Electron-rich heteroaroylphosphonates and their reaction with trimethyl phosphite†

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Dialkyl heteroaroylphosphonates based on thiophene, pyrrole or furan have been prepared and their reactions with trimethyl phosphite investigated. Deoxygenation of the carbonyl groups in these heteroaroylphosphonates occurs to give carbene intermediates, which then undergo further reaction. In the case of the furan-3-oylphosphonates and those systems containing a thiophene or pyrrole ring, the major reaction pathway involves intermolecular trapping of the carbene intermediates by the trimethyl phosphite, leading to the formation of ylidic phosphonates that can be readily converted into the corresponding 1,1-bisphosphonates. However, in some furan-2-oylphosphonates the carbenes generated undergo ring-opening to initially give acyclic alkynylphosphonates which may react further to give other novel phosphorus compounds. The effects of substituents on the extent to which intermolecular trapping of the initially formed carbene competes with intramolecular rearrangement has been investigated. The latter process appears to be suppressed by a substituent at the 5-position of the furan ring, the resulting ylidic phosphonates being a rare example of an efficient intermolecular trapping of a furan-2-yl carbene.

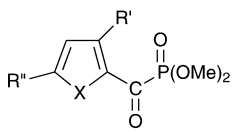
Introduction

The reactions of 2-substituted dialkyl benzoylphosphonates with trialkyl phosphites have proved to be a fruitful area for research and have led to the formation of some novel compounds, often *via* the intramolecular cyclisation of initially formed carbene intermediates.[1–5] In an attempt to broaden the scope of this research and to investigate their synthetic potential, we have now investigated the preparation and reactions of a range of heterocyclic analogues of the benzoylphosphonates. In this paper we report some of our studies on the reactions of trimethyl phosphite with 'electron-rich' heteroaroylphosphonates based on thiophene, pyrrole and furan.

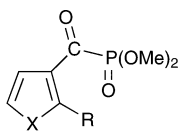
Results and discussion

The heteroaroylphosphonates **1a–1g** and **2a–2c** were prepared by the action of trimethyl phosphite on the corresponding acid chlorides, sometimes in the presence of an inert solvent. In general these reactions were carried out at room temperature, but, as discussed later, in some cases it was desirable to cool the reaction to avoid side reactions. Unfortunately, it proved to be very difficult to prepare the parent pyrrole-based aroylphosphonate **1h** in sufficient quantities for a meaningful study due to the tendency of the pyrrole-2-carbonyl chloride to decompose during its reaction with trimethyl phosphite. However, this problem did not arise with the *N*-substituted analogues **1f** and **1g**.

The heteroaroylphosphonates all gave a characteristic low-field large doublet in their ^{13}C NMR spectra for the carbonyl carbon adjacent to the phosphonate group and a ^{31}P NMR chemical shift around δ_P 0 ppm, although it is interesting to note that the ^{31}P NMR chemical shifts for the pyrrole systems **1f–h** were about 1.5–2 ppm downfield of those for the other aroylphosphonates studied to date. It is also interesting to note that some of the heteroaroylphosphonates were sufficiently stable to enable them to be purified by chromatography on silica. This contrasts with the behaviour of the benzoylphosphonates we have studied which usually readily hydrolyse and are thus difficult to purify if they cannot be distilled.



1a: X = S, R' = R" = H
1b: X = O, R' = R" = H
1c: X = O, R' = CH_2Ph, R" = H
1d: X = O, R' = H, R" = Me
1e: X = O, R' = H, R" = Ph
1f: X = NMe, R' = R" = H
1g: X = NPh, R' = R" = H
1h: X = NH, R' = R" = H



2a: X = S, R = H
2b: X = O, R = H
2c: X = O, R = $CH_2OCH_2C{\equiv}CH$

Moreover, although the deoxygenation reactions of the dialkyl benzoylphosphonates with trimethyl phosphite usually required heating before they proceeded at a reasonable rate, there was much greater variability in the reactivities of the heteroaroyl systems.

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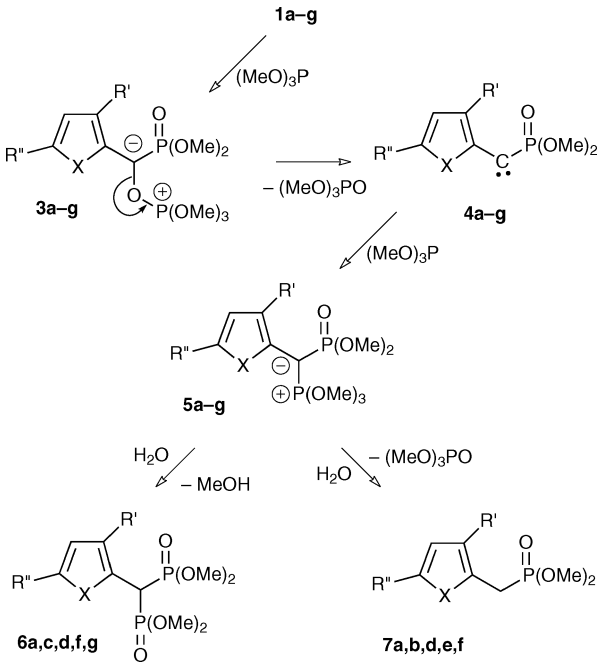
† Electronic supplementary information (ESI) available: A. Additional general details; B. Preparation, isolation and characterisation information for **1a–h** and **2a–c**; C. NMR spectral data for **6a**,**c–g**, **7a**,**d–f**, **10**, **15a–b**, **16a–c**, **17a**, **18a–b**, **19b**, **19b′**, 2,4-DNPH derivatives of **20b**, **20c**, **23** and **25**; D. Crystal data and X-ray experimental data for 2,4-DNPH derivative of **20b**. See DOI: 10.1039/b717130g

Thus, for example, while the reaction of the thiophene system **2a** with trimethyl phosphite still required heating at 100 °C, that involving the isomeric thiophene system **1a** required cooling to avoid overheating and charring.

