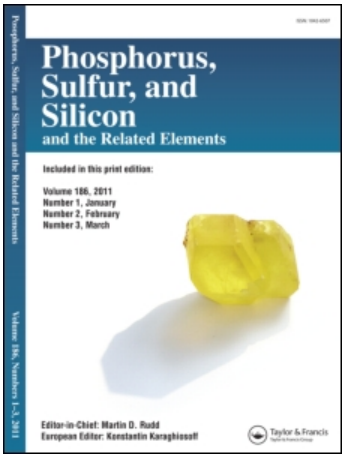

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SYNTHESIS OF 1,2-OXAPHOSPHOLANE OXIDES BY OXYGEN INSERTION INTO THE C-P BOND OF PHOSPHETANE OXIDES

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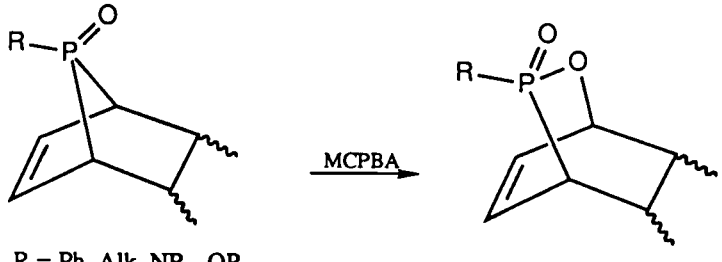
A number of phosphetane oxides with a variety of aromatic substituents on phosphorus underwent oxygen insertion into a C—P bond by the action of *m*-chloroperbenzoic acid, resulting in formation of 1,2-oxaphospholane oxides in high yield. The products were easily isolated and were characterized by ^{31}P and ^{13}C NMR. For 2,2,3,4,4-pentamethyl-substituted phosphetane oxides only one site of attack is possible and the reaction is assumed to proceed with retention of the stereochemistry of the starting material. For 2,2,3-trimethyl-substituted phosphetane oxides, regioisomers were formed, with that derived from O-insertion at the least substituted carbon accounting for 80–90% of the product.

Key words: phosphetane oxide, phospholane oxide, oxidation, peracid, NMR.

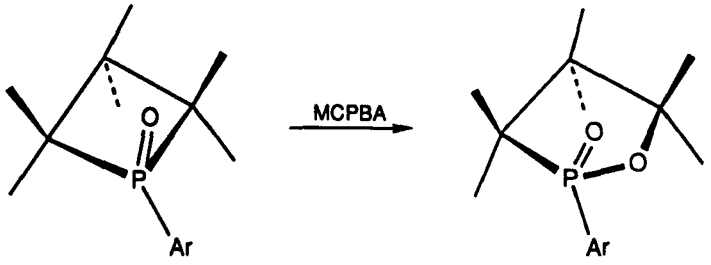
INTRODUCTION

The carbon-phosphorus bond in acyclic compounds is not known to be sensitive to attack by peracids, but several cases are now known[2–5] where cyclic compounds with especially strong contraction of the C—P—C bond angle do undergo an oxygen-insertion reaction with peracids under mild conditions. The process has overall resemblance to the well-known Baeyer-Villiger oxidation of ketones, which when cyclic are converted to lactones. Many of the reactive cyclic phosphorus compounds sensitive to this reaction have the framework of the norbornene system where the phosphorus function is located at the highly strained 7-position. A bond angle of 83° has been found[6] in a phosphine oxide with this structure, which is some 20° below the normal value.



R = Ph, Alk, NR_2, OR.

In our earlier work,[3] we found that two P-phenylphosphetane oxides, where the internal angle is similar to that of the 7-phosphanorbornenes (e.g. 79.4° in 2,2,3-trimethyl-1-phenylphosphetane-1-oxide[7]), were also sensitive to the O-insertion with *m*-chloroperbenzoic acid (MCPBA), thereby affording the 1,2-oxaphospholane system.



