Dialkyl phosphonates and tetraalkyl bis(phosphonate)s from the decomposition of quasi-phosphonium ylidic phosphonates in aqueous conditions

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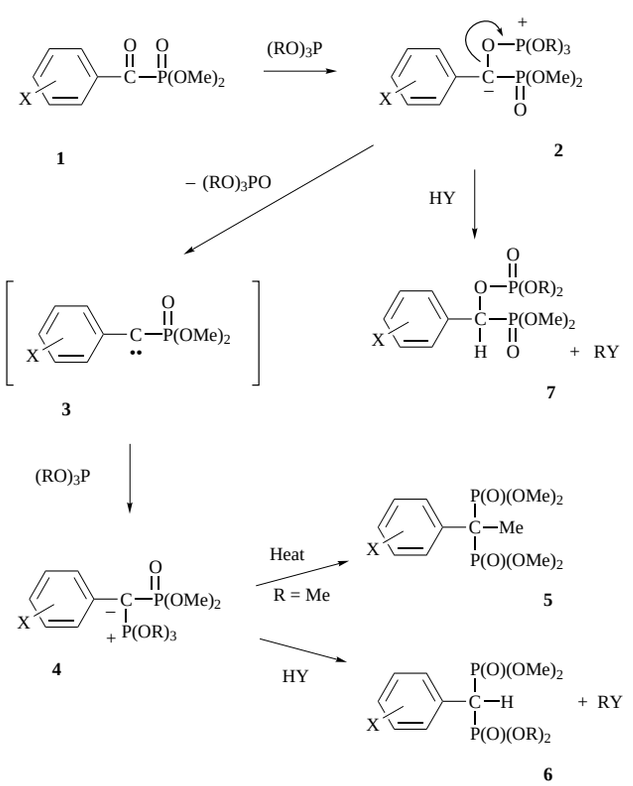
The reaction of dimethyl benzoylphosphonates 1 (X = 2-halogen or 2-CF_3O) with trialkyl phosphite leads to the formation of carbene intermediates 3 which are trapped by trialkyl phosphite to give the corresponding ylidic phosphonates 4. In acidic conditions these ylidic phosphonates decompose to give tetraalkyl phenylmethylene-1,1-bis(phosphonate)s 6 but in neutral or basic conditions they give mainly dimethyl benzylphosphonates and trialkyl phosphate. Factors influencing the mode of decomposition have been investigated.

We have previously reported[1] that, when trialkyl phosphites are heated with dialkyl benzoylphosphonates **1** in the absence of electrophiles, the reactions proceed *via* the carbene intermediates **3** following the initial formation of the anionic intermediates **2** (Scheme 1). We have also shown that, when a suitable



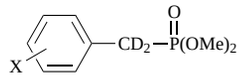
Scheme 1

ortho-substituent is present on the benzene ring, the carbene intermediates can undergo intramolecular reactions involving the substituent, often leading to the formation of cyclic products.[2,3,4]

Where no such *ortho*-substituent is present on the benzene ring, the carbenes **3** are readily trapped by the trialkyl phosphite present in the reaction mixture to give interesting ylidic phosphonates **4**.[1] For the ylides **4** (R = Me), formed when the carbenes react with trimethyl phosphite, there is a strong tendency for a subsequent rearrangement to occur under the reaction conditions to give the bis(phosphonate)s **5** and it is therefore difficult to obtain clean samples of these ylides. Moreover, the rate of rearrangement of the ylide **4** (X = 4-MeO R = Me) to the bis(phosphonate) **5** (X = 4-MeO) was similar in both a dilute solution in toluene and in the absence of solvent.[5] While this suggests that in some cases the rearrangement may be intramolecular, the mechanism involved in such cases has yet to be established. However, we have found that rearrangement of these ylides can be suppressed either by preparing the ylidic phosphonates **4** (R = Et or Pr^i) or by placing a substituent at the *ortho* position in the ylidic phosphonates **4** (R = Me).

To ensure that an ylidic phosphonate **4** is the major reaction product when employing this latter strategy, the substituent must not readily react with the carbene centre in the intermediates **3**, otherwise intramolecular cyclisation will occur. Thus, for example, the ylidic phosphonates **4** (X = 2-Me, R = Me) and **4** (X = 2-CF_3O, R = Me) were both produced in high yield by heating the appropriate benzoylphosphonates with trimethyl phosphite; both proved to be resistant to thermal rearrangement at 100 °C despite containing the methylenetrimethoxyphosphorane moiety. We attribute this to steric factors inhibiting nucleophilic attack by the carbanion on the alkyl groups on the adjacent phosphonium centre. The 2-trifluoromethoxy substituted case also confirms the lack of reactivity of the C–F bond to carbene insertion since the corresponding 2-methoxy-substituted system **1** (X = 2-MeO) readily cyclised under similar conditions to give dimethyl 2,3-dihydrobenzo[*b*]furan-3-ylphosphonate.[1]

While both the ylides **4** (X = 2-Me, R = Me) and **4** (X = 2-CF_3O, R = Me) were reluctant to rearrange to the corresponding bis(phosphonate)s **5**, they were readily converted to the analogous bis(phosphonate)s **6** (R = Me) under acidic conditions, such as by the addition of a hydrogen halide or dilute aqueous acid. However, differences in behaviour were observed when the ylides were decomposed in aqueous methanol in preparation for purification of the expected bis(phosphonate)s **6** (R = Me) by reversed-phase HPLC. Thus, while the ylide **4** (X = 2-Me, R = Me) once again gave only the bis(phosphonate) **6** (X = 2-Me, R = Me), decomposition of the ylide **4** (X = 2-CF_3O, R = Me) resulted mainly in the formation of equimolar quantities of the benzylphosphonate **9** (X = 2-CF_3O) (55%) and trimethyl phosphate, although a significant quantity of the bis(phosphonate) **6** (X = 2-CF_3O, R = Me) (45%) was also formed. Confirmation that both methylene hydrogens in the benzylphosphonate **9** (X = 2-CF_3O) had been derived from the water was obtained by repeating the decomposition using



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deuterium oxide, resulting in the formation of the α,α-dideuteriated benzylphosphonate derivative **8** (X = 2-CF_3O).

