Reactions of tert-Butylperoxy Esters, XIII
Reactions of Dialkyl tert-Butylperoxy Phosphates with Amines

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tert-Butylperoxy Esters, Dialkyl Cycloalkylammonium Phosphates, tert-Butylperoxy Phosphates, Dialkyl Phosphates, Amines

The interaction of dialkyl tert-butylperoxy phosphates, \((R'O)P(O)OOCH\) (1) with primary and secondary cycloalkylamines, \(R'R'''NH\), \(R' = \text{cyclo-C}_6\text{H}_{11}\), \(R'''' = \text{H} ; R' = R'' = \text{cyclo-C}_6\text{H}_{11} (2)\) in the presence and absence of water, produces the corresponding dialkyl cycloalkyl ammonium phosphates, \((R'O)P(O)O-N'\text{H}_2R'' (3)\), and tert-butanol. In carbon tetrachloride the reaction produces in addition to 3 the corresponding cyclohexylammonium chloride. Possible mechanisms of the reaction are discussed.

Introduction

The reaction of organophosphorus compounds with hydrogen peroxide in the presence of amines to produce colored products is known as the Schonemann reaction and it forms the basis of a sensitive method for the determination of phosphorus-containing nerve gases\(^1\)\(^{-}\)\(^3\). The reactions of isopropyl methylphosphono-fluoridate (Sarin)\(^4\)\(^{-}\)\(^6\) and diethyl p-nitrophenyl phosphate \(^1\)\(^{-}\)\(^3\)\(^,\)\(^7\) with hydrogen peroxide in aqueous alkaline solution in the absence of amines involve rapid nucleophilic attack by the hydroperoxy anion on the phosphorus ester. The peroxyacid then slowly undergoes either a bimolecu-

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\(^c\) Preliminary results were communicated in G. Sosnovsky and E. H. Zaret, Chem. Ind. 1967, 1297.

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Although organophosphate esters are found in all living systems many organophosphorus compounds are extremely toxic and have been used as insecticides and war gases. The toxicity of such compounds, e.g. Sarin, is ascribed to their ability to inhibit, through phosphorylation of histidine or serine or both, cholinesterase-type enzymes.

Disopropyl tert-buty1peroxy phosphate (1, \(R = i-C_3H_7\)) was shown in our laboratory\(^9\) to be a mild cholinesterase inhibitor in rats. Therefore, it was of interest to investigate the interaction of peroxyesters (1) with imidazole and histidine. Such a study is complicated by the extreme instability of dialkyl phosphorylated imidazolide\(^1\)\(^-\)\(^1\)\(^1\)\(^1\)\(^1\)\(^1\)\(^1\) and histidine derivatives. Thus, the reactions of peroxyesters (1) with cyclo-alkyl amines were chosen as model systems.
Results

The reaction of peroxyesters (1) \( (R = \text{C}_2\text{H}_5, \text{i-C}_3\text{H}_7) \) with cyclohexyl- \( (2, R' = \text{cyclo-C}_6\text{H}_{11}; R'' = \text{H}) \) and dicyclohexylamine \( (2, R' = R'' = \text{cyclo-C}_6\text{H}_{11}) \) yields, both in the presence and absence of water, the corresponding amine salt of the cognate phosphoric acid (3) and tert-butanol as the major products (Table I).

\[
\begin{align*}
\text{RO}_2\text{P(O)}\text{OCMe}_3 + R'R''\text{NH} &\rightarrow \text{RO}_2\text{P(O)}\text{O} + \text{H}_2\text{R'R''} + \text{Me}_3\text{COH} \\
\text{R} &\text{ = C}_2\text{H}_5, \text{i-C}_3\text{H}_7, R' = \text{cyclo-C}_6\text{H}_{11}, \text{R''} = \text{H}, \text{cyclo-C}_6\text{H}_{11}.
\end{align*}
\]

The reaction of peroxyesters (1) \( (R = \text{C}_3\text{H}_7, \text{n-C}_4\text{H}_9) \) with piperidine, phenethylamine, diphenylamine, aniline, and triethylamine failed to produce isolatable crystalline salts. However, the IR spectrum of each of the reaction mixtures evidenced the band at approximately 2200 cm\(^{-1}\) characteristic of ammonium salts. The reaction of peroxyester (1) \( (R = \text{i-C}_3\text{H}_7) \) with benzylamine at 40 °C did not proceed and the peroxyester and amine were recovered by distillation.

