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Generation and Trapping of Monomeric Metaphosphoric Acid Esters in Solution: Mechanistic Investigation into the Fragmentation of Mixed Carbonic-Phosphoric Acid Anhydrides and the Chelotropic Breakdown of Cyclic Pyrocarbonate Esters

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ABSTRACT

The generation of alkyl-substituted monomeric metaphosphoric acid esters ($ROPO_2$) **4** *in solution is described, utilizing two different methods based on the condensation of alkyl phosphorodichloridates either with anhydrous potassium hydrogen carbonate or with the novel disodium pyrocarbonate salt* **5**, *which is formed in quantitative yield from diethyl pyrocarbonate by treatment with two equivalents of sodium trimethylsilanolate in THF at 0°C. The first method is believed to proceed via a transient mixed carbonic-phosphoric anhydride* **3**, *which decomposes at room temperature with release of 1 mol each of hydrogen chloride and carbon dioxide to produce* **4**. *In the other method, ^{31}P NMR spectroscopy indicated the involvement of a cyclic pyrocarbonate phosphate (2-alkoxy-1,3,5-trioxaphosphorinane-4,6-dione-2-oxide)* **6**, *which decomposed in situ with the release of 2 mol of carbon dioxide. In both cases, the metaphosphate thus formed spontaneously self-condensed to produce polymeric species with P–O–P bonds having characteristic ^{31}P NMR signals clustered in the δ −12 and −24 regions. When metaphosphate* **4** *is generated by either process in the presence of styrene oxide, polymerization is avoided, and trapping occurs with the exclusive formation of a diastereomeric mixture of 2-alkoxy-1,3,2-dioxaphospholane-2-oxides* **7** *(cis, trans). In order to shed some mechanistic light on the formation*

Dedicated to Prof. Louis D. Quin on the occasion of his retirement from the Department of Chemistry at the University of Massachusetts at Amherst.

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of 7, ^{31}P *NMR studies have been carried out on the individual trapping reactions between (−)-menthyl metaphosphate* **4d** *and racemic styrene oxide, as well as its optically pure forms. Based on evidence that these transformations proceed by inversion of configuration at the phenyl-bearing carbon of styrene oxide, a mechanism is invoked whereby the dipolar metaphosphate* **4d** *reacts both as an electrophile and as a nucleophile in a self-catalyzed process via the activated complex* **9d**. © *1996 John Wiley & Sons, Inc.*

INTRODUCTION

Derivatives of metaphosphoric acid of the type $ROPO_2$ (where R = aryl or alkyl) have been reported in the chemical literature for many years as transient species or reactive intermediates, being renowned for their potent electrophilic properties both in biological systems [1–3] and aromatic substitution reactions (phosphorylations) [4,5]. Of late, such monomeric metaphosphoric acid esters have become of much interest to the synthetic organic chemist due to their ability to phosphorylate such functional groups as alcohols [4a,4d,6], amines [4e,7], epoxides [8], and carbonyl compounds [9], as well as *OH* groups on the surfaces of solids (i.e., silica gel, alumina, and zeolites) [10]. Such is the extent of the interest in these species that, since 1981, there have been four reviews on the subject [1,3,11].

The earliest procedure for the generation of an alkyl-substituted metaphosphate was carried out in the gas phase by Clapp and Westheimer [4e], who, in 1974, produced methyl metaphosphate via a retro Diels–Alder reaction by subjecting methyl 2-butenylphostonate to pyrolysis at 650°C. Early work in our laboratory also concentrated on the gas phase and involved the pyrolysis of 2-substituted 1,3,2-dioxaphospholanes **1** at 800°C to generate metaphosphate species by extrusion of ethylene. Depending upon the nature of the 2-substituent, the metaphosphate followed different reaction pathways, reacting either by an electrophilic substitution (path 1) [5] as shown in Scheme 1 or by a cyclic, concerted elimination reaction involving as the key step an unusual 1,2-methyl shift induced by competing α-and γ-hydrogen abstractions with loss of metaphosphoric acid (path 2), as shown by deuterium labeling studies [12].

More recently, most attention in this area has focussed on the generation of alkyl metaphosphates in solution with many different routes being reported [6a,7b,13]. One of the most notable is that of Quin et al., which involves either the thermal [15] or photochemical [4a] fragmentation of the 2,3-oxaphosphabicyclo[2.2.2]octene ring system **2** (Scheme 2). It has also been reported [14] from the same laboratory that thermal fragmentation of *O*-ethyl phosphoramidic acids serves as a source of ethyl metaphosphate, albeit only with sterically demanding *N*-substituents.

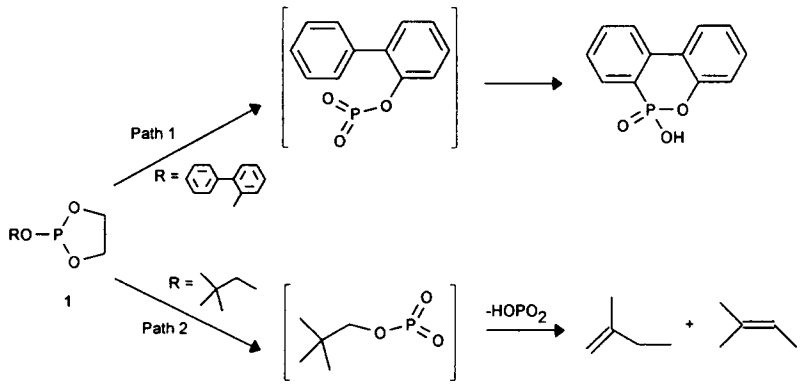
In our laboratory, initial attempts at the generation of alkyl metaphosphates in solution [8b] concentrated on the condensation of methyl phosphorodichloridate with potassium hydrogen carbonate to produce a transient mixed carbonic-phosphoric anhydride **3a**, which decomposed at room temperature with release of 1 mol of hydrogen chloride and carbon dioxide (Scheme 3) to produce methyl metaphosphate **4a**, as verified by trapping experiments with styrene oxide.