However, providing the reaction of the aroylphosphonate **1a** with trimethyl phosphite was kept cool, it proceeded cleanly to give the ylidic phosphonate **5a** [δ_P 52.4 and 29.3 ppm, J_{PP} 96 Hz] and trimethyl phosphate as the major products. Since such ylidic phosphonates have been shown to arise from the intermolecular trapping of the corresponding carbene intermediates by trimethyl phosphite,[5] this indicates that the reaction follows the deoxygenation pathway shown in Scheme 1 which is analogous to that previously observed for the benzoylphosphonates.

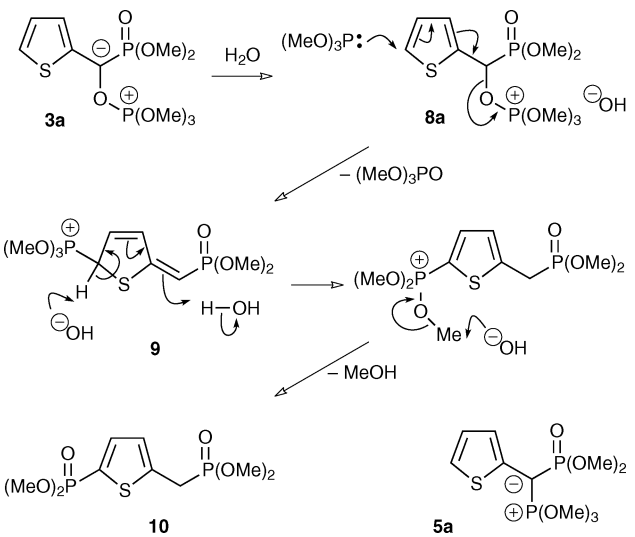


Scheme 1

Decomposition of the ylidic phosphonate **5a** in water produced a 2 : 1 mixture of the bisphosphonate **6a** and the monophosphonate **7a**. The route by which this occurs has been discussed previously for those ylidic phosphonates generated from benzoylphosphonates.[6]

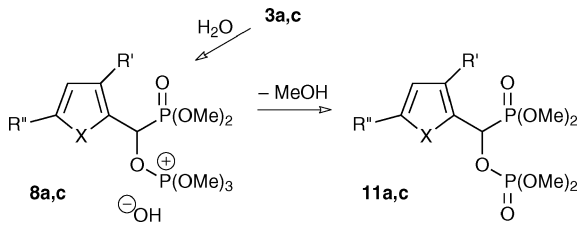
If moisture is not rigorously excluded during the reaction of the aroylphosphonate **1a** with trimethyl phosphite, two other products are formed in addition to the ylidic phosphonate **5a**. The first of these is the novel bisphosphonate **10** (Scheme 2). The presence of a methylene unit in this molecule clearly indicates the involvement of a proton donor in its formation and this was confirmed by adding a small quantity of water to the aroylphosphonate **1a** immediately prior to its reaction with trimethyl phosphite. This resulted in the formation of the bisphosphonate **10** as the major reaction product.

The likely route to the bisphosphonate **10** is that shown in Scheme 2. Under the reaction conditions it would seem that the quasiphosphonium salt **8a**, formed from the protonation of the initially formed anionic intermediate **3a**, preferentially undergoes attack on the heterocyclic ring and that the resulting system **9** then undergoes re-aromatisation and dealkylation to give the observed bisphosphonate **10**.



Scheme 2 X = S and R′ = R″ = H shown to simplify structures.

The direct dealkylation of the quasiphosphonium salt **8a** to give the phosphate-phosphonate **11a** [δ_P 2.3 and 18.7 ppm (d, J_{PP} 32)] (Scheme 3) was also observed in the presence of moisture, although this was less favoured than the formation of **10** under the reaction conditions used.



Scheme 3

In contrast, the 3-substituted thiophene system **2a** behaved more like the benzoylphosphonates in that it had to be heated with trimethyl phosphite before the reaction proceeded at a reasonable rate. Once again the reaction proceeded *via* a carbene intermediate (Scheme 4) to give initially the ylide **14a**, although prolonged heating caused this material to rearrange to the bisphosphonate **15a**. Attempts to purify the ylide **14a** by chromatography led to its decomposition and the isolation of its hydrolysis products, the bisphosphonate **16a** and the monophosphonate **17a**.

If moisture is not fully excluded, the reaction of **2a** with trimethyl phosphite also generates some of the phosphate-phosphonate **18a**.

Although the pyrrole-based heteroaroylphosphonates **1f** and **1g** both required heating with the trimethyl phosphite to achieve deoxygenation, they behaved similarly to the thiophene system **1a** giving the ylidic phosphonates **5f** and **5g** as the major products. There was no evidence for an intramolecular carbene insertion reaction into the *N*-phenyl ring following the formation of the carbene **4g**. The ylidic phosphonates **5f** and **5g** were isolated as their hydrolysis products, the corresponding bisphosphonates **6** and monophosphonates **7**. A similar pathway appears to occur with the parent system **1h**.

In contrast, the furan-2-oylphosphonate **1b** showed quite different behaviour in its reaction with trialkyl phosphites to the thiophene- and pyrrole-based aroylphosphonates.

