484,0.7073073297
H,0,-5.3461500636,1.8194671592,-0.3899793039
H,0,-4.7045301363,1.6326280959,-2.0280623673
```

Aldol Transition States re face, cis, B

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-cis-B-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95200368

```
 Zero-point correction=                           0.398089 (Hartree/Particle)
 Thermal correction to Energy=                    0.420753
 Thermal correction to Enthalpy=                  0.421697
 Thermal correction to Gibbs Free Energy=         0.343997
 Sum of electronic and zero-point Energies=          -1201.553915
 Sum of electronic and thermal Energies=             -1201.531251
 Sum of electronic and thermal Enthalpies=           -1201.530307
 Sum of electronic and thermal Free Energies=        -1201.608006

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.026             86.848            163.532
```

```
N,0,-5.3043277444,-0.4229609414,-1.3843587292
C,0,-4.2851674543,-1.3920473306,-1.8114466204
C,0,-3.0809162883,-1.4072368495,-0.8264623285
N,0,-3.2355035341,-0.2575350243,0.1500038909
C,0,-4.4924381642,-0.493361381,0.9695935929
C,0,-5.6908767589,-0.7145741664,0.003987824
C,0,-4.7362577155,0.9319403874,-1.4500295851
C,0,-3.4138190359,1.0267912008,-0.6351031501
C,0,-2.0246918186,-0.1871310814,1.1209229744
C,0,-0.7002436646,0.1813994671,0.5362231523
C,0,-0.4265827504,1.6060911421,0.4134428333
O,0,-0.9515188998,2.5090210508,1.0734981959
O,0,0.5535476108,1.8682969231,-0.4954542019
```

```
C,0,0.9627687356,3.2428917783,-0.6235070164
C,0,0.7455345715,-0.6356325707,1.7169902577
O,0,1.8393789224,-0.7201833815,1.0701318796
C,0,0.6931835221,0.2275119693,2.9588444166
C,0,1.6136659137,1.2761901956,3.1254264134
C,0,1.604056622,2.0615444317,4.2719416346
C,0,0.665694059,1.7810988441,5.2722683201
C,0,-0.2520993375,0.7327380543,5.1455597176
C,0,-0.2274993499,-0.0373087067,3.9875532294
N,0,0.6511909413,2.5935154565,6.4807311345
O,0,1.4716528733,3.5154494348,6.5838969391
O,0,-0.182364083,2.3329755872,7.3591950766
H,0,-2.3211638539,0.535086544,1.8834350478
H,0,1.7408267799,3.243985979,-1.3865458914
H,0,0.1232433023,3.8676729979,-0.9384354694
H,0,1.3600686925,3.6193242467,0.3219125638
H,0,-2.0069070113,-1.1868025837,1.5647878148
H,0,-0.3672333455,-0.4082517102,-0.3120779892
H,0,0.1320906722,-1.5507249938,1.8412984219
H,0,-0.9231735608,-0.8659123583,3.8904080335
H,0,-0.9560695126,0.5276199733,5.9421900363
H,0,2.3074905305,2.8745264592,4.402192474
H,0,2.3430341484,1.4585087916,2.3436685201
H,0,-2.127202879,-1.2784032374,-1.3372810617
H,0,-3.040294387,-2.3204492211,-0.2300497346
H,0,-3.4136132757,1.8472936195,0.0827452301
H,0,-2.5396718414,1.1262936338,-1.2784725172
H,0,-4.3034792417,-1.3571518647,1.6089806648
H,0,-4.6212610119,0.387857569,1.6004234087
H,0,-3.9524561305,-1.1230171436,-2.8168614747
H,0,-4.7351628694,-2.3865463306,-1.8602976395
H,0,-6.0387406854,-1.7491165812,0.0563865456
H,0,-6.521740865,-0.0646933923,0.2887091905
H,0,-5.4757883549,1.6364368466,-1.0615508474
H,0,-4.5453394722,1.1875702665,-2.4951191777
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-cis-B-M062X-631Gdp-PCM-methanol
E(RM062X) = -1201.44459244

```
 Zero-point correction=                    0.402705 (Hartree/Particle)
 Thermal correction to Energy=                  0.424965
 Thermal correction to Enthalpy=                 0.425909
```

```
Thermal correction to Gibbs Free Energy=         0.349384
Sum of electronic and zero-point Energies=          -1201.041887
Sum of electronic and thermal Energies=            -1201.019627
Sum of electronic and thermal Enthalpies=           -1201.018683
Sum of electronic and thermal Free Energies=        -1201.095209

                E (Thermal)           CV                S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total               266.670            85.625           161.062
```

```
N,0,-5.3417228854,-0.2975006746,-1.2810862935
C,0,-4.3803287422,-1.2678649042,-1.8104007531
C,0,-3.0257363146,-1.1601680457,-1.0662424323
N,0,-3.2315214849,-0.3368965548,0.1750807672
C,0,-4.4061233919,-0.8982692086,0.9305229009
C,0,-5.6874393294,-0.6749683584,0.0912305211
C,0,-4.7149876188,1.0261880568,-1.2612016046
C,0,-3.5569551775,1.0732061692,-0.2341856043
C,0,-1.9920125844,-0.3909513067,1.0844436755
C,0,-0.6991966319,0.0279498642,0.4921137566
C,0,-0.3935000971,1.432132918,0.5231646874
O,0,-0.9794466329,2.2904440653,1.1870394761
O,0,0.7080392837,1.7454910981,-0.2059733649
C,0,1.1280876454,3.1077976446,-0.144393758
C,0,0.8207917478,-0.8113355018,1.7305913704
O,0,1.8814654497,-0.9092547163,1.0727425738
C,0,0.7247594311,0.168779602,2.8660736666
C,0,1.6274400449,1.2356433639,2.9283527171
C,0,1.5504745739,2.1662810208,3.9551880818
C,0,0.5619063093,2.0019511003,4.9225806221
C,0,-0.3412116765,0.941858963,4.8990672493
C,0,-0.2478566158,0.0237015754,3.861462832
N,0,0.4745651403,2.9746287709,6.011220753
O,0,1.2780613241,3.8955479977,6.0303529785
O,0,-0.3984853221,2.8233949013,6.8535166635
H,0,-2.245862929,0.2516525458,1.933198789
H,0,2.0249419613,3.1688642854,-0.7593132951
H,0,0.3535860795,3.7687882697,-0.5410102411
H,0,1.3542851878,3.3976122047,0.8847017789
H,0,-1.9692942148,-1.4352207031,1.4177275646
H,0,-0.301706241,-0.5404926712,-0.3410830525
H,0,0.1730276365,-1.6980772346,1.871131253
H,0,-0.9332813774,-0.8196736811,3.8291533897
H,0,-1.0857894817,0.8432263732,5.6794288675
```

H,0,2.2354581932,3.0036072697,4.0158488254
H,0,2.3835453061,1.3191785292,2.1541033798
H,0,-2.2640040626,-0.6489786693,-1.6567974231
H,0,-2.639071889,-2.1325959877,-0.7530077642
H,0,-3.8171077131,1.610055223,0.6805462074
H,0,-2.64912859,1.510610029,-0.6479828717
H,0,-4.1942026221,-1.9573386917,1.0941718069
H,0,-4.4433686126,-0.3910441394,1.8965771496
H,0,-4.2303861222,-1.0821859346,-2.8761980001
H,0,-4.8035619166,-2.2688257794,-1.6957236817
H,0,-6.2837261342,-1.5897778119,0.0758075902
H,0,-6.2975555228,0.1215949099,0.5236179626
H,0,-5.4664290102,1.7767065322,-1.005744072
H,0,-4.34561137,1.2451192919,-2.2661196454

Aldol Transition States re face, cis, C

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-cis-C-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95483649

```
 Zero-point correction=                           0.397982 (Hartree/Particle)
 Thermal correction to Energy=                    0.420749
 Thermal correction to Enthalpy=                  0.421693
 Thermal correction to Gibbs Free Energy=         0.343130
 Sum of electronic and zero-point Energies=          -1201.556855
 Sum of electronic and thermal Energies=             -1201.534088
 Sum of electronic and thermal Enthalpies=           -1201.533143
 Sum of electronic and thermal Free Energies=        -1201.611707

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.024            86.909            165.350
```

N,0,-5.6103290183,0.1206629655,-1.4007609201
C,0,-4.8443474772,-1.10896236,-1.6514299035
C,0,-3.6816256455,-1.2634426275,-0.6283803228
N,0,-3.5858561505,0.0044544335,0.1969740747
C,0,-4.8772393209,0.1641044405,0.9799058579
C,0,-6.0781940046,0.1200814428,-0.0072490122
C,0,-4.7363652628,1.284181739,-1.6117186895
C,0,-3.4487594677,1.1847352598,-0.7436850426
C,0,-2.4126287649,-0.0778949799,1.2048366134

```
C,0,-1.0307551251,-0.1196273784,0.6512739701
C,0,-0.4028300181,1.1423554427,0.3119239981
O,0,-0.7296753888,2.2601312789,0.7230389683
O,0,0.701605353,0.9681215076,-0.4758695099
C,0,1.4659490057,2.1481552409,-0.7830135201
C,0,0.0359455567,-0.6274981539,2.358653812
O,0,-0.4466534089,-0.0477322675,3.3827901331
C,0,-0.0801256166,-2.1313550426,2.2321845936
C,0,-0.9621003076,-2.8437172392,3.060818763
C,0,-1.0616099665,-4.2293674304,2.9747544016
C,0,-0.2531272809,-4.9054354822,2.0555347916
C,0,0.6511933919,-4.2249503347,1.2294963615
C,0,0.7290887127,-2.841671299,1.326805824
N,0,-0.3457504472,-6.3560147954,1.9608890695
O,0,-1.1503336924,-6.9470042415,2.6938446008
O,0,0.3822664627,-6.9427131731,1.1487276844
H,0,-2.5293223113,0.7920287248,1.8523242104
H,0,2.2891388521,1.8063647878,-1.4102037629
H,0,0.8554211222,2.8748220023,-1.3248825956
H,0,1.8526382819,2.608663692,0.1294422956
H,0,-2.6359232193,-0.9758859105,1.7861302477
H,0,-0.7820549024,-0.9375152424,-0.0164185383
H,0,0.9891907528,-0.2666096443,1.9304827728
H,0,1.4277343005,-2.3011902245,0.6939711791
H,0,1.2738161001,-4.7761427364,0.5360954215
H,0,-1.7419603411,-4.7844034119,3.6086191368
H,0,-1.5548702369,-2.2948590837,3.7846903123
H,0,-2.7173541609,-1.4075000742,-1.1152920073
H,0,-3.8472974569,-2.0829059684,0.0733807205
H,0,-3.2762207284,2.0675653345,-0.1284778541
H,0,-2.5596590409,1.0024251227,-1.3468868109
H,0,-4.9095105795,-0.641649741,1.7150847859
H,0,-4.8044617115,1.1164293837,1.5077821602
H,0,-4.4521488389,-1.0696659115,-2.6705340817
H,0,-5.5164246265,-1.9676930769,-1.5818165896
H,0,-6.6765110805,-0.7793233936,0.1575343999
H,0,-6.7225505771,0.9879010837,0.1528032058
H,0,-5.2972871589,2.1875578921,-1.3597450637
H,0,-4.4670455567,1.3394254499,-2.6693221411
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-cis-C-M06-PCM-methanol
E(RM062X) = -1201.44614755

```
Zero-point correction=                           0.402500 (Hartree/Particle)
Thermal correction to Energy=                    0.424909
Thermal correction to Enthalpy=                  0.425853
Thermal correction to Gibbs Free Energy=         0.348491
Sum of electronic and zero-point Energies=          -1201.043648
Sum of electronic and thermal Energies=             -1201.021238
Sum of electronic and thermal Enthalpies=           -1201.020294
Sum of electronic and thermal Free Energies=        -1201.097656

                E (Thermal)          CV                S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total             266.635           85.713           162.823

N,0,-5.6590754837,0.2291285508,-1.3509902336
C,0,-4.8673828076,-0.9259827028,-1.7818810387
C,0,-3.7453763431,-1.232844186,-0.7593479339
N,0,-3.6011118876,-0.0476196766,0.1535975924
C,0,-4.8517145848,0.0702710567,0.982563406
C,0,-6.0764753989,0.0233016943,0.0377183011
C,0,-4.8176123386,1.4280096204,-1.414603938
C,0,-3.4710331917,1.191794742,-0.6895635065
C,0,-2.3961598409,-0.2218190483,1.088287318
C,0,-1.0588324599,-0.2446527307,0.4663105155
C,0,-0.4152032784,0.994517314,0.1703829704
O,0,-0.7520533055,2.115918305,0.5603541027
O,0,0.7354467694,0.8247716452,-0.547336168
C,0,1.4985582633,2.0053257474,-0.7860210457
C,0,0.0362178029,-0.5724206801,2.3721878751
O,0,-0.5526282734,0.040362589,3.2846326676
C,0,-0.0569921396,-2.0699617403,2.2736022463
C,0,-0.9900269925,-2.7576471029,3.0556687472
C,0,-1.0840188784,-4.1432046384,2.9868964013
C,0,-0.2165381626,-4.8213409323,2.1368969497
C,0,0.7388195884,-4.1663993386,1.3596587637
C,0,0.8092843681,-2.7835993453,1.4354962935
N,0,-0.3020350519,-6.2801813458,2.0599342108
O,0,-1.1533461969,-6.8458149398,2.7297978791
O,0,0.4813365051,-6.8662024193,1.3276301842
H,0,-2.4632806061,0.6046416088,1.8025653735
H,0,2.3668483578,1.6862668533,-1.3610079563
H,0,0.917017079,2.7344183967,-1.3553210775
H,0,1.8167283891,2.4585221893,0.1560263845
H,0,-2.6071614059,-1.1587587974,1.6171063901
```

```
H,0,-0.748947795,-1.1085767718,-0.1095613145
H,0,0.9536740491,-0.1608208064,1.9155218608
H,0,1.5380215051,-2.245471173,0.834279876
H,0,1.4016954324,-4.7341060445,0.7183526243
H,0,-1.8045017531,-4.6919408889,3.5810983811
H,0,-1.6309358033,-2.1918374408,3.7244669679
H,0,-2.7783976238,-1.3955478295,-1.2366580477
H,0,-3.9785847552,-2.0912935928,-0.1243793372
H,0,-3.1838930834,2.0074522512,-0.0245124677
H,0,-2.6495228049,1.0080531197,-1.3845664899
H,0,-4.8454020715,-0.7507925781,1.7021464243
H,0,-4.7759608512,1.0156531003,1.5245723272
H,0,-4.442554283,-0.7023541666,-2.7637413116
H,0,-5.5209352347,-1.7951956026,-1.8848747667
H,0,-6.5815490723,-0.9434951648,0.1066192558
H,0,-6.7907179501,0.8000281737,0.3201785002
H,0,-5.3648685942,2.2548351506,-0.9545306537
H,0,-4.6337388058,1.684045576,-2.4605455029
```

Aldol Transition States re face, cis, D

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-cis-D-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95184377

```
Zero-point correction=                           0.398011 (Hartree/Particle)
Thermal correction to Energy=                    0.420697
Thermal correction to Enthalpy=                  0.421641
Thermal correction to Gibbs Free Energy=         0.343622
Sum of electronic and zero-point Energies=       -1201.553832
Sum of electronic and thermal Energies=          -1201.531147
Sum of electronic and thermal Enthalpies=        -1201.530203
Sum of electronic and thermal Free Energies=     -1201.608222

                E (Thermal)         CV                S
                 KCal/Mol     Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total             263.991         86.900           164.205
```

```
C,0,-0.47537337,-2.9490210191,-0.239203384
C,0,-1.4843246257,-3.0171915621,0.7313310138
C,0,-1.6320289436,-1.9576172223,1.6161408916
C,0,-0.8004801641,-0.8255883859,1.5363620656
C,0,0.2110269977,-0.7943227033,0.5617260982
```

```
C,0,0.3815932722,-1.8495286704,-0.3315964472
C,0,-0.95355738,0.3039418523,2.5313130525
O,0,-1.3128982037,0.0244564658,3.7202269458
N,0,-0.3094729742,-4.0574167969,-1.1705654238
O,0,0.5864507422,-3.9853412001,-2.0223623458
O,0,-1.0728772934,-5.0275833028,-1.0756635346
C,0,-2.4143770572,1.379142728,1.547655033
C,0,-2.838859472,2.2449118959,2.6361264691
O,0,-3.8346854485,1.6904736405,3.3756814404
C,0,-4.2264209697,2.4005168832,4.5650583513
C,0,-1.7504165816,2.0438710591,0.3896316165
N,0,-2.6705742364,2.6389570842,-0.71766053
C,0,-3.6926490812,3.6030170917,-0.1508505231
C,0,-4.4624348052,4.2632940581,-1.331170414
O,0,-2.3342550215,3.331620715,2.9384706314
C,0,-1.8020768588,3.3930942926,-1.7078709558
C,0,-2.687890708,3.8744588701,-2.8922553008
C,0,-3.3971123022,1.5375710813,-1.4626488648
C,0,-4.3432261569,2.1853272335,-2.5151587753
H,0,-1.1474236696,2.8880355528,0.7300847284
H,0,-5.0019013756,1.7896221317,5.0266906777
H,0,-3.3780149844,2.5125633378,5.2439802965
H,0,-4.6230682581,3.3872544466,4.3130036205
H,0,-1.1122803458,1.3540931187,-0.1674695521
H,0,-3.1084197783,0.574900649,1.3223930291
H,0,0.8869271268,0.0548921139,0.5123771521
H,0,1.1637977798,-1.8307863888,-1.0800436831
H,0,-2.1279957589,-3.8864831429,0.7824728568
H,0,-2.3952145298,-1.9947001612,2.3861972128
H,0,-0.1898647913,1.0918328971,2.3777718041
H,0,-1.3526811567,4.2226002274,-1.1593666693
H,0,-1.009758911,2.7132359546,-2.0253605429
H,0,-2.6297550052,0.9109358725,-1.9207671907
H,0,-3.9403432352,0.9468248525,-0.7257299039
H,0,-4.3491153051,3.0214920257,0.4959444435
H,0,-3.1502199325,4.325132734,0.459967028
H,0,-2.532903762,4.9427325459,-3.0618604871
H,0,-2.4204222954,3.3453408174,-3.8101526452
H,0,-4.1762127255,1.7297169853,-3.494186982
H,0,-5.3881611735,2.0209092856,-2.2413325716
N,0,-4.1111651739,3.6339907703,-2.6129436404
H,0,-5.5391319105,4.1661675539,-1.1718205157
H,0,-4.2262521864,5.3284487319,-1.3920985755
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-cis-D-M06-PCM-methanol
E(RM062X) = -1201.44283592

```
 Zero-point correction=                           0.402811 (Hartree/Particle)
 Thermal correction to Energy=                    0.425080
 Thermal correction to Enthalpy=                  0.426024
 Thermal correction to Gibbs Free Energy=         0.348718
 Sum of electronic and zero-point Energies=          -1201.040025
 Sum of electronic and thermal Energies=             -1201.017756
 Sum of electronic and thermal Enthalpies=           -1201.016812
 Sum of electronic and thermal Free Energies=        -1201.094118

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.742             85.541            162.704
```

```
 C,0,-0.562039764,-3.0551231788,0.0441092509
 C,0,-1.3866050294,-3.0497779505,1.1693898517
 C,0,-1.4431831227,-1.8975825985,1.9373594874
 C,0,-0.6992959368,-0.7647429489,1.5811991707
 C,0,0.1309581296,-0.8076038035,0.4563150716
 C,0,0.2046969239,-1.955547619,-0.3261692787
 C,0,-0.768895919,0.4639166175,2.4452325448
 O,0,-1.0449304907,0.3611019971,3.6589456529
 N,0,-0.4915245876,-4.2669584962,-0.7720337765
 O,0,0.2260896737,-4.2575263074,-1.7614218413
 O,0,-1.1556027364,-5.2335660618,-0.4283042573
 C,0,-2.4410841907,1.3247976864,1.3289005698
 C,0,-2.9366831271,2.0522558432,2.4592704737
 O,0,-3.7932612124,1.316455292,3.208427931
 C,0,-4.2053348558,1.9018365849,4.4417916084
 C,0,-1.7603858024,2.0876601913,0.2617086161
 N,0,-2.6616338771,2.7373529251,-0.8055057156
 C,0,-3.7265329389,3.5954559818,-0.1758084097
 C,0,-4.4211216213,4.4047671938,-1.2971173447
 O,0,-2.593095765,3.1840452708,2.8105324573
 C,0,-1.8180355899,3.6060360578,-1.698160613
 C,0,-2.684732186,4.0734168934,-2.8921296331
 C,0,-3.3289594875,1.6920882858,-1.6541379094
 C,0,-4.3483092355,2.3979862361,-2.5816394096
 H,0,-1.1992122336,2.9244123117,0.689631951
 H,0,-4.8728229196,1.1769880429,4.9059359912
```

```
H,0,-3.3426638025,2.0869088857,5.0850667968
H,0,-4.7342008223,2.8416379887,4.2660500622
H,0,-1.0793965968,1.4624856951,-0.3269072768
H,0,-2.9847674235,0.4240589284,1.0646418547
H,0,0.7418229515,0.0535147232,0.1989236109
H,0,0.84684502,-2.0068836867,-1.1969321341
H,0,-1.9612735636,-3.9311074763,1.426725953
H,0,-2.0679281265,-1.8533931718,2.8238218218
H,0,-0.1220477954,1.2903798192,2.0928318767
H,0,-1.4712444126,4.4392462117,-1.0826255231
H,0,-0.9556251383,3.0138448798,-2.0114269201
H,0,-2.53458378,1.1881724305,-2.2103637874
H,0,-3.8029774303,0.9768704035,-0.9808636489
H,0,-4.4126881938,2.9147034981,0.3315062262
H,0,-3.2397554368,4.2206380482,0.5749617034
H,0,-2.5191490714,5.1375881387,-3.0743757968
H,0,-2.4184916375,3.5275775711,-3.8006851429
H,0,-4.2665267676,1.9943886552,-3.5933790668
H,0,-5.3693860803,2.2289439291,-2.2304455586
N,0,-4.1044798302,3.8425009824,-2.6135325518
H,0,-5.5030981965,4.3882069023,-1.1475712403
H,0,-4.0933479633,5.447369197,-1.281276698
```

Aldol Transition States re face, cis, E

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-cis-E-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95664402

```
 Zero-point correction=                           0.397990 (Hartree/Particle)
 Thermal correction to Energy=                    0.420765
 Thermal correction to Enthalpy=                  0.421709
 Thermal correction to Gibbs Free Energy=         0.342836
 Sum of electronic and zero-point Energies=         -1201.558654
 Sum of electronic and thermal Energies=            -1201.535879
 Sum of electronic and thermal Enthalpies=          -1201.534935
 Sum of electronic and thermal Free Energies=       -1201.613808

                 E (Thermal)             CV                S
                  KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total              264.034             86.876            166.004
```

```
C,0,2.1116884676,-1.2758925856,1.1487052655
```

```
C,0,3.1977682911,-1.7112045854,0.3985981619
C,0,4.0631885446,-0.7569500669,-0.1496257548
C,0,3.8616360502,0.6146522642,0.0422668343
C,0,2.7654475954,1.0284497797,0.7902899583
C,0,1.8714810583,0.095496886,1.3440334098
N,0,5.2080908031,-1.2026333626,-0.930889103
O,0,5.9723132862,-0.3488558729,-1.4013371268
C,0,0.7062334596,0.5522896079,2.1855156625
O,0,0.1660157061,-0.261155977,3.0021995482
O,0,5.3737411428,-2.4188946575,-1.0971448575
C,0,-0.7352664359,0.9783666286,0.7507662698
C,0,-1.1990462536,-0.3893538983,0.4016465538
N,0,-2.6784008082,-0.5547127178,-0.0342818869
C,0,-3.6227553146,-0.2254910672,1.1034620191
C,0,-5.0875423179,-0.3849135438,0.6013520442
C,0,-0.199718523,1.8080002043,-0.3111823836
O,0,-0.0891494091,3.116760022,0.0731357393
C,0,0.4801020328,4.0249701287,-0.8870069629
O,0,0.1889053303,1.4308031916,-1.4212997602
C,0,-2.897632886,-2.0027043597,-0.4322929543
C,0,-4.3978397673,-2.2111562814,-0.7850461001
C,0,-3.0163311503,0.3252015979,-1.2199631086
C,0,-4.4689825669,0.0088264841,-1.6805818228
H,0,0.7887940019,1.6194283347,2.4555589484
H,0,-0.6194721485,-0.7956727514,-0.428940354
H,0,-1.1039340456,-1.0422649316,1.276954144
H,0,-2.2715754696,0.1240525512,-1.9905962629
H,0,-2.9035382347,1.3568598916,-0.8877523932
H,0,-3.4045571054,0.7927065196,1.4234405621
H,0,-3.3813451628,-0.9091316182,1.9190761697
H,0,-2.2386501005,-2.1957157059,-1.2803792254
H,0,-2.5746399089,-2.618111098,0.4089700597
H,0,-1.3197917403,1.5220774388,1.4859907829
H,0,0.4816245246,4.9998449091,-0.3996923831
H,0,1.5000327981,3.7305948355,-1.1455426376
H,0,-0.1276698916,4.0582055471,-1.7948610972
H,0,4.5543975771,1.3298115996,-0.3830215876
H,0,2.6027764798,2.0898245771,0.9541012317
H,0,1.4395757807,-1.9945253536,1.6046575458
H,0,3.3856044441,-2.7660840469,0.2419117924
N,0,-5.1248876237,-0.9337754302,-0.7618917193
H,0,-5.6381448038,-1.0535322334,1.2674598397
H,0,-5.5959246673,0.5823573279,0.5995334473
H,0,-5.0557391827,0.9298070076,-1.7204691471
```

```
H,0,-4.4638194593,-0.4299317002,-2.6813649049
H,0,-4.4886525221,-2.6534326997,-1.7801014666
H,0,-4.8673518749,-2.8907137894,-0.06966599
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-cis-E-M062X-631Gdp-PCM-methanol
E(RM062X) = -1201.44923941

```
Zero-point correction=                       0.402321 (Hartree/Particle)
Thermal correction to Energy=                  0.424704
Thermal correction to Enthalpy=                0.425648
Thermal correction to Gibbs Free Energy=        0.348308
Sum of electronic and zero-point Energies=        -1201.046919
Sum of electronic and thermal Energies=           -1201.024536
Sum of electronic and thermal Enthalpies=         -1201.023592
Sum of electronic and thermal Free Energies=       -1201.100931

              E (Thermal)          CV             S
               KCal/Mol       Cal/Mol-Kelvin   Cal/Mol-Kelvin
Total              266.506          85.816         162.775
```

```
C,0,2.0305929456,-1.198218798,1.0236469407
C,0,3.0272868418,-1.5074777244,0.1082214406
C,0,3.8290263788,-0.473336348,-0.3704568878
C,0,3.6670071738,0.8496842153,0.031665109
C,0,2.6570511896,1.140335355,0.9389232147
C,0,1.8315719374,0.1249944407,1.4344507524
N,0,4.886717822,-0.7908706841,-1.3298689876
O,0,5.6221113004,0.1128102085,-1.6993511337
C,0,0.7557219265,0.4522404815,2.422506897
O,0,0.2484226659,-0.4268539834,3.1423614041
O,0,4.9857384928,-1.9450352115,-1.7197946733
C,0,-0.8282024503,0.9593631938,0.8852239641
C,0,-1.2743146306,-0.4207297598,0.6356314063
N,0,-2.6886200633,-0.5963757062,0.0576046686
C,0,-3.7297180875,-0.1202187332,1.0297158667
C,0,-5.107928606,-0.1600680856,0.3252065255
C,0,-0.1599735722,1.6597283529,-0.1602308146
O,0,0.1206668413,2.9561821891,0.1746883339
C,0,0.8361248168,3.7094902375,-0.8009127656
O,0,0.2225986344,1.1963784089,-1.2394473038
C,0,-2.9301500181,-2.0538682614,-0.2236735196
C,0,-4.4192795979,-2.2429894521,-0.600644293
```

```
C,0,-2.8463035027,0.1674886018,-1.2285934395
C,0,-4.1924229591,-0.2431395873,-1.8740116513
H,0,0.7369338406,1.5130071948,2.7224986169
H,0,-0.6197482551,-0.9075055395,-0.0949758237
H,0,-1.283479819,-1.0056837593,1.5653128392
H,0,-1.9781989324,-0.0608568512,-1.8496444697
H,0,-2.8120945635,1.226359873,-0.96522869
H,0,-3.4500897803,0.8869905951,1.339784086
H,0,-3.6786017861,-0.7870069378,1.8939934287
H,0,-2.2540457077,-2.3286016964,-1.0365861231
H,0,-2.6493572744,-2.6101648532,0.6728821854
H,0,-1.3214763453,1.5532661633,1.6459407558
H,0,0.9702019654,4.7015946647,-0.3712225595
H,0,1.808679957,3.2549918871,-1.0082668712
H,0,0.2688968785,3.7767800685,-1.7326094175
H,0,4.3172863946,1.622514994,-0.3600848894
H,0,2.5010246338,2.1654618099,1.2653192498
H,0,1.3955663273,-1.9774824705,1.4339135275
H,0,3.1940734863,-2.5238038323,-0.2275433307
N,0,-5.0372195263,-0.9502016216,-0.9065857409
H,0,-5.8521822879,-0.5985539328,0.9938045978
H,0,-5.4370995175,0.8496841006,0.0668013469
H,0,-4.7189091947,0.6456284329,-2.2291468646
H,0,-4.0256587149,-0.9027174954,-2.729472675
H,0,-4.5009137955,-2.8980841233,-1.4707640624
H,0,-4.9702554622,-2.7025530207,0.22371483
```

Aldol Transition States re face, cis, F

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-cis-F-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95419151

```
 Zero-point correction=                           0.397659 (Hartree/Particle)
 Thermal correction to Energy=                    0.420475
 Thermal correction to Enthalpy=                  0.421419
 Thermal correction to Gibbs Free Energy=         0.342562
 Sum of electronic and zero-point Energies=          -1201.556532
 Sum of electronic and thermal Energies=             -1201.533716
 Sum of electronic and thermal Enthalpies=           -1201.532772
 Sum of electronic and thermal Free Energies=        -1201.611629

                     E (Thermal)             CV                S
```

	KCal/Mol	Cal/Mol-Kelvin	Cal/Mol-Kelvin
Total	263.852	87.012	165.968

```
C,0,-0.6977660449,-2.6096206028,-0.6192702789
C,0,-1.3939469284,-2.8602680788,0.5683823333
C,0,-1.4346090807,-1.8680330049,1.541898004
C,0,-0.7997143811,-0.6325389034,1.3368569167
C,0,-0.0978872752,-0.4148017623,0.1389498339
C,0,-0.0417246242,-1.393117996,-0.8458572882
C,0,-0.8182108241,0.4208264623,2.4163121616
O,0,-1.1427611409,0.1116283347,3.602603169
N,0,-0.6463230405,-3.6436311688,-1.6433208224
O,0,-0.0346618807,-3.4056263721,-2.6939663525
O,0,-1.2175575055,-4.721065226,-1.4264803861
C,0,-2.1805961732,1.7849978652,1.5901970151
C,0,-2.1556886091,2.7602261437,2.717363149
N,0,-2.771104772,4.1645773719,2.4623275073
C,0,-4.2039619037,4.0828117603,1.977448139
C,0,-4.7843783164,5.5242794829,1.8877128976
C,0,-3.4056784406,1.0428172047,1.379519569
O,0,-3.5144975673,0.5584424808,0.104739219
C,0,-4.6563707126,-0.2711887253,-0.1721355787
O,0,-4.2624003997,0.7933174774,2.2354299047
C,0,-2.7508888631,4.9393087622,3.7676859186
C,0,-3.2456150894,6.3899998121,3.5040523801
C,0,-1.9575640462,4.9289969042,1.4376626584
C,0,-2.6317325921,6.3098313878,1.1898409642
H,0,-2.7013843562,2.361242521,3.5733189117
H,0,-4.5579934382,-0.5618501869,-1.2180268134
H,0,-4.6584737342,-1.157338606,0.4668237754
H,0,-5.5850478837,0.2854793193,-0.0216255366
H,0,-1.1329476552,2.9867635214,3.0291011127
H,0,-1.6498116802,2.0585763208,0.6832732936
H,0,0.4107008366,0.5321766062,-0.0210139175
H,0,0.4986130049,-1.2315557437,-1.770045593
H,0,-1.8837217097,-3.8144671436,0.7176940901
H,0,-1.9532457601,-2.0400375088,2.4786553086
H,0,-0.0210923891,1.1735608597,2.2549711352
H,0,-0.9490165246,5.0235828089,1.8442110681
H,0,-1.9179384603,4.3187729137,0.5355205911
H,0,-3.3965538415,4.3976097115,4.4608601449
H,0,-1.7275395648,4.9077990043,4.1452230465
H,0,-4.177500583,3.5888273093,1.0066539712
H,0,-4.7456424038,3.4467410344,2.6776287948
```

```
N,0,-3.741740355,6.532829657,2.1274384166
H,0,-1.8967095243,7.1091404939,1.3119248541
H,0,-3.0228822345,6.3654365885,0.1709429529
H,0,-4.0497527694,6.6408290491,4.1999550861
H,0,-2.4331785827,7.1046923456,3.656340216
H,0,-5.2172598598,5.6893215407,0.8980425399
H,0,-5.5762303199,5.662531974,2.6280055175
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-cis-F-M06-PCM-methanol
E(RM062X) = -1201.44804305

```
 Zero-point correction=                           0.402581 (Hartree/Particle)
 Thermal correction to Energy=                    0.424818
 Thermal correction to Enthalpy=                  0.425762
 Thermal correction to Gibbs Free Energy=         0.348594
 Sum of electronic and zero-point Energies=          -1201.045462
 Sum of electronic and thermal Energies=             -1201.023225
 Sum of electronic and thermal Enthalpies=           -1201.022281
 Sum of electronic and thermal Free Energies=        -1201.099449

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.577             85.670            162.413
```

```
C,0,-1.0820088374,-2.5977869633,-0.4365212
C,0,-1.7522004338,-2.6942553269,0.779370587
C,0,-1.5747323142,-1.6792731312,1.7114957638
C,0,-0.7474105853,-0.5902721717,1.4215517532
C,0,-0.0714731331,-0.5321831939,0.198182283
C,0,-0.233984348,-1.5353758575,-0.7455317065
C,0,-0.5847789635,0.5056685823,2.4300775724
O,0,-0.9706717141,0.3636936456,3.6064794063
N,0,-1.2679992563,-3.6573874623,-1.428064423
O,0,-0.69364788,-3.5510007842,-2.5018884694
O,0,-1.9910389661,-4.59990585,-1.1399462911
C,0,-1.9173776926,1.9614687055,1.399350986
C,0,-1.9872182699,2.8287004722,2.593648923
N,0,-2.7372881454,4.1644250526,2.4424422096
C,0,-4.142140485,3.9629259821,1.9414774509
C,0,-4.8944998539,5.3109859462,2.0555318135
C,0,-3.0472097731,1.1448640517,1.0877899589
O,0,-3.0054747983,0.6429862082,-0.179869281
```

```
C,0,-4.049094561,-0.26144062,-0.5306576363
O,0,-3.9611569083,0.8319868412,1.8582227411
C,0,-2.8052068097,4.8399904582,3.7854544192
C,0,-3.3488496253,6.2753807093,3.58843985
C,0,-2.0172727162,5.0735055792,1.4873273448
C,0,-2.8950392042,6.3260162905,1.2506267488
H,0,-2.495522882,2.3066298805,3.4101011002
H,0,-3.8126759486,-0.6122064992,-1.5352948254
H,0,-4.0828465199,-1.1045957991,0.1632627652
H,0,-5.0176191076,0.2458812302,-0.5280528863
H,0,-0.9915989679,3.127595824,2.9384657718
H,0,-1.273409323,2.2439552583,0.5728650379
H,0,0.574511375,0.3145043666,-0.0196888817
H,0,0.2753211553,-1.5060765937,-1.7009927022
H,0,-2.395587696,-3.5426180763,0.9794037233
H,0,-2.0757991465,-1.7162280808,2.6729474559
H,0,0.2373893242,1.2054620693,2.1917212612
H,0,-1.0571146141,5.315115365,1.9494182312
H,0,-1.8403959815,4.5075524984,0.5717310982
H,0,-3.4597278007,4.2260428508,4.4082977226
H,0,-1.7994532755,4.8270205524,4.210128753
H,0,-4.0549910074,3.6222427606,0.9079945873
H,0,-4.5881998811,3.1623464308,2.5331476942
N,0,-3.952742196,6.4152623337,2.2608602586
H,0,-2.2760143249,7.2248517602,1.2947198716
H,0,-3.3657987363,6.2858819941,0.2652588166
H,0,-4.0972331125,6.4952752661,4.3527888924
H,0,-2.544374924,7.0094357553,3.6789024036
H,0,-5.4686622544,5.4910550782,1.1437798484
H,0,-5.5916688798,5.2947306106,2.8970671985
```