This article describes in detail our work in this area and demonstrates how this procedure can be extended to generate alkyl-substituted metaphosphates in general. Of particular interest is the case where the alkyl substituent is replaced by a menthyl group as a chiral source. When the resulting metaphosphate is trapped with both (*R*)- and (*S*)-styrene oxide, and the course of the reaction followed by ^{31}P NMR spectroscopy, important information is obtained about the reaction mechanism involving metaphosphates and epoxides. We also describe an alternative procedure for the generation of alkyl metaphosphates in solution based on the reaction of alkyl phosphorodichloridates with the novel disodium pyrocarbonate salt **5** (Scheme 4). The resulting cyclic pyrocarbonate phosphate **6** subsequently undergoes chelotropic breakdown with the release of 2 moles of carbon dioxide to produce the desired alkyl metaphosphates.

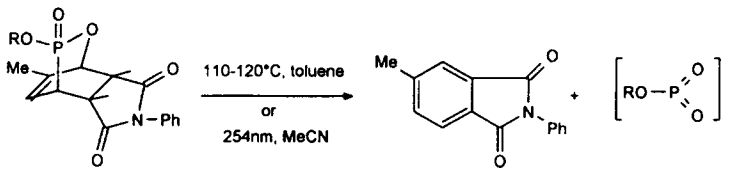
RESULTS AND DISCUSSION

Generation of Alkyl Metaphosphates by Reaction of Alkyl Phosphorodichloridates with Potassium Hydrogen Carbonate

We have previously demonstrated [8b] that reaction of methyl phosphorodichloridate with potassium hydrogen carbonate results in the generation of methyl metaphosphate in solution at room temperature. The course of this reaction is easily followed by ^{31}P NMR spectroscopy. The procedure simply involves the condensation of potassium hydrogen carbonate with methyl phosphorodichloridate in anhydrous dimethoxyethane (DME) at 0°C (Scheme 3) and then allowing the reaction mixture to warm to ambient temperature. At the start of the reaction, a single phosphorus signal is observed at δ 5.78, corresponding to the methyl phosphorodichloridate, which is



SCHEME 1



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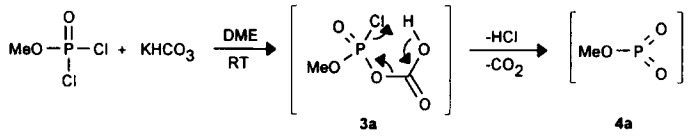

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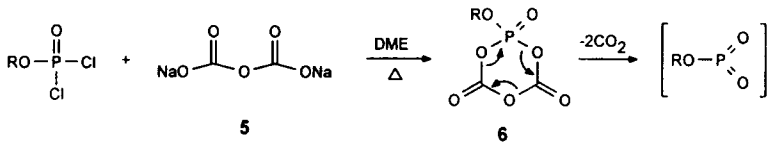
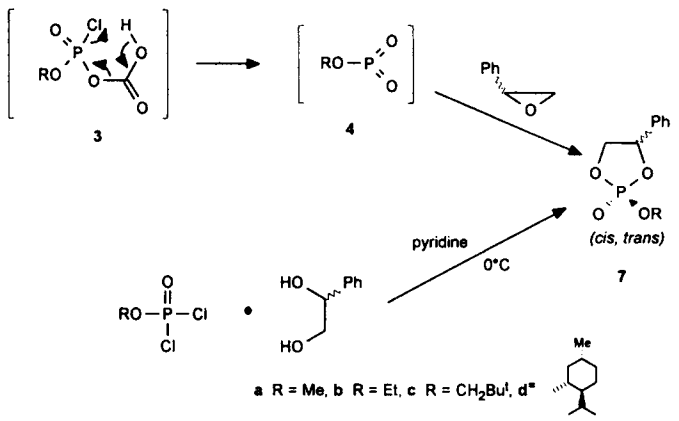


SCHEME 4

gradually replaced by peaks in the δ −12 and −24 regions. It is known [1] that when metaphosphates are generated in the absence of trapping reagents, they condense to give polyphosphates with characteristic ^{31}P NMR signals in such regions and so this was taken as strong evidence to support the generation of methyl metaphosphate. When the same reaction was repeated in the presence of styrene oxide, the signals at ca. δ −12 and −24 regions were not observed, but, instead, a closely matched pair of peaks at δ 16.83 and 17.03 appeared and grew in intensity as the reaction proceeded to completion. Such signals in the δ 16–18 region are unique to cyclic phosphates with five-membered rings [16], and by comparison with an authentic sample, prepared by the condensation of 1-phenylethanediol with methyl phosphorodichloridate in the presence of triethylamine at 0°C, the signals were identified as being due to a diastereomeric mixture of 2-methoxy-4-phenyl-1,3,2-dioxaphospholane-2-oxide **7a**.

The proposed mechanism is shown in Scheme 5 and involves generation of methyl metaphosphate **4a** by fragmentation of the mixed carbonic-phosphoric anhydride **3a** (which is transient and is not observed in the ^{31}P NMR spectrum) and its interception by styrene oxide to give rise to the 1,3,2-dioxaphospholane-2-oxide **7a**. This observation is in keeping with a similar trapping reaction reported by Quin and coworkers [8a] following the generation of ethyl metaphosphate by thermal fragmentation of the 2,3-oxaphosphabicyclo[2.2.2]octene ring system **2** (Scheme 2) and provides further compelling evi-



SCHEME 5

dence for the intermediacy of methyl metaphosphate in the foregoing reaction despite the failure to detect the intermediate **3a**.

In order to give this method of generating alkyl metaphosphates greater practical value, and moreover to emphasize its versatility, the method was extended to include ethyl **4b**, neopentyl **4c**, and metaphosphate **4d** derived from (−)-menthol. For every case, in the absence of trapping agents, signals in the δ −12 and −24 regions were observed in keeping with the products expected from the self-condensation reactions of monomeric alkyl metaphosphates. In the presence of styrene oxide, the reaction is diverted to afford exclusively 1,3,2-dioxaphospholane-2-oxides **7b–d**, all of which displayed a characteristic pair of signals in the δ 16–18 region.