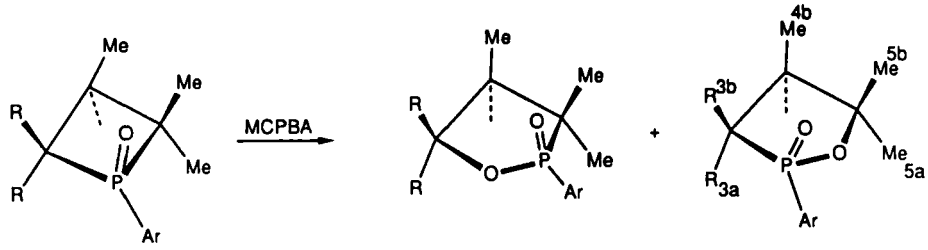
It appeared that this process could be of synthetic value, since other methods[8-10] used to generate the 1,2-oxaphospholane system cannot be characterized as being general and proceed in modest yields. We have therefore carried out further study of the O-insertion reaction with a variety of phosphetane oxides in order to explore the synthetic utility of the process. Our previous experiments were hampered by the very strong tendency of *m*-chlorobenzoic acid, as well as unreacted MCPBA, to cling to the product, making purification quite difficult. We have been able to improve the isolation procedure by the simple expedient of performing a complexation of the acids on the surface of solid potassium fluoride.[11] We are now able to describe the O-insertion process as a versatile, straightforward approach to the 1,2-oxaphospholane oxide system when the corresponding phosphetane oxides are available.

RESULTS AND DISCUSSION

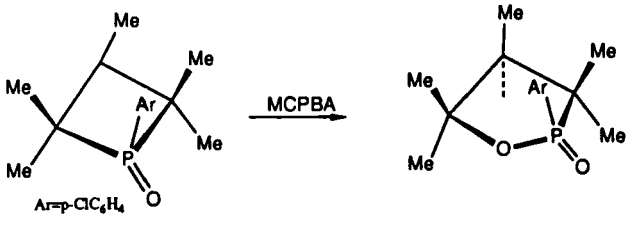
Six different 1-arylphosphetane oxides (**1–6**) were available from our earlier work.[12] This research provided improvements in the phosphetane oxide synthesis of McBride, *et al.*[13] based on the reaction of phosphonous dihalides and olefins in the presence of $AlCl_3$. These products were mixtures of *cis,trans* isomers with the *trans* isomer in predominance by the ratio of 9:1 or higher. One phosphetane oxide with predominantly *cis* structure (**16**) was also prepared by inclusion in the study.

The best results for the oxygen insertion reaction were obtained when the phosphetane oxide was oxidized in methylene chloride solution with a 3-fold excess of *m*-chloroperbenzoic acid for several days in the dark. Solid anhydrous potassium fluoride was then added to complex the acids, and the solid removed by filtration. The 1,2-oxaphospholane products were then purified by Kugelrohr distillation. Alternatively, column chromatography was used to separate the two regioisomers (*vide infra*) which formed in the reaction from unsymmetrically substituted phosphetane oxides. The reaction yields and the melting points and elemental analyses of the products are summarized in Table 1. Since the phosphetane oxides always consisted of a mixture of *cis* and *trans* isomers, and since in some cases two regioisomers were formed from each, the crude products could contain as many as four compounds. As noted, the regioisomers were found to be separable by column chromatography, but the *cis,trans* isomers were not readily separated and the elemental analyses were performed on the isomer mixture.

^{31}P NMR spectroscopy proved to be a useful tool for following the progress of the oxidation reactions as well as for determining the regiochemistry of the products. The ^{31}P NMR signals of the insertion products (see Table 2) were always downfield



	R	Ar (80-90% trans)		
1	H	p-FC_6H_4	7	8
2	Me	p-FC_6H_4	9	
3	H	p-ClC_6H_4	10	11
4	Me	p-ClC_6H_4	12	
5	Me	3,4-$Cl_2C_6H_3$	13	
6	H	2,4-$Cl_2C_6H_3$	14	15



16 17

SCHEME 1

TABLE I

Data for synthesis of 1,2-oxaphospholane-1-oxides

Compound[a]	Yield[%]	m.p.[°C]	Mol. Formula	Elemental analysis					
				Calculated			Found		
				C	H	P	C	H	P
7	84[b]	96-8	$C_{12}H_{16}FO_2P$	59.49	6.67	12.78	59.46	6.61	12.84
8		oil		59.49	6.67	12.78	59.42	6.62	12.92
9	80	156-8	$C_{14}H_{20}FO_2P$	62.21	7.47	11.46	62.06	7.31	11.38
10	47[b]	oil	$C_{12}H_{16}ClO_2P$	55.71	6.25	11.97	55.49	6.17	11.86
11		oil		55.71	6.25	11.97	55.57	6.28	12.12
12	73	145-8	$C_{14}H_{20}ClO_2P$	58.63	7.04	10.81	58.88	7.05	11.06
13	81	158-9	$C_{14}H_{19}Cl_2O_2P$	52.31	5.92	9.68	52.22	6.01	9.44
14	78[b]	oil	$C_{12}H_{15}Cl_2O_2P$	52.31	5.92	9.68	52.13	6.18	9.51
15		oil		52.31	5.92	9.68	52.45	5.99	9.81
17	77	oil	$C_{14}H_{20}ClO_2P$	58.63	7.04	10.81	58.52	7.25	10.62

[a] All compounds except **17** were a mixture of about 90% *trans* and 10% *cis* isomers. Compound **17** was a pure *cis* isomer.