Aldol Transition States re face, trans, A

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-trans-A-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95527120

```
 Zero-point correction=                           0.397863 (Hartree/Particle)
 Thermal correction to Energy=                    0.420807
 Thermal correction to Enthalpy=                  0.421751
 Thermal correction to Gibbs Free Energy=         0.341315
 Sum of electronic and zero-point Energies=          -1201.557408
 Sum of electronic and thermal Energies=             -1201.534464
```

```
Sum of electronic and thermal Enthalpies=           -1201.533520
Sum of electronic and thermal Free Energies=         -1201.613956

                    E (Thermal)             CV                S
                     KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total                   264.061              86.918             169.293

C,0,2.1576687627,-1.3826309739,0.7171384712
C,0,3.2310744664,-1.6046636742,-0.1372561962
C,0,4.0547201617,-0.5248786152,-0.4778583065
C,0,3.825826341,0.7613217138,0.0239628265
C,0,2.7423208767,0.9633182437,0.871252769
C,0,1.8877433293,-0.0976135398,1.2196970862
N,0,5.1857045566,-0.7475557881,-1.3676266561
O,0,5.9190896293,0.2115553617,-1.6439730234
C,0,0.7353097726,0.1247440838,2.1665795147
O,0,0.2590580635,-0.8600149359,2.816556304
O,0,5.3700161874,-1.8871384139,-1.816719557
C,0,-0.7772061508,0.7680702119,0.8881573297
C,0,-1.2306228983,-0.5249586908,0.3120817414
N,0,-2.7252663174,-0.6434958335,-0.0905326705
C,0,-3.6292649964,-0.4943213542,1.1164062579
C,0,-5.1097071504,-0.6506574543,0.6593768041
C,0,-0.2954399756,1.8512088726,0.0539336945
O,0,0.0773503782,1.4634880958,-1.2031656792
C,0,0.6330824101,2.4806714236,-2.0556571465
O,0,-0.1491231142,3.0193744149,0.4314100056
C,0,-2.9477468358,-2.0212962492,-0.6873897759
C,0,-4.4496597098,-2.1789497264,-1.0615882967
C,0,-3.1117925874,0.3950169737,-1.122087135
C,0,-4.5956051952,0.1654095285,-1.5341994843
H,0,0.7804068931,1.1206468799,2.6409163311
H,0,-0.6797802207,-0.7795798303,-0.5938892496
H,0,-1.0943443056,-1.3159559431,1.0595324305
H,0,-2.4182002937,0.2875086751,-1.9568345105
H,0,-2.9553751629,1.3704830467,-0.6619469748
H,0,-3.4330185067,0.4862511385,1.5485158393
H,0,-3.3257723811,-1.2600027021,1.832489716
H,0,-2.2920285419,-2.0963220982,-1.5563471894
H,0,-2.6228418073,-2.7468332475,0.0601045543
H,0,-1.3425376333,1.1390336262,1.7372180091
H,0,0.8879561543,1.9729795683,-2.985815858
H,0,-0.100941325,3.2682592561,-2.2446038793
H,0,1.527085343,2.9187214418,-1.6066169098
```

H,0,4.4885381337,1.5744164919,-0.2443965201
H,0,2.5565306436,1.9553820618,1.2719987857
H,0,1.5186759135,-2.2066374795,1.015373919
H,0,3.4406431114,-2.5911728394,-0.5316266477
N,0,-5.1938277982,-0.9440868486,-0.7781158488
H,0,-5.5883876845,-1.462344055,1.2125388762
H,0,-5.6656521152,0.2682681341,0.8606513461
H,0,-5.1799003068,1.0701907474,-1.3497927009
H,0,-4.6600071175,-0.06496518,-2.6003981554
H,0,-4.5489232276,-2.4140129429,-2.1240083399
H,0,-4.8987087686,-2.9958865758,-0.4916819013

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-trans-A-M06-PCM-methanol
E(RM062X) = -1201.44832886

```
 Zero-point correction=                           0.402601 (Hartree/Particle)
 Thermal correction to Energy=                    0.423889
 Thermal correction to Enthalpy=                  0.424833
 Thermal correction to Gibbs Free Energy=         0.351662
 Sum of electronic and zero-point Energies=          -1201.045727
 Sum of electronic and thermal Energies=             -1201.024440
 Sum of electronic and thermal Enthalpies=           -1201.023496
 Sum of electronic and thermal Free Energies=        -1201.096667

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  265.994             83.690            154.002
```

C,0,1.978731952,-1.3589490383,0.7144557567
C,0,2.8933097882,-1.5328680389,-0.3147809902
C,0,3.6634973754,-0.4393513432,-0.7049048589
C,0,3.5574923287,0.8090296852,-0.0978845501
C,0,2.6297417776,0.9662284115,0.9229006858
C,0,1.8264506633,-0.1076207703,1.3241927265
N,0,4.6312151816,-0.6129990665,-1.7890402953
O,0,5.3071252565,0.3498665917,-2.1202042366
C,0,0.8150242759,0.0753273536,2.4138248899
O,0,0.3366546925,-0.9006096426,3.0195075378
O,0,4.7166953456,-1.7124725068,-2.315949854
C,0,-0.8415141796,0.811206701,1.0643401068
C,0,-1.2216245134,-0.5070648392,0.5301388597
N,0,-2.6488393058,-0.6456681685,-0.0322400742

```
C,0,-3.6731742164,-0.4697916629,1.0518973928
C,0,-5.0783552947,-0.4635970651,0.40003731
C,0,-0.2425081045,1.8202625865,0.2548363943
O,0,0.1623908353,1.3742223766,-0.9737582105
C,0,0.8322994072,2.3240521723,-1.7974702414
O,0,-0.0069591134,2.982382918,0.6019487134
C,0,-2.8086595981,-2.0206549118,-0.6193086496
C,0,-4.2954954402,-2.2245411458,-1.0009380943
C,0,-2.9083474061,0.3668276677,-1.1129616115
C,0,-4.2621342876,0.0261944786,-1.7836142307
H,0,0.8239735659,1.0804254396,2.8678631382
H,0,-0.5748491569,-0.7997944246,-0.3015813597
H,0,-1.1677364694,-1.2707263545,1.3190288045
H,0,-2.0643311634,0.3251156923,-1.8036870937
H,0,-2.9109802696,1.3440578524,-0.6261609074
H,0,-3.4487064236,0.4657373647,1.5651091253
H,0,-3.5351515632,-1.3007404703,1.7480114693
H,0,-2.1441647031,-2.0682181533,-1.4851538992
H,0,-2.4645865912,-2.736537645,0.1297870637
H,0,-1.3462170166,1.1826092563,1.9492222165
H,0,1.1460794434,1.7772013957,-2.6862937783
H,0,0.1572465869,3.1380086676,-2.0748276111
H,0,1.7024277416,2.7405093585,-1.2855197163
H,0,4.1872950077,1.6276653009,-0.4250759978
H,0,2.5158294394,1.9328245557,1.4060198532
H,0,1.3673789401,-2.188800422,1.0552113026
H,0,3.0192907666,-2.4889658066,-0.8081381269
N,0,-5.0096023651,-0.9457641503,-0.9812796405
H,0,-5.7545781103,-1.1017145438,0.973191213
H,0,-5.492543609,0.5476950257,0.3898691251
H,0,-4.8585629444,0.9345010332,-1.8949474639
H,0,-4.1033711434,-0.3991513031,-2.7777588142
H,0,-4.3656441969,-2.6622295205,-1.9991279952
H,0,-4.7843941857,-2.9027758919,-0.2970213832
```

Aldol Transition States re face, trans, B

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-trans-B-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95241836

```
 Zero-point correction=                   0.397463 (Hartree/Particle)
 Thermal correction to Energy=                 0.419538
```

```
Thermal correction to Enthalpy=                 0.420482
Thermal correction to Gibbs Free Energy=        0.343818
Sum of electronic and zero-point Energies=        -1201.554955
Sum of electronic and thermal Energies=           -1201.532881
Sum of electronic and thermal Enthalpies=         -1201.531937
Sum of electronic and thermal Free Energies=      -1201.608601

                E (Thermal)           CV                S
                 KCal/Mol       Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              263.264           85.107          161.354
```

```
C,0,2.2271446379,-1.1295320388,1.0162013972
C,0,1.8098689291,-0.9854286548,-0.3180257031
C,0,2.6805195738,-0.3906444771,-1.2451404079
C,0,3.9333135214,0.0688727326,-0.8534736247
C,0,4.3175964595,-0.0818964879,0.4834674892
C,0,3.4760496018,-0.6818700593,1.4286291521
C,0,0.4721991309,-1.5221096544,-0.7619503183
O,0,0.2374601441,-1.7183081679,-1.9926133364
N,0,5.6299320835,0.3901277198,0.9021014415
O,0,5.9599667896,0.2459910654,2.0873841575
C,0,-0.8034348095,-0.056206707,0.0318984771
C,0,-0.3293260951,1.2196090818,-0.46653553
O,0,0.4468693617,1.9787330752,0.1241214497
C,0,-2.076127267,-0.6498645536,-0.4722931886
N,0,-3.4083685487,-0.1084063806,0.1218884525
C,0,-3.4975897699,-0.4097462872,1.6040519669
C,0,-4.8346288795,0.1660515145,2.1550239079
N,0,-5.6705309866,0.6986287217,1.0690955526
C,0,-5.8991127928,-0.3598345568,0.0752336123
C,0,-4.560480017,-0.8054275495,-0.5793149594
C,0,-3.5593724468,1.385252485,-0.0770668231
C,0,-4.968175515,1.8174502051,0.4238709721
O,0,-0.7622351865,1.501408602,-1.7339973461
O,0,6.3661837883,0.9194894022,0.0583005996
H,0,0.0601910123,-2.2313132097,-0.0164463457
H,0,-2.1702592818,-0.5168307317,-1.5499576538
H,0,-2.1231225804,-1.7190809038,-0.2501862596
H,0,-3.4055833406,1.5861211536,-1.1371253097
H,0,-2.7583056449,1.8603999275,0.4883619511
H,0,-2.6257168294,0.0404908845,2.0777013997
H,0,-3.4343364788,-1.4944994973,1.708183178
H,0,-4.4974060971,-0.5296114812,-1.6333336028
H,0,-4.3890602432,-1.8792857293,-0.4883300972
```

```
H,0,-0.5951288862,-0.1834912114,1.0902743313
H,0,3.8040249359,-0.7942885485,2.4542789672
H,0,1.5663589715,-1.6026665076,1.7375373025
H,0,2.3633458377,-0.3037882378,-2.2786534141
H,0,4.6090711994,0.5312574413,-1.5620789821
H,0,-5.3892242399,-0.6168039787,2.6779660847
H,0,-4.6366272773,0.9712273825,2.8666395958
H,0,-4.872519234,2.6364883883,1.1409110008
H,0,-5.5764209021,2.1716545167,-0.412053961
H,0,-6.5823023298,0.014043533,-0.6910588011
H,0,-6.3802468183,-1.2054991312,0.5724830186
C,0,-0.2808738451,2.7215283327,-2.324213489
H,0,-0.7335245523,2.7637763034,-3.3148758549
H,0,-0.5890766569,3.5864293271,-1.7311135153
H,0,0.8082715736,2.7095349468,-2.4067469336
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-trans-B-M06-PCM-methanol
E(RM062X) = -1201.44547366

```
 Zero-point correction=                           0.402300 (Hartree/Particle)
 Thermal correction to Energy=                    0.424632
 Thermal correction to Enthalpy=                  0.425576
 Thermal correction to Gibbs Free Energy=         0.348860
 Sum of electronic and zero-point Energies=          -1201.043174
 Sum of electronic and thermal Energies=             -1201.020842
 Sum of electronic and thermal Enthalpies=           -1201.019898
 Sum of electronic and thermal Free Energies=        -1201.096614

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.460             85.803           161.463
```

```
C,0,2.3352079537,-1.1273056763,0.9557783768
C,0,1.7184237404,-1.1113030982,-0.2989524862
C,0,2.3236802302,-0.4372106994,-1.3642557332
C,0,3.5296798193,0.2274353426,-1.1820015913
C,0,4.1193382376,0.1920856853,0.079133577
C,0,3.5447300363,-0.4779552307,1.1571161717
C,0,0.4168961312,-1.8227253858,-0.5118979894
O,0,-0.0024140374,-2.0624842517,-1.663897863
N,0,5.3929889154,0.8818269664,0.279968384
O,0,5.9013089751,0.8457243428,1.391219727
```

```
C,0,-0.8564753287,-0.2945823709,0.4338986002
C,0,-0.2135693381,0.9349086555,0.076855705
O,0,0.5617019627,1.5843528401,0.7807536756
C,0,-2.0655294662,-0.7684420613,-0.2751704646
N,0,-3.4075578021,-0.1340570781,0.1341177653
C,0,-3.636909405,-0.2781396862,1.6128434236
C,0,-5.0948869084,0.1418191198,1.9249544003
N,0,-5.6887460338,0.8421789328,0.7831547074
C,0,-5.8471987864,-0.1050501985,-0.3223746348
C,0,-4.5165206447,-0.8473093102,-0.5927597166
C,0,-3.4694129365,1.3256178088,-0.2179501704
C,0,-4.7826552659,1.9110400208,0.3590562158
O,0,-0.4621898678,1.3148038759,-1.21251534
O,0,5.8925518519,1.4646363753,-0.6715659462
H,0,0.1341779151,-2.4807241554,0.3304765143
H,0,-1.9825132009,-0.5976638272,-1.3513924537
H,0,-2.22663518,-1.8388817897,-0.1090428761
H,0,-3.4151532899,1.3866956292,-1.3072831042
H,0,-2.5860057902,1.8030547577,0.205442302
H,0,-2.9014854197,0.3604166229,2.1049574428
H,0,-3.4327692748,-1.3186433074,1.8749095162
H,0,-4.2517377157,-0.8658501461,-1.6518196419
H,0,-4.5266598444,-1.8720151591,-0.2145445989
H,0,-0.742049095,-0.5608847549,1.4805405453
H,0,4.0389836095,-0.4843022318,2.1208200054
H,0,1.8592721417,-1.6490655352,1.7821135241
H,0,1.8333916124,-0.440817822,-2.332490363
H,0,4.0124629248,0.7589156249,-1.9933406906
H,0,-5.7091930868,-0.7343147384,2.1472400829
H,0,-5.1104703901,0.7979296479,2.7979304076
H,0,-4.5707598417,2.5449122119,1.2238141308
H,0,-5.277269248,2.5247213695,-0.397026493
H,0,-6.1657759561,0.4499304543,-1.2079854139
H,0,-6.6285571669,-0.8261473904,-0.0728659709
C,0,0.2078997458,2.4929209038,-1.6541543248
H,0,-0.0800607366,2.6261157961,-2.69630849
H,0,-0.1033085819,3.3588345622,-1.0640253587
H,0,1.2910238366,2.3731303585,-1.5724534857
```

Aldol Transition States re face, trans, C

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-trans-C-Becke-631Gdp-PCM-methanol

```
E(RB3LYP) = -1201.95064107

 Zero-point correction=                           0.398149 (Hartree/Particle)
 Thermal correction to Energy=                    0.420847
 Thermal correction to Enthalpy=                  0.421791
 Thermal correction to Gibbs Free Energy=         0.343790
 Sum of electronic and zero-point Energies=         -1201.552492
 Sum of electronic and thermal Energies=            -1201.529794
 Sum of electronic and thermal Enthalpies=          -1201.528850
 Sum of electronic and thermal Free Energies=       -1201.606851

                E (Thermal)             CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total            264.086             86.877            164.168

 N,0,-5.3423969693,-0.6984968299,-1.2183467522
 C,0,-5.3506772581,-0.6076937703,0.2488648319
 C,0,-3.9099441533,-0.720394957,0.825590472
 N,0,-2.9211274855,-0.6949288562,-0.322731891
 C,0,-3.1682287031,-1.9167547331,-1.1895634848
 C,0,-4.6629402977,-1.938701141,-1.6195094898
 C,0,-4.6058979582,0.4499173201,-1.766242958
 C,0,-3.1758480642,0.5426594431,-1.1585527663
 C,0,-1.4547881704,-0.7546001866,0.2033478557
 C,0,-0.9667062495,0.3979295775,1.0179060637
 C,0,-0.5214818285,1.6157814701,0.3593070507
 O,0,-0.5211922822,2.7372543941,0.867563777
 O,0,0.0118264352,1.3958031369,-0.8810657488
 C,0,0.5561360297,2.540303901,-1.5618327934
 C,0,0.8163629533,-0.1877497344,1.8645652462
 O,0,1.4624381919,0.820703664,2.2976929545
 C,0,0.282398487,-1.1875424797,2.8667781856
 C,0,-0.1291750531,-0.7625562792,4.1428632561
 C,0,-0.5832474757,-1.6734763195,5.0872730757
 C,0,-0.6091041917,-3.034340068,4.7530398867
 C,0,-0.188442041,-3.4918450515,3.5016497594
 C,0,0.2557339474,-2.5597163724,2.5667184218
 N,0,-1.0790082049,-3.9989871937,5.7391817685
 O,0,-1.4490800008,-3.5808613698,6.8441729335
 O,0,-1.0922195991,-5.198885046,5.4334776897
 H,0,1.1667129642,-0.6868189485,0.9398517349
 H,0,-0.8485252381,-0.8913652153,-0.693415525
 H,0,-1.4424701024,-1.6822523447,0.7799466372
 H,0,-2.3952105077,0.584345918,-1.918493889
```

H,0,-3.0649228517,1.4002812265,-0.4952172581
H,0,-3.6629920017,0.1090686069,1.4874507101
H,0,-3.7449845198,-1.6583921543,1.3589162329
H,0,-2.4900816138,-1.8379408631,-2.0409271832
H,0,-2.8898731537,-2.7919823614,-0.6001645315
H,0,-1.5297039611,0.6183085441,1.9206279184
H,0,0.9143735845,2.16594696,-2.5207248173
H,0,-0.2135677417,3.3006321065,-1.7169413566
H,0,1.3823742142,2.9713374309,-0.9916429004
H,0,-0.2041975293,-4.5506695029,3.2758330299
H,0,0.6050534901,-2.9060831875,1.597958686
H,0,-0.0822628774,0.2942718125,4.3831172005
H,0,-0.9094700927,-1.3510352187,6.0681543925
H,0,-5.9753445083,-1.4082599353,0.652398238
H,0,-5.8010572148,0.3463331389,0.533393394
H,0,-5.1614518722,1.3650700009,-1.5478072454
H,0,-4.5516850949,0.3398408188,-2.8520968887
H,0,-4.735707637,-2.0496489215,-2.7040977245
H,0,-5.1810077923,-2.7833434293,-1.158882199

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-trans-C-M06-PCM-methanol
E(RM062X) = -1201.44159586

```
 Zero-point correction=                           0.402412 (Hartree/Particle)
 Thermal correction to Energy=                    0.424787
 Thermal correction to Enthalpy=                  0.425731
 Thermal correction to Gibbs Free Energy=         0.348481
 Sum of electronic and zero-point Energies=          -1201.039183
 Sum of electronic and thermal Energies=             -1201.016809
 Sum of electronic and thermal Enthalpies=           -1201.015865
 Sum of electronic and thermal Free Energies=        -1201.093115

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.558             85.748            162.588
```

N,0,-5.2980052226,-0.6848618477,-1.3125198421
C,0,-5.3800873906,-0.4066617536,0.1228851936
C,0,-4.0030315881,-0.6193752935,0.7996429396
N,0,-2.9544202541,-0.7053346077,-0.27373639
C,0,-3.1900185915,-1.9589990518,-1.0716180203
C,0,-4.6757729965,-1.9965031998,-1.5040984956

```
C,0,-4.4556059331,0.3345773643,-1.9430336469
C,0,-3.1081938961,0.476112889,-1.191881697
C,0,-1.5399082821,-0.7680151573,0.3478575198
C,0,-1.0997604133,0.4126809229,1.1223794288
C,0,-0.6219178236,1.5933188025,0.4679377912
O,0,-0.5597435537,2.7172428703,0.9619651468
O,0,-0.1133260824,1.3508869659,-0.7790752969
C,0,0.4357531204,2.4762151023,-1.4601501167
C,0,0.8988118481,-0.1156624557,1.8982912304
O,0,1.4666303274,0.9113489076,2.3190343204
C,0,0.372083424,-1.1435248762,2.8599757559
C,0,0.0157485798,-0.769886092,4.1622108547
C,0,-0.451822641,-1.7149458364,5.0629691764
C,0,-0.5436467434,-3.041826268,4.643263684
C,0,-0.1773486958,-3.4501530448,3.3653942313
C,0,0.2856429872,-2.4859122148,2.4765843823
N,0,-1.0364371253,-4.045384709,5.5875076503
O,0,-1.3375922229,-3.6797688822,6.7138681459
O,0,-1.1265904676,-5.2027739956,5.2055678268
H,0,1.1643504765,-0.5345452169,0.9091148644
H,0,-0.8811095415,-0.9628174668,-0.5039453131
H,0,-1.5878593078,-1.6651143113,0.9735554173
H,0,-2.244398327,0.4841206253,-1.8586081234
H,0,-3.0726293949,1.3679573084,-0.5627770552
H,0,-3.7298049889,0.2073678559,1.4559344048
H,0,-3.9523220323,-1.555447063,1.3614788868
H,0,-2.5075619782,-1.918862558,-1.9236445757
H,0,-2.9162219609,-2.8057999624,-0.4390317003
H,0,-1.5899897603,0.60936119,2.0708536675
H,0,0.7868606412,2.1001978052,-2.4204947852
H,0,-0.3261685747,3.2446460377,-1.6136800324
H,0,1.2677276332,2.9031183874,-0.8956609732
H,0,-0.2485631217,-4.4935248249,3.0834526185
H,0,0.5915057156,-2.7822587865,1.4764980607
H,0,0.1088127166,0.2716646821,4.4531732942
H,0,-0.7392948845,-1.4438683289,6.0714930054
H,0,-6.1208622128,-1.0677122277,0.5781646828
H,0,-5.7186638125,0.6240046944,0.2541307009
H,0,-4.98245406,1.2914041753,-1.9380678228
H,0,-4.2871687382,0.0457314911,-2.9834958862
H,0,-4.7476258427,-2.2815362098,-2.5560875032
H,0,-5.2306110069,-2.7304148354,-0.9141936053
```

Aldol Transition States re face, trans, D

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-trans-D-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95321923

```
 Zero-point correction=                           0.397967 (Hartree/Particle)
 Thermal correction to Energy=                    0.420810
 Thermal correction to Enthalpy=                  0.421755
 Thermal correction to Gibbs Free Energy=         0.342807
 Sum of electronic and zero-point Energies=         -1201.555252
 Sum of electronic and thermal Energies=            -1201.532409
 Sum of electronic and thermal Enthalpies=          -1201.531465
 Sum of electronic and thermal Free Energies=       -1201.610412

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.063             86.899           166.159
```

```
C,0,-1.3651800645,-0.6968680582,5.8484072598
C,0,-0.382949461,0.2577517863,5.5381520229
C,0,0.9698042287,-0.0609055117,5.7553259886
C,0,1.3428301663,-1.3043324357,6.249561687
C,0,0.3407880498,-2.2426532499,6.5293132928
C,0,-1.0133460341,-1.9520532112,6.3362643051
C,0,-0.7839735262,1.6268193862,5.0284003175
O,0,-1.9897111864,2.0120324297,5.1670478349
N,0,0.719398669,-3.5519576766,7.0440497042
O,0,1.9216340668,-3.7941751239,7.2159960626
O,0,-0.1747991525,-4.3734235525,7.2874272573
C,0,-1.1368550641,1.0535957017,0.0578938139
N,0,-1.5723115486,0.0827716718,1.1369849669
C,0,-2.9794029968,-0.3912218021,0.8187727469
C,0,-2.9652599616,-1.14640774,-0.5407724545
N,0,-1.6435803453,-1.0576116305,-1.1774745492
C,0,-1.2767693632,0.3578410795,-1.3273733567
C,0,-0.6502809639,-1.7240870199,-0.3231716061
C,0,-0.6482895764,-1.118754058,1.1107378346
C,0,-1.5867116434,0.7386161159,2.5417288546
C,0,-0.314752989,1.3396978702,3.0375816762
C,0,0.0819406663,2.6818842968,2.6515812953
O,0,-0.9529214751,3.4601346807,2.2181925975
C,0,-0.6480582935,4.8359648789,1.9258060915
O,0,1.2215139364,3.1435234213,2.7763019081
H,0,-1.5905636371,5.2814007449,1.6080523098
```

```
H,0,-0.2693945661,5.3448649152,2.8153037381
H,0,0.0923629365,4.905432153,1.1250567017
H,0,-1.9137329716,-0.0724703516,3.1974689642
H,0,-2.3784731714,1.4864342875,2.5023900731
H,0,-1.7618209927,1.9413263609,0.1526296498
H,0,-0.1056443078,1.3268613012,0.2800826601
H,0,0.3397914121,-0.7734768167,1.4134130305
H,0,-1.0228536003,-1.8179166536,1.8603364914
H,0,-3.297218906,-1.0266527955,1.6469185896
H,0,-3.6114466148,0.4980403452,0.7970581118
H,0,0.5418928977,0.6775691278,3.1111901682
H,0,-3.7122470169,-0.7171669619,-1.2129009525
H,0,-3.2100361051,-2.2010261757,-0.3934454959
H,0,-2.0459769411,0.8529848064,-1.9249881533
H,0,-0.3321713803,0.4227625111,-1.8727342965
H,0,0.3338850144,-1.6117567924,-0.7843114518
H,0,-0.8803970612,-2.7912737579,-0.2758109696
H,0,0.0365835359,2.3556606243,5.1655685859
H,0,1.736615887,0.6772315282,5.5360782385
H,0,2.3824965233,-1.5523874086,6.4223150036
H,0,-1.7658611699,-2.6940420629,6.5725753572
H,0,-2.4090149021,-0.4330891776,5.7159510943
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-trans-D-M06-PCM-methanol
E(RM062X) = -1201.44445184

```
 Zero-point correction=                           0.402923 (Hartree/Particle)
 Thermal correction to Energy=                    0.425287
 Thermal correction to Enthalpy=                  0.426232
 Thermal correction to Gibbs Free Energy=         0.348842
 Sum of electronic and zero-point Energies=          -1201.041529
 Sum of electronic and thermal Energies=             -1201.019164
 Sum of electronic and thermal Enthalpies=           -1201.018220
 Sum of electronic and thermal Free Energies=        -1201.095609

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.872             85.553            162.879
```

```
C,0,-1.3618072743,-0.7964867766,5.8042888165
C,0,-0.4983676856,0.2819744171,5.5893481277
C,0,0.8545508645,0.1712465349,5.9354968739
```

```
C,0,1.3525428471,-1.0060489729,6.4724628224
C,0,0.4704348152,-2.0706967259,6.6566679001
C,0,-0.8804681536,-1.9887728196,6.3339475051
C,0,-1.0305891633,1.5668827781,5.01933826
O,0,-2.2595026811,1.7751125778,4.9635933093
N,0,0.9845469489,-3.319674743,7.2189182709
O,0,2.1716007807,-3.379125006,7.5031467774
O,0,0.2044772077,-4.2470499723,7.3776221122
C,0,-1.1002951842,1.0334119247,0.0611471187
N,0,-1.6256109921,0.0473477833,1.0677622304
C,0,-3.0499501762,-0.2833154503,0.7104174542
C,0,-3.0543480467,-1.0651665579,-0.6248193452
N,0,-1.7592803646,-0.9348980203,-1.2969353132
C,0,-1.4005899635,0.4854534609,-1.3552131711
C,0,-0.7472033594,-1.6444112709,-0.5098804677
C,0,-0.8084758042,-1.2110762349,0.9753463756
C,0,-1.5856624462,0.6151936443,2.4939571135
C,0,-0.2816694627,1.1068520871,2.9834777048
C,0,0.1973813261,2.4217848785,2.6944924786
O,0,-0.7709280539,3.2689920102,2.2360816988
C,0,-0.3759475486,4.6256152925,2.042342036
O,0,1.3391664107,2.8378153507,2.9103703951
H,0,-1.2606483737,5.1417301156,1.6720779238
H,0,-0.0466800757,5.0707630827,2.9841537743
H,0,0.4334512689,4.6916686513,1.3115508435
H,0,-1.9516556825,-0.2113886856,3.1151310719
H,0,-2.3335442308,1.4118147276,2.5117440063
H,0,-1.5794336166,1.9921056157,0.2649304361
H,0,-0.0300600259,1.1317969767,0.253674551
H,0,0.177311312,-0.9914644463,1.3865638484
H,0,-1.3033703264,-1.9517130371,1.6085823355
H,0,-3.4685105825,-0.8599856432,1.5374351025
H,0,-3.5811126349,0.668430144,0.6398248375
H,0,0.503124998,0.3871024766,3.186444811
H,0,-3.8416855216,-0.6789602235,-1.2759526664
H,0,-3.246858477,-2.1268244471,-0.4507373442
H,0,-2.231168794,1.0303794053,-1.8112722471
H,0,-0.5224745382,0.6101322176,-1.9927041055
H,0,0.2349272602,-1.4238009588,-0.9354736278
H,0,-0.9163154612,-2.720662908,-0.5876562595
H,0,-0.3186220058,2.4075417843,5.1001622848
H,0,1.519626181,1.0153555903,5.7719108315
H,0,2.3954698089,-1.1078095001,6.7461107021
H,0,-1.5321814904,-2.837388154,6.502526152
```

```
H,0,-2.4140628325,-0.6842909735,5.5625286543
```

Aldol Transition States re face, trans, E

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-trans-E-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95484181

```
Zero-point correction=                          0.397871 (Hartree/Particle)
Thermal correction to Energy=                   0.420715
Thermal correction to Enthalpy=                 0.421659
Thermal correction to Gibbs Free Energy=        0.342478
Sum of electronic and zero-point Energies=         -1201.556971
Sum of electronic and thermal Energies=            -1201.534127
Sum of electronic and thermal Enthalpies=          -1201.533183
Sum of electronic and thermal Free Energies=       -1201.612364

                E (Thermal)             CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              264.003             86.915            166.651
```

```
C,0,-0.3911837096,-0.7966493608,1.4079163831
N,0,-1.5106621168,0.1949878335,1.1657238278
C,0,-1.2028723756,0.9814268356,-0.0917558179
C,0,-1.1138094559,-0.0049532355,-1.2935058826
N,0,-1.2721791179,-1.3976837595,-0.8513411099
C,0,-0.243958048,-1.7057139143,0.1524268533
C,0,-2.6008776187,-1.5629336283,-0.2458447813
C,0,-2.7960615023,-0.5814064567,0.9452384563
C,0,-1.7103696576,1.1249584015,2.3925393139
C,0,-0.5752140775,2.0120611083,2.7654374669
C,0,-0.436810481,3.3292281782,2.1768097822
O,0,0.6178934574,3.9646166947,2.0761123735
O,0,-1.6310953241,3.8829342409,1.7941686064
C,0,-1.5800689211,5.2160832158,1.257238353
C,0,-1.064244609,2.2289527147,4.8130655826
O,0,-1.4391612063,1.0889041399,5.2319740056
C,0,0.2331638455,2.8165670526,5.2969753745
C,0,1.2518152641,1.9838702235,5.7943682072
C,0,2.4364541724,2.5200552871,6.2815591173
C,0,2.5951380022,3.9123495271,6.2839732105
C,0,1.5944155474,4.766951128,5.8101207332
C,0,0.4185964443,4.2088012166,5.3195781569
```

```
N,0,3.8297407248,4.4844291194,6.8005743205
O,0,4.7072685578,3.7172999332,7.2206197561
O,0,3.9579970441,5.7166523269,6.7992772913
H,0,-2.6105717293,5.4699333234,1.0087045534
H,0,-1.1864218115,5.9175409255,1.9968330195
H,0,-0.9560436015,5.2486149911,0.3605463427
H,0,-1.9265238374,0.440538878,3.2211289949
H,0,-2.6077853175,1.7002798651,2.1602446832
H,0,-1.9985410793,1.718465369,-0.2086229477
H,0,-0.2635388395,1.5044704129,0.0864379403
H,0,0.512790793,-0.2227797226,1.6080244554
H,0,-0.6572468793,-1.357841252,2.3054316361
H,0,-3.0211741103,-1.0963517646,1.8805217988
H,0,-3.5782342981,0.1552618332,0.7548715004
H,0,0.3862277791,1.5292001946,2.9109791492
H,0,-3.3614386025,-1.3814043291,-1.0090833186
H,0,-2.7034880711,-2.5967087293,0.092956006
H,0,-1.8938030801,0.2186542157,-2.0253926694
H,0,-0.1462706704,0.0984975309,-1.7906409512
H,0,0.7391304359,-1.564577487,-0.3030843148
H,0,-0.3344795067,-2.756270569,0.4388757749
H,0,-1.8253510926,3.0056835464,4.6147326602
H,0,-0.3690805858,4.8620026366,4.9562206677
H,0,1.7402322115,5.8395361211,5.8331894492
H,0,3.2272791774,1.8848708687,6.6606123106
H,0,1.0965038775,0.9104063192,5.7969986786
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-trans-E-M06-PCM-methanol
E(RM062X) = -1201.44500905

```
 Zero-point correction=                           0.402102 (Hartree/Particle)
 Thermal correction to Energy=                    0.424719
 Thermal correction to Enthalpy=                  0.425663
 Thermal correction to Gibbs Free Energy=         0.345258
 Sum of electronic and zero-point Energies=         -1201.042907
 Sum of electronic and thermal Energies=            -1201.020290
 Sum of electronic and thermal Enthalpies=          -1201.019346
 Sum of electronic and thermal Free Energies=       -1201.099751

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.515             85.970           169.227
```

