

Stereochemistry of Oxidation of Organophosphorus Thiono-compounds and P^{III} Compounds by Nitric Acid and Dinitrogen Tetroxide

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Summary The stereochemical course of oxidation at the phosphorus atom in phosphorus thiono-derivatives, phosphines, and phosphites is shown to depend on structural factors as well as on the nature of the oxidising agent.

RECENTLY there has been considerable interest in the stereochemistry of optically active phosphorus compounds containing sulphur^{1,2} which have assumed great significance in the study of the reaction mechanisms of phosphorus compounds. Convenient methods of preparation of optically active thiono-esters $>P(S)OR$ and thionoanhydrides $>P(S)-O-P(O)<$ have been developed in these laboratories.^{1,3} The ready availability of such compounds has justified a search for a convenient general method of oxidising thiono-derivatives of phosphorus to the corresponding oxo-compounds with a high degree of stereospecificity. Although such conversions can be achieved, stereochemical studies have been limited to the oxidation of methylphenyl-n-propylphosphine sulphide by

potassium permanganate in pyridine.⁴ Retention of configuration was reported in that case. We report a study on oxidation of phosphorus compounds containing the thiono-group, $P=S$, by nitric acid and dinitrogen tetroxide in which configuration at the phosphorus atom was either retained or inverted depending on the nature of the oxidising agent. We have found that stereochemical direction of oxidation of the optically active acyclic phosphine (VI) runs parallel with that of the thiono-compounds (III) and (VII). Therefore, we also examined the behaviour of the cyclic phosphites (IX) and (X) on oxidation and found that different stereochemistry was involved.

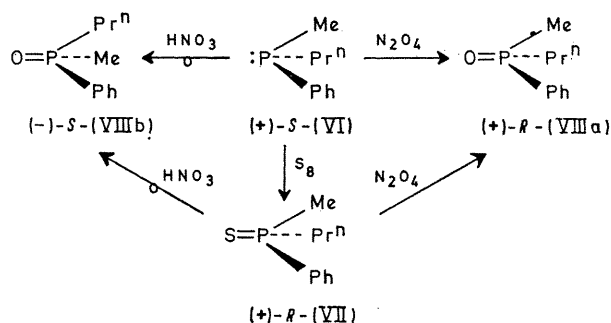
Oxidations with dinitrogen tetroxide were carried out in methylene chloride solution (1 g N_2O_4 in 10 ml CH_2Cl_2), at 15–20° in the case of thiono-compounds and at –40° for P^{III} compounds. Oxidations by conc. nitric acid (ca. 67%) were performed by adding the organophosphorus compound to a fourfold excess of the oxidising agent at room temperature. All reactions described were run for 0.5 h.† The reaction mixture was neutralised and the products‡ were extracted with chloroform. Nitric acid oxidation of

† This length of time in all cases was sufficient to achieve complete oxidation of the starting material.

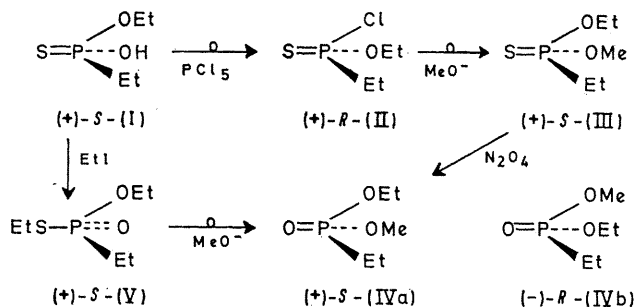
‡ The purity of compounds was checked by t.l.c. and g.l.c. Their integrated n.m.r. spectra were in accord with assigned structures, and satisfactory analyses were obtained.

O-ethyl *O*-methyl ethyl phosphono thionate (III) $[\alpha]_{578} + 2.3^\circ$ (neat) prepared from *O*-ethyl ethylphosphonochloridothionate⁵ (II) and sodium methoxide gave *O*-ethyl *O*-methyl ethylphosphonate (IVb) $[\alpha]_{578} - 0.848^\circ$ (neat). Oxidation of (III) with dinitrogen tetroxide gave (IVa), $[\alpha]_{578} + 0.135^\circ$ (neat). Methylphenyl-*n*-propylphosphine sulphide (VII), $[\alpha]_{578} + 16.3^\circ$ prepared by addition of sulphur to methyl phenyl-*n*-propylphosphine⁶ (VI) $[\alpha]_{578} + 13.5^\circ$ (toluene), was oxidised with nitric acid to give methylphenyl-*n*-propylphosphine oxide (VIIIb) $[\alpha]_{578} - 12.5^\circ$. Oxidation of (VII) $[\alpha]_{578} + 13.3^\circ$ with dinitrogen tetroxide gave (VIIIa) $[\alpha]_{578} + 1.0^\circ$. (VI) $[\alpha]_{578} + 12.1^\circ$ gave (VIIIb) $[\alpha]_{578} - 9.45^\circ$ when oxidised with nitric acid, but gave (VIIIa) $[\alpha]_{578} + 2.4^\circ$ when dinitrogen tetroxide was used. Oxidations of (VI) and (VII) with dinitrogen tetroxide were not fully reproducible and in some experiments full racemisation was observed. In order to elucidate the stereochemical course of oxidation by nitric acid and dinitrogen tetroxide the transformation shown in Schemes

