DI(HYDROPEROXY)ALKANE ADDUCTS OF PHOSPHINE OXIDES:
SAFE, SOLID, STOICHIOMETRIC AND SOLUBLE OXIDIZING AGENTS

A Dissertation

by

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ABSTRACT

Despite its importance and wide use as oxidizing agent, aqueous $\text{H}_2\text{O}_2$ has disadvantages. It easily decomposes, and when the substrates are not water-soluble, biphasic reaction mixtures are required. Thus, oxidizing agents that are anhydrous and soluble in organic solvents are desired. To this purpose, several $\text{H}_2\text{O}_2$ adducts of phosphine oxides, for example $[\text{Bu}_3\text{PO}\cdot\text{H}_2\text{O}_2]_2$ and $[\text{Ph}_3\text{PO}\cdot\text{H}_2\text{O}_2]_2\cdot\text{H}_2\text{O}_2$, have been synthesized and characterized. These adducts represent an extension to the adducts previously reported by the Bluemel group, and display comparable physical properties.

Furthermore, di(hydroperoxy)alkane adducts, $\text{R}_3\text{PO} \cdot (\text{HOO})_2\text{CRR'}\text{R''}$ ($\text{R}, \text{R'}, \text{R''} = \text{alkyl, aryl}$), were synthesized and fully characterized. These adducts can be constructed using a wide variety of alkanes and phosphine oxides. All di(hydroperoxy)alkane adducts are structurally well defined as proven by single crystal X-ray analysis, and they contain two active oxygen atoms per assembly.

These adducts of the type $\text{R}_3\text{PO} \cdot (\text{HOO})_2\text{CRR'}\text{R''}$ are highly soluble in organic solvents, allowing for oxidation reactions to occur in one phase. Moreover, there are many beneficial features to be harvested from their well-defined molecular structure and relatively anhydrous character. For example, selective and fast oxidation of dialkylsulfides to corresponding sulfoxides can be accomplished, without overoxidation to sulfones, because the solid oxidizing agents can easily be administered stoichiometrically. The adducts can also successfully oxidize substrates sensitive to hydrolysis, such as $\text{Ph}_2\text{P} \cdot \text{PPh}_2$, without cleaving the P-P bond.
The $\text{R}_3\text{PO}\cdot(\text{HOO})_2\text{CR'R''}$ adducts are robust and practically no decomposition is found after storing the solids for 100 days at 4 °C. At room temperature, the adducts slowly decompose over time, via the release of oxygen gas. When exposed to higher temperatures or mechanical stress such as hammering or grinding, no sudden release of energy and/or oxygen was observed, attesting to the stability of the adducts. In the presence of catalytic amounts of acid, adducts with di(hydroperoxy)cycloalkane moieties decompose by undergoing a Baeyer-Villiger oxidation, and the di(hydroperoxy)cycloalkanes are transformed into the corresponding lactones.

The $\text{R}_3\text{PO}\cdot(\text{HOO})_2\text{CR'R''}$ adducts are stable, solid, stoichiometric and soluble materials, and can serve as an excellent complement to aqueous $\text{H}_2\text{O}_2$ as oxidizing agents.
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Contributors

This work was supervised by a dissertation committee consisting of the chair, Professor Dr. Janet Bluemel, and Professors Dr. Simon North and Dr. Kim Dunbar of the Department of Chemistry, and Professor Dr. Hae-Kwon Jeong of the Department of Chemical Engineering.

All work for the dissertation was completed by the student, under the advisement of Professor Dr. Janet Bluemel of the Department of Chemistry.

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NOMENCLATURE

δ  chemical shift in ppm

λ  wavelength

$^{13}\text{C}$  carbon nucleus (NMR)

$^2\text{H}$  deuterium nucleus (NMR)

$^1\text{H}$  proton nucleus (NMR)

$^{31}\text{P}$  phosphorus nucleus (NMR)

{ $^1\text{H}$}  proton decoupled (NMR)

Å  Ångstrom

br  broad

Bu  butyl

COSY  Correlation Spectroscopy (2D NMR)

CP  cross-polarization

CP/MAS  cross-polarization/magic angle spinning

CSA  chemical shift anisotropy

Cy  cyclohexyl

d  doublet (NMR), days

D  deuterium ($^2\text{H}$) atom

DCM  dichloromethane

dppm  bis(diphenylphosphino)methane

dppe  bis(diphenylphosphino)ethane
<table>
<thead>
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<th>Abbreviation</th>
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<tr>
<td>dppp</td>
<td>bis(diphenylphosphino)propane</td>
</tr>
<tr>
<td>D$_2$O</td>
<td>deuterium oxide</td>
</tr>
<tr>
<td>eq</td>
<td>equivalents, equatorial (NMR)</td>
</tr>
<tr>
<td>FID</td>
<td>free induction decay (NMR)</td>
</tr>
<tr>
<td>FT</td>
<td>Fourier Transformation</td>
</tr>
<tr>
<td>h</td>
<td>hours</td>
</tr>
<tr>
<td>HSQC</td>
<td>heteronuclear single quantum coherence spectroscopy (2D NMR)</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
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<tr>
<td>i</td>
<td>ipso</td>
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<tr>
<td>J</td>
<td>scalar coupling constant (NMR)</td>
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<tr>
<td>IR</td>
<td>infrared</td>
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<td>m</td>
<td>multiplet (NMR)</td>
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<td>m</td>
<td>meta</td>
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<td>MAS</td>
<td>magic angle spinning</td>
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<td>Me</td>
<td>methyl</td>
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<td>NMR</td>
<td>nuclear magnetic resonance</td>
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<tr>
<td>o</td>
<td>ortho</td>
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<tr>
<td>p</td>
<td>para</td>
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<tr>
<td>Ph</td>
<td>phenyl</td>
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<td>ppm</td>
<td>parts per million</td>
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<tr>
<td>R</td>
<td>alkyl, aryl group</td>
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<td>RT</td>
<td>room temperature</td>
</tr>
<tr>
<td>Symbol</td>
<td>Definition</td>
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<td>t</td>
<td>triplet (NMR)</td>
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<tr>
<td>tert</td>
<td>tertiary</td>
</tr>
<tr>
<td>T</td>
<td>temperature, time</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>Δν₁/₂</td>
<td>signal width at half height</td>
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<tr>
<td>xs</td>
<td>excess</td>
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CHAPTER I

INTRODUCTION

H$_2$O$_2$ is an immensely important reagent for oxidation reactions in organic syntheses.$^1$ For example, Baeyer-Villiger oxidations$^{2,3}$ and sulfide oxidation processes,$^4$ as well as epoxidation reactions,$^5$ are mainly performed using H$_2$O$_2$. Most importantly, since the rise of the new propylene oxide processes that use aqueous H$_2$O$_2$ as the oxidant, it has turned into a commodity with world capacities well above 2 million tons per year.$^{1a}$ The reactions with H$_2$O$_2$ are very selective and efficient, with fast and quantitative reactions taking place at low temperatures. Additionally, many oxidation reactions with H$_2$O$_2$, for example, the transformation of phosphines to their oxides,$^6$ do not need any catalyst.

Aqueous H$_2$O$_2$ is an enticing oxidizing agent in industrial settings because it is cheap, available on a large scale and it can be applied in concentrations up to 85 wt%. Its major drawback, however, remains the water byproduct. Aqueous H$_2$O$_2$ solutions used in modern industrial processes are very pure and stable, with typical decomposition rates of 1% per year. On the other hand, in academic settings 30 wt% aqueous solutions are usually purchased as a compromise between potency and safety regulations. In practice, with many users, aqueous H$_2$O$_2$ decomposes at unpredictable rates, and the solutions have to be titrated$^7$ prior to each application when exact stoichiometry is needed. Furthermore, in case the reagents are not soluble in water, the oxidation has to be
performed in a biphasic system, which entails a slow reaction at the phase boundary and a phase separation requirement in the workup.

Different formulations of H$_2$O$_2$ are also in use, for example, urea hydrogen peroxide (UHP) adducts.$^8$ However, the UHP adducts are not stoichiometric in nature, and urea and water have to be removed after the reaction. Alternatively, alkali metal peroxocarbonates have been applied,$^9,^{10}$ but like UHP, they are caustic. Unfortunately, H$_2$O$_2$ is much less stable under basic conditions. Additionally, many oxidations performed with H$_2$O$_2$ are co-catalyzed by acids.$^{1a}$ Besides these materials, encapsulated$^{11}$ and immobilized versions of hydrogen peroxide are known.$^{12,13}$ Again, the stoichiometry of these materials is not very well defined. Furthermore, H$_2$O$_2$ adducts of metal complexes have been characterized.$^{14}$ Organic and silicon-containing peroxides are important, but can be difficult to synthesize and remove from reaction mixtures.$^{15}$

The ideal oxidizing agent is an easy to synthesize, solid and molecular H$_2$O$_2$ adduct of reproducible stoichiometry that is soluble in organic solvents. This thesis describes the discovery of two different peroxide containing adducts of phosphine oxides as oxidizing agents – the H$_2$O$_2$ and the di(hydroperoxy)alkane adducts of phosphine oxides. In contrast to urea hydrogen peroxide or peroxocarbonates, phosphine oxides are only moderate Lewis bases, and they could also function as ligands for Mo or W centers in oxidation reactions,$^{16}$ therewith playing a dual role.

For both types of adducts, once all active peroxide is consumed during an oxidation reaction, the remaining phosphine oxide can easily be removed from the reaction mixture via reversible adsorption on solid oxide materials, such as silica or
molecular sieves. Once the phosphine oxides are retrieved from the support by washing with polar solvents, they can undergo the synthetic procedure to regenerate the adduct.

In the following chapters, the synthetic methods of each type of adduct are described in detail and full characterization data are provided. Furthermore, the potential of each type of adduct as stoichiometric oxidizing agent for different oxidation reactions is explored.
CHAPTER II

HYDROGEN PEROXIDE ADDUCTS OF PHOSPHINE OXIDES

Introduction

H$_2$O$_2$ adducts of phosphine oxides, such as [Cy$_3$PO•H$_2$O$_2$]$_2$, have been described by the Bluemel group as stoichiometric, well-defined molecules with high melting points that are stable over months on the shelf and can easily be crystallized. Previously, a single crystal X-ray structure of [Cy$_3$PO•H$_2$O$_2$]$_2$ had been obtained, where the two H$_2$O$_2$ molecules bridge the two phosphine oxides to form a chair-like structure (Figure 2.1). This well-defined molecular structure of [Cy$_3$PO•H$_2$O$_2$]$_2$ allows for exact stoichiometric determination of per oxy groups and active oxygen atoms.

Figure 2.1. Single crystal X-ray structure of [Cy$_3$PO•H$_2$O$_2$]$_2$.

On the other hand, the structural data of (Ph₃PO)₂•H₂O₂ have been known for decades, where two phosphine oxide molecules are bridged by a single H₂O₂ molecule (Figure 2.2). Although H₂O₂ adducts of other phosphine oxide molecules have been reported, single crystal X-ray data have only been obtained for [Cy₃PO•H₂O₂]² and (Ph₃PO)₂•H₂O₂ when the work on this thesis was started. Therefore, it was difficult to determine the ratio R₃PO : H₂O₂ for a H₂O₂ adduct of any given phosphine oxide. Moreover, adducts of phosphine oxides with less steric bulk are often viscous oils.

![Figure 2.2. Single crystal X-ray structure of (Ph₃PO)₂•H₂O₂.](image)

The synthetic method described previously was applied to various different phosphine oxides in an attempt to crystallize another adduct and determine whether the chair-like structure found in [Cy₃PO•H₂O₂]² is unique to Cy₃PO, or if this is a general motif for trialkylphosphine oxides.

Previously, ³¹P NMR and IR spectroscopy have been used to confirm the presence of H₂O₂ and the absence of H₂O in adduct molecules. In the ³¹P NMR
spectrum, the phosphorus peak of an adduct \((R_3PO)_x(H_2O_2)_y\) is downfield shifted compared to the neat \(R_3PO\), as electron density is removed to form the \(P=O\) group by hydrogen bonding, and phosphorus is deshielded. In the IR spectrum, the O-H band for \(H_2O_2\) appears as a broad band around 3200 cm\(^{-1}\), distinct from the O-H band of H\(_2\)O at 3400 cm\(^{-1}\) (Figure B.1).

For the newly synthesized \(H_2O_2\) adducts, both \(^{31}\)P NMR and IR spectroscopy were performed, and the solubilities of these adducts in common organic solvents were measured.

**Results and Discussions**

In order to probe whether \([R_3PO\cdot H_2O_2]_2\) represents a general composition of hydrogen peroxide adducts of phosphine oxides, analogous compounds with different substituents (\(R = ^tBu, Ph\)) have been synthesized following the previously described method.\(^6\) Indeed, the adduct \([^tBu_3PO\cdot H_2O_2]_2\) (1) crystallized as a dimer with two \(H_2O_2\) molecules hydrogen-bonded between two phosphine oxide groups in a chair conformation (Figure 2.3).\(^18,20\) The tendency of \(P=O\) groups to eagerly form hydrogen bonds to \(H_2O_2\) molecules,\(^6\) \(H_2O^{17}\) and silanols\(^{17}\) has been described. Recently, hydrogen bonding between \(P=O\) and phenol -OH groups has also been used to create dimeric motifs.\(^21\)

Many triarylphosphine oxides do not follow this structural trend, and they can even lead to different adduct structures and stoichiometries for one given
triarylphosphine oxide. For example, an adduct of Ph₃PO has been described earlier and its composition has been determined as (Ph₃PO)₂•H₂O₂ with H₂O₂ bridging two Ph₃PO molecules.¹⁹ Two separate attempts to reproduce this result led to (Ph₃PO)₂•H₂O₂ (Figure 2.2)¹⁹ and a new adduct [Ph₃PO•H₂O₂]₂•H₂O₂ (2) (Figure 2.3).¹⁸,²² Most probably, due to the rigid nature and steric of the phenyl groups, additional H₂O₂ molecules can be accommodated in the space between the dimers, depending on the reaction conditions.

Figure 2.3. Single crystal X-ray structures of 1 (left)¹⁸,²⁰ and 2 (right).¹⁸,²²

The crystalline adduct [Cy₃PO•H₂O₂]₂ (3) was easily reproduced in high yield following the previously reported synthetic method.⁶ The absence of bulk water molecules was confirmed via NMR and IR spectroscopy.

When solubilized, the hydrogen bond between H₂O₂ and R₃PO reversibly forms, and proton exchange can occur between H₂O₂ and protic solvents. This exchange was observed when adduct 3 was dissolved in a CDCl₃/D₂O (6:1) mixture and stirred overnight. The resulting product was precipitated, and analyzed with ²H NMR and IR
spectroscopy. In the $^2$H NMR spectrum, a broad peak is observed at 10.51 ppm, corresponding to the peroxide-bound deuterium (Figure 2.4).

Figure 2.4. $^1$H NMR spectrum of 3 (top) and $^2$H NMR spectrum of partially deuterated 3 (bottom).

In the $^1$H NMR spectrum of a non-deuterated sample, the -OOH proton peak occurs in the same region, at 10.14 ppm. The IR spectrum shows signs of residual H$_2$O$_2$ (3165.2 cm$^{-1}$) as well as the exchanged D$_2$O$_2$ (2358.9 cm$^{-1}$) (Figure B. 4).
One of the most important advantages of the hydrogen peroxide adducts of phosphine oxides with respect to their application as oxidizing agents is that they are very soluble in organic solvents, rendering biphasic reaction mixtures obsolete. The solubilities of 2 and 3 in representative organic solvents have been quantified (Figure 2.5). They are substantially higher in polar solvents, with adduct 3 displaying remarkably high solubility especially in chlorinated solvents.

![Figure 2.5. Solubilities of 2 and 3 in representative solvents.](image)

**Conclusion**

In this chapter it has been demonstrated that the H$_2$O$_2$ adducts of trialkylphosphine oxides crystallize readily and reproducibly in a dimer structure with a
chair-type arrangement of the H₂O₂ moieties. Triarylphosphine oxides can lead to different H₂O₂ contents, and therefore quantification of the ratio R₃PO : H₂O₂ is necessary for each new batch. The described adducts do not contain an excess of water molecules and are very soluble in representative organic solvents, allowing oxidation reactions in a single organic phase.

Experimental

[¹Bu₃PO•H₂O₂]₂ (1)

¹Bu₃P (20 mg, 0.099 mmol) is weighed into a Schlenk flask inside a glove box. The flask is then sealed, brought outside, and acetone (40 mL) is added under a nitrogen stream. Once the phosphine is dissolved, aqueous H₂O₂ (1.0 mL, 10 mmol) is added and the reaction mixture is stirred for 1 h. 100 mL of EtOH is then added to the flask, and the azeotropic mixture of EtOH and H₂O is removed in vacuo at ambient temperature. The resulting viscous material is washed with toluene and left to crystallize. The adduct [¹Bu₃PO•H₂O₂]₂ is obtained in the form of white rhombic crystals (19 mg, 0.075 mmol, 76% yield).

NMR (δ, CDCl₃), ³¹P{¹H} 43.16 (s), ¹H 9.10 (br. s, H₂O₂), 1.41 (d, ³J(³¹P-¹H) = 12.5 Hz, -CH₃); ¹³C{¹H} 39.17 (d, ¹J(³¹P-¹³C) = 49.6 Hz, PC), 29.00 (s, -CH₃).

NMR (δ, (CD₃)₂CO), ³¹P{¹H} 65.61 (s); ¹H 1.34 (d, ³J(³¹P-¹H) = 12.0 Hz, -CH₃); ¹³C{¹H} 40.35 (d, ¹J(³¹P-¹³C) = 51.1 Hz, PC), 30.08 (s, -CH₃). mp 122-125 °C.
[Ph₃PO•H₂O₂]₂•H₂O₂ (2)

Ph₃P (150 mg, 0.572 mmol) is weighed into a Schlenk flask flushed with nitrogen gas. CH₂Cl₂ (150 mL) is added under a nitrogen stream. Once the phosphine is dissolved, aqueous H₂O₂ (1.0 mL, 10 mmol) is added and the reaction mixture is stirred for 30 min. The organic layer is collected via separation funnel, and the solvent is removed in vacuo. The resulting white precipitate is dissolved in acetone (60 mL), and after the addition of H₂O₂ (0.1 mL, 1 mmol), the sample is allowed to crystallize. [Ph₃PO•H₂O₂]₂•H₂O₂ is obtained in the form of colorless needles (286 mg, 0.434 mmol, 76% yield).

NMR (δ, CDCl₃), ³¹P{¹H} 32.84 (s); ¹H 11.24 (br. s, H₂O₂), 8.93 (br. s, H₂O₂), 7.67-7.62 (m, 6H, Hₜ), 7.58-7.55 (m, 3H, Hₚ), 7.49-7.45 (m, 6H, Hₘ); ¹³C{¹H} 132.43 (s, Cₚ), 132.04 (d, ²J(³¹P⁻¹³C) = 10.2 Hz, Cₙ), 130.71 (d, ¹J(³¹P⁻¹³C) = 108.8 Hz, Cᵢ), 128.69 (d, ³J(³¹P⁻¹³C) = 12.1 Hz, Cₘ). mp 143-155 °C.

Deuteration of [Cy₃PO•H₂O₂]₂ (3)

0.5 mL of D₂O was added to a solution of 50 mg (0.08 mmol) of [Cy₃PO•H₂O₂]₂, dissolved in 3 mL of CDCl₃, and the mixture was stirred vigorously for 24 h. The remaining CDCl₃ and D₂O were removed via slow evaporation, and the deuterated adduct was obtained as white crystalline powder. A sample was prepared for ²H NMR by dissolving the product in C₆H₆.
CHAPTER III

SYNTHESIS OF DI(HYDROPEROXY)ALKANE ADDUCTS OF PHOSPHINE
OXIDES*

Introduction

In an attempt to control the R₃PO : H₂O₂ ratio in H₂O₂ adducts of triaryl-
phosphine oxides, and to be able to work in one organic phase, the solvent for the
reaction was changed from CH₂Cl₂ to acetone. Contrary to anticipation, a new class of
adducts was discovered, with the molecular formula R₃PO•(HOO)₂CR'R'' (R, R', R'' =
alkyl, aryl). For these di(hydroperoxy)alkane adducts the number of active peroxide
groups is even higher than for H₂O₂ adducts, as two peroxy groups are bound to one
phosphine oxide group. The high tendency of these adducts to crystallize makes them an
ideal source for stoichiometric active peroxides.