```
C,0,-0.2789550464,-0.7238847858,1.1777446483
N,0,-1.4924767617,0.1615941419,1.1648560287
C,0,-1.4352898267,1.0318326275,-0.0582530644
C,0,-1.1880564839,0.1258739561,-1.2899588266
N,0,-1.4176210737,-1.2814837312,-0.953258394
C,0,-0.3858028703,-1.7147905489,-0.0076220391
C,0,-2.7268781762,-1.4037292719,-0.3084816189
C,0,-2.7155830627,-0.7086843776,1.0750913882
C,0,-1.5722356947,1.0095171847,2.4538897884
C,0,-0.3869381265,1.8244062988,2.7732244418
C,0,-0.2021754903,3.1355025212,2.256510724
O,0,0.8479899525,3.7870372008,2.2534197839
O,0,-1.3646015051,3.7076820191,1.7954036783
C,0,-1.2502155237,5.0373603954,1.2989356492
C,0,-1.1348190165,2.1924705752,4.9489123172
O,0,-1.486811016,1.0826404355,5.3741551292
C,0,0.1472689473,2.8301462425,5.376489765
C,0,1.1413558247,2.0615714826,5.9955093201
C,0,2.3169896505,2.6531681523,6.43068529
C,0,2.4707288772,4.02784528,6.2494452961
C,0,1.4972463127,4.8198123913,5.6501541029
C,0,0.3309300997,4.2055036401,5.2095980696
N,0,3.7033339956,4.6635551343,6.716285578
O,0,4.5640302139,3.9549116578,7.2171831509
O,0,3.8172410616,5.8731263923,6.5836404592
H,0,-2.2474350122,5.3150865191,0.9589457437
H,0,-0.917408669,5.721157881,2.0839003506
H,0,-0.5436274016,5.0811745976,0.4663462625
H,0,-1.7665563977,0.2728016962,3.2427080976
H,0,-2.4643534532,1.627278521,2.3153562126
H,0,-2.3874072955,1.5655856317,-0.1072729467
H,0,-0.6342235699,1.7553749076,0.0964847417
H,0,0.5871569306,-0.0655337883,1.0975887098
H,0,-0.2517221586,-1.2267327629,2.1472448459
H,0,-2.6508363462,-1.4219474589,1.9000162233
H,0,-3.585435138,-0.0675016137,1.2306057075
H,0,0.5249372743,1.3175763352,3.0709414399
H,0,-3.4762353444,-0.9500390295,-0.961971733
H,0,-2.9749891913,-2.4608245014,-0.1892638796
H,0,-1.8566844249,0.4158243177,-2.1034864271
H,0,-0.1588586474,0.2300384016,-1.6428115023
H,0,0.57468483,-1.7766131937,-0.5240132488
H,0,-0.6453916008,-2.7149170796,0.3482553451
```

H,0,-1.8761810344,2.8996853773,4.5350442303
H,0,-0.4440986238,4.8003433152,4.7339664863
H,0,1.6561109714,5.8847515076,5.5330794084
H,0,3.0997501466,2.0767539199,6.9083256091
H,0,0.9762348949,0.9975034852,6.1301846567

Aldol Transition States re face, trans, F

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-re-trans-F-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95074233

```
 Zero-point correction=                           0.398063 (Hartree/Particle)
 Thermal correction to Energy=                    0.420796
 Thermal correction to Enthalpy=                  0.421740
 Thermal correction to Gibbs Free Energy=         0.343528
 Sum of electronic and zero-point Energies=         -1201.552680
 Sum of electronic and thermal Energies=            -1201.529947
 Sum of electronic and thermal Enthalpies=          -1201.529003
 Sum of electronic and thermal Free Energies=       -1201.607214

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.053             86.864            164.610
```

C,0,-0.3091711099,-1.1205760423,0.9795678886
N,0,-1.4602855673,-0.1413609078,0.8582357101
C,0,-1.0874497618,0.9254636124,-0.1510103427
C,0,-0.7876188889,0.2424267587,-1.5176044244
N,0,-0.9528949599,-1.2149339327,-1.4333686446
C,0,-0.0336658141,-1.7488112466,-0.4189531037
C,0,-2.3351739932,-1.5213005439,-1.0418185675
C,0,-2.6754678115,-0.8918634169,0.3395462515
C,0,-1.8237012445,0.4711465202,2.2418824889
C,0,-0.768649426,1.2641728564,2.9455277394
C,0,-0.5520441162,2.6612712503,2.5965207773
O,0,0.4819064168,3.2939363773,2.820959231
O,0,-1.6511043281,3.2682336928,2.0543834916
C,0,-1.5306934134,4.6704102013,1.7554297232
C,0,-1.1891284339,1.2278334398,4.9242694389
O,0,-0.1618542162,1.5781613169,5.5928434421
C,0,-2.445744945,2.0670707056,5.0271115279
C,0,-2.3594486992,3.4197057628,5.3991336481

```
 C,0,-3.5013245201,4.2011131805,5.5267695744
 C,0,-4.7499615049,3.6126406992,5.2923144556
 C,0,-4.8720236059,2.2634444824,4.9433195069
 C,0,-3.7151498535,1.5013479747,4.8166277113
 N,0,-5.9533280667,4.4220021969,5.427509719
 O,0,-5.8324103441,5.6139848071,5.7408272404
 O,0,-7.0518310485,3.888308302,5.2209585718
 H,0,-2.4907523722,4.9609461764,1.3292729682
 H,0,-1.3311743216,5.2437741253,2.6635158028
 H,0,-0.7282657639,4.8431447404,1.0338215544
 H,0,-2.1085103387,-0.4056680394,2.8308719561
 H,0,-2.7146015708,1.0703732256,2.0520467416
 H,0,-1.9244622248,1.6221150661,-0.1995392558
 H,0,-0.2187339462,1.4487220491,0.246441851
 H,0,0.5482333842,-0.5644442989,1.3570886297
 H,0,-0.6021250594,-1.8642120774,1.7230004681
 H,0,-2.9268179506,-1.6432488829,1.0897873505
 H,0,-3.4905398214,-0.1688075562,0.2797946917
 H,0,0.1718728384,0.747960408,3.1113876309
 H,0,-3.0107957752,-1.1340006395,-1.8083976925
 H,0,-2.4569099263,-2.6063408641,-1.0015892359
 H,0,-1.4629935364,0.6273542404,-2.2854329321
 H,0,0.2367907476,0.4602913904,-1.8289752067
 H,0,0.9918993279,-1.5360806069,-0.7298110057
 H,0,-0.1543657411,-2.8337392463,-0.3732067085
 H,0,-1.4374494656,0.1488777991,4.8613998303
 H,0,-3.8030072135,0.4478668595,4.5669822692
 H,0,-5.8512348094,1.8289277523,4.7862232087
 H,0,-3.4391334728,5.2453517119,5.8067469298
 H,0,-1.3810897325,3.8453696204,5.5925140988
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-re-trans-F-M06-PCM-methanol
E(RM062X) = -1201.44441583

```
 Zero-point correction=                           0.402349 (Hartree/Particle)
 Thermal correction to Energy=                    0.424626
 Thermal correction to Enthalpy=                  0.425570
 Thermal correction to Gibbs Free Energy=         0.348898
 Sum of electronic and zero-point Energies=          -1201.042067
 Sum of electronic and thermal Energies=             -1201.019790
 Sum of electronic and thermal Enthalpies=           -1201.018846
 Sum of electronic and thermal Free Energies=        -1201.095518
```

	E (Thermal) KCal/Mol	CV Cal/Mol-Kelvin	S Cal/Mol-Kelvin
Total	266.457	85.668	161.370

```
C,0,-0.1787198622,-0.920936676,0.8701139842
N,0,-1.481380496,-0.170801851,0.9132359441
C,0,-1.4045243261,0.9691630891,-0.0645709384
C,0,-0.9492011553,0.405951449,-1.4342161237
N,0,-1.0388528127,-1.0559602567,-1.4521086029
C,0,-0.0545863791,-1.6027968039,-0.5151502653
C,0,-2.3788818908,-1.4504790428,-1.0134459343
C,0,-2.5827080132,-1.101178967,0.4802455365
C,0,-1.7866353271,0.3252821258,2.3405872637
C,0,-0.7322688411,1.1249368685,3.0070895966
C,0,-0.6171651869,2.5354999152,2.7764891884
O,0,0.3405959322,3.2414184635,3.090314253
O,0,-1.7476787805,3.0918915774,2.244784292
C,0,-1.7212074407,4.5042306839,2.056701145
C,0,-1.1865749179,1.1077929227,5.1095192458
O,0,-0.1641221644,1.4522340804,5.7398019793
C,0,-2.3877415894,2.0098417863,5.0647710036
C,0,-2.2349638655,3.3713200136,5.3501790762
C,0,-3.3228268207,4.2307251205,5.2847008783
C,0,-4.5651012518,3.6996596912,4.9462782576
C,0,-4.7562982347,2.3450937958,4.6855615639
C,0,-3.6536734242,1.5034544617,4.7502625952
N,0,-5.7189237929,4.596694469,4.8763698756
O,0,-5.5392038754,5.7873326477,5.085776739
O,0,-6.8099854021,4.1149351494,4.6085368666
H,0,-2.7090347695,4.7729278307,1.6834670792
H,0,-1.5224273799,5.0185706088,2.9996368589
H,0,-0.9546426815,4.7815937292,1.3280590255
H,0,-1.9915473959,-0.6022263182,2.8887663731
H,0,-2.7163810964,0.8924437242,2.2421756052
H,0,-2.398782886,1.4206086303,-0.0966553582
H,0,-0.701584279,1.6978849139,0.3392155206
H,0,0.6099404697,-0.1878834633,1.0458721322
H,0,-0.1857028827,-1.6377982543,1.6941857024
H,0,-2.51853289,-1.9798114278,1.1262261132
H,0,-3.5302384124,-0.5925163725,0.6684002701
H,0,0.2095499974,0.6337808575,3.2249478175
H,0,-3.1115159385,-0.9296179468,-1.6347537905
H,0,-2.5076440779,-2.524687057,-1.1634572342
H,0,-1.5765731359,0.8158687881,-2.2286915305
```

```
H,0,0.0862968831,0.6886510007,-1.6393677136
H,0,0.9496217832,-1.445006308,-0.9142348328
H,0,-0.2216985426,-2.6794421705,-0.4308338329
H,0,-1.4434360931,0.0364203962,5.0045974274
H,0,-3.779077224,0.4404278424,4.5594647534
H,0,-5.7442609644,1.9713219499,4.4458767958
H,0,-3.2235546572,5.2901896834,5.4894955795
H,0,-1.2485299082,3.7413556501,5.6107068188
```

Aldol Transition States si face, cis, A

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-cis-A-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95603982

```
 Zero-point correction=                           0.397666 (Hartree/Particle)
 Thermal correction to Energy=                    0.420585
 Thermal correction to Enthalpy=                  0.421529
 Thermal correction to Gibbs Free Energy=         0.341690
 Sum of electronic and zero-point Energies=          -1201.558374
 Sum of electronic and thermal Energies=             -1201.535455
 Sum of electronic and thermal Enthalpies=           -1201.534511
 Sum of electronic and thermal Free Energies=        -1201.614349

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  263.921             87.004            168.035
```

```
C,0,-3.6473522073,-1.5545965483,-0.5894843905
C,0,-2.4254454706,-1.7069388769,0.0532540868
C,0,-1.9841457007,-0.7624952117,0.9967210565
C,0,-2.8093141668,0.332055502,1.3037546371
C,0,-4.0395320981,0.4998124883,0.6774162437
C,0,-4.4439454139,-0.4475630244,-0.2690465847
C,0,-0.6824536627,-0.9599488342,1.725027488
O,0,-0.2033912229,-2.1277941101,1.859297904
N,0,-5.7297733928,-0.2832050525,-0.9316329116
O,0,-6.0771853657,-1.1292346728,-1.767139416
O,0,-6.4270160919,0.6973837808,-0.6369502504
C,0,0.6076841095,0.1025063258,0.4111334789
C,0,1.8817967138,-0.3443085929,1.0316560364
N,0,3.1594580489,-0.2955519511,0.1512286889
C,0,3.4218935025,1.0976560143,-0.3811349711
```

```
C,0,4.7836607354,1.0983673516,-1.134712402
C,0,0.2766264077,1.5094931084,0.4908453707
O,0,-0.587881438,1.9023987809,-0.4930927742
C,0,-1.0483389556,3.2640666524,-0.4398033504
O,0,0.6539027289,2.3007718489,1.3644310341
C,0,4.3422648562,-0.7148606682,1.0044449005
C,0,5.6171448603,-0.7668065242,0.1156306392
C,0,3.0533999074,-1.2522234596,-1.018905803
C,0,4.3452629911,-1.136675652,-1.8793412665
H,0,2.1231580155,0.2703831976,1.901630863
H,0,-1.7231852643,3.3766809686,-1.2882198473
H,0,-1.5810720723,3.458816785,0.4940483657
H,0,-0.2102488907,3.9598120114,-0.5297936553
H,0,1.801875115,-1.3925458039,1.3387890413
H,0,0.3063236752,-0.3864357212,-0.510137865
H,0,-0.5408994143,-0.2220610683,2.5364231787
H,0,-1.79820015,-2.5651056984,-0.1631462561
H,0,-3.9909437726,-2.2750361675,-1.3212352345
H,0,-4.6808328857,1.3396118001,0.9135485833
H,0,-2.4871373262,1.056044448,2.0467835961
H,0,2.9169656828,-2.2493472745,-0.5966712657
H,0,2.1587546491,-0.9833060031,-1.5795608817
H,0,2.5864260252,1.34584143,-1.0356037578
H,0,3.4095108357,1.7751415548,0.4733808846
H,0,4.4235656272,0.019355838,1.8078660219
H,0,4.0951092164,-1.6842300863,1.4401699832
N,0,5.3352888722,-0.2609883199,-1.2358454118
H,0,4.7867712778,-2.1259833912,-2.0222368671
H,0,4.1098689682,-0.7271111219,-2.8646908716
H,0,4.6519014078,1.5021282977,-2.1415493298
H,0,5.5080129074,1.7276653311,-0.6118326716
H,0,6.4090332237,-0.1613640026,0.5632841035
H,0,5.983515602,-1.7928326779,0.0322778497
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-cis-A-M062X-631Gdp-PCM-methanol
E(RM062X) = -1201.44748454

```
 Zero-point correction=                           0.402241 (Hartree/Particle)
 Thermal correction to Energy=                    0.424695
 Thermal correction to Enthalpy=                  0.425639
 Thermal correction to Gibbs Free Energy=         0.347914
 Sum of electronic and zero-point Energies=          -1201.045244
```

```
Sum of electronic and thermal Energies=           -1201.022790
Sum of electronic and thermal Enthalpies=          -1201.021845
Sum of electronic and thermal Free Energies=        -1201.099571

                E (Thermal)           CV               S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total               266.500           85.987           163.587

C,0,-3.7466033498,-1.3500111543,-0.4646913603
C,0,-2.5634126637,-1.6927538721,0.1731939766
C,0,-1.9842708832,-0.8223923344,1.1034160746
C,0,-2.613624476,0.3855871456,1.4175522544
C,0,-3.8031111773,0.7435684759,0.7954812691
C,0,-4.3434965151,-0.1322102558,-0.1408351231
C,0,-0.7073830192,-1.1926561186,1.7879663694
O,0,-0.3030707343,-2.3611186931,1.8380100173
N,0,-5.5917715856,0.2383076259,-0.8094571254
O,0,-6.0621655344,-0.5398524108,-1.6258592987
O,0,-6.1051945358,1.3096293341,-0.5230757372
C,0,0.6254213926,-0.1417005036,0.1797110568
C,0,1.853899512,-0.509047208,0.9012050184
N,0,3.1791167937,-0.3323258509,0.1251747991
C,0,3.3148461991,1.068582241,-0.4029890807
C,0,4.752862938,1.2435938239,-0.9474741721
C,0,0.1772159767,1.2042228912,0.2162094884
O,0,-0.7798712628,1.4738500277,-0.7237249435
C,0,-1.3438781163,2.7807368599,-0.6830960285
O,0,0.5232348418,2.0802879019,1.0225154088
C,0,4.3336038882,-0.6079124225,1.0473834625
C,0,5.6349687148,-0.6416564161,0.2098687896
C,0,3.2539003251,-1.288629922,-1.0293568145
C,0,4.5095049409,-0.942292893,-1.8668521087
H,0,1.9850899609,0.1130652027,1.7930910135
H,0,-2.1062195004,2.8002913026,-1.4619715444
H,0,-1.7996103244,2.9820387982,0.2899021147
H,0,-0.5822633693,3.5390050916,-0.8827773396
H,0,1.8532187258,-1.566564866,1.1909162277
H,0,0.2727592712,-0.7670715518,-0.6328660281
H,0,-0.3473776473,-0.434778102,2.5080645992
H,0,-2.0690684955,-2.6327434144,-0.0496600517
H,0,-4.2063024506,-2.0033487209,-1.1960700378
H,0,-4.302404581,1.6780866924,1.021154561
H,0,-2.1609727646,1.0565196612,2.143853623
H,0,3.2983277185,-2.2928217579,-0.6006143889
```

```
H,0,2.3301383408,-1.1844261518,-1.5998454293
H,0,2.5561534576,1.1806596904,-1.1798515191
H,0,3.0747614921,1.7499294429,0.415649302
H,0,4.3359689676,0.1930538231,1.7904630757
H,0,4.1321123711,-1.5559386042,1.5501044924
N,0,5.4051158314,-0.0590356538,-1.1146883868
H,0,5.0421464025,-1.8586228236,-2.1308028162
H,0,4.2267549687,-0.4355117367,-2.79317489
H,0,4.7229840189,1.759041572,-1.9101030093
H,0,5.3567855395,1.8419459936,-0.2604626822
H,0,6.4189988784,-0.0797740523,0.7222334022
H,0,5.983062519,-1.6693631073,0.0784555194
```

Aldol Transition States si face, cis, B

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-cis-B-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95483649

```
 Zero-point correction=                           0.397982 (Hartree/Particle)
 Thermal correction to Energy=                    0.420749
 Thermal correction to Enthalpy=                  0.421693
 Thermal correction to Gibbs Free Energy=         0.343130
 Sum of electronic and zero-point Energies=          -1201.556855
 Sum of electronic and thermal Energies=             -1201.534088
 Sum of electronic and thermal Enthalpies=           -1201.533144
 Sum of electronic and thermal Free Energies=        -1201.611707

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.024             86.909            165.350
```

```
N,0,5.5231268672,-0.4249262783,-1.5066717343
C,0,4.6377360142,0.5881371862,-2.0998641177
C,0,3.3806446061,0.824199318,-1.2136945802
N,0,3.5543469043,0.068832077,0.0885902839
C,0,4.8708014762,0.4928526247,0.715722247
C,0,6.0378533572,0.0804230509,-0.2258703629
C,0,4.7541840157,-1.6544110135,-1.2645239733
C,0,3.6273781936,-1.4139075587,-0.2181573003
C,0,2.4162282071,0.3709940608,1.0947789213
C,0,1.0166064884,0.1414075633,0.6408022038
C,0,0.3723625918,1.1970057285,-0.1159729669
```

O,0,0.7083123372,2.3848591176,-0.1535073278
O,0,-0.7573589886,0.7560278683,-0.7484461249
C,0,-1.5365153691,1.7483160064,-1.4407738664
C,0,0.0103771726,0.3026787631,2.4497949046
O,0,0.5249770609,1.2128210566,3.1741645929
C,0,0.1282658381,-1.1440970521,2.8787388481
C,0,-0.7081979972,-2.1294775902,2.3233638347
C,0,-0.6279698684,-3.453045631,2.7365569857
C,0,0.3065618757,-3.791806114,3.7240220935
C,0,1.1429032169,-2.8332265108,4.3048277759
C,0,1.0406831764,-1.5113812376,3.8810216063
N,0,0.4018755067,-5.1771560859,4.1638375989
O,0,-0.3507916595,-6.0140831045,3.6472380616
O,0,1.2332125666,-5.4658363221,5.0352669039
H,0,2.5511631864,1.4164771841,1.374747282
H,0,-2.3790294169,1.2077743457,-1.8718361277
H,0,-1.8940198928,2.5140551195,-0.7479488826
H,0,-0.9476666809,2.2210644027,-2.23082268
H,0,2.6627594779,-0.2539006862,1.9566833471
H,0,0.7488362457,-0.86192324,0.3273830514
H,0,-0.9582804483,0.4900269071,1.9509463773
H,0,1.6553496872,-0.7408158782,4.3338190667
H,0,1.8465786927,-3.1236415851,5.0750394243
H,0,-1.2714307221,-4.2143780999,2.3139366368
H,0,-1.430062563,-1.8520737786,1.5600396848
H,0,3.820072589,-1.9211506587,0.7289484202
H,0,2.6477919349,-1.7178967338,-0.5864731809
H,0,2.4724136132,0.4414159484,-1.6786485552
H,0,3.225366117,1.8723520708,-0.9589346134
H,0,4.811990585,1.5728726614,0.8605355172
H,0,4.9312433501,0.0117365694,1.6932924228
H,0,5.4317677471,-2.4338286607,-0.9076758513
H,0,4.3275810253,-1.9873800051,-2.2137757154
H,0,4.3325768352,0.2548727749,-3.094812747
H,0,5.2031274433,1.5162392521,-2.2146320823
H,0,6.6836705431,0.9410872352,-0.4158712
H,0,6.6451050612,-0.7013930672,0.2368118978

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-cis-B-M06-PCM-methanol
E(RM062X) = -1201.44614719

Zero-point correction= 0.402499 (Hartree/Particle)

```
Thermal correction to Energy=                    0.424909
Thermal correction to Enthalpy=                  0.425853
Thermal correction to Gibbs Free Energy=         0.348486
Sum of electronic and zero-point Energies=          -1201.043649
Sum of electronic and thermal Energies=             -1201.021238
Sum of electronic and thermal Enthalpies=           -1201.020294
Sum of electronic and thermal Free Energies=        -1201.097661

                E (Thermal)         CV                S
                 KCal/Mol      Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              266.634           85.713           162.832
```

```
N,0,5.5730890416,-0.306348144,-1.5016018494
C,0,4.7251711346,0.7934126983,-1.9716971763
C,0,3.4048130635,0.8504297461,-1.1666177032
N,0,3.5682401486,0.0042343965,0.0667602984
C,0,4.8456478569,0.4063611972,0.7534978345
C,0,6.0379624549,0.0064333894,-0.1483948534
C,0,4.7719052797,-1.5321333886,-1.4537347619
C,0,3.6863141378,-1.4339921932,-0.353501289
C,0,2.3962343225,0.1943288455,1.0395090273
C,0,1.0387841891,-0.0428563914,0.5133557911
C,0,0.3804266627,1.0076215391,-0.1939848518
O,0,0.7256199334,2.1910504723,-0.2526886003
O,0,-0.7931669803,0.5969374989,-0.7614359422
C,0,-1.56874548,1.6148190199,-1.3902399289
C,0,0.0100946301,0.3590254318,2.4423234189
O,0,0.6270009508,1.25813204,3.0470964603
C,0,0.1062250823,-1.0714623979,2.8956076201
C,0,-0.7846922483,-2.0350074562,2.4057264555
C,0,-0.7109368797,-3.350205444,2.8389339921
C,0,0.2727650811,-3.6832898588,3.7701386117
C,0,1.1654301205,-2.7484389294,4.2840364254
C,0,1.0679273269,-1.4330691623,3.8440044831
N,0,0.3618311432,-5.0697918232,4.2296357515
O,0,-0.4430130678,-5.8766315863,3.7885023481
O,0,1.2373774138,-5.3581164556,5.0319259777
H,0,2.4841788065,1.2241040924,1.3994631251
H,0,-2.4546606055,1.1149725772,-1.7796571646
H,0,-1.8567503141,2.3839321767,-0.6694126483
H,0,-1.0097809499,2.0801113835,-2.2056726717
H,0,2.6287261384,-0.4861948605,1.8670768117
H,0,0.7130069891,-1.0548764295,0.3042879144
H,0,-0.9239093192,0.5828052814,1.8971290799
```

H,0,1.7285623492,-0.6671522027,4.237868002
H,0,1.9078063968,-3.0477068372,5.0138303726
H,0,-1.3925580058,-4.1076465178,2.4719941329
H,0,-1.5354957541,-1.7481117821,1.6735476095
H,0,3.944286622,-2.0026827145,0.5434627783
H,0,2.704413255,-1.7516408007,-0.7060882023
H,0,2.5610120528,0.4323449146,-1.7187721256
H,0,3.1370636606,1.8552690152,-0.8370085629
H,0,4.7844913425,1.4851052408,0.9142152667
H,0,4.8669238974,-0.0944841552,1.7233871987
H,0,5.4250666417,-2.3844045611,-1.2530286381
H,0,4.3132567568,-1.679470331,-2.4347932292
H,0,4.5050448182,0.6507082343,-3.0321379215
H,0,5.2843650392,1.7264505095,-1.8642820174
H,0,6.7582470116,0.8264310919,-0.1933427276
H,0,6.5489058531,-0.8725143693,0.2527720782

Aldol Transition States si face, cis, C

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-cis-C-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95200363

```
 Zero-point correction=                           0.398088 (Hartree/Particle)
 Thermal correction to Energy=                    0.420752
 Thermal correction to Enthalpy=                  0.421697
 Thermal correction to Gibbs Free Energy=         0.343993
 Sum of electronic and zero-point Energies=          -1201.553916
 Sum of electronic and thermal Energies=             -1201.531251
 Sum of electronic and thermal Enthalpies=           -1201.530307
 Sum of electronic and thermal Free Energies=        -1201.608010

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.026             86.848            163.540
```

N,0,5.2225682664,-0.9226592327,-1.2816141416
C,0,4.6477292847,0.3191226442,-1.8204203082
C,0,3.3526362261,0.7171817133,-1.0547646295
N,0,3.2050494206,-0.1891062433,0.1512801644
C,0,4.4892562922,-0.1195999661,0.9594931929
C,0,5.6558889098,-0.6893129562,0.10393514
C,0,4.1933558518,-1.9718718561,-1.2913545577

```
C,0,3.0224130691,-1.6150101226,-0.3310475293
C,0,2.0267755392,0.2423230026,1.0673827071
C,0,0.6823766488,0.3828557749,0.4312239144
C,0,0.3996536887,1.6660920508,-0.1957440444
O,0,0.9428841442,2.7433195125,0.0707028892
O,0,-0.6109666551,1.5860139164,-1.1055421657
C,0,-1.029168609,2.8218860461,-1.7147203923
C,0,-0.7205586447,0.0673741614,1.8749055377
O,0,-1.8348812858,-0.2385607765,1.339402284
C,0,-0.6303214826,1.324705114,2.7121265583
C,0,0.3248462213,1.4468249048,3.736221331
C,0,0.3849265556,2.5870809482,4.5304271079
C,0,-0.5319945877,3.6170154112,4.293887273
C,0,-1.503952392,3.5199778008,3.291036927
C,0,-1.5486143521,2.3695531411,2.5126415142
N,0,-0.4804864619,4.8152599404,5.1198230584
O,0,0.3826173717,4.8871233941,6.005419653
O,0,-1.3004434021,5.7180840902,4.9045498825
H,0,2.3456921417,1.190878587,1.5026449456
H,0,-1.8320609722,2.550438685,-2.3997634623
H,0,-1.3963086049,3.5216957249,-0.9605047599
H,0,-0.2027935583,3.2806676723,-2.2633167705
H,0,2.0273101739,-0.5253526479,1.8467087852
H,0,0.3236127977,-0.4734257524,-0.1311546352
H,0,-0.1000084701,-0.74401121,2.3058717537
H,0,-2.3041011881,2.2593963306,1.7422724843
H,0,-2.2056561045,4.3303088601,3.1370894556
H,0,1.1156088275,2.6816906615,5.3237869082
H,0,1.0199494762,0.6341454148,3.9269232293
H,0,3.0048586288,-2.2462069801,0.5592315665
H,0,2.0518611168,-1.6737324354,-0.8226610096
H,0,2.457330763,0.5819544508,-1.6614767596
H,0,3.3731970917,1.7434441601,-0.6874864714
H,0,4.6356816565,0.9301888227,1.2194766512
H,0,4.3246849365,-0.6877826867,1.876412003
H,0,4.645090619,-2.9191494023,-0.9871976514
H,0,3.8265905799,-2.0865579054,-2.3142247539
H,0,4.4214187364,0.1762047239,-2.8798383558
H,0,5.3971473077,1.1104266788,-1.7407519593
H,0,6.4933553626,0.0123965239,0.1041611257
H,0,6.0090450653,-1.6359056895,0.5201993143
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-cis-C-M06-PCM-methanol
E(RM062X) = -1201.44459215

```
 Zero-point correction=                           0.402707 (Hartree/Particle)
 Thermal correction to Energy=                    0.424966
 Thermal correction to Enthalpy=                  0.425910
 Thermal correction to Gibbs Free Energy=         0.349385
 Sum of electronic and zero-point Energies=          -1201.041885
 Sum of electronic and thermal Energies=             -1201.019626
 Sum of electronic and thermal Enthalpies=           -1201.018682
 Sum of electronic and thermal Free Energies=        -1201.095207

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.670             85.624            161.061
```

```
N,0,5.2645585118,-0.7692109261,-1.2292456202
C,0,4.6349011305,0.475566854,-1.6758018322
C,0,3.5104386871,0.9056325379,-0.7018177477
N,0,3.2025172212,-0.2538898653,0.2051059403
C,0,4.4025282508,-0.5104632395,1.0767135772
C,0,5.6554441878,-0.6214561323,0.1745390892
C,0,4.2894614018,-1.8572052077,-1.3365118308
C,0,2.9592676983,-1.4724417152,-0.6416455884
C,0,1.9931858191,0.0397832411,1.1092273372
C,0,0.6806180383,0.2244201752,0.4452525497
C,0,0.3719031381,1.5452831701,-0.0304588668
O,0,0.9763546251,2.5816795499,0.2545762465
O,0,-0.7534812748,1.5799220308,-0.7890490485
C,0,-1.1756016191,2.8739850305,-1.217234766
C,0,-0.7958255689,-0.0898221623,1.9511983299
O,0,-1.8769224884,-0.4120852413,1.4081902875
C,0,-0.666365014,1.2367409147,2.645977434
C,0,0.3382010655,1.4570396811,3.5947380292
C,0,0.462111932,2.6901739148,4.2211332426
C,0,-0.4430100157,3.6934649431,3.8832947173
C,0,-1.4627102541,3.5014585647,2.9540674072
C,0,-1.5698248746,2.2605068542,2.3417177409
N,0,-0.3236429331,4.996051914,4.5374222486
O,0,0.576677649,5.1555931071,5.3489169224
O,0,-1.1290670953,5.8672489497,4.2435164269
H,0,2.2723016046,0.9461413008,1.6554595908
H,0,-2.0919154284,2.7137870441,-1.7837194993
H,0,-1.3695621183,3.5221379573,-0.3590532519
```

```
H,0,-0.4162918785,3.3372116422,-1.8520033256
H,0,1.9844003814,-0.8097896975,1.8022196723
H,0,0.2584831679,-0.6058262697,-0.10957688
H,0,-0.1413286686,-0.8694811631,2.3864210168
H,0,-2.3507052942,2.0618659996,1.6144610242
H,0,-2.1479574034,4.3090444098,2.7255080614
H,0,1.2317135607,2.8770951478,4.9599592257
H,0,1.024784125,0.6541712787,3.8519109251
H,0,2.585843181,-2.2592473729,0.017694811
H,0,2.1773496189,-1.2060018766,-1.3543297479
H,0,2.5884708316,1.1695296263,-1.2185652464
H,0,3.7983828048,1.7375869676,-0.0556250449
H,0,4.4694051679,0.3147602898,1.7883685369
H,0,4.1991163554,-1.4342031331,1.6231982417
H,0,4.7191278931,-2.7505958666,-0.8766888169
H,0,4.104658254,-2.0730003882,-2.3911025184
H,0,4.2326841429,0.3149225496,-2.6791195659
H,0,5.3919684544,1.2606751292,-1.7362653088
H,0,6.2768833609,0.2724851222,0.266175519
H,0,6.2535656685,-1.4838606407,0.4765033552
```

Aldol Transition States si face, cis, D

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-cis-D-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95419149

```
 Zero-point correction=                           0.397659 (Hartree/Particle)
 Thermal correction to Energy=                    0.420475
 Thermal correction to Enthalpy=                  0.421419
 Thermal correction to Gibbs Free Energy=         0.342561
 Sum of electronic and zero-point Energies=         -1201.556532
 Sum of electronic and thermal Energies=            -1201.533716
 Sum of electronic and thermal Enthalpies=          -1201.532772
 Sum of electronic and thermal Free Energies=       -1201.611630

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                 263.852             87.011            165.971
```

```
N,0,-5.4220313391,-0.188512215,-1.0979182246
C,0,-4.5515923767,-1.1969807881,-1.7194157969
C,0,-3.2339454741,-1.3752948032,-0.9103180311
```

N,0,-3.1821263718,-0.3221568212,0.1779554471
C,0,-4.348831828,-0.5486410551,1.1224558301
C,0,-5.6699839159,-0.5630656336,0.3020222719
C,0,-4.7464332262,1.1169311007,-1.131328369
C,0,-3.3432265618,1.0414618473,-0.4619370313
C,0,-1.8635568273,-0.4370888048,0.9929073757
C,0,-0.5887137741,-0.1347133668,0.281895142
C,0,-0.2113640399,1.2573003128,0.1555933645
O,0,-0.5618118469,2.1776097489,0.903270749
O,0,0.6626063766,1.4738906914,-0.8743526592
C,0,1.1659310638,2.8134987316,-1.0190472877
C,0,0.6963096563,-0.9487592732,1.7260333046
O,0,0.4284158636,-0.5004158021,2.8816485144
C,0,2.0345822807,-0.6602063609,1.0928604799
C,0,2.4967147658,-1.4355931893,0.0157530005
C,0,3.7442714328,-1.2038152484,-0.5499180024
C,0,4.539614899,-0.1797164057,-0.0205211971
C,0,4.1119391393,0.6007083815,1.0593128542
C,0,2.8608703921,0.3493596224,1.6120940232
N,0,5.8495751651,0.0733164058,-0.6040298044
O,0,6.2123714446,-0.6184031184,-1.5655570494
O,0,6.5507675452,0.9716296476,-0.1186893807
H,0,-1.9923097293,0.2380981995,1.8397702934
H,0,1.8433962032,2.7791253375,-1.8722237452
H,0,0.3502200106,3.5146905402,-1.2137754228
H,0,1.7051276414,3.1263453461,-0.1218687329
H,0,-1.8836862636,-1.4663930857,1.3598222667
H,0,-0.3347541482,-0.7566926052,-0.5711784516
H,0,0.3255077009,-1.9527412936,1.4386947327
H,0,2.509762668,0.9277512285,2.4596023322
H,0,4.7536648982,1.3795687963,1.4520388573
H,0,4.1061354362,-1.7988733827,-1.3788639656
H,0,1.8708018409,-2.2302421352,-0.3814678075
H,0,-2.3462761436,-1.2449896769,-1.5290810346
H,0,-3.1776201841,-2.3449223593,-0.4122764892
H,0,-3.203639898,1.7847096791,0.3231459374
H,0,-2.5358228909,1.1439294186,-1.1863410251
H,0,-4.1663978628,-1.4921825257,1.639387331
H,0,-4.3197412113,0.2618278942,1.8525963911
H,0,-4.3309469845,-0.8808278348,-2.741964558
H,0,-5.0879549149,-2.1476861589,-1.7697447204
H,0,-6.1208384554,-1.5582603065,0.3206590528
H,0,-6.3853835123,0.1390215662,0.7368900371
H,0,-5.375924025,1.8456196661,-0.6146750811

```
H,0,-4.6451186191,1.4378530883,-2.1709517209
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-cis-D-M06-PCM-methanol
E(RM062X) = -1201.44804296

```
 Zero-point correction=                           0.402579 (Hartree/Particle)
 Thermal correction to Energy=                    0.424817
 Thermal correction to Enthalpy=                  0.425761
 Thermal correction to Gibbs Free Energy=         0.348590
 Sum of electronic and zero-point Energies=          -1201.045464
 Sum of electronic and thermal Energies=             -1201.023226
 Sum of electronic and thermal Enthalpies=           -1201.022282
 Sum of electronic and thermal Free Energies=        -1201.099453