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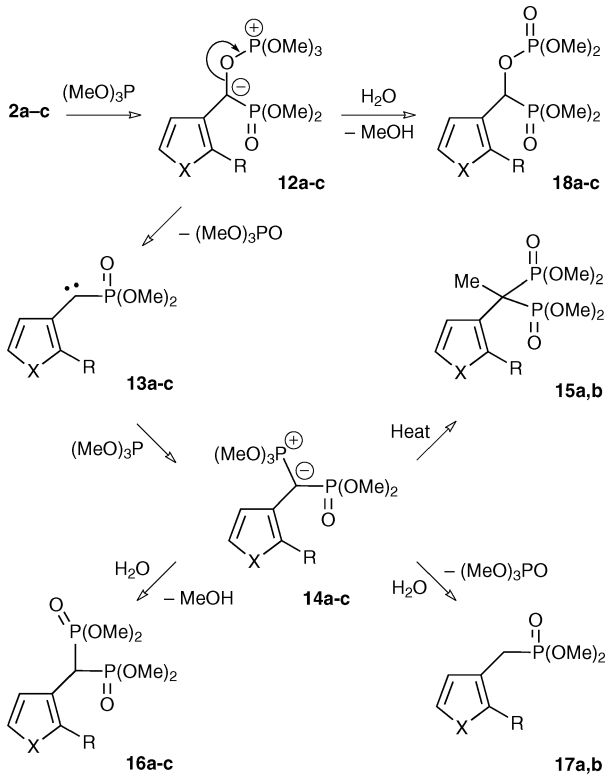
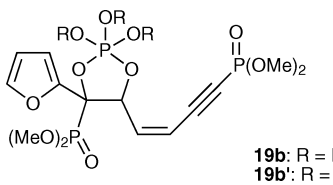
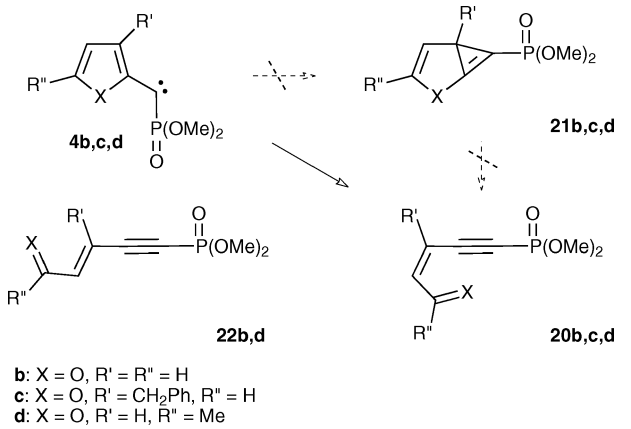


Scheme 4



Firstly, the reaction needed to be carried out at low temperature since at room temperature an exothermic reaction occurred leading to extensive charring. Secondly, at low temperature and in toluene, the reaction proceeded cleanly to give one major product, a triphosphorus compound **19b** [δ_P −48.3 (d, J_{PP} 41), −3.4 (s) and 19.0 (d, J_{PP} 41)] that can be seen to arise from two molecules of the furanoylphosphonate **1b** and one of the trimethyl phosphite. This was confirmed by repeating the reaction using triethyl phosphite which gave the corresponding triphosphorus compound **19b′** [δ_P −51.4 (d, J_{PP} 41), −3.4 (s) and 19.0 (d, J_{PP} 41)]. A small quantity of the ylidic phosphonate **5b** was also produced under these conditions [δ_P 28.9 (d, J_{PP} 89) and 52.6 (d, J_{PP} 89)] together with other minor components including one [δ_P −4.9] later identified as the aldehyde **20b**.

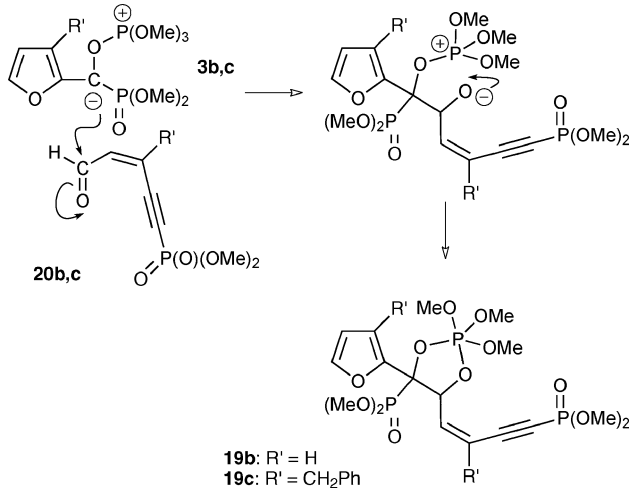
The presence of the alkynylphosphonate portion of **19b** was confirmed from the high field shift of this phosphonate resonance [δ_P −3.4 ppm] and by the exceptionally large coupling (J_{PC} 298 Hz) between the phosphonate group and the adjacent carbon atom. A similar large coupling has been seen in related structures[7] and reflects the high degree of s character in this P–C bond. To explain the formation of **19b** we propose that the initially formed carbene intermediate **4b** undergoes ring opening to give the aldehyde **20b** (Scheme 5).



Scheme 5

The formation of analogous aldehydes has been observed previously when attempts have been made to prepare other furan-2-yl carbenes.[8] Computational studies[9] support the concept of a spontaneous ring-opening of the furan-2-yl carbenes leading to these aldehydes rather than the involvement of an intermediate such as **21b**. Furthermore, no experimental evidence has yet been obtained to support the formation of such cyclopropene intermediates.[10]

The reaction of the anionic intermediate **3b**, initially formed from the reaction of **1b** with trimethyl phosphite, with the aldehyde **20b** then explains the formation of the observed triphosphorus compound **19b** (Scheme 6).



Scheme 6 X = O and R″ = H shown to simplify structures.

