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SYNTHESIS AND STEREOCHEMISTRY OF 3,4-EPOXYPHOSPHOLANES; ^{13}C NMR EVIDENCE FOR PREFERENTIAL EPOXIDATION anti TO PHOSPHORYL IN 3-PHOSPHOLENE OXIDES

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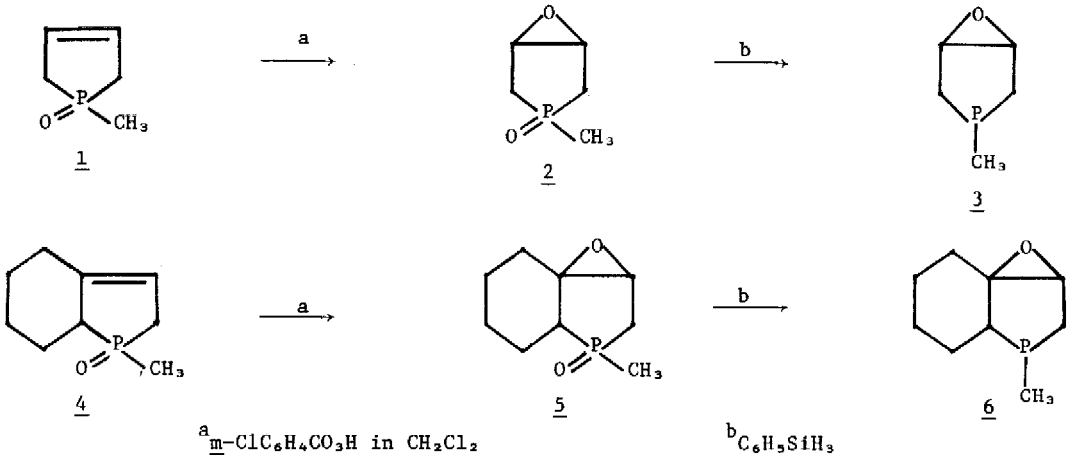
We have synthesized the first known compounds containing a trivalent phosphorus function and an epoxide ring. The compounds are stable at room temperature and can be distilled in vacuo. They show no tendency to experience transfer of oxygen to phosphorus, although under more vigorous conditions phosphines have been used to effect deoxygenation of epoxides to olefins.[1]

The epoxy phosphines 3 and 6 were prepared as shown in Scheme I.

Scheme I



[a] m-$ClC_6H_4CO_3H$ in CH_2Cl_2 [b] $C_6H_5SiH_3$

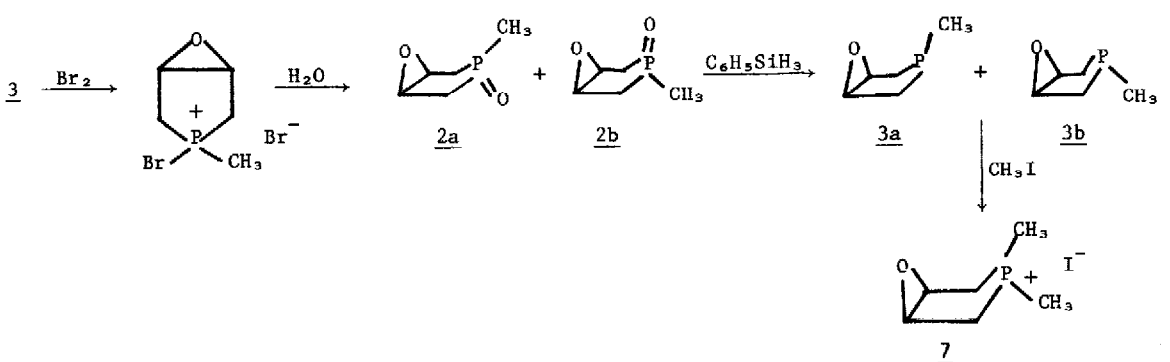
3-Phospholene oxides have been converted to epoxides previously by oxidation with peracetic acid,[2] or via the bromohydrin.[3] We have found that the epoxidation of phospholene oxides 1 and 4 with m-chloroperbenzoic acid proceeds well in refluxing methylene chloride. Thus, reaction of 1 with a slight excess of the peracid in methylene chloride gave epoxide 2 (81%, bp 81-82°/0.05 mm) as a hygroscopic solid; pmr ($CDCl_3$) δ 1.66 (d, $^2J_{PH}$ = 14 Hz, P-CH_3), 2.00-2.64 (m, -CH_2-), 3.70 (d, $^3J_{PH}$ = 26 Hz, epoxy H); ^{31}P NMR ($CDCl_3$) δ -60.5 ppm (downfield from 85% H_3PO_4). Similarly, phospholene oxide 4 (as a 30:70 mixture of cis:trans isomers)[4] gave 5 (76%, bp 120-123°/0.1 mm) as a hygroscopic solid; pmr ($CDCl_3$) δ 1.21-2.65 (m, ring CH_2), 1.56 (d, $^2J_{PH}$ = 14 Hz, P-CH_3), 1.63 (d, $^2J_{PH}$ = 14 Hz, P-CH_3), 3.45 (d, $^3J_{PH}$ = 25 Hz, epoxy H), 3.62 (d, $^3J_{PH}$ = 22 Hz, epoxy H); ^{31}P NMR ($CDCl_3$) δ -61.4 (33%) and -62.4 ppm (67%). Both 2 and 5 gave correct analyses.

