

Studies of Geometric Isomers of Cyclic Phosphites

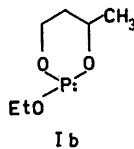
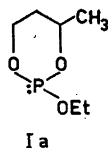
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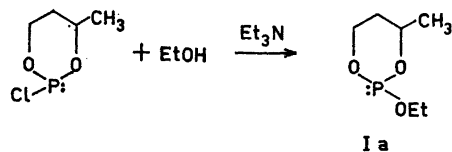
The paper reports studies of geometrical isomers of the cyclic phosphites 2-ethoxy-4-methyl-1,3,2-dioxaphosphorinan and 2-ethoxy-4-methyl-1,3,2-dioxaphospholan. It is shown that the reaction of the stable isomer of 2-chloro-4-methyl-1,3,2-dioxaphosphorinan with ethanol in ether in presence of triethylamine gives the unstable isomer of 2-ethoxy-4-methyl-1,3,2-dioxaphosphorinan in nearly pure form. This result is interpreted as an inversion of configuration around the phosphorus atom due to a S_N2 reaction between the nucleophilic oxygen in the alcohol and the electrophilic phosphorus atom in the chlorophosphite.

During an attempted gas chromatographic purification of the six-membered cyclic phosphite, 2-ethoxy-4-methyl-1,3,2-dioxaphosphorinan, two partially resolved peaks were obtained. When the temperature on the chromatographic column was altered the ratio between the two peaks was also altered. The result was interpreted as a partial separation of two geometric isomers (Ia) and (Ib), but that isomerization on the chromatographic column prevented their complete separation.

Recently Denney and Denney¹ have reported similar incomplete gas chromatographic separation of 2-methoxy-4-methyl-1,3,2-dioxaphosphorinan.



Further studies of the isomeric mixture showed that the isomerization was strongly sensitive to acid catalysis. Traces of acid caused rapid isomerization, after which only one peak was observed in the gas chromatogram (Fig. 1). Of the two isomers originally present, one must therefore be considerably less stable than the other. The unstable isomer was successfully obtained in nearly pure form from the corresponding cyclic chlorophosphite and ethanol in presence of excess triethylamine in ether:



The isomer ratio in the mixture was determined by treating the isomer mixture with sulphur in carbon disulphide, whereupon the stable thiophosphate (IIa) and (IIb) resulted. The mild condition under which sulphur is added, is assumed to have no influence on the ratio between the phosphite isomers originally present.

In Fig. 2 is shown the gas chromatogram of the thioisomers made from (Ia). Intergration of the area under the peaks shows that the unstable isomer (Ia) contains approximately 4 % of the stable isomer (Ib). The almost exclusive formation of the unstable isomer (Ia) from the chlorophosphite on treatment with ethanol in presence of excess triethylamine suggests an S_N2 -displacement on a single chlorophosphite isomer. The presence of only one cyclic chlorophosphite isomer was confirmed by treating the chlorophosphite with sulphur in carbon disulphide. The resulting thiophosphate gave a single peak in the gas chromatogram (Fig. 3). In comparison with the easy isomerization of the phosphite ester, a still easier isomerization of the chlorophosphite is to be expected since the P-Cl bond is much more reactive than the P-OEt bond.

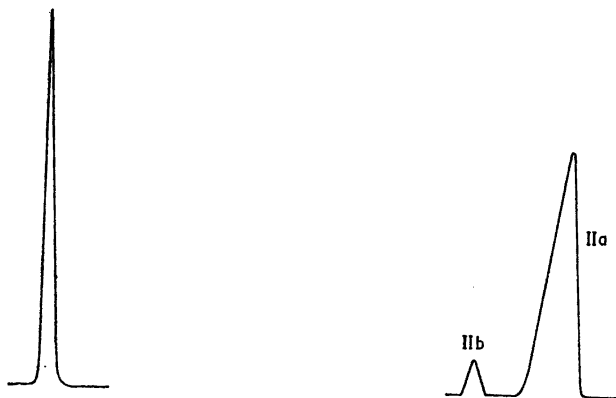
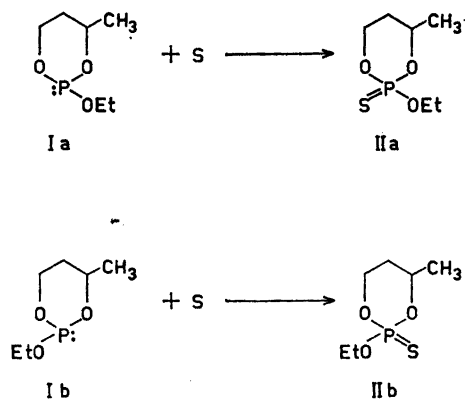


Fig. 1. Gas chromatogram of the stable phosphite isomer, 2-ethoxy-4-methyl-1,3,2-dioxaphosphorinan (Ib), after addition of traces of HCl to the isomer mixture (Ia + Ib). Column: $5' \times 1/8''$ packed with 20 % PDEAS on 60–80 mesh firebrick. Temperature: 110°C .

Fig. 2. Gas chromatogram of the thiophosphate isomers made by adding sulphur to the unstable isomer, 2-ethoxy-4-methyl-1,3,2-dioxaphosphorinan (Ia) in carbon disulphide. IIb (4 %) is identical with the thiophosphate made by adding sulphur to the stable phosphite isomer (Ib Fig. 1). Column: $5' \times 1/8''$ packed with 20 % PDEAS on 60–80 mesh firebrick. Temperature: 170°C .



