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ELECTROPHILIC CATALYSIS OF N-->O PHOSPHYL MIGRATION

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Summary: 2-N-Benzoyl-N-phenylamino-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (3a) undergoes rearrangement to (2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinanyl)(N-phenyliminobenzoyl)oxide (4a). This transformation is shown to be catalysed by electrophilic reagents such as benzoyl chloride, trimethylsilyl chloride, p-toluenesulphonyl chloride.

We originally observed that aqueous work-up of the reaction mixture from treatment of O,O-dialkyl phosphoranilidate (1) in pyridine with an excess of benzoyl chloride leads to O,O-dialkyl phosphate (2)[1]. This prompted us to carry out more detailed studies, which indicated that the most probable course of events includes N-benzoylation, and the key-intermediate N-benzoyl-O,O-dialkyl phosphoranilidate (3) undergoes a slow rearrangement to O,O-dialkylphosphoric-N-phenyliminobenzoic mixed anhydride (4). Hydrolysis of 4 occurs with attack of water exclusively at N-phenylimino-carbon atom leading to 2 and benzanilidate[2]. On the basis of ^{31}P NMR studies of reaction of [^{15}N] and [^{18}O]-labeled *cis*- and *trans*-2-N-phenylamino-2-oxo-4-methyl-1,3,2-dioxaphosphorinanes[3] we established that rearrangement 3-->4 occurs with retention of configuration; we formulated the working hypothesis that the rearrangement 3-->4 is catalysed by pyridine. In order to evaluate the validity of this hypothesis more detailed studies were undertaken. As a model phosphoryl system we chose derivatives of 2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane.

In this report we present independent preparations of N-benzoyl-O,O-dialkyl phosphoranilidate (3) and O,O-dialkylphosphoric-N-phenyliminobenzoic anhydride (4). Additionally we present studies on the influence of reaction medium (pyridine) and benzoyl chloride on the stability of both 3 and 4.

2-Methoxy-5,5-dimethyl-1,3,2-dioxaphosphorinane[4] in reaction with phenyl azide gave 2-methoxy-2-N-phenylimino-5,5-dimethyl-1,3,2-dioxaphosphorinane (5)[5]. This compound when treated with stoichiometric equivalent of benzoyl chloride in benzene gave 2-N-benzoyl-N-phenylamino-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (3a)[6]. Independent studies on reaction between 2-tributylstannyloxy-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (6)[7] and N-phenylbenzimidoyl chloride (7)[9], performed in pyridine solution and monitored by ^{31}P NMR, had shown the appearance of two products absorbing at -10.8 ppm and -16.4 ppm (spectrum recorded 5 min. after mixing of reagents, intensity ratio was ca.1:4, respectively). However, the intensities of signals at -10.8 ppm and -16.4 ppm were time dependent and after 2 h the ratio was ca 2:1, while after 20 h it was ca 4:1. The signal at -16.4 ppm has been interpreted as characteristic for (5,5-dimethyl-1,3,2-dioxaphosphorinyl)(N-phenyliminobenzoyl)oxide (4a), while the one at -10.8ppm was recognized as corresponding to 3a, which has been confirmed by addition of a genuine sample of 3a to the NMR tube. Similarly, condensation of 2-trimethylsilyloxy-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (8) with N-phenylbenzimidoyl chloride (7), performed in pyridine solution, had shown in ^{31}P NMR assay a similar pattern of signals (-10.8 ppm and -16.4 ppm, ratio 1:2 one hr after mixing of reagents, and 5:1 after 20 h, respectively).

These results clearly indicated that compound 4a is, under the reaction conditions, the thermodynamically less stable product and undergoes slow rearrangement to 3a. This was unambiguously proved by results of condensation between 2-tributylstannyloxy-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (6) and [^{15}N]N-phenylbenzimidoyl chloride, since the signal appearing at -10.8 ppm showed the splitting pattern in Fig.1, indicating the presence of direct ^{15}N-^{31}P bond in 3a. Higher thermodynamic stability of 2-N-benzoyl-N-phenylamino-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane 3a under the aforementioned experimental conditions was consistent with earlier results of Mikołajczyk et.al.[10], who proved that the primary products of condensation of dialkyl phosphorothioic acid with DCC undergoes O-->N phosphyl migration.

