The Reaction of Dimethyl Dioxirane with Diazomethylphosphonates; the First Synthesis of a Formylphosphonate Hydrate

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Formylphosphonate hydrate **8**, synthesized for the first time by the reaction of diethyl diazomethylphosphonate with dimethyl dioxirane (DMD), reacts with primary amines to provide imines **9** and **10**; compound **9** is also prepared by the reaction of the anion of diethyl methylenebisphosphonate with nitrosobenzene.

Acylphosphonates[1] **1** and their derived imines **2** are readily available and MO calculations† suggest that these compounds should undergo Diels–Alder reactions. However, we have been unable to observe such reactions even with highly reactive dienes, which suggests that steric effects are of overriding importance. In view of this, formylphosphonate esters **3** are of substantial interest as synthetic reagents both in general organic synthesis and for the preparation of other organophosphorus compounds. The only reported[3,4] method of the synthesis of these compounds involves the formylation of dialkyl phosphites with formic acetic anhydride. We have been unable to repeat this procedure and the ^{1}H NMR data given in the original publication[4] do not support the proposed structure. The diethyl acetal derivative **4** of **3** is available from the reaction of triethyl phosphite and triethyl orthoformate.[5] However, attempts to convert **4** into the corresponding aldehyde by acid hydrolysis gave only diethyl phosphonate and ethyl formate.[6,7] We now report the synthesis of the hydrate of diethyl formylphosphonate and derived imines.

Glyoxals **6** have been conveniently prepared in good yields by the oxidation of α-diazoacetates **5** with dimethyldioxirane (DMD) in acetone solution (Scheme 1).[8] Treatment of diethyl diazomethylphosphonate[9] **7**, available from the aminomethylphosphonate by diazotisation, with DMD in acetone at room temp. gave, as indicated by ^{1}H and ^{13}C NMR and mass spectra,‡ diethyl formylphosphonate hydrate **8** in quantitative yield (Scheme 2).

The addition of aniline to a solution of **8** in acetone gave an oil which displayed a doublet at δ 8.22 ($^1J_{\mathrm{PH}}$ = 61.2 Hz) in its ^{1}H NMR spectrum and a molecular ion at m/z = 241.085642 indicating a molecular formula of $C_{11}H_{16}NO_3P$.§ The ^{13}C NMR spectrum of the product included a doublet at δ 157.79 ($^1J_{\mathrm{PC}}$ = 222.5 Hz) and a ^{1}H^{13}C COSY confirmed a direct coupling of this carbon with the proton observed at δ 8.22. All these data are fully consistent with the *N*-phenylimine structure **9**; interestingly the $^1J_{\mathrm{PH}}$ and $^1J_{\mathrm{PC}}$ values of 61.2 and 222.5 Hz, respectively, are among the largest so far reported.¶ A similar reaction of **8** with *tert*-butylamine gave imine **10** whose structure is supported by spectral data.|| The related imines **13** and **14** bearing electron-withdrawing groups on the nitrogen atom have been generated *in situ* by the dehydrobromination of **11** and **12**, respectively; however, no spectra data were reported (Scheme 3).[14]

The reaction of **8** with secondary amines is exemplified by that with morpholine which gives a quantitative yield of diethyl phosphonate and *N*-formyl morpholine, presumably *via* fragmentation of the initially formed amine hydrate.

A possible alternative route to the imine **9** was suggested by reports[15] that imines are among the products of Wittig-type reactions with nitrosobenzene. Treatment of the anion of tetraethyl methylenediphosphonate with two molar equivalents of nitrosobenzene in THF at −78 °C gave a green oil with spectral characteristics identical to those of the product obtained by reaction of aniline with diethyl formylphosphonate hydrate **8** (Scheme 4).

We are currently investigating the use of **8** and derived imines in synthesis.

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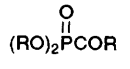
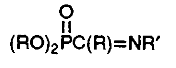


$(RO)_2\overset{O}{\overset{\|}{P}}COR$

1

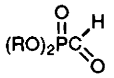
R = Aryl,Alkyl



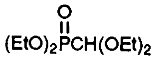
$(RO)_2\overset{O}{\overset{\|}{P}}C(R){=}NR'$