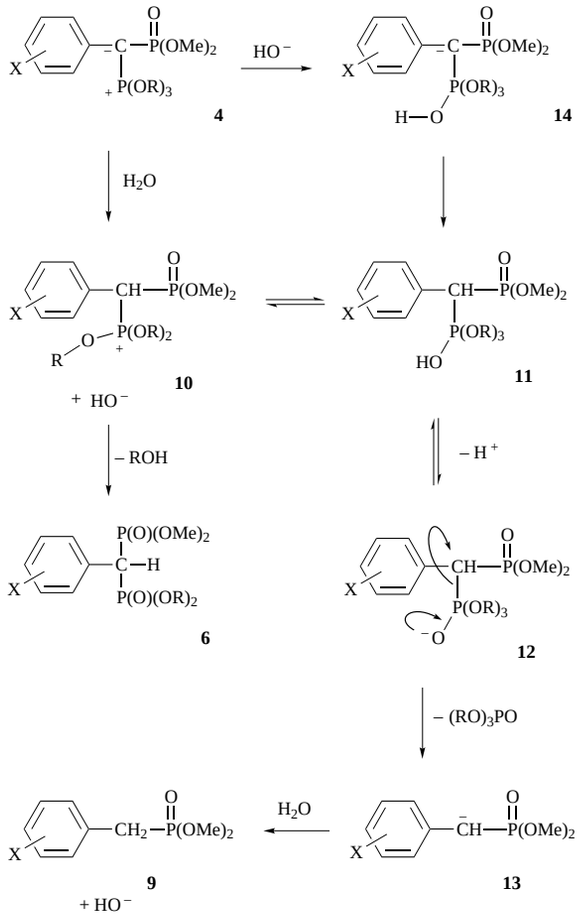
Since the trifluoromethoxy substituent on a benzene ring has been shown to exhibit similar electronic characteristics to those of the halogens,[6,7] we have also studied the hydrolysis of the 2-halogenated ylidic phosphonates **4** (X = 2-F, 2-Cl, 2-Br and 2-I, R = Me) to see how changing the electronegativity and size of the *ortho*-substituent affects the mode of ylide hydrolysis.

Fortunately, all four ylidic phosphonates **4** (X = 2-F, 2-Cl, 2-Br and 2-I, R = Me) could be prepared in a reasonable state of purity by reaction of the appropriate benzoylphosphonate with trimethyl phosphite. As anticipated the small fluorine substituent was least effective at inhibiting rearrangement of the ylides **4** to the bis(phosphonate)s **5**, but even here formation of the ylidic phosphonate **4** (X = 2-F, R = Me) could be achieved without significant thermal rearrangement, by careful control of the reaction conditions.

As expected, in all cases the decomposition of the ylides **4** (X = 2-F, 2-Cl, 2-Br and 2-I, R = Me) in acidic aqueous conditions resulted in the formation of the corresponding bis-(phosphonate)s **6** in high yield, but on addition of water at pH 7 trimethyl phosphate and the benzylphosphonates **9** became the major decomposition products. Benzylphosphonate formation was least prevalent for the iodo-substituted case **4** (X = 2-I, R = Me) where it accounted for about 60% of the hydrolysis product, the yield increasing with the electronegativity of the halogen substituent (X = 2-Br, 60%; 2-Cl, 65%; 2-F, 85%). In contrast, increasing the bulk of the alkoxy groups on the phosphorus caused an increase in the proportion of bis-(phosphonate) formed at pH 7, rising from 40% for **4** (X = 2-I, R = Me) to 60% for **4** (X = 2-I, R = Et) and to essentially 100% for **4** (X = 2-I, R = Pr^i).

The decomposition of phosphonium ylides and phosphonium salts under basic conditions has been well studied[8] and is known to result in most cases in the formation of a phosphine oxide and a hydrocarbon, although other reactions can occur in specific cases.[9,10,11] However, in the case of the trialkoxy quasi-phosphonium ylides **4** there is the additional possibility of bis(phosphonate) formation occurring *via* nucleophilic attack at one of the alkoxy groups on the quasi-phosphonium salt **10** which results from protonation of the initial ylide **4** (Scheme 2).

Formation of the benzylphosphonates **9** *via* attack of the hydroxide anion on the phosphonium centre in the ylide **4** to give hydroxyphosphorane **14** can be ruled out since increasing the basicity of the hydrolysis conditions resulted in a marked slowing of the rate of ylide decomposition. For example, when decomposition of the ylides **4** (X = 2-I, R = Me) was attempted in strongly basic aqueous medium (pH 14) it was found that the ylide did not hydrolyse even after several days. We must therefore conclude that both the formation of the bis(phosphonate) **6** and the benzylphosphonate **9** proceed *via* an initial protonation of the ylide to give the quasi-phosphonium salt **10**. Attack by hydroxide anion at one of the alkoxy groups on the phosphonium centre in **10** results in dealkylation and formation of the bis(phosphonate) **6**, whereas direct attack at the phosphonium centre gives the phosphorane **11** which then reacts *via* **13** as shown in Scheme 2 to give the benzylphosphonate **9**. The ratio of benzylphosphonate **9** to bis(phosphonate) **6** formation will therefore be affected by steric factors and the stability of the carbanion **13** displaced on formation of the trialkyl phosphate. This latter factor accounts for the observed increase in benzylphosphonate formation with increasing electronegativity of the *ortho* substituent.



Scheme 2

It is interesting to note that while increasing the bulk of the alkoxy substituents around the quasi-phosphonium centre would normally reduce the proportion of product derived from dealkylation of one of these groups, in this particular case the cumulative steric effects of the three alkoxy substituents have a much greater impact at the phosphonium centre. With more bulky alkoxy groups as in **4** (X = 2-I, R = Pr^i) reaction therefore proceeds essentially exclusively *via* dealkylation of one of the isopropoxy groups on the initially formed phosphorane **10** (X = 2-I, R = Pr^i) leading to bis(phosphonate) formation.

In contrast, a significant increase in the preference for benzylphosphonate **9** formation was noted as the pH of the hydrolysis medium was increased [from 60% at pH 7 to 75% at pH 9 for **4** (X = 2-I, R = Me)]. Since a higher pH will facilitate deprotonation of the phosphorane **11** and encourage formation of the anionic species **12**, it is probably this factor which accounts for the observed increasing preference for benzylphosphonate formation in more basic solutions.