In addition to the major products the reactions produce intractable colored oils. In the case of the interaction of peroxyester (1) \( (R = \text{i-C}_3\text{H}_7) \) with cyclohexylamine in benzene, traces of cyclohexanone oxime, diisopropyl N-cyclohexylphosphoramidate \( (4, R = \text{i-C}_3\text{H}_7; R' = \text{cyclo-C}_6\text{H}_{11}) \) and at least two unknown components have been elucidated by tlc analysis of the residual colored oil. In addition to the tert-butanol, the volatile products have been shown by glc to contain traces of acetone and methanol. In order to obtain some clues on the mechanism of the reaction of peroxyesters (1) and amines (2), the reaction was carried out in carbon tetrachloride. The reaction of amines with carbon tetrachloride has been shown\(^{12-13}\) to produce the corresponding amine hydrochlorides among other products. The reaction seems to involve ionic, charge transfer, and radical species, and therefore, one could assume that this solvent might have an influence on our reaction. However, the results shown in Table I indicate that no substantial change of product composition has occurred. Thus, the reaction of equimolar amounts of diisopropyl tert-butylperoxy phosphate (1, \( R = \text{i-C}_3\text{H}_7 \)) and cyclohexylamine in carbon tetrachloride solution at 25 °C produces a 26% yield of cyclohexylammonium chloride and a 26% yield of diisopropyl cyclohexylammonium phosphate \( (3, R = \text{i-C}_3\text{H}_7; R' = \text{cyclo-C}_6\text{H}_{11}; \text{R''} = \text{H}) \).

<table>
<thead>
<tr>
<th>Peroxyester ( R ) mol</th>
<th>( R' )</th>
<th>( R'R''\text{NH} ) mol</th>
<th>Solvent</th>
<th>Time [h]</th>
<th>Temp [°C]</th>
<th>Salt 3 Yield [%]</th>
<th>( R'R''\text{N} + H_2\text{Cl}^- ) Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.02</td>
<td>none</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>( \text{C}_6\text{H}_6 )</td>
<td>0.05</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.10</td>
<td>C( _6\text{H}_6 ) (25)</td>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.04</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.05</td>
<td>C( _6\text{H}_6 ) (15)</td>
<td>14</td>
<td>25</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.02</td>
<td>C( _6\text{H}_6 ) (25)</td>
<td>504</td>
<td>25</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.05</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.1</td>
<td>C( _6\text{H}_6 ) (50)</td>
<td>5</td>
<td>70</td>
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<tr>
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<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.04</td>
<td>C( _6\text{H}_6 ) (25)</td>
<td>18</td>
<td>40</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.04</td>
<td>C( _6\text{H}_6 ) (25)</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.25</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.05</td>
<td>CCl(_4) (50)</td>
<td>168</td>
<td>25</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.05</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.05</td>
<td>CCl(_4) (50)</td>
<td>168</td>
<td>25</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.05</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.05</td>
<td>CCl(_4) (50)</td>
<td>2</td>
<td>25</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.03</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.039</td>
<td>CCl(_4) (25)</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.02</td>
<td>CH(_3)OH (25)</td>
<td>9</td>
<td>25</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.02</td>
<td>CH(_3)OH (25)</td>
<td>17.5</td>
<td>40</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.04</td>
<td>CH(_3)OH (25)</td>
<td>18</td>
<td>40</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.04</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>0.048</td>
<td>28</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>H</td>
<td>0.02</td>
<td>cyclo-C( <em>6\text{H}</em>{11} )</td>
<td>0.02</td>
<td>48</td>
</tr>
</tbody>
</table>

\(^a\) Yield of salt 3 lowered by removal for titration of five 0.5-ml aliquots of the reaction mixture before the salt was isolated.  
\(^b\) Reaction carried out in the presence of 0.002 mol galvinoxyl (9).  
\(^c\) Yield of salt 3 lowered by removal for titration of three 0.5-ml aliquots before the salt was isolated.  
\(^d\) Reaction carried out in the presence of 0.05 mol water.  
\(^e\) Reaction carried out in a glovebox filled with dry nitrogen.  
\(^f\) In addition, 46 percent peroxyester was recovered.  
\(^g\) Reaction carried out in the presence of 0.01 mol sodium methoxide.
The mechanism by which peroxyesters (1) react with amines to produce the corresponding dialkyl N-alkylammonium phosphates remains unclear. Nucleophilic attack on phosphorus by the amine can be expected to yield the corresponding dialkyl N-alkylphosphoramidate (4) and tert-butyl hydroperoxide.

\[
\begin{align*}
\text{(RO)}_2\text{P(O)}\text{OOCMe}_3 + \text{R'NH}_2 &\rightarrow 1 \\
\text{(RO)}_2\text{P(O)}\text{NHR}'+ \text{Me}_3\text{COOH} &\rightarrow 4
\end{align*}
\]

Reaction of tert-butyl hydroperoxide with the amine might then yield the corresponding imine and tert-butanol.

\[
\begin{align*}
\text{Me}_3\text{COOH} + \text{R''CHNH}_2 &\rightarrow \\
\text{R''}=(-\text{CH}_2-)_{5}
\end{align*}
\]

Our results indicate that, although tert-butanol is a major product, the reaction of peroxyester (1) \((R=\text{C}_3\text{H}_7)\) with cyclohexylamine produces only traces of diisopropyl N-cyclohexylphosphoramidate (4, \(R=\text{C}_3\text{H}_7;\ R'=\text{cyclo-C}_8\text{H}_{11}\)) and cyclohexanone oxime.