In an effort to obtain support for the involvement of the intermediate aldehyde **20b** in the formation of **19b**, the reaction of furan-2-oyl chloride with trimethyl phosphite was investigated under a variety of conditions to see if the quantity of this aldehyde in the reaction mixture could be increased. Fortunately, by using low temperatures with acetonitrile as the solvent and by restricting the quantity of trimethyl phosphite used, it was possible to obtain a reaction mixture that contained a significant quantity of a component [δ_P −4.9] that gave NMR spectra consistent with the aldehyde **20b**. This component was isolated from the reaction

mixture as its 2,4-dinitrophenylhydrazone derivative, the structure of which was determined using X-ray crystallography (Fig. 1).[11]

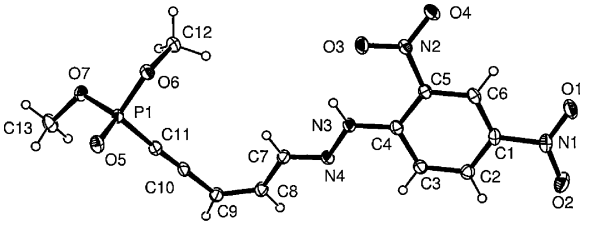


Fig. 1 X-ray structure of the 2,4-dinitrophenylhydrazone derivative of **20b**.

It is interesting to note that while the aldehyde **20b** is initially produced with a *Z*-configuration at the alkene (CH=CH, $^{3}J_{HH}$ 11.2) it slowly isomerises under the reaction conditions to give the corresponding *E*-configuration **22b** (CH=CH, $^{3}J_{HH}$ 16.2) as the major component.

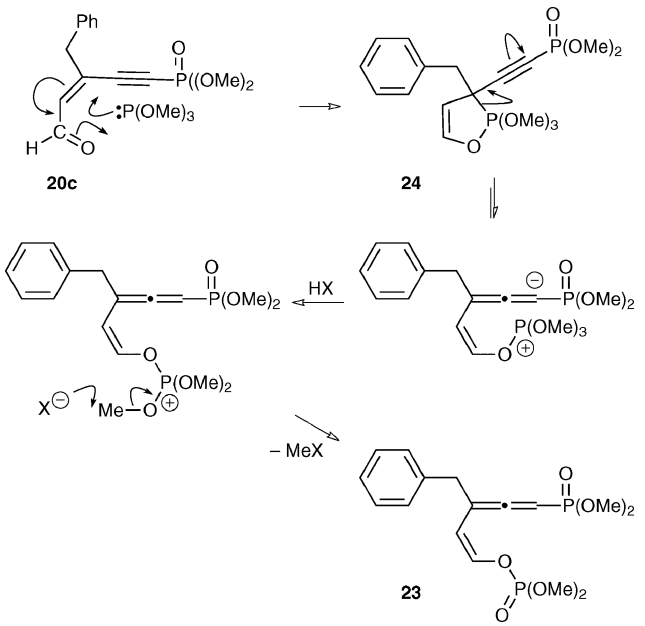
We have also investigated the influence of placing substituents at the 3- and 5-positions on the furan ring. In particular we were interested to see how this might affect the ease of ring opening of the furan-2-yl carbenes **4c–e**. We were also interested to see if it might be possible to achieve an intramolecular insertion reaction into a substituent at the 3-position on the ring as an alternative reaction pathway for the carbene **4c**.

Interestingly, with the 3-benzyl-substituted system **1c** there was no evidence for the formation of any of the triphosphorus compound analogous to **19b** when it was reacted with trimethyl phosphite, even though formation of the aldehyde **20c** was the major reaction pathway following carbene formation. The benzyl substituent had thus clearly inhibited further reaction of the aldehyde **20c** with the anionic intermediate **3c**. Some intermolecular trapping of the carbene **4c** by the trialkyl phosphite to give the ylidic phosphonate **5c** was also observed, suggesting that this carbene intermediate is slightly longer-lived than that for the unsubstituted system, but there was no evidence for products arising from an interaction between the carbene centre and the benzyl substituent in **4c**.

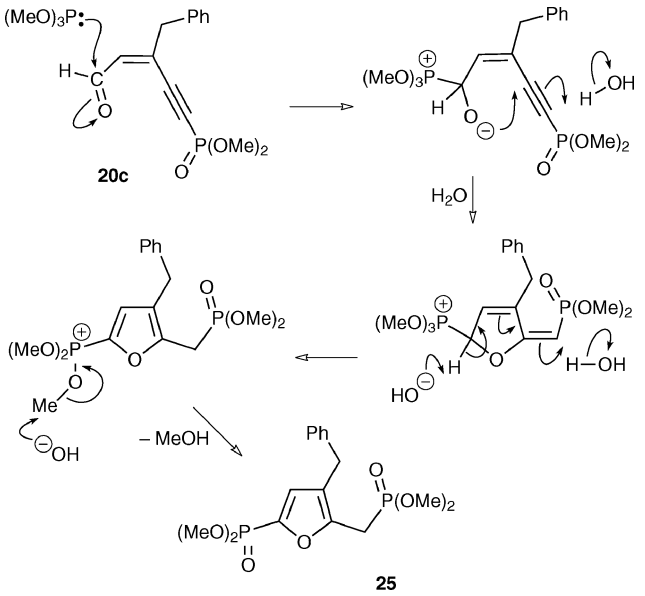
We also observed that if a proton donor was present in the reaction mixture the initially formed aldehyde could react with further trimethyl phosphite to give a product giving two singlets in the ^{31}P NMR spectrum at δ_P −1.9 and 17.3 ppm. This product was identified as the novel allene **23**, the formation of which can be rationalised as shown in Scheme 7. This allene showed a characteristic resonance in the ^{13}C NMR spectrum at δ_C 215.7 ppm for the sp-hybridised carbon in an allene and a broad band in the IR spectrum at ν_{max} 1940 cm^{-1} typical of an allene.