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.577             85.672            162.420
```

```
N,0,-5.4302956546,0.0528124463,-0.9643550271
C,0,-4.6658704223,-0.9536375146,-1.7059615966
C,0,-3.3976903107,-1.3653998871,-0.9201698009
N,0,-3.1647408012,-0.3541689379,0.1662156513
C,0,-4.2834768794,-0.4620415784,1.1669521464
C,0,-5.6306867393,-0.4239652935,0.4064996315
C,0,-4.6539618752,1.2953121075,-0.9197629758
C,0,-3.2063643576,1.0204862748,-0.4451496425
C,0,-1.8282481719,-0.6212585148,0.8818089201
C,0,-0.5960799913,-0.4473229017,0.0850478782
C,0,-0.0875143574,0.875112154,-0.0964879392
O,0,-0.3661189992,1.8681748581,0.5839314424
O,0,0.8423454778,0.9538675901,-1.0913437616
C,0,1.4679160381,2.2221108036,-1.2657033548
C,0,0.6846566457,-1.1944751099,1.7461571768
O,0,0.2559413863,-0.7417380862,2.8251510074
C,0,1.9810676822,-0.7192386115,1.1646723245
C,0,2.585352481,-1.4202373503,0.1157004913
C,0,3.7758584862,-0.9731038728,-0.4376281017
C,0,4.3492922518,0.1854627215,0.0841443733
C,0,3.783255758,0.8932981361,1.1402826995
C,0,2.5910346371,0.42780472,1.6810847633
N,0,5.6006528797,0.6714378019,-0.4976015101
O,0,6.0764699816,0.0563659336,-1.4407771742
```

```
O,0,6.1129648895,1.6716869166,-0.0167936669
H,0,-1.8225474159,0.0587186254,1.7391998554
H,0,2.2223779754,2.0771302919,-2.0390031869
H,0,0.7396686091,2.9716152852,-1.5871399154
H,0,1.9399468161,2.5539371999,-0.3379897497
H,0,-1.9323347006,-1.6467724153,1.2519264887
H,0,-0.3479040969,-1.1774633544,-0.6784169437
H,0,0.3964502325,-2.2078815331,1.4108530943
H,0,2.1171960415,0.9474141366,2.5071001291
H,0,4.2684819521,1.7848815132,1.5188519035
H,0,4.2565668588,-1.49777515,-1.254204399
H,0,2.109066647,-2.314378411,-0.2783910261
H,0,-2.5043989689,-1.3807557158,-1.546027056
H,0,-3.505581213,-2.3345187658,-0.4272451235
H,0,-2.8530966097,1.7244238396,0.3096014041
H,0,-2.493046502,1.0120778388,-1.2714973054
H,0,-4.1400847482,-1.3925284247,1.7198441056
H,0,-4.1665290658,0.3789684604,1.854183773
H,0,-4.3969916726,-0.5315071625,-2.6773965057
H,0,-5.294323303,-1.8300915243,-1.8789227057
H,0,-6.0778394455,-1.4200858061,0.3617905695
H,0,-6.3281020551,0.2388527638,0.9231662271
H,0,-5.157724458,1.9895604553,-0.2424647055
H,0,-4.6364569125,1.7459060477,-1.914768882
```

Aldol Transition States si face, cis, E

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-cis-E-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95664402

```
 Zero-point correction=                           0.397990 (Hartree/Particle)
 Thermal correction to Energy=                    0.420765
 Thermal correction to Enthalpy=                  0.421709
 Thermal correction to Gibbs Free Energy=         0.342828
 Sum of electronic and zero-point Energies=          -1201.558654
 Sum of electronic and thermal Energies=             -1201.535879
 Sum of electronic and thermal Enthalpies=           -1201.534935
 Sum of electronic and thermal Free Energies=        -1201.613816

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.034             86.876            166.021
```

```
N,0,-5.3208540269,-0.4677047864,-1.3725973447
C,0,-4.2876354913,-1.4257645054,-1.7918278468
C,0,-3.0528318635,-1.3709436323,-0.8455956843
N,0,-3.2409837263,-0.2331336086,0.1365745003
C,0,-4.4750287767,-0.5225470695,0.9711645209
C,0,-5.689283032,-0.7398943305,0.0242022279
C,0,-4.7822077032,0.8972681962,-1.4698505467
C,0,-3.4752737478,1.047234956,-0.6380737544
C,0,-2.0253634031,-0.1129567577,1.0923963861
C,0,-0.7168509183,0.2595335187,0.495186428
C,0,-0.3915308565,1.6688966958,0.3917516288
O,0,-0.9345098929,2.6005528674,0.9941313407
O,0,0.6828885396,1.8835383464,-0.4282056365
C,0,1.1276216713,3.2452103969,-0.5653909447
C,0,0.5937443328,-0.733872101,1.7653969196
O,0,0.155697041,-1.9246809034,1.8683430257
C,0,0.604259167,0.160897584,2.9794157525
C,0,1.4606242909,1.2739434192,3.0425246165
C,0,1.5017687955,2.0840057133,4.1714649866
C,0,0.6717350696,1.7689578524,5.2533747412
C,0,-0.1833523796,0.6607250027,5.2259480881
C,0,-0.2038620325,-0.139688036,4.0898866093
N,0,0.7062728663,2.6096730223,6.4415718528
O,0,1.4750515896,3.5807626062,6.4575909974
O,0,-0.0358330296,2.3230887975,7.3910563906
H,0,-2.333579471,0.6197371129,1.8400902381
H,0,1.9776311699,3.2062240668,-1.2464363465
H,0,0.3355169773,3.8697182195,-0.9864117403
H,0,1.4356713628,3.6541850384,0.3997972017
H,0,-1.9481382219,-1.1048757143,1.5524459485
H,0,-0.3720696536,-0.3375925244,-0.3429193981
H,0,1.4439352565,-0.5234959431,1.0935023207
H,0,-0.8391613215,-1.0177515653,4.0517810216
H,0,-0.8062490027,0.4360025514,6.0827449999
H,0,2.1623807753,2.9401153958,4.225412799
H,0,2.10632237,1.5024264294,2.1995064157
H,0,-2.1260384751,-1.1840813233,-1.3867662556
H,0,-2.9363899851,-2.2802090479,-0.2535091327
H,0,-3.5239776645,1.8576507019,0.0898283181
H,0,-2.5992282354,1.1977015619,-1.2684036938
H,0,-4.2523742159,-1.4022646427,1.5772000668
H,0,-4.6104913162,0.3337387896,1.6338872937
H,0,-3.9916057371,-1.1896774629,-2.8168655108
```

```
H,0,-4.7146523507,-2.4315215496,-1.7877825945
H,0,-6.048444556,-1.7695290892,0.0940236922
H,0,-6.5088503814,-0.0765616693,0.3110835733
H,0,-5.5428793496,1.5958782352,-1.112876445
H,0,-4.5832114575,1.1249191851,-2.5199290268
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-cis-E-M062X-631Gdp-PCM-methanol
E(RM062X) = -1201.44923941

```
Zero-point correction=                           0.402323 (Hartree/Particle)
Thermal correction to Energy=                    0.424705
Thermal correction to Enthalpy=                  0.425649
Thermal correction to Gibbs Free Energy=         0.348312
Sum of electronic and zero-point Energies=         -1201.046917
Sum of electronic and thermal Energies=            -1201.024534
Sum of electronic and thermal Enthalpies=          -1201.023590
Sum of electronic and thermal Free Energies=       -1201.100928

                 E (Thermal)             CV                S
                  KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              266.506              85.815           162.770
```

```
N,0,5.0328735412,-0.8278571509,-0.8843289434
C,0,5.0860651837,0.1919512839,0.1662867596
C,0,3.7297144072,0.2857039693,0.9071620229
N,0,2.6951201508,-0.4347026879,0.0909247368
C,0,3.0266001588,-1.9016258322,0.0883341124
C,0,4.5133826788,-2.0703271912,-0.3071330481
C,0,4.1138782451,-0.3776017478,-1.9342128013
C,0,2.7626426774,0.0694357606,-1.3246813976
C,0,1.2898115964,-0.2351017936,0.6829223835
C,0,0.7586480528,1.1374251759,0.6782208814
C,0,0.0138383341,1.5765887992,-0.4542275755
O,0,-0.3681161776,0.8876678066,-1.4056761312
O,0,-0.3441339342,2.8940825822,-0.3660649691
C,0,-1.1376210442,3.3959077949,-1.4383098523
C,0,-0.7409363601,0.8473795662,2.350285297
O,0,-0.1540457624,0.1596002026,3.2052088669
C,0,-1.8208224734,0.2673271134,1.4911066375
C,0,-2.72763575,1.1132099559,0.842988567
C,0,-3.7418678463,0.5888681757,0.0530492587
C,0,-3.8254677483,-0.7947645631,-0.0769857545
```

```
C,0,-2.9415651557,-1.6638036199,0.5592996257
C,0,-1.9415768088,-1.1204529377,1.3541809152
N,0,-4.8870157623,-1.3585741704,-0.9107963487
O,0,-5.6925870743,-0.5916668331,-1.4176186799
O,0,-4.9189780449,-2.5707517295,-1.0642537861
H,0,0.6485319024,-0.8948631749,0.0890634758
H,0,-1.3261842929,4.4430536707,-1.2041918005
H,0,-0.6039620642,3.3132561616,-2.3884220732
H,0,-2.0826692775,2.8510739924,-1.5122280242
H,0,1.366004348,-0.6242097797,1.7073037999
H,0,1.2327649089,1.8981941425,1.2874607943
H,0,-0.7854057007,1.9455716614,2.4372954732
H,0,-1.243254038,-1.7636783192,1.8809015566
H,0,-3.0487867255,-2.7345504471,0.4348847181
H,0,-4.4544157684,1.2285177576,-0.4536271646
H,0,-2.6320319357,2.1900699911,0.9569784929
H,0,3.3916357132,1.3153196802,1.0271440535
H,0,3.7494886334,-0.1999733069,1.8858956527
H,0,1.8940714669,-0.3288396529,-1.8523320116
H,0,2.6645272735,1.1553553815,-1.2708901088
H,0,2.8107282451,-2.2867446677,1.0869364591
H,0,2.3470447047,-2.3714402681,-0.6264390575
H,0,5.3381378362,1.149257275,-0.2971268642
H,0,5.8777756317,-0.0603540373,0.8753319437
H,0,5.1183159815,-2.3243685015,0.5668573251
H,0,4.6136430572,-2.877597303,-1.0359566962
H,0,3.9670748993,-1.2014819825,-2.6373048512
H,0,4.5681437677,0.4542301046,-2.4772734993
```

Aldol Transition States si face, cis, F

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-cis-F-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95184377

```
 Zero-point correction=                           0.398011 (Hartree/Particle)
 Thermal correction to Energy=                    0.420697
 Thermal correction to Enthalpy=                  0.421641
 Thermal correction to Gibbs Free Energy=         0.343622
 Sum of electronic and zero-point Energies=          -1201.553832
 Sum of electronic and thermal Energies=             -1201.531147
 Sum of electronic and thermal Enthalpies=           -1201.530203
 Sum of electronic and thermal Free Energies=        -1201.608221
```

```
              E (Thermal)           CV               S
               KCal/Mol       Cal/Mol-Kelvin   Cal/Mol-Kelvin
Total             263.991           86.900          164.204
```

```
N,0,-5.5198065171,0.0396745162,-1.4224238102
C,0,-4.6974002004,-1.1419067958,-1.7216792817
C,0,-3.5421912196,-1.2946442415,-0.689855713
N,0,-3.5035264848,-0.0578305738,0.1846230623
C,0,-4.8036396236,0.0169574069,0.9641355914
C,0,-5.9950699756,-0.0453595768,-0.0337394975
C,0,-4.6961317196,1.2481937768,-1.5753831698
C,0,-3.4100577553,1.1663701142,-0.7030246174
C,0,-2.3250303023,-0.1353822534,1.2005198939
C,0,-0.9407118524,-0.073544713,0.649553869
C,0,-0.3956212263,1.2536987973,0.4133085981
O,0,-0.7144057535,2.2866208893,1.0119923445
O,0,0.5989422196,1.2438140617,-0.5123042082
C,0,1.3059285539,2.4817167699,-0.7123107628
C,0,0.3258072493,-0.686951043,2.1586279626
O,0,1.521063436,-0.3100077421,1.9349545
C,0,0.0143237804,-2.1671177949,2.1228140693
C,0,-0.9249413925,-2.7267002242,3.0052470498
C,0,-1.1868920187,-4.0948949659,3.003595452
C,0,-0.4922480317,-4.9076166796,2.1042818958
C,0,0.4615887954,-4.3822830939,1.2217929168
C,0,0.7121745077,-3.0169779742,1.2452781216
N,0,-0.7602943601,-6.3399066358,2.090278042
O,0,-1.6043532332,-6.7915125563,2.8758026264
O,0,-0.1352129534,-7.0497157855,1.2912412696
H,0,-2.4983719496,0.6951413784,1.8877648566
H,0,2.0705874046,2.263157787,-1.457425177
H,0,0.6300836668,3.2574447817,-1.0810809327
H,0,1.7688712219,2.8158873383,0.2189766439
H,0,-2.5154054125,-1.0748490989,1.7244784169
H,0,-0.6803049457,-0.8032997567,-0.1112938879
H,0,-0.2594879013,-0.1636388559,2.9403871265
H,0,1.4575355017,-2.5895548008,0.5830390781
H,0,0.989136589,-5.0392619443,0.5415959021
H,0,-1.9059995608,-4.5297764183,3.6863332439
H,0,-1.4435637861,-2.0897986928,3.7164638591
H,0,-2.5682804405,-1.3872577363,-1.1694920905
H,0,-3.6887539787,-2.1454566803,-0.0220093044
H,0,-3.2842546216,2.0296087322,-0.0489824996
```

H,0,-2.5095138307,1.050336908,-1.305536006
H,0,-4.8042381704,-0.8141883224,1.6712220048
H,0,-4.7775289941,0.953132586,1.5243032863
H,0,-4.2950620475,-1.0354639161,-2.7319748672
H,0,-5.3308232046,-2.0320894711,-1.703776201
H,0,-6.5472406551,-0.9805248759,0.0871496144
H,0,-6.6844988531,0.7802359333,0.1588102513
H,0,-5.2966108211,2.1150754453,-1.2890442651
H,0,-4.4235911332,1.3606509969,-2.6276082569

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-cis-F-M06-PCM-methanol
E(RM062X) = -1201.44283597

```
 Zero-point correction=                           0.402805 (Hartree/Particle)
 Thermal correction to Energy=                    0.425076
 Thermal correction to Enthalpy=                  0.426020
 Thermal correction to Gibbs Free Energy=         0.348701
 Sum of electronic and zero-point Energies=          -1201.040031
 Sum of electronic and thermal Energies=             -1201.017760
 Sum of electronic and thermal Enthalpies=           -1201.016816
 Sum of electronic and thermal Free Energies=        -1201.094135

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.739             85.544            162.731
```

N,0,-5.6257270863,0.2180728621,-1.4026022615
C,0,-4.8618693537,-0.991143478,-1.7210176997
C,0,-3.7907872167,-1.2624065728,-0.6361920579
N,0,-3.6292454588,-0.0165602679,0.1883501808
C,0,-4.899324141,0.2083604527,0.9625633676
C,0,-6.0943635814,0.1268146139,-0.0174495828
C,0,-4.7414916954,1.3813050629,-1.5224116352
C,0,-3.4259408721,1.1505314263,-0.7408386038
C,0,-2.4560652806,-0.1582783939,1.1767263438
C,0,-1.100585121,-0.2243482298,0.5914876766
C,0,-0.4450866787,1.0111154807,0.2808432908
O,0,-0.730731473,2.1250395482,0.7280123825
O,0,0.6360793234,0.8328545519,-0.5164480383
C,0,1.4444543464,1.9863047082,-0.7395114017
C,0,0.1582897623,-0.6094401885,2.3380574189
O,0,1.2804890205,-0.0766874965,2.2088379191

```
C,0,0.0158367253,-2.1025567547,2.2316397098
C,0,-1.0014443822,-2.7789643724,2.9129300177
C,0,-1.1137841242,-4.1628672583,2.8252308153
C,0,-0.1866614184,-4.8508785434,2.0499019034
C,0,0.84913674,-4.2074027951,1.3722243757
C,0,0.9454459859,-2.8287726906,1.4753490038
N,0,-0.2961094613,-6.306182804,1.9513054302
O,0,-1.2134873508,-6.8588662927,2.5402924559
O,0,0.5341112789,-6.903237346,1.2821765797
H,0,-2.5462550584,0.7134669659,1.8325559262
H,0,2.2588358974,1.6578381839,-1.383923314
H,0,0.8682070997,2.7727459785,-1.2327255065
H,0,1.8396752891,2.3655758856,0.2050576003
H,0,-2.7088631831,-1.0615277999,1.74354114
H,0,-0.8385157245,-1.0737979621,-0.0302007374
H,0,-0.608241179,-0.1361863311,2.9815644009
H,0,1.7395840387,-2.2899513194,0.9683099858
H,0,1.554957084,-4.7824632093,0.7854269805
H,0,-1.8921850866,-4.7021451294,3.3510535595
H,0,-1.7001503654,-2.2254052776,3.5344721367
H,0,-2.8160052948,-1.5017449213,-1.06286052
H,0,-4.0846023737,-2.0572419599,0.0539235956
H,0,-3.1262623638,2.004600781,-0.1307435483
H,0,-2.594649739,0.8834050509,-1.3959721339
H,0,-4.9449905224,-0.5521267788,1.7449631792
H,0,-4.8083683964,1.1919576154,1.429094069
H,0,-4.3931410932,-0.8546349661,-2.6988536532
H,0,-5.5427524009,-1.8427353921,-1.7872525146
H,0,-6.6303276835,-0.8178457892,0.1036073021
H,0,-6.7930709693,0.9419670256,0.1836054296
H,0,-5.2714249196,2.2564013433,-1.1376055141
H,0,-4.5176135421,1.5582477839,-2.5768684542
```

Aldol Transition States si face, trans, A

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-trans-A-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95074241

```
 Zero-point correction=                           0.398063 (Hartree/Particle)
 Thermal correction to Energy=                    0.420796
 Thermal correction to Enthalpy=                  0.421740
 Thermal correction to Gibbs Free Energy=         0.343529
```

```
Sum of electronic and zero-point Energies=          -1201.552680
Sum of electronic and thermal Energies=             -1201.529947
Sum of electronic and thermal Enthalpies=           -1201.529003
Sum of electronic and thermal Free Energies=        -1201.607213

                E (Thermal)          CV               S
                 KCal/Mol      Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total             264.053           86.864          164.608
```

```
C,0,2.0531797977,-1.2825232016,0.7199554063
C,0,3.0807273254,-1.6062142041,-0.1601404419
C,0,3.9775847961,-0.6021798406,-0.5403893603
C,0,3.8704114776,0.7041117544,-0.0479676082
C,0,2.8390961007,1.0036794807,0.8337448842
C,0,1.9073273157,0.0239228705,1.2176102989
N,0,5.0575519541,-0.9275707126,-1.4619242502
O,0,5.8473692597,-0.0311325424,-1.7878057364
C,0,0.8100526292,0.3668025444,2.2037153897
O,0,0.9917676812,1.3377131495,3.0095226648
O,0,5.1432948234,-2.0877332999,-1.8872151343
C,0,-0.7803067195,0.7484223572,1.0126386423
C,0,-1.2053007659,-0.5450308288,0.3933640833
N,0,-2.6827884611,-0.6645474017,-0.0804072913
C,0,-3.6438434142,-0.5000381332,1.0806089987
C,0,-5.0992004729,-0.6939580454,0.5602494708
C,0,-0.4010648213,1.871918585,0.1673343898
O,0,0.0407929511,1.501122146,-1.0726339396
C,0,0.5032664823,2.5567681248,-1.9338545121
O,0,-0.3922543796,3.0524158065,0.5223559093
C,0,-2.8788485398,-2.0502117385,-0.6723996594
C,0,-4.3527722569,-2.198219865,-1.1475863356
C,0,-3.0204004795,0.3633731402,-1.1411130116
C,0,-4.492901613,0.1488132541,-1.5990663849
H,0,0.3175228233,-0.5513968121,2.5833016024
H,0,-0.6128461879,-0.7785388616,-0.4916700086
H,0,-1.1096802776,-1.3679890274,1.1078045091
H,0,-2.3012563947,0.2322130351,-1.9497520498
H,0,-2.8681311226,1.3441994645,-0.6925277209
H,0,-3.483373327,0.4955719281,1.4928669668
H,0,-3.3645787446,-1.2416592812,1.8312873042
H,0,-2.1641605547,-2.1470218723,-1.4912838516
H,0,-2.6181495622,-2.7670147418,0.1078875924
H,0,-1.3696680738,1.075532995,1.8636489588
H,0,0.7979736872,2.0675155623,-2.8620320421
```

```
H,0,-0.2959223648,3.2778340806,-2.1230813498
H,0,1.3582916783,3.0715522704,-1.4898910536
H,0,4.5866440695,1.457445873,-0.351591919
H,0,2.7435343955,2.0027000823,1.2443512124
H,0,1.365747736,-2.0616525338,1.036592284
H,0,3.1979815491,-2.612846721,-0.5412979991
N,0,-5.1166509695,-0.9718067916,-0.882505404
H,0,-5.576758647,-1.5260613241,1.083003968
H,0,-5.6880947462,0.206504467,0.7500960419
H,0,-5.0789469325,1.0519610452,-1.4127685999
H,0,-4.5256292281,-0.0597670287,-2.6711129739
H,0,-4.3832573512,-2.4053892966,-2.2200885307
H,0,-4.833842125,-3.0310149107,-0.6291514092
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-trans-A-M06-PCM-methanol
E(RM062X) = -1201.44441610

```
 Zero-point correction=                           0.402346 (Hartree/Particle)
 Thermal correction to Energy=                    0.424625
 Thermal correction to Enthalpy=                  0.425569
 Thermal correction to Gibbs Free Energy=         0.348879
 Sum of electronic and zero-point Energies=          -1201.042070
 Sum of electronic and thermal Energies=             -1201.019791
 Sum of electronic and thermal Enthalpies=           -1201.018847
 Sum of electronic and thermal Free Energies=        -1201.095537

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.456             85.669            161.408
```

```
C,0,1.9764722274,-1.2399128443,0.7015525219
C,0,2.8831064261,-1.4648256703,-0.3259384659
C,0,3.6892941554,-0.4053113269,-0.7344449017
C,0,3.6315845695,0.8536151874,-0.1415095198
C,0,2.7230424996,1.0555971966,0.8880903076
C,0,1.877730156,0.0200293747,1.3021653565
N,0,4.6449396348,-0.6293914083,-1.8195228378
O,0,5.334099856,0.3109209259,-2.1864586092
C,0,0.8792925323,0.275847559,2.3958713582
O,0,1.0342929312,1.2388891918,3.1767958786
O,0,4.7084769883,-1.7463544924,-2.312064787
C,0,-0.8246162736,0.6765269049,1.1455385803
```

```
C,0,-1.2291304746,-0.6205578405,0.5545163154
N,0,-2.6501634824,-0.6984673926,-0.0381038557
C,0,-3.6788417097,-0.2625487736,0.9685180147
C,0,-5.0828152138,-0.6007233716,0.4083409797
C,0,-0.3046233548,1.7322701808,0.3263066732
O,0,0.1320710761,1.3042017191,-0.8969656305
C,0,0.7247486835,2.2953443811,-1.7319163048
O,0,-0.1560777822,2.9045469022,0.6695640196
C,0,-2.9342369491,-2.1255513307,-0.4237550559
C,0,-4.2787549913,-2.1749164495,-1.188294612
C,0,-2.7880988045,0.1653679265,-1.2613347067
C,0,-4.272794534,0.1492041849,-1.7038944087
H,0,0.3632513327,-0.6419831793,2.7366267871
H,0,-0.5706333522,-0.9067391033,-0.2702619544
H,0,-1.2275646836,-1.4199227536,1.3053670307
H,0,-2.1127645073,-0.2485308086,-2.013660739
H,0,-2.4451516545,1.165074901,-0.99453682
H,0,-3.5364149653,0.8088712793,1.1168959397
H,0,-3.4618729692,-0.7814807997,1.9048203614
H,0,-2.093333134,-2.4723049891,-1.0275707382
H,0,-2.9622064148,-2.6985200811,0.5059381337
H,0,-1.3636816907,1.0203780885,2.0212569272
H,0,1.0582681788,1.7698151386,-2.6262799004
H,0,-0.0067787859,3.063559644,-1.9968411589
H,0,1.5747762382,2.7664454783,-1.2332213999
H,0,4.2861412867,1.6456620159,-0.485716334
H,0,2.6443366034,2.0201234642,1.3793526582
H,0,1.3422060642,-2.053821904,1.0442056313
H,0,2.9754514738,-2.4335925145,-0.8015307176
N,0,-5.0086130271,-0.9168435711,-1.020038046
H,0,-5.5080670964,-1.4621405628,0.9292260634
H,0,-5.7521466256,0.2495906612,0.5551735648
H,0,-4.7527584106,1.1024740225,-1.4689992574
H,0,-4.3343526107,-0.0047390554,-2.783398593
H,0,-4.1096229018,-2.3343790327,-2.256021388
H,0,-4.8879765145,-3.0002220724,-0.8131603607
```

Aldol Transition States si face, trans, B

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-trans-B-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95484181

```
Zero-point correction=                          0.397872 (Hartree/Particle)
Thermal correction to Energy=                   0.420715
Thermal correction to Enthalpy=                 0.421659
Thermal correction to Gibbs Free Energy=        0.342481
Sum of electronic and zero-point Energies=         -1201.556970
Sum of electronic and thermal Energies=            -1201.534127
Sum of electronic and thermal Enthalpies=          -1201.533183
Sum of electronic and thermal Free Energies=       -1201.612361

                 E (Thermal)             CV                S
                  KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              264.003            86.915           166.644

C,0,2.1028900173,-1.4089640944,1.0130586926
C,0,1.7605075904,-0.9745239637,-0.2801815127
C,0,2.6538381818,-0.146916975,-0.9803521282
C,0,3.8555721536,0.256242422,-0.4076290516
C,0,4.161181018,-0.1799496643,0.8856864062
C,0,3.294038819,-1.0121154501,1.6062654084
C,0,0.4892744208,-1.4459419272,-0.9316870184
O,0,-0.0519548772,-2.5320987466,-0.5534133119
N,0,5.4160935302,0.2344795398,1.4954722153
O,0,5.6770780686,-0.1612140414,2.6401530215
C,0,-0.7860506078,0.1310318385,-0.3269652259
C,0,-0.3701454865,1.349009113,-0.9933901492
O,0,0.4192966846,2.1836631445,-0.5390853524
C,0,-2.0760596375,-0.5255846561,-0.6723828214
N,0,-3.3384827934,-0.0607640359,0.1022397711
C,0,-3.2111933945,-0.3564248783,1.5826501402
C,0,-4.5058623264,0.1206991354,2.3041201791
N,0,-5.492554618,0.6333912176,1.3432593954
C,0,-5.803183689,-0.4180809947,0.3648500038
C,0,-4.5334408767,-0.8263287772,-0.4359386972
C,0,-3.5958212457,1.4208643866,-0.079493874
C,0,-4.9253823899,1.7931654184,0.6407449117
O,0,-0.8762169918,1.4762068793,-2.2610783373
O,0,6.1754719095,0.9688145878,0.8482305807
H,0,0.4382405332,-1.1632132078,-1.9991090203
H,0,-2.3285850497,-0.3823225161,-1.7240560028
H,0,-2.0071830057,-1.5992655839,-0.4621962812
H,0,-3.6307597967,1.608154958,-1.1535861392
H,0,-2.7361868617,1.9431490403,0.3399352911
H,0,-2.3246364028,0.1643282835,1.94233483
H,0,-3.0491836376,-1.4317807123,1.6755046372
```

```
H,0,-4.6117014946,-0.5799454026,-1.4960728757
H,0,-4.300522094,-1.8880167711,-0.3401924736
H,0,-0.509429228,0.1277340721,0.7228810761
H,0,3.5614603937,-1.3379093471,2.6037064798
H,0,1.4218328913,-2.0666221852,1.5423031408
H,0,2.408728369,0.178530495,-1.9869012444
H,0,4.5490087332,0.8908148983,-0.9449341052
H,0,-4.9518287194,-0.7083219399,2.8588769788
H,0,-4.2704568794,0.9146471028,3.0169332452
H,0,-4.746649378,2.5908412985,1.3658272696
H,0,-5.659672259,2.1547943876,-0.0831966741
H,0,-6.5732837143,-0.0492038278,-0.3169227919
H,0,-6.2100899422,-1.2809324319,0.8976914041
C,0,-0.4574703815,2.631183811,-3.008650476
H,0,-0.9662107038,2.5565558775,-3.9697742377
H,0,-0.7505743145,3.551039262,-2.4963236529
H,0,0.6255684836,2.6279159608,-3.1536246235
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-trans-B-M06-PCM-methanol
E(RM062X) = -1201.44507800

```
 Zero-point correction=                           0.401999 (Hartree/Particle)
 Thermal correction to Energy=                    0.424503
 Thermal correction to Enthalpy=                  0.425447
 Thermal correction to Gibbs Free Energy=         0.347717
 Sum of electronic and zero-point Energies=          -1201.043079
 Sum of electronic and thermal Energies=             -1201.020575
 Sum of electronic and thermal Enthalpies=           -1201.019631
 Sum of electronic and thermal Free Energies=        -1201.097361

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.379             86.013            163.596
```

```
C,0,2.2954269582,-1.4718560955,0.9539372207
C,0,1.7621809338,-1.1270805966,-0.2940339519
C,0,2.4469301546,-0.2360586567,-1.1244596567
C,0,3.6562719191,0.3168651224,-0.7222111525
C,0,4.1550131857,-0.0358225318,0.5274074639
C,0,3.494620385,-0.9208826534,1.3796392258
C,0,0.4836506851,-1.7395140079,-0.7638414508
O,0,0.0100516785,-2.7605310631,-0.2463348028
```

```
N,0,5.4253498531,0.5434978287,0.9647228594
O,0,5.8467744257,0.2429828071,2.0719700058
C,0,-0.8193646644,0.0049160505,0.055685974
C,0,-0.2627957786,1.1912163216,-0.4943810963
O,0,0.6077488037,1.9035205223,0.0167910888
C,0,-2.0530086515,-0.6076877164,-0.4673530868
N,0,-3.3825991055,-0.0813164928,0.1229064992
C,0,-3.3842158237,-0.190201277,1.6206603215
C,0,-4.813076464,0.1255156626,2.129997128
N,0,-5.616985103,0.7412472986,1.0705476702
C,0,-5.8524882306,-0.2514095023,0.0194285405
C,0,-4.5188488053,-0.9072252684,-0.4134192977
C,0,-3.6136276982,1.3538470525,-0.2563777923
C,0,-4.865434396,1.8619841326,0.4989695912
O,0,-0.7273543693,1.4766398199,-1.7566573178
O,0,6.0076955979,1.3023237602,0.2039308039
H,0,0.19203971,-1.4372015343,-1.7865646215
H,0,-2.1591751974,-0.4500728666,-1.5444814855
H,0,-2.078901286,-1.6829257209,-0.2521072105
H,0,-3.7351267407,1.3723572974,-1.3422473386
H,0,-2.7115339047,1.908424716,0.0046069282
H,0,-2.6414364746,0.5200213633,1.9865268128
H,0,-3.0590238645,-1.2018534071,1.8743007484
H,0,-4.4056852085,-0.9540233292,-1.4983821081
H,0,-4.3949842703,-1.9116560411,-0.002025062
H,0,-0.5292426793,-0.2025299708,1.0803079988
H,0,3.9218554767,-1.1672589444,2.3439523627
H,0,1.7561676308,-2.1733650882,1.5822651367
H,0,2.0288347531,0.0279382877,-2.092834448
H,0,4.2013849374,1.0077982376,-1.3532933154
H,0,-5.3170971998,-0.7874274605,2.4571856958
H,0,-4.7585893684,0.8065472639,2.9822022039
H,0,-4.5789775313,2.533247773,1.312751981
H,0,-5.5104673567,2.4167763018,-0.1860353129
H,0,-6.3281084658,0.2503403074,-0.8269574685
H,0,-6.5384542687,-1.0161974396,0.3903916278
C,0,-0.1682357645,2.6281515685,-2.3807997986
H,0,-0.6527285176,2.7038999032,-3.3536860236
H,0,-0.3670845092,3.5261721543,-1.7902174874
H,0,0.9119636098,2.5186811116,-2.5067976028
```

Aldol Transition States si face, trans, C

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-trans-C-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.95321923

```
 Zero-point correction=                           0.397967 (Hartree/Particle)
 Thermal correction to Energy=                    0.420810
 Thermal correction to Enthalpy=                  0.421755
 Thermal correction to Gibbs Free Energy=         0.342806
 Sum of electronic and zero-point Energies=         -1201.555252
 Sum of electronic and thermal Energies=            -1201.532409
 Sum of electronic and thermal Enthalpies=          -1201.531465
 Sum of electronic and thermal Free Energies=       -1201.610413

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.062             86.899            166.160
```

```
N,0,-5.3050083711,-0.5616777572,-1.3589803448
C,0,-5.255184963,-0.8131927498,0.088404496
C,0,-3.7898327327,-1.0183521933,0.5712916286
N,0,-2.8492466931,-0.7409119505,-0.5847776558
C,0,-3.1366976052,-1.7472814914,-1.6849723042
C,0,-4.6429026953,-1.6680914889,-2.0643711597
C,0,-4.5938252618,0.6903052219,-1.6544196351
C,0,-3.1330600801,0.6486883476,-1.1186492161
C,0,-1.3712698843,-0.9082039894,-0.1474666691
C,0,-0.8453329851,0.0298322209,0.8862287554
C,0,-0.3642290073,1.3513336979,0.5256739027
O,0,-0.1831746105,2.2776119073,1.3234966925
O,0,-0.0178191556,1.4727629106,-0.7895046761
C,0,0.5716816969,2.7233354627,-1.1893765931
C,0,0.9255147154,-0.9101280133,1.3827562207
O,0,1.4881005624,-1.406843934,0.3540746961
C,0,0.3786190791,-1.8397633581,2.4465678902
C,0,0.1008757972,-1.3662568285,3.741673799
C,0,-0.373743308,-2.2190354389,4.7301237772
C,0,-0.5731193045,-3.5687891897,4.4119893944
C,0,-0.2945191057,-4.0728707212,3.1377525929
C,0,0.1885351737,-3.2024468194,2.164972069
N,0,-1.0746500316,-4.4725288098,5.4387799864
O,0,-1.3116532779,-4.0143763539,6.5646266013
O,0,-1.2473291519,-5.6633816335,5.1460684024
H,0,1.3410599247,0.0089387755,1.8366030144
H,0,-0.7892715142,-0.8373926289,-1.0661229705
H,0,-1.3267229071,-1.9410266393,0.2076272389
```

H,0,-2.3914250572,0.8545423863,-1.8901571758
H,0,-2.9773424013,1.3400402608,-0.2908677597
H,0,-3.5202174836,-0.3375090762,1.3780710691
H,0,-3.5953795499,-2.0426108705,0.8939481961
H,0,-2.480955567,-1.493919369,-2.5195666064
H,0,-2.8528660975,-2.7288057646,-1.3020168182
H,0,-1.3591001703,0.0408161058,1.8420516132
H,0,0.779797911,2.6193743261,-2.2540721378
H,0,-0.122869371,3.549543151,-1.0184121318
H,0,1.497119566,2.9073972997,-0.638688499
H,0,-0.4478778082,-5.123569761,2.9251919231
H,0,0.4406819949,-3.570767053,1.1762975746
H,0,0.262170296,-0.3172993958,3.97531506
H,0,-0.5847631765,-1.8598233166,5.729482802
H,0,-5.8493614695,-1.7016059411,0.3159129539
H,0,-5.7093399814,0.0368260807,0.6032462355
H,0,-5.1344499766,1.5212757313,-1.194950744
H,0,-4.5972029509,0.842879218,-2.7364090032
H,0,-4.7480823968,-1.5155609248,-3.1412489232
H,0,-5.1509126133,-2.5997956423,-1.804190562