It is further highly likely that the stable configuration of the chlorophosphite corresponds to the stable configuration of the phosphite ester (Ib). Since the reaction of ethanol with the stable chlorophosphite isomer gives the unstable phosphite ester isomer, inversion of configuration around the phosphorus atom must have occurred. This shows that the phosphorus atom in the chlorophosphite behaves electrophilic towards the oxygen atom of the ethanol in the substitution process. On treatment of the same chlorophosphite with



Fig. 3. Gas chromatogram of 2-chloro-2-thio-4-methyl-1,3,2-dioxaphosphorinan made from the corresponding chlorophosphite and sulphur. Column; 5' × 1/8" packed with 20 % PDEAS on 60-80 mesh firebrick. Temperature: 160°C.

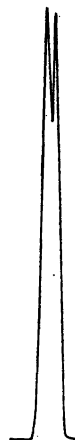


Fig. 4. Gas chromatogram of the thiophosphate isomers, 2-ethoxy-2-thio-4-methyl-1,3,2-dioxaphospholan made from the corresponding mixture of phosphite isomers. Column: 5' × 1/8" packed with 20 % PDEAS on 60-80 mesh firebrick. Temperature: 160°C.

sodium methoxide in ether, Denney and Denney¹ reported the formation of two cyclic phosphite ester isomers in varying ratios. It is reasonable to expect that the strongly nucleophilic methoxide ions unlike the mixture of ethanol and triethylamine may bring about an easier isomerization of the unstable methoxy isomer which is formed from the chlorophosphite.

Studies of the corresponding five-membered cyclic phosphite, 2-ethoxy-4-methyl-1,3,2-dioxaphospholan suggest a still easier isomerization of these isomers than observed for the six-membered analogs. Earlier, the presence of isomers in five-membered cyclic phosphites has been detected by NMR spectroscopy.² In the present study the isomers were treated with sulphur in carbon disulphide, and the stable thiophosphates thus obtained were subjected to gas chromatographic purification. Fig. 4 shows that complete separation of the two thioisomers has not been obtained, but the approximately equal size of the peaks suggests comparable amounts of the two isomers. The chromatogram was unchanged when the isomeric phosphite mixture was treated with catalytic amount of acid prior to treatment with sulphur in carbon disulphide. These findings compared with the formation of only one of the isomers of the six-membered cyclic phosphites under corresponding conditions, points to the conclusion that there is less energy difference between the isomers in the phospholan system than between the isomers in the phosphorinan system.

EXPERIMENTAL

2-Chloro-4-methyl-1,5,2-dioxaphosphorinan and *2-chloro-4-methyl-1,3,2-dioxaphospholan* were synthesized from 1,3-butandiol, and 1,2-propandiol, respectively, and phosphorus trichloride in chloroform according to descriptions by Lucas *et al.*³ Chlorophosphorinan: b.p.₁₄ 71°C, n_D^{20} 1.4403 (reported: b.p.₈ 63–64°C, n_D^{20} 1.4410). (Found: Cl 22.43. Calc. for $C_4H_8O_2PCl$: Cl 22.95). Chlorophospholan: b.p.₁₅ 50°C, n_D^{19} 1.4767 (reported: b.p.₂₈ 58°C, n_D^{25} 1.4707).

2-Thio-2-chloro-4-methyl-1,3,2-dioxaphosphorinan and *2-thio-2-chloro-4-methyl-1,3,2-dioxaphospholan* were made by adding equivalent amounts of the above chlorophosphorinan, respectively chlorophospholan, to a solution of sulphur in carbon disulphide (1.5 g sulphur in 50 ml carbon disulphide). The thio isomers were isolated by gas chromatography.

2-Ethoxy-4-methyl-1,3,2-dioxaphosphorinan and *2-ethoxy-4-methyl-1,3,2-dioxaphospholan* were synthesized from the respective chlorides with ethanol in ether in the presence of excess triethylamine. Example: To a solution of 13 g (0.28 M) ethanol and 30 g (0.30 M) triethylamine in 300 ml ether is added with stirring 40 g (0.26 M) of 2-chloro-4-methyl-1,3,2-dioxaphosphorinan. The temperature is kept below 10°C during the addition. Triethylamine hydrochloride is filtered off and the ether and excess triethylamine are distilled off at reduced pressure keeping the distillation temperature at room temperature. The rest in the distilling flask is the nearly pure isomer (Ia). This can be distilled unchanged at reduced pressure. Addition of catalytic amounts of dry HCl gas to the isomer (Ia) followed by distillation or gas chromatography gave the pure isomer (Ib) (Fig. 1).

2-Thio-2-ethoxy-4-methyl-1,3,2-dioxaphosphorinan and *2-thio-2-ethoxy-4-methyl-1,3,2-dioxaphospholan* were made by adding the respective cyclic phosphites to an equivalent amount of sulphur in carbon disulphide (1.6 g sulphur dissolved in 50 ml carbon disulphide). Unreacted sulphur was filtered off and the isomeric thiophosphates isolated by gas chromatography (Figs. 2 and 4).

REFERENCES

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