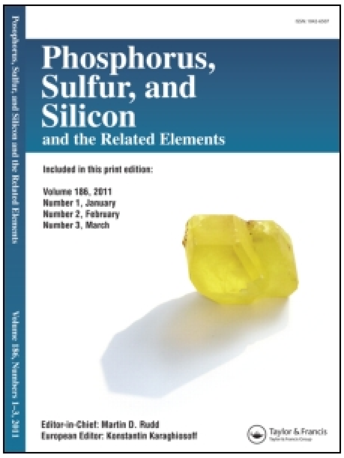

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# REACTIONS OF PHOSPHITES WITH ACID CHLORIDES. Phosphite Attack at the Carbonyl Oxygen of α-Ketophosphonates

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# REACTIONS OF PHOSPHITES WITH ACID CHLORIDES

## Phosphite Attack at the Carbonyl Oxygen of α-Ketophosphonates

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The reaction of 4-nitro and 3,5-dinitrobenzoyl chloride with trimethyl phosphite gives the diphosphorus compounds **2a** and **2c** derived from the reaction of two molecules of phosphite with two molecules of acid chloride. The mechanism has been shown to involve an anionic intermediate and proceeds via the expected α-ketophosphonate **1**.

## RESULTS AND DISCUSSION

The Michaelis-Arbusov reaction involving the addition of trialkyl phosphite to carboxylic acid chlorides has been successfully used to prepare a wide range of α-ketophosphonates. Although complications have arisen when unsaturated acid chlorides have been employed, e.g. *trans*-2-butenoyl chloride[1] or cinnamoyl chloride,[2] few problems have been reported concerning the saturated acyl or simple aroyl chlorides. Thus most α-aroylphosphonates **1** are readily prepared by the reaction of phosphites with the appropriate acid chloride (Eq. 1).

$$\mathrm{ArCOCl} + (\mathrm{RO})_3\mathrm{P} \longrightarrow \underset{\mathbf{1}}{\mathrm{ArCOPO(OR)_2}} + \mathrm{RCl} \qquad (1)$$

We have used $^{31}$P n.m.r. spectroscopy to monitor a number of these reactions and have observed that the reaction of trimethyl phosphite with 4-nitrobenzoyl chloride proceeds to give the diphosphorus compound **2a**, $\delta^{31}$P −2.29, 13.90 p.p.m.,[3] $J_{PP}$ 1.8 Hz, rather than the expected α-ketophosphonate (**1**, R = Me, Ar = 4-nitrophenyl). The structure of the diphosphorus compound was established as **2a** by $^1$H, $^{13}$C and $^{31}$P n.m.r. studies (see Table I). This is somewhat surprising in view of previous claims[4] that diethyl 4-nitrobenzoylphosphonate (**1**, R = Et, Ar = 4-nitrophenyl) can be prepared by reaction of triethyl phosphite with 4-nitrobenzoyl chloride. Such a claim is not supported by our n.m.r. studies which indicate that, regardless of the mode of addition, at no time during the course of the reaction is there any signifi-

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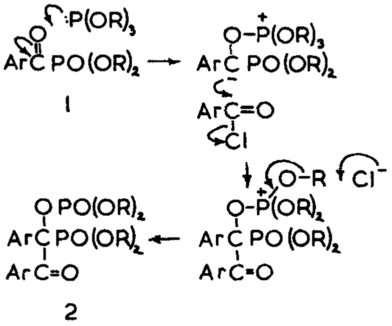
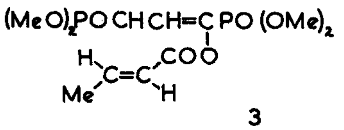
TABLE I

$^1$H and $^{13}$C N.M.R. Data for the Phosphates **2a** and **5a**

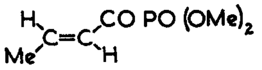
| $\delta^{13}C(J_{CP})$ | **2a** | **5a** |
|---|---|---|
| O—Me | 55.61(6),55.28(7)<br>54.61(6),54.26(7) | 54.73(6),54.50(6)<br>54.28(4),53.99(4) |
| Ar—C | 88.75(4,164) | 73.44(6,169) |
| Ar 1 | 139.72(4,11) | 140.35(2,2) |
| 2,6 | 126.92(4) | 128.08(6) |
| 3,5 | 123.34(3) | 123.45(3) |
| 4 | 147.97(3) | 147.87(3) |
| C=O | 190.50(1,2) | — |
| COAr 1 | 138.10(7) | — |
| 2,6 | 130.87 | — |
| 3,5 | 123.06 | — |
| 4 | 149.67 | — |
| $\delta^1H(J_{HP})$ | | |
| O—Me | 3.49(11.6)<br>3.81(11.2)<br>3.88(11.7)<br>3.93(11.2) | 3.65(11.3)<br>3.78(10.8)<br>3.78(10.8)<br>3.82(11.3) |
| Ar—CH | — | 5.72(10.6,14.7) |
| Ar | 7.75(2.1),8.28<br>($J_{HH}$ 8) | 7.69(2.2),8.26<br>($J_{HH}$ 8.8) |
| COAr | 7.82,8.14<br>($J_{HH}$ 8) | — |