While di(hydroperoxy)alkanes have been known for a long time, the only
preceding report of this class of phosphine oxide adduct was made when H₂O₂ and
bis(diphenylphosphino)ethane (dppe) were reacted in acetone in the presence of R₂SnCl₂
(R = Me or n-Bu) as catalyst to form (Ph₂P(O)CH₂CH₂P(O)Ph₂)•((HOO)₂CMe₂)₂. The
authors proposed that this adduct could only form with a chelating phosphine that has
two methylene carbons in the chain between the two P atoms.

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Phosphine Oxides as Stoichiometric and Soluble Oxidizing Agents” Ahn, S. H.; Cluff, K. J.;
Bhuvanesh, N.; Blümel, J. Angew. Chem. 2015, 127, 13539-13543. Copyright Wiley-VCH Verlag
GmbH & Co. KGaA.
Here, it will be demonstrated that di(hydroperoxy)alkane adducts of phosphine oxides are actually easy to synthesize with a large variety of alkane moieties. Moreover, the active oxygen content and the structural mode remain the same for different phosphine oxides. A description of the general synthetic method and its mechanism are provided in this chapter.

**Results and Discussion**

Di(hydroperoxy)alkane adducts of various phosphine oxides and alkanes (4-15) were successfully synthesized and obtained in nearly quantitative yields as giant crystals (Scheme 3.1). Adducts of the bulky Cy$_3$PO crystallize especially readily, and thus Cy$_3$PO was used most often in adduct syntheses. In order to improve the atom economy of active oxygen, and to probe the general structure of the di(hydroperoxy)alkane adducts, 1,2-bis(diphenylphosphino)ethane (dppe) and 1,2-bis(diphenylphosphino)-methane (dppm) were treated with acetone and aqueous H$_2$O$_2$. While dppm dioxide only formed the adduct with one molecule of (HOO)$_2$CMe$_2$, dppe dioxide formed hydrogen bonds with (HOO)$_2$CMe$_2$ at both P=O groups. Encouraged by this success, the dppe dioxide adduct synthesis was repeated with 3-pentanone to produce (Ph$_2$P(O)CH$_2$CH$_2$P(O)Ph$_2$)$\ast$(HOO)$_2$CEt$_2$)$_2$ (15). The discrepancy in the ratio of dppm dioxide and (HOO)$_2$CMe$_2$ is studied in detail in the following chapter.

It is important to note that the di(hydroperoxy)alkane adducts can be generated at room temperature and without addition of a strong acid or catalyst.$^{18,23a,25}$ This prevents the formation of potentially dangerous cyclic peroxide trimers.$^{26}$ In fact, none of the
adducts 4-15 displayed any violent release of energy when being ground, hammered, stored over months, or heated up.

Scheme 3.1. (HOO)$_2$CR'R" adducts of the phosphine oxides 4-12 and the diphosphine dioxides 13-15.

The adducts can be synthesized in a variety of ways (Scheme 3.2). One option is to start from the phosphine oxides or their corresponding H$_2$O or H$_2$O$_2$ adducts.
Alternatively, the phosphines can be used as educts. When starting from the phosphine oxides, exclusion of air is not necessary during the adduct synthesis. However, starting from the phosphines entails the risk of formation of other unwanted products from oxygen insertion into the P-C bonds, and thus the synthesis must be performed in inert atmosphere.\textsuperscript{6}

For all starting materials, the adduct formation can be achieved by adding the corresponding ketone and H\textsubscript{2}O\textsubscript{2}, or the pre-formed di(hydroperoxy)alkane moiety,\textsuperscript{23a} if available in stable form. The ketone can serve a dual role as the reaction solvent, or CH\textsubscript{2}Cl\textsubscript{2} can be used instead, as the phosphines and phosphine oxides are highly soluble in polar chlorinated solvents.

\textbf{Scheme 3.2.} General synthesis routes for the adducts R\textsubscript{3}PO•(HOO)\textsubscript{2}CR'R" (R, R', R" = alkyl, aryl).

The mechanism for the formation of the adducts is suggested in Scheme 3.3.\textsuperscript{18} Two hydroperoxides perform a nucleophilic attack on the carbonyl carbon atom to form
the di(hydroperoxyl)alkane, which then attaches to the phosphine oxide via hydrogen bonds.

![Scheme 3.3](image)

**Scheme 3.3.** Suggested mechanism for the formation of adducts R₃PO•(HOO)₂CR'R" (R, R', R" = alkyl, aryl).

In order to remove excess water from the solution without decomposing the peroxide groups, ethanol is used to form an azeotropic mixture with water. This mixture is then removed in a mild vacuum at room temperature, and the adduct is crystallized from the remaining solution. Starting from larger ketones, the ensuing (HOO)₂CR'R" molecule can be safely isolated and dried,²³a and combined with pure phosphine oxide at a later time to form the adduct. Thus, an azeotropic mixture is unnecessary. Excess solvent is removed in vacuo at room temperature, as the peroxide functionality can decompose at higher temperatures. The adduct is obtained in the form of crystals from the concentrated solution.

The general synthetic routes outlined in Scheme 3.2 allow for easy recycling of the adducts. Once the peroxide oxygen atoms are consumed in the course of an oxidation
reaction, the remaining phosphine oxide can be removed and the adduct is regenerated by stirring the phosphine oxide in a solution of excess H$_2$O$_2$ together with the corresponding ketone.

**Conclusion**

Di(hydroperoxy)alkane adducts of phosphine oxides are successfully synthesized at room temperature, without the use of acid or metal catalysts. Phosphine, phosphine oxide, and H$_2$O or H$_2$O$_2$ adducts of phosphine oxides can be used as the starting materials. While the high solubility of these starting materials make CH$_2$Cl$_2$ an attractive solvent, the corresponding ketone can be used as the solvent instead. This one-pot, general synthetic approach can be applied to a wide variety of phosphine oxides and ketones, and the resulting adducts can be safely and easily isolated in the form of large crystals.

**Experimental**

Ph$_3$PO•(HOO)$_2$CMe$_2$ (4)

Ph$_3$P (200 mg, 0.762 mmol) is weighed into a Schlenk flask flushed with nitrogen gas. Acetone (100 mL) is added under a nitrogen flow. Once the phosphine is all dissolved, H$_2$O$_2$ (1.0 mL, 10 mmol) is added and the reaction mixture is stirred for 3 h. The sample is concentrated *in vacuo* to 5 mL, then allowed to crystallize.
(Ph₃PO)•(HOO)₂CMe₂ (4) is obtained as colorless rectangular crystals (243 mg, 0.629 mmol, 82.5% yield).

NMR (δ, CDCl₃), ³¹P{¹H} 34.74 (s); ¹H 11.29-10.90 (br. s, -OOH), 7.68-7.61 (m, 6H, \(H_α\)), 7.60-7.55 (m, 3H, \(H_β\)), 7.51-7.46 (m, 6H, \(H_m\)), 1.47 (m, 6H, CH₃); ¹³C{¹H} 132.57 (s, \(C_p\)), 132.10 (d, \(^2J⁹³P⁻¹³C = 10.7\) Hz, \(C_o\)), 130.56 (d, \(^1J⁹³P⁻¹³C = 106.07\) Hz, \(C_i\)), 128.77 (d, \(^3J⁹³P⁻¹³C = 12.6\) Hz, \(C_m\)), 109.28 (s, CH₃C), 20.64 (s, CH₃).

NMR (δ, (CD₃)₂CO), ³¹P{¹H} 31.21 (s); ¹H 10.97 (br. s, -OOH), 7.76-7.68 (m, 6H, \(H_α\)), 7.67-7.62 (m, 3H, \(H_β\)), 7.60-7.53 (m, 6H, \(H_m\)), 1.35 (m, CH₃); ¹³C{¹H} 133.14 (d, \(^4J⁹³P⁻¹³C = 2.3\) Hz, \(C_p\)), 132.58 (d, \(^2J⁹³P⁻¹³C = 10.2\) Hz, \(C_o\)), 132.51 (d, \(^1J⁹³P⁻¹³C = 104.7\) Hz, \(C_i\)), 129.52 (d, \(^3J⁹³P⁻¹³C = 12.1\) Hz, \(C_m\)), 109.03 (s, CH₃C), 20.97 (s, CH₃). IR: ν(PO) = 1152 cm⁻¹. mp (decomp.) 75 °C.

Cy₃PO•(HOO)₂CMe₂ (5)

Cy₃P (100 mg, 0.357 mmol) is weighed into a Schlenk flask inside a glove box. The flask is then sealed, brought outside, and acetone (60 mL) is added under a nitrogen flow. Once the phosphine is all dissolved, H₂O₂ (0.5 mL, 5.1 mmol) is added and the reaction mixture is stirred for 1 h. 100 mL of EtOH is then added to the flask, and the azeotropic mixture of EtOH and H₂O is removed in vacuo at ambient temperature. (Cy₃PO)•(HOO)₂CMe₂ (5) is obtained as colorless hexagonal crystals (126 mg, 0.327 mmol, 91.6% yield)
NMR (δ, CDCl₃), ³¹P{¹H} 55.59 (s); ¹H 1.97-1.80 (m, 15H, PCHaxCHeqCHeq), 1.77-1.70 (s, 3H, PCH(CH₂)₂CHeq), 1.49-1.36 (s, 12H, PCHCHax, CH₃), 1.36-1.21 (m, 9H, PCHCH₂CHaxCHax); ¹³C{¹H} 108.91 (s, CH₃C), 34.79 (d, ³¹P-¹³C) = 60.9 Hz, PCH), 26.74 (d, ³J(³¹P-¹³C) = 12.7 Hz, PCHCH₂CH₂), 25.98 (d, ²J(³¹P-¹³C) = 3.6 Hz, PCHCH₂), 25.92 (d, ⁴J(³¹P-¹³C) = 1.8 Hz, PCH(CH₂)₂CH₂), 20.63 (s, CH₃).

NMR (δ, (CD₃)₂CO), ³¹P{¹H} 56.44 (s); ¹H 11.45 (br. s, -OOH), 2.02-1.89 (m, 9H, PCHaxCHeq), 1.86-1.76 (m, 6H, PCHCH₂CHeq), 1.74-1.66 (m, 3H, PCH(CH₂)₂CHeq), 1.52-1.38 (m, 6H, PCHCHax), 1.37-1.19 (m, 9H, PCHCH₂CHaxCHax), 1.30 (s, CH₃); ¹³C{¹H} 108.61 (s, (CH₃)₂C(OOH)₂), 35.53 (d, ¹J(³¹P-¹³C) = 61.0 Hz, PCH), 27.36 (d, ³J(³¹P-¹³C) = 12.1 Hz, PCHCH₂CH₂), 26.74 (s, PCH(CH₂)₂CH₂), 26.73 (d, ²J(³¹P-¹³C) = 2.8 Hz, PCHCH₂). IR: ν(PO) = 1125 cm⁻¹. mp (decomp.) 70 °C.

Ph₃PO•(HOO)₂CMeEt (6)

Ph₃P (300 mg, 1.1 mmol) was placed in a round bottom flask and dissolved in toluene (40 mL). 2-Butanone (0.12 mL, 1.3 mmol) and H₂O₂ (0.5 mL, 5 mmol) were added, and the reaction mixture was stirred overnight. The solution was concentrated to approximately 3 mL in vacuo and the product was allowed to crystallize. Adduct 6 was obtained in the form of colorless crystals (294 mg, 0.71 mmol, 65% yield).

NMR (δ, CDCl₃), ³¹P{¹H} 30.52 (s); ¹H 11.38 (s, 2H, OOH), 7.69-7.64 (m, 6H, Hₖ), 7.60-7.55 (m, 3H, Hₚ), 7.51-7.46 (m, 6H, Hₘ), 1.79 (q, ³J(¹H-¹H) = 7.6 Hz, 2H,
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CH₂CH₃), 1.41 (s, 3H, CCH₃), 1.01 (t, ³J(¹H·¹H) = 7.6 Hz, 3H, CH₂CH₃); ¹³C{¹H} 132.32 (d, ⁴J(³¹P·¹³C) = 2.7 Hz, Cp), 132.08 (d, ²J(³¹P·¹³C) = 10.0 Hz, Co), 131.29 (d, ¹J(³¹P·¹³C) = 105.4 Hz, Ci), 128.66 (d, ³J(³¹P·¹³C) = 12.3 Hz, Cm), 111.56 (s, CH₃C), 26.09 (s, CH₂CH₃), 17.46 (s, CCH₃), 8.38 (s, CH₂CH₃).

NMR (δ, C₆D₆), ³¹P{¹H} 31.42 (s); ¹H 11.95 (s, 2H, OOH), 7.62-7.56 (m, 6H, Ho), 7.03-6.98 (m, 3H, Hp), 6.96-6.91 (m, 6H, Hm), 2.09 (q, ³J(¹H·¹H) = 7.6 Hz, 2H, CH₂CH₃), 1.65 (s, 3H, CCH₃), 1.11 (t, ³J(¹H·¹H) = 7.6 Hz, 3H, CH₂CH₃); ¹³C{¹H} 132.32 (d, ²J(³¹P·¹³C) = 10.4 Hz, Co), 132.11 (d, ¹J(³¹P·¹³C) = 104.0 Hz, Ci), 132.10 (d, ⁴J(³¹P·¹³C) = 3.2 Hz, Cp), 128.72 (d, ³J(³¹P·¹³C) = 12.3 Hz, Cm), 111.70 (s, CH₃C), 26.94 (s, CH₂CH₃), 18.16 (s, CCH₃), 8.78 (s, CH₂CH₃). IR: ν(PO) = 1142 cm⁻¹. mp (decomp.) 54 °C.

Cy₃PO•(HOO)₂CMeEt (7)

[Cy₃PO•H₂O₂]₂ (300 mg, 0.91 mmol) was placed in a round bottom flask and dissolved in 30 mL of butanone (0.33 mol). After addition of H₂O₂ (0.5 mL, 5 mmol) the solution was stirred overnight. Excess butanone was removed in vacuo until a precipitate appeared. Subsequently, 50 mL of EtOH was added to the flask, and the azeotropic mixture of EtOH and H₂O was removed in vacuo at ambient temperature to give white crystals of 7 (345 mg, 0.82 mmol, 90% yield).
NMR ($\delta$, CDCl$_3$), $^{31}$P{$^{1}$H} 58.77 (s); $^1$H 11.47 (s, 2H, OOH), 1.97-1.80 (m, 15H, PCHCH$_{eq}$CH$_{eq}$), 1.73 (q, $^3J(^1$H-$^1$H) = 7.6 Hz, 2H, CH$_2$CH$_3$), 1.76-1.72 (m, 3H, PCH(CH$_2$)$_2$CH$_{eq}$), 1.48-1.39 (m, 6H, PCHCH$_{ax}$), 1.38 (s, 3H, CCH$_3$), 1.29-1.23 (m, 9H, PCHCH$_2$CH$_{ax}$CH$_{ax}$), 0.97 (t, $^3J(^1$H-$^1$H) = 7.6 Hz, 2H, CH$_2$CH$_3$); $^{13}$C{$^{1}$H} 111.26 (s, CH$_3$C), 34.72 (d, $^1J(^{31}$P-$^{13}$C) = 60.5 Hz, PC), 26.72 (d, $^3J(^{31}$P-$^{13}$C) = 12.1 Hz, PCHCH$_2$CH$_2$), 26.02 (s, CH$_2$CH$_3$), 25.96 (d, $^2J(^{31}$P-$^{13}$C) = 2.8 Hz, PCHCH$_2$), 25.91 (d, $^4J(^{31}$P-$^{13}$C) = 1.4 Hz, PCH(CH$_2$)$_2$CH$_2$), 17.41 (s, CCH$_3$), 8.36 (s, CH$_2$CH$_3$). IR: $\nu$(PO) = 1124 cm$^{-1}$. mp (decomp.) 108 °C.

Cy$_3$PO•(HOO)$_2$CEt$_2$ (8)

[Cy$_3$PO•H$_2$O$_2$]$_2$ (330 mg, 1.0 mmol) was placed in a round bottom flask and combined with 3-pentanone (0.4 mL, 2 mmol) and H$_2$O$_2$ (0.2 mL, 2 mmol). The mixture was stirred for 1 h, then left to crystallize by slow evaporation of solvent. Cy$_3$PO•(HOO)$_2$CEt$_2$ (8) was obtained in the form of white, rod-shaped crystals (425 mg, 1.0 mmol, 98% yield).

NMR ($\delta$, CDCl$_3$), $^{31}$P{$^{1}$H} 58.35 (s); $^1$H 10.82 (br. s, 2H, OOH), 1.96-1.81 (m, 15H, PCH$_{ax}$CH$_{eq}$CH$_{eq}$), 1.76-1.71 (m, 3H, PCH(CH$_2$)$_2$CH$_{eq}$), 1.81 (t, $^3J(^1$H-$^1$H) = 6.4 Hz, 4H, CCH$_2$), 1.68 (q, $^3J(^1$H-$^1$H) = 7.6 Hz, 4H, CCH$_2$), 1.47-1.37 (m, 8H, PCHCH$_{ax}$, CCH$_2$CH$_2$CH$_2$), 1.30-1.22 (m, 9H, PCHCH$_2$CH$_{ax}$CH$_{ax}$), 0.94 (t, $^3J(^1$H-$^1$H) = 7.6 Hz, 6H, CCH$_2$CH$_3$); $^{13}$C{$^{1}$H} 113.76 (s, CCH$_3$), 34.64 (d, $^1J(^{31}$P-$^{13}$C) = 60.5 Hz, PC), 26.68 (d, $^3J(^{31}$P-$^{13}$C) = 11.6 Hz, PCHCH$_2$CH$_2$), 25.93 (d, $^2J(^{31}$P-$^{13}$C) = 3.3 Hz, PCHCH$_2$), 25.87 (d,
$^4J(^{31}\text{P}-^{13}\text{C}) = 0.9 \text{ Hz, PCH(CH}_2\text{)}_2\text{CH}_2$, 21.64 (s, CH$_2$CH$_3$), 7.91 (s, CH$_2$CH$_3$). IR: $\nu$(PO) = 1126 cm$^{-1}$. mp 138 °C.

Cy$_3$PO•(HOO)$_2$C(CH$_2$)$_4$ (9)

In a round bottom flask [Cy$_3$PO•H$_2$O$_2$]$_2$ (996 mg, 3 mmol) is dissolved in cyclopentanone (4.6 mL, 52 mmol). H$_2$O$_2$ (1 mL, 10 mmol) is added to the flask, the contents is stirred for 1 h, then left to crystallize by slow evaporation of the solvent. Cy$_3$PO•(HOO)$_2$C(CH$_2$)$_4$ (9) is obtained in the form of colorless, cubic crystals (1049 mg, 2.3 mmol, 76% yield).

NMR ($\delta$, CDCl$_3$), $^{31}$P{${^1}$H} 57.14 (s); $^1$H 11.61 (br. s, 2H, OO$\text{H}$), 1.93 (t, 4H, $^3J(\text{H}-\text{H}) = 7.58$ Hz, CCH$_2$), 1.95-1.81 (m, 15H, PCH$_{\text{ax}}$CH$_{\text{eq}}$CH$_{\text{eq}}$), 1.75-1.71 (m, 3H, PCH(CH$_2$)$_2$CH$_{\text{eq}}$), 1.70 (t, 4H, $^3J(\text{H}-\text{H}) = 7.58$ Hz, CCH$_2$CH$_2$), 1.47-1.37 (m, 6H, PCHCH$_{\text{ax}}$), 1.31-1.21 (m, 9H, PCHCH$_2$CH$_{\text{ax}}$CH$_{\text{ax}}$); $^{13}$C{${^1}$H} 120.92 (s, CCH$_3$), 34.80 (d, $^{1}J(^{31}\text{P}-^{13}\text{C}) = 60.5$ Hz, PC), 33.14 (s, CCH$_2$), 26.76 (d, $^3J(^{31}\text{P}-^{13}\text{C}) = 11.6$ Hz, PCHCH$_2$CH$_2$), 26.01 (d, $^2J(^{31}\text{P}-^{13}\text{C}) = 3.3$ Hz, PCHCH$_2$), 25.95 (d, $^4J(^{31}\text{P}-^{13}\text{C}) = 1.4$ Hz, PCH(CH$_2$)$_2$CH$_2$), 24.66 (s, CCH$_2$CH$_2$). IR: $\nu$(PO) = 1123 cm$^{-1}$. mp 152 °C.