Since the formation of the benzylphosphonates **9** can only result *via* attack by water or hydroxide anions at the phosphonium centres in the initially formed phosphoranes **10**, the presence of other nucleophiles in the hydrolysis medium will not contribute to the formation of **9**. However, the presence of other nucleophiles in the reaction mixture can affect the rate of dealkylation of the quasi-phosphonium salts **10** to give the bis(phosphonate)s **6**. This is clearly shown in the decomposition of the ylides **4** in dilute hydrochloric acid where the chloride ions readily dealkylate one of the alkoxy groups on the phosphonium centre to give exclusively the bis(phosphonate)s **6**, while the weakly nucleophilic water molecules[12] play little part in either the formation of bis(phosphonate)s **6** or benzylphosphonates **9**. Hydrolysis of the ylides with water or dilute aqueous alkali, however, proceeds *via* attack by the more nucleophilic hydroxide anion at both the phosphonium centre and the

adjacent alkoxy groups, although even here we were able to demonstrate that it was possible to substantially affect the product ratio by the addition of other nucleophilic species. Thus, hydrolysis of the ylide **4** (X = 2-I, R = Me) in an aqueous solution of potassium iodide (1 mol dm^{-3}) resulted in exclusive formation of the bis(phosphonate) **6** (X = 2-I, R = Me) even at pH 11, this reflecting the higher nucleophilicity of iodide anions relative to hydroxide anions for carbon electrophiles.[12] In contrast, a similar hydrolysis carried out using aqueous potassium fluoride rather than potassium iodide showed no increase in bis(phosphonate) formation, in keeping with the lower nucleophilicity of the fluoride anion for carbon electrophiles.[12,13] Instead, the presence of the additional potassium fluoride seems to enhance benzylphosphonate formation (85%) relative to the case where only sodium hydroxide is present (75%). It is less easy to be certain about the causes of this, but this may simply reflect the higher ionic strength of the hydrolysis medium. This would not necessarily affect equally the two reaction pathways from the quasi-phosphonium salt **10** (X = 2-I, R = Me) to the bis(phosphonate) **6** (X = 2-I, R = Me) and the benzylphosphonate **9** (X = 2-I).

Finally, while we might expect that benzylphosphonate formation will be more prevalent in those cases where the substituents on the benzene ring facilitate stabilisation of the carbanionic intermediate **13**, it is interesting to note that we also observed the formation of some benzylphosphonate **9** (X = 2-PhS) on hydrolysis of the ylidic phosphonate **4** (X = 2-PhS, R = Me)[4] and this example would suggest that other factors may also play a part in controlling the course of the hydrolysis reaction.

Experimental

NMR spectra were determined on JEOL EX90 and EX270 spectrometers. FAB mass spectra were run by M-Scan Ltd. on a VG Autospec E spectrometer using *m*-nitrobenzyl alcohol as the matrix.

Preparation of dimethyl benzoylphosphonates

The dimethyl benzoylphosphonates were prepared in high yield by the addition of an equimolar quantity of trimethyl phosphite to the appropriate benzoyl chloride in dry toluene. They were purified by short path distillation *in vacuo* unless otherwise indicated. Distillation temperatures refer to that of the heating bath. Where the benzoyl chlorides were not readily available they were prepared by the action of thionyl chloride on the corresponding benzoic acid. In such cases all thionyl chloride must be removed from the benzoyl chloride before addition of the trimethyl phosphite.

Dimethyl 2-fluorobenzoylphosphonate 1 (X = 2-F). This compound was distilled at 112 °C at 0.02 mmHg and obtained as a pale yellow oil (2.89 g, 98%); $\delta_P(CDCl_3)$ −0.7; $\delta_C(CDCl_3)$ 53.3 (2 d, J_{PC} 7, MeOP), 115.9 (dd, J_{FC} 20, J_{PC} 2, C-3), 123.60 (dd, J_{FC} 10, J_{PC} 64, C-1), 123.63 (d, J_{FC} 4, C-5), 130.7 (s, C-6), 135.4 (d, J_{FC} 10, C-4), 160.3 (dd, J_{FC} 262, J_{PC} 4, C-2) and 195.3 (d, J_{PC} 183, C=O); δ_H(270 MHz; $CDCl_3$) 3.95 (6 H, d, J_{PH} 11, MeOP), 7.24 (1 H, m, 2-H), 7.33 (1 H, tm, J_{HH} 7.5, 5-H), 7.67 (1 H, m, 4-H) and 8.18 (1 H, td, J_{HH} 7.5 and 2, J_{HF} 7.5, 6-H).

The 2,4-dinitrophenylhydrazone derivative of **1** (X = 2-F) was recrystallised from ethanol as a yellow solid, mp 151 °C; $\delta_P(CDCl_3)$ 6.5 (Found: C, 43.85; H, 3.45; N, 13.7. $C_{15}H_{14}FN_4O_7P$ requires C, 43.70; H, 3.42; N, 13.59%).

Dimethyl 2-chlorobenzoylphosphonate 1 (X = 2-Cl). This compound was distilled at 119 °C at 0.05 mmHg (lit.,[14] bp 102–109 °C at 0.1 mmHg) and obtained as a pale yellow oil (1.40 g, 94%); $\delta_P(CDCl_3)$ −1.4; $\delta_C(CDCl_3)$ 53.9 (2 d, J_{PC} 8, MeOP), 126.4 (s, C-5), 131.0 (d, J_{PC} 3, C-6), 131.2 (s, C-3), 131.7 (d, J_{PC} 6, C-2), 133.3 (C-4), 134.4 (d, J_{PC} 64, C-1) and 199.2 (d, J_{PC} 181, C=O); δ_H(270 MHz; $CDCl_3$) 3.88 (6 H, d, J_{PH} 11, MeOP), 7.33–7.52 (3 H, m, 3-H, 4-H, 5-H) and 8.14 (1 H, dm, J_{HH} 8, 6-H).

The 2,4-dinitrophenylhydrazone derivative of **1** (X = 2-Cl) was recrystallised from ethanol as a yellow solid, mp 158–159 °C; $\delta_P(CDCl_3)$ 6.0 (Found: C, 41.95; H, 3.25; N, 13.1. $C_{15}H_{14}ClN_4O_7P$ requires C, 42.02; H, 3.29; N, 13.07%).