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-trans-C-M06-PCM-methanol
E(RM062X) = -1201.44445178

```
 Zero-point correction=                           0.402915 (Hartree/Particle)
 Thermal correction to Energy=                    0.425285
 Thermal correction to Enthalpy=                  0.426229
 Thermal correction to Gibbs Free Energy=         0.348787
 Sum of electronic and zero-point Energies=          -1201.041536
 Sum of electronic and thermal Energies=             -1201.019167
 Sum of electronic and thermal Enthalpies=           -1201.018223
 Sum of electronic and thermal Free Energies=        -1201.095665

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.870             85.557           162.990
```

N,0,-5.2971445917,-0.4938169659,-1.554477898
C,0,-5.3289284729,-0.7346963816,-0.109440211
C,0,-3.9216124394,-1.1167096946,0.4111045466
N,0,-2.9141155504,-0.766537832,-0.6482407681
C,0,-3.1374051645,-1.6675812003,-1.8331618902

```
C,0,-4.6385796983,-1.6285099603,-2.2061448941
C,0,-4.5123963614,0.7172347455,-1.813271172
C,0,-3.1498576291,0.6542308759,-1.0811257911
C,0,-1.4850296146,-0.9715879096,-0.1250274822
C,0,-1.0389469407,-0.0871581447,0.9706667943
C,0,-0.5164064312,1.2214134894,0.7326753338
O,0,-0.2956874876,2.0781684342,1.5932681351
O,0,-0.1572945091,1.439727817,-0.566906307
C,0,0.4786319384,2.6866788299,-0.8401731321
C,0,0.9249668429,-1.0900541766,1.2051076556
O,0,1.2336622357,-1.6374929944,0.127282222
C,0,0.4530358814,-1.9117417295,2.3718426826
C,0,0.4030631231,-1.351121532,3.6546808051
C,0,-0.0200762251,-2.1043732141,4.7390802826
C,0,-0.3921228229,-3.4298758806,4.515151235
C,0,-0.3428778465,-4.0193098637,3.2558109422
C,0,0.0921877449,-3.249216874,2.1827578612
N,0,-0.8440521814,-4.234052486,5.6506909564
O,0,-0.8794998226,-3.7076074068,6.7529671597
O,0,-1.1667973464,-5.3948647078,5.4455867032
H,0,1.3872574491,-0.1326518585,1.5047815705
H,0,-0.8367626862,-0.8664251368,-0.9984926013
H,0,-1.4692218545,-2.0226857448,0.188007276
H,0,-2.3070712588,0.9465506405,-1.7091808996
H,0,-3.1339242502,1.2609864516,-0.1735218782
H,0,-3.6488783341,-0.570525934,1.3146559888
H,0,-3.8194998402,-2.1889012851,0.5966486921
H,0,-2.4972545456,-1.2912814532,-2.6341232033
H,0,-2.7992876091,-2.6666810671,-1.5517780132
H,0,-1.4784069979,-0.2137495406,1.9535143682
H,0,0.6812933733,2.6876080992,-1.9102636283
H,0,-0.1775463709,3.52029029,-0.5792735497
H,0,1.4123037891,2.7755850372,-0.2798743693
H,0,-0.6321796935,-5.0553862799,3.1287405173
H,0,0.1682220302,-3.6792213204,1.1889810199
H,0,0.6909498501,-0.3125487389,3.7964325991
H,0,-0.0637732793,-1.6864471432,5.7372604586
H,0,-6.0341786352,-1.5397417922,0.1084818857
H,0,-5.6881668269,0.1730954366,0.3817223456
H,0,-5.0736135169,1.5904996383,-1.4734621036
H,0,-4.3661621484,0.8068236996,-2.8928006483
H,0,-4.7474528462,-1.5382671833,-3.2892111274
H,0,-5.1399444281,-2.5463860523,-1.8889414693
```

Aldol Transition States si face, trans, D

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-trans-D-Becke-631Gdp-PCM-MeOH
E(RB3LYP) = -1201.95241824

```
 Zero-point correction=                           0.397462 (Hartree/Particle)
 Thermal correction to Energy=                    0.419538
 Thermal correction to Enthalpy=                  0.420482
 Thermal correction to Gibbs Free Energy=         0.343810
 Sum of electronic and zero-point Energies=          -1201.554956
 Sum of electronic and thermal Energies=             -1201.532881
 Sum of electronic and thermal Enthalpies=           -1201.531936
 Sum of electronic and thermal Free Energies=        -1201.608608

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                 263.264             85.108            161.369
```

C,0,-0.5411737407,-1.0061061666,1.2587261752
N,0,-1.5545526527,0.1160038896,1.1610952852
C,0,-1.2035491889,0.9810381959,-0.0313455208
C,0,-1.3054259619,0.1187769727,-1.3230796701
N,0,-1.561663598,-1.2929066443,-1.0024249867
C,0,-0.5143263184,-1.7788613853,-0.0921865889
C,0,-2.8668910738,-1.4028350631,-0.33562992
C,0,-2.9245228024,-0.4943192294,0.9254073314
C,0,-1.6048097333,0.9312259642,2.4854976761
C,0,-0.3737974985,1.672596672,2.8871590259
C,0,-0.0488518448,2.9529200868,2.2904284188
O,0,1.0799644072,3.4528314705,2.2313880647
O,0,-1.1468544249,3.6378064291,1.8447788019
C,0,-0.9127806383,4.9473970571,1.298035768
C,0,-0.9674386311,2.0646877999,4.8620664182
O,0,-2.1280246818,2.574261046,4.9007278573
C,0,0.2247594026,2.8476723946,5.3520048821
C,0,1.4212764642,2.1890654948,5.6831097515
C,0,2.512094314,2.8916604792,6.1798424021
C,0,2.3958055716,4.2772998309,6.3471009371
C,0,1.2153492514,4.9599236603,6.0334692448
C,0,0.1345047774,4.2358783621,5.5419625684
N,0,3.5309876467,5.0254909655,6.8684923805
O,0,4.5684294295,4.4084707444,7.1470537906

```
O,0,3.4176134387,6.2505486012,7.0122689612
H,0,-1.8940781203,5.3191386887,1.0031555849
H,0,-0.4683638542,5.6069305757,2.0468396635
H,0,-0.2531744877,4.8915832309,0.4282030393
H,0,-1.8662303698,0.1756774522,3.2308596555
H,0,-2.4502428487,1.6094110886,2.3704196259
H,0,-1.8914831153,1.8262987016,-0.029691159
H,0,-0.1931113346,1.3526429173,0.1362792601
H,0,0.4205574104,-0.5522809683,1.496086563
H,0,-0.8496920403,-1.6358064908,2.0952827784
H,0,-3.1880649572,-1.049229188,1.8273232434
H,0,-3.6215528209,0.3375632275,0.8108355451
H,0,0.5125681435,1.0739392187,3.0761171752
H,0,-3.650777307,-1.1134502261,-1.0395571415
H,0,-3.0297066923,-2.4476376408,-0.0603507407
H,0,-2.1165880849,0.4817197904,-1.9590668364
H,0,-0.3749176974,0.1897276421,-1.8916226585
H,0,0.4548248165,-1.6548038053,-0.5813339369
H,0,-0.6672188631,-2.8458898946,0.0866313211
H,0,-0.8479565679,0.9832232313,5.0733727983
H,0,-0.7990474374,4.7357944902,5.3077601828
H,0,1.1542755438,6.0310940089,6.179872306
H,0,3.4346465775,2.3885288619,6.4404575521
H,0,1.4953401936,1.11263346,5.5541411239
```

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-trans-D-M06-PCM-methanol
E(RM062X) = -1201.44547374

```
 Zero-point correction=                           0.402300 (Hartree/Particle)
 Thermal correction to Energy=                    0.424632
 Thermal correction to Enthalpy=                  0.425576
 Thermal correction to Gibbs Free Energy=         0.348860
 Sum of electronic and zero-point Energies=          -1201.043174
 Sum of electronic and thermal Energies=             -1201.020842
 Sum of electronic and thermal Enthalpies=           -1201.019898
 Sum of electronic and thermal Free Energies=        -1201.096614

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.460             85.803            161.462
```

```
C,0,-0.5494575754,-1.017247063,1.0675579418
```

```
N,0,-1.5548288352,0.0947509971,1.180190275
C,0,-1.2963203213,1.0845180957,0.0792982477
C,0,-1.2338282075,0.314610862,-1.2636845062
N,0,-1.7416901193,-1.0495748503,-1.107529235
C,0,-0.8293612536,-1.7991850181,-0.2400058167
C,0,-3.0586723644,-0.9899961428,-0.4698939303
C,0,-2.9310765956,-0.4845477904,0.9871538277
C,0,-1.489939351,0.7513320086,2.5714714382
C,0,-0.1732988438,1.2651415935,3.0092076929
C,0,0.3254536235,2.528725359,2.5541189192
O,0,1.5009532895,2.897826768,2.5696824079
O,0,-0.664654738,3.3857838148,2.1620537372
C,0,-0.2399373006,4.6879039745,1.7669181036
C,0,-0.9117921183,1.7142966081,5.0347914756
O,0,-2.1143783713,2.0474435207,4.9776642886
C,0,0.1484877716,2.7147553668,5.3817192739
C,0,1.4264624793,2.2886175818,5.7561670383
C,0,2.4099354161,3.2097074589,6.0870944217
C,0,2.0892232001,4.5643073587,6.0289294208
C,0,0.8265272008,5.0204236335,5.6588545608
C,0,-0.146124984,4.0811844943,5.3407534436
N,0,3.1183099944,5.5443667741,6.3735033011
O,0,4.2236559922,5.1333314763,6.6957409516
O,0,2.8282853183,6.7309621707,6.3232591655
H,0,-1.1488722836,5.235151508,1.519726392
H,0,0.2909844156,5.1837594727,2.5832652942
H,0,0.4152315793,4.6323445772,0.8936581665
H,0,-1.8501098097,-0.035065931,3.2432071469
H,0,-2.2357012497,1.5498313453,2.5482376775
H,0,-2.1087110103,1.8137972537,0.1178748061
H,0,-0.3583404809,1.5906354824,0.3065776175
H,0,0.4354190284,-0.5473921413,1.0732449392
H,0,-0.6492335944,-1.6390336115,1.9599855024
H,0,-3.0341645472,-1.2897114665,1.7180846096
H,0,-3.6508140808,0.3011189928,1.2254102847
H,0,0.6054258289,0.5433330348,3.2373572926
H,0,-3.6944946178,-0.3216226342,-1.0553979357
H,0,-3.5107666196,-1.9841292223,-0.4779655453
H,0,-1.8277144769,0.8368256469,-2.0170074804
H,0,-0.2035962449,0.2583865176,-1.6241879821
H,0,0.1083587287,-1.9767872815,-0.7709946397
H,0,-1.2840887775,-2.7682695894,-0.0197993679
H,0,-0.6346979485,0.6752030843,5.2916851741
H,0,-1.1452907031,4.3930600593,5.0539196449
```

```
H,0,0.6194925254,6.0834722074,5.6290886834
H,0,3.4035105799,2.8973106033,6.3841959133
H,0,1.652368452,1.2256790396,5.7827813615
```

Aldol Transition States si face, trans, E

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-trans-E-M06-PCM-methanol
E(RM062X) = -1201.44857883

```
 Zero-point correction=                           0.402630 (Hartree/Particle)
 Thermal correction to Energy=                    0.424802
 Thermal correction to Enthalpy=                  0.425746
 Thermal correction to Gibbs Free Energy=         0.349344
 Sum of electronic and zero-point Energies=         -1201.045949
 Sum of electronic and thermal Energies=            -1201.023777
 Sum of electronic and thermal Enthalpies=          -1201.022833
 Sum of electronic and thermal Free Energies=       -1201.099235

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.567             85.616            160.803
```

```
C,0,-0.1510313259,-0.8975904167,0.8876016684
N,0,-1.4500020777,-0.1421418631,0.9134903602
C,0,-1.3808047888,0.9627873972,-0.1029030691
C,0,-0.9232564314,0.3545913385,-1.4515339864
N,0,-1.0255991173,-1.1067363655,-1.4226492086
C,0,-0.0420037277,-1.6314882728,-0.4716324192
C,0,-2.3664573546,-1.4768582057,-0.9631484379
C,0,-2.5569909048,-1.0819433426,0.5213720418
C,0,-1.739091992,0.413627469,2.3191272106
C,0,-0.6862168818,1.238829771,2.9355106339
C,0,-0.6326653682,2.6554077043,2.7790803932
O,0,0.2791571053,3.3929360539,3.1670432846
O,0,-1.760651331,3.190272173,2.2194862024
C,0,-1.7900438076,4.6097478713,2.1021917416
C,0,-1.3035382578,0.9106059264,5.0697355043
O,0,-1.4976250678,-0.3151738907,5.1726318927
C,0,-2.4478346742,1.8775587415,5.0518388952
C,0,-2.2286982367,3.2313075121,5.3329522872
C,0,-3.2803437276,4.1371083136,5.2988890009
C,0,-4.5491545299,3.6614452909,4.9797510354
```

```
C,0,-4.8037019851,2.3171763812,4.7161763155
C,0,-3.7416724453,1.4251885198,4.7652616627
N,0,-5.6624547154,4.6101178557,4.9305506252
O,0,-5.431086983,5.7859177606,5.170682863
O,0,-6.7724081804,4.183456332,4.6480955854
H,0,-2.7776374243,4.855115319,1.7124768845
H,0,-1.6403421452,5.0852145491,3.0738860328
H,0,-1.0160191491,4.9553824113,1.4118165432
H,0,-1.9260959891,-0.4813010134,2.9296248058
H,0,-2.6707019855,0.9743019544,2.2038709513
H,0,-2.3795254963,1.403116721,-0.1529216357
H,0,-0.6872629128,1.7123678185,0.2796117894
H,0,0.6410672017,-0.1610686167,1.029058922
H,0,-0.1536400152,-1.5812101608,1.7397424022
H,0,-2.4906393981,-1.9399047635,1.1940994569
H,0,-3.5014130437,-0.5644591194,0.7011029882
H,0,0.2638059796,0.7733646498,3.1738765224
H,0,-3.0992515241,-0.9694835646,-1.595374983
H,0,-2.5040301546,-2.5540851636,-1.0805581421
H,0,-1.5438282812,0.7436317711,-2.262031691
H,0,0.1154142077,0.6218475387,-1.6617632301
H,0,0.9623032591,-1.5014670316,-0.8807087591
H,0,-0.2219827899,-2.7023784547,-0.3480564585
H,0,-0.3431782461,1.3628058049,5.3694382773
H,0,-3.9001830972,0.3679111661,4.5766932953
H,0,-5.8103108702,1.9908155767,4.4846147691
H,0,-3.1318376897,5.1892455505,5.5106772476
H,0,-1.2253036292,3.5763450022,5.5667579282
```

Aldol Transition States si face, trans, F

*B3LYP/6-31+G** PCM solvent model in methanol*

cc-si-trans-F-Becke-meoh
E(RB3LYP) = -1201.95064112

```
 Zero-point correction=                           0.398148 (Hartree/Particle)
 Thermal correction to Energy=                    0.420846
 Thermal correction to Enthalpy=                  0.421791
 Thermal correction to Gibbs Free Energy=         0.343788
 Sum of electronic and zero-point Energies=          -1201.552493
 Sum of electronic and thermal Energies=             -1201.529795
 Sum of electronic and thermal Enthalpies=           -1201.528851
 Sum of electronic and thermal Free Energies=        -1201.606853
```

	E (Thermal) KCal/Mol	CV Cal/Mol-Kelvin	S Cal/Mol-Kelvin
Total	264.085	86.877	164.170

```
C,0,-0.4670014347,-1.0779272287,1.0546118578
N,0,-1.4801631227,0.0434569466,1.1687197351
C,0,-1.2025445333,1.0640833804,0.0841332069
C,0,-1.4000468018,0.3858788598,-1.3029499646
N,0,-1.6171108542,-1.0612105928,-1.1605721023
C,0,-0.5035184748,-1.6406439574,-0.3955765425
C,0,-2.8719754349,-1.2875910067,-0.4292993959
C,0,-2.8624131633,-0.5394687005,0.9344215409
C,0,-1.4500023067,0.6786920738,2.5921196072
C,0,-0.2016365695,1.3865452308,3.0051807978
C,0,0.0435286963,2.7480594977,2.556535557
O,0,1.1538496014,3.2677987818,2.4420937316
O,0,-1.1032789497,3.4674707736,2.3601269626
C,0,-0.9434909511,4.8511859081,2.0004051033
C,0,-0.3579457302,1.7313627183,5.0290575714
O,0,0.4882255469,2.6062634163,5.4039004162
C,0,-0.1933273574,0.310421574,5.5219991855
C,0,-1.3157209874,-0.4806916101,5.818470524
C,0,-1.1729534552,-1.772660929,6.3191848833
C,0,0.1162123858,-2.2710426721,6.5238430876
C,0,1.2557504621,-1.5026695298,6.2493686651
C,0,1.0900152676,-0.2145012342,5.7584621321
N,0,0.279394976,-3.6224133278,7.0444223836
O,0,-0.7352592206,-4.2891618252,7.2879486091
O,0,1.426883467,-4.0523972823,7.2209737878
H,0,-1.9546663519,5.2394356909,1.8790045702
H,0,-0.4210901375,5.3970207362,2.7895441743
H,0,-0.3875846309,4.9460128123,1.064147746
H,0,-1.6566810953,-0.1746285626,3.2419534482
H,0,-2.3105809335,1.3491617658,2.6100018366
H,0,-1.8830304276,1.9002010361,0.2468978975
H,0,-0.1799329795,1.4111978681,0.2311415728
H,0,0.5073620091,-0.6651548006,1.3140008627
H,0,-0.7432955481,-1.8254418751,1.8005162694
H,0,-3.0806264247,-1.2000806055,1.7751776027
H,0,-3.5621520643,0.2976737627,0.9562309763
H,0,0.7097301037,0.7951689706,2.9941240908
H,0,-3.7078223415,-0.9367648603,-1.0393963298
H,0,-2.995180137,-2.3623055491,-0.2750364667
```

H,0,-2.2627413844,0.8160135924,-1.8176106483
H,0,-0.5182810098,0.5530965515,-1.9261529518
H,0,0.4293919366,-1.4116731901,-0.9163644859
H,0,-0.6160787171,-2.7271901064,-0.3690319496
H,0,-1.4259703352,2.0178482936,4.9639665542
H,0,1.9555324548,0.4070674707,5.5551391819
H,0,2.2414644224,-1.9149896323,6.4250881756
H,0,-2.035960009,-2.3826288191,6.5547878696
H,0,-2.313512455,-0.0752268142,5.6752936629

*M06-2X/6-31+G** PCM solvent model in methanol*

cc-si-trans-F-M06-PCM-methanol
E(RM062X) = -1201.44159600

```
 Zero-point correction=                           0.402413 (Hartree/Particle)
 Thermal correction to Energy=                    0.424787
 Thermal correction to Enthalpy=                  0.425731
 Thermal correction to Gibbs Free Energy=         0.348485
 Sum of electronic and zero-point Energies=          -1201.039183
 Sum of electronic and thermal Energies=             -1201.016809
 Sum of electronic and thermal Enthalpies=           -1201.015865
 Sum of electronic and thermal Free Energies=        -1201.093111

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  266.558             85.748           162.580
```

C,0,-0.3988335637,-1.0571693763,0.9341450524
N,0,-1.4449977609,-0.0049569384,1.1739085401
C,0,-1.2848896605,1.0764790246,0.1408035751
C,0,-1.6351277348,0.4791669369,-1.2449559972
N,0,-1.6847677549,-0.9837648165,-1.1832609541
C,0,-0.4537622476,-1.4712109794,-0.5575265146
C,0,-2.8248877496,-1.3833228223,-0.355760678
C,0,-2.8013710397,-0.6316820523,0.9971588436
C,0,-1.3375959008,0.5549414478,2.6113314833
C,0,-0.0894320425,1.2695862026,2.956264757
C,0,0.1265338877,2.6250434001,2.5481543893
O,0,1.2150947231,3.1911082478,2.4722333662
O,0,-1.0351192228,3.3168994324,2.3374116839
C,0,-0.8899432927,4.6911977901,1.9882172864
C,0,-0.3035212952,1.8147466783,5.0855341475
O,0,0.5621358905,2.6594003207,5.3877476979

```
C,0,-0.1874652779,0.3971818255,5.5711082674
C,0,-1.3369632437,-0.3756910824,5.7655180137
C,0,-1.2441827316,-1.6806191445,6.2373866921
C,0,0.0200697447,-2.1889075953,6.5151718296
C,0,1.1841464079,-1.4386461715,6.3501615484
C,0,1.0690915816,-0.1383898913,5.8819509568
N,0,0.1326733003,-3.5620615928,7.0084668701
O,0,-0.8919563199,-4.2158218597,7.1360877826
O,0,1.2462729291,-3.9929761259,7.2678217528
H,0,-1.9019515048,5.0741795364,1.8613583679
H,0,-0.3757605341,5.2403244894,2.7801467482
H,0,-0.3292614726,4.795968487,1.0558862079
H,0,-1.4757063528,-0.3366840596,3.2314232562
H,0,-2.2157607725,1.1997429922,2.7142358434
H,0,-1.9383373062,1.9012505293,0.4297511798
H,0,-0.248219309,1.4145035649,0.1997873224
H,0,0.5641894071,-0.6276169951,1.2115453205
H,0,-0.6294916977,-1.8861737508,1.6079503204
H,0,-2.9687143294,-1.2951170391,1.8480728332
H,0,-3.5282855823,0.1828326619,1.0354931754
H,0,0.8239446091,0.6879215347,3.0337964716
H,0,-3.753395228,-1.1608651863,-0.8863021655
H,0,-2.7739354264,-2.4635308119,-0.1976090424
H,0,-2.6082873817,0.8419773962,-1.5850962428
H,0,-0.8847899306,0.7840484132,-1.9778625333
H,0,0.3968020618,-1.0564073602,-1.10398139
H,0,-0.4119055172,-2.5595392851,-0.6400143033
H,0,-1.3467313262,2.1293316678,4.8927105212
H,0,1.9508622423,0.4800750367,5.7473093202
H,0,2.1475417039,-1.8725652255,6.5885463227
H,0,-2.1252753342,-2.2907594043,6.3942040764
H,0,-2.3149686442,0.0492249498,5.5545739972
```

Intermediate 2, after aldol addition

*B3LYP/6-31+G** PCM solvent model in methanol*

```
doc-cc-re-cis-A-B3PCMopttoprod
E(RB3LYP) = -1201.96169328
```

```
 Zero-point correction=                           0.400068 (Hartree/Particle)
 Thermal correction to Energy=                    0.422912
 Thermal correction to Enthalpy=                  0.423856
 Thermal correction to Gibbs Free Energy=         0.345196
```

```
Sum of electronic and zero-point Energies=         -1201.561625
Sum of electronic and thermal Energies=           -1201.538781
Sum of electronic and thermal Enthalpies=          -1201.537837
Sum of electronic and thermal Free Energies=       -1201.616498

                E (Thermal)         CV              S
                 KCal/Mol       Cal/Mol-Kelvin   Cal/Mol-Kelvin
Total              265.381          87.343          165.555

C,0,4.7324490988,-0.4115061822,-0.0443149713
C,0,3.8531958938,-1.3274458768,-0.6386541141
C,0,2.5931749765,-1.5003324841,-0.0809303909
C,0,2.1883191248,-0.7654615454,1.0477565291
C,0,3.0970321919,0.136570081,1.6237597789
C,0,4.3693853748,0.3232289823,1.0873752445
C,0,0.8060052539,-1.0080263627,1.6689750615
O,0,0.5016988532,-2.307081804,1.7949941715
N,0,6.0575610872,-0.2241358358,-0.6169000933
O,0,6.8220632298,0.5950897817,-0.088336424
O,0,6.370869612,-0.8893353722,-1.6140116726
C,0,-0.3165170938,-0.2268787185,0.7401818576
C,0,-1.6482440595,-0.5332853024,1.4069192478
N,0,-2.8997374868,-0.5070369773,0.5310219088
C,0,-2.8873068106,-1.6328552547,-0.4891799704
C,0,-4.1633499223,-1.5190578123,-1.3724127448
C,0,-0.0173994414,1.2440947939,0.6576797175
O,0,0.5676207172,1.584577795,-0.5084910111
C,0,0.9809216424,2.962489488,-0.6520146698
O,0,-0.2244052816,2.0483887374,1.5572997807
C,0,-4.1060372444,-0.707229612,1.4398238197
C,0,-5.3850745851,-0.8233885509,0.5657212576
C,0,-3.0706259875,0.8129953513,-0.1974883017
C,0,-4.452660618,0.8137937009,-0.9141379266
H,0,-1.8366658018,0.1719433653,2.2189388161
H,0,1.4198844565,3.0291777937,-1.6461956547
H,0,0.118853344,3.6274337857,-0.5678571838
H,0,1.7191766047,3.2175107383,0.1109006001
H,0,-1.5815794809,-1.5499240175,1.8036381603
H,0,-0.2275386035,-0.681529328,-0.2477423837
H,0,0.7873119936,-0.4335278122,2.6247213579
H,0,2.8076375473,0.6976711814,2.5080522464
H,0,5.0707430096,1.0180654905,1.532361711
H,0,4.1626198312,-1.8846619441,-1.5141465045
H,0,1.9070961093,-2.2224538229,-0.5109734339
```

```
H,0,-1.9732911022,-1.542201993,-1.0742887628
H,0,-2.8483365455,-2.5640070894,0.0779449829
H,0,-2.9835613726,1.605443745,0.5469421961
H,0,-2.244527486,0.8963861061,-0.903714279
H,0,-3.9148114965,-1.6044227325,2.0299950631
H,0,-4.1341867349,0.153771789,2.109390543
N,0,-5.0883783676,-0.5090068458,-0.8393538884
H,0,-3.8958661369,-1.2376813038,-2.3937123766
H,0,-4.6720280181,-2.4852326379,-1.4108507159
H,0,-5.792928958,-1.8357126004,0.6158715434
H,0,-6.1486097585,-0.133718195,0.9332770485
H,0,-5.1196485369,1.5462685256,-0.4533094706
H,0,-4.3238760217,1.0883727817,-1.9637186995
```

*M06-2X/6-31+G** PCM solvent model in methanol*

Int2-M06-meoh
E(RM062X) = -1201.45929073

```
 Zero-point correction=                           0.405342 (Hartree/Particle)
 Thermal correction to Energy=                    0.427516
 Thermal correction to Enthalpy=                  0.428460
 Thermal correction to Gibbs Free Energy=         0.351912
 Sum of electronic and zero-point Energies=          -1201.053949
 Sum of electronic and thermal Energies=             -1201.031775
 Sum of electronic and thermal Enthalpies=           -1201.030831
 Sum of electronic and thermal Free Energies=        -1201.107379

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  268.270             85.590            161.109
```

```
H,0,-1.1250603714,0.9090779875,1.3439140683
C,0,0.6341751749,4.2097949078,-1.5811081035
C,0,-0.567507221,3.5097353382,-1.6548803101
C,0,-0.7786069977,2.4736620285,-0.7542404759
C,0,0.1890095517,2.1369709487,0.2014782317
C,0,1.3732210922,2.8786917534,0.2585375961
C,0,1.6125378351,3.9158029911,-0.635422391
N,0,0.8698517131,5.3024576429,-2.5245827288
H,0,-1.3102570645,3.7793096414,-2.3959907856
H,0,-1.7174258196,1.9246611607,-0.7857303908
H,0,2.0920014647,2.632171514,1.0335258631
H,0,2.5285725146,4.4935828114,-0.6040782779
```

```
C,0,1.7965863602,-0.4240390755,0.1248040053
H,0,2.0058337989,-0.0191891035,-0.8687590866
H,0,2.288208106,0.1787683003,0.8944718193
N,0,2.4683656523,-1.777321696,0.1751940484
C,0,1.768071932,-2.7949553403,-0.6889493772
H,0,1.58894335,-2.3275753598,-1.6586106346
C,0,2.6646273496,-4.0544430862,-0.7778801581
H,0,0.8078850648,-3.0062277573,-0.2130893938
C,0,2.5382723046,-2.2968325207,1.5890384327
H,0,1.5397775582,-2.2390013303,2.0216334992
C,0,3.0820057185,-3.7449654969,1.5470358498
H,0,3.194435327,-1.6143532582,2.1334038546
C,0,3.8827448606,-1.6266144792,-0.3327572842
C,0,4.6458818154,-2.9443584312,-0.0604991943
H,0,3.8041235118,-1.3995192417,-1.3980612415
H,0,4.3224068094,-0.7701654754,0.1815764066
C,0,0.3091745293,-0.4084680153,0.4031525888
H,0,0.0055624872,-1.1560666656,1.1401992738
C,0,-0.5190944963,-0.5901765298,-0.8369683463
O,0,-1.8053490051,-0.8069283034,-0.5371031948
O,0,-0.115860173,-0.5075712398,-1.9819954414
C,0,-2.7004966226,-0.9314727091,-1.6506420617
H,0,-3.683356388,-1.1057209563,-1.2186348557
H,0,-2.6977017027,-0.0122541624,-2.240614904
H,0,-2.4020963097,-1.7705822034,-2.2814020483
C,0,-0.0259471456,0.9793625342,1.1886767116
O,0,0.7053101554,1.0571989048,2.3009949333
O,0,1.9339223157,5.9010820622,-2.4632636089
O,0,-0.0069348068,5.5674533893,-3.3341091954
H,0,2.052842161,-4.949618024,-0.6483027357
H,0,3.1487149238,-4.1129394997,-1.7558922239
H,0,5.2337996429,-3.2163198578,-0.9397251633
H,0,5.3298854215,-2.8280751297,0.7839127207
N,0,3.7058340079,-4.0232751464,0.2514924479
H,0,3.8177425076,-3.8829604222,2.3423297804
H,0,2.2747121059,-4.4647253992,1.702212482
```

Elimination, simplest proton shuttle

*B3LYP/6-31+G** PCM solvent model in methanol*

elim-H-shuttle-Becke-meoh
E(RB3LYP) = -1317.69666653

```
Zero-point correction=                        0.449340 (Hartree/Particle)
Thermal correction to Energy=                 0.475823
Thermal correction to Enthalpy=               0.476767
Thermal correction to Gibbs Free Energy=      0.390392
Sum of electronic and zero-point Energies=        -1317.247326
Sum of electronic and thermal Energies=           -1317.220844
Sum of electronic and thermal Enthalpies=         -1317.219900
Sum of electronic and thermal Free Energies=      -1317.306274

              E (Thermal)         CV              S
               KCal/Mol     Cal/Mol-Kelvin   Cal/Mol-Kelvin
Total           298.583           98.931          181.791

H,0,-0.2077117535,0.3999479603,1.9494181017
C,0,2.8457646012,-0.1182795062,0.3742967312
H,0,2.8177120015,-0.0468368277,-0.7146330101
H,0,3.2085805244,0.82907756,0.776714592
N,0,4.010774145,-1.0956302063,0.6497074248
C,0,3.6454783568,-2.536471614,0.3397740451
H,0,3.1958246296,-2.5461530185,-0.6525213265
C,0,4.9307875774,-3.406230643,0.4419079037
H,0,2.8947258727,-2.8239428647,1.0750549913
C,0,4.4788701508,-1.0122464509,2.0912179939
H,0,3.6135761655,-1.202609636,2.7237366249
C,0,5.6027258179,-2.0642187905,2.308800738
H,0,4.8300729515,0.0102272651,2.2426472857
C,0,5.1689564338,-0.6951218508,-0.2464097873
C,0,6.4118339652,-1.5549466451,0.116519027
H,0,4.8388805667,-0.8558404846,-1.2741057156
H,0,5.3407601097,0.3723443612,-0.0971530416
C,0,1.4740100437,-0.4656141375,0.9345761428
H,0,1.5290747058,-1.3833526089,1.9067154351
C,0,0.5947322669,-1.051047966,-0.093957743
O,0,-0.7232949882,-1.0534041847,0.2475943725
O,0,0.97742576,-1.5631370002,-1.1482714893
C,0,-1.6240540526,-1.7171553196,-0.6598753773
H,0,-2.6129105721,-1.6102479671,-0.2147684775
H,0,-1.5979193721,-1.2451419544,-1.6446904221
H,0,-1.3632648097,-2.7738574286,-0.7555428664
C,0,0.8507518273,0.6550249987,1.8257110445
O,0,1.4866283265,0.6863900147,3.103311242
H,0,1.5291064131,-0.2645739876,3.3899550438
O,0,1.6184080556,-1.9689255218,3.0648280625
H,0,-0.4199380727,-2.1961345812,3.5131893879
```

```
C,0,1.0003404491,4.574562602,0.0434122385
C,0,1.8510539825,4.288235097,1.1129087734
C,0,1.796400763,3.0231988293,1.6943693878
C,0,0.9090594181,2.0460441988,1.2160999235
C,0,0.0583075243,2.3704284985,0.1427452685
C,0,0.0966396167,3.6266910934,-0.4497986674
N,0,1.0480642977,5.8974378484,-0.5696866481
H,0,2.5350293973,5.0428945309,1.4805066146
H,0,2.437539496,2.7881614752,2.5352414874
H,0,-0.6469390117,1.6328952382,-0.2268877781
H,0,-0.5601948932,3.878200073,-1.2728194257
C,0,0.5021565406,-2.782330311,3.3538704397
H,0,0.2946106933,-3.5033865905,2.5446994002
H,0,0.6775874344,-3.3666214157,4.2701478149
O,0,0.2848676184,6.1374679441,-1.5138542883
O,0,1.8502698821,6.7269418038,-0.1225920723
H,0,6.4584322471,-1.5973319372,2.8033750253
H,0,5.2458523267,-2.8749520467,2.9492962988
H,0,4.7330410453,-4.2841046409,1.0623299621
H,0,5.2388395901,-3.7564703591,-0.5467901031
N,0,6.0445102474,-2.6453245159,1.0311715337
H,0,6.8455636261,-1.979433219,-0.7924116011
H,0,7.1760300612,-0.940855161,0.599379482
```