Cy$_3$PO•(HOO)$_2$C(CH$_2$)$_5$ (10)

0.3 mL of H$_2$SO$_4$ (5 mmol) and 13.5 mL of H$_2$O$_2$ (0.135 mol) were combined with THF (25 mL) in a round bottom flask. Cyclohexanone (1.00 mL, 9.7 mmol) was added dropwise over a period of 15 min, while stirring vigorously. After 5 h, 10 mL of
CH$_2$Cl$_2$ was added, and NaHCO$_3$ was used to neutralize the mixture to pH 7. The organic layer was collected, washed with H$_2$O (4x3 mL) and dried with MgSO$_4$. Solvent from the filtrate was removed in vacuo, to produce (HOO)$_2$C(CH$_2$)$_5$. The $^1$H and $^{13}$C NMR spectra of (HOO)$_2$C(CH$_2$)$_5$ matched those in the literature.$^{23a}$ [Cy$_3$PO•H$_2$O$_2$]$_2$ (297 mg, 0.9 mmol) was dissolved in 5 mL of benzene and added to the flask. The mixture was stirred for 2 h and subsequently concentrated in vacuo to about 2 mL at ambient temperature. Cy$_3$PO•(HOO)$_2$C(CH$_2$)$_5$ (10) was obtained as clear, hexagonal crystals (235 mg, 0.53 mmol, 59% yield).

NMR (δ, CDCl$_3$), $^{31}$P{$^1$H} 58.01 (s); $^1$H 10.66 (br. s, 2H, OO$_2$H), 1.97-1.79 (m, 15H, PCH$_{ax}$CH$_{eq}$CH$_{eq}$), 1.81 (t, $^3$J($^1$H-$^1$H) = 6.4 Hz, 4H, CCH$_2$), 1.75-1.71 (m, 3H, PCH(CH$_2$)$_2$CH$_{eq}$), 1.58 (quin, $^3$J($^1$H-$^1$H) = 6.4 Hz, 4H, CCH$_2$CH$_2$), 1.47-1.37 (m, 8H, PCHCH$_{ax}$, CCH$_2$CCH$_2$CH$_2$), 1.31-1.22 (m, 9H, PCHCH$_2$CH$_{ax}$CH$_{ax}$); $^{13}$C{$^1$H} 109.52 (s, CCH$_3$), 34.67 (d, $^1$J($^{31}$P-$^{13}$C) = 60.5 Hz, PC), 29.68 (s, CCH$_2$), 26.69 (d, $^3$J($^{31}$P-$^{13}$C) = 12.1 Hz, PCHCH$_2$CH$_2$), 25.94 (d, $^2$J($^{31}$P-$^{13}$C) = 3.3 Hz, PCHCH$_2$), 25.89 (d, $^4$J($^{31}$P-$^{13}$C) = 0.9 Hz, PCH(CH$_2$)$_2$CH$_2$), 25.55 (s, CCH$_2$CCH$_2$CH$_2$), 22.53 (s, CCH$_2$CH$_2$). IR: ν(PO) = 1123 cm$^{-1}$. mp 121 ºC.

Cy$_3$PO•(HOO)$_2$C(CH$_2$)$_6$ (11)

[Cy$_3$PO•H$_2$O$_2$]$_2$ (831 mg, 2.5 mmol), dissolved in cycloheptanone (3.0 mL, 25 mmol), is placed into a round bottom flask. H$_2$O$_2$ (1 mL, 10 mmol) is added to the flask,
the contents is stirred for 1 h, and then left to crystallize. Cy₃PO•(HOO)₂C(CH₂)₆ (11) is obtained in the form of colorless, cubic crystals (1067 mg, 2.2 mmol, 88% yield).

NMR (δ, CDCl₃), ³¹P{¹H} 56.63 (s); ¹H 11.57 (br. s, 2H, OOH), 1.93-1.81 (m, 19H, PCHₐxCHₑqCHₑq, CCH₂), 1.75-1.71 (m, 3H, PCH(CH₂)₂CHₑq), 1.61-1.53 (m, CCH₂CH₂CH₂), 1.47-1.36 (m, 6H, PCHCHₐx), 1.31-1.21 (m, 9H, PCHCH₂CHₐxCHₐx); ¹³C{¹H} 114.33 (s, CCH₃), 34.80 (d, ¹J(³¹P-¹³C) = 60.9 Hz, PC), 32.36 (s, CCH₂), 30.23 (s, CCH₂CH₂), 26.75 (d, ²J(³¹P-¹³C) = 11.6 Hz, PCHCH₂CH₂), 26.00 (d, ²J(³¹P-¹³C) = 2.7 Hz, PCHCH₂), 25.95 (d, ⁴J(³¹P-¹³C) = 0.9 Hz, PCH(CH₂)₂CH₂), 22.84 (s, CCH₂CH₂CH₂). IR: ν(PO) = 1123 cm⁻¹. mp 138 °C.

Cy₃PO•(HOO)₂CMePh (12)

[Cy₃PO•H₂O₂]₂ (425 mg, 1.30 mmol) was dissolved in 3 mL of acetophenone (25.7 mmol) in a round bottom flask. Then, H₂O₂ (1.3 mL, 130 mmol) was added, and the solution was stirred for 4 h. The solution was concentrated in vacuo to about 3 mL, then allowed to crystallize. Cy₃PO•(HOO)₂CMePh (12) was obtained in the form of colorless crystals (327 mg, 0.70 mmol, 54%).

³¹P{¹H} NMR (δ, CDCl₃), ³¹P 58.31 (s); ¹H 11.89 (br. s, 2H, OOH), 7.59-7.56 (m, 2H, Hₐ), 7.38-7.33 (m, 2H, Hₘ), 7.31-7.27 (m, 1H, Hₚ), 1.94-1.80 (m, 15H, PCHₐxCHₑqCHₑq), 1.75-1.71 (m, 3H, PCH(CH₂)₂CHₑq), 1.66 (s, 3H, CH₃), 1.47-1.37 (m, 6H, PCHCHₐx), 1.30-1.20 (m, 9H, PCHCH₂CHₐxCHₐx); ¹³C{¹H} 140.09 (s, Cₐ), 127.98 (s, Cₘ), 127.82 (s,
$C_p$, 125.94 (s, $C_m$), 110.18, (S, CCH$_3$), 34.68 (d, $^1J(^{31}P-^{13}C) = 60.5$ Hz, PC), 26.70 (d, $^3J(^{31}P-^{13}C) = 12.1$ Hz, PCHCH$_2$CH$_2$), 25.95 (d, $^2J(^{31}P-^{13}C) = 3.3$ Hz, PCHCH$_2$), 25.89 (d, $^4J(^{31}P-^{13}C) = 1.4$ Hz, PCH(CH$_2$)$_2$CH$_2$), 23.40 (CCH$_3$). IR: $\nu$(PO) = 1123 cm$^{-1}$. mp (decomp.) 100 °C.

Ph$_2$P(O)CH$_2$P(O)Ph$_2$•(HOO)$_2$CMe$_2$ (13)

In a round bottom flask Ph$_2$PCH$_2$PPPh$_2$ (384 mg, 1 mmol) was dissolved in 60 mL of CH$_2$Cl$_2$. Then H$_2$O$_2$ (0.5 mL, 5 mmol) was added, and the solution was stirred for 1 h. The organic layer was collected in a separation funnel, and the solvent was removed in vacuo. The resulting white precipitate (Ph$_2$P(O)CH$_2$P(O)Ph$_2$) was dissolved in 5 mL of acetone, and after the addition of another 0.5 mL of H$_2$O$_2$, the sample was allowed to crystallize via slow evaporation of the solvent. Adduct 14 was obtained in the form of white, needle-like crystals (364 mg, 0.76 mmol, 76% yield).

NMR ($\delta$, CDCl$_3$), $^{31}P\{^1H\}$ 30.33 (s); $^1$H 11.01 (br. s, 2H, OOH), 7.72-7.66 (m, 8H, $H_o$), 7.47-7.42 (m, 4H, $H_p$), 7.38-7.33 (m, 8H, $H_m$), 3.62 (t, $^3J(^{31}P-^1H) = 14.7$ Hz, 2H, PCH$_2$), 1.48 (s, 6H, CCH$_3$); $^{13}$C$\{^1H\}$ 132.21 (s, $C_p$), 131.07 (d, $^1J(^{31}P-^{13}C) = 107.0$ Hz, $C_i$), 130.86 (virtual quintet, $J(^{31}P-^{13}C) = 5.1$ Hz, $C_o$), 128.64 (virtual quintet, $J(^{31}P-^{13}C) = 6.1$ Hz, $C_m$), 109.21 (s, CCH$_3$), 21.26 (PCH$_2$), 20.63 (s, CCH$_3$).

NMR ($\delta$, (CD$_3$)$_2$CO), $^{31}P\{^1H\}$ 26.63 (s); $^1$H 10.49 (br. s, OOH), 7.87-7.81 (ddd, $^3J(^{31}P-^1H) = 12.2$ Hz, $^3J(^{1}H-^{1}H) = 8.3$ Hz, $^4J(^{1}H-^{1}H) = 1.2$ Hz, $H_o$), 7.52-7.47 (td $^3J(^{1}H-^{1}H) =$
7.3 Hz, $^4J(^1H^-^1H) = 1.2$ Hz, $H_p$), 7.43-7.38 (td $^3J(^1H^-^1H) = 8.3$ Hz, $^3J(^1H^-^1H) = 7.3$ Hz, $H_m$), 3.99 (t, $^2J(^{31}P^-^1H) = 13.9$ Hz, -CH$_2$-), 1.36 (s, -CH$_3$); $^{13}$C{^1H} 133.46 (d, $^1J(^{31}P^-^{13}C) = 106.2$ Hz, $C_i$), 131.74 (s, $C_p$), 130.89 (virtual quintet 29.3 Hz, $C_o$), 128.38 (virtual quintet, 30.5 Hz, $C_m$), 108.34 (s, CH$_3$C), 20.43 (s, PCH$_2$), 20.25 (s, -CH$_3$). IR: $\nu$(PO) = 1163.1 cm$^{-1}$. mp (decomp.) 120 °C.

(Ph$_2$P(O)CH$_2$CH$_2$P(O)Ph$_2$)$\cdot$((HOO)$_2$CMe$_2$)$_2$ (14)

Ph$_2$P(O)CH$_2$CH$_2$P(O)Ph$_2$ (20 mg, 0.05 mmol) was dissolved in 0.5 mL of acetone (6.8 mmol) in a round bottom flask. Subsequently, H$_2$O$_2$ (0.1 mL, 1 mmol) was added and the solution was stirred for 1 h, then left to crystallize via slow evaporation of the solvent. Adduct 14 crystallized in the form of colorless, needle-like crystals (27 mg, 0.04 mmol, 84% yield).

NMR ($\delta$, CDCl$_3$), $^{31}$P{^1H} 38.78 (s); $^1H$ 11.34 (s, 2H, OOH), 7.71 (dd, 8H, $^3J(^{31}P^-^1H) = 11.5$ Hz, $^3J(^1H^-^1H) = 7.3$ Hz, $H_o$), 7.52 (t, 4H, $^3J(^1H^-^1H) = 7.3$ Hz, $H_p$), 7.45 (dd, 8H, $^3J(^1H^-^1H) = 11.5$ Hz, $^2J(^1H^-^1H) = 7.3$ Hz, $H_m$), 2.52 (d, 4H, $^2J(^{31}P^-^1H) = 2.5$ Hz, PCH$_2$-), 1.51 (s, 12H, -CH$_3$); $^{13}$C{^1H} = 132.70 (s, $C_p$), 130.68 (virtual triplet, $J(^{31}P^-^{13}C) = 4.9$ Hz, $C_o$), 129.86 (d, $^1J(^{31}P^-^{13}C) = 100.0$ Hz, $C_i$), 129.21 (virtual triplet, $J(^{31}P^-^{13}C) = 6.1$ Hz, $C_m$), 109.38 (s, CH$_3$C), 21.08 (virtual triplet, $J(^{31}P^-^{13}C) = 33.0$ Hz, PCH$_2$), 20.68 (s, -CH$_3$). IR: $\nu$(PO) = 1148 cm$^{-1}$. mp (decomp.) 80 °C.
(Ph₂P(O)CH₂CH₂P(O)Ph₂)((HOO)₂C₂Et₂)₂ (15)

Ph₂P(O)CH₂CH₂P(O)Ph₂ (20 mg, 0.05 mmol) was dissolved in 0.3 mL of pentanone (2.8 mmol) in a round bottom flask. Subsequently, H₂O₂ (0.1 mL, 1 mmol) was added and the solution was stirred for 1 h, then left to crystallize via slow evaporation of the solvent. Adduct 15 crystallized in the form of colorless, needle-like crystals (22 mg, 0.04 mmol, 78% yield).

NMR (δ, CDCl₃), ³¹P{¹H} 39.42 (s); ¹H 10.81 (virtual doublet, J(³¹P-¹H = 82.2 Hz, 2H, OOHO), 7.81-7.75 (m, 8H, Hₜ), 7.58-7.53 (m, 4H, Hₚ), 7.51-7.46 (m, 8H, Hₜ), 2.66 (d, ³J(³¹P-¹H) = 2.7 Hz, 2H, PCH₂), 1.75 (q, ³J(¹H-¹H) = 7.6 Hz, 8H, CH₂CH₃), 1.00 (t, ³J(¹H-¹H) = 7.6 Hz, 12H, CH₂CH₃); ¹³C{¹H} 132.74 (s, Cp), 130.67 (virtual quintet, J(³¹P-¹³C) = 5.1 Hz, Cₜ), 129.61 (d, J(³¹P-¹³C) = 102.8 Hz, C₁), 129.23 (virtual quintet, J(³¹P-¹³C) = 6.1 Hz, Cₚ), 114.13 (s, CCH₃), 21.81 (s, CH₂CH₃), 21.05 (virtual triplet, J(³¹P-¹³C) = 33.0 Hz, PCH₂), 7.99 (s, CH₃). IR: ν(PO) = 1150 cm⁻¹. mp (decomp.) 82 °C.
CHAPTER IV

CHARACTERIZATION OF THE ADDUCTS $R_3PO\cdot(HOO)_2CR'R'$

Introduction

It is known that acetone and hydrogen peroxide can form triacetone triperoxide (TATP) and other oligomers in the presence of acid, which can be explosive in the solid form.$^{26-27}$ Because both acetone and hydrogen peroxide are involved in the synthesis of the first few adducts, it was important to have analytical tools for determining the identity of the product in solution, prior to crystallization. NMR spectroscopy is especially useful in this respect, and attention is given to some of these characterization data, as they can be used diagnostically during the synthesis, prior to isolation of the product.

In an FT-IR spectrum, the characteristic peroxide band $\nu$(O-H) is easily differentiable from the broad water band $\nu$(O-H). Therefore, IR spectroscopy can be used as a quick analytical check for confirming the absence of water in the material prior to applying the adduct in organic reactions.

Single crystal X-ray crystallography allows for exact structural determination of these adducts, as well as providing information regarding the phosphine oxide to


28
(HOO)$_2$CR'R" ratio. A trend with respect to the elongation of the P=O bond length is also observed with the increase of the number of hydrogen bonds and their strengths.

The characteristic signals in each of these analytical methods are unique to the R$_3$PO•(HOO)$_2$CR'R" adducts. Thus, the properties of the newly discovered adducts are studied via multinuclear NMR spectroscopy, single crystal X-ray crystallography and IR spectroscopy, and the results of these analyses are described in detail.

**Results and Discussion**

All adducts 4-15 have been obtained in the form of large single crystals, and they have been characterized with single crystal X-ray crystallography (Figure 4.1, Figure 4.2).

![Figure 4.1](image_url)  
*Figure 4.1. Large single crystals of (a) 4, (b) 9, (c) 10, and (d) 11.*
Figure 4.2. Single crystal X-ray structures of adducts 4-15.\textsuperscript{28-40}
For monodentate phosphine oxides, X-ray structures of the adducts 4-12 confirm that each P=O group forms two hydrogen bridges to one (HOO)\textsubscript{2}CR'R" moiety. This means that there are two active oxygen atoms per P=O group, and thus the molar ratio of active peroxide is twice as high as for the H\textsubscript{2}O\textsubscript{2} adducts presented previously.\textsuperscript{6,18} This is also true for the bidentate dppe dioxide. Each P=O group forms two hydrogen bonds, with both (HOO)\textsubscript{2}CMe\textsubscript{2} (14)\textsuperscript{38} and (HOO)\textsubscript{2}CET\textsubscript{2} (15).\textsuperscript{39}

Regarding the dppe dioxide, however, only one of the two P=O groups is bonded to the (HOO)\textsubscript{2}CMe\textsubscript{2} moiety (13).\textsuperscript{40} The two P=O groups are only separated by one methylene group, and thus the interaction with a second (HOO)\textsubscript{2}CMe\textsubscript{2} unit may be sterically hindered. The distances between the two P=O oxygen atoms and the terminal oxygen atom of one OOH group are practically identical with 2.816 and 2.817 Å (Figure 4.3). Therefore, one could imagine that the hydrogen atom interacts with both P=O oxygen atoms equally.
Figure 4.3. X-ray structure of 13 with corresponding bond distances. Only the hydrogen-bonded H atoms and ipso carbon atoms of the phenyl rings are shown for clarity.\textsuperscript{40}

However, the P=O bond lengths differ. The P=O bond of the group carrying the adduct is lengthened to 1.495 Å, while the free P=O bond remains in the typical range of undisturbed P=O bond lengths with 1.488 Å, and thus the interaction of the proton with both P=O groups is not likely in the solid state.\textsuperscript{17} As for adducts 4-12 and 14-15, a significant elongation of the P=O bond is observed between neat phosphine oxide and adducts as a result of hydrogen bonding (Table 4.1).
Table 4.1. Comparison of the P=O bond lengths of the pure phosphine oxides Ph$_3$PO, Cy$_3$PO, Ph$_2$P(O)CH$_2$P(O)Ph$_2$ and Ph$_2$P(O)CH$_2$CH$_2$P(O)Ph$_2$ with the adducts 4-15.