2

R = Aryl,Alkyl

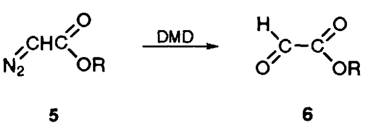


3

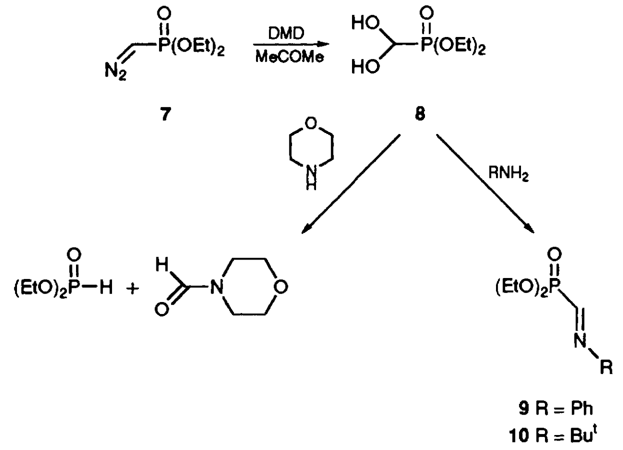


$(EtO)_2\overset{O}{\overset{\|}{P}}CH(OEt)_2$

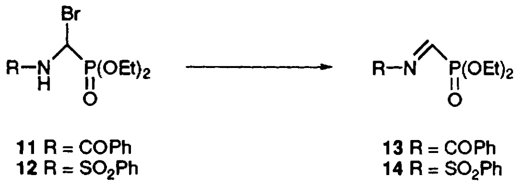
4



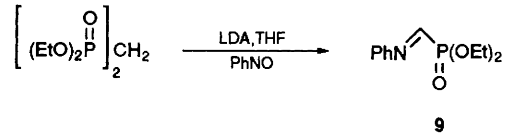
Scheme 1



Scheme 2



Scheme 3



Scheme 4

Footnotes

† The cycloaddition reaction of (Ts)N=CHCO$_2$R with various dienes is known to occur.[2] Our calculations (AM1 M O program) give a LUMO/HOMO energy difference of 6.2412 eV for the reaction of (TS)N=CHCO$_2$Et with Danishefsky's diene. Analogous calculations on a number of phosphonate analogues give comparable or lower LUMO/HOMO differences of Diels–Alder reactions with Danishefsky's diene, *e.g.* N(Ts)=C(Ph)P(O)(OPh)$_2$: LUMO/HOMO energy difference = 5.3807 eV.

‡ *Selected spectral data* for **8**: ^{1}H NMR (CDCl$_3$) δ 1.36 [m, 6H, (*Me*CH$_2$O)$_2$P], 4.22 [m, 4H, (MeC*H*$_2$O)$_2$P], 5.13 [d, *J* 9.07 Hz, 1H, PC*H*(OH)$_2$]; ^{13}C NMR (CDCl$_3$) δ 17.0 (s, *Me*CH$_2$O), 64.33 (MeCH$_2$O), 88.17 (d, *J* 210.04 Hz, PCH); M$^+$ at *m/z* = 166.0392.

§ *Selected spectral data* for **9**: ^{1}H NMR (CDCl$_3$) δ 1.38 [m, 6H, (*Me*CH$_2$O)$_2$P], 4.26 [m, 4H, (MeC*H*$_2$O)$_2$P], 6.8–7.4 (m, 5H, CH=N*Ph*), 8.22 (d, *J* 61.16 Hz, 1H, PCH=N); ^{13}C NMR (CDCl$_3$) δ 17.00 (s, *Me*CH$_2$O), 63.99 (s, Me*C*H$_2$O), 115–130 (=NPh), 157.79 (d, *J* 222.54 Hz, PCH=N).

¶ The $^1J_{PC}$ value for an sp hybridised carbon, *e.g.* (EtO)$_2$P(O)CCH, has been reported as $^1J_{PC}$ = 294.0 Hz,[10] however, the largest $^1J_{PC}$ values reported for an sp^2 hydridised carbon are, for *e.g.* (EtO)$_2$P(O)-CH=CH$_2$: $^1J_{PC}$ = 182.1 Hz;[10,11] (Pr^{i}O)$_2$P(O)CH=C(OTs)CO$_2$Me: $^1J_{PC}$ = 186.4 Hz.[12] The largest $^2J_{PH}$ values found in the literature are, for *e.g.* Cl$_2$P(O)CH$_a$=CHCMe=CH$_2$: $^2J_{PHa}$=36.2 Hz; Cl$_2$P-(O)CH$_a$=CHCMe=CHMe: $^2J_{PHa}$ = 37 Hz.[13]

‖ *Selected spectral data* for **10**: ^{1}H NMR (CDCl$_3$) δ 1.23 (s, 9H, Me$_3$C), 1.36 [m, 6H, (*Me*CH$_2$O)$_2$P], 4.18 [m, 4H, (MeC*H*$_2$O)$_2$P], 7.94 (d, *J* 65.1 Hz, 1H, PCH=N); ^{13}C NMR (CDCl$_3$) δ 17.22 (s, *Me*CH$_2$O), 29.44 (s, *Me*$_3$C), 52.00 (s, Me$_3$*C*), 63.89 (s, Me*C*H$_2$O), 153.61 (d, *J* 208.78 Hz, PCH=N).

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