Dimethyl 2-bromobenzoylphosphonate 1 (X = 2-Br). This compound was distilled at 123 °C at 0.03 mmHg and obtained as a pale yellow oil (1.25 g, 95%); $\delta_P(CDCl_3)$ −0.8; $\delta_C(CDCl_3)$ 53.7 (2 d, J_{PC} 7, MeOP), 119.0 (d, J_{PC} 6, C-2), 126.7 (s, C-5), 130.0 (d, J_{PC} 3, C-6), 130.9 (s, C-3), 133.1 (s, C-4), 135.8 (d, J_{PC} 64, C-1) and 199.7 (d, J_{PC} 181, C=O); δ_H(270 MHz; $CDCl_3$) 3.91 (6 H, d, J_{PH} 11, MeOP), 7.37–7.51 (2 H, m, 4-H, 5-H), 7.68 (1 H, dm, J_{HH} 8, 3-H) and 8.14 (1 H, dm, J_{HH} 8, 6-H).

The 2,4-dinitrophenylhydrazone derivative of **1** (X = 2-Br) was recrystallised from ethanol as a yellow solid, mp 168 °C; $\delta_P(CDCl_3)$ 5.8 (Found: C, 38.05; H, 3.0; N, 11.85. $C_{15}H_{14}BrN_4O_7P$ requires C, 38.08; H, 2.98; N, 11.84%).

Dimethyl 2-iodobenzoylphosphonate 1 (X = 2-I). This compound (1.2 g) was obtained as a pale yellow solid in essentially quantitative yield and was purified by washing the crystals with diethyl ether, mp 62 °C (Found: C, 31.75; H, 3.0. $C_9H_{10}IO_4P$ requires C, 31.79; H, 2.96%); $\delta_P(CDCl_3)$ −1.4; $\delta_C(CDCl_3)$ 54.4 (2 d, J_{PC} 7, MeOP), 91.6 (s, C-2), 128.0 (s, C-5), 132.3 (s, C-6), 133.8 (s, C-4), 138.2 (d, J_{PC} 67, C-1), 142.0 (d, J_{PC} 2, C-3) and 200.3 (d, J_{PC} 181, C=O); δ_H(270 MHz; $CDCl_3$) 3.92 (6 H, d, J_{PH} 11, MeOP), 7.25 (1 H, td, J_{HH} 7.5 and 2, 4-H), 7.51 (1 H, td, J_{HH} 7.5 and 2, 5-H), 8.04 (1 H, dm, J_{HH} 7.5, 3-H) and 8.25 (1 H, dd, J_{HH} 8 and 2, 6-H).

Dimethyl 2-trifluoromethoxybenzoylphosphonate 1 (X = 2-CF_3O). This compound was distilled at 120 °C at 0.01 mmHg and obtained as a pale yellow oil (0.6 g, 90%); *m*/*z* 298; $\delta_P(CDCl_3)$ −1.3; $\delta_C(CDCl_3)$ 54.4 (2 d, J_{PC} 7, MeOP), 120.4 (q, J_{FC} 259, CF_3), 122.1 (br s, CH), 127.2 (d, J_{PC} 64, Q), 127.3 (CH), 132.0 (s, CH), 135.0 (CH), 146.9 (m, Q) and 198.8 (d, J_{PC} 185, C=O); δ_H(90 MHz; $CDCl_3$) 3.90 (6 H, d, J_{PH} 11, MeOP), 7.30–7.78 (3 H, m, 3-H, 4-H, 5-H) and 8.20 (1 H, ddd, J_{HH} 7.5, 2 and 0.5, 6-H).

The reaction of dimethyl 2-trifluoromethoxybenzoylphosphonate with trimethyl phosphite

A mixture of dimethyl 2-trifluoromethoxybenzoylphosphonate **1** (X = 2-CF_3O) (2.2 g, 9.7 mmol) and trimethyl phosphite (4 g, 32 mmol) was heated under dry nitrogen at 105 °C for 3 h. ^{31}P NMR spectroscopy indicated the formation of equimolar quantities of trimethyl phosphate and the ylide, [(dimethoxyphosphinoyl)(2-trifluoromethoxyphenyl)methylene]trimethoxyphosphorane **4** (X = 2-CF_3O, R = Me); $\delta_P(CDCl_3)$ 51.8 [d, J_{PP} 89, $P(OMe)_3$] and 29.5 [d, J_{PP} 89, $P(O)(OMe)_2$]. The volatile components in the reaction mixture were removed by heating the yellow solution under reduced pressure (85 °C at 0.01 mmHg) to give the crude ylide **4** (X = 2-CF_3O, R = Me). Decomposition of a sample of this ylide by the addition of dilute hydrochloric acid resulted in the formation of **6** (X = 2-CF_3O, R = Me) while decomposition by the addition of aqueous methanol (70%) resulted in the formation of **6** (X = 2-CF_3O, R = Me) (45%) and **9** (X = 2-CF_3O) (55%). Both products were isolated by reversed-phase HPLC using aqueous methanol (70%) as eluent.

Tetramethyl (2-trifluoromethoxyphenyl)methylene-1,1-bis(phosphonate) 6 (X = 2-CF_3O, R = Me). This material was isolated as a colourless oil; *m*/*z* 392; $\delta_P(CDCl_3)$ 20.4; δ_H(270 MHz; $CDCl_3$) 3.67 (6 H, d, J_{PH} 11, POMe), 3.77 (6 H, d, J_{PH} 11, POMe), 4.36 (1 H, t, J_{PH} 25, αCH), 7.26–7.41 (3 H, m, 3-H, 4-H, 5-H) and 7.95 (1 H, m, 6-H); $\delta_C(CDCl_3)$ 36.4 (t, J_{PC} 135, αC), 53.7 (2 m, POMe), 54.0 (2 m, POMe), 120.5 (q, J_{FC} 259, CF_3), 119.7 (m, CH), 122.3 (t, J_{PC} 7, Q), 126.7 (t, J_{PC} 2, CH), 129.4 (t, J_{PC} 2, CH), 131.9 (t, J_{PC} 5, CH) and 147.2 (tq, J_{PC} 8, J_{FC} 1, Q).