It is of particular interest to note that, when metaphosphate **4d** was generated in the presence of *racemic* styrene oxide, the ^{31}P NMR spectrum consisted of not two, but four closely spaced signals of almost 1:1:1:1 intensity in the δ 16–18 region. The explanation for the presence of four signals on this occasion is that, for the first time, all four possible diastereomers are being observed due to the chiral discrimination provided by the enantiomerically pure (−)-menthyl component of the 1,3,2-dioxaphospholane-2-oxide **7d**. In all previous examples that have been reported [8], the generated alkyl metaphosphates contain nonchiral components, and although four diastereomers are still present in the trapped products, two pairs are present as enantiomers, which are indistinguishable by ^{31}P NMR spectroscopy, thus giving rise to only the two signals. The four possible products (and enantiomeric pairs) from the reaction of alkyl metaphosphates with racemic styrene oxide are shown in Figure 1.

We believe that the ability of the chiral component in the 1,3,2-dioxaphospholane-2-oxide **7d** to facilitate the observation of all four possible diastereomers (Figure 1) in the ^{31}P NMR spectrum provides us with a mechanistic tool that can be used to provide important information on the course of reaction of alkyl metaphosphates with epoxides, a reaction that is still not yet fully understood (vide infra).

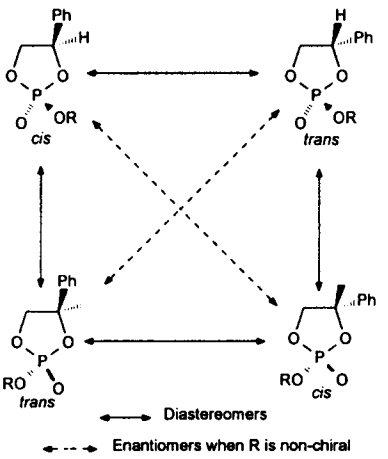


FIGURE 1 All four possible diastereomeric products from the trapping of metaphosphates ($ROPO_2$) with styrene oxide.

Generation of Alkyl Metaphosphates by Reaction of Alkyl Phosphorodichloridates with Disodium Pyrocarbonate 5

Our initial attempts to prepare dialkali pyrocarbonate salts revolved around the hydrolysis of diethyl pyrocarbonate with potassium hydroxide at 0°C [8b]. Unfortunately, detailed examination of the product obtained showed that, during its attempted preparation, decomposition of dipotassium pyrocarbonate had occurred in situ, despite careful precau-

tions, to afford potassium hydrogen carbonate, a result that led to the work detailed earlier. Renewed attempts to synthesize such pyrocarbonate salts were given encouragement by the work of Laganis and Chenard [17], who found that alkali metal trimethylsilanolates converted carboxylic acid derivatives (acid chlorides and esters) into their corresponding anhydrous salts under mild anhydrous conditions. Application of this method to diethyl pyrocarbonate by treatment with two equivalents of sodium trimethylsilanolate in THF at 0°C led to the precipitation of a colorless solid in almost quantitative yield. FAB-MS analysis of the solid [$(M^+ + 1)$ 150.96199, $C_2HNa_2O_5$ requires 150.96200] confirmed its identity to be disodium pyrocarbonate **5**, formed from diethyl pyrocarbonate by spontaneous elimination of volatile ethyl trimethylsilyl ether (Scheme 6). Additional evidence to support the structure of **5** came from spectroscopic studies, viz., solid-state ^{13}C NMR spectroscopy that showed a singlet at δ 162.2 (C = O) and the shift observed for the carbonyl group in the FT-IR spectrum (1610 vs. 1820, 1760 cm^{-1} for the diethyl ester).

Thermal gravimetric analysis (TGA) of a sample of the disodium pyrocarbonate salt **5** also revealed that, over a temperature range of 65–145°C, the salt underwent decomposition via loss of 1 mol of carbon dioxide to produce sodium carbonate (Scheme 6). Analysis of the residue from TGA by FT-IR spectroscopy confirmed the residue to be sodium carbonate by comparison with an authentic sample.

The reaction of disodium pyrocarbonate **5** with methyl phosphorodichloridate was carried out in boiling anhydrous DME, and the course of the reaction followed by ^{31}P NMR spectroscopy. After only 1 hour, it was evident that methyl metaphosphate **4a** had in fact been generated due to the disappearance of the peak for the starting methyl phosphorodichloridate at δ 5.78 and its replacement by the characteristic signals in the δ −12 and −24 regions due to polyphosphates (vide supra). A minor signal at δ 0.13 was also observed and was assigned to methyl phosphonic acid. A possible mechanism for the intermediacy of **4a** is shown in Scheme 7 and involves the initial formation of cyclic pyrocarbonate phosphate (2-methoxy-1,3,5-trioxaphosphorinane-4,6-dione-2-oxide) **6a**, which subsequently undergoes chelotropic breakdown with the release of 2 moles of carbon dioxide. When the ^{31}P NMR spectrum of the reaction mixture was recorded after only 15 minutes, it was found that, apart from starting material and the first traces of polyphosphates from the self-condensation of methyl metaphosphate, peaks for two major phosphorus-containing products had appeared at δ −4.04 and −16.69. These signals gradually disappeared to be replaced after 1 hour by absorbances for polyphosphates in the δ −12 and −24 regions. We believe that the signal at −16.69 is due to the cyclic pyrocarbonate phosphate **6a**, while we have tentatively assigned the signal at −4.04 to the mixed phosphoric-pyrocarbonic anhydride, sodium salt **8a**.

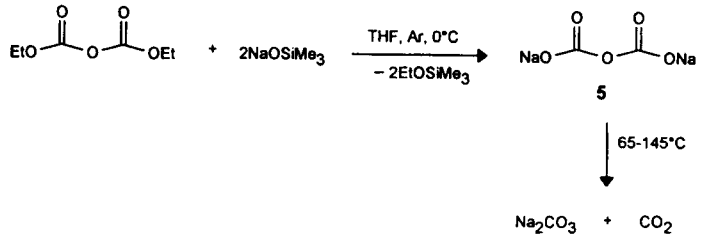
Attempts to trap methyl metaphosphate in this reaction were also carried out, again by the use of styrene oxide. When the reaction was repeated in the presence of one equivalent of styrene oxide, the signals in the δ −12 and −24 regions were not observed, but instead a closely matched pair of signals of almost 1:1 intensity at δ 16.60 and 16.70 appeared and grew in intensity as the reaction proceeded to completion. As discussed earlier, these signals are due to a diastereomeric mixture of 1,3,2-dioxaphospholane-2-oxides **7a** [8], the formation of which provides compelling evidence for the intermediacy of monomeric methyl metaphosphate generated by ring fragmentation of **6a**.