SCHEME 1 **2a** R = methyl, Ar = 4-nitrophenyl
**2b** R = ethyl, Ar = 4-nitrophenyl
**2c** R = methyl, Ar = 3,5-dinitrophenyl



**3**



**4**

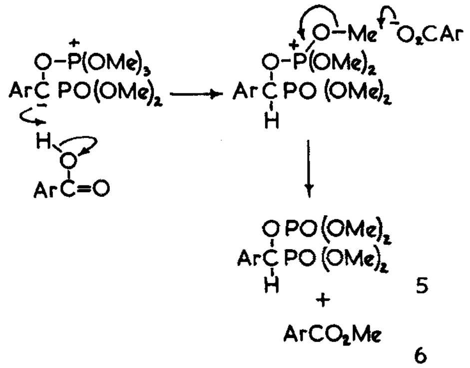
cant concentration of the α-ketophosphonate (**1**, R = Me or Et, Ar = 4-nitrophenyl) in the reaction mixture.

It is interesting to note that since both compounds (**1**, R = Et, Ar = 4-nitrophenyl) and **2b** give the same values for microanalysis and both have a carbonyl absorption band in the infra red spectrum it is unlikely that earlier workers would have been alerted to the possibility of an anomolous reaction occurring. Furthermore the formation of the diphosphorus compound **2b** might account for the abnormally large difference in the predicted and observed dipole moment reported[4] for the α-ketophosphonate (**1**, R = Et, Ar = 4-nitrophenyl).

We have recently reported[1] that the reaction of *trans*-2-butenoyl chloride with trimethyl phosphite can lead to the formation of the diphosphonate **3**. This reaction involves the attack by phosphite on the initially formed α-ketophosphonate **4** followed by reaction with another molecule of acid chloride. We believe that this basic reaction sequence also occurs during the formation of the diphosphorus compound **2a** but that the mechanisms in the two reactions are different. The proposed mechanism for the formation of the diphosphorus compound **2a** is shown in Scheme 1.

The mechanism proposed involves the attack by trimethyl phosphite on the carbonyl oxygen of the initially formed α-ketophosphonate (**1**, R = Me, Ar = 4-nitrophenyl) to give an anionic intermediate in which the negative charge is stabilised by the electron-withdrawing 4-nitrophenyl group in addition to the phosphoryl group. This anionic intermediate then undergoes further reaction with another acid chloride molecule to give the diphosphorus compound **2a**. This formation of an anionic intermediate by phosphite attack on the carbonyl oxygen of an α-ketophosphonate has also been postulated to occur in the case of a number of ortho-substituted benzoylphosphonates, e.g. (**1**, R = Et, Ar = 2-methoxyphenyl).[5] In this latter case it has been proposed that the anionic intermediate is first protonated by proton transfer from the methoxyl group followed by an intramolecular cyclisation involving the expulsion of the attacking phosphite as phosphate. The product is thus another phosphonate rather than a diphosphorus compound. Moreover the reaction of these ortho-substituted aroylphosphonates with trialkyl phosphites are reported to require several hours at temperatures of 80–100°C. In contrast the reactivity of the phosphite towards the carbonyl oxygen of the α-ketophosphonate (**1**, R = Me or Et, Ar = 4-nitrophenyl) is obviously higher than towards the carbonyl carbon in the 4-nitrobenzoyl chloride since $^{31}$P n.m.r. indicates that at no time during the reaction are significant quantities of the α-ketophosphonate (**1**, R = Me or Et, Ar = 4-nitrophenyl) present in the reaction mixture. The presence of small quantities of the α-ketophosphonate (**1**, R = Me, Ar = 4-nitrophenyl) in the final product mixture during the production of **2a** was confirmed by adding Brady's reagent. Recrystallisation of the resulting hydrazone from ethanol produced a small quantity of the 2,4-dinitrophenylhydrazone derivative of dimethyl 4-nitrobenzoylphosphonate, the identity of which was confirmed by microanalysis and $^{1}$H n.m.r. spectroscopy.

Further evidence for the anionic intermediate shown in Scheme 1 was obtained by adding one equivalent of 4-nitrobenzoic acid to the 4-nitrobenzoyl chloride before the addition of the trimethyl phosphite. Under these conditions the $^{31}$P n.m.r. spectrum showed that the diphosphorus compound **2a** was no longer formed to any significant extent and the major product was now the diphosphorus compound **5a**, $\delta^{31}$P 1.25, 17.36 p.p.m.[3], $J_{PP}$ 29.5 Hz, whose structure was established by n.m.r. spectroscopy (see Table I). This product is consistent with the protonation of the anionic intermediate by the 4-nitrobenzoic acid as in Scheme 2. The methyl 4-nitrobenzoate (**6**, Ar = 4-nitrophenyl) was also isolated and identified.