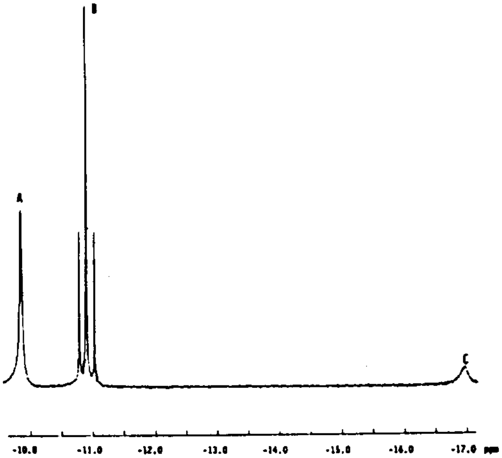
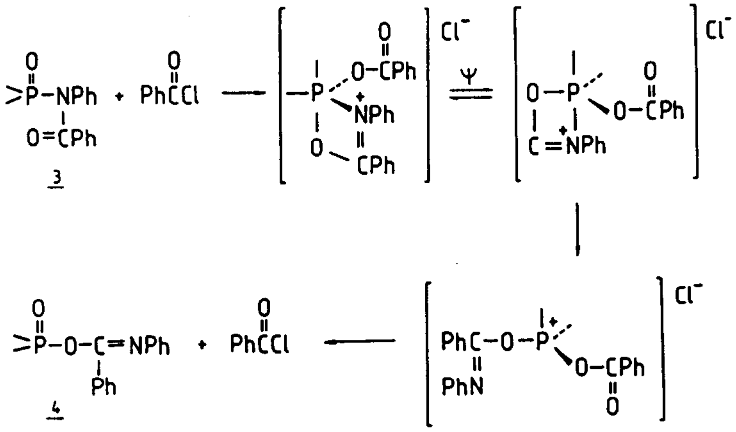


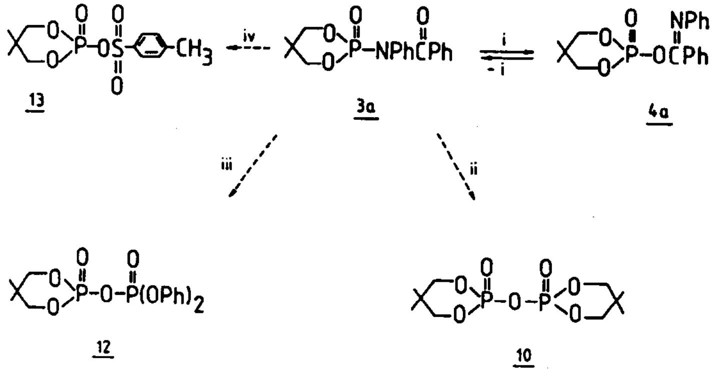
Figure 1. ^{31}P MNR spectrum of the reaction mixture between 2-tributylstannyloxy -2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (6) and [^{15}N]N-phenylbenzimidoyl chloride. 6, 3a, 4a are explained in the text

Careful analysis of all previous reports[11], as well as the results presented *vide supra*, prompted us to study the influence of benzoyl chloride on the stability of N-benzoyl-O,O-dialkyl phosphoranilidates (3) and O,O-dialkylphosphoric-N-phenyliminobenzoic anhydrides (4). However, when 3a in pyridine solution ($\delta^{31}P$ -10.8 ppm) was treated with an excess of benzoyl chloride, the ^{31}P NMR spectra, recorded 11 h after mixing of reagents, showed the presence of two signals of nearly equal intensities at -10.8 ppm and -16.4 ppm, while after 96 h only the signal at -16.4 ppm was present, which is characteristic of 4. This result unambiguously proved that N-->O phosphyl migration (rearrangement 3a-->4a) is caused by the electrophilic assistance of benzoyl chloride, and presumably occurs *via* phosphoryl oxygen involvement, increasing the electron deficit at phosphorus and making it more susceptive for intramolecular attack by the carbonyl oxygen. Moreover, the presence of an excess of benzoyl chloride increases the stability of structure 4 (Scheme 1).