<table>
<thead>
<tr>
<th>Species</th>
<th>P=O bond length (Å)</th>
<th>Δ Bond length</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>1.502</td>
<td>+0.023</td>
</tr>
<tr>
<td>5</td>
<td>1.507</td>
<td>+0.017</td>
</tr>
<tr>
<td>6</td>
<td>1.507/1.505</td>
<td>+0.017/0.015</td>
</tr>
<tr>
<td>7</td>
<td>1.510</td>
<td>+0.020</td>
</tr>
<tr>
<td>8</td>
<td>1.508</td>
<td>+0.018</td>
</tr>
<tr>
<td>9</td>
<td>1.513</td>
<td>+0.023</td>
</tr>
<tr>
<td>10</td>
<td>1.512</td>
<td>+0.022</td>
</tr>
<tr>
<td>11</td>
<td>1.505</td>
<td>+0.015</td>
</tr>
<tr>
<td>12</td>
<td>1.510</td>
<td>+0.020</td>
</tr>
<tr>
<td>13</td>
<td>1.488/1.495</td>
<td>average: 1.492</td>
</tr>
<tr>
<td>14</td>
<td>1.505</td>
<td>+0.015</td>
</tr>
<tr>
<td>15</td>
<td>1.501</td>
<td>+0.011</td>
</tr>
<tr>
<td>Ph$_3$PO</td>
<td>1.479$^{41}$</td>
<td>-</td>
</tr>
<tr>
<td>Cy$_3$PO</td>
<td>1.490$^{42}$</td>
<td>-</td>
</tr>
<tr>
<td>Ph$_2$P(O)CH$_2$P(O)Ph$_2$</td>
<td>1.491$^{43}$</td>
<td>-</td>
</tr>
<tr>
<td>Ph$_2$P(O)CH$_2$CH$_2$P(O)Ph$_2$</td>
<td>average: 1.490$^{44}$</td>
<td>-</td>
</tr>
</tbody>
</table>

In determining whether the reaction product is safe to isolate and crystallize, $^{13}$C NMR spectroscopy is especially useful, as the signal of the quaternary carbon nucleus in the (HOO)$_2$CR'R” moieties occurs in a narrow range and unique region (108-120 ppm) of the carbon spectrum and can therefore be used as a diagnostic signal (Figure 4.4,
Table 4.2.\textsuperscript{18} In the case of shock-sensitive DADP (diacetone diperoxide) or TATP, the quaternary peak appears more upfield shifted, at about 105 ppm.\textsuperscript{26}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure4.png}
\caption{\textsuperscript{13}C NMR spectrum of Ph$_3$PO•(HOO)$_2$CMe$_2$ in CDCl$_3$.}
\end{figure}

\begin{table}
\centering
\begin{tabular}{|c|c|c|}
\hline
Adduct & C$_q$ (ppm) & Adduct & C$_q$ (ppm) \\
\hline
4 & 109.28 & 10 & 109.52 \\
5 & 108.91 & 11 & 114.34 \\
6 & 111.56 & 12 & 110.18 \\
7 & 111.26 & 13 & 109.21 \\
8 & 113.76 & 14 & 109.38 \\
9 & 120.92 & 15 & 114.13 \\
\hline
\end{tabular}
\caption{\textsuperscript{13}C NMR Chemical shifts of the quaternary carbon signals of the adducts R$_3$PO• (HOO)$_2$CR’R” in CDCl$_3$.}
\end{table}
The $^{31}$P NMR signals of the adducts $R_3PO\cdot(HOO)\_2CR'R''$ are shifted downfield as compared to the neat phosphine oxides $R_3PO$ (Table 4.3). This downfield shift is caused by the decrease in electron density around the phosphorus nucleus of the P=O group, as the electrons get pulled towards the oxygen atom to support the hydrogen bonds. The change in the $^{31}$P chemical shift is most significant for Cy$_3$PO, with $\Delta\delta$ being larger than 6 ppm in most cases.

**Table 4.3.** $^{31}$P NMR chemical shifts for the adducts $R_3PO\cdot(HOO)\_2CR'R''$ and the corresponding neat $R_3PO$ in CDCl$_3$. The differences are given as $\Delta\delta$ (ppm).

<table>
<thead>
<tr>
<th>Adduct</th>
<th>$\delta(^{31}P)$ (ppm)</th>
<th>$\Delta\delta$ (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>34.74</td>
<td>5.64</td>
</tr>
<tr>
<td>5</td>
<td>55.59</td>
<td>5.68</td>
</tr>
<tr>
<td>6</td>
<td>30.52</td>
<td>1.42</td>
</tr>
<tr>
<td>7</td>
<td>58.77</td>
<td>8.86</td>
</tr>
<tr>
<td>8</td>
<td>58.35</td>
<td>8.44</td>
</tr>
<tr>
<td>9</td>
<td>57.14</td>
<td>7.23</td>
</tr>
<tr>
<td>10</td>
<td>58.01</td>
<td>8.10</td>
</tr>
<tr>
<td>11</td>
<td>56.63</td>
<td>6.72</td>
</tr>
<tr>
<td>12</td>
<td>58.31</td>
<td>8.40</td>
</tr>
<tr>
<td>13</td>
<td>30.33</td>
<td>5.47</td>
</tr>
<tr>
<td>14</td>
<td>38.78</td>
<td>6.10</td>
</tr>
<tr>
<td>15</td>
<td>39.42</td>
<td>6.74</td>
</tr>
<tr>
<td>Ph$_3$PO</td>
<td>29.16</td>
<td>-</td>
</tr>
<tr>
<td>Cy$_3$PO</td>
<td>49.91</td>
<td>-</td>
</tr>
<tr>
<td>Ph$_2$P(O)CH$_2$P(O)Ph$_2$</td>
<td>24.86</td>
<td>-</td>
</tr>
<tr>
<td>Ph$_2$P(O)CH$_2$CH$_2$P(O)Ph$_2$</td>
<td>32.68</td>
<td>-</td>
</tr>
</tbody>
</table>
Many of these adducts could easily be obtained as large single crystals (Figure 4.1). This rare opportunity could be seized to perform single crystal solid-state NMR measurements of 4. The chemical shift anisotropy (CSA) obtained from the span of the $^{31}$P wideline NMR spectrum of polycrystalline 4 amounts to 166 ppm (Figure 4.5).\textsuperscript{18}

\begin{figure}[ht]
\centering
\includegraphics[width=0.5\textwidth]{figure4.5.png}
\caption{\textsuperscript{31}P CP wideline NMR spectrum of polycrystalline 4. The CSA, defined as the span of the signal, $\delta_{11}-\delta_{33}$, amounts to 166.3 ppm. $\delta_{11} = 95.4$, $\delta_{22} = 85.0$, $\delta_{33} = -70.9$, $\delta_{\text{iso}} = 36.5$ ppm.\textsuperscript{18}}
\end{figure}

Figure 4.6 displays the $^{31}$P CP spectra of a single crystal of 4 recorded with different random orientations. The random orientations were obtained by ejecting and reinserting the rotors into the probehead. Two resonances, corresponding to two magnetically inequivalent $^{31}$P nuclei in the unit cell, are obtained in most cases. The two resonances can overlap by accident, but this event is statistically less favored. The chemical shift changes of the two signals with the orientation of the crystal in the external magnetic field are different, as expected and described for other cases.\textsuperscript{17,45}
Figure 4.6. $^{31}$P CP NMR spectra of a large single crystal of 4 at different random orientations with respect to the external magnetic field.

For adduct 5, all protons of the adducts are accounted for in the $^1$H NMR spectra, and all signals have been successfully assigned with the help of 2-dimensional $^{13}$C,$^1$H COSY NMR spectroscopy (Figure 4.7, Figure A.18). While the peroxide protons appear downfield shifted to about 11.5 ppm (Table 4.4), the absence of any obvious water signal corroborates the assumption that the sample is water-free (Figure 4.7).
Figure 4.7. $^1$H NMR spectrum of 5 in CDCl$_3$, with complete signal assignment. The peroxide proton peak is visible at 11.45 ppm.

Table 4.4. $^1$H Chemical shifts of the peroxide protons of the adducts 4-15.

<table>
<thead>
<tr>
<th>Adduct</th>
<th>$\delta(^1$H) OOH (ppm)</th>
<th>Adduct</th>
<th>$\delta(^1$H) OOH (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>11.15</td>
<td>10</td>
<td>10.66</td>
</tr>
<tr>
<td>5</td>
<td>11.45</td>
<td>11</td>
<td>11.57</td>
</tr>
<tr>
<td>6</td>
<td>11.38</td>
<td>12</td>
<td>11.89</td>
</tr>
<tr>
<td>7</td>
<td>10.90</td>
<td>13</td>
<td>10.73</td>
</tr>
<tr>
<td>8</td>
<td>10.82</td>
<td>14</td>
<td>11.28</td>
</tr>
<tr>
<td>9</td>
<td>11.61</td>
<td>15</td>
<td>10.81</td>
</tr>
</tbody>
</table>
Additionally, the IR spectra of 4-15 show no H$_2$O hydroxyl stretching band at 3400 cm$^{-1}$ (Figure B.5-Figure B.18), and thus it can be confirmed that no water is present in these adducts. Instead, all adducts display a broad band around 3200 cm$^{-1}$, corresponding to the hydroperoxy stretching band $\nu$(O-H) (Table 4.5).

**Table 4.5.** Stretching bands $\nu$(O-H), $\nu$(C-O), $\nu$(O-O) and comparison of the $\nu$(P=O) IR values of the pure phosphine oxides with those of the adducts 4-15, given as $\Delta \nu$(P=O).

<table>
<thead>
<tr>
<th>Species</th>
<th>$\nu$(O-H) (cm$^{-1}$)</th>
<th>$\nu$(P=O) (cm$^{-1}$)</th>
<th>$\nu$(C-O) (cm$^{-1}$)</th>
<th>$\nu$(O-O) (cm$^{-1}$)</th>
<th>$\Delta \nu$(P=O) (cm$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>3256</td>
<td>1152</td>
<td>1118</td>
<td>885</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>3192</td>
<td>1125</td>
<td>1099</td>
<td>891, 856</td>
<td>32</td>
</tr>
<tr>
<td>6</td>
<td>3250</td>
<td>1142</td>
<td>1118</td>
<td>889, 851</td>
<td>40</td>
</tr>
<tr>
<td>7</td>
<td>3196</td>
<td>1124</td>
<td>1101</td>
<td>893, 854</td>
<td>33</td>
</tr>
<tr>
<td>8</td>
<td>3194</td>
<td>1126</td>
<td>1103</td>
<td>891, 858</td>
<td>31</td>
</tr>
<tr>
<td>9</td>
<td>3167</td>
<td>1123</td>
<td>1101</td>
<td>891, 860</td>
<td>34</td>
</tr>
<tr>
<td>10</td>
<td>3196</td>
<td>1123</td>
<td>1103</td>
<td>893, 860</td>
<td>34</td>
</tr>
<tr>
<td>11</td>
<td>3186</td>
<td>1123</td>
<td>1101</td>
<td>891, 856</td>
<td>34</td>
</tr>
<tr>
<td>12</td>
<td>3176</td>
<td>1123</td>
<td>1101</td>
<td>889, 851</td>
<td>34</td>
</tr>
<tr>
<td>13</td>
<td>3291</td>
<td>1163</td>
<td>1099</td>
<td>871</td>
<td>25</td>
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<tr>
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<td>3242</td>
<td>1148</td>
<td>1097</td>
<td>872</td>
<td>24</td>
</tr>
<tr>
<td>15</td>
<td>3275</td>
<td>1150</td>
<td>1097</td>
<td>858</td>
<td>22</td>
</tr>
<tr>
<td>Ph$_3$PO</td>
<td>-</td>
<td>1182</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cy$_3$PO</td>
<td>-</td>
<td>1157$^1$</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ph$_2$P(O)CH$_2$P(O)Ph$_2$</td>
<td>-</td>
<td>1188</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ph$_2$P(O)CH$_2$CH$_2$P(O)Ph$_2$</td>
<td>-</td>
<td>1172</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Representative FT-IR spectra of 6 and 7 are shown in Figure 4.8. In general, the P=O band is observed around 1150 cm\(^{-1}\) for aryl phosphine oxide adducts and 1120 cm\(^{-1}\) for Cy\(_3\)PO adducts (Table 4.5).

![IR spectra](image)

**Figure 4.8.** Representative IR spectra of adduct 4 (top) and 5 (bottom).

The ν(P=O) bands of the adducts 4-15 are lower in frequency as compared to the neat R\(_3\)PO analogs, due to the P=O bond strength being weakened by the hydrogen bonds. The change in wavenumber is similar for most of the R\(_3\)PO adducts incorporating one PO group, with a shift of 30-34 cm\(^{-1}\). The red shift is less significant for the adducts.
13-15 with two PO bonds each, which agrees with the smaller change in P=O bond lengths of the adducts 13-15 (Table 4.1). The ν(P=O) stretching bands for Cy₃PO adducts often overlap with strong ν(C-O) bands that occur around 1101 cm⁻¹. Finally, the ν(O-O) stretching frequency can be observed as sharp signals around 890 and 860 cm⁻¹, as expected (Table 4.5), the only problem being potential overlap with other fingerprint IR absorptions in this region.⁴⁶-⁴⁷

Conclusion

¹³C NMR spectroscopy is an excellent tool for confirming the synthesis of a new adduct prior to its isolation. The diagnostic signal at 108-120 ppm in CDCl₃ is unique to a quaternary carbon bound to two peroxide functionalities, and yet is different enough from the quaternary carbon of the shock-sensitive oligomers DADP or TATP. At this point, no specific trend is observed between the changing R' and R" groups of the moiety (HOO)₂CR'R" and the shift in the quaternary signal.

Single crystal X-ray crystallography provides indisputable proof that the adducts are systematic molecule-type assemblies with an exact ratio between the phosphine oxide groups and the (HOO)₂CR'R" moieties. Significant P=O bond elongation is observed in connection with the formation of multiple hydrogen bonds.

The weakened P=O bond strength is also observed in the IR spectra, as the ν(P=O) bands undergo red shifts of around 30 cm⁻¹. Along with the ¹H NMR peaks at
10-11 ppm, the peroxide $\nu$(O-H) stretching bands around 3200 cm$^{-1}$ in the IR spectra confirm the presence of peroxide protons in the adduct molecules.
CHAPTER V

SOLUBILITY STUDY

Introduction

In Chapter II, it was mentioned that one of the most important advantages of the hydrogen peroxide adducts \([R_3PO\cdot H_2O_2]_2\) with respect to their application as oxidizing agents is that they are very soluble in organic solvents, rendering biphasic reaction mixtures obsolete. The same is true for the adducts \(R_3PO\cdot (HOO)_2CR'R''\) (\(R, R', R'' =\) alkyl, aryl), and therefore the solubilities of selected adducts in common organic solvents were quantified.

Results and Discussion

The solubilities of the adducts in organic solvents are measured by dissolving 20 mg of each adduct in the determined minimum amount of solvent, and measuring the mass of the solvent upon complete solvation. The results of the solubility tests for the representative adducts 4-11 are summarized in Figure 5.1. The solubilities are remarkably high in chloroform and dichloromethane, but even in aromatic solvents such as toluene and benzene, the solubilities are substantial.

The total concentration of active peroxide in a sample solution can be increased even more by dissolving two or more adducts with different phosphine oxides in the same solution. For instance, 20 mg of 6 and 20 mg of 7 were both dissolved together in a minimum amount of CH$_2$Cl$_2$ (84 mg, 0.063 mL). Therefore, in this mixture, 6 and 7 each display a solubility of 317 mg/mL, for a total of 3.0 M concentration of active peroxide in CH$_2$Cl$_2$. When compared to the individual solubilities of 636 mg/mL of 6 and 374 mg/mL of 7 in CH$_2$Cl$_2$ (Figure 5.1), the solubilities of the mixture of 6 and 7 appear reduced. However, the 3.0 M concentration of active peroxide is comparable to that of 7 (3.18 M in CH$_2$Cl$_2$), and significantly increased compared to 6 (1.79 M in CH$_2$Cl$_2$). Therefore, the mixture contains overall a much higher concentration of peroxide than each single component by itself.
In an analogous experiment, 19 mg of 7 were dissolved in a minimum amount of CH₂Cl₂ (27 mg, 0.05 mL). To this completely saturated solution, a powder sample of 6 was added in very small portions and the mixture was swirled to facilitate dissolution. The process was continued until the powder did not dissolve anymore, at which point a total of 17 mg of 6 had been added. In this mixture, the solubility of 6 was 333 mg/mL and 7 was 374 mg/mL, for a combined concentration of 3.4 M active peroxide in CH₂Cl₂. This is in the same order of magnitude as the 35 wt% aqueous H₂O₂, with a 10 M concentration of active peroxide.

As evidenced from these two tests, the saturation with one adduct does not completely prohibit the dissolution of another adduct in the same sample, although the solubility of the second adduct may be decreased as compared with its solubility in pristine solvent.

Conclusion

Similar to the H₂O₂ adducts of phosphine oxides, the adducts of the type R₃PO•(HOО)₂CR'R" (R, R', R" = alkyl, aryl) display high solubility in common organic solvents. The concentration of active peroxide can be increased even more by combining adducts of multiple different phosphine oxides. When applied to organic reactions, these adducts are very appealing, as the reactions can be performed in one phase, and the volume of solvent can be decreased to reduce costs.
CHAPTER VI

SHELF LIFE AND DECOMPOSITION STUDY*

Introduction

Aqueous H$_2$O$_2$ gradually decomposes to form oxygen gas and H$_2$O. Therefore, aqueous H$_2$O$_2$ is often administered in excess because the oxidant decomposes at unpredictable rates, and thus the concentration at any given time is unknown. For applications requiring exact stoichiometry, the solution has to be titrated prior to use.\(^7\)

In the case of the adducts $R_3$PO•(HOO)$_2$CR'R" (R, R', R" = alkyl, aryl) the hydrogen bonds between the peroxide and the phosphine oxide groups do not break easily, and therefore the phosphine oxides act as stable, solid carriers of the peroxide. However, in order to ensure accurate stoichiometry at the time of use, the study of stability and shelf life of the adducts is essential. Decomposition of these adducts occurs via the release of oxygen gas from the peroxide functionality.\(^8c,48\) In addition to shelf life, the safety of these adducts during decomposition was of interest, and thus the adducts were exposed to mechanical and thermal stress on a small scale.

In this chapter, the results of the decomposition tests are reported, and a quantitative NMR (QNMR) method is described in which $^{31}$P NMR spectroscopy is utilized to determine the % decomposition of active peroxide in the adducts over time.\(^49\)


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In order to determine the number of active peroxide groups remaining in a sample of \( R_3PO\cdot(HOO)_2CR'R' \), a known mass of the adduct was used as an oxidant for PPh\(_3\), and the degree of its oxidation was observed through NMR spectroscopy. Oxidation of PPh\(_3\) was chosen for strategic reasons: PPh\(_3\) is solid and air-stable even in most solvents, and therefore it is easy to handle and any oxidation is not due to admission of air, but only to the oxidant. When dissolved in a solvent together with the above adduct, oxidation of PPh\(_3\) occurs immediately, with OPPh\(_3\) being the sole product. PPh\(_3\) and OPPh\(_3\) display two far apart, distinct peaks in the \( ^{31}P \) NMR spectrum which are easy to identify and integrate.\(^{49a-c}\)

A series of \( ^{31}P \) NMR spectra is collected following the addition of adduct to a weighed excess of PPh\(_3\). The samples are carefully prepared so that the concentration of each analyte exceeds 20 mM.\(^{50}\) The proton decoupler is turned off, because the Nuclear Overhauser Effect (NOE) can alter the peak intensities.\(^{49d}\) Three peaks occur in the spectrum, belonging to the carrier phosphine oxide of the spent adduct, OPPh\(_3\) and the remaining PPh\(_3\) (Figure 6.1). A capillary insert with neat ClPPh\(_2\) as the chemical shift standard is centered in the NMR tube (Figure 6.2).\(^{6,50-51}\) ClPPh\(_2\) is an ideal standard, as its peak occurs at 81.92 ppm, clear of the region of interest.\(^{6,49a,52}\)
Figure 6.1. $^{31}$P NMR spectrum obtained following the partial oxidation of an excess of PPh$_3$ with 5.

Figure 6.2. Capillary insert with ClPPh$_2$ centered inside a 5 mm NMR tube.

By integrating the OPPh$_3$ and PPh$_3$ peaks, one can calculate what percentage of the original PPh$_3$ has been oxidized. The number of moles of oxidized PPh$_3$ corresponds to the number of moles of active peroxide groups that remain in the applied adduct after long term storage. Comparison of this number with the mole of peroxide that the
measured amount of pristine adduct contains, provides the degree of decomposition of the adduct.