either dinitrogen tetroxide or nitric acid under the same reaction conditions for 2 h. Full racemisation of (VIII)



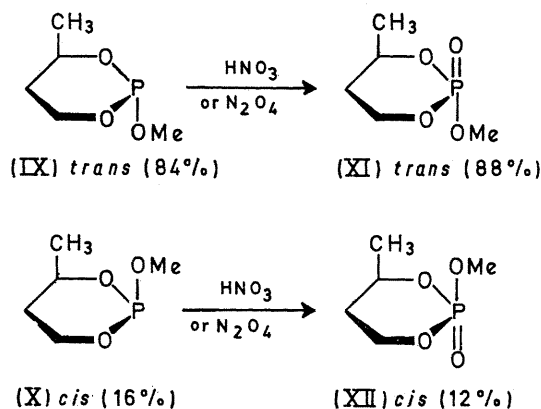
SCHEME 2



SCHEME 1. The absolute configuration of the monothio-acid (I) is taken from ref. 14.

1—3 were carried out. There is no bond breaking at the phosphorus atom in the transformation (I) \rightarrow (V) and, by analogy with closely related reactions,^{1-3,7} the transformations (I) \rightarrow (II), (II) \rightarrow (III), and (V) \rightarrow (IVa) should proceed with inversion of configuration. Therefore, formation of the dextrorotatory stereoisomers (IVa) in the dinitrogen tetroxide oxidation of (III) indicates retention of configuration. The formation of the laevorotatory stereoisomers in the nitric acid oxidation shows that inversion takes place. The stereochemical assignments in Scheme 2, which is based on the work of Horner and his colleagues,^{8,9} show that oxidations by nitric acid lead to inversion but that those by dinitrogen tetroxide lead to retention with considerable racemisation. These results indicate a clear difference in the course of oxidations by nitric acid and dinitrogen tetroxide. The highly stereospecific oxidation with nitric acid gave a rather unexpected inversion of configuration. The high degree of racemisation in addition to retention observed in oxidations by dinitrogen tetroxide is, at least in the case of the reaction (III) \rightarrow (IVa), most likely to result from the mechanism of oxidation and not from racemisation of (IVa) by the oxidant. Compound (IV) racemises to only a slight extent when treated with

was observed, however, in the presence of dinitrogen tetroxide after 45 min.[¶] This racemisation is somewhat similar to stereomutations of sulfoxides in the presence of dinitrogen tetroxide.¹¹ In contrast to the oxidations of the acyclic phosphine, diastereomeric *trans*-(IX) and *cis*-(X) 2-methoxy-4-methyl-1,3,2-dioxaphosphorinane were oxidised by both nitric acid and dinitrogen tetroxide with full retention of configuration at the phosphorus atom to diastereomeric 2-oxo-2-methoxy-4-methyl-1,3,2-dioxaphos-



SCHEME 3

pharinar *trans*-(XI) and *cis*-(XII).^{12,13} The diastereomeric ratios ($\pm 5\%$) of phosphites and phosphates were determined from n.m.r. spectra and g.l.c., respectively. The difference in the stereochemistry of acyclic phosphine and cyclic phosphite oxidations is particularly interesting and illustrates once again that stereochemical conclusions drawn from acyclic systems cannot always be applied to cyclic systems and *vice versa*.

Note added in proof. Oxidation of the optically active phosphine sulphide (VII) with N_2O_4 in the presence of

§ Rotations refer to solvent methanol unless otherwise stated.

¶ The racemisation of an acyclic phosphine oxide by N_2O_4 has been mentioned recently.¹⁰

$\text{CF}_3\text{CO}_2\text{H}$ gave optically active phosphine oxide (VIII) indicates the importance of protonation in the mechanism with partial *inversion* of configuration. This clearly involved.

(Received, September 7th, 1970; Com. 1503.)

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