Scheme 1.

Electrophilic assistance in the rearrangement 3-->4 has been proven by independent experiments with electrophiles other than benzoyl chloride. If 3a was treated with trimethylsilyl chloride/pyridine, it underwent complete rearrangement to 4a. However, removal of trimethylsilyl chloride by vacuum evaporation reversed the process, (rearrangement 4-->3). Treatment of 4a, resulting from reaction 3a and Me$_3$SiCl/Py, with water, caused disappearance of 4a and the formation of 2-hydroxy-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane (2a)[13].



Scheme 2 : i) Me$_3$SiCl ; ii) P(O)Cl ; iii) (PhO)$_2$P(O)Cl ;
iv) CH$_3$–C$_6$H$_4$–SO$_2$Cl

The results presented on electrophilic assistance in the rearrangement 3-->4 do not provide strong evidence for covalent electrophilic catalysis, since the volatile trimethylsilyl chloride can be removed by evaporation, which results in the reverse 4-->3 rearrangement. However, when a pyridine solution of 3a was treated with 2-chloro-2-oxo-5,5-

dimethyl-1,3,2-dioxaphosphorinane (9)[13] the ^{31}P NMR control showed the appearance of the symmetrical pyrophosphate, namely bis(2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinanyl)oxide (10)[13] (Scheme 2), while similar treatment with O,O-diphenyl phosphorochloridate (11) gave unsymmetrical pyrophosphate, namely (2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinanyl)(O,O-diphenyl phosphoryl)oxide (12, two doublets at $\delta^{31}P$ -20.8 ppm and -23.16 ppm, ^{2}J=19.2 Hz). Analogous reaction of a pyridine solution of 3a with p-toluenesulphonyl chloride led to the appearance of mixed phosphoric-sulphonic anhydride, namely (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinanyl)(p-toluenesulphonyl)oxide (13, $\delta^{31}P$ -20.3 ppm); its identity was proved by addition of a genuine sample of 13, prepared according to Michalski et al.[14]. These results strengthen the hypothesis concerning electrophilic assistance (phosphoryl chloride, p-toluenesulphonyl chloride) in the process of 3-->4 rearrangement, since formation of structures such as these in compounds 10, 12 and 14 is possible only if N-benzoyl-O,O-dialkyl phosphoranilidate (3) undergoes rearrangement to anhydride 4, but also indicate the phosphorylating properties of 4.

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5. 5: yield 63%; m.p. 99-101°C; MS(70eV) m/z 255(M^{+},80%), 187(100%); $\delta^{31}P$ -9.0 ppm($CDCl_3$).
6. 3a: yield 52%; m.p. 137-159°C; MS(70eV) m/z 345(M^{+},20%), 105(100%); $\delta^{31}P$ -9.4 ppm ($CDCl_3$).
7. Compound 6 had been obtained according to procedure described by Hata et al.[8], in the reaction between 2-hydroxy-2-oxo-5,5-dimethyl-1,3,2-dioxaphosphorinane and tri-n-butyltin methoxide in methylene chloride at room temperature. This compound is a white sticky solid and had been used without any purification after complete removal of solvent, $\delta^{31}P$ -9.9 ppm (C_5H_5N).
8. K.Yanaguchi, T.Kamimura, T.Hata; J.Am.Chem.Soc. 102, 4534 (1980).
9. N-Phenylbenzimidoyl chloride had been obtained in the reaction between benzanilide and thionyl chloride. Yield 89%, m.p. 40-41°C, b.p. 175°C/12 mm Hg.
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11. Modro had reported that N-benzoyl-O,O-dialkyl phosphoramidates undergo rearrengement to O,O-dialkylphosphoric-N-phenyliminocarboxylic anhydrides under condition of electron impact mass spectrometer (70eV,200°C)[12].
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