For an accurate determination of the integrals it is important that the signals are defined by a sufficient number of data points. A representative $^{31}$P NMR point spectrum of a sample after PPh$_3$ oxidation (Figure 6.3) shows that the signals are defined by a sufficient number of data points, ensuring the quality of the integration. Since the intensity of a signal, and therewith the integral, when comparing the intensities of different signals, is calculated by adding the discrete height values of the data points, it is important that each peak incorporates a sufficient number of data points.$^{49d}$ The digital resolution used typically for determining the integrals in this project is 0.56 Hz per point (65536 data points for a sweep width of 36764.71 Hz). Furthermore, it is important to allow for enough area around the signals when choosing the boundaries for their integration. Figure 6.3 shows representative signals with a sufficient number of data points and ample space around them. The integration extends 100 Hz in each direction from the center of PPh$_3$ and OPPh$_3$ peaks. It has been previously reported that integration should be performed over an area of 20-30 times the linewidth of the signal of interest for accurate analysis.$^{49a,49d}$
Figure 6.3. Point display of the $^{31}$P NMR signals obtained after the partial oxidation of PPh$_3$ with 5.

This quantitative NMR method was furthermore tested against multiple criteria to validate its consistency. Specifically, it was tested whether the following factors influenced the integration of the signals: (1) the depth of insertion of the sample into the probehead, (2) the spectral range or sweep width, and (3) the applied relaxation delay. For checking factor (1), the sample is placed in three different positions within the probehead so that the bottom of the NMR tube would be 1.5 cm (A), 1.0 cm (B), and 0.5 cm (C) below the region with the optimal RF (radio frequency) coil transmission and reception. Figure 6.4 indicates the bottom of the NMR tube in the sample gauge with a red line, and the area that the coil would stretch over in the probehead with a blue rectangle. The same sample was placed at the different positions into the probehead and $^{31}$P NMR spectra were measured with varying spectral windows and relaxation delays ranging from 1 to 40 seconds.
Collecting NMR spectra of the sample at different positions within the probehead tests for equal RF homogeneity for the solubilized adduct, the initial PPh₃ and the product OPPh₃. Theoretically, if all components are homogeneously dispersed throughout the CDCl₃ solution, changing the extent of the sample tube that is exposed to the region with optimal RF homogeneity should not change the ratio between PPh₃ and OPPh₃. However, the response of the various substances to the RF excitation could be different, thus leading to a deviating integral.

When the spectral window is changed by moving it, the maximal intensity of the excitation pulse, which is in the center of the spectrum, is also moved. The closer the maximal intensity of the excitation pulse is to a signal of the sample, the more intense it will be in the spectrum (Figure 6.5).⁴⁹ᵃ
Figure 6.5. \(^{31}\text{P}\) NMR spectra obtained following the oxidation of an excess of PPh\(_3\) with 5. The change in the integrals with the change of the center of the excitation pulse is demonstrated.

The different \(^{31}\text{P}\) nuclei in a sample require different relaxation times after a RF pulse is applied. Optimally, a subsequent pulse would not be applied until each nucleus is fully relaxed again. In case the next pulse is applied before the magnetization of one sort of nuclei is returned to the Boltzmann distribution equilibrium, it would reach eventually a steady state situation where the intensity of the signal does not show to its full extent. For maximum integration accuracy, all magnetizations of all species need to entirely return to equilibrium. Therefore, in order to obtain correct integral ratios between the PPh\(_3\) and OPPh\(_3\) peaks, it is paramount that the relaxation delay chosen is longer than the relaxation time that the involved nuclei require.\(^{49a,49d,52}\)
Results and Discussion

The decomposition temperatures of neat \((\text{HOO})_2\text{CR'R''}\) adducts range from 70 to 150 °C (Table C.1). Prior to recording the actual melting points, the adducts have been tested regarding their thermal stability by exposing them to gradually increasing temperatures in an oil bath to expedite decomposition. It should be noted that no explosive TATP or other explosive oligomers are formed during this process. The representative adducts 4 and 5 have also been tested by applying mechanical stress. No sudden release of oxygen occurred during forceful grinding or hammering of the pure powders. This may be due to the low weight% of active oxygen in the molecules, which is 7.9% for \(\text{Cy}_3\text{PO}•(\text{HOO})_2\text{CMe}_2\) and 8.3% for \(\text{Ph}_3\text{PO}•(\text{HOO})_2\text{CMe}_2\). The \(^{31}\text{P}\) NMR spectra before and after the grinding only show the starting materials. Thermogravimetric analyses (TGA) of 4 and 5 indicated that the \((\text{HOO})_2\text{CMe}_2\) moiety, as a whole or in fragments, is lost upon heating (80-110 °C), and this is followed by the loss of \(\text{H}_2\text{O}_2\) molecules at 150 °C, leaving the phosphine oxides behind (Figure 6.6).
Figure 6.6. Thermogravimetric analysis (TGA) of 5.

Even in solution, the R$_3$PO•(HOO)$_2$CR'R" adducts are remarkably stable in the absence of a reducing agent. For example, heating a benzene solution of 4 to 90 °C and monitoring the solution with $^{13}$C NMR showed that three days were needed to decompose about 80% of 4. The main products remaining in solution were Ph$_3$PO•H$_2$O$^{6,17}$ and acetone, besides traces of isopropanol, formic acid, and acetic acid (Figure A.79).

Next, a QNMR method was developed to observe the shelf life of the representative adducts. The oxidation yields from the integrals of PPh$_3$ and OPPh$_3$ under varying factors, as described above, are summarized in Table 6.1. Comparing the results of A, B and C, the position of the NMR tube within the probe does not exhibit a
significant influence on the integral ratio. This was expected, since both the phosphine and the phosphine oxide are dispersed homogeneously in the NMR sample. On the other hand, changing the spectral ranges and therefore the point of irradiation with maximal intensity, shows a definite trend. As the excitation pulse frequency with maximal intensity moves closer, the OPPh₃ peak intensity grows for all constellations A, B and C. Finally, the relaxation delay has to be longer than 35 seconds, in order for the phosphine oxide to relax completely.

Table 6.1. Comparison of experimental and theoretical yields of OPPh₃, expressed as %, following the oxidation of PPh₃ with freshly synthesized 5. Experimental yields were calculated from the integral ratio of OPPh₃ and PPh₃ peaks in the $^{31}$P NMR spectra.

![Table 6.1](image)
Ph₃P oxidation was performed with representative adducts after they have been stored in polycrystalline form under different conditions. The adducts were exposed to the atmosphere at room temperature with and without light, and at -4 °C and -20 °C in the dark. At regular intervals aliquots were removed from the stored samples and the described Ph₃P oxidation test was performed. ³¹P NMR spectra were recorded with a spectral range from 100 to -100 ppm and a relaxation delay of 35 seconds. In this way the oxidative power of the adducts was monitored for up to 100 days (Figure 6.7, Figure C.1-Figure C.3).

**Figure 6.7.** Oxidative power of 5 after being stored at the indicated conditions. 100% equals to two moles of active oxygen per mole of 5.
At -20 and 4 °C the adducts retain most of their oxidative power over months. Exposure to light did not influence the decomposition, while the temperature played a dominant role. Furthermore, the exposed surface area of the materials made a difference. For example, large crystals (3×3×1 mm\(^3\)) of 4-7, 9 and 10 retained 99% oxidative power after 100 days of being exposed to the ambient atmosphere and light at room temperature. Under the same conditions, the polycrystalline materials retain 60 to 70% of their oxidative power in the course of months. It is possible that the peroxides on the surface of the adduct are decomposing while the shielded molecules in the interior of the crystals remain unchanged.

Decomposition may also occur in a stepwise manner, in which only one of the peroxide groups loses an oxygen atom, to initially form \(R_3\text{PO} \cdot \text{(HOO)} \cdot \text{(HO)CR'CR''}\). Indeed, a single crystal X-ray structure obtained from large crystals of \(\text{Cy}_3\text{PO} \cdot \text{(HOO)} \cdot \text{(HO)C(CH}_2)_5\) (16) (Figure 6.8)\(^{53}\) demonstrates that such a molecule is stable enough to assemble systematically and it might slow down decomposition.

![Figure 6.8. Large crystals (left) and single crystal X-ray structure (right) of 16.\(^{53}\)](image-url)
Since this hydroperoxy(hydroxy)alkane adduct (16) is stable and melts without decomposition at 33 °C, it was possible to perform full characterization. In the IR spectrum two distinct stretching bands are observed, one each for the hydroxy O-H and the hydroperoxy O-H group (Figure B.19). In comparison to the di(hydroperoxy)-cyclohexane adduct 10, the P=O bond is stronger, as evidenced from the frequency of P=O stretching band ν(P=O), which lies in between the values of neat Cy$_3$PO and adduct 10 (Table 6.2). The stronger P=O bond of 16 as compared to 10 can also be assumed due to the shorter bond length of the P=O group in the X-ray structure.

Table 6.2. Comparison of IR and X-ray crystallographic data of Cy$_3$PO, 16 and 10.

<table>
<thead>
<tr>
<th>Species</th>
<th>ν(O-H) (cm$^{-1}$)</th>
<th>ν(P=O) (cm$^{-1}$)</th>
<th>Δν(P=O) (cm$^{-1}$)</th>
<th>P=O (Å)</th>
<th>Δ Bond length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cy$_3$PO</td>
<td>-</td>
<td>1157</td>
<td>-</td>
<td>1.490$^{42}$</td>
<td>-</td>
</tr>
<tr>
<td>16</td>
<td>3323/3246</td>
<td>1144</td>
<td>13</td>
<td>1.509</td>
<td>+0.019</td>
</tr>
<tr>
<td>10</td>
<td>3196</td>
<td>1123</td>
<td>24</td>
<td>1.512</td>
<td>+0.022</td>
</tr>
</tbody>
</table>

The trend is continued in $^{31}$P NMR spectroscopy. Less electron density is removed from the P=O bond, and thus the phosphorus nucleus is more shielded than 10, and the signal for 16 appears more upfield shifted and closer to Cy$_3$PO, with a Δδ value of approximately half of that of 10. The quaternary carbon on the (HOO)(HO)C(CH$_2$)$_3$ moiety is also observed more upfield shifted compared to 10 (Table 6.3). Nonetheless, this monoperoxy adduct 16 is still capable of stoichiometrically oxidizing Ph$_3$P to Ph$_3$PO.
Table 6.3. Comparison of $^{13}$C and $^{31}$P NMR chemical shifts of Cy$_3$PO, 16 and 10.

<table>
<thead>
<tr>
<th>Adduct</th>
<th>$\delta$($^{13}$C) C$_{q}$ (ppm)</th>
<th>$\delta$ ($^{31}$P) P=O (ppm)</th>
<th>$\delta$ ($^{31}$P) neat R$_3$PO (ppm)</th>
<th>$\Delta$δ (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>102.65</td>
<td>53.34</td>
<td>49.91</td>
<td>3.43</td>
</tr>
<tr>
<td>10</td>
<td>109.52</td>
<td>58.01</td>
<td></td>
<td>8.10</td>
</tr>
</tbody>
</table>

Finally, the solubility of 16 was compared with those of the cyclic adducts 9-11 (Figure 6.9). Adduct 16 shows slightly higher solubility than 9-11 in most solvents with the exception of chlorinated solvents, benzene, and THF.
Conclusion

The decomposition of the adducts of the type R₃PO•(HOO)₂CR'R" was studied from multiple perspectives. The adducts were first exposed to thermal and mechanical stress, during which sudden release of energy was never observed, once again confirming the safety of these adducts.

Next, the decomposition rate of these adducts was studied under various storage conditions to test for their shelf life. In order to quantify the rate of decomposition, a quantitative NMR method was developed, involving the use of precise ³¹P NMR peak integration. Using this method, it was shown that the adducts decompose over time to about 70% when stored at room temperature in powder form. However, when the powder is stored at decreased temperatures of -4 °C, there is essentially no decomposition even after months. Moreover, when the adducts are stored as large single crystals, the decomposition is insignificant even at room temperature.

Since the adducts decompose much faster as powders than in the form of large crystals, it is hypothesized that the surface area plays a role in the decomposition of the peroxide groups. This decomposition can occur simultaneously at both peroxide positions, or it could take place in a stepwise manner, to form R₃PO•(HOO)(HO)CR'R" as an intermediate. The latter assumption is supported by successful characterization of Cy₃PO•(HO)(HO)C(CH₂)₅ via single crystal X-ray crystallography, NMR and IR spectroscopy.
Experimental

Cy$_3$PO•(HOO)(HO)C(CH$_2$)$_5$ (16)

300 mg of [Cy$_3$PO•H$_2$O$_2$]$_2$ (0.45 mmol) was dissolved in 10 mL of cyclohexanone (97 mmol) in a 20 mL vial. 1.5 mL aqueous H$_2$O$_2$ (15 mmol) was added to the vial, and the solution was stirred vigorously overnight, then left to crystallize via slow evaporation. Colorless rhombic crystals appeared after three days (327 mg, 0.76 mmol, 84% yield).

NMR (δ, CDCl$_3$), $^{31}$P{$^1$H} 53.34 (s); $^1$H 10.37 (s, 1H, OOHO), 9.51 (s, 1H, OH), 1.95-1.78 (m, 17H, PCH$_{ax}$CH$_{eq}$CH$_{eq}$, OCCCH) 1.74-1.68 (m, 3H, PCH(CH$_2$)$_2$CH$_{eq}$), 1.67-1.60 (m, 2H, CCH), 1.58-1.52 (m, 4H, CCH$_2$CH$_2$), 1.47-1.34 (m, 8H, PCHCH$_{ax}$, CCH$_2$CH$_2$CH$_2$), 1.31-1.19 (m, 9H, PCHCH$_2$CH$_{ax}$CH$_{ax}$); $^{13}$C{$^1$H} 102.65 (s, COO), 35.01 (d, $^1$J($^{31}$P-$^{13}$C) = 60.6 Hz, PC), 34.15 (s, CCH$_2$), 26.80 (d, $^3$J($^{31}$P-$^{13}$C) = 11.8 Hz, PCHCH$_2$CH$_2$), 26.11 (d, $^2$J($^{31}$P-$^{13}$C) = 3.4 Hz, PCHCH$_2$), 26.00 (d, $^4$J($^{31}$P-$^{13}$C) = 1.7 Hz, PCH(CH$_2$)$_2$CH$_2$), 25.40 (s, CCH$_2$CH$_2$CH$_2$), 22.93 (s, CCH$_2$CH$_2$). IR: ν(PO) = 1143 cm$^{-1}$. 
CHAPTER VII

APPLICATIONS IN OXIDATION REACTIONS*

Introduction

The ultimate objective of this project is to apply the adducts of the type R_3PO•(HOO)_2CR'R'' (R, R', R'' = alkyl, aryl) as stoichiometric and soluble oxidizing agents in organic reactions. In the previous chapter, it was demonstrated that these adducts are capable of oxidizing PPh_3 to OPPh_3 selectively and stoichiometrically. The well-defined and reproducible composition of the adducts allows for stoichiometric application in reactions that are sensitive to overoxidation. This property of the adducts also makes them an attractive option in reactions such as sulfoxidations,\(^{4b,4c,54}\) where the sulfoxide (R_2SO) is preferred to the sulfone (R_2SO_2).

One particular example where selective oxidation to the sulfoxide is desired is in the neutralization of the chemical warfare agent mustard gas (bis(2-chloroethyl)sulfide, codename HD). Upon contact with an oxidant, the sulfide in HD is initially oxidized to the harmless HD-sulfoxide. However, overoxidation to the vesicant HD-sulfone occurs over time in the presence of excess oxidizing agent (Scheme 7.1).\(^{55}\)

Scheme 7.1. Oxidation of HD to HD-sulfoxide and HD-sulfone in the presence of excess oxidant.

Because the adducts $R_3PO\cdot(HOO)_2CR'R''$ (R, R', R'' = alkyl, aryl) are stored in solid form, it is relatively easy to use them in reactions that require air- and moisture-free conditions. Moreover, due to their high solubility in organic solvents, the oxidation reaction can occur in one phase, eliminating the need for phase transfer agents. The oxidation of PPh$_3$ is relatively easy, as PPh$_3$ is not air-sensitive in the solid state and in most solvents, and OPPh$_3$ is the sole product with no occurrence of overoxidation. In the case of alkyl- and other phosphines which are sensitive to overoxidation and hydrolysis, it is interesting to probe whether oxidation with the adducts of the type $R_3PO\cdot(HOO)_2CR'R''$ can proceed in a stoichiometric manner, and whether the reaction conditions would remain sufficiently anhydrous to prevent hydrolysis.

For instance, 1,1,2,2-tetraphenyldiphosphine dioxide, Ph$_2$P(O)-P(O)Ph$_2$, is a species of interest because of its structural similarity to hypophosphoric acid, (RO)$_2$P(O)-P(O)(OR)$_2$, which exhibits anti-tumor activity. The oxidation of 1,1,2,2-tetraphenyldiphosphine, Ph$_2$P-PPh$_2$, to the dioxide is traditionally performed in dry solvents with oxygen gas, as the P-P bond is sensitive to hydrolysis. In the presence of moisture, the P-P bond is cleaved to produced a mixture of oxidized species, including Ph$_2$P(O)H and Ph$_2$P(O)OH. Therefore, this method of oxidation is inconvenient, also
because it involves the use of an oxygen gas cylinder. When exposed to dry air at merely atmospheric pressure, the oxidation is extremely slow and incomplete, with a mixture of diphosphine dioxide and diphosphine monoxide in the product mixture (Scheme 7.2, Figure A.92).\textsuperscript{56a}

![Scheme 7.2. Oxidation of 1,1,2,2-tetraphenyldiphosphine in dry air.](image)

More recent approaches to the 1,1,2,2,-tetraphenyldiphosphine dioxide involve 1) the reaction between an electrophilic $R_2P(O)X$ ($X = \text{Cl, Br}$) and deprotonated $R_2POH$, 2) an alkali metal reduction of $R_2P(O)X$, or 3) the reaction of $R_2PCI$ with $R_2P(O)H$ and oxygen gas in anhydrous conditions.\textsuperscript{56a} However, all of these methods result in a mixture of products, including $R_2P(O)-P(O)R_2$ and $R_2P(O)-O-PR_2$. On the other hand, $R_3PO\cdot(HOO)_2CR'R''$ adducts are dry, solid materials that can simply be weighed in and administered in a stoichiometric manner. If successful, this provides a new and efficient way of selectively oxidizing 1,1,2,2,-tetraphenyldiphosphine to the diphosphine dioxide.

Additionally, the potency of the adducts as oxidants in epoxidation reactions is studied. On one hand, the anhydrous properties of the adducts make them desirable, as the absence of water molecules should prevent the hydrolysis of the generated epoxide. However, the adducts are milder oxidants than aqueous $H_2O_2$, and thus may not be strong enough to activate all types of olefins.\textsuperscript{8b,33}
Finally, the reactivity of the di(hydroperoxy)cycloalkane adducts 9-11 under Baeyer-Villiger reaction conditions is explored.\textsuperscript{2,58} Baeyer-Villiger oxidations are used to transform a cyclic ketone to its corresponding lactone. In the case of the adducts 9-11, a cyclic ketone is already used to generate the adduct molecule, which incorporates two moles of peroxides as potent oxidants. In this chapter, the transformation of the moiety \((\text{HOO})_2\text{C(CH}_2\text{)}_n\) \((n = 4-6)\) in the adducts to the corresponding lactone, with and without offering additional ketone, is studied in detail.

\textbf{Results and Discussion}

\textit{Sulfoxidation}

To study the application of the adducts \(\text{R}_3\text{PO}^\bullet(\text{HOO})_2\text{CR}'\text{R}''\) as oxidants for reactands that are air-sensitive and prone to overoxidation, tetrahydrothiophene (THT) oxidation was selected.\textsuperscript{4b,4c,54} When 3 or 4 was combined with THT in a 1 : 2 molar ratio in benzene, it was selectively and quantitatively oxidized to tetramethylene sulfoxide at ambient temperatures within two hours (Scheme 7.3)

\begin{center}
\begin{tikzpicture}
\node (A) at (0,0) {\text{R}_3\text{PO}^\bullet(\text{HOO})_2\text{CR}'\text{R}'' + \text{C}_6\text{H}_6 \rightarrow \text{O} + \text{S}};
\node (B) at (-1.5,0) {1 : 2};
\node (C) at (1.5,0) {100\%};
\node (D) at (3,0) {0\%};
\end{tikzpicture}
\end{center}

\textbf{Scheme 7.3.} Stoichiometric oxidation of THT with \(\text{R}_3\text{PO}^\bullet(\text{HOO})_2\text{CR}'\text{R}''\) (4-8, 12).
Generally, with adducts incorporating sterically more shielding substituents, the reaction times were increased (Table 7.1). However, the sulfoxide was still produced selectively, with the only other reaction products being the corresponding phosphine oxide carriers and the regenerated ketones. The resulting water molecule remains hydrogen bonded to the phosphine oxide group.¹⁷ This fast and clean reaction in one organic phase compares favorably to earlier studies which required biphasic mixtures and added catalysts.⁴ｂ,⁴ｃ,⁵⁴

Table 7.1. Selective and complete oxidation of THT to tetramethylene sulfoxide.