Other alkyl metaphosphates that have been generated using this method include **4b**, **4c**, and **4d**. In each case, in the absence of trapping agent, the expected signals in the δ −12 and −24 regions are observed in keeping with the products expected from the self-condensation reactions of monomeric alkyl metaphosphates. On the other hand, in the presence of styrene oxide, all of the metaphosphate was trapped as 1,3,2-dioxaphospholane-2-oxides **7b–d** (*cis, trans*) with characteristic ^{31}P NMR signals in the ca. δ 15–18 region.

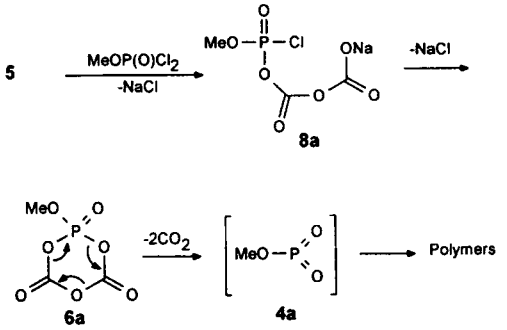
Mechanistic Considerations of the Alkyl Metaphosphate-Epoxide Reaction: (−)-Menthol-Derived Metaphosphate **4d** *as a Mechanistic Tool*

The reaction of alkyl metaphosphates with epoxides to form 1,3,2-dioxaphospholane-2-oxides proceeds via a mechanistic pathway that is complex and not yet fully understood. Hitherto, a number of mechanisms have been proposed [8], and, as shown in Figure 2, a key feature in each mechanism is the common step involving the initial formation of the Lewis salt **9** from reaction of styrene oxide with the alkyl metaphosphate. The formation of **9** is generally accepted since alkyl metaphosphates are recognized to be extremely powerful electrophiles and are believed to coordinate with ethereal oxygen [1].

Mechanism (1) involves ring opening by the more favored internal nucleophilic substitution at the phenyl-bearing carbon, but constraints on approach angles make this mechanism most unlikely, even though it has been invoked [18] to explain the



SCHEME 6



SCHEME 7

formation of a 1,3,2-dithiaphospholane sulfide in the reaction of an epoxide with the presumed species $ArPS_2$.

By contrast, it is proposed that mechanism (2) involves the ring opening of intermediate **9** to form a stabilized carbocation that subsequently collapses to the 1,3,2-dioxaphospholane-2-oxide **7**. It is possible that a carbocation could also be formed by ring opening at the adjacent methylenic carbon atom, although one would expect the secondary carbocation shown in mechanism (2) to be formed preferentially due to added stabilization from the adjacent aromatic ring. Quin [8a] has proposed evidence against this mechanism on the grounds that, if the phenyl group were replaced by a *tert*-butyl group, then methyl migration should occur to form a new carbocation (Scheme 8) and, subsequently, the six-membered 1,3,2-dioxaphosphorinane-2-oxide **10**, which he failed to observe.

Finally, the proposed mechanism (3) is much more elaborate in that it involves the key intermediate **9** undergoing rearrangement by way of a [1,2]-hydrogen shift to form **11**. Thereafter, a further [1,5]-hydrogen shift takes place to produce enol phosphate **12**, which, upon attack of another molecule of styrene oxide, leads to the hydroxyalkyl ester **13**. This is then envisaged to undergo an intramolecular displacement of the enolic grouping to afford

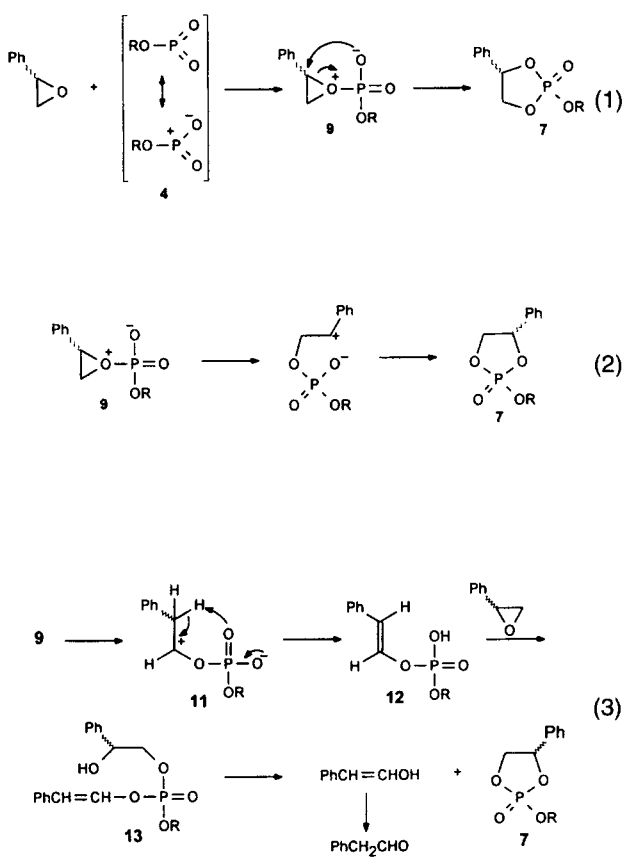
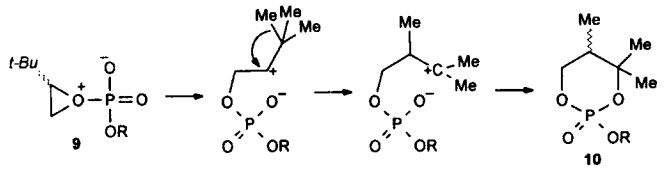


FIGURE 2 The three possible mechanisms that have been proposed to explain the reaction of alkyl metaphosphates with epoxides to form 1,3,2-dioxaphospholane-2 oxides **7**.

the 1,3,2-dioxaphospholane-2-oxide **7**. The only evidence put forward by Quin in support of this mechanism was the detection of propionaldehyde by GC-MS in the reaction products from condensation of 2-methyloxirane and ethyl metaphosphate **4b**, although the amount detected was quite small, being only 0.53% of theory.