Dimethyl 2-trifluoromethoxybenzylphosphonate 9 (X = 2-CF_3O). This compound was isolated as a colourless oil; *m*/*z* 284; $\delta_P(CDCl_3)$ 27.8; δ_H(270 MHz; $CDCl_3$) 3.26 (2 H, d, J_{PH} 22,

αCH$_2$), 3.70 (6 H, d, J_{PH} 11, POMe), 7.22–7.32 (3 H, m, 3-H, 4-H, 5-H) and 7.48 (1 H, m, 6-H); δ_C($CDCl_3$) 26.4 (d, J_{PC} 141, αC), 52.9 (2 d, *J* 7, POMe), 120.6 (q, J_{FC} 258, CH_3), 124.2 (d, J_{PC} 9, Q), 126.8 (d, J_{PC} 3, CH), 128.6 (d, J_{PC} 4, CH), 132.1 (d, J_{PC} 6, CH) and 147.6 (dq, J_{PC} 8, J_{FC} 2, Q).

The reaction of dimethyl 2-fluorobenzoylphosphonate with trimethyl phosphite

A mixture of dimethyl 2-fluorobenzoylphosphonate **1** (X = 2-F) (1.0 g, 4.3 mmol) and trimethyl phosphite (1.06 g, 8.6 mmol) was heated under dry nitrogen at 105 °C for 4 h. ^{31}P NMR spectroscopy indicated the formation of equimolar quantities of trimethyl phosphate and the ylide, [(dimethoxyphosphinoyl)-(2-fluorophenyl)methylene]trimethoxyphosphorane **4** (X = 2-F, R = Me); δ_P($CDCl_3$) 52.5 [d, J_{PP} 90, P(OMe)$_3$] and 30.3 [d, J_{PP} 90, P(O)(OMe)$_2$]. A small quantity of the phosphate **7** (X = 2-F) {δ_P($CDCl_3$) 1.1 [d, J_{PP} 32, OP(O)(OMe)$_2$] and 17.8 [d, J_{PP} 32, P(O)(OMe)$_2$]} was also present in the reaction mixture. The volatile components in the reaction mixture were removed by heating the yellow solution under reduced pressure (70 °C at 0.02 mmHg) to give the crude ylide **4** (X = 2-F, R = Me). Decomposition of a sample of the ylide by the addition of dilute hydrochloric acid resulted in the formation of **6** (X = 2-F, R = Me), while decomposition by the addition of water (pH 7) resulted in the formation of **6** (X = 2-F, R = Me) (15%) and **9** (X = 2-F) (85%). Both products were isolated by reversed-phase HPLC using aqueous methanol (70%) as eluent.

Tetramethyl (2-fluorophenyl)methylene-1,1-bis(phosphonate) 6 (X = 2-F, R = Me). This compound was isolated as a colourless oil [HRMS(FAB): found MH^+, 327.0563. $C_{11}H_{18}FO_6P_2$ requires *M*, 327.0563]; δ_P($CDCl_3$) 20.7; δ_H(270 MHz, $CDCl_3$) 3.62 (6 H, d, J_{PH} 11, POMe), 3.75 (6 H, d, J_{PH} 11, POMe), 4.22 (1 H, t, J_{PH} 25, αCH), 7.02 (1 H, br t, J_{HH} 9, 4-H), 7.11 (1 H, br t, J_{HH} 8, 5-H), 7.24 (1 H, m, 3-H) and 7.76 (1 H, br t, *J* 7, 6-H); δ_C($CDCl_3$) 35.2 (br t, J_{PC} 135, αC), 53.7 (2 m, POMe), 54.0 (2 m, POMe), 115.4 (d, J_{FC} 22, C-3), 117.2 (m, C-1), 124.4 (br s, C-5), 129.6 (br d, J_{FC} 9, C-6), 131.5 (br s, C-4) and 160.2 (dt, J_{FC} 248, J_{PC} 8, C-2).

Dimethyl 2-fluorobenzylphosphonate 9 (X = 2-F). This compound was isolated as a colourless oil [HRMS(FAB): found MH^+, 219.0586. $C_9H_{13}FO_3P$ requires *M*, 219.0586]; δ_P($CDCl_3$) 27.8 (d, J_{PF} 6); δ_H(270 MHz; $CDCl_3$) 3.23 (2 H, d, J_{PH} 22, αCH$_2$), 3.71 (6 H, d, J_{PH} 11, POMe), 7.03 (1 H, br t, J_{HH} 8, 5-H), 7.11 (1 H, br t, J_{HH} 7.5, 4-H), 7.25 (1 H, m, 3-H) and 7.36 (1 H, tm, J_{HH} 7.5, 6-H); δ_C($CDCl_3$) 25.3 (dd, J_{FC} 3, J_{PC} 141, αC), 52.9 (2 d, *J* 7, POMe), 115.4 (dd, J_{FC} 22.5, J_{PC} 3, C-3), 118.7 (dd, J_{FC} 16, J_{PC} 10, C-1), 124.2 (dd, J_{FC} 4, J_{PC} 3, C-5), 128.8 (dd, J_{FC} 4, J_{PC} 8, C-6), 131.7 (dd, J_{FC} 5, J_{PC} 4, C-4) and 160.7 (dd, J_{FC} 247, J_{PC} 7, C-2).

The reaction of dimethyl 2-chlorobenzoylphosphonate with trimethyl phosphite

A mixture of dimethyl 2-chlorobenzoylphosphonate **1** (X = 2-Cl) (1.0 g, 4.3 mmol) and trimethyl phosphite (1.06 g, 8.6 mmol) was heated under dry nitrogen at 105 °C for 4 h. ^{31}P NMR spectroscopy indicated the formation of equimolar quantities of trimethyl phosphate and the ylide, [(dimethoxyphosphinoyl)(2-chlorophenyl)methylene]trimethoxyphosphorane **4** (X = 2-Cl, R = Me); δ_P 50.9 [d, J_{PP} 90, P(OMe)$_3$] and 30.0 [d, J_{PP} 90, P(O)(OMe)$_2$]. A small quantity of the phosphate **7** (X = 2-Cl) {δ_P 1.3 [d, J_{PP} 32, OP(O)(OMe)$_2$] and 18.3 [d, J_{PP} 32, P(O)(OMe)$_2$]} was also present in the reaction mixture. The volatile components in the reaction mixture were removed by heating the yellow solution under reduced pressure (70 °C at 0.02 mmHg) to give the crude ylide **4** (X = 2-Cl, R = Me). Decomposition of a sample of the ylide by the addition of dilute hydrochloric acid resulted in the formation of **6** (X = 2-Cl, R = Me), while decomposition by the addition of water (pH 7) resulted in the formation of **6** (X = 2-Cl, R = Me) (35%) and **9** (X = 2-Cl) (65%). Both products were isolated by reversed-phase HPLC using aqueous methanol (70%) as eluent.