Marsi has reported that phenylsilane reduction of phospholane oxides proceeds in good yield with retention of configuration at phosphorus.[5] We have applied this method to the epoxyphospholane oxides, and have obtained exclusive reaction at phosphorus, with no detectable side reaction at the epoxide function. Reaction of 2 with phenylsilane gave 3 (67%) as a distillable liquid, bp 60-61°/16 mm; pmr ($CDCl_3$) δ 1.10 (d, $^2J_{PH}$ = 4 Hz, P-CH_3), 1.76-2.12 (m, -CH_2), 3.66 (d, $^3J_{PH}$ = 4 Hz, epoxy H); ^{31}P NMR (C_6H_5) δ +36.4. Likewise, oxide 5 gave epoxyphosphine 6 (67%) as a mixture of cis, trans isomers, bp 105-110°/15 mm; pmr ($CDCl_3$) δ 1.00 and 1.10 (both d, $^2J_{PH}$ = 4 Hz cis and trans P-CH_3), 1.00-2.15 (m, ring -CH_2-), 3.56 and 3.64 (both m, epoxy H). Methiodides formed from the phosphines gave the correct analysis; the precipitate from 3 had mp 185-6°, from 6 mp 178-182°.

Arubzov and co-workers had reported previously[2] that peracetic acid oxidation of 3-phospholene oxides occurred at only one face of the ring and gave a single epoxide isomer which was suggested from dipole moment measurements to be that with phosphoryl oxygen and epoxide oxygen trans to one another.[6] In our work, m-chloroperbenzoic acid epoxidation also gave one (by ^{31}P NMR) isomer. We have used ^{13}C NMR techniques to deduce the relationship of the oxirane ring to the phosphoryl oxygen, and have arrived at the same conclusion on the directive effect of the phosphoryl group on epoxidation as did Arbuzov. For the purpose of this structure assignment, both the cis (2b) and trans (2a) isomers were required. An isomer mixture was therefore prepared by another method (Scheme II). This involves addition of bromine to a n-hexane solution at 0° of 3 from Scheme I to form the bromophosphonium bromide, followed by hydrolysis in an ice-aqueous $NaHCO_3$ slurry. The resulting epoxy phospholane oxide mixture was dominated (90%) by the same isomer as obtained from the direct oxidation.

Reduction of this oxide mixture with phenylsilane at 80° for 1 hr gave a phosphine mixture, again with the predominant isomer (90%) identical to the product of Scheme I. While the formation of the other isomer proceeds in only low yield by this method, an adequate concentration was obtained for comparative spectral measurements on both the oxide and the phosphine.

Scheme II



The ^{13}C NMR spectra are given in the Table. It might be expected that there would be a pronounced difference in chemical shifts for CH_3 of an isomer pair; this carbon would be δ-oriented to the epoxy oxygen, and it is known from a study of steroidal epoxides,[7] as well as

of alicyclic alcohols,[8] that greater δ-deshielding of CH_3 occurs when syn to oxygen than when anti. On the basis of its CH_3 signal being the more downfield (by 2.9 ppm), the major epoxy oxide isomer resulting from Scheme II and the single isomer from epoxidation of 1 may be assigned structure 2a. The same ^{13}C NMR relation is observed for the phosphines resulting from P-deoxygenation; the major isomer from Scheme II and the single isomer from Scheme I had the more downfield (by 3.0 ppm) CH_3 signal and is assigned structure 3a.