Although phosphoramidates (4) are difficult to crystallize they are readily purified by sublimation as was shown using a synthetic mixture of a dialkyl cyclohexylammonium phosphate and the corresponding dialkyl N-cyclohexylphosphoramidate. Moreover, if 1 is interacted with cyclohexylamine in the presence of phosphoramidate (4) the reaction proceeds normally to yield salt 3, and 4 is recovered without difficulty. These observations, coupled with tlc evidence, lead us to believe that if phosphoramidates (4) had been formed in more than trace amounts we would have been able to isolate them.

There is evidence that nitrogen compounds will participate in nucleophilic displacements on oxygen even though the picture is often clouded by data which could be just as readily explained on the basis of a free radical interaction. Nucleophilic attack by the amine on the peroxide linkage can be envisioned as follows.

\[
\begin{align*}
\text{(RO)}_2\text{P(O)}\text{O}^\text{6-}\text{O}^\text{6-C(CH}_3)_3 + \text{R'NH}_2 &\rightarrow 1 \\
\text{[R'N-H}_2\text{OC(CH}_3)_3]\text{[(RO)}_2\text{P(O)}\text{O}^\text{-}] &\rightarrow 5
\end{align*}
\]

Intermediate 5 might then decompose by two different routes as shown in schemes (a) and (b).

(a) A proton transfer

\[
\begin{align*}
\text{[(R'N+H}_2\text{OOC(CH}_3)_3\text{)][(RO)}_2\text{P(O)}\text{O}^\text{-}] &\rightarrow 5 \\
\text{[R'NHOC(CH}_3)_3\text{]} &\rightarrow 6 \\
\text{[R'NHOC(CH}_3)_3\text{]} &\rightarrow 7
\end{align*}
\]

(b) A cleavage to give radicals

\[
\begin{align*}
\text{[(R'N+H}_2\text{OOC(CH}_3)_3\text{)][(RO)}_2\text{P(O)}\text{O}^\text{-}] &\rightarrow 5 \\
\text{R'N}^+\text{H}_2 + [(\text{CH}_3\text{O})^\text{+}(\text{CH}_3)_2] &\rightarrow 6 \\
\text{R'N}^+\text{H}_2 + [(\text{CH}_3\text{O})^\text{+}(\text{CH}_3)_2] &\rightarrow 7
\end{align*}
\]

An alternative mechanism (c) involving nucleophilic attack on the peroxide in a concerted manner can also be envisioned.

(c) A nucleophilic displacement

\[
\begin{align*}
\text{(RO)}_2\text{P(O)}\text{O}^\text{-}\text{OOC(CH}_3)_3 + \text{R'NH}_2 &\rightarrow \text{[R'NHOC(CH}_3)_3\text{]} \rightarrow 5 \\
\text{[R'NHOC(CH}_3)_3\text{]} &\rightarrow 6 \\
\text{[R'NHOC(CH}_3)_3\text{]} &\rightarrow 7
\end{align*}
\]

Our results do not permit a choice to be made between these or any other theoretically possible routes. On the basis of the product analysis, none of the routes shown is satisfactory since each involves some intermediates which were not intercepted. However, the reactions always produce.
intractable tars and, therefore, product analysis is not a sufficient criterion for determination of the mechanism. Routes (a) and (c) are intriguing in that they explain the production of salt 3 without involving water. However, failure to isolate either methyl isopropenyl ether (8) or the O-tert-butyl hydroxylamine derivative (7) is disappointing. Methyl isopropenyl ether (8) is a product of the thermal decomposition of peroxyesters and although it is very reactive under the present reaction conditions probably would have been detected. O-tert-Butyl N-cyclohexyl hydroxylamine (7, $R' = \text{cyclo-C}_6\text{H}_{11}$) has not been reported. However, an analogous compound, O,N-di-tert-butyl hydroxylamine (7, $R' = (\text{CH}_3)_3\text{C}$), has been prepared and isolated either as the hydrobromide or hydrochloride and has been shown to survive treatment with aqueous acid solution. Under the relatively mild reaction conditions employed in our experiments, it might be expected that 7 ($R' = \text{cyclo-C}_6\text{H}_{11}$) would have survived. The major fault with the sequences is that they do not explain the production of tert-butanol as a primary reaction product.