Two other components were also produced small quantities which arose as a result of traces of moisture in the reaction mixture, the phosphate-phosphonate **11c** and the bisphosphonate **25**.

Although we earlier proposed that the formation of thiophene-based bisphosphonate **10** involved attack by phosphite on the quasiphosphonium salt **8a** (Scheme 2), we believe that the formation of the furan-based system **25** is more likely to be derived from the alternative mechanism shown in Scheme 8. This is supported by the observation that treatment of the aldehyde **20c** with trimethyl phosphite without the rigorous exclusion of moisture leads to cyclisation and formation of the bisphosphonate **25**.



Scheme 7



Scheme 8

Although the ring opening of thiophen-2-yl carbenes has been reported[12] we saw no evidence for this occurring with the thiophen-2-yl carbene intermediate **4a** generated by the action of trialkyl phosphite on the aroylphosphonate **1a**. We have therefore ruled out a pathway analogous to that shown in Scheme 8 to explain the formation of the corresponding thiophene-based bisphosphonate **10**.

To investigate the influence of a substituent at the 5-position on the furanyl carbenes **4** (X = O), we prepared the methyl- and phenyl-substituted furanoylphosphonates **1d** and **1e**.

The reaction of the 5-methyl substituted system **1d** with trimethyl phosphite in toluene gave largely the ylidic phosphonate **5d**, subsequently isolated as its decomposition products **6d** and **7d**, although a small quantity of the ring-opened ketone **20d**

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(*ca.* 2%) was also produced. As with the aldehyde **20b** previously discussed, the ketone was initially produced as the *Z*-isomer **20d** [CH=CH, $^{3}J_{HH}$ 12 Hz] but subsequently isomerised under the reaction conditions to give the corresponding *E*-form **22d** [CH=CH, $^{3}J_{HH}$ 16.3 Hz] as the major isomer.

The ability of substituents at the 5-position on the furan ring to affect the ease of ring-opening of the corresponding furanyl carbene **4** was even more marked in the case of the 5-phenyl-substituted furan-2-yl carbene **4e** where no ring-opening to give phenyl ketones analogous to **20d** or **22d** was observed under the conditions used. In this case only intermolecular trapping of the carbene intermediate **4e** by the trialkyl phosphite was observed leading to the formation of the ylidic phosphonate **5e**. It is interesting to note that early studies had concluded that the presence of alkyl or aryl groups at the 5-position of some simpler furan-2-yl carbenes had not had a significant effect on the efficiency of ring opening although they had seen a marked effect if an electron-withdrawing group was placed at the 5-position.[12] It is also interesting to note that it has proved extremely difficult to intercept furan-2-yl carbene intermediates before ring opening occurs.[13] The formation of the ylidic phosphonate **5e** in the presence of trimethyl phosphite is therefore a rare example of the efficient intermolecular trapping of such a carbene intermediate.[14]

The effect of moving the ketophosphonate group to the 3-position on the furan ring was also investigated. Whereas the reaction the furan-2-oylphosphonates **1b** and **1e** with trialkyl phosphites had required cooling to avoid side reactions, the furan-3-oylphosphonates **2b** and **2c** required heating with trimethyl phosphite before the reaction occurred at any significant rate. However, under these conditions both **2b** and **2c** reacted to give the corresponding ylidic phosphonates **14b** and **14c** together with trimethyl phosphate, indicating that these reactions too were proceeding *via* carbene intermediates as had been observed with the analogous thiophene system **2a** (Scheme 4). In the case of the parent furan system **2b**, the initially formed ylidic phosphonate **14b** showed a tendency to rearrange to the corresponding bisphosphonate **15b** if the reaction mixture was heated for an extended period, but this was not observed with the 2-substituted system **14c**. This is consistent with the behaviour of the ylidic phosphonates from benzoylphosphonates where the analogous rearrangement was inhibited by the presence of an *ortho* substituent.[5] Both ylidic phosphonates could be readily converted into the corresponding bisphosphonates **16b** and **16c** by the action of a suitable proton donor such as hydrogen chloride. There was no evidence for any interaction between the carbene centre and the adjacent substituent in **13c**.

Summary

The reactions of trimethyl phosphite with heteroaroylphosphonates **1a–h** and **2a–c** have been shown to proceed *via* deoxygenation of the carbonyl group to give carbene intermediates **4a–h** and **13a–c** whose subsequent reactions depend on the nature of the heterocyclic ring. With those 2-heteroaroyl systems **1a**, **1f–h** that contained the more aromatic thiophene and pyrrole heterocyclic systems, and with all the 3-heteroaroyl systems **2a–c** studied, the major reaction pathway involves the intermolecular trapping of the carbene intermediates by the trimethyl phosphite in the reaction mixture. The resulting ylidic phosphonates **5** and **14** can be used as precursors for the preparation of some novel 1,1-bisphosphonates. In contrast, the major reaction pathway with the furan-2-yl systems **1b** and **1c**, where there is no substituent on the 5-position of the furan ring, involves ring opening of the carbene intermediates **4b,c** to give novel alkynylphosphonates **20b,c** and **22b**. There was no evidence for any reaction between the benzyl substituent in **4c** and the carbene centre.