In order to shed further light on the mechanism operating between alkyl metaphosphates and styrene oxide, trapping reactions were carried out with



SCHEME 8

metaphosphate species **4d** in the presence of both (*R*)- and (*S*)-styrene oxide. It was argued that, irrespective of which mechanism held true, upon attachment of a chiral component to the resulting 1,3,2-dioxaphospholane-2-oxide **7d**, the ^{31}P NMR spectrum of the reaction products should display all four diastereomeric signals due to *racemization* at the chiral center on the styrene oxide, or only two signals due to *inversion* or *retention* of configuration at the same chiral center. For this scenario, it is also argued with confidence that the menthyl moiety is sited too remotely from the bond-breaking and -forming center adjacent to the phenyl ring to bring about any discrimination in the activation energies for the different transition states of the possible diastereomers; i.e., the transformation is not diastereodifferentiating.

Thus, according to mechanism (1) for which internal nucleophilic substitution takes place in a single step at the chiral carbon center of the styrene epoxide ring, no loss of chirality occurs, and one would expect to observe two diastereomeric products as two closely spaced signals of almost 1:1 intensity in the ^{31}P NMR spectrum. Alternatively, for the reaction to proceed via mechanism (2), a stabilized carbocation on the chiral carbon center of the styrene oxide ring is formed, resulting in racemization of the chiral center with the observation of all four possible diastereomeric products as four closely spaced signals of 1:1:1:1 intensity in the ^{31}P NMR spectrum. Finally, in the case of mechanism (3), the 1,3,2-dioxaphospholane-2-oxide **7d** is formed from the hydroxyalkyl ester **13** that is generated by attack of intermediate **12** on a second mole of styrene oxide with retention of configuration. Ultimately, this leads again to the observation of two signals of almost equal intensity in the ^{31}P NMR spectrum for the resulting product **7d**.

Before carrying out these mechanistic studies, it was first necessary to identify which two of the four possible diastereomeric signals in the ^{31}P NMR spectrum resulted from **7d** having the (*R*)-configuration at the phenyl-bearing ring carbon and which two signals had the (*S*)-configuration. To this end, (−)-menthyl phosphorodichloridate was condensed separately with both (*R*)- and (*S*)-1-phenylethanediol in the presence of pyridine at 0°C to produce **7d** with known configuration at the phenyl-bearing ring carbon center. From the ^{31}P NMR spectra of the two sets of reaction products, we were able to establish that **7d** with the (*S*)-configuration at the ring carbon corresponded to the two diastereomeric signals with chemical shifts at δ 14.75 and 14.99, while the other two signals at δ 14.60 and 14.85 corresponded to the products with the (*R*)-configuration. Figure 3a shows all of these products formed as a 1:1:1:1 mixture from the trapping of metaphosphate **4d**, obtained by reaction of disodium pyrocarbonate **5** with (−)-menthyl phosphorodichloridate, with racemic styrene oxide; the configuration at the phenyl-bearing ring carbon is indicated for each signal.

When the individual trapping reactions of metaphosphate **4d** in the presence of both (*R*)- and (*S*)-styrene oxide were carried out in the same manner, the results proved to be conclusive in ruling out two of the three proposed mechanisms. Thus, in the case of (*S*)-styrene oxide, the ^{31}P NMR spectrum of the reaction mixture (Figure 3b) showed the dominating presence of only two of the four possible diastereomers, with the two major signals corresponding to inversion of configuration at the ring carbon center. A similar result was obtained for (*R*)-styrene oxide with the ^{31}P NMR spectrum of the reaction mixture being of the opposite configuration to that obtained with (*S*)-styrene oxide, proving conclusively that the trapping reaction of alkyl metaphosphates occurs predominately with inversion of configuration at the phenyl-bearing carbon center of styrene oxide. These observations rule out the possibility of the reaction proceeding via mechanism (3), since this mechanism, viz., **13**→**7**, would result solely in retention of configuration at the ring carbon center. The results are also conclusive in ruling out mechanism (2) since, irrespective of whether (*R*)- or (*S*)-styrene oxide is used, the same intermediate carbocation is formed on going from **9**→**7**, and due to its planarity, would lead to identical product mixtures and, consequently, identical ^{31}P NMR spectra consisting of four signals of equal intensity.

A plausible explanation for the observed inversion involves a variation of mechanism (1) whereby ring opening of the initially formed intermediate **9d** occurs intermolecularly by nucleophilic attack from

another complexed metaphosphate species (Scheme 9). Whether or not cyclization of the derived intermediate **11d** to **7d** (*cis, trans*) occurs concertedly as depicted, or in stages, needs further investigation possibly involving molecular modeling, but the overall process results in regeneration of metaphosphate and explains the quantitative nature of the reaction. The capacity of the dipolar metaphosphate species to react both as an electrophile and as a nucleophile (via **9d**) in a self-catalyzed process is, to our knowledge, without precedent, but the need to invoke an activated complex such as **9** is required by both the ease of ring opening and the preferred attack at the more highly substituted carbon position that is akin to nucleophilic attack at protonated epoxides [19]. It is interesting to note that Quin [8a] did not comment on the possibility that mechanism (3) proceeded by attack of **12** on the activated intermediate **9**, instead of free styrene oxide, and inevitably result in inversion of configuration as we observed. For such a mechanism to operate, two equivalents of epoxide are required, and based on this fact, trapping of metaphosphate **4d** was repeated with only one equivalent from which a yield of over 60% of 1,3,2,-dioxaphospholane-2-oxide **7d** was isolated after workup and purification by column chromatography. Since the maximum yield for mechanism (3) to be valid is only 50%, it can be argued that the reaction does not proceed by this mechanism. Nonetheless, it is worth noting the comments made by a referee that the small amount of aldehyde detected, albeit propionaldehyde from the condensation of propylene oxide