<table>
<thead>
<tr>
<th>Adduct</th>
<th>23 °C</th>
<th>50 °C</th>
<th>60 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>2</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>6</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

While the challenge regarding the oxidation of dialkyl sulfides lies in the selective oxidation to sulfoxides, oxidations of diaryl sulfides and thiophenes are intrinsically difficult due to low reactivity in the absence of a catalyst.⁴ａ-ｃ,⁴ｅ,⁵４,⁵９ Following the successful selective oxidation of THT to tetramethylene sulfoxide, oxidation of diphenylsulfide was attempted using the adducts 4, 5, 7 and 8 (Scheme 7.4).
Upon addition of the adduct and SPh₂ in a 1 : 2 ratio in benzene at room temperature, no oxidation occurred even after a prolonged time period of 100 hours. When the reaction temperature was increased to 70 °C, conversion to the corresponding sulfoxide took place, with some overoxidation to the sulfone in two cases (Table 7.2).

**Table 7.2.** Yields (%) of oxidized products Ph₂SO and Ph₂SO₂ after reacting Ph₂S with selected adducts R₃PO•(HOO)₂CR'R".

<table>
<thead>
<tr>
<th>Adduct</th>
<th>Ph₂SO</th>
<th>Ph₂SO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>60</td>
<td>11</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>8</td>
</tr>
<tr>
<td>7</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>30</td>
<td>0</td>
</tr>
</tbody>
</table>

Adducts 4 and 5 exhibited the highest activities, oxidizing Ph₂S in moderately high yields to Ph₂SO without any catalyst, albeit extended reaction times of 100 h were required and some overoxidation to Ph₂SO₂ occurred. To increase the sulfoxide yield and minimize overoxidation to the sulfone, the oxidation reaction was repeated with adduct 7 at room temperature, in the presence of catalytic amounts of silica and Br₂, which have...
been shown to be useful by another group previously.\textsuperscript{60} With the addition of silica and Br\textsubscript{2}, the sulfoxide yield remained 43\% in acetonitrile and 47\% in benzene, both after 100 h of stirring (Table 7.3 entries 6 and 7). When silica was added without Br\textsubscript{2}, diphenylsulfoxide and diphenylsulfone are produced in almost equal amounts (Entries 3 and 4). When Br\textsubscript{2} is added without silica, the sulfoxide is obtained as the only product; however, the yield is decreased (Entry 5). Increasing the reaction temperature to 50 °C resulted in a high conversion of 86\% after only one day of stirring. However, the major product was diphenylsulfone (53\%), and the yield of diphenylsulfoxide was merely 33\% (Entry 8).

**Table 7.3.** Yields (\%) of the oxidation products Ph\textsubscript{2}SO and Ph\textsubscript{2}SO\textsubscript{2} after reaction of Ph\textsubscript{2}S with selected adducts R\textsc{3}PO•(HOO)\textsubscript{2}CR'\textsc{R}'', with and without catalytic amounts of SiO\textsubscript{2} and Br\textsubscript{2}.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Adduct</th>
<th>SiO\textsubscript{2} (g)</th>
<th>Br\textsubscript{2}</th>
<th>Ph\textsubscript{2}SO</th>
<th>Ph\textsubscript{2}SO\textsubscript{2}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>46\textsuperscript{[a]}</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>0.5</td>
<td>-</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>2.0</td>
<td>-</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>0.5</td>
<td>-</td>
<td>43</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>7</td>
<td>0.5</td>
<td>1 drop</td>
<td>47\textsuperscript{[b]}</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>7</td>
<td>0.5</td>
<td>1 drop</td>
<td>33\textsuperscript{[c]}</td>
<td>53\textsuperscript{[c]}</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>0.5</td>
<td>-</td>
<td>49</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>5</td>
<td>0.5</td>
<td>-</td>
<td>46</td>
<td>0</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]} Reaction temperature 70 °C; \textsuperscript{[b]} Reaction was performed in benzene; \textsuperscript{[c]} Reaction temperature 50 °C.
Assured that conducting the oxidation reaction at room temperature does not yield the sulfone, the sulfoxidation was attempted with adducts 5 and 10, using the same reaction conditions. In both cases, no overoxidation to the sulfone was observed, in contrast to previous results. The yields for the sulfoxide were similar to the ones obtained with adduct 7, with 49% for 5 and 46% for 10 (Table 7.3, entries 9 and 10).

Finally, the oxidation of thiophene was attempted using the adducts. Thiophene and adduct 7 were combined in a 2 : 1 ratio, and dissolved in acetonitrile (Scheme 7.5). After stirring for 4 days at room temperature, no oxidation occurred without silica and Br2 (Table 7.4, entry 1). With addition of catalytic amounts of silica and Br2, 41% conversion was observed, with thiophene oxide being the only product (Entry 2). No overoxidation was detected.

![Scheme 7.5. Oxidation of thiophene with the R3PO•(HOO)2CR’R” adduct 7.](image)

**Table 7.4. Product yields (%) after oxidation of thiophene with 7.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>SiO2 / Br2</th>
<th>Thiophene 1-oxide</th>
<th>Thiophene 1,1-dioxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>- / -</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0.5 g / 1 drop</td>
<td>41</td>
<td>0</td>
</tr>
</tbody>
</table>
**Epoxidation**

Epoxidations of styrene and cyclohexene were attempted using the adducts 4-8 (Scheme 7.6) in benzene.\(^{8b,48d,61}\)

![Scheme 7.6. Epoxidation attempts with R₃PO•(HOO)₂CR'R'' adducts.](image)

In the absence of any catalyst, no reaction occurs, even at elevated temperatures (70 °C). This is plausible, as the adducts are milder oxidants than aqueous H₂O₂. When 0.01 mol% of methyltrioxo rhenium (MTO) is added to the reaction mixture, 100% conversion is achieved, but the product is fully hydrolyzed to trans-1,2-cyclohexanediol.\(^{5c,61-62}\) Further epoxidation attempts were discontinued due to time constraints.

**Phosphine oxidation**

When Cy₃PO•(HOO)₂CMe₂ (5) and Ph₂P-PPh₂ were added in a 1:1 ratio to dry benzene, the diphosphine dioxide was obtained as the main product (Scheme 7.7). While the resulting water adduct of the phosphine carrier, Cy₃PO•H₂O, is highly soluble in benzene, 1,1,2,2,-tetraphenyldiphosphine dioxide (17) is insoluble and precipitates out of the solution, allowing for easy separation from the reaction mixture (Figure A.93). In the
solid form, **17** is air-stable and can be stored for weeks without P-P bond cleavage due to hydrolysis or oxygen insertion.

![Scheme 7.7](image)

**Scheme 7.7.** Stoichiometric oxidation of 1,1,2,2-tetraphenyldiphosphine with Cy₃PO•(HOO)₂CMe₂ (5) in benzene.

**17** was intended to serve as a diphosphine dioxide carrier for di(hydroperoxy)alkanes. The interest was to extend the known diphosphine dioxide adducts from those with two methylene groups between the P atoms (14, 15), via the one with one CH₂ group (13) to an adduct with no carbon between the two PO groups. Therefore, an adduct synthesis with **17** as a new diphosphine dioxide carrier was attempted. However, when **17** was brought in contact with equal molar amounts of (HOO)₂C(CH₄)₅ crystals, the P-P bond was immediately hydrolyzed to the phosphinic acid Ph₂P(O)OH even in the absence of any solvent.

**Baeyer-Villiger oxidation**

For each cycloalkane adduct Cy₃PO•(HOO)₂C(CH₂)₅ (n = 4-6) there is a cyclic ketone inherently present, arranged favorably with respect to its oxidation with two active peroxide groups attached to the quaternary carbon. In the presence of a catalytic
amount of H$_2$SO$_4$, these (HOO)$_2$C(CH$_2$)$_n$ moieties immediately form the corresponding free lactones in quantitative yields (Scheme 7.8).

Scheme 7.8. Formation of lactones from the cycloalkane adducts Cy$_3$PO•(HOO)$_2$C(CH$_2$)$_n$ in the presence of trace amounts of acid.

It is not yet clear whether the oxidation takes place while the di(hydroperoxy)cycloalkanes are still attached to the phosphine oxide carriers, or whether they are released from the phosphine oxides prior to the oxidation. Even though there are two peroxo groups per (HOO)$_2$C(CH$_2$)$_n$ moiety, no further oxidation of the lactones is observed, and the only other product remaining in the reaction mixture is Cy$_3$PO•H$_2$O (Table 7.5, entry 1).
Table 7.5. Baeyer-Villiger oxidation of substrate ketone and (HOO)$_2$C(CH$_2$)$_n$ moieties in the presence of a drop (< 1 mg) of H$_2$SO$_4$.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Adduct</th>
<th>Substrate</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
<td>-</td>
<td><img src="image" alt="100%" /></td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td><img src="image" alt="1 eq" /></td>
<td><img src="image" alt="58%" /></td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td><img src="image" alt="2 eq" /></td>
<td><img src="image" alt="55%" /></td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td><img src="image" alt="1 eq" /></td>
<td>![9 + <img src="image" alt="5%" /> <img src="image" alt="52%" /></td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td><img src="image" alt="1 eq" /></td>
<td>![21% + <img src="image" alt="23%" /></td>
</tr>
<tr>
<td>6</td>
<td>10</td>
<td><img src="image" alt="1 eq" /></td>
<td>![24% + <img src="image" alt="22%" /></td>
</tr>
</tbody>
</table>

For comparison, the Baeyer-Villiger oxidation was attempted with cyclopentanone and the hydrogen peroxide adduct [Cy$_3$PO•H$_2$O$_2$]$_2$ in a 2 : 1 molar ratio, again with only a trace amount of H$_2$SO$_4$. The corresponding δ-valerolactone is the only product, however, the yield is decreased to 55% (Table 7.5, entry 3). When the molar ratio of adduct to substrate is increased to 1 : 1, such that there are two active peroxide
groups per cyclopentanone, a mixture of δ-valerolactone and adduct 9 is obtained (Scheme 7.9, Table 7.5, entry 4).

Scheme 7.9. Oxidation of cyclopentanone to δ-valerolactone and di(hydroperoxy)-cyclopentane in the presence of 3 and trace amounts of acid.

In order to test whether the peroxo groups show selectivity with the attached cycloalkyl group over freshly added cyclic ketone, adduct 9 was reacted with cyclohexanone, and adduct 10 was reacted with cyclopentanone in a 1 : 1 molar ratio. In both cases, mixtures of δ-valerolactone and ε-caprolactone (Table 7.5, entries 5 and 6) are obtained, in approximately 1 : 1 molar ratio. Therefore, one can conclude that there is no preference for the oxidation of phosphine oxide-bound di(hydroperoxy)cycloalkanes over the lactone formation from added free ketones.
Conclusion

The anhydrous and stoichiometric character of the di(hydroperoxy)alkane adducts \( \text{R}_3\text{PO} \cdot \text{(HOO)}_2\text{CR'}\text{R''} \) \( (\text{R}, \text{R'}, \text{R''} = \text{alkyl, aryl}) \) places them in a unique position in organic oxidation reactions. As demonstrated by the successful selective oxidation of tetrahydrothiophene and 1,1,2,2-tetraphenyldiphosphine, these adducts can be applied as oxidants in reactions that require air- and water-free conditions, as well as reactions with desired products that are sensitive to overoxidation.

The selectivity of these adducts stems from their exact stoichiometry and their mild oxidizing power, relative to aqueous \( \text{H}_2\text{O}_2 \). In the case of reluctant reactions such as diarylsulfide oxidation, a catalyst or initiator can be used in combination with the adducts to push the reaction forward. Overoxidation to \( \text{R'}\text{R''SO}_2 \) does not occur under optimized reaction conditions, and the corresponding sulfoxide \( \text{R'}\text{R''SO} \) is obtained as the only product in good yields. In the presence of trace amounts of \( \text{H}_2\text{SO}_4 \), the di(hydroperoxy)cycloalkane moieties of 9-11 produce the corresponding lactones, leaving the phosphine oxide carriers behind.

While reactions such as epoxidations, which involve the activation of C=C bonds, are possible with the adducts \( \text{R}_3\text{PO} \cdot \text{(HOO)}_2\text{CR'}\text{R''} \) in the presence of a catalyst like MTO, the adducts are most favorable for reactions that require mild oxidants, such as the oxidation of 1,1,2,2-tetraphenyldiphosphine. Because the oxidizing power of the adducts is mild, the P-P bond is not cleaved and the diphosphine dioxide 17 is obtained quantitatively. However, the scope of applications of these adducts is still being
expanded in every direction, including oxidations of substrates that contain sensitive functional groups.

**Experimental**

* Tetrahydrothiophene (THT) oxidation

  46 mg (0.1 mmol) of Cy₃PO•(HOO)₂C(CH₂)₄ (9) and 9 mg (0.1 mmol) of THT are weighed into a 20 mL vial inside a glove box and dissolved in 0.6 mL of C₆D₆. The vial is capped, and the contents are stirred. Every 10 minutes, an aliquot is transferred to an NMR tube, and the product identity and yield are determined by ¹H and ¹³C NMR analyses.

  Tetrahydrothiophene NMR (δ, C₆D₆), ¹H 2.55-2.42 (m, 4H, SCH₂), 1.48-1.36 (m, 4H, SCH₂CH₂); ¹³C 31.37 (s, SCHR₂), 30.85 (s, SCH₂C).⁶³

  Tetramethylene sulfoxide NMR (δ, C₆D₆), ¹H 2.89-2.74 (m, 4H, SCH₂), 2.47-2.04 (m, 4H, SCH₂CH₂); ¹³C 53.98 (s, SC), 25.02 (s, SCH₂C).⁶⁴

* SPh₂ oxidation

  In a representative reaction, 84 mg (0.2 mmol) of 7 and 78 mg (0.4 mmol) of Ph₂S are weighed into a 20 mL vial. The mixture is then dissolved in 3 mL of distilled acetonitrile. Finally, 0.5 g of dry SiO₂ and 1 drop (less than 1 mg) of Br₂ are added to the vial, and the contents is stirred for 4 days. The reaction progress is monitored every 12 hours via ¹H and ¹³C NMR spectroscopy.
Ph$_2$S NMR ($\delta$, C$_6$D$_6$), $^1$H 7.47-7.26 (m, 10H); $^{13}$C 135.83 (s, $C_i$), 131.00 (s, $C_o$), 129.11 (s, $C_m$), 126.94 (s, $C_p$).

Ph$_2$SO NMR ($\delta$, C$_6$D$_6$), $^1$H 7.71-7.63 (m, 4H, $H_o$), 7.50-7.46 (m, 2H, $H_p$), 7.45-7.41 (m, 4H, $H_m$); $^{13}$C 145.76 (s, $C_i$), 130.96 (s, $C_p$), 129.25 (s, $C_m$), 124.67 (s, $C_o$).

Ph$_2$SO$_2$ NMR ($\delta$, C$_6$D$_6$), $^1$H 7.95-7.91 (m, 4H, $H_o$), 7.55-7.53 (m, 2H, $H_m$), 7.52-7.49 (m, 4H, $H_p$); $^{13}$C 141.53 (s, $C_i$), 133.21 (s, $C_p$), 129.27 (s, $C_m$), 127.54 (s, $C_o$).

**Thiophene oxidation**

84 mg (0.2 mmol) of 7 and 34 mg (0.4 mmol) of C$_4$H$_4$S are weighed into a 20 mL vial. The mixture is then dissolved in 3 mL of distilled acetonitrile. Finally, 0.5 g of dry SiO$_2$ and 1 drop (less than 1 mg) of Br$_2$ are added to the vial, and the contents is stirred for 4 days. The reaction progress is monitored every 12 hours via $^1$H and $^{13}$C NMR spectroscopy.

Thiophene NMR ($\delta$, C$_6$D$_6$), $^1$H 7.34-7.30 (m, 2H, SCH), 7.09-7.06 (m, 2H, SCHCH); $^{13}$C 126.82 (s, SCC), 125.08 (s, SC).

Thiophene-1-oxide NMR ($\delta$, C$_6$D$_6$), $^1$H 7.34-7.30 (m, 2H, SCH), 7.09-7.06 (m, 2H, SCHCH); $^{13}$C 140.93 (s, SC), 126.48 (s, SCC).

**Baeyer-Villiger oxidation**

23 mg (0.05 mmol) of Cy$_3$PO•(HOO)$_2$C(CH$_2$)$_4$ is dissolved in 3 mL of benzene in a 20 mL vial, and a drop of H$_2$SO$_4$ (98 wt%) is added. The contents of the vial is
stirred for 20 min, and subsequently an NMR sample is prepared for $^1$H and $^{13}$C NMR analyses. δ-Valerolactone is produced in 100% yield, with respect to the di(hydroperoxy)cyclopentane moiety.

In a new vial, 92 mg (0.2 mmol) of Cy$_3$PO•(HOO)$_2$C(CH$_2$)$_4$ (9) and 17 mg (0.2 mmol) of cyclopentanone are dissolved in CDCl$_3$ (1.0 mL). 1 drop of H$_2$SO$_4$ (98 wt%) is added, and the contents is stirred for 20 min. Both (HOO)$_2$C(CH$_2$)$_4$ and cyclopentanone are oxidized to δ-valerolactone (58% yield according to $^{13}$C NMR).

In another 20 mL vial, [Cy$_3$PO•H$_2$O$_2$]$_2$ (33 mg, 0.05 mmol) is reacted with 10 mg (0.12 mmol) of cyclopentanone and one drop of H$_2$SO$_4$ (98 wt%) in 1.0 mL of CDCl$_3$. After stirring for 20 min, δ-valerolactone is produced in 55% yield with respect to the (HOO)$_2$C(CH$_2$)$_4$ moiety, according to $^1$H NMR spectroscopy.

When [Cy$_3$PO•H$_2$O$_2$]$_2$ (3) (66 mg, 0.11 mmol) is reacted with 10 mg (0.12 mmol) of cyclopentanone and H$_2$SO$_4$ (98 wt%), 100% conversion occurs, but the product is a mixture of δ-valerolactone and adduct 9.

When 9 (46 mg, 0.1 mmol) is reacted with 10 mg (0.1 mmol) of cyclohexanone and one drop of H$_2$SO$_4$ (98 wt%) in 1.0 mL of CDCl$_3$, a mixture of δ-valerolactone (21% yield) and ε-caprolactone (23% yield) are produced. Reacting adduct 10 with cyclopentanone in a 1 : 1 ratio results in a mixture of δ-valerolactone (24% yield) and ε-caprolactone (22% yield) as well (Scheme 7.10).
Scheme 7.10. δ-Valerolactone (left) and ε-caprolactone (right), numbered for the purpose of NMR signal assignment.