In the case of the unsubstituted furan-2-oylphosphonate **1b**, the initially formed anionic intermediate **3b** reacts with the aldehyde portion of the subsequently formed alkynylphosphonate **20b** to give the triphosphorus system **19b**. However, with the benzyl-substituted alkynylphosphonate **20c** such a subsequent reaction is inhibited. In contrast, the presence of a substituent at the 5-position on the furan ring in the carbene intermediates **4d** and **4e** appears to discourage ring-opening, and trapping of the carbene by trimethyl phosphite to give the ylidic phosphonates **5d** and **5e** becomes the dominant reaction pathway. Indeed, in the case of the 5-phenyl substituted carbene **4e** this intermolecular trapping pathway was the only carbene decomposition pathway observed under the conditions used and as such it is a rare example of a successful intermolecular trapping of a furan-2-yl carbene.[8]

Finally, these studies have shown that some unexpected products can be generated when the reaction of trimethyl phosphite with the heteroaroylphosphonates occurs in the presence of a proton donor such as moisture. Thus, for example, in the presence of moisture the alkynylphosphonate **20c** reacts with trimethyl phosphite to give the novel allene **23** while the reaction of **1a** with trimethyl phosphite in the presence of moisture gave the unexpected bisphosphonate **10**. Other reactions of this type will be the subject of a future publication.[15]

Experimental

General details[21]

NMR spectra were recorded on JEOL EX-270, Bruker AMX400 and Bruker AV600 spectrometers. ^{31}P NMR spectra are referenced to 85% phosphoric acid, ^{1}H NMR spectra to Me_4Si, and ^{13}C NMR spectra to $CDCl_3$ at 77.23 ppm. *J* values are given in Hz; '*J*' indicates the apparent coupling in a second order spectrum.

The carboxylic acids used were either available commercially or prepared by literature methods. 3-Benzylfuran-2-carboxylic acid[16] was prepared from 3-benzylfurfural,[16] and 5-methylfuran-2-carboxylic acid[17] by the oxidation of 5-methylfurfural.[17] 5-Phenylfuran-2-carboxylic acid[18] was prepared from furan-2-carboxylic acid, 1-phenylpyrrole-2-carboxylic acid[19] from 1-phenylpyrrole, and 2-(prop-2-ynyloxymethyl)furan-3-carboxylic acid[20] from methyl 2-methylfuran-3-carboxylate.

Typical procedure for the preparation of the aroylphosphonates 1a–h and 2a–c.[21]

The aroylphosphonates **1a–h** and **2a–c** were prepared by the action of trimethyl phosphite on the corresponding acid chlorides, which were usually prepared *in situ* by the action of thionyl chloride or oxalyl chloride on the carboxylic acid.

Dimethyl thiophene-2-carbonylphosphonate 1a

The phosphonate **1a** was obtained as a pale yellow oil in essentially quantitative yield; δ_P(109.3 MHz, $CDCl_3$) 0.1; δ_C(67.9 MHz, $CDCl_3$) 188.6 (d, $^1J_{PC}$ 182, C=O).[21]

Dimethyl furan-2-carbonylphosphonate 1b

The phosphonate **1b** (4.0 g, 58%) was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) −0.1; δ_C(67.9 MHz, $CDCl_3$) 183.7 (d, J_{PC} 190, C=O).[21]

Dimethyl 3-benzylfuran-2-carbonylphosphonate 1c

A sample of the pure phosphonate **1c** (1.2 g, 63%) was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 0.9; δ_C(67.9 MHz, $CDCl_3$) 186.2 (d, J_{PC} 186, C=O).[21]

Dimethyl 5-methylfuran-2-carbonylphosphonate 1d

The phosphonate **1d** (5.1 g, 60%) was obtained as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 0.6; δ_C(67.9 MHz, $CDCl_3$) 182.3 (d, J_{PC} 189, C=O).[21]

Dimethyl 5-phenylfuran-2-carbonylphosphonate 1e

The phosphonate **1e** (0.09 g, 20%) was isolated as a pale yellow oil, bp 130 °C at 0.005 mmHg; δ_P(109.3 MHz, $CDCl_3$) 0.6; δ_C(67.9 MHz, $CDCl_3$) 183.0 (d, J_{PC} 189, C=O).[21]

Dimethyl 1-methylpyrrole-2-carbonylphosphonate 1f

The phosphonate ester **1f** (1.04 g, 60%) was isolated as a pale yellow oil, bp 137 °C at 0.005 mmHg; δ_P(109.3 MHz, $CDCl_3$) 2.5; δ_C(67.9 MHz, $CDCl_3$) 184.2 (d, J_{PC} 183, C=O).[21]

Dimethyl 1-phenylpyrrole-2-carbonylphosphonate 1g

The phosphonate ester **1g** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 2.1; δ_C(100.63 MHz, $CDCl_3$) 183.6 (d, J_{PC} 184, C=O).[21]

Dimethyl thiophene-3-carbonylphosphonate 2a

The phosphonate **2a** was isolated in essentially quantitative yield as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 0.75; δ_C (67.9 MHz, $CDCl_3$) 191.0 (d, J_{PC} 178, C=O).[21]

Dimethyl furan-3-carbonylphosphonate 2b

The phosphonate **2b** (12.4 g, 68%) was obtained as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) −0.4; δ_C(67.9 MHz, $CDCl_3$) 192.0 (d, J_{PC} 183, C=O).[21]

Dimethyl 2-(prop-2-ynyloxymethyl)furan-3-carbonylphosphonate 2c

The phosphonate ester **2c** was obtained as a pale yellow oil in essentially quantitative yield; δ_P(109.3 MHz, $CDCl_3$) 0.2; δ_C(67.9 MHz, $CDCl_3$) 193.9 (d, J_{PC} 185, C=O).[21]

Reaction of dimethyl thiophene-2-carbonylphosphonate 1a with trimethyl phosphite

Trimethyl phosphite (2.23 g, 18 mmol) was added slowly to a stirred sample of the phosphonate **1a** (1.32 g, 6 mmol) at 0 °C. The solution was then allowed to warm to room temperature and after a period of 12 h ^{31}P NMR spectroscopy showed the formation of trimethyl phosphate, the ylidic phosphonate **5a** [δ_P 29.3 and 52.4 ppm (d, J_{PP} 96)] and a small quantity of the bisphosphonate **6a**. Volatile components were then removed *in vacuo* (50 °C at 0.005 mmHg). Decomposition of the ylide **5a** by the addition of water resulted in the formation of the bisphosphonate **6a** and the monophosphonate **7a** in a 5 : 1 ratio. Pure samples of products in the residue were isolated by a combination of column chromatography on silica gel using ethyl acetate as the eluent and reverse-phase HPLC on a C_{18} column using water–methanol mixtures as the eluent.