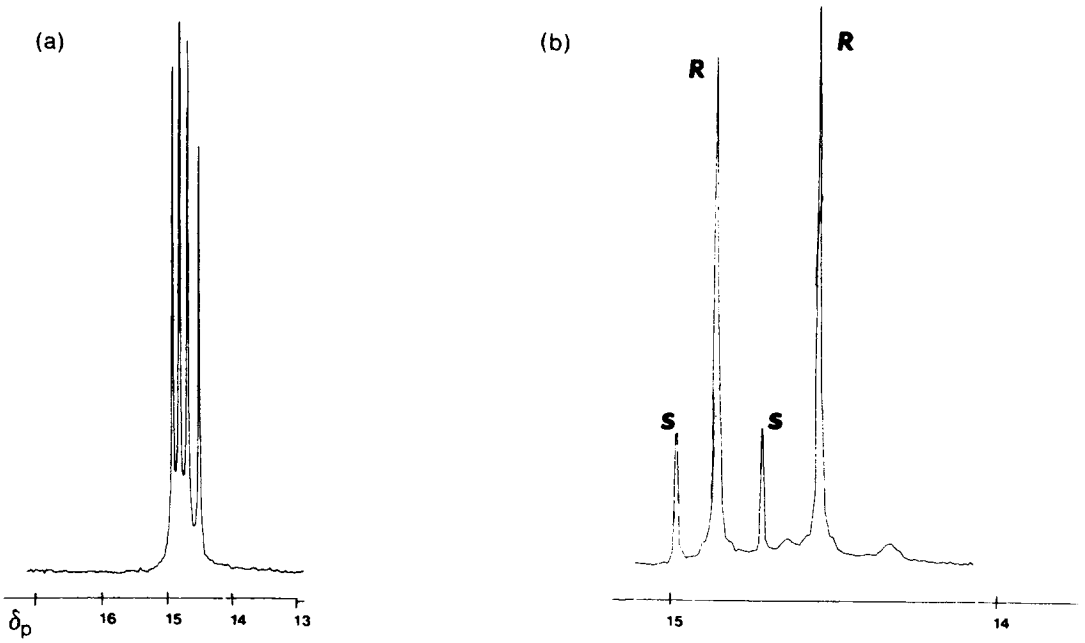
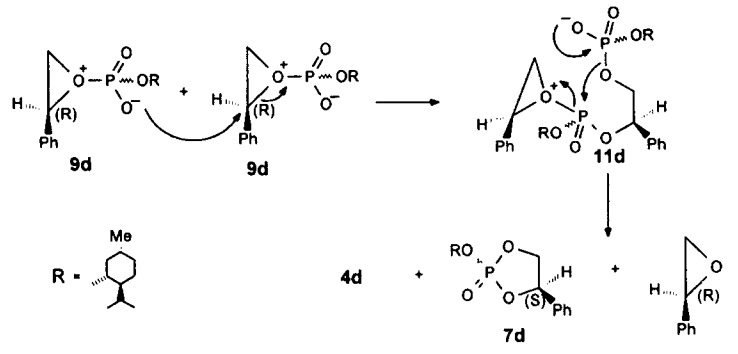


FIGURE 3



SCHEME 9

with metaphosphate **4b** (vide supra), may indicate it is competitively phosphorylated by metaphosphate **4b** to reproduce the key intermediate **12b**. If this is the case, only one equivalent of styrene oxide would be required to complete the condensation, and mechanism (3) may hold provided that attack by phosphoric acid **12** occurs at the phenyl-bearing carbon of protonated styrene oxide. This aspect awaits further investigation, but it is evident that the small amount of diastereomeric products observed with retained stereochemistry (see Figure 3b) arises from leakage by another mechanism, but at this stage, it is not possible to say whether this occurs with retention of configuration or racemization.

EXPERIMENTAL

^{1}H NMR spectra were determined at 60 MHz using a JEOL PMX-60 spectrometer, at 200 MHz using a Bruker WP-200 spectrometer, or at 360 MHz using a Bruker WH-360 spectrometer. All coupling constants are quoted in Hertz. ^{13}C NMR spectra were determined at 50.3 MHz using a Bruker WP-200 spectrometer, with all coupling constants quoted in Hertz. Solid-state ^{13}C NMR spectra were obtained at 100.6 MHz using a Bruker NSL-400 spectrometer. ^{31}P NMR spectra were determined either at 36.23 MHz with a JEOL FX-90Q spectrometer or at 101.26 with a Bruker AC-250 spectrometer using 85% H_3PO_4 as an external reference with positive signs downfield, negative signs upfield. All ^{31}P NMR spectra were determined in ^{1}H decoupled mode. Where stated, in cases where reactions were to be monitored, ^{31}P NMR spectra were recorded by placing a sample directly from the reaction mixture into an NMR tube along with a [$^2H_6$]-acetone capillary lock. Mass spectra were determined by use of a Kratos MS-50TC (high resolution or FAB) instrument. A Stanton Redcroft TG750/770 thermal analyzer was used to obtain thermal gravimetric analysis (TGA). Both methyl and ethyl phosphorodichloridate were prepared according to published procedures [20]. All solvents were dried by standard methods. All reactants and reagents were supplied by the Aldrich Chemical Company unless otherwise stated.

Neopentyl Phosphorodichloridate

To a solution of neopentyl alcohol (2.00 g, 2.27×10^{-2} mol) in dry toluene (20 cm^3) at 0°C under argon was added butyllithium (1.6 mol dm^3 in hexane, 15 cm^3, 2.40×10^{-2} mol), and the reaction mixture was brought to room temperature gradually with stirring. The resultant mixture was transferred dropwise via a cannula into a solution of phosphoryl chloride (6.97 g, 4.54×10^{-2} mol) in toluene (20 cm^3) and stirred at room temperature for 3 hours. Solvents were then removed under vacuum and the residue purified by Kugelrohr distillation to give the title compound (3.63 g, 78%) as a colorless oil, bp 95°C (15 mmHg) [21]; ν_{max} (thin film)/cm^{-1} 1289; δ_H (60 MHz, $CDCl_3$), 4.06 (2H, d, J 7.10), and 1.04 (9H, s); δ_C (50.3 MHz, $CDCl_3$), 85.23 (d, J 10.6), 32.64 (d, J 6.8), and 26.32; δ_P (36.23 MHz, $CDCl_3$) 7.40.