A mechanistic explanation of the products of the reactions of peroxyesters (1) with amines is made even more difficult by the following observations.

1. The reaction of peroxyester (1, $R = \text{C}_2\text{H}_5$) in benzene in the presence of cyclohexylamine is much faster than is the disappearance of the peroxyester in benzene alone and the rate appears to be dependent on the amine concentration. The amine thus appears to be inducing the decomposition of the peroxyester.

2. The reaction of peroxyesters (1) with cyclohexylamine is faster in ethanol than in benzene. This could imply an ionic intermediate in the rate determining step.

3. The reaction of peroxyesters (1) with cyclohexylamine is accelerated by the addition of galvinoxyl [2,6-di-tert-butyl-a-(3,5-di-tert-butyl-4-oxo-2,5-cyclohexadien-1-ylidene)] (9), a free radical trap which usually retards free radical reactions.

4. The reaction of peroxyesters (1) with cyclohexylamine is accelerated by the addition of 2,6-di-tert-butyl phenol, a compound which usually retards free radical reactions.

5. The reaction of peroxyesters (1) with cyclohexylamine is inhibited by the addition of azobisisobutyronitrile which usually serves as an initiator of free radical reactions. The inhibition, in this case, can be explained by a reaction sequence involving the oxidation of the amine by peroxyesters to a nitroxyl radical followed by the formation of an adduct arising from the combination of the nitroxyl with radicals derived from the azobisisobutyronitrile.

\[
\text{Oxidation by 1} \quad \begin{array}{c}
\text{R'NH}_2 \\
\text{R'NH}
\end{array} \quad \begin{array}{c}
\text{CN\(\text{C}(\text{CH}_3)_2\)} \\
\text{C(CH}_3)_3\text{CN}
\end{array}
\]

Observations 1, 2, and 4 point to an ionic reaction as the rate determining step. If the rate determining step is indeed ionic, then the acceleration of the amine-peroxyester interaction by galvinoxyl points to the formation of free radicals at some point in the process. This conclusion is based (a) upon the production of phenol (10) and aldehyde (11) from the interaction of galvinoxyl with tert-butoxy radicals, (b) upon the previously discussed interaction of inorganic peroxyphosphates with aromatic amines in the presence of carbonyl compounds, and (c) upon our observation that 2,6-di-tert-butyl phenol accelerates the amine-peroxyester interaction.

The results of this investigation, therefore, are not amenable to interpretation by either simple ionic or free radical mechanisms.

**Experimental**

Boiling points and melting points are uncorrected. IR spectra were obtained on a Perkin-Elmer model 137 spectrophotometer. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Illinois, or on an F & M Carbon Hydrogen Nitrogen Analyzer, model 185. Gas chromato-
graphic analyses were performed on Varian Aerograph instruments models 1700 and A-90P3 equipped with thermal conductivity detectors using wx filaments on a 10 ft × 1/8 in steel column packed with 100–200 mesh Porapak Q. Unless otherwise noted, materials were concentrated at less than 50 °C on a rotating evaporator at 10–15 mm Hg.

Dialkyl phosphoric acids were prepared by the method of Zwierzak and we have previously reported methods for the preparation of dialkyl tert-butylperoxy phosphates. Cyclohexylamine and the other amines were distilled over zinc under nitrogen and were stored over sodium hydroxide under nitrogen. Carbon tetrachloride was stored over calcium chloride. All other materials were the best commercial grade. With the exceptions of the solvents and inorganic reagents, all materials were purified by suitable techniques of distillation, recrystallization, sublimation, or chromatography before use. Unless otherwise noted, the petroleum ether used had b.p. 20–40 °C.

### Preparation of dialkyl ammonium phosphates (3).

**General procedure (Table II)**

Equimolar amounts of the dialkyl phosphoric acid (6) and the amine were stirred at ambient temperature in the solvent indicated. The reaction mixture was concentrated on a rotating evaporator and the residual oils were crystallized and recrystallized as indicated.

### Determination of active oxygen content of peroxyesters

The peroxide content of solutions of dialkyl tert-butylperoxy phosphates was determined in analogy with the method of Silbert and Swern. Thus, 15 ml glacial acetic acid containing 0.1% ferric chloride hexahydrate was purged with dry nitrogen for 5 min and 2 ml of a saturated aqueous solution of sodium iodide was added. The sample was added and the flask was stoppered and stored at ambient temperature for 5 min. Water (50 ml) was added followed by 5 ml of a stable starch solution (Fisher Chemicals, Inc.). The solution was titrated to a colorless end point with 0.1 N sodium thiosulfate solution. The procedure typically required a titration blank of 0.5 ml sodium thiosulfate.