δ-Valerolactone NMR (δ, CDCl₃), ¹H 4.35-4.31 (m, 2H, H5), 2.58-2.51 (m, 2H, H2), 2.15-1.63 (m, 4H, H3, H4); ¹³C 172.01 (s, C1), 69.45 (s, C5), 29.53 (s, C2), 21.96 (s, C4), 18.68 (s, C3).⁶⁶

ε-Caprolactone NMR (δ, CDCl₃), ¹H 4.24-4.20 (m, 2H), 2.65-2.61 (m, 2H), 1.88-1.82 (m, 2H), 1.79-1.70 (m, 4H); ¹³C 176.22 (s, C1), 69.30 (s, C6), 34.57 (s, C2), 29.34 (s, C4), 28.93 (s, C5), 22.99 (s, C3).⁶⁷

Styrene oxidation

In a representative styrene epoxidation attempt, 44 mg (0.1 mmol) of Cy₃PO•(HOO)₂CMeEt (7) and 23 mg of styrene (0.2 mmol) are combined in a 25 mL Schlenk flask and flushed with N₂ gas. The mixture is dissolved in 3 mL of benzene and stirred overnight at each of following temperatures: room temperature, 40 °C, 50 °C, 60 °C, and 70 °C. The reaction is monitored with ¹H and ¹³C NMR spectroscopy. No conversion of styrene is observed.
440 mg (1 mmol) of Cy$_3$PO•(HOO)$_2$CMeEt (7), 230 mg (2 mmol) of styrene and 5 mg (0.02 mmol, 1 mol%) of CH$_3$ReO$_3$ (MTO) are placed in a 100 mL Schlenk flask, flushed with N$_2$ gas and dissolved in 40 mL of benzene. The reaction mixture is stirred for 2 h at room temperature. $^1$H and $^{13}$C NMR spectra show the hydrolyzed phenylethane-1,2-diol as the only product.$^{68}$

Phenylethane-1,2-diol NMR ($\delta$, CDCl$_3$), $^1$H 7.35-7.21 (m, 5H, aryl-$H$), 4.74-4.71 (m, 1H, PhCH$_3$), 3.69-3.57 (m, 2H, CH$_2$OH), 3.08 (s, 2H, OH); $^{13}$C 140.55 (s, $C$), 128.42 (s, $C_m$), 127.78 (s, $C_p$), 126.09 (s, $C_o$), 74.71 (PhC), 67.95 (CH$_2$).$^{68}$

**Ph$_2$P-PPh$_2$ oxidation**

1,1,2,2-Tetraphenyldiphosphane Ph$_2$P-PPh$_2$ is synthesized according to a literature method in 83% isolated yield.$^{69}$ The $^1$H and $^{13}$C NMR peaks are determined using $^{13}$C,$^1$H HMBC and COSY NMR spectra. The $^1$H and $^{31}$P NMR signals agree with literature values,$^{69}$ and $^{13}$C NMR signals agree with trends found in the literature for arylphosphines.$^6$

NMR ($\delta$, CDCl$_3$), $^{31}$P -14.84 (s); $^1$H 7.39-7.35 (m, 8H, $H_o$), 7.26 (m, 4H, $H_p$), 7.20 (m, 8H, $H_m$),$^{69}$ $^{13}$C 135.64 (virtual t, $J^{(31}\text{P-13}\text{C}) = 5.1$ Hz, $C_i$) 134.30 (virtual t, $J^{(31}\text{P-13}\text{C}) = 12.6$ Hz, $C_o$), 128.66 (s, $C_p$), 128.20 (virtual t, $J^{(31}\text{P-13}\text{C}) = 3.3$ Hz, $C_m$). mp 96-98 °C.

41 mg (0.11 mmol) of Ph$_2$P-PPh$_2$ and 47 mg (0.12 mmol) of Cy$_3$PO•(HOO)$_2$CMe$_2$ are filled into an NMR tube flushed with N$_2$ gas. When 0.4 mL of
C₆D₆ is added to the tube, it heats up immediately. Initially, the sample forms a cloudy solution. However, after a few minutes, Ph₂P(O)-P(O)Ph₂ precipitates as a white powder and settles at the bottom of the tube. The water adduct of the phosphine oxide carrier, Cy₃PO•H₂O, remains dissolved in C₆D₆, allowing for easy separation of the product Ph₂P(O)-P(O)Ph₂ via filtration. The solid Ph₂P(O)-P(O)Ph₂ is redissolved in 0.5 mL of CDCl₃ and characterized with ¹H, ¹³C and ³¹P NMR spectroscopy. The ¹H and ³¹P NMR signals agree with literature values.⁵⁶a ¹³C NMR signal assignment is reported for the first time in this dissertation.

NMR (δ, CDCl₃), ³¹P 23.71 (s); ¹H 7.93 (dd, ³J(³¹P-¹H) = 12.5 Hz, ³J(¹H-¹H) = 7.6 Hz, 8H, H₀), 7.49 (t, ³J(¹H-¹H) = 7.6 Hz, 4H, Hₚ), 7.40 (t, ³J(¹H-¹H) = 7.6 Hz, 8H, Hₘ),⁵⁶a ¹³C 132.43 (s, Cᵢ) 131.80 (virtual t, J(³¹P-¹³C) = 5.1 Hz, Cᵦ), 128.57 (virtual t, J(³¹P-¹³C) = 6.1 Hz, Cₘ), 128.32 (s, Cₚ).
CHAPTER VIII
MISCELLANEOUS RESULTS

Introduction

Di(hydroperoxy)alkane adducts of phosphine oxides are easily synthesized and crystallized. The synthetic method was tested across a wide scope of phosphine oxides and ketones, and all starting materials have successfully produced the expected adducts. However, in one case a completely different species was obtained as product.

In the absence of phosphine oxide, butanone is known to react with $\text{H}_2\text{O}_2$ to form 2,2'-peroxydi(butane-2-peroxol), \([\text{HOOCMeEtO}^-]_2\), commonly referred to as methylethylketone peroxide (MEKPO).

This substance is used in the polymer industry as a catalyst for acrylic resins or as curing agent for unsaturated polyester resins, and is produced by addition of aqueous $\text{H}_2\text{O}_2$ to 2-butanol in the presence of acid.

Regarding the previously described adducts of phosphine oxides, the strong hydrogen bond between the phosphine oxide and the 2,2-di(hydroxy)butane prevents the formation of MEKPO. However, in one case the MEKPO came into existence nonetheless, forming a network of hydrogen bonds with the phosphine oxides in the reaction mixture.

Following a similar line of thought, it was hypothesized that diketones which normally undergo cyclization upon reaction with $\text{H}_2\text{O}_2$ could instead form di(hydroperoxy) moieties from each carbonyl group and become attached to diphosphine dioxides with a fitting distance between the PO groups, through hydrogen bonding. Surprisingly, it turned out that bidentate phosphine oxides can act as bystander
molecules, and from a series of experiments different forms of cyclized products were isolated and crystallized. In this chapter, the synthesis and characterization of these serendipitously found molecules, which do not align with the adducts 4-15, are described in detail.

**Results and Discussion**

When acetone and 3-pentanone were combined with bis(diphenylphosphino)ethane dioxide (dppe dioxide), the adducts 14 and 15 were formed, respectively. However, when butanone was combined with this diphosphine dioxide and an excess of aqueous H₂O₂, the crystallized product obtained in 83% yield, poly(2,2′-peroxydi(butane-2-peroxol)-bis(diphenylphosphino)ethane dioxide) (18), shows a polymeric structure, consisting of dppe dioxide and MEKPO (Figure 8.1). The two phosphine oxide groups point in opposite directions and form hydrogen bonds with the hydroperoxy functionalities of different MEKPO molecules.
Perhaps the ideal packing of the phenyl groups in dppe dioxide promotes the formation of MEKPO as opposed to the di(hydroperoxy)butane moieties found in the adducts 6 and 7. Another factor favoring the structure of the material is the similar lengths of the P-C-C-P and C-O-O-C units, which allow for their parallel arrangement and strainless stacking in the crystal. The slight difference in the lengths is made up for by the hydrogen bonds. It is yet to be seen whether a similar polymer forms with the cyclohexyl analog of dppe dioxide, [Cy₂P(O)CH₂]₂.

Since dppe dioxide is able to form multiple hydrogen bonds to di(hydroperoxy)alkanes, the next step in synthesis involved expanding the scope of ketones to diketones. It was interesting to see whether both carbonyl groups would undergo nucleophilic attack to each form the di(hydroperoxy)alkane moiety, and finally bind to phosphine oxides, as shown for one example in Scheme 8.1.
To test this idea, dppm dioxide and dppp dioxide were chosen as the phosphine oxides, and acetylacetone was selected as the diketone. While the two P=O groups in dppe dioxide point away from each other in the structures we have obtained so far, the P=O groups in dppm dioxide and dppp dioxide point in the same direction, and are in close enough proximity to form hydrogen bonds, should the acetylacetone successfully form di(hydroperoxy)alkane moieties at both carbonyl positions (Scheme 8.1).

Scheme 8.1. Attempted synthesis of the shown desired adduct.

Unfortunately, the two carbonyl groups in acetylacetone are so close to each other that as soon as one carbonyl group undergoes a nucleophilic attack by hydrogen peroxide, the second carbonyl group is attacked by the resulting hydroperoxide, forming a five-membered ring (Scheme 8.2).\textsuperscript{46,75} Unlike the cases of previous adducts, where the phosphine oxides favorably formed hydrogen bonds with the di(hydroperoxy)alkane moieties and thereby prohibited the cyclic condensation of acetone peroxide or butanone peroxide, the presence of dppm dioxide or dppp dioxide does not prevent the formation of the cycloperoxide according to the pathway displayed in Scheme 8.2 below.
Scheme 8.2. Synthesis of cyclic di(hydroxy)peroxide.

Depending on the concentration of the aqueous H₂O₂ in the reaction mixture, the 3,5-dimethyl-1,2-dioxolane-3,5-diol (19) or the 3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane (20) are obtained. An orderly network of hydrogen bonds is formed for both 19 and 20, and both crystallize easily, without any interaction with the phosphine oxide in solution (Figure 8.2, Figure 8.3). As seen from the X-ray structures, both compounds form the trans isomer. The same compounds could also be synthesized just as easily in the absence of chelating phosphine oxides, but with acid catalysis.⁴⁶

Figure 8.2. Single crystal X-ray structure of a single molecule of 19 (left) and 19 in the unit cell (right).⁷⁶
These diol and dioxolane compounds have been known for some time, but the X-ray crystal structures have not been reported yet. Previous reports state that reactions of diketones with aqueous H$_2$O$_2$ at room temperature form inseparable mixtures of the di(hydroxy)peroxide (19), di(hydroperoxy)peroxide (20), and hydroperoxyperoxides (Figure 8.4). Contrary to this, in our hands 19 and 20 were both obtained as isolated products in high yields, without the need for further purification.

**Figure 8.3.** Single crystal X-ray structure of a single molecule of 20 (left) and 20 in the unit cell (right).

**Figure 8.4.** Potential products from reaction of acetylacetone with aq. H$_2$O$_2$. 

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Conclusion

Unlike the cases of the adducts 6 and 7, reacting H₂O₂ with butanone in the presence of dppe dioxide gives the methylethylketone peroxide molecule (MEKPO). The hydroperoxides at either end of the MEKPO molecule form hydrogen bonds with phosphine oxide groups of different dppe dioxide molecules, thereby generating the polymeric adduct 18. This adduct is stable and it has been obtained in the form of large single crystals.

The presence of dppm dioxide does not prohibit the cyclization of the diketone when being treated with aqueous H₂O₂. Acetylacetone undergoes nucleophilic attack by aqueous H₂O₂ to form the trans-cycloperoxides 19 and 20. These two species were successfully characterized by single crystal X-ray crystallography, and the structures show intricate networks of intermolecular hydrogen bonds.

Experimental
Poly(2,2’-peroxydi(butane-2-peroxol)-bis(diphenylphosphino)ethane dioxide) (18)

In a round bottom flask, dppe dioxide (103 mg, 0.24 mmol) was dissolved in 10 mL of toluene. 10 mL (112 mmol) of butanone and 0.1 mL (1 mmol) of aqueous H₂O₂ was added, and the solution was stirred overnight. The solution was concentrated in vacuum to 5 mL, then the mixture was left so that the product could crystallize. Adduct 19 was obtained in the form of large, colorless, rectangular crystals (126 mg, 0.20 mmol, 83% yield).
NMR (δ, CDCl₃, ³¹P{¹H} 36.91 (s); ¹H 11.27 (br. s, 2H, OOOH), 7.76-7.71 (m, 8H, Hp), 7.56-7.51 (m, 4H, Hp), 7.49-7.45 (m, 8H, Hm), 2.59 (d, ²J(³¹P-¹H) = 2.7 Hz, 4H, PC₃H₂), 1.81 (q, ³J(¹H-¹H) = 7.6 Hz, 4H, CH₂CH₃), 1.44 (s, 6H, CC₃H₃), 1.03 (t, ³J(¹H-¹H) = 7.6 Hz, 6H, CH₂CH₃); ¹³C{¹H} 132.49 (s, Cp), 130.73 (d, ¹J(³¹P-¹³C) = 102.8 Hz, C), 130.70 (virtual triplet, J(³¹P-¹³C) = 4.7 Hz, Co), 129.08 (virtual triplet, J(³¹P-¹³C) = 6.1 Hz, Cm), 111.73 (s, CCH₃), 26.15 (s, CH₂CH₃), 21.31 (t, ³J(³¹P-¹³C) = 33.0 Hz, PCH₂), 17.49 (s, CCH₃), 8.39 (s, CH₂CH₃). IR: ν(PO) = 1437.0 cm⁻¹.

3,5-Dimethyl-1,2-dioxolane-3,5-diol (19)

Dppp (1.001 g, 2.43 mmol) is dissolved in 60 mL of CH₂Cl₂. Aqueous H₂O₂ (5.0 mL, 0.05 mol) is added, and the solution is stirred for 1 h. The organic layer is collected using a separation funnel, and the solvent is removed in vacuo. The resulting white residue is dissolved in 2.5 mL (24.3 mmol) of acetylacetone, followed by the addition of excess aqueous H₂O₂ (0.1 mL, 1.0 mmol). The solution is stirred for 3 days, then the mixture is allowed to stand for crystallization. The unintentional product 19 is obtained in the form of white, crystalline needles (94 mg, 0.71 mmol, 71% yield with respect to amount of H₂O₂ added into the acetylacetone), while an oily liquid remains.

The procedure is repeated without phosphine oxide. 100 mg (1 mmol) of acetylacetone is weighed into a vial, followed by 0.15 mL (1.5 mmol) of H₂O₂. The solution is stirred overnight, and excess water is removed with vacuum. Benzene (1.0 mL) is used to precipitate the product, which is filtered and dried in vacuo. (83 mg, 0.62 mmol, 62% yield). ¹H and ¹³C NMR data match the literature values.⁴⁶
NMR (δ, CDCl$_3$), $^1$H 2.74 (s, 2H, CH$_2$), 1.63 (s, 6H, CH$_3$); $^{13}$C 105.50 (s, OC), 55.23 (CH$_2$), 22.59 (CH$_3$). mp (decomp.) 82 °C.

3,5-Dihydroperoxy-3,5-dimethyl-1,2-dioxolane (20)

100 mg (1 mmol) of acetylacetone is weighed into a vial and combined with 1.0 mL (10 mmol) of aqueous H$_2$O$_2$. The solution is stirred overnight, and the excess of water is removed with vacuum. Benzene (1.0 mL) is used to precipitate the product (113 mg, 0.68 mmol, 68% yield). $^1$H and $^{13}$C NMR data match the literature values.$^{46}$

NMR (δ, CDCl$_3$), $^1$H 8.54 (s, 2H, OH), 2.74 (s, 2H, CH$_2$), 1.63 (s, 6H, CH$_3$); $^{13}$C 112.99 (s, OC), 51.11 (CH$_2$), 17.52 (CH$_3$). mp (decomp.) 98 °C.
CHAPTER IX
SUMMARY

Hydrogen peroxide and di(hydroperoxy)alkane adducts of phosphine oxides are presented as solid, safe, stoichiometric and soluble oxidizing agents. Structural motifs of H₂O₂ adducts with different R₃PO : H₂O₂ ratios are highlighted by single crystal analyses, and the physical properties of all adducts are described in detail.

Di(hydroperoxy)alkane adducts of phosphine oxides are successfully synthesized at room temperature in high yields, without the use of acid or metal catalysts. Phosphines, phosphine oxides, and H₂O or H₂O₂ adducts of phosphine oxides can be used as the starting materials. While high solubility of these starting materials in CH₂Cl₂ renders it an attractive solvent, the corresponding ketone can just as well be used as the solvent. This one-pot, general synthetic method has been applied to a wide variety of phosphine oxides and ketones, and the resulting adducts can be safely and easily isolated in the form of large crystals. The general synthetic approach also allows for easy recycling of the phosphine oxide carriers. The adducts can be regenerated by simply stirring the phosphine oxides in a solution of excess H₂O₂ and ketone.

All adducts have been fully characterized, using mostly the methods multinuclear NMR and IR spectroscopy, X-ray crystallography and melting point analyses. ¹³C NMR spectroscopy is especially valuable as a diagnostic tool, as the quaternary carbon on the (HOO)₂CR'R" moiety displays a unique signal at 108-120 ppm, and the product can be identified prior to its isolation. X-Ray crystallography and IR spectroscopy show
significant elongation and weakening of the P=O bond as a result of hydrogen bonding to the \((\text{HOO})_2\text{CR}'\text{R}''\) moiety.

IR spectroscopy also confirms the absence of water molecules in the adducts. Moreover, the adducts are insoluble in H$_2$O, but they show high solubility in many common organic solvents. Thus, when used as oxidizing agents, the oxidation reaction can be performed in a single organic phase.

Because these adducts have a well-defined molecular structure, the exact number of active oxygen atoms can be easily calculated. The anhydrous and stoichiometric character of the adducts of the type \(\text{R}_3\text{PO}\cdot(\text{HOO})_2\text{CR}'\text{R}''\) allows for their application as oxidants in reactions that require air- and water-free conditions, as well as reactions that are sensitive to overoxidation. Indeed, dialkyl sulfides were selectively oxidized to sulfoxides, and 1,1,2,2-tetraphenyldiphosphine was transformed quantitatively into the corresponding dioxide without hydrolysis of the P-P bond or oxygen insertion.

In the case of reluctant educts such as diarylsulfides, a catalyst or initiator can be used in combination with the adducts to push the reaction forward. Overoxidation to the sulfones \(\text{R}'\text{R}''\text{SO}_2\) can be prevented by careful control of the reaction conditions. In the presence of acid, but no other substrate, the di(hydroperoxy)cycloalkane moieties are transformed into the corresponding free lactones and the phosphine oxide carriers.

Decomposition of the adducts \(\text{R}_3\text{PO}\cdot(\text{HOO})_2\text{CR}'\text{R}''\) under thermal and mechanical stress was studied in more detail. Upon heating, hammering and grinding, no sudden release of oxygen or other sign of violent decomposition was observed, confirming the safety of these adducts. Furthermore, the long term stability and shelf life
of the adducts was studied by storing them under various conditions. A quantitative NMR method was developed to study the rate of decomposition. The oxidation capacity of the stored adducts was monitored by the oxidation of Ph₃P, and the amount of oxidized Ph₃P was calculated via $^{31}$P NMR peak integration. This number was compared to the mass of adduct used for the oxidation to quantify the number of active peroxide groups remaining in the adduct. Using this method, it has been shown that the adducts decompose to about 70% of their original oxidative power when stored as powders at room temperature for several months. However, when the powders are stored at a lower temperature of -4 °C, there is essentially no decomposition even after months. Moreover, when the adducts are stored as large single crystals, decomposition is insignificant even at room temperature.

In one particular case, adduct synthesis with 2-butanone in the presence of a stoichiometric amount of dppe dioxide resulted in the condensation to methylethylketone peroxide (MEKPO), which then formed hydrogen bonds to two molecules of dppe dioxide. The resulting adduct displayed a polymeric structure, as opposed to the discrete molecular structures observed for $R_3PO\cdot(HOO)_2CMeEt$ ($R = $ Cy, Ph). It is hypothesized that the steric of dppe dioxide is favorable for packing with MEKPO, and thus unlike the previous adducts, condensation of 2,2-di(hydroperoxy)butane to MEKPO is not prohibited by the presence of phosphine oxide bonds.

