A Reinvestigation of the Reaction Between 2-Methoxy-5,5-dimethyl-1,3,2dioxaphosphorinan-2-one and 2-Chloro-5,5-dimethyl-1,3,2-dioxaphosphorinan-2-one

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The title compounds together give pyrophosphate and methyl chloride probably *via* a cycle of reactions involving cyclic phosphate diester and hydrogen chloride as carriers; rapid formation of dioxadiphosphetanes from intermediate five-co-ordinate phosphoranes and a slower intermolecular scrambling account for the distributions of ¹⁸O observed starting with various patterns of ¹⁸O labelling.

Phosphoryl esters, R1R2P(O)OR3, are weakly nucleophilic. Their nucleophilic site is usually assumed to be the phosphoryl oxygen1 and this has been demonstrated by means of ¹⁸O-labelling in the case of reaction with phosgene.² However, in 1975, Simpson and Zwierzak³ treated the ¹⁸O-labelled ester (1) with the phosphoryl chloride (2) and analysed the resulting pyrophosphate (3) by reaction with sodium methoxide and estimation of the ¹⁸O content of the resulting methyl ester. One half of the ester formed from (3a) will contain ¹⁸O whereas (3b) can lead only to unlabelled ester. Starting with methyl ester (1) containing 10.2% ¹⁸O in the phosphoryl oxygen, Simpson and Zwierzak recovered ester containing 2.9% ¹⁸O. They concluded that the pyrophosphate was a 60:40 mixture of (3a) and (3b) and that, whereas (3b) resulted from the expected nucleophilic attack of phosphoryl oxygen, (3a) was the result of nucleophilic attack on (2) by the methoxy oxygen of (1). We have reinvestigated



this reaction with the advantages of high levels of isotopic substitution and high-field ^{31}P n.m.r. spectroscopy and provide a different interpretation of these results.

When the methyl ester (1) and the phosphoryl chloride (2),



Figure 1. ³¹P N.m.r. spectrum at 121 MHz in $CDCl_3$ of pyrophosphate formed from ester (1) and phosphoryl chloride (2), both labelled with 95% ¹⁸O in their phosphoryl oxygens, in xylene at 120 °C for 24 h.

Table 1. Pyrophosphates formed from ester (1) and phosphoryl chloride (2), both labelled with 95% ¹⁸O in their phosphoryl oxygens, in xylene at 120 °C.

	P O P						
	(3)	(3 a)	(3b)	(3c)	(3d)	(3e)	
Found(%) $\begin{cases} 24 h \\ 2 h \end{cases}$	4.9 1.8	15.8 11.4	9.9 7.7	15.7 21.8	28.4 44.2	24.3 13.0	
scrambling	4.9	17.0	8.5	14.7	29.4	25.2	





Scheme 1. (i), pseudorotation; (ii) - Cl-.

both labelled with 95% ¹⁸O in the phosphoryl oxygen, were heated together in xylene at 120 °C for 24 h the ³¹P n.m.r. spectrum of the resulting pyrophosphate (Figure 1) showed the ¹⁸O to be almost completely scrambled among the three exocyclic oxygens (Table 1). In this system a P¹⁸O single bond produces an upfield ³¹P n.m.r. shift of 0.023 p.p.m. and a P¹⁸O double bond a shift of 0.035 p.p.m.; the effects are additive. In unsymmetrically labelled molecules an extreme AB system leads to one apparent signal halfway between the two expected; *e.g.* the signal at 4.9 Hz to high field of unlabelled pyrophosphate is due to (**3d**) in which the two phosphorus signals would individually be at 2.7 and 7.1 Hz relative to (**3**).⁴

Under the conditions used by Simpson and Zwierzak, 2 h refluxing in xylene, scrambling was extensive but not complete (Table 1). This scrambling is most easily envisaged as involving exchange between (3) and traces of cyclic phosphodiester (4).

Attempts to prepare an authentic sample of (3a) by reaction of unlabelled phosphodiester anion (4) with ¹⁸O-labelled (2a)in CDCl₃ at 30 °C revealed unexpected complexity. The reaction gave, even in its first stages, a 1:1 mixture of (3a) and (3b). Similarly monolabelled anion (4a) with unlabelled (2)



gave (3a) and (3b) in a ratio of 3:1 throughout the course of the reaction. Clearly whichever oxygen of (4) or (4a) attacks the phosphoryl chloride it becomes equivalent at some stage of the reaction sequence with the phosphoryl oxygen of the phosphoryl chloride. This is probably *via* the topomeric dioxadiphosphetanes (6) and (7) formed from the initial five-co-ordinate phosphorane (5) which must pseudorotate before expelling chloride anion⁵ (Scheme 1).

Application of a similar dioxadiphosphetane hypothesis to the Simpson-Zwierzak reactions described above, *i.e.* (a) labelled (1) with unlabelled (2) and (b) labelled (1) with labelled (2a), predicted that in their early stages, before intermolecular scrambling became important, reaction (a) would lead to a 1:1 ratio of (3a) and (3b) whereas reaction (b) would give entirely (3d). Neither prediction was correct; reaction (a) gave (3a) and (3b) in a ratio of 3:1 and reaction (b) gave (3d) and (3c) in a ratio of 3:1. These are the ratios of isomeric pyrophosphates expected from attack of cyclic phosphodiester anion (4a) on phosphoryl chlorides (2a) and (2) respectively!

The rate of a Simpson-Zwierzak reaction is inversely related to the purity of the starting materials and to the precautions taken to exclude moisture. We conclude that the formation of pyrophosphate is initiated by a small amount of phosphodiester (4). This reacts with the phosphoryl chloride (2) to give pyrophosphate and HCl which then reacts with methyl ester to give methyl chloride and (4),⁶ see Scheme 2. This hypothesis, together with the formation of dioxadiphosphetanes from the intermediate five-co-ordinate phosphoranes and a slower intermolecular scrambling in the product, account for the experimental observations.

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