### Thin layer chromatography

Peroxyphosphates and tert-butyl hydroperoxide were visualized by spraying the dried developed plate with a solution of sodium iodide in nitrogen-saturated glacial acetic acid. They appeared as brown spots on a white background. All phosphorus esters could be visualized by spraying the dried developed plates with concentrated hydrochloric acid followed by exposure to iodine vapor and appeared as brown spots on a white background. This procedure is capable of detecting 5 μg of phosphorus compound in a spot. The phosphor-amidates were visualized by exposing the dried developed plates to iodine vapor, and they appeared as brown spots on a white background.

### Reaction of diethyl tert-butyl peroxy phosphate (I, \( R = C_2H_5 \)) with cyclohexylamine

Diethyl tert-butylperoxy phosphate (11.31 g, 0.05 mol) was added in one portion to a solution of 9.2 g (0.10 mol) cyclohexylamine and 25 ml benzene and the resulting mixture was stored at room temperature for 16 h. Filtration of the precipitate which had formed yielded a hydroscopic solid, m.p. 78–80 °C. Repeated recrystallization of the solid from benzene yielded 7.2 g (53%) diethyl cyclohexylammonium phosphate monohydrate.

**Analysis:** Caled for \( C_{10}H_{23}NO_4P \cdot H_2O \): C 46.50; H 9.65. Found: C 46.44; H 9.55.

### Table II. Dialkyl cycloalkylammonium phosphates (3) prepared from dialkyl phosphates (6).

<table>
<thead>
<tr>
<th>Dialkyl phosphate (6)</th>
<th>Amine</th>
<th>Solvent</th>
<th>Reaction time [h]</th>
<th>Salt 3*</th>
<th>Recrys. solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃</td>
<td>H</td>
<td>CHCl₃</td>
<td>1</td>
<td>77.5–78.5</td>
<td>Ether-Pentane</td>
</tr>
<tr>
<td>i-Pr</td>
<td>H</td>
<td>C₂H₅</td>
<td>1</td>
<td>198–199</td>
<td>Acetone</td>
</tr>
<tr>
<td>n-Pr</td>
<td>H</td>
<td>C₂H₅</td>
<td>6</td>
<td>81.5–83</td>
<td>Ligroin or Ether</td>
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<tr>
<td>n-Bu</td>
<td>H</td>
<td>CHCl₃</td>
<td>1</td>
<td>81–82</td>
<td>Ether Pentane</td>
</tr>
<tr>
<td>i-Bu</td>
<td>H</td>
<td>C₂H₅</td>
<td>200–201.5</td>
<td>Ligroin-Acetone</td>
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<tr>
<td>Me</td>
<td>C₆H₁₁</td>
<td>CHCl₃</td>
<td>24</td>
<td>159.5–160.5</td>
<td>Acetone</td>
</tr>
<tr>
<td>Et</td>
<td>C₆H₁₁</td>
<td>CHCl₃</td>
<td>24</td>
<td>133.5–134.5</td>
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<td>C₂H₅</td>
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<td>172–173</td>
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</tr>
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<td>C₆H₁₁</td>
<td>C₂H₅</td>
<td>3</td>
<td>133–134</td>
<td>Acetone</td>
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<tr>
<td>n-Bu</td>
<td>C₆H₁₁</td>
<td>CCl₄</td>
<td>60</td>
<td>106–107</td>
<td>Ligroin</td>
</tr>
<tr>
<td>i-Bu</td>
<td>C₆H₁₁</td>
<td>C₂H₅</td>
<td>3</td>
<td>165.0–165.5</td>
<td>Acetone</td>
</tr>
<tr>
<td>i-Bu</td>
<td>C₆H₁₁</td>
<td>C₂H₅</td>
<td>1</td>
<td>181.0–181.5</td>
<td>Benzene</td>
</tr>
</tbody>
</table>

* C, H, N analyses were within 0.3% of the theoretical values.
Reaction of diisopropyl tert-butylperoxy phosphate \((1, R = i-C_3H_7)\) with cyclohexylamine in the absence of solvent

Cyclohexylamine (1.98 g, 0.02 mol) was added in one portion without cooling to 5.08 g (0.02 mol) diisopropyl tert-butylperoxy phosphate. The resulting mixture was stirred at room temperature for 12 h during which time it slowly solidified. Repeated recrystallization of the resulting brown solid from acetone yielded 3.1 g (55\%) diisopropyl cyclohexylammonium phosphate: m.p. 192–196 °C.