Tetramethyl (2-chlorophenyl)methylene-1,1-bis(phosphonate) 6 (X = 2-Cl, R = Me). This compound was isolated as a colourless oil [HRMS(FAB): found MH^+, 343.0253, 345.0232. $C_{11}H_{18}ClO_6P_2$ requires *M*, 343.0267, 345.0237]; δ_P($CDCl_3$) 20.6; δ_H(270 MHz; $CDCl_3$) 3.67 (6 H, d, J_{PH} 11, POMe), 3.82 (6 H, d, J_{PH} 11, POMe), 4.36 (1 H, t, J_{PH} 25, αCH), 7.22–7.36 (2 H, m, 4-H, 5-H), 7.43 (1 H, dm, J_{HH} 7, 3-H) and 7.92 (1 H, dm, J_{HH} 7, 6-H); δ_C($CDCl_3$) 39.8 (t, J_{PC} 134, αC), 53.7 (2 m, POMe), 54.0 (2 m, POMe), 127.0 (t, J_{PC} 3, C-5), 127.6 (t, J_{PC} 7, C-2), 129.1 (t, J_{PC} 2, C-3), 129.6 (t, J_{PC} 1, C-4), 131.5 (t, J_{PC} 4, C-6) and 134.3 (t, J_{PC} 9, C-1).

Dimethyl 2-chlorobenzylphosphonate 9 (X = 2-Cl).[15] This compound was isolated as a colourless oil [HRMS(FAB): found MH^+, 235.0285, 237.0258. $C_9H_{13}ClO_3P$ requires *M*, 235.0290, 237.0261]; δ_P($CDCl_3$) 27.9; δ_H(270 MHz; $CDCl_3$) 3.32 (2 H, d, J_{PH} 22, αCH$_2$), 3.63 (6 H, d, J_{PH} 11, POMe), 7.09–7.19 (2 H, m, 4-H, 5-H) and 7.28–7.37 (2 H, m, 3-H, 6-H); δ_C($CDCl_3$) 29.6 (d, J_{PC} 140, αC), 53.9 (2 d, J_{PC} 7, POMe), 126.9 (d, J_{PC} 3, C-5), 128.4 (d, J_{PC} 4, C-4), 129.5 (d, J_{PC} 10, C-1), 129.6 (d, J_{PC} 3, C-3), 131.6 (d, J_{PC} 5, C-6) and 134.0 (d, J_{PC} 8, C-2).

The reaction of dimethyl 2-bromobenzoylphosphonate with trimethyl phosphite

A mixture of dimethyl 2-bromobenzoylphosphonate **1** (X = 2-Br) (1.0 g, 4.3 mmol) and trimethyl phosphite (1.06 g, 8.6 mmol) was heated under dry nitrogen at 105 °C for 4 h. ^{31}P NMR spectroscopy indicated the formation of equimolar quantities of trimethyl phosphate and the ylide, [(dimethoxyphosphinoyl)(2-bromophenyl)methylene]trimethoxyphosphorane **4** (X = 2-Br, R = Me); δ_P($CDCl_3$) 49.7 [d, J_{PP} 90, P(OMe)$_3$] and 29.9 [d, J_{PP} 90, P(O)(OMe)$_2$]. A small quantity of the phosphate **7** (X = 2-Br) {δ_P($CDCl_3$) 1.0 [d, J_{PP} 32, OP(O)(OMe)$_2$] and 17.8 [d, J_{PP} 32, P(O)(OMe)$_2$]} was also present in the reaction mixture. The volatile components in the reaction mixture were removed by heating the yellow solution under reduced pressure (70 °C at 0.02 mmHg) to give the crude ylide **4** (X = 2-Br, R = Me). Decomposition of a sample of the ylide by the addition of dilute hydrochloric acid resulted in the formation of **6** (X = 2-Br, R = Me), while decomposition by the addition of water (pH 7) resulted in the formation of **6** (X = 2-Br, R = Me) (40%) and **9** (X = 2-Br) (60%). Both products were isolated by reversed-phase HPLC using aqueous methanol (70%) as eluent.

Tetramethyl (2-bromophenyl)methylene-1,1-bis(phosphonate) 6 (X = 2-Br, R = Me). This compound was isolated as a colourless oil (Found: C, 34.1; H, 4.55. $C_{11}H_{17}BrO_6P_2$ requires C, 34.11; H, 4.39%); δ_P($CDCl_3$) 20.5; δ_H(270 MHz; $CDCl_3$) 3.66 (6 H, d, J_{PH} 11, POMe), 3.83 (6 H, d, J_{PH} 11, POMe), 4.65 (1 H, t, J_{PH} 25, αCH), 7.18 (1 H, td, J_{HH} 8 and 1.5, 4-H), 7.35 (1 H, br t, J_{HH} 7.5, 5-H), 7.62 (1 H, br d, J_{HH} 8, 3-H) and 7.94 (1 H, dm, J_{HH} 8, 6-H); δ_C($CDCl_3$) 42.0 (t, J_{PC} 134, αC), 52.8 (2 m, POMe), 53.0 (2 m, POMe), 124.6 (t, J_{PC} 10, C-1), 127.4 (br s, CH), 128.4 (br s, CH), 128.6 (t, J_{PC} 7, C-2), 130.6 (t, J_{PC} 4, CH) and 132.1 (br s, CH).