(−)-Menthyl Phosphorodichloridate

To a solution of phosphoryl chloride (4.50 g, 2.90×10^{-2} mol) in dry ether (60 cm^3) at 0°C under argon was added a solution of (−)-menthol (4.59 g, 2.90×10^{-2} mol) and pyridine (2.32 g, 2.90×10^{-2} mol) in ether (50 cm^3) at a rate of 1 cm^3/min via a perfusor. Once the addition was complete, the reaction mixture was allowed to stir overnight at room temperature, after which time the reaction mixture was filtered, the precipitate washed with dry ether (2×50 cm^3), and the filtrate evaporated to yield the title compound (7.2 g, 90%) as a viscous colorless oil. Attempts to purify the oil by Kugelrohr distillation under vacuum led to decomposition, and consequently the isolated product was used in future stages without further purification. ν_{max} (thin film)/cm^{-1} 1295; δ_H (200 MHz, $CDCl_3$), 4.69–4.51 (1H, m), 2.34–2.26 (1H, m), 2.09–2.01 (1H, m), 1.74–1.50 (1H, m), 1.48–0.98 (6H, m), 0.93 (3H, d, J 6.8), 0.90 (3H, d, J 6.8), and 0.80 (3H, d, J 6.9); δ_C (50.3 MHz, $CDCl_3$), 86.3 (d, J 10.8), 47.9 (d, J 8.1), 41.9, 33.4, 31.5, 25.2, 22.7, 21.5, 20.5, and 15.5; δ_P (36.23 MHz, $CDCl_3$) 7.2; m/z 271 ($M^+ + 1$).

Generation of Alkyl Metaphosphates **4a–d** *by the Reaction of Alkyl Phosphorodichloridates with Potassium Hydrogen Carbonate*

General Procedure. To a stirred suspension of anhydrous potassium hydrogen carbonate (1.00 g, 9.98 mmol) in dry DME (10 cm^3) at room temperature under an argon atmosphere was added a solution of the appropriate alkyl phosphorodichloridate (9.98 mmol) in DME (3 cm^3) and the resultant mixture left to stir at room temperature for 24 hours. After this period, monitoring of the reaction mixture by ^{31}P NMR spectroscopy showed signals in the δ −12 and −24 regions, which are characteristic of linear, branched, and cyclic phosphates formed from the self-condensation reactions of the title compounds **4a–d**. In the case of **4d**, the reaction required a further 1 hour of heating under reflux before these

such were observed. We found that the composition of the reaction mixtures changed with time to ultimately consist of a mixture of alkyl dihydrogen phosphates (^{31}P NMR shifts around δ 0) and alkyl pyrophosphates (^{31}P NMR shifts around δ −13).

General Procedure in the Presence of Styrene Oxide. To a stirred suspension of anhydrous potassium hydrogen carbonate (1.00 g, 9.98 mmol) in dry DME (10 cm^3) at room temperature under argon was added styrene oxide (1.20 g, 9.98 mmol) followed immediately by a solution of the appropriate alkyl phosphorodichloridate (9.98 mmol) in dry DME (3 cm^3) and the resultant mixture left to stir at room temperature for 24 hours. After this period, the reaction mixture consisted of two closely spaced δ_P signals of almost 1:1 intensity in the δ 16–18 region that were attributed to diastereomeric mixtures of 2-alkoxy-4-phenyl-1,3,2-dioxaphospholane-2-oxides **7a–c** formed by the trapping of alkyl metaphosphates **4a–c** by styrene oxide. In the case of the generation of (−)-menthol-derived metaphosphate **4d**, the reaction required a further 1 hour of heating under reflux before **4d** could be generated and trapped by styrene oxide to form **7d**. **7d** was observed as not two, but four closely spaced δ_P signals of almost 1:1:1:1 intensity in the δ 16–18 region.

Disodium Pyrocarbonate **5**

To a solution of sodium trimethylsilanolate (1.45 g, 1.29×10^{-2} mol) in anhydrous THF (30 cm^3) at 0°C under an argon atmosphere was added a solution of diethyl pyrocarbonate (1.05 g, 6.48×10^{-3} mol) in THF (15 cm^3) at a rate of 1 cm^3/min via a perfusor. Once the addition was complete, the reaction mixture was allowed to warm to room temperature and stirred overnight. The precipitate was filtered off, washed with anhydrous ether (2×50 cm^3), and dried in vacuo to yield the title compound **5** (0.91 g, 94%) as a colorless solid, which was used in future stages without purification. TGA of **5** resulted in the loss of 1 mol of CO_2 in the temperature range 65–145°C (found: $M^+ + H$, 150.96199, $C_2HNa_2O_5$ requires 150.96200); ν_{max} (KBr disc)/cm^{-1} 1610; δ_C (CPMAS) 162.2.

Generation of Alkyl Metaphosphates **4a–d** *by the Reaction of Alkyl Phosphorodichloridates with Disodium Pyrocarbonate* **5**

General Procedure. To a stirred suspension of disodium pyrocarbonate **5** (1.00 g, 6.66 mmol) in anhydrous DME (15 cm^3) at room temperature under an argon atmosphere was added a solution of the appropriate alkyl phosphorodichloridate (6.66 mmol) in DME (5 cm^3), and the resulting mixture was heated under reflux for 1 hour. After this time, ^{31}P NMR spectra of the reaction mixtures showed characteristic δ_P signals in the δ −12 and −24 regions for linear, branched, and cyclic phosphates formed from the self-condensation reactions of the title compounds **4a–d**.