Reaction of diisopropyl tert-butylperoxy phosphate \((1, R = i-C_3H_7)\) with cyclohexylamine in benzene solution

I. At ambient temperature

A. A solution of 10.2 g of (0.04 mol) diisopropyl tert-butylperoxy phosphate, 5 g (0.05 mol) cyclohexylamine, and 15 ml benzene was stirred at ambient temperature for 14 h. The mixture was concentrated. Crystallization of the residual oil from acetone yielded 6.0 g (54\%) diisopropyl cyclohexylammonium phosphate.

B. A solution of 5.08 g (0.02 mol) diisopropyl tert-butylperoxy phosphate, 1.98 g (0.02 mol) cyclohexylamine, and 25 ml benzene was stirred at room temperature for 3 weeks and was then concentrated to an orange oil. Crystallization of this oil under 20–40 °C petroleum ether yielded 4.7 g (84\%) of a tan solid. Recrystallization of this solid produced 1.5 g diisopropyl cyclohexylammonium phosphate: m.p. 184–187 °C; and an uncrystallizable oil whose IR spectrum was essentially superimposable with the IR spectrum of pure diisopropyl cyclohexylammonium phosphate.

II. At 70 °C

A. Into a 100 ml, 3-necked, round bottom flask equipped with thermometer, reflux condenser, drying tube, a —78 °C trap, magnetic stirrer, and gas buret filled with saturated sodium chloride solution, and the entire system purged with nitrogen gas, was added a solution of 12.7 g (0.05 mol) diisopropyl tert-butylperoxy phosphate and 25 ml benzene. To this solution was added a solution of 9.9 g (0.10 mol) cyclohexylamine in 25 ml benzene and the reaction flask was immersed in a 70 °C oil bath. When thermal equilibrium had been achieved (15 min) the flow of nitrogen gas was stopped and the gas buret opened. Gas evolution occurred for the first hour and 59 ml (5.3\%) of unidentified gas was collected. The mixture was heated at 70 °C for 4 h more and was then kept overnight at room temperature. Concentration by distillation of the benzene at atmospheric pressure under nitrogen gave a black residue. Crystallization of the residue from acetone yielded 11 g (79\%) diisopropyl cyclohexylammonium phosphate, m.p. 194–196 °C; and 7.4 g of a black uncrystallizable oil which was analyzed by tlc on alumina using benzene, ether, and ethyl acetate as eluants and was found to be comprised of at least five components of which diisopropyl N-cyclohexylphosphoramide, cyclohexanone oxime, and diisopropyl cyclohexylammonium phosphate were identified by comparison with authentic samples. The tlc investigation eliminated the possibility of the oil containing cyclohexylamine or cyclohexanone. The benzene distillate was shown by gle to contain tert-butanol (41\%) with traces of methanol, water and acetone.

B. A solution of 5.08 g (0.02 mol) diisopropyl tert-butylperoxy phosphate in 15 ml benzene was purged at room temperature with nitrogen. A solution of 3.96 g (0.04 mol) cyclohexylamine in 10 ml benzene was added in one portion and the reaction flask was immersed in a 40 °C oil bath. The reaction mixture was then concentrated. Repeated recrystallization of the residue from acetone yielded 3.8 g (68\%) diisopropyl cyclohexylammonium phosphate. Aliquots (0.05 ml) of the reaction mixture were periodically titrated for peroxide content.

Elapsed time [h]: 0 1 3 6 10.
Percent peroxide: 100 96 96 78 54.

A duplicate experiment was performed simultaneously; however, the amine solution also contained 0.84 g (0.002 mol) galvinoxyl. Analogous work-up after 1 h yielded 3.1 g (55\%) diisopropyl cyclohexylammonium phosphate. Titration of the reaction mixture after 1 h was not possible because the mixture had almost solidified.

Reaction of diisopropyl tert-butylperoxy phosphate \((1, R = i-C_3H_7)\) with cyclohexylamine in carbon tetrachloride

A. In the presence of water

A mixture of 6.35 g (0.025 mol) diisopropyl tert-butylperoxy phosphate, 4.95 g (0.05 mol) cyclohexylamine, 0.9 ml water, and 50 ml carbon tetrachloride was stirred at room temperature for 7 days. The reaction mixture was filtered to remove a small amount of cyclohexylammonium chloride. Recrystallization of the filtrate from ligroin yielded in several crops, 4 g (57\%) diisopropyl cyclohexylammonium phosphate: m.p. 191–193 °C.