Dimethyl 2-bromobenzylphosphonate 9 (X = 2-Br).[16] This compound was isolated as a colourless oil [HRMS(FAB): found MH^+, 278.9783, 280.9771. $C_9H_{13}BrO_3P$ requires *M*, 278.978 56, 280.9765]; δ_P($CDCl_3$) 27.8; δ_H(270 MHz; $CDCl_3$) 3.33 (2 H, d, J_{PH} 22, αCH$_2$), 3.61 (6 H, d, J_{PH} 11, POMe), 7.02 (1 H, br t, J_{HH} 7, 5-H), 7.18 (1 H, br t, J_{HH} 7.5, 4-H), 7.35 (1 H, br d, J_{HH} 7.5, 3-H) and 7.46 (1 H, br d, J_{HH} 7.5, 6-H); δ_C($CDCl_3$) 32.3 (d, J_{PC} 138, αC), 52.7 (2 d, J_{PC} 7, POMe), 124.5 (d, J_{PC} 8, C-2), 127.3 (d, J_{PC} 4, C-4), 128.4 (d, J_{PC} 4, C-5), 131.2 (d, J_{PC} 9, C-1), 131.3 (d, J_{PC} 5, C-6) and 132.7 (d, J_{PC} 3, C-3).

The reaction of dimethyl 2-iodobenzoylphosphonate with trimethyl phosphite

A mixture of dimethyl 2-iodobenzoylphosphonate **1** (X = 2-I) (1.0 g, 4.3 mmol) and trimethyl phosphite (1.06 g, 8.6 mmol)

was heated under dry nitrogen at 105 °C for 4 h. ^{31}P NMR spectroscopy indicated the formation of equimolar quantities of trimethyl phosphate and the ylide, [(dimethoxyphosphinoyl)-(2-iodophenyl)methylene]trimethoxyphosphorane **4** (X = 2-I, R = Me); δ_P 50.0 [d, J_{PP} 90, P(OMe)$_3$] and 28.4 [d, J_{PP} 90, P(O)(OMe)$_2$]. A small quantity of the phosphate **7** (X = 2-I) {δ_P(CDCl$_3$) 2.0 [d, J_{PP} 32, OP(O)(OMe)$_2$] and 18.7 [d, J_{PP} 32, P(O)(OMe)$_2$]} was also present in the reaction mixture. The volatile components in the reaction mixture were removed by heating the yellow solution under reduced pressure (70 °C at 0.02 mmHg) to give the crude ylide **4** (X = 2-I, R = Me). Decomposition of a sample of the ylide by the addition of dilute hydrochloric acid resulted in the formation of **6** (X = 2-I, R = Me), while decomposition by the addition of water (pH 7) resulted in the formation of **6** (X = 2-I, R = Me) (40%) and **9** (X = 2-I) (60%). Decomposition by the addition of dilute aqueous sodium hydroxide (pH 9) resulted in the formation of **6** (X = 2-I, R = Me) (25%) and **9** (X = 2-I) (75%). When decomposition of the ylide **4** (X = 2-I, R = Me) was carried out using aqueous solutions of potassium iodide and potassium fluoride (1 M, adjusted to pH 9 with sodium hydroxide) the viscosity of the ylide **4** (X = 2-I, R = Me) was reduced by the addition of a small quantity of acetone before addition of the aqueous solutions to facilitate mixing of the reactants. Decomposition with the potassium iodide solution resulted in the formation of only **6** (X = 2-I, R = Me), while decomposition with the potassium fluoride solution resulted in the formation of **6** (X = 2-I, R = Me) (15%) and **9** (X = 2-I) (85%). Both products were isolated by reversed-phase HPLC using aqueous methanol (70%) as eluent.

Tetramethyl (2-iodophenyl)methylene-1,1-bis(phosphonate) 6 (X = 2-Cl, R = Me). This compound was isolated as a colourless oil (Found: C, 30.65; H, 3.9. $C_{11}H_{17}IO_6P_2$ requires C, 30.48; H, 3.93%); δ_P(CDCl$_3$) 20.6; δ_H(270 MHz; CDCl$_3$) 3.65 (6 H, d, J_{PH} 11, POMe), 3.83 (6 H, d, J_{PH} 11, POMe), 4.53 (1 H, t, J_{PH} 25, αCH), 7.00 (1 H, tm, J_{HH} 7.5, 4-H), 7.38 (1 H, br t, J_{HH} 8, 5-H), 7.90 (1 H, dd, J_{HH} 8 and 1, 3-H) and 7.94 (1 H, dm, J_{HH} 7.5, 6-H); δ_C(CDCl$_3$) 48.8 (t, J_{PC} 133, αC), 53.9 (2 m, POMe), 54.1 (2 m, POMe), 103.2 (t, J_{PC} 9, C-2), 128.5 (s, C-5), 129.5 (s, C-4), 130.9 (t, J_{PC} 4, C-6), 133.2 (t, J_{PC} 7, C-1) and 140.0 (s, C-3).

Dimethyl 2-iodobenzylphosphonate 9 (X = 2-I). This compound was isolated as a colourless oil [HRMS(FAB): found MH$^+$, 326.9627. $C_9H_{13}IO_3P$ requires *M*, 326.9647]; δ_P(CDCl$_3$) 28.0; δ_H(270 MHz; CDCl$_3$) 3.44 (2 H, d, J_{PH} 22, αCH$_2$), 3.70 (6 H, d, J_{PH} 11, POMe), 6.94 (1 H, tt, J_{HH} 8 and 2, 5-H), 7.31 (1 H, br t, J_{HH} 7.5, 4-H), 7.46 (1 H, dm, J_{HH} 8, 3-H) and 7.84 (1 H, br d, J_{HH} 8, 6-H); δ_C(CDCl$_3$) 37.7 (d, J_{PC} 138, αC), 52.9 (2 d, J_{PC} 7, POMe), 101.1 (d, J_{PC} 10, C-2), 128.4 (d, J_{PC} 3, C-5), 128.7 (d, J_{PC} 4, C-4), 130.7 (d, J_{PC} 6, C-1), 135.1 (d, J_{PC} 9, C-6) and 139.8 (d, J_{PC} 3, C-3).