*M06-2X/6-31+G** PCM solvent model in methanol*

```
elim-H-shuttle-M06-meoh
E(RM062X) = -1317.14208850

 Zero-point correction=                           0.455158 (Hartree/Particle)
 Thermal correction to Energy=                    0.480945
 Thermal correction to Enthalpy=                  0.481889
 Thermal correction to Gibbs Free Energy=         0.397426
 Sum of electronic and zero-point Energies=          -1316.686930
 Sum of electronic and thermal Energies=             -1316.661143
 Sum of electronic and thermal Enthalpies=           -1316.660199
 Sum of electronic and thermal Free Energies=        -1316.744662

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  301.798             97.112           177.768

 H,0,-0.097447337,0.3339398239,2.1079486232
 C,0,2.8801358708,-0.0827573976,0.3821659987
```

```
H,0,2.8268590984,0.0302339997,-0.7043409625
H,0,3.2488049818,0.8509739796,0.817579111
N,0,4.0109500084,-1.0750185653,0.6132867915
C,0,3.604240342,-2.4909218946,0.281584535
H,0,3.0921204341,-2.4623898695,-0.6810393831
C,0,4.8801595998,-3.3667439533,0.2732407839
H,0,2.9003282431,-2.7947175472,1.059492311
C,0,4.4894035154,-1.0310703871,2.0419191219
H,0,3.6182329694,-1.1348291501,2.6870549943
C,0,5.5005759843,-2.1827249265,2.2437052259
H,0,4.941396819,-0.0460188416,2.1828744404
C,0,5.1672739696,-0.6973902482,-0.2758500019
C,0,6.3978095112,-1.539304374,0.1348107831
H,0,4.847946832,-0.8966114123,-1.3014493876
H,0,5.3343186308,0.3753421932,-0.1588879284
C,0,1.5346619558,-0.4638226828,0.9668167941
H,0,1.6396317286,-1.3813442228,1.8722771046
C,0,0.6202808292,-0.9990740994,-0.0587553404
O,0,-0.6761361365,-0.9991801786,0.3169820283
O,0,0.9676383687,-1.4612130976,-1.1378809796
C,0,-1.5915405012,-1.6176573479,-0.5910809043
H,0,-2.5733661176,-1.5173876,-0.1320989226
H,0,-1.569378284,-1.1134317552,-1.5591339326
H,0,-1.3390205267,-2.6718809899,-0.7245277851
C,0,0.9468608308,0.6101340182,1.9155583242
O,0,1.6739623844,0.6265996201,3.1294728215
H,0,1.7057218101,-0.3223582428,3.4144007411
O,0,1.7086141597,-2.0286026119,3.0458815981
H,0,0.5675975033,-3.511020606,3.9373940637
C,0,0.960815154,4.5004604596,0.1348290946
C,0,1.8502258661,4.2458988992,1.1712535326
C,0,1.8374691476,2.9852342701,1.7610386418
C,0,0.9517596611,1.9997709906,1.3153016188
C,0,0.0648103062,2.2935395757,0.2695560677
C,0,0.0605101687,3.5444411734,-0.3298311156
N,0,0.9659748837,5.8257477794,-0.488438964
H,0,2.5313806093,5.0194846533,1.5047916067
H,0,2.5125544911,2.7588551838,2.5785886774
H,0,-0.6357138517,1.5347601903,-0.0684970312
H,0,-0.623434971,3.785167454,-1.1344022862
C,0,0.4865025603,-2.6937246998,3.2057250744
H,0,-0.3180551613,-2.0226256156,3.5560507119
H,0,0.1367930083,-3.1425593847,2.2587676749
O,0,0.1876569581,6.0336220371,-1.406846345
```

```
O,0,1.7484769474,6.6612496197,-0.0616108494
H,0,6.3467143949,-1.8308945434,2.8387633294
H,0,5.0307644979,-3.013086941,2.7781527986
H,0,4.6763184608,-4.3137873213,0.7782014415
H,0,5.1936021243,-3.5902869963,-0.7500571624
N,0,5.9842267418,-2.6819484231,0.9526683577
H,0,6.9129167014,-1.8974765206,-0.759280868
H,0,7.1025238234,-0.937353473,0.7143353265
```

Elimination, zero methanols, methoxide deprotonation, OH away

*B3LYP/6-31+G** PCM solvent model in methanol*

elim-methox-B-OH-away-Becke-meoh
E(RB3LYP) = -1317.68651404

```
Zero-point correction=                           0.448338 (Hartree/Particle)
Thermal correction to Energy=                    0.475186
Thermal correction to Enthalpy=                  0.476130
Thermal correction to Gibbs Free Energy=         0.389075
Sum of electronic and zero-point Energies=         -1317.238176
Sum of electronic and thermal Energies=            -1317.211328
Sum of electronic and thermal Enthalpies=          -1317.210384
Sum of electronic and thermal Free Energies=       -1317.297440

                 E (Thermal)             CV                S
                  KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total               298.184            100.084           183.224
```

```
O,0,-2.6651702782,2.0185063493,1.150493442
O,0,-0.0255841865,0.13442909,2.3446644373
C,0,0.5409326161,0.8504652716,1.2408389774
C,0,-0.5199558385,0.8205225867,0.1094242572
C,0,-0.2512034869,1.7468514453,-1.0217195466
O,0,0.2966594023,2.9229695906,-0.6251713014
C,0,0.4841717022,3.9258686534,-1.6445579775
C,0,1.8991019224,0.2663932413,0.8481676294
C,0,2.8478561116,1.0757279591,0.1962453382
C,0,4.0825449621,0.5670887568,-0.1915230423
C,0,4.3739353553,-0.7720960481,0.0848934496
```

```
C,0,3.4632203973,-1.598753322,0.7457724873
C,0,2.2325045521,-1.0701041509,1.1267783861
N,0,5.66801577,-1.3165972841,-0.3164503389
O,0,6.4679243165,-0.5692108754,-0.8923550732
O,0,5.9109169057,-2.5033739793,-0.0658492174
C,0,-0.8190439728,-0.5931257355,-0.383517838
N,0,-2.2868559916,-1.0439370676,-0.3537654879
C,0,-3.1827526656,-0.1051180004,-1.1448840648
C,0,-2.809393152,-1.141886561,1.0693191216
C,0,-2.3645958553,-2.4208896547,-0.9880952217
O,0,-0.5582842843,1.5444575,-2.1943635807
H,0,0.929563085,4.778053612,-1.1324247784
H,0,1.1531465402,3.5584318487,-2.4258937839
H,0,-0.4750029784,4.2056921901,-2.0855737588
H,0,-1.5308350908,1.3878724185,0.6398383546
H,0,-0.3052246226,-1.3378503402,0.2243317329
H,0,-0.5179041039,-0.7229126763,-1.4245284987
H,0,0.6930861581,1.897833582,1.5173600428
H,0,1.5293598784,-1.6990156126,1.6610659861
H,0,3.7186564112,-2.6290334034,0.9591870092
H,0,4.8130098372,1.1913411063,-0.6904373615
H,0,2.6161643957,2.1157316296,-0.0051013694
H,0,-2.0485735192,-2.3066533156,-2.0266334439
H,0,-1.6446321261,-3.0569599023,-0.4703621047
H,0,-2.1846153041,-1.8791738154,1.57618303
H,0,-2.6722688887,-0.1594591509,1.5232803023
H,0,-3.1676822074,0.8513206742,-0.6217584549
H,0,-2.7269233018,0.0093075084,-2.128323412
C,0,-4.3055846741,-1.5595367743,1.0172514398
C,0,-4.6107296655,-0.7188691822,-1.2056263847
C,0,-3.8203748511,-2.9524342333,-0.8669236909
H,0,-4.4784817703,-2.418180583,1.6715743928
H,0,-4.9381361314,-0.7386303511,1.3650602967
H,0,-4.8635332297,-1.0057885937,-2.2299284381
H,0,-5.3444505843,0.0201341933,-0.8734692087
H,0,-4.1783018953,-3.2802971918,-1.8462199694
H,0,-3.8585856311,-3.8100949619,-0.1906271803
N,0,-4.7196819246,-1.9118022638,-0.3506339742
```

```
H,0,0.5603583337,0.2288559639,3.1090796295
C,0,-2.3608271398,3.0335661018,2.0620686875
H,0,-3.2110698665,3.2489879511,2.7373594805
H,0,-1.5048268846,2.7798635759,2.7192287356
H,0,-2.1035837032,3.9963717474,1.5748369834
```

Elimination, zero methanols, methoxide deprotonation, intramolecular OH

*B3LYP/6-31+G** PCM solvent model in methanol*

deprotonationFullSysmethoxideINTRAMeOH
E(RM062X) = -1317.13102674

```
 Zero-point correction=                           0.456947 (Hartree/Particle)
 Thermal correction to Energy=                    0.482465
 Thermal correction to Enthalpy=                  0.483409
 Thermal correction to Gibbs Free Energy=         0.399530
 Sum of electronic and zero-point Energies=          -1316.674079
 Sum of electronic and thermal Energies=             -1316.648562
 Sum of electronic and thermal Enthalpies=           -1316.647618
 Sum of electronic and thermal Free Energies=        -1316.731497

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  302.751             96.550            176.537
```

```
O,0,0.5985318291,1.7460884155,1.9697956676
C,0,-0.7963699772,-0.6277050274,-0.6516206033
H,0,-0.6132082594,-0.5104209524,-1.7216834945
H,0,-0.107086877,-1.3905414292,-0.278911041
N,0,-2.1624112836,-1.2643348232,-0.5415790607
C,0,-3.2541615304,-0.3432602395,-1.0375727832
H,0,-2.9324775305,0.0385357035,-2.0076596529
C,0,-4.5688751204,-1.1576532764,-1.1148744555
H,0,-3.3136972707,0.4661809836,-0.3046712565
C,0,-2.4580621948,-1.6574188167,0.8857399211
H,0,-2.3122270848,-0.7741974709,1.5082309024
C,0,-3.9212734838,-2.1535196755,0.951814086
H,0,-1.7363656406,-2.4379187583,1.1420622067
C,0,-2.179729599,-2.5118173447,-1.3882522287
C,0,-3.4911720824,-3.2808935289,-1.1009954729
H,0,-2.1066123143,-2.182382858,-2.4273170466
H,0,-1.2909759875,-3.0942572797,-1.1373892356
```

```
C,0,-0.6205849381,0.6828342801,0.1135840493
H,0,-1.6041157495,0.9474345083,0.7612132228
C,0,-0.4666376228,1.880508715,-0.7610321787
O,0,-1.0794713868,1.7634125895,-1.9433271172
O,0,0.0948674589,2.9190922662,-0.4308837258
C,0,-1.1009957089,2.9381425807,-2.7665487876
H,0,-1.652336594,2.6569310594,-3.6610614469
H,0,-1.6066287346,3.7503685313,-2.2407320204
H,0,-0.0833598509,3.2393906363,-3.0187286739
C,0,0.4800924773,0.5676235206,1.1991227491
H,0,0.1393158183,-0.2128328404,1.8912796029
O,0,-2.8189535103,1.3059717297,1.5818491947
H,0,-2.3388785342,3.3391396067,1.677765404
C,0,4.2853556458,-0.7205925873,-0.3127806475
C,0,3.5103388154,-1.6177499237,0.410191082
C,0,2.2817019724,-1.1789582733,0.8944058538
C,0,1.8351089332,0.12502124,0.6583948213
C,0,2.6509623507,1.0048736366,-0.0670844048
C,0,3.8807780396,0.5882977217,-0.5597660096
N,0,5.5834607593,-1.1670708519,-0.8287222103
H,0,3.8638071379,-2.6250722549,0.5927848826
H,0,1.6684982924,-1.8617207324,1.4766938634
H,0,2.3269310935,2.0254357103,-0.2426470258
H,0,4.5190384661,1.2586302473,-1.1223412449
C,0,-3.0362207304,2.6200499868,1.2025413856
H,0,-2.9214942435,2.7765784876,0.1036093269
H,0,-4.0566558913,2.9723008929,1.4424443447
O,0,6.2488297824,-0.3743207964,-1.4763974491
O,0,5.9359573154,-2.3107816742,-0.5865873546
H,0,-3.9342188633,-3.6165036272,-2.0413231961
H,0,-3.2925640212,-4.1618512577,-0.4854170428
N,0,-4.4427528599,-2.4257302161,-0.3905464667
H,0,-3.9766161409,-3.0638202557,1.5534431964
H,0,-4.553833057,-1.3938771086,1.4182647209
H,0,-5.3836232895,-0.5754460079,-0.6777804356
H,0,-4.8298175353,-1.3813942042,-2.1526169699
H,0,0.5298973115,2.4992870436,1.3596072549
```

*M06-2X/6-31+G** PCM solvent model in methanol*

deprotonationFullSysmethoxideINTRAMeOH
E(RM062X) = -1317.13102674

Zero-point correction= 0.456947 (Hartree/Particle)

```
Thermal correction to Energy=                    0.482465
Thermal correction to Enthalpy=                  0.483409
Thermal correction to Gibbs Free Energy=         0.399530
Sum of electronic and zero-point Energies=         -1316.674079
Sum of electronic and thermal Energies=            -1316.648562
Sum of electronic and thermal Enthalpies=          -1316.647618
Sum of electronic and thermal Free Energies=       -1316.731497

                E (Thermal)           CV                S
                 KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              302.751           96.550           176.537
```

```
O,0,0.5985318291,1.7460884155,1.9697956676
C,0,-0.7963699772,-0.6277050274,-0.6516206033
H,0,-0.6132082594,-0.5104209524,-1.7216834945
H,0,-0.107086877,-1.3905414292,-0.278911041
N,0,-2.1624112836,-1.2643348232,-0.5415790607
C,0,-3.2541615304,-0.3432602395,-1.0375727832
H,0,-2.9324775305,0.0385357035,-2.0076596529
C,0,-4.5688751204,-1.1576532764,-1.1148744555
H,0,-3.3136972707,0.4661809836,-0.3046712565
C,0,-2.4580621948,-1.6574188167,0.8857399211
H,0,-2.3122270848,-0.7741974709,1.5082309024
C,0,-3.9212734838,-2.1535196755,0.951814086
H,0,-1.7363656406,-2.4379187583,1.1420622067
C,0,-2.179729599,-2.5118173447,-1.3882522287
C,0,-3.4911720824,-3.2808935289,-1.1009954729
H,0,-2.1066123143,-2.182382858,-2.4273170466
H,0,-1.2909759875,-3.0942572797,-1.1373892356
C,0,-0.6205849381,0.6828342801,0.1135840493
H,0,-1.6041157495,0.9474345083,0.7612132228
C,0,-0.4666376228,1.880508715,-0.7610321787
O,0,-1.0794713868,1.7634125895,-1.9433271172
O,0,0.0948674589,2.9190922662,-0.4308837258
C,0,-1.1009957089,2.9381425807,-2.7665487876
H,0,-1.652336594,2.6569310594,-3.6610614469
H,0,-1.6066287346,3.7503685313,-2.2407320204
H,0,-0.0833598509,3.2393906363,-3.0187286739
C,0,0.4800924773,0.5676235206,1.1991227491
H,0,0.1393158183,-0.2128328404,1.8912796029
O,0,-2.8189535103,1.3059717297,1.5818491947
H,0,-2.3388785342,3.3391396067,1.677765404
C,0,4.2853556458,-0.7205925873,-0.3127806475
C,0,3.5103388154,-1.6177499237,0.410191082
```

```
C,0,2.2817019724,-1.1789582733,0.8944058538
C,0,1.8351089332,0.12502124,0.6583948213
C,0,2.6509623507,1.0048736366,-0.0670844048
C,0,3.8807780396,0.5882977217,-0.5597660096
N,0,5.5834607593,-1.1670708519,-0.8287222103
H,0,3.8638071379,-2.6250722549,0.5927848826
H,0,1.6684982924,-1.8617207324,1.4766938634
H,0,2.3269310935,2.0254357103,-0.2426470258
H,0,4.5190384661,1.2586302473,-1.1223412449
C,0,-3.0362207304,2.6200499868,1.2025413856
H,0,-2.9214942435,2.7765784876,0.1036093269
H,0,-4.0566558913,2.9723008929,1.4424443447
O,0,6.2488297824,-0.3743207964,-1.4763974491
O,0,5.9359573154,-2.3107816742,-0.5865873546
H,0,-3.9342188633,-3.6165036272,-2.0413231961
H,0,-3.2925640212,-4.1618512577,-0.4854170428
N,0,-4.4427528599,-2.4257302161,-0.3905464667
H,0,-3.9766161409,-3.0638202557,1.5534431964
H,0,-4.553833057,-1.3938771086,1.4182647209
H,0,-5.3836232895,-0.5754460079,-0.6777804356
H,0,-4.8298175353,-1.3813942042,-2.1526169699
H,0,0.5298973115,2.4992870436,1.3596072549
```

Elimination, zero methanols, methoxide deprotonation, OH H-bonded to methoxide, ester switched

*M06-2X/6-31+G** PCM solvent model in methanol*

deprotonationFullSysmethoxideMethanolB
E(RM062X) = -1317.14070851

```
 Zero-point correction=                           0.455202 (Hartree/Particle)
 Thermal correction to Energy=                    0.481073
 Thermal correction to Enthalpy=                  0.482018
 Thermal correction to Gibbs Free Energy=         0.397265
 Sum of electronic and zero-point Energies=          -1316.685506
 Sum of electronic and thermal Energies=             -1316.659635
 Sum of electronic and thermal Enthalpies=           -1316.658691
 Sum of electronic and thermal Free Energies=        -1316.743444

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
```

Total	301.878	97.090	178.377

```
H,0,0.6914422978,2.1249072922,1.2442574947
C,0,-0.6750237641,-0.5030529074,-0.5529314254
H,0,-0.4392935263,-0.5647174762,-1.6179191414
H,0,-0.0201028877,-1.1957427024,-0.0154523038
N,0,-2.0572084326,-1.1333162452,-0.4288846689
C,0,-3.145290596,-0.2341637074,-0.9636111069
H,0,-2.807908561,0.1379150867,-1.9315335084
C,0,-4.4517210077,-1.0598148396,-1.0518901817
H,0,-3.2272350918,0.5989809261,-0.2623914497
C,0,-2.3717341445,-1.4801286179,1.0035175321
H,0,-2.1935510611,-0.5931055822,1.607793075
C,0,-3.8443186724,-1.9430557086,1.0735155474
H,0,-1.6685051391,-2.2670107712,1.2884986007
C,0,-2.0701403738,-2.4101505103,-1.2283282566
C,0,-3.3755001755,-3.1769818618,-0.9072665325
H,0,-2.0033781774,-2.1195533405,-2.2792844729
H,0,-1.1750995325,-2.9747505556,-0.9588282785
C,0,-0.5283108756,0.9085443856,-0.0142967112
H,0,-1.5451204411,1.2590749801,0.7010487555
C,0,-0.3892184002,1.9630767191,-1.0381224659
O,0,-0.9710931272,1.6424323348,-2.2147202124
O,0,0.1393209012,3.0538515287,-0.8733294885
C,0,-0.9403420576,2.6516948506,-3.2284775811
H,0,-1.4588977783,2.2242554998,-4.084729449
H,0,-1.4506899969,3.5523965114,-2.8821930659
H,0,0.0911759027,2.8956710496,-3.4893453721
C,0,0.5108004363,1.0483311031,1.1259913307
O,0,-0.001135368,0.5030359723,2.3271178546
H,0,-0.9026341197,0.9071561337,2.4210104683
O,0,-2.3502318322,1.5650943004,1.7352738162
H,0,-1.5604669976,3.4535841497,2.1576251432
C,0,4.2442352817,-0.7947253864,0.1405474665
C,0,3.4374870283,-1.4051630032,1.0929571218
C,0,2.2296053633,-0.7988250499,1.4264000036
C,0,1.8378458124,0.3940339387,0.810499309
C,0,2.6796483431,0.985082438,-0.143005885
C,0,3.8886486216,0.3976038164,-0.4862880203
N,0,5.5182307137,-1.4243681522,-0.2120008985
H,0,3.7531012367,-2.3293119298,1.5616734753
H,0,1.5839461219,-1.2458622219,2.1741984464
H,0,2.3826056015,1.9186689293,-0.61208288
H,0,4.5483710247,0.8488273614,-1.217240473
```

```
C,0,-2.4577925212,2.9618266284,1.741280642
H,0,-2.6000031761,3.3656622031,0.7229523045
H,0,-3.3172103567,3.2956809659,2.3411796816
O,0,6.2315294459,-0.863190516,-1.0298633129
O,0,5.8091862658,-2.4817915213,0.3264403487
H,0,-3.8047169523,-3.5745815423,-1.8297357033
H,0,-3.1750335427,-4.0164237428,-0.2367272001
N,0,-4.3445213364,-2.2893809526,-0.260367655
H,0,-3.927196153,-2.8118842764,1.7307278664
H,0,-4.4746887096,-1.1473170551,1.4798233615
H,0,-5.2867500115,-0.4628040517,-0.6781612583
H,0,-4.668515501,-1.3364138773,-2.0871096866
```

Elimination, one methanol, methoxide deprotonation, OH turned

*B3LYP/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideOneMeohOHturnedAB3PCM
E(RB3LYP) = -1433.43478052

```
 Zero-point correction=                           0.501393 (Hartree/Particle)
 Thermal correction to Energy=                    0.532801
 Thermal correction to Enthalpy=                  0.533745
 Thermal correction to Gibbs Free Energy=         0.434906
 Sum of electronic and zero-point Energies=         -1432.933388
 Sum of electronic and thermal Energies=            -1432.901979
 Sum of electronic and thermal Enthalpies=          -1432.901035
 Sum of electronic and thermal Free Energies=       -1432.999874

                E (Thermal)          CV              S
                 KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
 Total             334.338          113.267          208.024

    1     8     0    -0.585371    2.318145   -0.912784
    2     6     0     0.521343   -1.066842    0.344141
    3     1     0     0.146684   -1.541239    1.252150
    4     1     0     0.011000   -1.517412   -0.508429
    5     7     0     1.960517   -1.600405    0.215566
    6     6     0     2.863565   -1.083801    1.323248
    7     1     0     2.343724   -1.261551    2.264494
    8     6     0     4.229879   -1.819592    1.229770
    9     1     0     2.960531   -0.011972    1.152605
   10     6     0     2.568520   -1.242995   -1.127956
   11     1     0     2.510492   -0.162098   -1.233312
```

12	6	0	4.037947	-1.751102	-1.157616
13	1	0	1.947583	-1.724635	-1.885899
14	6	0	1.905008	-3.115066	0.317460
15	6	0	3.322846	-3.691408	0.046622
16	1	0	1.545931	-3.347722	1.321424
17	1	0	1.167798	-3.463515	-0.407942
18	6	0	0.306700	0.447089	0.393815
19	1	0	1.437386	1.148612	0.158258
20	6	0	-0.029095	0.860797	1.780137
21	8	0	-0.582873	2.091900	1.880464
22	8	0	0.239886	0.202098	2.787426
23	6	0	-0.827773	2.579621	3.213554
24	1	0	-1.280366	3.562219	3.082260
25	1	0	-1.509490	1.915752	3.750177
26	1	0	0.109390	2.664978	3.768681
27	6	0	-0.619207	0.895111	-0.772583
28	1	0	-0.184794	0.443157	-1.674642
29	8	0	2.552854	1.774594	-0.086926
30	1	0	2.092763	3.620753	0.798256
31	6	0	-4.678243	-0.556173	-0.508214
32	6	0	-3.771919	-1.210026	-1.344469
33	6	0	-2.470012	-0.721157	-1.426041
34	6	0	-2.061436	0.395370	-0.676791
35	6	0	-3.007347	1.042075	0.140180
36	6	0	-4.312943	0.573005	0.232157
37	7	0	-6.047328	-1.056254	-0.414563
38	1	0	-4.085104	-2.069993	-1.922817
39	1	0	-1.769963	-1.209629	-2.097486
40	1	0	-2.710488	1.919927	0.700104
41	1	0	-5.041532	1.068064	0.861785
42	6	0	2.812787	2.787192	0.859118
43	1	0	2.781074	2.404303	1.894468
44	1	0	3.817530	3.210643	0.705731
45	8	0	-6.843351	-0.457240	0.318515
46	8	0	-6.354539	-2.059352	-1.070101
47	1	0	3.592727	-4.396312	0.836985
48	1	0	3.342774	-4.228905	-0.904707
49	7	0	4.324824	-2.617377	-0.003553
50	1	0	4.218727	-2.311766	-2.078415
51	1	0	4.731568	-0.906985	-1.135597
52	1	0	5.042716	-1.088756	1.241127
53	1	0	4.368969	-2.488750	2.082942
54	1	0	-1.067030	2.548553	-1.719775
55	1	0	3.100360	2.160757	-1.584259

56	8	0	3.484631	2.361858	-2.489530
57	6	0	2.801540	3.475284	-3.046259
58	1	0	3.227396	3.678987	-4.034110
59	1	0	1.726130	3.281276	-3.171710
60	1	0	2.916567	4.381198	-2.432661

Elimination, one methanol, methoxide deprotonation, OH turned, ester switched

*B3LYP/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideOneMeohOHturnedBB3PCM
E(RB3LYP) = -1433.43358533

```
Zero-point correction=                          0.501165 (Hartree/Particle)
Thermal correction to Energy=                   0.532802
Thermal correction to Enthalpy=                 0.533746
Thermal correction to Gibbs Free Energy=        0.432914
Sum of electronic and zero-point Energies=       -1432.932421
Sum of electronic and thermal Energies=          -1432.900784
Sum of electronic and thermal Enthalpies=        -1432.899840
Sum of electronic and thermal Free Energies=     -1433.000672

                E (Thermal)         CV              S
                 KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
Total              334.338          113.344          212.219
```

O,0,0.3795849648,-2.3280981022,-0.4800180863
C,0,0.0923645469,1.2841979501,0.5786634898
H,0,0.5350405867,1.7597299737,1.4528517262
H,0,0.6846422616,1.5795748237,-0.2898847948
N,0,-1.2338385493,2.0452850587,0.3779037445
C,0,-2.1779268685,1.8596590688,1.5542801948
H,0,-1.6201125614,2.1397423139,2.4481643287
C,0,-3.4368027284,2.7448172685,1.3253923995
H,0,-2.4210202528,0.7970272545,1.5861434032
C,0,-1.9319835184,1.6186208622,-0.8992315309
H,0,-2.1158723036,0.5491142831,-0.8264315583
C,0,-3.2532132959,2.4287502417,-1.0425760674
H,0,-1.234468824,1.8175792341,-1.7150296487
C,0,-0.9046747426,3.5245520264,0.264762821
C,0,-2.2151612002,4.3184348099,-0.0021911022
H,0,-0.4271484264,3.8129759395,1.2024590322
H,0,-0.1810138522,3.6326686625,-0.5448671998

C,0,0.0495771938,-0.2393699186,0.7301749327
H,0,-1.2007632763,-0.7224134788,0.7000362983
C,0,0.5009798259,-0.7018967057,2.0659700459
O,0,0.1712705061,0.1830220014,3.0552092318
O,0,1.0339026913,-1.7730357711,2.3376840331
C,0,0.4700825779,-0.2194428707,4.4047604242
H,0,0.1580934322,0.6153745827,5.0319814157
H,0,-0.0870535412,-1.121512239,4.6692036555
H,0,1.5398199393,-0.4050658933,4.5248264971
C,0,0.7114305516,-0.9363312423,-0.4896152376
H,0,0.2525442952,-0.4719486199,-1.3734538345
O,0,-2.4396805568,-1.1634002499,0.6637312207
H,0,-2.0751583505,-3.1204711036,1.3176227772
C,0,4.9649660248,-0.3299116704,-0.916033326
C,0,4.0838636833,0.432850842,-1.6843052169
C,0,2.7157570284,0.2163301358,-1.5365786174
C,0,2.2203328225,-0.7345577494,-0.6277327755
C,0,3.137911537,-1.4990276469,0.1170163022
C,0,4.50766219,-1.3011622345,-0.0191595115
N,0,6.4024848823,-0.1168888233,-1.0629788106
H,0,4.463612154,1.1642284277,-2.3864182886
H,0,2.0270337723,0.7858977793,-2.1536483153
H,0,2.7626212654,-2.2432749931,0.8073689581
H,0,5.215977405,-1.8856843658,0.5544832832
C,0,-2.6168799498,-2.2023861828,1.6011985472
H,0,-2.2669635277,-1.9127774877,2.6068486062
H,0,-3.6823801375,-2.4636335584,1.6962290066
O,0,7.1723127873,-0.8085532164,-0.3855750676
O,0,6.7920248271,0.748083473,-1.8571117425
H,0,-2.3424636133,5.0945716503,0.7565386137
H,0,-2.1699729067,4.8060496579,-0.9791029441
N,0,-3.3845196393,3.4303860761,0.0248230477
H,0,-3.2770717777,2.9379509776,-2.0093130813
H,0,-4.1134111839,1.7569350432,-0.9937590721
H,0,-4.3366607795,2.1252071886,1.3564457906
H,0,-3.5212637752,3.5001326217,2.1110443002
H,0,0.7024799801,-2.7181529586,-1.3045899367
H,0,-3.0477463123,-1.603136815,-0.7876671913
O,0,-3.4223138157,-1.8479555973,-1.6885557344
C,0,-4.8399597728,-1.8500270592,-1.6130136266
H,0,-5.2367313176,-2.093005954,-2.6041726333
H,0,-5.2162203229,-2.6011524213,-0.9024366455
H,0,-5.2412030528,-0.8690472993,-1.31739853

Elimination, one methanol, methoxide deprotonation, intramolecular OH

*M06-2X/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideOneMeohINTRAM062X
E(RM062X) = -1432.83117542

```
 Zero-point correction=                           0.509705 (Hartree/Particle)
 Thermal correction to Energy=                    0.539523
 Thermal correction to Enthalpy=                  0.540467
 Thermal correction to Gibbs Free Energy=         0.447295
 Sum of electronic and zero-point Energies=          -1432.321471
 Sum of electronic and thermal Energies=             -1432.291652
 Sum of electronic and thermal Enthalpies=           -1432.290708
 Sum of electronic and thermal Free Energies=        -1432.383881

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  338.556            109.873           196.098
```

O,0,0.6436917405,-2.2372407289,-1.6360474805
C,0,-0.1951243501,0.7051533567,0.6270295142
H,0,0.1176287551,0.8003631412,1.6685717413
H,0,0.4529641096,1.3523872499,0.028852739
N,0,-1.5539861354,1.3776606391,0.5688417576
C,0,-2.5379085317,0.7030560104,1.4930202307
H,0,-2.1413843965,0.8309789521,2.5030832187
C,0,-3.9240145218,1.3656666001,1.2952562262
H,0,-2.5501740495,-0.3562692651,1.2339611806
C,0,-2.1079606196,1.3890241021,-0.8337365974
H,0,-2.3123498944,0.3518060436,-1.102057226
C,0,-3.389639872,2.2609789065,-0.8465720735
H,0,-1.3246866204,1.7909473214,-1.4811872122
C,0,-1.3889418136,2.8086202221,1.0154330756
C,0,-2.7898493115,3.4569703776,1.1288488044
H,0,-0.8575014726,2.7928293493,1.9685151344
H,0,-0.7616422545,3.2979504647,0.2669194254
C,0,-0.1362157012,-0.7366274387,0.1483825597
H,0,-1.289894305,-1.2063218568,-0.2045765032
C,0,0.20375201,-1.7056206381,1.2107940893
O,0,-0.2344617828,-1.3428052753,2.4269342602
O,0,0.7410560095,-2.7957316437,1.0289001777
C,0,-0.0872481405,-2.3152102435,3.4690237595
H,0,-0.518206398,-1.8584933339,4.3575687276

H,0,-0.6244347631,-3.2292642903,3.206932391
H,0,0.9677108895,-2.5437030891,3.6281307392
C,0,0.7003176907,-0.9125103363,-1.1425241403
H,0,0.2280348916,-0.285885239,-1.9097759552
O,0,-2.4540356587,-1.7844517735,-0.5671283434
H,0,-1.8313543207,-3.7574675848,-0.3322093916
C,0,4.7460956253,0.4650916579,-0.7168660755
C,0,3.8208376356,1.2855959694,-1.3487981116
C,0,2.5183749177,0.8174368038,-1.4909134559
C,0,2.1430068913,-0.4391404429,-1.0020607303
C,0,3.110462306,-1.2442489324,-0.3835988177
C,0,4.4171843307,-0.7992533751,-0.2353576331
N,0,6.1228761001,0.943896583,-0.5638223341
H,0,4.1176559156,2.2565243513,-1.7261243467
H,0,1.7892464872,1.4383443738,-2.0049146804
H,0,2.839519716,-2.2280970188,-0.0163132121
H,0,5.1708111127,-1.4148545948,0.2403713552
C,0,-2.5277463263,-3.0168721486,0.0931758592
H,0,-2.2878404482,-2.9264506479,1.1695579262
H,0,-3.5412657024,-3.4408884338,0.0305107201
O,0,6.9321437271,0.2062584181,-0.023431882
O,0,6.3946935221,2.0584919347,-0.982788211
H,0,-3.0561576662,3.6108481304,2.1774058742
H,0,-2.7872952322,4.4297960288,0.6317758167
N,0,-3.8047893554,2.6013096074,0.5160525231
H,0,-3.2182569824,3.1893001214,-1.3972998594
H,0,-4.1942476703,1.7033662731,-1.3296125426
H,0,-4.5858776836,0.687602231,0.7519490868
H,0,-4.3645684507,1.5964375477,2.2681756466
H,0,0.7214052588,-2.8310338707,-0.8702455262
H,0,-3.8240574786,-1.1834247264,-0.8717535695
O,0,-4.7012211369,-0.7439405651,-1.1384762843
C,0,-4.727277621,-0.6801283195,-2.5459700942
H,0,-5.6512764968,-0.1850417899,-2.8601232605
H,0,-3.8801809322,-0.1023355181,-2.9493980626
H,0,-4.6997255461,-1.6777026476,-3.0055259475

Elimination, one methanol, methoxide deprotonation B, intramolecular OH

*M06-2X/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideOneMeohINTRABM062XPCM
E(RM062X) = -1432.82893732

Zero-point correction= 0.508810 (Hartree/Particle)
Thermal correction to Energy= 0.538865
Thermal correction to Enthalpy= 0.539809
Thermal correction to Gibbs Free Energy= 0.444850
Sum of electronic and zero-point Energies= -1432.320128
Sum of electronic and thermal Energies= -1432.290073
Sum of electronic and thermal Enthalpies= -1432.289128
Sum of electronic and thermal Free Energies= -1432.384087

	E (Thermal) KCal/Mol	CV Cal/Mol-Kelvin	S Cal/Mol-Kelvin
Total	338.143	110.240	199.858

1	8	0	0.637977	2.146840	1.537745
2	6	0	-0.443104	-0.694244	-0.746013
3	1	0	-0.155592	-0.801311	-1.794140
4	1	0	0.170320	-1.385728	-0.161278
5	7	0	-1.843580	-1.270664	-0.660605
6	6	0	-2.830519	-0.449821	-1.458641
7	1	0	-2.382775	-0.286646	-2.440102
8	6	0	-4.163990	-1.232105	-1.526335
9	1	0	-2.934904	0.501383	-0.933035
10	6	0	-2.303601	-1.365336	0.773137
11	1	0	-2.140824	-0.400719	1.252450
12	6	0	-3.797963	-1.761683	0.767534
13	1	0	-1.670124	-2.121377	1.246039
14	6	0	-1.834761	-2.666944	-1.231706
15	6	0	-3.202281	-3.325162	-0.929068
16	1	0	-1.647566	-2.563777	-2.303000
17	1	0	-1.002253	-3.205384	-0.774829
18	6	0	-0.288311	0.734490	-0.247234
19	1	0	-1.388860	1.211044	0.221359
20	6	0	0.030679	1.720369	-1.300041
21	8	0	-0.438864	1.387379	-2.512400
22	8	0	0.588265	2.799306	-1.111338
23	6	0	-0.289018	2.370737	-3.544418
24	1	0	-0.726926	1.926760	-4.436017
25	1	0	-0.818657	3.285190	-3.270594
26	1	0	0.767096	2.592434	-3.705154
27	6	0	0.622219	0.838797	1.001560
28	1	0	0.164884	0.205206	1.772930
29	8	0	-2.506541	1.735714	0.790599
30	1	0	-1.707381	3.659452	0.884426