B. In the absence of water

1. A solution of 4.95 g (0.05 mol) cyclohexylamine, 6.35 g (0.025 mol) diisopropyl tert-butylperoxy phosphate, and 50 ml carbon tetrachloride was stirred at ambient temperature for 7 days. The solution was filtered to remove 2 g (30\%) cyclohexylammonium chloride. The filtrate was concentrated. Crystallization of the residue from acetone yielded 2.1 g (30\%) diisopropyl cyclohexylammonium phosphate.

2. Cyclohexylamine (4.95 g, 0.05 mol) was added over 9 min at 22–25 °C to a solution of 6.35 g (0.025 mol) diisopropyl tert-butylperoxy phosphate and 50 ml carbon tetrachloride. The resulting
mixture was stirred at 25 °C for 2 h and was filtered to remove 1.1 g (16%) cyclohexylamine dichloride. The filtrate was concentrated. Crystallization of the residue from acetone yielded 1.5 g (21%) diisopropyl cyclohexylammonium phosphate; m. p. 186 °C.

3. A glove box was purged with dried (H₂SO₄) nitrogen and at intervals during the reaction the chamber’s drying-train was activated. The carbon tetrachloride (reagent grade) was dried over calcium chloride. The diisopropyl tert-butylperoxy phosphate was doubly distilled and was stored at —10 °C but was warmed to ambient temperature and opened in the glove box. A solution of 10.08 g (0.0394 mol) di-isopropyl c.p. tert-butylperoxy phosphate in 15 ml absolute ethanol (1:1) and benzene-ethyl acetate (4:1) solution of 0.54 g (0.01 mol) sodium methoxide, 1.98 g (0.02 mol) cyclohexylamine, 5.01 g (0.02 mol) diisopropyl tert-butylperoxy phosphate, and 25 ml methanol was stirred at ambient temperature for 9 h and was then concentrated to a yellow solid. Recrystallization of the solid from acetone yielded 1.8 g (32%) diisopropyl cyclohexylammonium phosphate, m. p. 194–196 °C.

**Reaction of diisopropyl tert-butylperoxy phosphate (I, R = i-C₃H₇) with cyclohexylamine in the presence of sodium methoxide**

A mixture of 0.54 g (0.01 mol) sodium methoxide, 1.98 g (0.02 mol) cyclohexylamine, 5.01 g (0.02 mol) diisopropyl tert-butylperoxy phosphate, and 25 ml methanol was stirred at 40 °C for 17.5 h and was concentrated to a yellow oil. Repeated recrystallization from acetone gave 1.8 g (32%) diisopropyl cyclohexylammonium phosphate, m. p. 194–196 °C; and 1.9 g of an intractable brown oil, nD²⁰ 1.4300.

**Reaction of diisopropyl tert-butylperoxy phosphate (I, R = i-C₃H₇) with cyclohexylamine in ethanol**

To a solution of 5.08 g (0.02 mol) diisopropyl tert-butylperoxy phosphate in 15 ml absolute ethanol which had been purged with dry nitrogen was added in one portion a solution of 3.96 g (0.04 mol) cyclohexylamine in 10 ml absolute ethanol. The reaction mixture was immediately immersed in a preheated 40 °C oil bath and 0.5 ml aliquots were periodically removed for titration of the peroxide content.

Elapsed time [h]: 0 3 7 17.
Percent peroxide: 100 98 20 0.

After 17 h the reaction mixture was concentrated. Repeated recrystallization of the residue from acetone yielded 3.1 g (56%) cyclohexylammonium phosphate, m. p. 186–192 °C.

An identical experiment was carried out in which the reaction residue was sublimated in an unsuccessful effort to isolate diisopropyl N-cyclohexylphosphoramidate had it been formed.

**Reaction of diethyl tert-butylperoxy phosphate (I, R = C₂H₅) with dicyclohexylamine in benzene**

A. Diethyl tert-butylperoxy phosphate (4.52 g, 0.02 mol) was added to 3.62 g (0.02 mol) dicyclohexylamine. The mixture was diluted with 10 ml benzene and was stirred in a stoppered flask for 2 days at ambient temperature. The mixture was filtered to remove 0.2 g dicyclohexylammonium chloride. The filtrate was concentrated leaving a darkbrown solid. Recrystallization of the solid from skellysolve B yielded 4.0 g (59%) diethyl dicyclohexylammonium phosphate, m. p. 138–139 °C, which was identified by comparison with an authen tic sample by tlc on silica gel G plates using acetone ethanol (1:1) and benzene-ethyl acetate (4:1) solutions as eluants and iodine to visualize the spots.