Tetramethyl thiophen-2-ylmethane-1,1-bisphosphonate **6a** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 19.7; δ_H(400 MHz, $CDCl_3$) 4.12 (1 H, t, J_{PH} 25.0, α-CH); δ_C(100.63 MHz, $CDCl_3$) 39.5 (t, J_{PC} 136, α-C); *m/z* (EI) 314.0143 (M^+. $C_9H_{16}O_6P_2S$ requires 314.0143).[21]

Dimethyl thiophen-2-ylmethylphosphonate **7a** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 27.3; δ_H(400 MHz, $CDCl_3$) 3.37 (2 H, d, J_{PH} 20.8, CH_2); δ_C(100.63 MHz, $CDCl_3$) 27.1 (d, J_{PC} 144, CH_2); *m/z* (ESI) 229.0059 (M + Na^+. $C_7H_{11}O_3PSNa$ requires 229.0064).[21]

Dimethyl 5-(dimethoxyphosphorylmethyl)thiophen-2-ylphosphonate **10**, was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 15.2 (d, J_{PP} 3) and 26.3 (d, J_{PP} 3); δ_H(400 MHz, $CDCl_3$) 3.34 (2 H, d, J_{PH} 21.2, CH_2); δ_C(100.63 MHz, $CDCl_3$) 26.3 (d, J_{PC} 143, CH_2), 124.7 (dd, J_{PC} 211 and 4, C-2); *m/z* (EI) 314.0143 (M^+. $C_9H_{16}O_6P_2S$ requires 314.0143).[21]

Reaction of dimethyl furan-2-carbonylphosphonate 1b with trimethyl phosphite

Trimethyl phosphite (1.8 g, 14.7 mmol) was added dropwise to a solution of the phosphonate **1b** (1.0 g, 4.9 mmol) in dry toluene (3 cm^3) at −48 °C under an atmosphere of dry nitrogen. This mixture was then allowed to warm to room temperature and stirred for a further 16 h. Volatile components were then removed *in vacuo* (55 °C at 0.005 mmHg). The NMR spectra of the product confirmed the formation of the triphosphorus compound **19b**, δ_P(109.3 MHz, $CDCl_3$) −48.3 [d, J_{PP} 41, $P(OMe)_3$], −3.4 [s, $CCP(O)(OMe)_2$] and 19.0 [d, J_{PP} 41, $P(O)(OMe)_2$],[21] as the major compound (*ca.* 90%) although small quantities of the ylidic phosphonate **5b** [δ_P 28.9 ppm (d, J_{PP} 90) and 52.6 ppm (d, J_{PP} 90)] and the aldehydes **20b** and **22b** [δ_P −4.8 and −4.9 ppm] were also present. Attempts to obtain a pure sample of the triphosphorus compound **19b** by chromatography on silica led to its decomposition.

The reaction can also be carried out in the absence of a solvent without any significant change in product.

Use of triethyl phosphite rather than trimethyl phosphite led to the formation of **19b**′ in a good state of purity; δ_P(109.3 MHz, $CDCl_3$) 19.0 (d, J_{PP} 41), −3.4 (s) and −51.4 (d, J_{PP} 41).[21]

Dimethyl (*Z*)-5-oxo-pent-3-en-1-ynylphosphonate 20b

A solution of furan-2-carbonyl chloride (1.82 g, 14 mmol) in dry acetonitrile (2 cm^3) was cooled to −78 °C and trimethyl phosphite (2.10 g, 16 mmol) added under an atmosphere of dry nitrogen. The mixture was then allowed to warm to room temperature over a period of 12 h. ^{31}P NMR spectroscopy indicated that the reaction had proceeded to form two products, the aroylphosphonate **1b**

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(*ca.* 60%) and the aldehyde **20b** (*ca.* 40%). **20b**: δ_P(109.3 MHz, $CDCl_3$) −4.9; δ_H(400 MHz, $CDCl_3$) 3.85 (6 H, d, J_{HH} 12.4, POMe), 6.47 (1 H, ddd, J_{HH} 11.2 and 7.6, J_{PH} 1.2, 4-H), 6.62 (1 H, dd, J_{HH} 11.2, J_{PH} ~4, 3-H), 10.07 (1 H, d, J_{HH} 7.6, CHO); δ_C(100.63 MHz, $CDCl_3$) 53.5 (x2)(d, J_{PC} 6, POMe), 87.5 (d, J_{PC} 293, C-1), 92.2 (d, J_{PC} 51, C-2), 124.0 (d, J_{PC} 6, C-3), 142.2 (d, J_{PC} 3, C-4) and 189.8 (C-5). Under the reaction conditions **20b** slowly isomerises to give the (*E*)-isomer **22b** as the major component (*ca.* 70%). **22b**: δ_P(109.3 MHz, $CDCl_3$) −4.8 ppm; δ_H(400 MHz, $CDCl_3$) 3.84 (6 H, d, J_{HH} 12.4, POMe), 6.56 (1 H, dd, J_{HH} 16.2, J_{PH} 3.2, 3-H), 6.62 (1 H, ddd, J_{HH} 16.2 and 7.0, J_{PH} 0.8, 4-H), 9.58 (1 H, d, J_{HH} 7.0, CHO); δ_C(100.63 MHz, $CDCl_3$) 53.6 (x2)(d, J_{PC} 6, POMe), 88.9 (d, J_{PC} 294, C-1), 94.0 (d, J_{PC} 51, C-2), 127.1 (d, J_{PC} 6, C-3), 143.2 (d, J_{PC} 3, C-4) and 191.8 (C-5).