31	6	0	4.594626	-0.642561	0.322982
32	6	0	3.679092	-1.456337	0.977200
33	6	0	2.399538	-0.956815	1.199462
34	6	0	2.037937	0.324371	0.767967
35	6	0	2.995422	1.120376	0.122939
36	6	0	4.279127	0.644037	-0.105297
37	7	0	5.948448	-1.152455	0.087315
38	1	0	3.967573	-2.445559	1.310845
39	1	0	1.680011	-1.570890	1.734783
40	1	0	2.734787	2.123097	-0.197852
41	1	0	5.026780	1.250838	-0.601363
42	6	0	-2.533330	3.088316	0.428172
43	1	0	-2.449471	3.215363	-0.666258
44	1	0	-3.475550	3.565696	0.734889
45	8	0	6.753065	-0.416319	-0.462123
46	8	0	6.207443	-2.289555	0.450083
47	1	0	-3.559944	-3.852472	-1.816309
48	1	0	-3.109642	-4.051146	-0.117487
49	7	0	-4.183220	-2.312052	-0.535338
50	1	0	-3.986265	-2.503814	1.547547
51	1	0	-4.422343	-0.886514	0.969399
52	1	0	-4.996269	-0.551616	-1.332481
53	1	0	-4.308835	-1.673794	-2.515542
54	1	0	0.694884	2.763013	0.788780
55	1	0	-2.285216	1.446433	2.289432
56	8	0	-2.198449	1.145538	3.255145
57	6	0	-3.393737	0.492704	3.613882
58	1	0	-3.548649	0.584648	4.693958
59	1	0	-4.265077	0.928705	3.106049
60	1	0	-3.366087	-0.582663	3.374767

Elimination, one methanol, methoxide deprotonation B, OH turned away

*M06-2X/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideOneMeohOHturnedBM062XPCM
E(RM062X) = -1432.82358864

```
 Zero-point correction=                           0.509001 (Hartree/Particle)
 Thermal correction to Energy=                    0.538959
 Thermal correction to Enthalpy=                  0.539903
 Thermal correction to Gibbs Free Energy=         0.446986
 Sum of electronic and zero-point Energies=       -1432.314588
```

```
Sum of electronic and thermal Energies=            -1432.284630
Sum of electronic and thermal Enthalpies=          -1432.283686
Sum of electronic and thermal Free Energies=       -1432.376602

               E (Thermal)          CV              S
                KCal/Mol      Cal/Mol-Kelvin   Cal/Mol-Kelvin
Total             338.202          110.690          195.560
```

```
O,0,0.7911548519,-1.8922550134,-1.9285406092
C,0,-0.2888596809,0.6885117865,0.5741253263
H,0,-0.1487470303,0.6427224528,1.6558924358
H,0,0.450094609,1.3905486406,0.1775335916
N,0,-1.6154673058,1.4080376355,0.3934699256
C,0,-2.7470191639,0.6467646651,1.0379793827
H,0,-2.4278350642,0.4093815766,2.0543300904
C,0,-4.0182466069,1.5306185521,0.9931793195
H,0,-2.8558394103,-0.2788596412,0.4699938077
C,0,-1.9244807449,1.6287271242,-1.0641874023
H,0,-1.8621576532,0.6620132582,-1.5655282729
C,0,-3.3428383391,2.2424652229,-1.1756793974
H,0,-1.1446362054,2.2966341135,-1.4420009276
C,0,-1.519665695,2.7552030369,1.0632657564
C,0,-2.7988036828,3.5633092724,0.7345890145
H,0,-1.4092724312,2.5632846418,2.1328018938
H,0,-0.6139265776,3.2405132899,0.6944442572
C,0,-0.1517909052,-0.6787050954,-0.0815966099
H,0,-1.2574319327,-1.0707342119,-0.6794204827
C,0,0.0442432321,-1.7670971368,0.9022018851
O,0,-0.7664527894,-1.6020398982,1.9788657123
O,0,0.7571395161,-2.7503269445,0.8002839572
C,0,-0.7394077111,-2.6481517893,2.9512319808
H,0,-1.4322450636,-2.3418669526,3.7333287124
H,0,-1.0636873946,-3.5905511863,2.5039286993
H,0,0.2660164727,-2.7679767379,3.3593697396
C,0,0.8459497822,-0.6486901719,-1.252539958
H,0,0.4898722991,0.1477029727,-1.9252576453
O,0,-2.3151811876,-1.5203069358,-1.3296785549
H,0,-1.3703837021,-3.350163402,-1.5720652802
C,0,4.850024211,0.4290498003,-0.1663154201
C,0,4.0115802825,1.4030375822,-0.6941162536
C,0,2.7207039593,1.0280050485,-1.0516782619
C,0,2.2733540195,-0.2855375499,-0.8702384132
C,0,3.1531916311,-1.2453693894,-0.3512041984
C,0,4.4484922835,-0.8929987135,0.0064606814
```

```
N,0,6.2156266042,0.8061767922,0.2104352908
H,0,4.3672775884,2.4167522812,-0.8311337681
H,0,2.0560611012,1.7654071042,-1.4955494109
H,0,2.8038310707,-2.2640066916,-0.2295104644
H,0,5.1409810069,-1.6212484585,0.4107112083
C,0,-2.2990540467,-2.9158673956,-1.1752711474
H,0,-2.3822363082,-3.2155389619,-0.1144915005
H,0,-3.1434878903,-3.3794137265,-1.707190352
O,0,6.948725745,-0.0599265681,0.6617742529
O,0,6.5557222317,1.96923757,0.0567504423
H,0,-3.1980727245,4.0084377062,1.6488243723
H,0,-2.5723586345,4.3706664271,0.0335609288
N,0,-3.814555734,2.7006218059,0.1333450322
H,0,-3.3261442482,3.0865930791,-1.869235326
H,0,-4.0455426502,1.4904909487,-1.5418967675
H,0,-4.8487894058,0.9438824677,0.594976679
H,0,-4.279844181,1.881938448,1.9948499159
H,0,1.3116340815,-1.8198226893,-2.7385366856
H,0,-3.7811648641,-1.0475295423,-1.3498009703
O,0,-4.7568522616,-0.7785394585,-1.2652377593
C,0,-5.323467299,-1.5759809936,-0.2505579854
H,0,-6.302524761,-1.1662055963,0.017752739
H,0,-5.4659269263,-2.6173222262,-0.5721785797
H,0,-4.7013273665,-1.5901992249,0.6587003736
```

Elimination, one methanol, methoxide deprotonation D, OH turned away

*M06-2X/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideOneMeohOHturnedDM062XPCM
E(RM062X) = -1432.82347607

```
 Zero-point correction=                           0.507888 (Hartree/Particle)
 Thermal correction to Energy=                    0.538389
 Thermal correction to Enthalpy=                  0.539333
 Thermal correction to Gibbs Free Energy=         0.442673
 Sum of electronic and zero-point Energies=          -1432.315588
 Sum of electronic and thermal Energies=             -1432.285087
 Sum of electronic and thermal Enthalpies=           -1432.284143
 Sum of electronic and thermal Free Energies=        -1432.380803

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  337.844            110.943           203.439
```

1	8	0	-0.549823	2.108976	-1.142732
2	6	0	0.642014	-1.152605	0.240888
3	1	0	0.248927	-1.685674	1.110659
4	1	0	0.272189	-1.645988	-0.661555
5	7	0	2.128864	-1.456695	0.235975
6	6	0	2.818597	-0.867634	1.445060
7	1	0	2.224180	-1.153056	2.314359
8	6	0	4.264801	-1.415466	1.488902
9	1	0	2.788593	0.216243	1.319371
10	6	0	2.773660	-0.944462	-1.026714
11	1	0	2.465564	0.088874	-1.176454
12	6	0	4.302797	-1.070441	-0.866770
13	1	0	2.383641	-1.564900	-1.838670
14	6	0	2.335191	-2.949014	0.277157
15	6	0	3.835423	-3.235088	0.019322
16	1	0	2.007771	-3.282681	1.264504
17	1	0	1.689169	-3.395154	-0.481674
18	6	0	0.271925	0.323711	0.265426
19	1	0	1.320780	1.118532	0.161109
20	6	0	-0.205432	0.715312	1.612660
21	8	0	-0.873303	1.878915	1.625493
22	8	0	0.040801	0.106359	2.645829
23	6	0	-1.287507	2.355298	2.907525
24	1	0	-1.821891	3.284476	2.716126
25	1	0	-1.945209	1.630608	3.392282
26	1	0	-0.418933	2.540307	3.543400
27	6	0	-0.621254	0.709252	-0.932131
28	1	0	-0.194137	0.189567	-1.803204
29	8	0	2.380638	1.916415	0.135581
30	1	0	0.985199	3.438745	0.325305
31	6	0	-4.680197	-0.619454	-0.483000
32	6	0	-3.750429	-1.485934	-1.046155
33	6	0	-2.444426	-1.036482	-1.203516
34	6	0	-2.067560	0.248124	-0.790621
35	6	0	-3.038634	1.099865	-0.247548
36	6	0	-4.350805	0.673210	-0.087938
37	7	0	-6.061470	-1.078195	-0.316567
38	1	0	-4.049862	-2.477198	-1.363675
39	1	0	-1.720813	-1.694346	-1.675759
40	1	0	-2.752412	2.101842	0.048146
41	1	0	-5.108067	1.324448	0.331362
42	6	0	2.022986	3.194890	0.593364
43	1	0	2.115804	3.276663	1.689339
44	1	0	2.675922	3.965513	0.153727

```
 45      8      0     -6.873940   -0.298860    0.157063
 46      8      0     -6.335621   -2.218704   -0.657505
 47      1      0      4.185174   -4.006757    0.708777
 48      1      0      3.988723   -3.596700   -1.000644
 49      7      0      4.630749   -2.018930    0.203872
 50      1      0      4.745002   -1.409508   -1.806788
 51      1      0      4.733926   -0.096603   -0.619602
 52      1      0      4.957111   -0.600149    1.712199
 53      1      0      4.373646   -2.175348    2.267348
 54      1      0     -0.985502    2.314286   -1.979939
 55      1      0      3.283090    2.008382   -1.104531
 56      8      0      3.801490    2.053144   -1.976637
 57      6      0      2.864387    2.364231   -2.981870
 58      1      0      3.384470    2.435448   -3.941773
 59      1      0      2.085988    1.590158   -3.074563
 60      1      0      2.359797    3.322891   -2.793128
```

Elimination, one methanol, methoxide deprotonation, OH bonded to methoxide

*M06-2X/6-31+G** PCM solvent model in methanol*

doc-deprotonationFullSysTwoMeOHinMethanolM062X
E(RM062X) = -1432.83889593

```
 Zero-point correction=                           0.509264 (Hartree/Particle)
 Thermal correction to Energy=                    0.539603
 Thermal correction to Enthalpy=                  0.540547
 Thermal correction to Gibbs Free Energy=         0.444060
 Sum of electronic and zero-point Energies=          -1432.329632
 Sum of electronic and thermal Energies=             -1432.299293
 Sum of electronic and thermal Enthalpies=           -1432.298349
 Sum of electronic and thermal Free Energies=        -1432.394836

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  338.606            110.220            203.074
```

```
 H,0,0.9023605913,2.1926648529,1.3402905514
 C,0,-0.6649916324,-0.4052130801,-0.3338046983
 H,0,-0.5417514699,-0.4354182092,-1.4196485314
 H,0,0.0407062409,-1.1077917659,0.1195815186
 N,0,-2.0276701787,-1.0418929694,-0.0914247303
 C,0,-3.1469216243,-0.181452703,-0.6173417572
```

```
H,0,-2.9747215826,-0.0752682114,-1.6904800849
C,0,-4.4960069321,-0.8600913062,-0.2671639619
H,0,-3.0495010284,0.7977124119,-0.145790469
C,0,-2.2572923373,-1.3092227474,1.3738554444
H,0,-2.3147489092,-0.3391068933,1.8669569716
C,0,-3.5677655085,-2.121900761,1.5289151388
H,0,-1.378967794,-1.8449683346,1.7400131783
C,0,-2.0580183417,-2.3623565626,-0.8177556433
C,0,-3.4755813568,-2.971852622,-0.6951554859
H,0,-1.7782435354,-2.1669460301,-1.8543038954
H,0,-1.2903788625,-2.9880606733,-0.3566760804
C,0,-0.4604027121,0.9989959164,0.1915525268
H,0,-1.4207880571,1.4463952814,1.0064093415
C,0,-0.4937543387,1.9928812303,-0.8912304715
O,0,0.0959969147,3.1666458713,-0.5740900238
O,0,-1.0572324379,1.8347470289,-1.9671624163
C,0,-0.0562679061,4.2214272813,-1.5269790183
H,0,0.4764238999,5.0740940265,-1.1096991494
H,0,0.3743769693,3.934634666,-2.4881258089
H,0,-1.1137229858,4.4616342073,-1.6600884971
C,0,0.6825366263,1.1246882105,1.220717418
O,0,0.2832992759,0.5730701975,2.4668936486
H,0,-0.5644499359,1.0083213718,2.687290661
O,0,-2.1044711158,1.8804282908,2.0056946921
H,0,-1.0907925896,3.6810110847,2.2732572632
C,0,4.2443148434,-0.8354129065,-0.1187839857
C,0,3.5644266274,-1.3698725359,0.9679828756
C,0,2.4168594671,-0.7210890568,1.415631018
C,0,1.9589931133,0.4370140949,0.7810255531
C,0,2.6737739307,0.9521004454,-0.3101281484
C,0,3.8216052726,0.3221519649,-0.7690023519
N,0,5.4517930071,-1.5110537664,-0.5990837722
H,0,3.9261343475,-2.2701820843,1.4495625951
H,0,1.8672936413,-1.1114520956,2.2641480007
H,0,2.3288625175,1.8581388495,-0.8010566323
H,0,4.3838819808,0.7111445822,-1.6089661895
C,0,-2.0821753429,3.2900794501,1.9992754566
H,0,-2.3371098957,3.6950139039,1.0077198995
H,0,-2.8107409799,3.6864793378,2.7187992238
O,0,6.0473178512,-1.0226788496,-1.5473878203
O,0,5.8066475947,-2.5320304385,-0.029969186
H,0,-3.9795746129,-2.9600716755,-1.6645795952
H,0,-3.4055415975,-4.0092309746,-0.3598556981
N,0,-4.2848073148,-2.2124326699,0.2556736508
```

```
H,0,-3.352226237,-3.1356658567,1.8762204527
H,0,-4.2123247097,-1.6292362248,2.2596367575
H,0,-5.0093465317,-0.2770389719,0.5002263082
H,0,-5.1249000551,-0.9182173801,-1.1586527143
H,0,-3.577435009,1.3406888598,2.2602093987
O,0,-4.4569972578,0.9200034054,2.4941646512
C,0,-4.3841284705,0.5436338944,3.8530726538
H,0,-5.3098946415,0.0265846907,4.1210855011
H,0,-3.5424361119,-0.139786123,4.0449675011
H,0,-4.2699357726,1.4126630709,4.5146859654
```

Elimination, two methanols, methoxide deprotonation, intramolecular OH

*B3LYP/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideTwoMeohINTRAB3PCM
E(RB3LYP) = -1549.19164165

```
 Zero-point correction=                           0.556064 (Hartree/Particle)
 Thermal correction to Energy=                    0.591621
 Thermal correction to Enthalpy=                  0.592565
 Thermal correction to Gibbs Free Energy=         0.482639
 Sum of electronic and zero-point Energies=          -1548.635578
 Sum of electronic and thermal Energies=             -1548.600021
 Sum of electronic and thermal Enthalpies=           -1548.599077
 Sum of electronic and thermal Free Energies=        -1548.709003

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  371.247            125.722            231.358
```

```
O,0,-0.4984406302,2.3001747438,-1.9043621232
C,0,0.7507697597,-0.4326582077,0.4668760967
H,0,0.5055673321,-0.4385558012,1.5293881541
H,0,0.0764646671,-1.1344799862,-0.0285271885
N,0,2.1157063163,-1.1403363088,0.396455563
C,0,3.201567427,-0.3472257932,1.1015191461
H,0,2.8320153267,-0.1302955153,2.1038691657
C,0,4.5099338014,-1.1891027619,1.1079239663
H,0,3.3110064774,0.5868374894,0.5523936141
C,0,2.530302779,-1.4053999261,-1.038244878
H,0,2.5319287997,-0.4512951501,-1.5598476541
C,0,3.9334139484,-2.077511238,-1.0385149573
```

```
H,0,1.7599101317,-2.0481119869,-1.4687731208
C,0,1.9822664225,-2.4822312495,1.0982946964
C,0,3.320534656,-3.2620674456,0.955516184
H,0,1.7325391003,-2.2683721287,2.138710244
H,0,1.1430500686,-3.0054578527,0.637092019
C,0,0.6217172612,0.9663364857,-0.1344635002
H,0,1.7680287348,1.4283202762,-0.7492554582
C,0,0.4018263733,2.0314907426,0.8583586446
O,0,0.9471741601,1.7800519504,2.0709396359
O,0,-0.1505558683,3.1187082968,0.6296836816
C,0,0.8751634909,2.8353479317,3.0535836696
H,0,1.369659071,2.4369789729,3.9385443914
H,0,1.3941002361,3.7262271869,2.693838375
H,0,-0.1652221229,3.0806870293,3.2758711784
C,0,-0.3855564179,0.9993997986,-1.327141573
H,0,0.0351173481,0.3646671027,-2.1140891581
O,0,2.7842641855,1.8719584346,-1.3890341602
H,0,1.8761575741,3.7174448071,-1.7711831471
C,0,-4.3055228036,-0.6094286432,-0.4741934221
C,0,-3.4386465444,-1.319691614,-1.3050426663
C,0,-2.1795216769,-0.7820607002,-1.5664449966
C,0,-1.7765984056,0.4414717625,-1.0080383167
C,0,-2.6806602947,1.1339941191,-0.1806218671
C,0,-3.9427240426,0.6183027332,0.090423864
N,0,-5.6300071863,-1.1582084272,-0.1928193444
H,0,-3.7472795749,-2.2625338354,-1.7385807137
H,0,-1.5051410892,-1.3207448287,-2.2259509234
H,0,-2.3983999386,2.088386904,0.2490690281
H,0,-4.6395922501,1.1506643607,0.725431822
C,0,2.7980013987,3.2944380267,-1.3502205581
H,0,2.9079543062,3.6711197157,-0.3219964095
H,0,3.6439037332,3.6783643596,-1.9365539692
O,0,-6.3931238345,-0.5097025045,0.5328932014
O,0,-5.9332403769,-2.2492052275,-0.6902818875
H,0,3.6708394906,-3.5804674168,1.9406046712
H,0,3.1758932358,-4.1563416655,0.3441606049
N,0,4.3524931549,-2.4264466253,0.327993758
H,0,3.9105154873,-2.9845399076,-1.6477678116
H,0,4.6736396676,-1.3935106,-1.4582502106
H,0,5.3206328441,-0.6027708481,0.671635775
H,0,4.7857319796,-1.4576254871,2.1309830739
H,0,-0.502918569,2.9281272854,-1.1536986378
H,0,4.4587662798,1.3865389022,-1.3913356484
O,0,5.4047490812,1.0932169374,-1.4250424458
```

```
C,0,6.2087010646,2.0061019729,-0.6863205967
H,0,7.2373328261,1.6343632128,-0.7024029427
H,0,6.1998011409,3.0130694072,-1.12620196
H,0,5.8881917629,2.0836519081,0.3626072697
H,0,2.6332426107,1.3530263949,-3.0524455644
O,0,2.5738321644,0.9696605109,-3.9647943901
C,0,2.3916918321,2.020196457,-4.9073935737
H,0,2.3169063904,1.5689573314,-5.9012892939
H,0,1.4708008953,2.5888520024,-4.7177580097
H,0,3.2387608312,2.7208481304,-4.9121704152
```

*M06-2X/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideTwoMeohINTRAM062XPCM
E(RM062X) = -1548.52612931

```
 Zero-point correction=                           0.563147 (Hartree/Particle)
 Thermal correction to Energy=                    0.597780
 Thermal correction to Enthalpy=                  0.598724
 Thermal correction to Gibbs Free Energy=         0.492979
 Sum of electronic and zero-point Energies=          -1547.962982
 Sum of electronic and thermal Energies=             -1547.928349
 Sum of electronic and thermal Enthalpies=           -1547.927405
 Sum of electronic and thermal Free Energies=        -1548.033151

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  375.113            123.598            222.561
```

```
O,0,-0.5249395328,2.2699077383,-1.9182094355
C,0,0.7926264119,-0.4519922012,0.3805231553
H,0,0.617299801,-0.5070433461,1.4572647578
H,0,0.1209073125,-1.1681422415,-0.1022083731
N,0,2.1747483216,-1.0519694473,0.186373163
C,0,3.2359871079,-0.2225466719,0.8638134112
H,0,2.8886446828,-0.0331652889,1.8810251305
C,0,4.5715769065,-1.0052576829,0.8136543943
H,0,3.2840168211,0.7214465861,0.3181433827
C,0,2.5090273911,-1.1967041496,-1.2759773317
H,0,2.3453767517,-0.2315097,-1.7579903254
C,0,3.9801785768,-1.6700566993,-1.3935996708
H,0,1.7990632377,-1.9236825359,-1.680323296
C,0,2.1884045627,-2.4254811457,0.8077540746
```

```
C,0,3.5254864844,-3.1166826587,0.4472378418
H,0,2.0675793143,-2.2806479471,1.8836075559
H,0,1.3217496253,-2.9670897154,0.423873542
C,0,0.5781842148,0.9476556875,-0.1652018619
H,0,1.6483576626,1.4774371029,-0.7679688823
C,0,0.3436302385,1.9739130391,0.8614888213
O,0,0.9763878342,1.7273928164,2.0223111008
O,0,-0.2779451284,3.0226607466,0.6925104394
C,0,0.908919238,2.759727215,3.013214071
H,0,1.480651882,2.3878075554,3.8610663992
H,0,1.3501300493,3.6809035334,2.6277108567
H,0,-0.1276428253,2.9427304556,3.3006844161
C,0,-0.4317512616,0.9824283134,-1.3381997545
H,0,-0.0239544808,0.3340033477,-2.1249479919
O,0,2.5877425873,2.0464275576,-1.4535761018
H,0,1.6271606339,3.8852741203,-1.6166985669
C,0,-4.2857831262,-0.5826566274,-0.2743940208
C,0,-3.4166275215,-1.381125499,-1.0063454088
C,0,-2.1775380146,-0.8523552025,-1.35526562
C,0,-1.8089531912,0.4419115766,-0.9712223312
C,0,-2.7204598557,1.2213890283,-0.2440088943
C,0,-3.9639935511,0.7163465682,0.1096847243
N,0,-5.5955757908,-1.1242021066,0.0983673289
H,0,-3.7099701212,-2.3815221852,-1.3002343194
H,0,-1.4948107707,-1.4545878257,-1.9493371741
H,0,-2.4539757746,2.2317479637,0.0467092619
H,0,-4.6748371367,1.3095028049,0.6719614747
C,0,2.5384585417,3.4339625469,-1.2008874419
H,0,2.5599469963,3.6455616287,-0.1197836292
H,0,3.4034319719,3.9361330154,-1.6549144906
O,0,-6.3654292169,-0.3988321899,0.7088188055
O,0,-5.8543892091,-2.2755602491,-0.2162862591
H,0,3.9523310028,-3.5802120286,1.3395113665
H,0,3.3638918479,-3.8995335532,-0.2979543498
N,0,4.4748423297,-2.1474260776,-0.0997174924
H,0,4.0495724581,-2.4751964832,-2.1291569364
H,0,4.6185185062,-0.8410014566,-1.70806073
H,0,5.3648473657,-0.3411944999,0.4640236386
H,0,4.8367624915,-1.3794780903,1.805764188
H,0,-0.5795468475,2.9069083655,-1.1860348949
H,0,4.164617447,1.6351391954,-1.5056888765
O,0,5.1353171951,1.4236892932,-1.4163829042
C,0,5.6529531321,2.2268624562,-0.3757124126
H,0,6.6512890062,1.8609364361,-0.1194732136
```

```
H,0,5.7380898269,3.2804994727,-0.6723134528
H,0,5.028786468,2.1790999114,0.5297838707
H,0,1.9953592287,1.5943770519,-2.9813091654
O,0,1.8401062278,1.1454898979,-3.8491862945
C,0,3.1152974725,0.8380724205,-4.3757785189
H,0,2.9776277151,0.3353271513,-5.3361314393
H,0,3.7198145736,1.7400622055,-4.5379930153
H,0,3.6818399019,0.1657247004,-3.7147982947
```

Elimination, two methanols H-bonded to OH, methoxide deprotonation, OH H-bonded to methoxide

*M06-2X/6-31+G** PCM solvent model in methanol*

```
doc-deprotonationFSTwoMeOHSetToMaxOHtransM062XPCM
E(RM062X) = -1548.51854502
```

```
 Zero-point correction=                           0.562729 (Hartree/Particle)
 Thermal correction to Energy=                    0.597619
 Thermal correction to Enthalpy=                  0.598563
 Thermal correction to Gibbs Free Energy=         0.491235
 Sum of electronic and zero-point Energies=          -1547.955816
 Sum of electronic and thermal Energies=             -1547.920926
 Sum of electronic and thermal Enthalpies=           -1547.919982
 Sum of electronic and thermal Free Energies=        -1548.027310

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  375.011            123.646           225.891
```

```
H,0,-0.7989640257,-0.4213265538,2.2683247372
C,0,0.8946807402,-0.7721181959,-0.7236851735
H,0,0.788517625,-1.7392156062,-1.2209353965
H,0,0.201572374,-0.0678471019,-1.1951923768
N,0,2.2703956627,-0.270118932,-1.1496567826
C,0,3.3912616532,-1.0138324544,-0.4679308468
H,0,3.169639628,-2.0781700636,-0.5499043938
C,0,4.722149186,-0.6171059092,-1.1538865053
H,0,3.3623272641,-0.7201519317,0.5832174111
C,0,2.4226743679,1.2013616784,-0.8685831785
H,0,2.1776131872,1.358384935,0.1816314875
C,0,3.8802881222,1.6098143405,-1.1873412734
```

```
H,0,1.6891805152,1.7188061175,-1.492238728
C,0,2.4044525062,-0.4776272302,-2.6365944859
C,0,3.6884612598,0.2361535471,-3.1218457031
H,0,2.4419155576,-1.5574639336,-2.7971055425
H,0,1.5009928394,-0.080351308,-3.1036238833
C,0,0.6399572393,-0.8672862408,0.7680012595
H,0,1.5531957077,-0.2315240642,1.4925104025
C,0,0.6234572771,-2.2330191061,1.324776074
O,0,1.348342673,-3.1111377716,0.5984747305
O,0,0.0738708452,-2.5740052806,2.3635502583
C,0,1.4573212613,-4.4346905107,1.1317121968
H,0,2.0562424927,-4.9917974603,0.4136581052
H,0,1.9520194441,-4.4109288073,2.1047494033
H,0,0.4688443993,-4.8851071918,1.2366140669
C,0,-0.5450619123,-0.0190720363,1.2795606224
O,0,-0.1566672455,1.3475942097,1.4260643377
H,0,0.757902385,1.2983185034,1.89399102
O,0,2.110018059,0.6758561972,2.244627007
H,0,1.207406607,0.0670981662,4.0283226457
C,0,-4.0539346195,-0.3947795649,-1.1407875851
C,0,-3.3526719784,0.8026278802,-1.1878752707
C,0,-2.2129249947,0.9360236203,-0.399561185
C,0,-1.787013003,-0.1133214832,0.4196371502
C,0,-2.5221848884,-1.3080622857,0.4440651605
C,0,-3.659803743,-1.4602565244,-0.3347244399
N,0,-5.2556477855,-0.5428055935,-1.9663720209
H,0,-3.6919154165,1.6104996136,-1.8246249306
H,0,-1.6669213029,1.8718916666,-0.4237800762
H,0,-2.2012460337,-2.120398917,1.0905376142
H,0,-4.238848194,-2.3753843628,-0.3198255331
C,0,2.1974081361,0.1607689422,3.5528229996
H,0,2.6609886957,-0.8377649367,3.5577264625
H,0,2.8101982039,0.8142193641,4.1862185613
O,0,-5.8637315353,-1.6006911096,-1.9136642412
O,0,-5.5909568794,0.3981607263,-2.6689538046
H,0,4.2355118055,-0.4162637674,-3.806164798
H,0,3.4404653412,1.1569495938,-3.6557379804
N,0,4.5461665306,0.577060737,-1.9852829644
H,0,3.8869094613,2.553572531,-1.7381808751
H,0,4.4482195793,1.7508754898,-0.2634379758
H,0,5.4805749113,-0.4177924125,-0.3935547439
H,0,5.0861128047,-1.4274893953,-1.7908543874
H,0,-1.5612781507,2.2954476078,2.1832835588
O,0,-2.344592378,2.7108987511,2.5867096472
```

```
C,0,-3.2672688324,1.6933513563,2.9362719845
H,0,-4.0275461554,2.1406316149,3.580314537
H,0,-3.7643176959,1.2714323079,2.0527779743
H,0,-2.7839527679,0.8778379976,3.4890060193
H,0,0.0500040866,2.6923580346,0.201139066
O,0,0.1597062297,3.4081743539,-0.451347139
C,0,1.1355363417,4.3140006468,0.0354853585
H,0,1.2558409116,5.1024335431,-0.7095093572
H,0,0.8282267038,4.7698016723,0.9837960995
H,0,2.1091952386,3.8264958295,0.1825673172
```

Elimination, two methanols on methoxide, methoxide deprotonation, OH pointing away

*B3LYP/6-31+G** PCM solvent model in methanol*

elim-twomeoh-cis-Becke-meoh
E(RB3LYP) = -1549.19205971

```
 Zero-point correction=                           0.555228 (Hartree/Particle)
 Thermal correction to Energy=                    0.591118
 Thermal correction to Enthalpy=                  0.592062
 Thermal correction to Gibbs Free Energy=         0.482443
 Sum of electronic and zero-point Energies=          -1548.636832
 Sum of electronic and thermal Energies=             -1548.600942
 Sum of electronic and thermal Enthalpies=           -1548.599998
 Sum of electronic and thermal Free Energies=        -1548.709617

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  370.932            126.589            230.713
```

```
H,0,-0.9225025695,-1.7582364908,1.3759365747
C,0,-0.09993454,0.957651561,-0.6294628806
H,0,-0.4810700313,0.9872174489,-1.6522435317
H,0,-0.7329772348,1.5866045961,-0.0028515358
N,0,1.2223146652,1.7417656356,-0.703232917
C,0,2.271109004,1.0112917071,-1.5218161446
H,0,1.8002495509,0.7299580249,-2.4635573834
C,0,3.4992842752,1.9472452138,-1.7056347352
H,0,2.522260325,0.1049017099,-0.9752650101
C,0,1.7754552081,2.0233635523,0.6801998446
```

```
H,0,1.8472423194,1.0692831109,1.1991072669
C,0,3.1487550775,2.7349207049,0.5290421749
H,0,1.0334312233,2.6434939104,1.1862098916
C,0,0.9448585773,3.074043761,-1.3782784671
C,0,2.2333166675,3.9413513676,-1.3278195247
H,0,0.6332355317,2.8476521271,-2.3993519083
H,0,0.1085437097,3.5369622314,-0.8516677711
C,0,-0.0457170437,-0.4682490843,-0.1001533824
H,0,1.1722088724,-0.8939731452,0.430365276
C,0,-0.1649109584,-1.4535650423,-1.1911151059
O,0,-0.4682953953,-2.7082423824,-0.7590643525
O,0,0.0620690776,-1.2273116266,-2.3806003564
C,0,-0.4644543897,-3.7521548016,-1.7523975364
H,0,-0.7437620441,-4.6598775049,-1.218050783
H,0,-1.1890968004,-3.5377551535,-2.5411102073
H,0,0.5311338257,-3.8599209205,-2.1887622439
C,0,-0.9788193326,-0.698110593,1.1131818516
O,0,-0.4567186382,0.0963194473,2.1879267445
H,0,-0.9562915033,-0.1023488255,2.9928485819
O,0,2.2372967621,-1.3984998156,0.8874843784
H,0,1.3798385294,-1.9686205417,2.7080523412
C,0,-5.1264701735,0.2085144967,0.3113306842
C,0,-4.3411126041,1.1656801148,0.9563031906
C,0,-3.0068850107,0.8680525703,1.2241840023
C,0,-2.4493711728,-0.3663835645,0.8505573365
C,0,-3.2748092543,-1.3143326076,0.2169885324
C,0,-4.6084894848,-1.0363077509,-0.0597327426
N,0,-6.526427781,0.5099654118,0.0274315434
H,0,-4.7694469351,2.117793207,1.2433185914
H,0,-2.3959825515,1.5981947815,1.7430387674
H,0,-2.8661880272,-2.2803192057,-0.0587588491
H,0,-5.243291556,-1.7667994421,-0.545110358
C,0,1.9377758016,-2.392225076,1.8609118923
H,0,1.3410403044,-3.2097307939,1.4315417584
H,0,2.8675687735,-2.8261897632,2.2529869586
O,0,-7.2081070595,-0.3478670033,-0.5467908744
O,0,-6.9736720284,1.6111582152,0.3707020311
H,0,3.1813075951,3.6179386188,1.1728453324
H,0,3.9522269441,2.0578378423,0.8291024292
H,0,4.4134915069,1.4129668868,-1.4360779982
H,0,3.5892403736,2.263493136,-2.7482314279
N,0,3.3809322258,3.1493002838,-0.8648329547
H,0,2.449270222,4.3400261231,-2.3222901802
H,0,2.0994496859,4.7863226866,-0.6476715306
```

H,0,3.030277965,-2.2115771381,-0.4280576543
O,0,3.4674410236,-2.6643405055,-1.195092567
C,0,4.7305097552,-3.1698022508,-0.7776095005
H,0,5.2171907608,-3.6183485907,-1.6488906368
H,0,5.382430392,-2.37604324,-0.3878549033
H,0,4.6290981262,-3.9452872305,-0.0045604226
H,0,3.6771560694,-0.6085748539,1.4407361154
O,0,4.5285907408,-0.2022285703,1.7475318338
C,0,4.4402531187,0.0737031909,3.1403145018
H,0,5.3899154322,0.5157567175,3.4556178218
H,0,3.6368702814,0.7884030166,3.3708626969
H,0,4.2717409662,-0.837286434,3.7314286497

*M06-2X/6-31+G** PCM solvent model in methanol*

elim-twomeoh-cis-M06-meoh
E(RM062X) = -1548.52728146

```
 Zero-point correction=                           0.562856 (Hartree/Particle)
 Thermal correction to Energy=                    0.597315
 Thermal correction to Enthalpy=                  0.598259
 Thermal correction to Gibbs Free Energy=         0.493948
 Sum of electronic and zero-point Energies=          -1547.964426
 Sum of electronic and thermal Energies=             -1547.929967
 Sum of electronic and thermal Enthalpies=           -1547.929022
 Sum of electronic and thermal Free Energies=        -1548.033333

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                 374.821            124.134            219.541
```

H,0,0.8084654813,1.6530963088,1.4516094036
C,0,0.0320325271,-1.0190279875,-0.6048083068
H,0,0.4369350806,-1.0493815229,-1.6207233972
H,0,0.6406656873,-1.6598691652,0.038953
N,0,-1.2992004266,-1.7482895178,-0.6981226131
C,0,-2.3100006661,-0.9685631677,-1.5003386922
H,0,-1.8121804394,-0.6445193243,-2.4160338182
C,0,-3.5366317212,-1.8813749108,-1.7520554217
H,0,-2.5688963277,-0.0899158123,-0.9077396482
C,0,-1.8694424419,-2.0167779033,0.6700327231
H,0,-1.8819332884,-1.0658343461,1.2065214865
C,0,-3.2804975223,-2.6305791808,0.4940586731
H,0,-1.1693525943,-2.6941127829,1.1659500101