B. A solution of 6.50 g (0.029 mol) diethyl tert-butylperoxy phosphate, 10.5 g (0.048 mol) dicyclohexylamine, and 20 ml benzene was stored at room temperature for 39 h and was concentrated to a thick oil. Crystallization of the oil from petroleum ether yielded 5.27 g (54%) diethyl dicyclohexylammonium phosphate, m. p. 131–133 °C, a portion of which was recrystallized from cyclohexane yielding white crystals, m. p. 140–140.5 °C.

**Analysis:** Calculated for C₃₆H₇₄N₄O₄P: C 57.29; H 10.22; N 4.18. Found: C 57.47; H 10.41; N 4.32.

**Reaction of di-n-butyl tert-butylperoxy phosphate (I, R = n-C₄H₉) with cyclohexylamine and galvinoxyl. Determination of the volatile products**

A solution of 7.05 g (0.025 mol) di-n-butyl tert-butylperoxy phosphate, 1.05 g (0.0025 mol) galvinoxyl, 4.92 g (0.05 mol) cyclohexylamine, and 25 ml benzene was heated under nitrogen at 65 °C for 4 h. Nitrogen was gently bubbled through the reaction mixture for 1 h and 1.2 g of a benzene solution of the volatile products was collected in a tap at —78 °C. Analysis of this solution by glc on Porapak Q showed it to contain (% yield) water (1.6%), methanol (4%), acetone (0.8%), tert-butanol (9%), and an unidentified component in trace amounts.

The analogous reaction of a solution of 14.1 g (0.05 mol) di-n-butyl tert-butylperoxy phosphate, 4.95 g (0.05 mol) cyclohexylamine, and 50 ml...
benzene at 65 °C for 24 h yielded as identified by 
glc analysis (% yield) water (0.7%), methanol (1.5%), acetone (0.7%), and tert-butanol (1.4%).

**Reaction of diisopropyl phosphate** \((6, R = i-C_3H_7)\) with diisopropyl N-cyclohexylphosphoramidate 
\((4, R = i-C_3H_7; R' = cyclo-C_6H_{11})\)

A mixture of 2.73 g (0.015 mol) diisopropyl phosphate, 3.96 g (0.015 mol) diisopropyl N-cyclohexylphosphoramidate, 4 ml water, and 30 ml benzene was stirred at 60 °C for 24 h and was concentrated. Sublimation of the residual oil at 50 °C (0.1 mm) yielded 3.6 g (99%) diisopropyl N-cyclohexylphosphoramidate. The mother liquor was concentrated.

Effect of galvinoxyl, azobisisobutyronitrile (AIBN), and 2,6-di-tert-butyl phenol on the reactions of dialkyl tert-butoxyperoxy phosphates \((1, R = C_2H_5, i-C_3H_7)\) with cyclohexylamine. General procedure

A. Solutions of 2.26 g (0.01 mol) diethyl tert-butoxyperoxy phosphate, 10 ml benzene, and 0.002 mol of the additive, where required, were stirred at the temperature specified for 20 min under nitrogen. Then 1.98 g (0.02 mol) cyclohexylamine was injected and heat was applied. Aliquots (0.5 ml) were titrated for peroxide content periodically.

a. At 73 °C a solution of peroxyester \((1)\) in benzene contained 96% of the peroxide after 3 h.

b. At 73 °C a solution of peroxyester \((1)\) and the amine in benzene contained no titratable peroxide after 1 h.

c. At 73 °C a solution of peroxyester \((1)\), the amine, AIBN, and benzene contained 95% of the peroxide after 3 h.

d. At 73 °C a solution of peroxyester \((1)\), the amine, galvinoxyl, and benzene contained no peroxide after 0.25 h.

E. At 30 °C a solution of peroxyester \((1)\), the amine, and benzene contained 85% of the peroxide after 1 h.

f. At 30 °C a solution of peroxyester \((1)\), the amine, galvinoxyl, and benzene contained 33% of the peroxide after 1 h.

B. Analogous reactions using diisopropyl tert-butoxyperoxy phosphate \((1, R = i-C_3H_7)\), the additive, and benzene were performed at 73 °C.

a. A solution of 0.005 mol peroxyester \((1)\), 0.005 mol amine, and 10 ml benzene contained 68% of the peroxide after 40 min.

b. A solution of 0.005 mol peroxyester \((1)\), 0.01 mol amine, 0.0006 mol AIBN, and 10 ml benzene contained 75% of the peroxide after 40 min.

c. A solution of 0.005 mol peroxyester \((1)\), 0.108 mol amine, 0.0013 mol 2,6-di-tert-butyl phenol, and 10 ml benzene contained 37% of the peroxide after 40 min.

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2 B. Gehauf, Anal. Chem. 29, 278 [1957].