SCHEME 2 **5a** Ar = 4-nitrophenyl
**5b** Ar = 3,5-dinitrophenyl

The formation of such anionic intermediates should also occur in reactions involving other acid chlorides which possess strong electron-withdrawing groups on the aryl ring. Thus it is not surprising that 3,5-dinitrobenzoyl chloride reacts with trimethyl phosphite to give **2c**, $\delta^{31}$P −2.55, 12.44 p.p.m., $J_{PP}$ 8.1 Hz, in the absence of a proton donor and **5b**, $\delta^{31}$P 0.84, 16.28 p.p.m., $J_{PP}$ 29.0 Hz, in the presence of a proton donor. As expected many of the features in the n.m.r. spectra of **5b** ($\delta^{13}C_{\alpha C}$ 72.2 p.p.m., $J_{PC}$ 5 and 172 Hz; $\delta^{1}H_{\alpha C-H}$ 5.89 p.p.m., $J_{PH}$ 11 and 14 Hz) are similar to those of **5a** (see Table I) and likewise those of **2c** ($\delta^{13}C_{\alpha C}$ 87.6 p.p.m., $J_{PC}$ 4 and 169 Hz) are similar to **2a** (see Table I). It is interesting to note, however, that the value of $J_{PCOP}$ in **2c** is significantly different from that in **2a**. Since it is unlikely that changing the aryl ring from 4-nitrophenyl to 3,5-dinitrophenyl would significantly alter the nature of the bonding between the phosphorus atoms in these two compounds it would seem that we are observing a change in the preferred dihedral angle of the P—O—C—P system.

## EXPERIMENTAL

$^{1}$H, $^{13}$C and $^{31}$P n.m.r. spectra were determined on a JEOL FX 100 spectrometer.

### *Dimethyl[dimethoxyphosphoryl(4-nitrobenzoyl)(4-nitrophenyl)methyl]phosphate* (**2a**)

4-Nitrobenzoyl chloride (3.7g), purified by vacuum sublimation, was dissolved in dry toluene and freshly distilled trimethyl phosphite (7.5g) was then added dropwise at room temperature. An exothermic reaction was observed and methyl chloride was evolved slowly. When reaction was complete $^{31}$P n.m.r. indicated that only one major phosphorus component was present accounting for at least 85% of the observed signals. The toluene was removed under reduced pressure to leave an oil which solidified on standing. This material was recrystallised from toluene and then chromatographed on Merck Kieselgel 60 $PF_{254}$ using an eluant of 5% methanol in ethyl acetate. The product was shown by n.m.r. to be a single compound which could be isolated as pale yellow glassy solid with an ill-defined melting point ~110°C (for n.m.r. data see Table I). Found: C, 40.80; H, 3.78; N, 5.24 $C_{18}H_{20}N_2O_{12}P_2$ requires C, 41.70; H, 3.86; N, 5.40.

### *Dimethyl 4-nitrobenzoylphosphonate 2,4-dinitrophenylhydrazone*

Addition of Brady's reagent to some of the crude product from the previous reaction produced a yellow precipitate which was filtered off and recrystallised from ethanol to give the 2,4-dinitrophenyl hydrazone of (**1**, R = Me, Ar = 4-nitrophenyl), m.p. 227°–229°C. This material gave $^1$H n.m.r. $\delta$(CDCl$_3$) 3.92 (6H, d, $J_{PH}$ 11.6Hz), 8.01 (2H, d, 8Hz), 8.29 (2H, d, 8Hz), 8.17 (1H, d, 8.5Hz), 8.45 (1H, dd, 8.5, 2.3Hz), 9.16 (1H, d, 2.3Hz), 14.2 (1H, broad s). Found: C, 40.86; H, 3.14; N, 15.90 $C_{15}H_{14}N_5O_9P$ requires C, 41.00; H, 3.12; N, 15.90.

### *Dimethyl[dimethoxyphosphoryl(4-nitrophenyl)methyl]phosphate* (**5a**)

4-Nitrobenzoyl chloride (3.7g) and 4-nitrobenzoic acid (3.7g) were added to dry toluene and cooled in an ice bath. Trimethylphosphite (5g) was added dropwise and the reaction stirred for 1 hour. The mixture was filtered and the toluene removed under reduced pressure. $^{31}$P n.m.r. showed that the resulting oil contained at least 80% of the desired product. A sample of the pure product m.p. 78°–79°C was obtained by column chromatography using florisil with chloroform followed by methanol as the eluant. Found: C, 35.94; H, 4.59; N, 3.83 $C_{11}H_{17}NO_9P_2$ requires C, 35.77; H, 4.60; N, 3.79, (for n.m.r. data see Table I). Methyl 4-nitrobenzoate was eluted prior to the product.

## ACKNOWLEDGMENT

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