General Procedure in the Presence of Styrene Oxide. To a stirred suspension of disodium pyrocarbonate **5** (1.00 g, 6.66 mmol) in anhydrous DME (15 cm^3) at room temperature under an argon atmosphere was added styrene oxide (6.66 mmol), followed by a solution of the appropriate alkyl phosphorodichloridate (6.66 mmol) in DME (5 cm^3), and the resulting mixture was then heated under reflux for 1 hour. After this period, the reaction mixture was subjected to analysis by ^{31}P NMR spectroscopy and found to consist of two closely spaced δ_P signals of almost 1:1 intensity in the 16–18 region that were assigned on the basis of comparison with authentic samples to diastereomeric mixtures of 2-alkoxy-4-phenyl-1,3,2-dioxaphospholane-2-oxides **7a–c**, resulting from the trapping of alkyl metaphosphates **4a–c** by styrene oxide. In the case of (−)-menthyl metaphosphate **4d**, the trapped product **7d** was observed as four, not two, closely spaced δ_P signals of almost 1:1:1:1 intensity in the 16–18 region.

Cis- and trans-Isomers of 2-Menthyloxy-4-phenyl-1,3,2-dioxaphospholane-2-oxide **7d** *from the Reaction of (−)-Menthyl Phosphorodichloridate with Disodium Pyrocarbonate* **5** *in the Presence of Styrene Oxide*

A solution of (−)-menthyl phosphorodichloridate (1.24 g, 4.5×10^{-3} mmol) in anhydrous DME (3 cm^3) was added dropwise to a stirred suspension of disodium pyrocarbonate **5** (0.68 g, 4.5×10^{-3} mmol) and styrene oxide (0.54 g, 4.5×10^3 mmol) in DME (5 cm^3) at room temperature under an argon atmosphere. Once the addition was complete, the reaction mixture was heated under reflux for 1.5 hours, cooled, and then filtered. The precipitate was washed with DME (2×10 cm^3) and the combined filtrate evaporated in vacuo. The resulting residue was purified by flash column chromatography (30 g, Fluka SiO_2, 0.040–0.063 mm) using gradient elution with *n*-hexane:ethyl acetate (100:0 to 0:100) to yield the title compound as two fractions containing *cis* (Rf = 0.23, 0.57 g) and *trans* (Rf = 0.4, 0.38 g) isomers

both as colorless solids (overall yield 0.95 g, 62%). From the ^{31}P NMR spectrum of the two fractions, it was observed that each fraction contained two closely spaced signals in the region around δ 16, suggesting that one fraction contained the two *cis* isomers with the other containing the two *trans* isomers. Physical data for the *cis* isomers (found: $M^+ + H$, 339.17208; $C_{18}H_{27}O_4P + H$ requires 339.17252); ν_{max}(nujol)/cm^{-1} 1260; δ_H (360 MHz, $CDCl_3$) 7.43–7.33 (5H, m), 5.60–5.54 (1H, m), 4.64–4.53 (1H, m), 4.42–4.33 (1H, m), 4.15–4.05 (1H, m), 2.28–2.06 (2H, m), 1.68–1.63 (1H, m), 1.51–0.97 (6H, m), 0.92 (3H, d, *J* 6.7), 0.90 (3H, d, *J* 6.8), and 0.83 (3H, d, *J* 6.9); δ_C (50.3 MHz, $CDCl_3$) 135.6, 129.3, 128.8, 125.9, 80.9 (d, *J* 6.7), 79.1, 71.8, (d, *J* 18.2), 48.1 (d, *J* 7.5), 42.5, 33.8, 31.3, 25.8, 22.9, 21.7, 20.6, and 15.7; δ_P (36.23 MHz, $CDCl_3$) 16.11 and 16.05; *m/z* 339 ($M^+ + H$).

Preparation of Authentic Mixtures of cis- and trans-2-Alkoxy-4-phenyl-1,3,2-dioxaphospholane-2 Oxides **7a–d**

To a solution of the appropriate alkyl phosphorodichloridate (4.98 mmol) in anhydrous ether (150 cm^3) at 0°C under argon was added a solution of 1-phenyl-1,2-ethanediol (4.98 mmol), triethylamine (4.98 mmol), and DMAP (5%) in ether (40 cm^3) at a rate of 1 cm^3/min via a perfusor. Once the addition was complete, the reaction mixture was heated under reflux for 1 hour, after which time the title compounds **7a–d** were observed by ^{31}P NMR spectroscopy as two closely spaced signals of almost 1:1 intensity in the region δ_P 16–18, with **7d** being observed in the same region as four, not two, closely spaced signals of almost 1:1:1:1 intensity. These samples were then compared to those generated by the trapping of alkyl metaphosphates **4a–d** with styrene oxide by peak enhancement experiments.

Reaction of Disodium Pyrocarbonate **5** *with (−)-Menthyl Phosphorodichloridate in the Presence of Chiral Styrene Oxide*

The procedure described earlier for the reaction of (−)-menthyl phosphorodichloridate with disodium pyrocarbonate **5** in the presence of styrene oxide was followed.

(S)-Styrene Oxide. After the reaction was carried out with (*S*)-styrene oxide as a trapping agent, ^{31}P NMR spectroscopy showed the reaction mixture to consist of all four possible diastereomers of (−)-2-menthyloxy-4-phenyl-1,3,2-dioxaphospholane-2-oxide **7d** by the appearance of signals at δ_P 14.36, 14.26, 14.13, and 13.98 in the ratio 1.0:4.6:1.0:4.9. The two major signals had (*R*)-configuration at the phenyl-bearing ring carbon atom by comparison with authentic samples.

(R)-Styrene Oxide. After the reaction was carried out using (*R*)-styrene oxide as a trapping agent, ^{31}P NMR spectroscopy showed the reaction mixture to consist of all four possible diastereomers of 2-menthyloxy-4-phenyl-1,3,2-dioxaphospholane-2 oxide **7d** at δ_P 14.39, 14.26, 14.15, and 13.98 in the ratio 3.8:1.0:4.6:1.4. The two major signals had (*S*)-configuration at the phenyl-bearing ring carbon atom.

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