[b] Yield of combined regioisomers.

TABLE II

Carbon-13 and Phosphorus-31 data for 1,2-oxaphospholane-1-oxides[a]

	^{31}P NMR δ		^{13}C NMR												
			C-3	C-4	C-5	C-3a	C-3b	C-4a	C-4b	C-5a	C-5b	Ar-1	Ar-2	Ar-3	Ar-4	Ar-
	63.2	δ	35.9	41.3	72.5	21.1	14.8	—	9.3	—	—	125.4	134.4	115.4	164.9	115.
		J(P-C)	85.7	9.9	3.3	4.4	2.2	—	9.9	—	—	123.0	11.0	6.7	3.3	6.
	50.9	δ	33.8	43.3	89.0	—	—	—	15.6	27.0	22.8	[c]	133.7	115.8	170.6	115.
		J(P-C)	82.4	2.2	2.2	—	—	—	15.4	8.7	0.0	[c]	12.1	3.3	0.0	3.
	61.6	δ	37.8	52.4	87.4	29.4	24.3	—	9.2	26.0	18.9	125.8	134.6	115.4	[c]	115.
		J(P-C)	84.6	0.0	3.3	7.7	0.0	—	11.0	3.3	0.0	134.0	9.9	13.7	[c]	13.
	66.1	δ	36.1	41.3	72.5	21.1	14.8	—	9.4	—	—	128.0	133.3	128.4	138.6	128.
		J(P-C)	84.6	9.9	3.3	4.4	2.2	—	9.9	—	—	119.3	11.0	13.2	3.3	13.
	51.5	δ	33.9	43.5	89.3	—	—	—	15.7	27.6	23.0	130.5	132.7	128.8	138.6	128.
		J(P-C)	81.9	0.0	2.7	—	—	—	16.1	8.1	0.0	[c]	12.3	13.8	2.7	13.
	61.7	δ	37.9	52.6	87.5	29.4	26.0	—	9.2	24.3	18.9	128.3	133.5	128.4	138.4	128.
		J(P-C)	83.2	6.7	4.0	6.7	2.7	—	10.7	0.0	2.7	128.9	10.7	13.4	4.1	13.
	60.3	δ	38.4	52.4	88.1	29.9	24.5	—	4.4	26.2	19.0	129.4	133.3	131.3	137.0	134.
		J(P-C)	84.6	6.6	3.3	10.8	0.0	—	14.4	0.0	0.0	[c]	13.2	9.9	0.0	11.
	63.2	δ	37.5	41.8	72.7	20.9	15.7	—	10.5	—	—	127.2	135.5	126.8	139.0	130.
		J(P-C)	95.7	9.9	4.4	4.4	0.0	—	8.8	—	—	122.0	7.7	9.9	3.3	8.
	48.1	δ	32.6	41.7	89.2	—	—	—	15.2	27.1	23.0	129.6	134.1	126.7	138.6	129.
		J(P-C)	84.6	2.2	4.4	—	—	—	16.5	8.8	0.0	132.9	6.6	11.0	3.3	8.
	57.7	δ	39.6	49.1	88.5	31.4	[c]	8.4	—	22.5	24.7	[c]	133.8	128.5	138.7	128.
		J(P-C)	85.5	4.4	2.2	[c]	[c]	10.7	—	0.0	0.0	[c]	7.9	13.2	3.3	13.