The reaction of dimethyl 2-iodobenzoylphosphonate with triethyl phosphite

A mixture of dimethyl 2-iodobenzoylphosphonate **1** (X = 2-I) (1.0 g, 4.3 mmol) and triethyl phosphite (1.0 g, 7.4 mmol) in toluene (3 cm^3) was heated under dry nitrogen at 105 °C for 18 h. ^{31}P NMR spectroscopy indicated the formation of equimolar quantities of triethyl phosphate and the ylide, [(dimethoxyphosphinoyl)(2-iodophenyl)methylene]triethoxyphosphorane **4** (X = 2-I, R = Et); δ_P(CDCl$_3$) 46.3 [d, J_{PP} 91, P(OEt)$_3$], 29.7 [d, J_{PP} 91, P(O)(OMe)$_2$]; δ_C([^{2}H$_6$]acetone) 37.1 (dd, J_{PC} 210 and 225, αC). The volatile components in the reaction mixture were removed by heating the yellow solution under reduced pressure (60 °C at 0.01 mmHg) to give the crude ylide **4** (X = 2-I, R = Et). Decomposition of a sample of this ylide by the addition of water (pH 7) resulted in the formation of **6** (X = 2-I, R = Et) (60%) and **9** (X = 2-I) (40%).

Diethyl dimethyl (2-iodophenyl)methylene-1,1-bis(phosphonate) 6 (X = 2-I, R = Et). This compound was isolated as a colourless oil by reversed-phase HPLC using aqueous methanol (70%) as eluent (Found: C, 33.8; H, 4.8. $C_{13}H_{21}IO_6P_2$ requires C, 33.79; H, 4.58%); δ_P(CDCl$_3$) 20.9 [d, J_{PP} 4, P(O)(OMe)$_2$] and 17.9 [d, J_{PP} 4, P(O)(OEt)$_2$]; δ_H(270 MHz; CDCl$_3$) 1.16 (3 H, t, J_{HH} 7, Me), 1.32 (3 H, d, J_{HH} 7, Me), 3.65 (3 H, d, J_{PH} 11, POMe), 3.83 (3 H, d, J_{PH} 11, POMe), 3.97 (2 H, m, CH$_2$), 4.19 (2 H, m, CH$_2$), 4.50 (1 H, t, J_{PH} 25, αCH), 7.00 (1 H, tm, J_{HH} 8, 4-H), 7.37 (1 H, m, 5-H), 7.88 (1 H, br d, J_{HH} 8, 3-H) and 7.97 (1 H, dm, J_{HH} 8, 6-H); δ_C(CDCl$_3$) 16.2 (d, J_{PC} 6, Me), 16.3 (d, J_{PC} 6, Me), 49.0 (t, J_{PC} 133, αC), 53.8 (d, J_{PC} 7, POMe), 54.0 (d, J_{PC} 7, POMe), 103.3 (t, J_{PC} 10, C-2), 128.5 (t, J_{PC} 3, C-5), 129.5 (t, J_{PC} 3, C-4), 131.0 (t, J_{PC} 4, C-6), 133.4 (t, J_{PC} 8, C-1) and 139.9 (t, J_{PC} 2, C-3).

The reaction of dimethyl 2-iodobenzoylphosphonate with triisopropyl phosphite

A mixture of dimethyl 2-iodobenzoylphosphonate **1** (X = 2-I) (1.0 g, 4.3 mmol) and triisopropyl phosphite (1.5 g, 7.4 mmol) in toluene (3 cm^3) was heated under dry nitrogen at 105 °C for 48 h. ^{31}P NMR spectroscopy indicated the formation of equimolar quantities of triisopropyl phosphate and the ylide, [(dimethoxyphosphinoyl)(2-iodophenyl)methylene]triisopropoxyphosphorane **4** (X = 2-I, R = Pr^i); δ_P(acetone) 40.4 [d, J_{PP} 97, P(OPr^i)$_3$] and 29.0 [d, J_{PP} 97, P(O)(OMe)$_2$]; δ_C(CDCl$_3$) 37.8 (dd, J_{PC} 213 and 227, αC). The volatile components in the reaction mixture were removed by heating the yellow solution under reduced pressure (60 °C at 0.01 mmHg) to give the crude ylide **4** (X = 2-I, R = Pr^i). Decomposition of a sample of this ylide by the addition of water (pH 7) resulted in the formation of only **6** (X = 2-I, R = Pr^i) and no **9** (X = 2-I).

Diisopropyl dimethyl (2-iodophenyl)methylene-1,1-bis(phosphonate) 6 (X = 2-I, R = Pr^i). This compound was isolated as a colourless oil by reversed-phase HPLC using aqueous methanol (70%) as eluent (Found: C, 36.55; H, 5.0. $C_{15}H_{25}IO_6P_2$ requires C, 36.75; H, 5.14%); δ_P(CDCl$_3$) 20.7 [d, J_{PP} 4, P(O)(OMe)$_2$] and 15.8 [d, J_{PP} 4, P(O)(OPr^i)$_2$]; δ_H(270 MHz; CDCl$_3$) 0.96 (3 H, d, J_{HH} 6, Me), 1.25 (3 H, d, J_{HH} 6, Me), 1.31 (3 H, d, J_{HH} 6.5, Me), 1.35 (3 H, d, J_{HH} 6.5, Me), 3.66 (3 H, d, J_{PH} 11, POMe), 3.85 (3 H, d, J_{PH} 11, POMe), 4.44 (1 H, t, J_{PH} 26, αCH), 4.55 (1 H, m, CH), 4.79 (1 H, m, CH), 6.97 (1 H, tm, J_{HH} 8, 4-H), 7.38 (1 H, br t, J_{HH} 8, 5-H), 7.88 (1H, dm, J_{HH} 8, 3-H) and 7.99 (1 H, dm, J_{HH} 8, 6-H); δ_C(CDCl$_3$) 22.9 (d, J_{PC} 6, Me), 23.8 (d, J_{PC} 6, Me), 24.0 (d, J_{PC} 4, Me), 24.4 (d, J_{PC} 3, Me), 49.6 (dd, J_{PC} 132 and 135, αC), 53.6 (d, J_{PC} 7, POMe), 53.9 (d, J_{PC} 7, POMe), 72.0 (d, J_{PC} 7, POCH), 72.7 (d, J_{PC} 7, POCH), 103.7 (t, J_{PC} 10, C-2), 128.3 (t, J_{PC} 3, C-5), 129.3 (t, J_{PC} 3, C-4), 131.0 (t, J_{PC} 4, C-6), 133.8 (t, J_{PC} 7, C-1) and 139.8 (br s, C-3).

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