C,0,-1.0698364335,-3.0678897654,-1.3880273953
C,0,-2.3662702527,-3.9060188733,-1.298959948
H,0,-0.7936127996,-2.8339713843,-2.4186240789
H,0,-0.2233716177,-3.5503439511,-0.8954244291
C,0,-0.0294144038,0.3923866207,-0.0682582287
H,0,-1.2251624342,0.7991520295,0.4371647818
C,0,0.1043096887,1.3976183971,-1.1322909845
O,0,0.3251630732,2.6447330407,-0.6609095659
O,0,-0.0420731944,1.1838522217,-2.329140612
C,0,0.3494898037,3.6847010706,-1.6431648027
H,0,0.5743563008,4.5994052167,-1.0962338747
H,0,1.124196788,3.4884520118,-2.3875334305
H,0,-0.6267195687,3.755656682,-2.128256592
C,0,0.8665753282,0.5983479366,1.1599159204
O,0,0.3300411536,-0.2283558725,2.1851615274
H,0,0.7848228614,-0.0388290146,3.016285527
O,0,-2.2829844112,1.317765887,0.8892006957
H,0,-1.5522416487,1.5063996999,2.8274396921
C,0,4.9645528725,-0.339619032,0.297676151
C,0,4.2065209811,-1.2688157417,0.998429229
C,0,2.8828805329,-0.9555768285,1.292798071
C,0,2.3278334461,0.2627935858,0.8882932854
C,0,3.1264694108,1.1800178113,0.1896168332
C,0,4.4490519135,0.8871485663,-0.1127572745
N,0,6.3601652789,-0.6586801049,-0.0138054509
H,0,4.6444579556,-2.210329164,1.306880853
H,0,2.276941682,-1.6628710953,1.849485845
H,0,2.7061051631,2.1342077241,-0.1152313919
H,0,5.0751691209,1.5894186564,-0.649421885
C,0,-1.9978505049,2.1099014025,2.0242686782
H,0,-1.2993925532,2.9232793772,1.7779922232
H,0,-2.9207258454,2.565083509,2.4091196043
O,0,7.0186459852,0.1709390155,-0.6219444512
O,0,6.7987112444,-1.7395082217,0.3487175904
H,0,-3.3950857094,-3.4874137588,1.1627805244
H,0,-4.0446033193,-1.8875849202,0.7363271396
H,0,-4.4530605149,-1.323838555,-1.5452561529
H,0,-3.565738497,-2.2135300257,-2.7931215882
N,0,-3.4915511317,-3.0655079933,-0.8900453535
H,0,-2.580854034,-4.3567438437,-2.2707546167
H,0,-2.2547890139,-4.7104439131,-0.5677671873
H,0,-2.6548050972,2.368473603,-0.4002638927
O,0,-2.8545549665,3.0372954368,-1.1003433601
C,0,-2.7970256972,4.313001484,-0.4939562934

```
 H,0,-2.9835729776,5.0665279055,-1.2640086943
 H,0,-3.5557313958,4.4280993425,0.2915518541
 H,0,-1.809991941,4.5088038708,-0.0528766965
 H,0,-3.7631430626,0.6722505516,1.1052616383
 O,0,-4.6315806719,0.2532829683,1.3531878505
 C,0,-4.5183294474,-0.1668671003,2.6976498962
 H,0,-5.3600699069,-0.8257393952,2.928220408
 H,0,-3.5876042492,-0.72659956,2.8744667928
 H,0,-4.5410564529,0.6802534512,3.3961061157
```

Elimination, two methanols on methoxide, methoxide deprotonation, OH pointing away

*B3LYP/6-31+G** PCM solvent model in methanol*

```
doc-deprotonationFSmethoxideTwoMeohOHturnedB3PCM
E(RB3LYP) = -1549.18445151

 Zero-point correction=                           0.555263 (Hartree/Particle)
 Thermal correction to Energy=                    0.591164
 Thermal correction to Enthalpy=                  0.592108
 Thermal correction to Gibbs Free Energy=         0.482506
 Sum of electronic and zero-point Energies=          -1548.629188
 Sum of electronic and thermal Energies=             -1548.593288
 Sum of electronic and thermal Enthalpies=           -1548.592344
 Sum of electronic and thermal Free Energies=        -1548.701946

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  370.961            126.649            230.677

O,0,-0.3853221565,2.1716050623,-1.9633862732
 C,0,0.7614070097,-0.7451500994,0.1391592077
 H,0,0.4257963788,-0.9448520499,1.1579169952
 H,0,0.2116859683,-1.4054565801,-0.5333232954
 N,0,2.1898591182,-1.321807451,0.1052844185
 C,0,3.1380088859,-0.5452929102,1.0009069833
 H,0,2.6584606538,-0.4709270348,1.9765236216
 C,0,4.503712987,-1.2878496465,1.0418177266
 H,0,3.2202480974,0.4521710375,0.5723396544
 C,0,2.7423463199,-1.3548238048,-1.3066872153
 H,0,2.680968162,-0.3454158311,-1.7065573438
 C,0,4.2049692895,-1.8819489833,-1.258651416
```

```
H,0,2.0823132877,-2.0081654943,-1.8808704101
C,0,2.1291208287,-2.7516334107,0.6171009949
C,0,3.5338926567,-3.4007927641,0.4690193314
H,0,1.8020250385,-2.6970586936,1.6567145678
H,0,1.3659381416,-3.2727544083,0.0366531
C,0,0.5559861743,0.7246528934,-0.2252276046
H,0,1.69685114,1.3607697318,-0.7295457988
C,0,0.30680171,1.514389619,1.0027333295
O,0,-0.2798800788,2.71742759,0.794682582
O,0,0.6682406165,1.1746609073,2.1330107279
C,0,-0.443473674,3.5614014962,1.9497332311
H,0,-0.934768285,4.4619454717,1.581638487
H,0,-1.0641629759,3.0717891918,2.7037753005
H,0,0.5275742924,3.8105795771,2.3841720303
C,0,-0.4282301906,0.8475396607,-1.4218495134
H,0,-0.049986905,0.147159211,-2.1788486188
O,0,2.7043684996,1.9461444621,-1.2128935002
H,0,1.6096616157,3.7167501835,-1.3550772175
C,0,-4.4868180803,-0.3681471644,-0.5768813052
C,0,-3.6263653774,-1.2571815471,-1.2231539563
C,0,-2.3247888938,-0.843166954,-1.4963741449
C,0,-1.8697569447,0.4327856725,-1.1215020352
C,0,-2.7712398651,1.3104250635,-0.4906361589
C,0,-4.0760322355,0.9185196739,-0.2129985125
N,0,-5.8552759992,-0.7873263245,-0.2871670337
H,0,-3.9746238025,-2.2401376294,-1.5140215115
H,0,-1.6625114942,-1.521287692,-2.0264348791
H,0,-2.4404537051,2.3058106678,-0.2230975089
H,0,-4.7700484812,1.5921895761,0.2737717185
C,0,2.5866221868,3.3514742708,-1.0168676973
H,0,2.706544106,3.6234152065,0.0430198567
H,0,3.367915562,3.874964544,-1.5848661032
O,0,-6.6101244766,0.0152854182,0.2751013921
O,0,-6.2037514211,-1.9285468168,-0.6137935088
H,0,3.8327040166,-3.8561849558,1.4166371116
H,0,3.5131046674,-4.1866168641,-0.2902495469
N,0,4.5357038852,-2.3999969696,0.0785064025
H,0,4.3345946015,-2.681112599,-1.993048136
H,0,4.9018077167,-1.0749991064,-1.4947874823
H,0,5.3051576399,-0.5884217385,0.7957305095
H,0,4.6922146168,-1.6908206114,2.0403986839
H,0,-0.897653542,2.1727242827,-2.7843063227
H,0,4.4131723014,1.6196094512,-1.1333159859
O,0,5.3867934993,1.4339318788,-1.1224893825
```

```
C,0,6.0153924716,2.2819174788,-0.1680969095
H,0,7.0815543734,2.0376290381,-0.1540911535
H,0,5.9093489263,3.3445507977,-0.4272705087
H,0,5.6154159856,2.1312290937,0.8450091838
H,0,2.7296998507,1.6364780405,-2.9326159028
O,0,2.8035537258,1.373860338,-3.8863414447
C,0,2.3951402488,2.4596882442,-4.710096663
H,0,2.4739445088,2.1374402571,-5.7527563229
H,0,1.3538027785,2.7531775954,-4.5178169287
H,0,3.0356950427,3.34287145,-4.5752928959
```

Elimination, two methanols on methoxide, methoxide deprotonation, OH pointing away, ester switched

*B3LYP/6-31+G** PCM solvent model in methanol*

doc-deprotonationFSmethoxideTwoMeohOHturnedConf2B3PCM
E(RB3LYP) = -1549.18334725

```
 Zero-point correction=                           0.555341 (Hartree/Particle)
 Thermal correction to Energy=                    0.591250
 Thermal correction to Enthalpy=                  0.592194
 Thermal correction to Gibbs Free Energy=         0.480883
 Sum of electronic and zero-point Energies=          -1548.628007
 Sum of electronic and thermal Energies=             -1548.592097
 Sum of electronic and thermal Enthalpies=           -1548.591153
 Sum of electronic and thermal Free Energies=        -1548.702464

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  371.015            126.663           234.275
```

```
O,0,-0.4057841796,1.7392679422,-2.2653358307
 C,0,0.8145720313,-0.427545248,0.5723582457
 H,0,0.6436660354,-0.2811395216,1.6383267646
 H,0,0.1382947247,-1.2167462361,0.2375142438
 N,0,2.2000859388,-1.1048934084,0.5157712281
 C,0,3.2862627626,-0.2071712942,1.0792333963
 H,0,2.9557601277,0.0945940446,2.0731578129
 C,0,4.627085041,-0.9956712243,1.0999758265
 H,0,3.3292908847,0.6714036957,0.4375932205
 C,0,2.5607320667,-1.5202256567,-0.895922183
 H,0,2.5221743553,-0.6308167946,-1.5200685485
```

```
C,0,3.9762928014,-2.1679798693,-0.8826871627
H,0,1.7874044252,-2.2200859072,-1.2187643163
C,0,2.1393653272,-2.3602591949,1.3694216554
C,0,3.5019776301,-3.1047269395,1.2718510398
H,0,1.9107409507,-2.0380482663,2.3866689762
H,0,1.3085977791,-2.9621990469,0.9977457408
C,0,0.5902180781,0.8613978369,-0.219978991
H,0,1.7177637771,1.3103444063,-0.9097664884
C,0,0.331434218,2.0352689312,0.6432731167
O,0,1.0403829892,1.9773247972,1.8135092336
O,0,-0.3510765481,3.0207624235,0.3776765454
C,0,0.9402276253,3.1193690207,2.6834790948
H,0,1.5610358024,2.881840386,3.5472586128
H,0,1.3122909859,4.0174469923,2.1844444012
H,0,-0.0948472132,3.2799642708,2.9939861911
C,0,-0.4230489798,0.6223999567,-1.3707828374
H,0,-0.0502533181,-0.2618141536,-1.9061509589
O,0,2.7140214291,1.7352411014,-1.5671186485
H,0,1.6321738852,3.3932372125,-2.2317260525
C,0,-4.4534660297,-0.3474717908,-0.1589258748
C,0,-3.5991826853,-1.3691658707,-0.5764194002
C,0,-2.3059401275,-1.0336565057,-0.9708886708
C,0,-1.8534947353,0.2967008649,-0.93856292
C,0,-2.7479835468,1.3039184923,-0.5294295133
C,0,-4.0447977757,0.9904058496,-0.1373387673
N,0,-5.8137397373,-0.6837694255,0.2530386049
H,0,-3.9457299223,-2.3944444918,-0.6032039044
H,0,-1.6480732692,-1.8211491458,-1.3268479675
H,0,-2.4104231635,2.3322305948,-0.5168897028
H,0,-4.7339996873,1.7626354305,0.1807518358
C,0,2.5863341874,3.1412900332,-1.7522195348
H,0,2.6427756337,3.6820039797,-0.7953953773
H,0,3.4005200166,3.5107904136,-2.3905611622
O,0,-6.5681770505,0.2336147628,0.5983537936
O,0,-6.1560295431,-1.8726183366,0.2420196759
H,0,3.9060617684,-3.274226456,2.2729589413
H,0,3.3688701035,-4.0781368079,0.7929926133
N,0,4.4734352468,-2.327247591,0.4921722603
H,0,3.9417623777,-3.1480199897,-1.3651510228
H,0,4.6809222321,-1.5397623758,-1.4316689442
H,0,5.3808244049,-0.4405107566,0.5380277886
H,0,4.9787791263,-1.1228836228,2.1271634469
H,0,-0.9382827331,1.5090565361,-3.0397856434
H,0,4.4318382578,1.4369955242,-1.4798995172
```

```
O,0,5.4068997997,1.2677833819,-1.430371722
C,0,6.0277716116,2.3263309222,-0.709838162
H,0,7.0959901475,2.1017160729,-0.639366737
H,0,5.9125994687,3.294161231,-1.2176037571
H,0,5.6289207241,2.4213216725,0.310399312
H,0,2.6922840914,0.9930212234,-3.1504794737
O,0,2.7217028708,0.5011599635,-4.0114106049
C,0,2.5625003184,1.4216844668,-5.0848866911
H,0,2.5920467646,0.854674094,-6.020136379
H,0,1.6009062751,1.9514692467,-5.0340420375
H,0,3.3691671461,2.1679301534,-5.1108511138
```

Elimination, two methanols on OH, methoxide deprotonation, OH H-bonded to methoxide, ester switched

*B3LYP/6-31+G** PCM solvent model in methanol*

doc-deprotonationFullSysTwoMeOHonOHB3LYPPCM
E(RB3LYP) = -1549.19016730

```
 Zero-point correction=                           0.555321 (Hartree/Particle)
 Thermal correction to Energy=                    0.591475
 Thermal correction to Enthalpy=                  0.592420
 Thermal correction to Gibbs Free Energy=         0.477672
 Sum of electronic and zero-point Energies=          -1548.634846
 Sum of electronic and thermal Energies=             -1548.598692
 Sum of electronic and thermal Enthalpies=           -1548.597748
 Sum of electronic and thermal Free Energies=        -1548.712495

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                 371.156            125.826            241.507
```

```
H,0,-0.9700678725,0.7564407128,2.0396932703
C,0,0.9104282788,-1.1419548763,-0.169035169
H,0,0.8519952354,-2.2201483928,-0.0173387511
H,0,0.2295043482,-0.8787714966,-0.9805478706
N,0,2.3083184888,-0.9349124015,-0.7992056129
C,0,3.4312657478,-1.1520005925,0.1971851754
H,0,3.2629124707,-2.1234808796,0.6602254796
C,0,4.790980293,-1.0677927337,-0.5567114299
H,0,3.3293243293,-0.3748792212,0.9533544267
C,0,2.4460840847,0.4504370671,-1.4037059308
```

```
H,0,2.2762785761,1.1678637044,-0.6036856309
C,0,3.8699015262,0.5922881321,-2.013761853
H,0,1.6592553763,0.545434034,-2.1531030409
C,0,2.4605342955,-1.9549243988,-1.9149339847
C,0,3.8131061748,-1.7156378952,-2.6441616745
H,0,2.4091419035,-2.9399009268,-1.4481132103
H,0,1.6018481825,-1.8356020492,-2.577767652
C,0,0.5704003435,-0.3751177566,1.1027815217
H,0,1.4465941186,0.6128591779,1.3826557975
C,0,0.5616189152,-1.1763959189,2.3444623987
O,0,1.3277579411,-2.2987023392,2.2664144958
O,0,-0.0100028034,-0.8714322323,3.3918972045
C,0,1.448149241,-3.0861560739,3.4676305376
H,0,2.0820321627,-3.930157796,3.1973508141
H,0,1.9130316904,-2.5006370312,4.2640129813
H,0,0.4677053292,-3.4368746857,3.7969641256
C,0,-0.6759649903,0.5537816778,1.0051366122
O,0,-0.3356115401,1.8116126509,0.3806921881
H,0,0.553006385,2.0648487535,0.7989785292
O,0,1.9890600389,1.7785429873,1.4660410306
H,0,1.3190468397,2.3436270872,3.3736066043
C,0,-4.073019896,-1.2939201781,-0.8892983057
C,0,-3.3409546166,-0.3511215104,-1.6118534914
C,0,-2.2459232557,0.2615247298,-1.004497057
C,0,-1.8771988268,-0.0619039606,0.310817143
C,0,-2.6440183369,-1.0100183341,1.0152900036
C,0,-3.737780646,-1.6318494811,0.4261556535
N,0,-5.221655458,-1.9386161293,-1.5190090945
H,0,-3.6256053322,-0.1025602644,-2.6264944404
H,0,-1.6821622065,0.9990031597,-1.5625024298
H,0,-2.381657925,-1.2571838632,2.0389998902
H,0,-4.3287906669,-2.357901616,0.9697962042
C,0,2.245450678,2.1789006697,2.79914239
H,0,2.842302059,1.4276189716,3.3404647804
H,0,2.8136140281,3.1200966217,2.8109348958
O,0,-5.8576960349,-2.7751599994,-0.8662696096
O,0,-5.5115241257,-1.623676447,-2.6796842896
H,0,4.3898396703,-2.6434927123,-2.6705219824
H,0,3.6391830974,-1.3979634091,-3.6751875847
N,0,4.6027309026,-0.6812256546,-1.9627211133
H,0,3.8000106197,0.9202717251,-3.0539880511
H,0,4.4441349032,1.3417277145,-1.4630835975
H,0,5.4382145625,-0.3315442293,-0.0737289668
H,0,5.3016483433,-2.0338308921,-0.528775229
```

```
H,0,-1.5821404607,3.1044073549,0.8477872883
O,0,-2.2557372278,3.7668163402,1.1063914028
C,0,-1.7014281443,4.61382417,2.1110373935
H,0,-2.4752438454,5.32934234,2.4014338048
H,0,-1.3999821206,4.0480365908,3.0029054631
H,0,-0.8325804084,5.1746923203,1.7406243519
H,0,-0.0906274982,2.4244134402,-1.3985001075
O,0,0.049119224,2.6994431295,-2.3249959216
C,0,-0.49729852,4.0055338718,-2.5120223904
H,0,-0.3450649811,4.2743387892,-3.5603470464
H,0,-1.5733252393,4.0324265458,-2.2970467054
H,0,0.0070755744,4.7515109089,-1.8840656338
```

Preelimination intermediate to product

*B3LYP/6-31+G** PCM solvent model in methanol*

preelimination-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -1201.96701341

```
 Zero-point correction=                           0.398941 (Hartree/Particle)
 Thermal correction to Energy=                    0.422198
 Thermal correction to Enthalpy=                  0.423142
 Thermal correction to Gibbs Free Energy=         0.342631
 Sum of electronic and zero-point Energies=          -1201.568072
 Sum of electronic and thermal Energies=             -1201.544816
 Sum of electronic and thermal Enthalpies=           -1201.543872
 Sum of electronic and thermal Free Energies=        -1201.624383

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  264.933             88.794            169.450
```

```
C,0,0.5295018448,0.7975403901,-0.6623944061
C,0,-0.4196018342,-0.1561800269,-0.2397513519
O,0,-1.7305082973,0.2352431784,-0.5377310568
O,0,-0.2267610542,-1.2386505314,0.3548882759
C,0,-2.7704415433,-0.7032324541,-0.2396226243
H,0,-3.7013302129,-0.2147728547,-0.5319552005
H,0,-2.6426997588,-1.6276386235,-0.810820882
H,0,-2.7946111306,-0.9431316182,0.8270224013
C,0,1.9366850772,0.5600961265,-0.3536075839
H,0,2.1610092199,-0.4986999184,-0.2105992268
```

```
H,0,2.6323839384,0.9936568003,-1.0775154689
N,0,2.503465598,1.19632455,1.0348157519
C,0,2.3855554501,2.6981172354,1.0128888915
H,0,2.9532232426,3.0498611826,0.1486282851
H,0,1.3306903157,2.9314418167,0.8607181582
C,0,2.94336428,3.2683043538,2.3508078841
C,0,3.9539837407,0.8237416043,1.194262554
H,0,4.4822402764,1.1943243553,0.3132553375
C,0,4.4942513034,1.4485968608,2.5155161836
H,0,4.0077674505,-0.2669084921,1.1984563356
C,0,1.7334688871,0.6626030705,2.2150502896
C,0,2.3243216526,1.2731501091,3.5195154891
H,0,0.6900876429,0.9337025528,2.0545111556
H,0,1.8139574249,-0.4244247894,2.1827783502
C,0,0.1062672145,2.0186542059,-1.442623921
H,0,1.0052994533,2.6136431944,-1.6475819063
C,0,-1.5169906482,1.2609452533,-5.3845763076
C,0,-2.0913742179,2.2618815335,-4.5968255064
C,0,-1.5754093487,2.4937615326,-3.3243149208
C,0,-0.5070911293,1.7325881025,-2.8229671744
C,0,0.0509804608,0.7376351494,-3.6451372546
C,0,-0.441638845,0.4947183533,-4.9223810701
N,0,-2.047534069,1.0114009665,-6.7186409691
H,0,-2.9211736368,2.8439934282,-4.9779430387
H,0,-2.0072900965,3.2706556619,-2.7051209725
H,0,0.8731367868,0.1377827517,-3.2694890316
H,0,-0.0111468922,-0.2738906733,-5.5519336749
O,0,-0.7442994585,2.9267071995,-0.6977471342
H,0,-1.4633020386,2.3749921679,-0.3488067412
O,0,-1.5223168754,0.1267315064,-7.4075701445
O,0,-3.0025594668,1.693649664,-7.1129466553
N,0,3.4369111905,2.1896091904,3.2210835976
H,0,4.8723736772,0.6650532034,3.1770479485
H,0,5.3169786675,2.1355517846,2.3015588007
H,0,3.7647143089,3.9620379685,2.1535166599
H,0,2.1623099937,3.8150170506,2.8854718159
H,0,1.554337013,1.8273412087,4.062687052
H,0,2.6930864427,0.4804187183,4.1757010063
```

*M06-2X/6-31+G** PCM solvent model in methanol*

preelimination-M06-meoh
E(RM062X) = -1201.46860432

```
Zero-point correction=                           0.404386 (Hartree/Particle)
Thermal correction to Energy=                    0.427002
Thermal correction to Enthalpy=                  0.427946
Thermal correction to Gibbs Free Energy=         0.349684
Sum of electronic and zero-point Energies=       -1201.064218
Sum of electronic and thermal Energies=          -1201.041603
Sum of electronic and thermal Enthalpies=        -1201.040658
Sum of electronic and thermal Free Energies=     -1201.118920

                E (Thermal)         CV                S
                 KCal/Mol     Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total             267.948          86.967           164.715

C,0,0.6004261213,0.8427155927,-0.6862630247
C,0,-0.3738381556,-0.0708954336,-0.2640953447
O,0,-1.6587075425,0.345655392,-0.5914808335
O,0,-0.2227092453,-1.1408494614,0.3566872001
C,0,-2.7109016265,-0.563563525,-0.2964859229
H,0,-3.6301059999,-0.0698322944,-0.6124821391
H,0,-2.5845138264,-1.4993382232,-0.8476727618
H,0,-2.7527198278,-0.7842337221,0.7730310422
C,0,2.0000412172,0.5715904853,-0.3519730231
H,0,2.1964624744,-0.4977041264,-0.2271982052
H,0,2.7093915955,0.9913205915,-1.0740921016
N,0,2.5029158624,1.1762503672,1.008341443
C,0,2.4111024433,2.6725471476,0.9851804173
H,0,3.1219976044,3.0181398549,0.2292613486
H,0,1.3965696909,2.9290074266,0.6707658271
C,0,2.7496578755,3.2042502877,2.4003629712
C,0,3.9303907064,0.7826616017,1.2380483477
H,0,4.489191867,1.0255437936,0.3314487679
C,0,4.4575988865,1.5441847648,2.4797039182
H,0,3.9396205096,-0.3009981797,1.377765183
C,0,1.6743606791,0.6635267395,2.1504495728
C,0,2.335025332,1.1193691656,3.4742631383
H,0,0.6724660518,1.0735155568,2.0095614347
H,0,1.6160189172,-0.4212956912,2.0466171239
C,0,0.2105524041,2.0615744202,-1.473648369
H,0,1.129167614,2.614958763,-1.7148097944
C,0,-1.5515934919,1.2046451985,-5.3048207531
C,0,-2.1107917054,2.2129638625,-4.5281741822
C,0,-1.5447062254,2.4855637937,-3.2869044681
C,0,-0.4479605483,1.7534529432,-2.8208881089
C,0,0.0909603377,0.7477893496,-3.6345362861
```

```
C,0,-0.450423692,0.4648498946,-4.8806302249
N,0,-2.1374592829,0.9121967968,-6.6123841844
H,0,-2.9671281948,2.7677561207,-4.8918088983
H,0,-1.9612045408,3.2706255162,-2.6667139321
H,0,0.9375375792,0.1721588572,-3.2729647237
H,0,-0.0397518129,-0.3126449994,-5.5132489805
O,0,-0.5860020397,3.0027024106,-0.7385093856
H,0,-1.3105357916,2.4864361067,-0.3540705305
O,0,-1.6391498705,0.0198674561,-7.2830563226
O,0,-3.0987379737,1.5732492134,-6.9773697909
N,0,3.3486252809,2.1488021002,3.2224747486
H,0,4.9976635085,0.85783315,3.1359376712
H,0,5.1453482509,2.3394374177,2.1808171054
H,0,3.4462039083,4.0426606057,2.3272550517
H,0,1.8462483407,3.5577952807,2.9040745209
H,0,1.5771367082,1.5213983418,4.1508342784
H,0,2.8205296265,0.2763022899,3.9729781796
```

MBH product

*B3LYP/6-31+G** PCM solvent model in methanol*

productBeckePCMmethanol
E(RB3LYP) = -856.619807271

```
Zero-point correction=                           0.211791 (Hartree/Particle)
Thermal correction to Energy=                    0.227630
Thermal correction to Enthalpy=                  0.228574
Thermal correction to Gibbs Free Energy=         0.166164
Sum of electronic and zero-point Energies=           -856.408016
Sum of electronic and thermal Energies=              -856.392177
Sum of electronic and thermal Enthalpies=            -856.391233
Sum of electronic and thermal Free Energies=         -856.453643

                 E (Thermal)             CV                S
                  KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
Total              142.840             58.233           131.354
```

```
C,0,-2.2611273099,-0.8273355466,-0.8832497709
C,0,-2.6971597205,0.1223707721,0.042211853
C,0,-1.8868697643,0.544901353,1.0991556317
C,0,-0.6110673192,0.0033120269,1.2190971298
C,0,-0.1409416805,-0.949895877,0.2999849049
C,0,-0.9816413765,-1.3603729467,-0.7443036989
```

C,0,1.2492905679,-1.5736630749,0.4785266808
O,0,1.6242755682,-2.3934796155,-0.6248345413
C,0,2.3215105488,-0.5357904032,0.7940224477
C,0,2.6834736263,0.3794442814,-0.3283794339
O,0,2.3299047526,0.1755880598,-1.4873777903
C,0,2.9326102188,-0.4711538836,1.984579973
O,0,3.4294817185,1.4256806665,0.0358948021
C,0,3.8556623107,2.3228605358,-1.0182148813
H,0,2.6803765712,-1.1660016223,2.780269433
H,0,3.6959315035,0.2704588495,2.1915293629
H,0,4.4471783702,3.0874845751,-0.5184431254
H,0,4.4599595497,1.7824639816,-1.7490773325
H,0,2.9861313439,2.7654420186,-1.5072658716
H,0,1.1917429826,-2.2521622272,1.3364985285
H,0,1.8319286614,-1.7899572942,-1.3606345594
N,0,-4.0382884802,0.6879809263,-0.0957283572
H,0,-2.2505219931,1.2801770835,1.8055978968
H,0,0.022796489,0.330385222,2.0366084297
H,0,-0.6333756668,-2.1043400244,-1.450575389
H,0,-2.9114190025,-1.1401017771,-1.6903680607
O,0,-4.7420872631,0.3093481288,-1.0389938839
O,0,-4.4126846813,1.5216132818,0.7370333984

*M06-2X/6-31+G** PCM solvent model in methanol*

product-M06-meoh
E(RM062X) = -856.262525405

```
 Zero-point correction=                           0.214813 (Hartree/Particle)
 Thermal correction to Energy=                    0.230507
 Thermal correction to Enthalpy=                  0.231452
 Thermal correction to Gibbs Free Energy=         0.169306
 Sum of electronic and zero-point Energies=          -856.047712
 Sum of electronic and thermal Energies=             -856.032018
 Sum of electronic and thermal Enthalpies=           -856.031074
 Sum of electronic and thermal Free Energies=        -856.093220

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
 Total                  144.646             57.523            130.797
```

C,0,-2.2099382042,-0.816300007,-0.897985381
C,0,-2.6317011256,0.1393308862,0.0181467078
C,0,-1.8378899156,0.5556147344,1.0819905772

```
C,0,-0.5753535974,-0.0066456312,1.2199118302
C,0,-0.1166776762,-0.9684708913,0.3115948674
C,0,-0.9437451423,-1.3699346855,-0.7403422611
C,0,1.2604742474,-1.6008387949,0.5013377717
O,0,1.6387097717,-2.4051647551,-0.5977997553
C,0,2.3140587089,-0.5565135524,0.8191125789
C,0,2.6109676633,0.3903875514,-0.2956956772
O,0,2.1639776993,0.235606036,-1.4203085061
C,0,2.9493735662,-0.4872851439,1.9900364344
O,0,3.40412082,1.4001482792,0.0421414723
C,0,3.7504104032,2.3109744253,-1.0129677539
H,0,2.7328638225,-1.1974596223,2.7828330364
H,0,3.6962061585,0.2758078185,2.1810801921
H,0,4.4046961737,3.0492002882,-0.5556336846
H,0,4.2677002166,1.7765413966,-1.8111610973
H,0,2.8496628715,2.7837545598,-1.4072667243
H,0,1.1986976606,-2.2802347378,1.3586066653
H,0,1.7860654739,-1.8115803161,-1.3515317006
N,0,-3.9638672608,0.7310146848,-0.1397533881
H,0,-2.203322369,1.3014677048,1.7770431835
H,0,0.0581867862,0.3100559984,2.0428953875
H,0,-0.596851876,-2.1230875856,-1.4382370749
H,0,-2.858551888,-1.1172849303,-1.7114436949
O,0,-4.6452678908,0.3698125385,-1.0863053777
O,0,-4.3279320973,1.5563407513,0.6832643722
```

MBH Anisaldehyde Product

*B3LYP/6-31+G** PCM solvent model in methanol*

product-A-Becke-631Gdp-PCM-methanol
E(RB3LYP) = -766.635441016

```
 Zero-point correction=                           0.241830 (Hartree/Particle)
 Thermal correction to Energy=                    0.257749
 Thermal correction to Enthalpy=                  0.258693
 Thermal correction to Gibbs Free Energy=         0.196901
 Sum of electronic and zero-point Energies=           -766.393611
 Sum of electronic and thermal Energies=              -766.377692
 Sum of electronic and thermal Enthalpies=            -766.376748
 Sum of electronic and thermal Free Energies=         -766.438540

                     E (Thermal)             CV                S
                      KCal/Mol        Cal/Mol-Kelvin    Cal/Mol-Kelvin
```

```
 Total                 161.740              58.948             130.053
```

```
 C,0,-2.2096263392,-0.9467920702,-0.9271676731
 C,0,-2.6908920236,0.0428061541,-0.0619688188
 C,0,-1.8694337043,0.5090433905,0.9769061478
 C,0,-0.5864317883,-0.0051582998,1.1377490724
 C,0,-0.0832925738,-0.9939669083,0.2739878689
 C,0,-0.9159207858,-1.4545786645,-0.7487027433
 C,0,1.3119966957,-1.5915122661,0.4935146816
 O,0,1.7320083103,-2.4144475227,-0.5974683698
 C,0,2.3610047162,-0.5324282675,0.8150074781
 C,0,2.7306968756,0.3807679496,-0.3067969443
 O,0,2.4289626002,0.156133955,-1.4760603352
 C,0,2.9516889133,-0.444747187,2.0146394758
 O,0,3.4316572421,1.4559562207,0.0712540882
 C,0,3.8754396963,2.3479576178,-0.978624823
 H,0,2.6991244449,-1.1388722569,2.8110608167
 H,0,3.6967356587,0.3128265566,2.2304160483
 H,0,4.4275616422,3.1352054281,-0.4686265475
 H,0,4.5216443131,1.8137009761,-1.6776492297
 H,0,3.0154775049,2.7614101093,-1.508667603
 H,0,1.2654347379,-2.2685686421,1.3534739973
 H,0,1.9090914227,-1.8121462562,-1.3415677519
 H,0,-2.249534713,1.2748412054,1.6460723295
 H,0,0.0299787277,0.3733852179,1.9480431615
 H,0,-0.5583336242,-2.2262961832,-1.4217547017
 H,0,-2.820036434,-1.3307121624,-1.735694877
 O,0,-3.9329653567,0.6108721517,-0.1455688681
 C,0,-4.8110084898,0.1776609572,-1.1874869913
 H,0,-5.7252477011,0.7585056704,-1.0652293623
 H,0,-4.3807949936,0.3761009327,-2.1756003224
 H,0,-5.0406329743,-0.8897048061,-1.0934442036
```

*M06-2X/6-31+G** PCM solvent model in methanol*

product-A-M06-PCM-methanol
E(RM062X) = -766.308284588

```
 Zero-point correction=                           0.245363 (Hartree/Particle)
 Thermal correction to Energy=                    0.260934
 Thermal correction to Enthalpy=                  0.261879
 Thermal correction to Gibbs Free Energy=         0.201228
 Sum of electronic and zero-point Energies=           -766.062922
 Sum of electronic and thermal Energies=              -766.047350
```

```
Sum of electronic and thermal Enthalpies=           -766.046406
Sum of electronic and thermal Free Energies=         -766.107056

                E (Thermal)           CV              S
                 KCal/Mol     Cal/Mol-Kelvin   Cal/Mol-Kelvin
Total                163.739           57.996           127.649

C,0,-2.1848338659,-0.9502199357,-0.918018044
C,0,-2.645892081,0.0568678897,-0.0687037853
C,0,-1.8204199977,0.5258174035,0.9611062962
C,0,-0.5496292463,-0.0044318868,1.1297763462
C,0,-0.0681175618,-1.0118963807,0.2818811161
C,0,-0.9021114872,-1.47449832,-0.7317449647
C,0,1.3175115826,-1.6148392333,0.4979670974
O,0,1.7342893377,-2.4110040781,-0.5980113509
C,0,2.347150647,-0.550300157,0.8276619612
C,0,2.6678957584,0.3905775911,-0.2859632056
O,0,2.2889456897,0.2114857587,-1.4315656151
C,0,2.9460635334,-0.4547382093,2.0161346808
O,0,3.4105445655,1.4320295601,0.0782389256
C,0,3.7871866251,2.3352340481,-0.9723673575
H,0,2.714344642,-1.1604135221,2.8087801092
H,0,3.6724575616,0.3234106777,2.224267793
H,0,4.3796468351,3.1097424259,-0.4912729878
H,0,4.3768024219,1.808002254,-1.7242197932
H,0,2.8963534615,2.7622466953,-1.4352666854
H,0,1.2729356463,-2.2988868221,1.3526433974
H,0,1.8466145212,-1.8115667733,-1.352965478
H,0,-2.1930173673,1.3077475345,1.615153729
H,0,0.0783311211,0.3744852207,1.9318377604
H,0,-0.5535445731,-2.2609157668,-1.393119362
H,0,-2.8025851012,-1.3353064402,-1.720304491
O,0,-3.8723599661,0.6392814686,-0.1620354885
C,0,-4.7328310279,0.1997482076,-1.2018506646
H,0,-5.6450586068,0.7864995048,-1.1064433242
H,0,-4.2834598507,0.3774437346,-2.184671247
H,0,-4.968861217,-0.8643594495,-1.0928803673
```