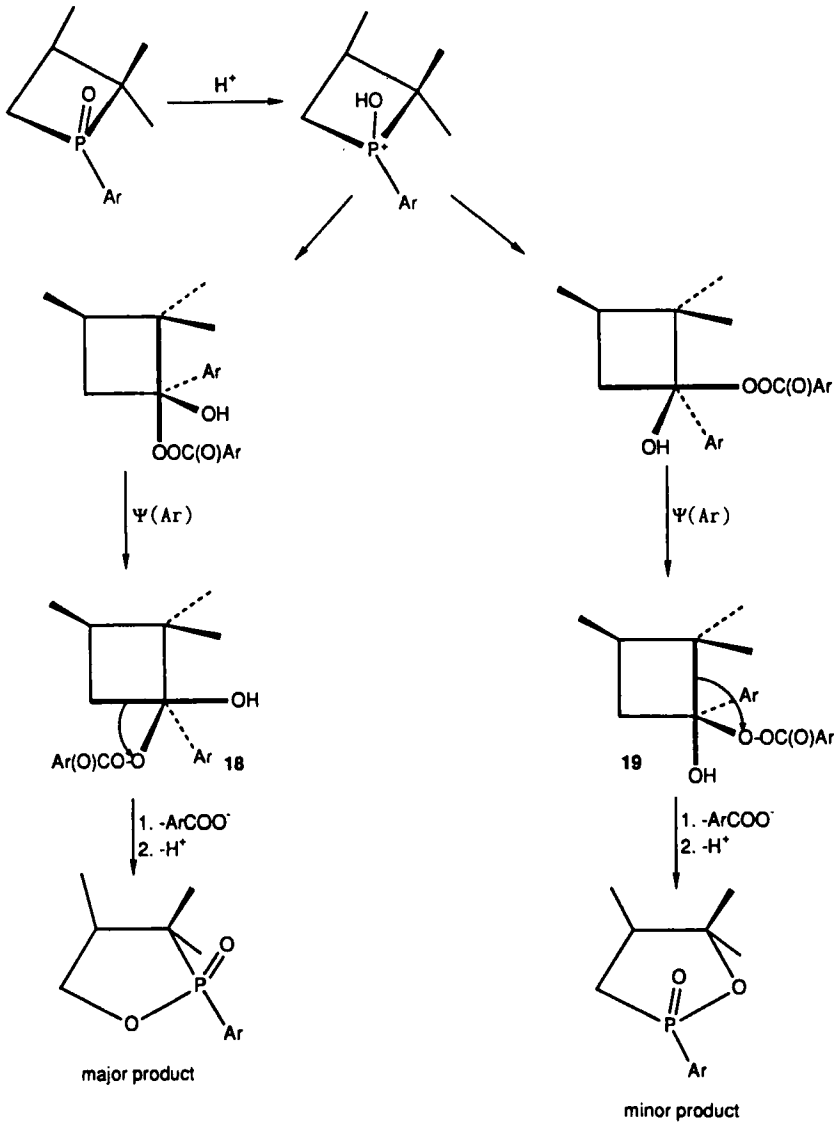
Spectra were taken in $CDCl_3$ solution as a mixture of *trans* (80–90%) and *cis* isomers; only the values for *trans* isomer are shown here. I
pure *cis* isomer.
C-F couplings were of the expected size but are not reported.
Not clearly observed.

of the phosphetane oxides, which is consistent with the creation of a 5-membered ring.[14] The downfield shifts ranged from 20 ppm for the *trans* isomers, where products had two methyls in the β-position to the P atom, to 2 ppm for the *cis* isomer **17**. It was also noted that the regioisomer from insertion next to a methylene group always had a more downfield signal than that from insertion next to a CMe_2 group, by some 12–15 ppm. Since carbon atoms in the β-position relative to phosphorus generally cause downfield shifts,[15] this is the result to be anticipated.

^{13}C NMR was useful in determining the structure of the regioisomers, since the carbon attached to oxygen was strongly deshielded and easily recognized. For a pair of regioisomers, the carbon bearing two methyl substituents (C-5 in **8**, **11**, and **15**) was downfield by some 17 ppm from the methylene carbons in the isomers (C-5 in **7**, **10**, and **14**, respectively) due to the α-substituent effect of the methyls. The ^1H NMR spectra of the regioisomers also were useful in assigning structures, since the CH_2 signals next to O were significantly downfield from the CH_2 next to P (δ 4.2 and 2.1, respectively). Other signals on the ^{13}C NMR spectra were easily assigned and are recorded in Table 1. Weak signals for the *cis* isomers also appeared on the spectra but are not reported in this table. The two regioisomers have some pronounced differences in the chemical shifts of the C-methyl groups, which probably result from conformational differences and the degree of shielding experienced from γ-interaction of the methyls. To illustrate, the methyl at ring carbon 4 is consistently found at about δ 9–10 in the major regioisomers, and at about δ 15–16 in the minor isomers. The conformational differences could come about from the greater crowding in the major isomer where there are substituents on three adjacent ring atoms, as compared to the minor isomer where the sequence is interrupted by the O atom.