The presence of phosphine oxide also does not interfere with cyclization of diketones with H₂O₂. Acetylacetone undergoes nucleophilic attack by aqueous H₂O₂ to form trans-cycloperoxides. Depending on the concentration of H₂O₂, either 3,5-
dimethyl-1,2-dioxolane-3,5-diol or 3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane is isolated as the sole product. Both species form an intricate network of hydrogen bonds with neighboring molecules and crystallize easily. This might be the reason why no interactions with the offered diphosphine dioxides are observed.
REFERENCES


(20) CCDC 1033533 contains the supplementary crystallographic data of 1. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., C_{12}H_{27}O_{11}P_{1}.H_{2}O_{2} unit cell parameters: a 8.266(2), b 15.032(4), c 12.467(4), P2_1/n.

(22) CCDC 1033531 contains the supplementary crystallographic data of 2. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_rdquest/cif., \((C_{18}H_{15}O_1P_1)_2(H_2O_2)_3\) unit cell parameters: a 9.6284(3), b 16.8881(6), c 10.9317(4), \(P_2_1/n\).


(26) Oxley, J. C.; Smith, J. L.; Bowden, P. R.; Rettinger, R. C. Propellants Explos. Pyrotech. 2013, 38, 244-254.


(28) CCDC 1033532 contains the supplementary crystallographic data of 4. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_rdquest/cif., \((C_{18}H_{15}O_1P_1)(C_3H_8O_4)\) unit cell parameters: a 9.1646(19), b 21.719(5), c 10.053(2), \(P_2_1/n\).

(29) CCDC 1033530 contains the supplementary crystallographic data OF 5. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_rdquest/cif., \((C_{18}H_{33}O_1P_1)(C_3H_8O_4)\) unit cell parameters: a 10.158(3), b 10.645(3), c 11.169(3), \(P-1\).

(30) CCDC 1449060 contains the supplementary crystallographic data of 6. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_rdquest/cif., \((C_{18}H_{15}O_1P_1)(C_4H_{16}O_4)\) unit cell parameters: a 13.212(3), b 10.652(2), c 15.084(3), \(Pc\).

(31) CCDC 1449059 contains the supplementary crystallographic data of 7. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_rdquest/cif., \((C_{18}H_{33}O_1P_1)(C_4H_{16}O_4)\) unit cell parameters: a 10.952(5), b 18.674(0), c 11.503(1), \(P2_1/c\).
CCDC 1451015 contains the supplementary crystallographic data of 8. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., \( \text{C}_{18}\text{H}_{33}\text{O}_1\text{P}_1\cdot(\text{C}_3\text{H}_1\text{O}_4) \) unit cell parameters: a 11.000(7), b 18.599(0), c 11.828(2), \( P_2_1/c \).

CCDC 1451754 contains the supplementary crystallographic data of another polymorph of 8. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., \( \text{C}_{18}\text{H}_{33}\text{O}_1\text{P}_1\cdot(\text{C}_5\text{H}_{12}\text{O}_4) \) unit cell parameters: a 9.629(2), b 11.173(5), c 12.034(9), \( P-1 \).

CCDC 1561376 contains the supplementary crystallographic data of 9. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., \( \text{C}_{18}\text{H}_{33}\text{O}_1\text{P}_1\cdot(\text{C}_5\text{H}_1\text{O}_4) \) unit cell parameters: a 10.995(3), b 18.254(3), c 11.838(4), \( P_2_1/c \).

CCDC 1451014 contains the supplementary crystallographic data of 10. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., \( \text{C}_{18}\text{H}_{33}\text{O}_1\text{P}_1\cdot(\text{C}_6\text{H}_1\text{O}_4) \) unit cell parameters: a 10.874(2), b 18.629(3), c 11.959(1), \( P_2_1/c \).

CCDC 1561375 contains the supplementary crystallographic data of 11. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., \( \text{C}_{18}\text{H}_{33}\text{O}_1\text{P}_1\cdot(\text{C}_7\text{H}_1\text{O}_4) \) unit cell parameters: a 10.841(2), b 18.222(4), c 12.877(3), \( P_2_1/c \).

CCDC 1449062 contains the supplementary crystallographic data of 12. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., \( \text{C}_{18}\text{H}_{33}\text{O}_1\text{P}_1\cdot(\text{C}_8\text{H}_1\text{O}_4) \) unit cell parameters: a 19.226(0), b 10.972(3), c 25.247(4), \( C_{2/c} \).

CCDC 1044831 contains the supplementary crystallographic data of 14. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., \( [(\text{C}_{26}\text{H}_{24}\text{O}_2\text{P}_2)\cdot(\text{C}_3\text{H}_5\text{O}_4)_2] \) unit cell parameters: a 10.8389(17), b 19.838(3), c 15.277(2), \( P_2_1/c \).

CCDC 1449063 contains the supplementary crystallographic data of 15. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., \( [(\text{C}_{26}\text{H}_{24}\text{O}_2\text{P}_2)\cdot(\text{C}_3\text{H}_1\text{O}_4)_2] \) unit cell parameters: a 8.794(4), b 12.076(3), c 17.271(4), \( P_2_1/n \).
Centre via www.ccdc.cam.ac.uk/data_request/cif., $\text{C}_{25}\text{H}_{22}\text{O}_2\text{P}_2\cdot(\text{C}_3\text{H}_8\text{O}_4)$ unit cell parameters: a 23.661(2), b 11.106(0), c 21.401(6), $\text{Pbcn}$.


(53) CCDC 1561377 contains the supplementary crystallographic data of 16. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., $\text{C}_{18}\text{H}_{33}\text{O}_4\text{P}_1\cdot(\text{C}_6\text{H}_7\text{O}_3)$ unit cell parameters: a 11.055(1), b 18.209(2), c 11.971(9), $\text{P}2_1/c$. 

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(74) CCDC 1449057 contains the supplementary crystallographic data of 18 for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_rdquest/cif., \([\text{C}_{26}\text{H}_{24}\text{O}_{2}\text{P}_{2}(\text{C}_{8}\text{H}_{18}\text{O}_{6})]\), unit cell parameters: \(a\ 8.635(2)\), \(b\ 9.022(9)\), \(c\ 11.547(7)\), \(P-1\).

CCDC 1449061 contains the supplementary crystallographic data of 19 for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., C₅H₁₀O₄ unit cell parameters: a 8.9984(5), b 8.984(5), c 8.500(7), P₄ᵥ₂₁₂.

CCDC 1452863 contains the supplementary crystallographic data of 20 for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif., C₅H₁₀O₆ unit cell parameters: a 5.566(1), b 15.416(7), c 8.854(5), P₂₁/n.
APPENDIX A

NMR SPECTRA

**Figure A.1.** $^1$H NMR spectrum of 1 in CDCl$_3$.

**Figure A.2.** $^{13}$C{$^1$H} NMR spectrum of 1 in CDCl$_3$. 
Figure A.3. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of 1 in CDCl$_3$.

Figure A.4. $^1\text{H}$ NMR spectrum of 1 in acetone-d$_6$. 
**Figure A.5.** $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of 1 in acetone-$d_6$.

**Figure A.6.** $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of 1 in acetone-$d_6$. 
Figure A.7. $^1$H NMR spectrum of 4 in CDCl$_3$.

Figure A.8. $^{13}$C{$^1$H} NMR spectrum of 4 in CDCl$_3$. 
Figure A.9. Expansion of aryl region of $^{13}\text{C}[^{1}\text{H}]$ NMR spectrum of 4 in CDCl$_3$.

Figure A.10. $^{31}\text{P}[^{1}\text{H}]$ NMR spectrum of 4 in CDCl$_3$. 
Figure A.11. $^1$H NMR spectrum of 4 in acetone-$d_6$.

Figure A.12. $^{13}$C[$^1$H] NMR spectrum of 4 in acetone-$d_6$. 
Figure A.13. $^{13}$C($^1$H) NMR spectrum of 4 in acetone-$d_6$, aryl region expansion.

Figure A.14. $^{31}$P($^1$H) NMR spectrum of 4 in acetone-$d_6$. 
Figure A.15. $^1$H NMR spectrum of 5 in CDCl$_3$ (top), alkyl region expansion (bottom).
Figure A.16. $^{13}$C{$^1$H} NMR spectrum of 5 in CDCl$_3$.

Figure A.17. $^{13}$C{$^1$H} NMR spectrum of 5 in CDCl$_3$, alkyl region expansion.
Figure A.18. $^{13}$C, $^1$H COSY NMR spectrum of 5 in CDCl$_3$. 
Figure A.19. $^{31}\text{P}[^{1}\text{H}]$ NMR spectrum of 5 in CDCl$_3$.

Figure A.20. $^{1}\text{H}$ NMR spectrum of 5 in acetone-$d_6$. 
Figure A.21. $^1$H NMR spectrum of 5 in acetone-$d_6$, alkyl region expansion.

Figure A.22. $^{13}$C{$^1$H} NMR spectrum of 5 in acetone-$d_6$. 
Figure A.23. $^{13}$C($^1$H) NMR spectrum of 5 in acetone-$d_6$, alkyl region expansion.

Figure A.24. $^{31}$P($^1$H) NMR spectrum of 5 in acetone-$d_6$. 
Figure A.25. $^1$H NMR spectrum of 6 in CDCl$_3$.

Figure A.26. $^{13}$C($^1$H) NMR spectrum of 6 in CDCl$_3$. 
Figure A.27. $^{31}\text{P}[^1\text{H}]$ NMR spectrum of 6 in CDCl$_3$.

Figure A.28. $^1\text{H}$ NMR spectrum of 6 in C$_6$D$_6$. 

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Figure A.29. $^{13}$C{$^1$H} NMR spectrum of 6 in C$_6$D$_6$.

Figure A.30. $^{31}$P{$^1$H} NMR spectrum of 6 in C$_6$D$_6$. 

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Figure A.31. $^1$H NMR spectrum of 7 in CDCl$_3$ (top), alkyl region expansion (bottom).
Figure A.32. $^{13}$C/$^1$H NMR spectrum of 7 in CDCl$_3$.

Figure A.33. $^{13}$C/$^1$H NMR spectrum of 7 in CDCl$_3$, alkyl region expansion.
Figure A.34. $^{31}\text{P}^{1\text{H}}$ NMR spectrum of 7 in CDCl$_3$. 
Figure A.35. $^1$H NMR spectrum of 8 in CDCl$_3$.

Figure A.36. $^1$H NMR spectrum of 8 in CDCl$_3$, alkyl region expansion.
Figure A.37. $^{13}\text{C}[^1\text{H}]$ NMR spectrum of 8 in CDCl$_3$.

Figure A.38. $^{13}\text{C}[^1\text{H}]$ NMR spectrum of 8 in CDCl$_3$, alkyl region expansion.
Figure A.39. $^{31}\text{P}^{\text{'H}}$ NMR spectrum of 8 in CDCl$_3$. 
Figure A.40. $^1$H NMR spectrum of 9 in CDCl$_3$.

Figure A.41. $^1$H NMR spectrum of 9 in CDCl$_3$, alkyl region expansion.
Figure A.42. $^{13}$C($^1$H) NMR spectrum of 9 in CDCl$_3$.

Figure A.43. $^{13}$C($^1$H) NMR spectrum of 9 in CDCl$_3$, alkyl region expansion.
Figure A.44. $^{31}\text{P}^{[\text{H}]}$ NMR spectrum of 9 in CDCl$_3$. 

$^{31}\text{P}$ NMR

CDCl$_3$

CIPPh$_2$

57.14

$\delta$ (ppm)
Figure A.45. $^1$H NMR spectrum of 10 in CDCl$_3$.

Figure A.46. $^1$H NMR spectrum of 10 in CDCl$_3$, alkyl region expansion.
Figure A.47. $^{13}\text{C}^{'\text{H}}$ NMR spectrum of 10 in CDCl$_3$.

Figure A.48. $^{13}\text{C}^{'\text{H}}$ NMR spectrum of 10 in CDCl$_3$, alkyl region expansion.
Figure A.49. $^{31}\text{P}$-$^1\text{H}$ NMR spectrum of 10 in CDCl$_3$. 
Figure A.50. $^1$H NMR spectrum of 11 in CDCl$_3$.

Figure A.51. $^1$H NMR spectrum of 11 in CDCl$_3$, alkyl region expansion.
Figure A.52. $^{13}$C($^1$H) NMR spectrum of 11 in CDCl$_3$.

Figure A.53. $^{13}$C($^1$H) NMR spectrum of 11 in CDCl$_3$, alkyl region expansion.
Figure A.54. $^{31}\text{P}^{1\text{H}}$ NMR spectrum of 11 in CDCl$_3$. 
Figure A.55. $^1$H NMR spectrum of 12 in CDCl$_3$.

Figure A.56. $^1$H NMR spectrum of 12 in CDCl$_3$, alkyl region expansion.
Figure A.57. $^{13}$C-$^1$H NMR spectrum of 12 in CDCl$_3$.

Figure A.58. $^{13}$C-$^1$H NMR spectrum of 12 in CDCl$_3$, alkyl region expansion.
Figure A.59. $^{31}$P{¹H} NMR spectrum of 12 in CDCl$_3$. 
Figure A.60. $^1$H NMR spectrum of 13 in CDCl$_3$.

Figure A.61. $^1$H NMR spectrum of 13 in CDCl$_3$, aryl region expansion.
Figure A.62. $^{13}$C($^1$H) NMR spectrum of 13 in CDCl$_3$.

Figure A.63. $^{13}$C($^1$H) NMR spectrum of 13 in CDCl$_3$, aryl region expansion.
Figure A.64. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of 13 in CDCl$_3$.

Figure A.65. $^1\text{H}$ NMR spectrum of 13 in acetone-d$_6$. 
Figure A.66. $^1$H NMR spectrum of 13 in acetone-$d_6$, aryl region expansion.

Figure A.67. $^{13}$C[$^1$H] NMR spectrum of 13 in acetone-$d_6$. 

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Figure A.68. $^{13}$C($^1$H) NMR spectrum of 13 in acetone-$d_6$, aryl region expansion.

Figure A.69. $^{31}$P($^1$H) NMR spectrum of 13 in acetone-$d_6$. 
**Figure A.70.** $^1$H NMR spectrum of 14 in CDCl$_3$.

**Figure A.71.** $^{13}$C($^1$H) NMR spectrum of 14 in CDCl$_3$. 
Figure A.72. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of 14 in CDCl$_3$, aryl region expansion.

Figure A.73. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of 14 in CDCl$_3$. 
Figure A.74. $^1$H NMR spectrum of 15 in CDCl$_3$.

Figure A.75. $^1$H NMR spectrum of 15 in CDCl$_3$, aryl region expansion.
Figure A.76. $^{13}$C{$^{1}$H} NMR spectrum of 15 in CDCl$_3$.

Figure A.77. $^{13}$C{$^{1}$H} NMR spectrum of 15 in CDCl$_3$, aryl region expansion.
Figure A.78. $^{31}\text{P}^{\text{1H}}$ NMR spectrum of 15 in CDCl$_3$. 

$^{31}\text{P NMR}$

CDCl$_3$

$\delta$ (ppm)
Figure A.79. $^{13}$C NMR spectrum of 4 in benzene after heating at 90 °C for 3 days.
Figure A.80. $^1$H NMR spectrum of 16 in CDCl$_3$.

Figure A.81. $^1$H NMR spectrum of 16 in CDCl$_3$, alkyl region expansion.
Figure A.82. $^{13}$C{$^1$H} NMR spectrum of 16 in CDCl$_3$.

Figure A.83. $^{13}$C{$^1$H} NMR spectrum of 16 in CDCl$_3$, alkyl region expansion.
Figure A.84. $^{31}\text{P}^{[1\text{H}]}$ NMR spectrum of 16 in CDCl$_3$. 

$^{31}\text{P}$ NMR
CDCl$_3$

53.34
Figure A.85. $^1$H NMR spectrum of 1,1,2,2-tetraphenyldiphosphine in CDCl$_3$.

Figure A.86. $^1$H NMR spectrum of 1,1,2,2-tetraphenyldiphosphine in CDCl$_3$, aryl region expansion.
Figure A.87. $^{13}\text{C}^{1}\text{H}$ NMR spectrum of 1,1,2,2-tetraphenyl-diphosphine in CDCl$_3$.

Figure A.88. $^{13}\text{C}^{1}\text{H}$ NMR spectrum of 1,1,2,2-tetraphenyl-diphosphine in CDCl$_3$, aryl region expansion.
**Figure A.89.** $^{13}$C, $^1$H HSQC NMR spectrum of 1,1,2,2-tetraphenyldiphosphine in CDCl$_3$. 
Figure A.90. $^{13}$C, $^1$H HMBC NMR spectrum of 1,1,2,2-tetraphenylidiphosphine in CDCl$_3$. 
Figure A.91. $^{31}\text{P}^{1\text{H}}$NMR spectrum of 1,1,2,2-tetraphenyldiphosphine in CDCl$_3$. 
Figure A.92. Oxidation of 1,1,2,2-tetraphenyldiphosphine in air over a period of 5 days.
Figure A.93. Stoichiometric oxidation of 1,1,2,2-tetraphenyldiphosphine with 5 as oxidant; starting phosphine in C<sub>6</sub>D<sub>6</sub> (bottom), product 1,1,2,2-tetraphenyldiphosphine dioxide and consumed adduct in C<sub>6</sub>D<sub>6</sub> (middle), and 1,1,2,2-tetraphenyldiphosphine dioxide isolated via simple filtration and dissolved in CDCl<sub>3</sub> (top).
Figure A.94. $^1$H NMR spectrum of 1,1,2,2-tetraphenyldiphosphine dioxide (17) in CDCl$_3$.

Figure A.95. $^1$H NMR spectrum of 17 in CDCl$_3$, aryl region expansion.
Figure A.96. $^{13}$C{\(^1\)H} NMR spectrum of 17 in CDCl$_3$.

Figure A.97. $^{13}$C{\(^1\)H} NMR spectrum of 17 in CDCl$_3$, aryl region expansion.
Figure A.98. $^{31}\text{P}$ [$^1\text{H}$] NMR spectrum of 17 in CDCl$_3$. 
Figure A.99. $^1$H NMR spectrum of 18 in CDCl$_3$.

Figure A.100. $^1$HNMR spectrum of 18 in CDCl$_3$, alkyl region expansion.
Figure A.101. $^1$H NMR spectrum of 18 in CDCl$_3$, aryl region expansion.

Figure A.102. $^{13}$C{ $^1$H} NMR spectrum of 18 in CDCl$_3$. 

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Figure A.103. $^{13}\text{C}\{^{1}\text{H}\}$ NMR spectrum of 18 in CDCl$_3$, aryl region expansion.

Figure A.104. $^{31}\text{P}\{^{1}\text{H}\}$ NMR spectrum of 18 in CDCl$_3$. 
Figure B.1. IR spectra of aqueous H$_2$O$_2$ in 35 wt% (top) and 17 wt% (bottom).
Figure B.2. IR spectrum of 1.

Figure B.3. IR spectrum of 2.
Figure B. 4 IR spectra of 3 before (bottom) and after (top) deuteration.
Figure B.5. IR spectrum of 4.

Figure B.6. IR spectrum of 5.
**Figure B.7.** IR spectrum of 6.

**Figure B.8.** IR spectrum of 7.
Figure B.9. IR spectrum of 8.

Figure B.10. IR spectrum of 9.
Figure B.11. IR spectrum of 10.

Figure B.12. IR spectrum of 1,1-di(hydroperoxy)cyclohexane.
Figure B.13. IR spectrum of 11.

Figure B.14. IR spectrum of 1,1-di(hydroperoxy)heptane.
Figure B.15. IR spectrum of 12.

Figure B.16. IR spectrum of 13.
Figure B.17. IR spectrum of 14.

Figure B.18. IR spectrum of 15.
Figure B.19. IR spectrum of 16.

Figure B.20. IR spectrum of 18.
Figure C.1. Oxidizing power of 3 after being stored at the indicated conditions. 100% equals to 2 moles of active oxygen per mole of 3.
Figure C.2. Oxidizing power of 4 after being stored at the indicated conditions. 100% equals to 2 moles of active oxygen per mole of 4.
Figure C.3. Oxidizing power of 6 after being stored at the indicated conditions. 100% equals to 2 moles of active oxygen per mole of 6.

Table C.1. Decomposition temperature of adducts 4-15.

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