^{13}C NMR was used in another way to confirm the structures of the phosphines. Epoxyphospholane 3 from Scheme I was quaternized (retention[9]) with methyl iodide, and the ^{13}C spectrum of the product (7) showed two P-CH_3 resonances (δ 13.7 and δ 10.4 ppm) through the δ-deshielding effect. Quaternization of 3 with CD_3I gave the corresponding deuteriomethyl iodide salt 8 whose spectrum as expected from the deuterium coupling effect showed only one P-CH_3 resonance (δ 13.9 ppm). That it is the upfield P-CH_3 resonance that is missing implies that the new methyl group is being incorporated on the side of the ring opposite to the epoxide moiety and that this was the position originally occupied by phosphoryl oxygen.

Further evidence that the P-CH_3 and epoxide ring were cis to one another in the phosphine 3 was provided by the lithium aluminum hydride reduction (in THF at room temperature) to 1-methyl-3-phospholanol (81%, bp 100-101°/16 mm). The single product had ^1H and ^{31}P NMR spectra identical to those reported for the cis phospholanol isomer as obtained by a different method,[10] and also exhibited the characteristic aromatic solvent-induced shift reported for that isomer. Since hydride reduction of epoxides gives retained configuration at the carbinol site,[11] phosphine 3 is shown to have the cis structure 3a.

Based on these results, the single isomer obtained on epoxidation of each of the cis, trans forms of bicyclic oxide 4 can be assigned structures with the epoxy group opposite to phosphoryl oxygen.

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Table. ^{13}C NMR Data[a]

Compound	P-CH_3	C-2,5	C-3,4
2a	20.4(60)	30.1(65)	53.5(5)
2b	17.5(60)	30.8(62)	55.0(3)
3a	15.0(18)	28.2(15)	60.2(5)
3b	12.0(15)	30.8(18)	62.8(3)
7[b]	13.7(50), 10.4(50)	28.1(52)	59.3(s)
8[b]	13.9(50)	28.4(54)	59.5(2)

[a]Proton noise-decoupled ^{13}C NMR spectra were obtained on $CDCl_3$ solutions at 22.62 MHz on a Bruker HFX-10 spectrometer using the Fourier transform technique. Chemical shifts are in ppm (± 0.1 ppm) downfield from internal TMS; ^{31}P-^{13}C coupling constants (± 1 Hz) are given in parentheses. [b]Methanol solution.

References

1. (a) M. J. Boskin and D. B. Denny, Chem. and Ind. (London), 330 (1959).
   (b) G. Wittig and W. Haag, Chem. Ber., 88, 1654 (1955).
2. B. A. Arbuzov, A. P. Rakov, A. O. Vizel, L. A. Shapshinskaya, and N. P. Kulikova, Izv. Akad. Nauk. SSSR. Ser. Khim., 8, 1313 (1968).
3. D. G. Smith and D. J. H. Smith, Tetrahedron Lett., 1249 (1973).
4. C. Symmes, Jr. and L. D. Quin, J. Org. Chem., 41, 238 (1976).
5. K. L. Marsi, J. Org. Chem., 39, 265 (1974).
6. B. A. Arbuzov, A. P. Anastaseva, A. N. Vereshchagin, A. O. Vizel, and A. P. Rakov, Izv. Akad. Nauk. SSSR. Ser. Khim., 8, 1729 (1968).
7. K. Tori and T. Komeno, Tetrahedron Lett., 1157 (1974).
8. S. H. Grover and J. B. Stothers, Can. J. Chem., 52, 870 (1974).
9. (a) L. Horner, H. Winkler, A. Rapp, A. Mentrup, H. Hoffmann and P. Beck, Tetrahedron Lett., 161 (1961).
   (b) L. D. Quin and T. P. Barket, J. Amer. Chem. Soc., 92, 4303 (1970).
10. L. D. Quin and R. C. Stocks, J. Org. Chem., 39, 1339 (1974).
11. L. W. Trevoy and W. G. Brown, J. Amer. Chem. Soc., 71, 1675 (1949).