From the results with the three unsymmetrically substituted phosphetane oxides **1**, **3**, and **6**, used in this study, as well as with 2,2,3-trimethyl-1-phenylphosphetane oxide used in our previous work,[3] it is clear that the O-insertion occurs predominantly at the least substituted carbon, which is the opposite of the outcome of the Baeyer-Villiger reaction with ketones.[16] We believe that this difference arises from the special mechanism open to phosphorus wherein a pentacoordinate intermediate can be formed by addition of the peracid to the P=O bond. Such P(V) intermediates have well-defined requirements in their formation and decomposition, and in Scheme 2 we apply the mechanism first outlined for O-insertion in 7-phosphanorbornene oxides[3] to the phosphetane oxides. As shown in Scheme 2, the reaction can take two pathways, thus accounting for the regioisomers. A major difference in the P(V) intermediates **18** and **19** is found at the carbon in the apical position of the trigonal bipyramid; the intermediate leading to the major isomer has the less sterically demanding methylene group in this position, while the intermediate leading to the minor isomer has the bulky $C(CH_3)_2$ group at this position. Another explanation may be that the former substituent is more electronegative than the latter,[17] and it is well known that the more electronegative groups prefer the apical rather than the equatorial positions.

In the mechanism depicted in Scheme 2, it is assumed that the O-insertion occurs with retention of configuration at phosphorus. This stereochemical event has been confirmed in studies with 7-phosphanorbornenes with the aid of X-ray crystallographic analyses.[5,18] Although there is no direct proof that retention occurs with



SCHEME 2

the phosphetane system, it is reasonable to argue that the stereochemistry of the O-insertion is the same in the two ring systems.

EXPERIMENTAL

Phosphetane oxides were available from an earlier study.[12] All spectra were recorded in $CDCL_3$ solutions. ^1H NMR spectra were obtained on an IBM NR-80 spectrometer, using tetramethylsilane as internal standard. ^{31}P NMR FT spectra were obtained on a JEOL FX-90Q spectrometer at 36.2 MHz, using 85% phosphoric acid as external standard with internal deuterium lock. Positive shifts are downfield of the reference. ^{13}C NMR spectra (FT) were obtained on the same instrument at 22.5 MHz with

tetramethylsilane as internal standard. Broad-band noise-decoupling was employed on all ^{13}C and ^{31}P spectra. Melting points were taken on a Mel-Temp apparatus, and are corrected. Microanalyses were performed by MHW Laboratories, Phoenix, Arizona and are listed in Table 1.

General procedure for O-insertion reaction. All reactions were performed by the same procedure; that for the reaction of oxide *1* is typical. A mixture of 3.4 g (0.015 mol) of 1-(*p*-fluorophenyl)-2,2,3-trimethylphosphetane 1-oxide (**1**, 90% *trans*) and 13 g (0.06 mol) of *m*-chloroperbenzoic acid (85%) in 70 ml of CH_2Cl_2 was stirred at room temperature in the dark for 9 days. Anhydrous KF (4.4 g) was added at that time and the resulting mixture was stirred for 1 h. The solid complex was filtered off, and the filtrate was washed twice with water (50 ml) and dried with $MgSO_4$. Solvent was removed under reduced pressure and the residue was purified by Kugelrohr distillation which provided 2.7 g (74%) of a mixture of regioisomers **7** and **8**. Alternatively the residue was separated by column chromatography on silica gel (hexane:ethyl acetate 1:2) affording 2.55 g of 2-(*p*-fluorophenyl)-3,3,4-trimethyl-1,2-oxaphospholane-1-oxide (**7**, 70% yield) and 0.51 g of 2-(*p*-fluorophenyl)-4,5,5-trimethyl-1,2-oxaphospholane-1-oxide (**8**, 14% yield). Information on these products, as well as the products from oxygen-insertion in phosphetane oxides **2–6**, is given in Tables 1 and 2.

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1. Work performed at Duke University. Present addresses: J. Szewczyk, Chemistry and Life Sciences, Research Triangle Institute, P.O. Box 12194, Research Triangle Park, N.C. 27709; E.-Y. Yao, Department of Chemistry, Nankei University, Tianjin, People's Republic of China; L. D. Quin, Department of Chemistry, University of Massachusetts, Amherst, MA 01003.
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