Reaction of the initially formed aldehyde **20b** with methanolic 2,4-dinitrophenylhydrazine solution gave an orange brown precipitate of the corresponding hydrazone which was purified by chromatography on silica gel using ethyl acetate–petroleum ether (bp 60–80 °C) as the eluent. Recrystallisation of this product from hot methanol gave orange brown crystals suitable for X-ray structure analysis;[11] mp 151–153 °C; *m/z* (ESI) 391.0414 (M + Na^+. $C_{13}H_{13}N_4O_7PNa$ requires 391.0419).[21]

Reaction of dimethyl 3-benzylfuran-2-carbonylphosphonate 1c with trimethyl phosphite

To a solution of 3-benzylfuran-2-carbonyl chloride (1 g, 4.5 mmol) in deuterochloroform (2.5 cm^3) cooled to −78 °C was added trimethyl phosphite (0.56 g, 4.5 mmol). The mixture was then allowed to warm to room temperature and ^{31}P NMR spectroscopy showed the formation of the phosphonate **1c** (δ_P 0.9). A further quantity of trimethyl phosphite (1.12 g, 9 mmol) was then added and the reaction mixture left at room temperature until the reaction was complete (*ca.* 1 h). Volatile components were then removed from the reaction mixture *in vacuo* (40 °C at 0.005 mmHg). The ^{31}P NMR spectrum of the residue showed the formation of several components subsequently identified as the ylidic phosphonate **5c** [δ_P 28.5 ppm (d, J_{PP} 102) and 53.7 ppm (d, J_{PP} 102)] (*ca.* 31%), the bisphosphonate **6c** (*ca.* 16%), the allene **23** (*ca.* 33%), the bisphosphonate **25** (*ca.* 11%) and some aldehyde **20c** (*ca.* 9%).[22] The major components in this residue were isolated by chromatography on silica gel using mixtures of dichloromethane, ethyl acetate and methanol of increasing polarity as the eluent.

Dimethyl (Z)-3-benzyl-5-oxo-pent-3-en-1-ynylphosphonate **20c** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) −4.5; δ_H(400 MHz, $CDCl_3$) 6.34 (1 H, dq, *J* 8 and 1.2, CH=), and 10.05 (1 H, d, J_{HH} 8, CHO); δ_C(100.63 MHz, $CDCl_3$) 88.2 (d, J_{PC} 291, C-1), 94.1 (d, J_{PC} 50, C-2), and 191.1 (s, C-5); *m/z* (ESI) 279.0781 (M + H^+. $C_{14}H_{16}O_4P$ requires 279.0786).[21]

Tetramethyl 3-benzylfuran-2-ylmethane-1,1-bisphosphonate **6c** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 19.5; δ_H(400 MHz, $CDCl_3$) 4.03 (1 H, t, J_{PH} 25.7, α-H); δ_C(100.63 MHz, $CDCl_3$) 37.5 (t, J_{PC} 136, α-CH)); *m/z* (ESI) 411 (M + Na^+. $C_{16}H_{22}O_7P_2Na$ requires 411).[21]

Dimethyl (Z)-3-benzyl-5-(dimethoxyphosphoryloxy)penta-1,2,4-trienylphosphonate **23** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) −1.9 and 17.3; δ_H(400 MHz, $CDCl_3$) 4.82 (1 H, ddt, J_{HH} 6.4 and 1.6, J_{PH} 2.7, 4-H), 5.35 (1 H, tddd, J_{HH} 2.7, 1.6 and 1.6, J_{PH} 1.4, 1-H), 6.46 (1 H, dddd, J_{HH} 6.4 and 1.6, J_{PH} 6.6 and 3.2, 5-H); δ_C(100.63 MHz, $CDCl_3$) 80.0 (d, J_{PC} 199, C-1), 100.3 (d, J_{PC} 17.5, C-3), 107.1 (dd, J_{PC} 10.2 and 9.8, C-4), 137.7 (dd, J_{PC} 5.3 and 5.1, C-5), 137.7 (d, J_{PC} 4, C-1′), 215.7 (d, J_{PC} 3, C-2); *m/z* (ESI) 389.0912 (M + H^+. $C_{16}H_{23}O_7P_2$ requires 389.0919).[21]

Dimethyl 4-benzyl-5-(dimethoxyphosphorylmethyl)furan-2-ylphosphonate **25** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 7.6, (d, J_{PP} 4) and 25.1 (d, J_{PP} 4); δ_H(400 MHz, $CDCl_3$) 3.26 (2 H, d, J_{PH} 21, PCH_2); δ_C(100.63 MHz, $CDCl_3$) 25.0 (d, J_{PC} 143, PCH_2), 141.6 (dd, J_{PC} 245 and 4, C-2); *m/z* (EI) 388.0836 (M^+. $C_{16}H_{22}O_7P_2$ requires, 388.0841).[21]

Reaction of (*Z*)-3-benzyl-5-oxo-pent-3-en-1-ynylphosphonate 20c with trimethyl phosphite without the rigorous exclusion of moisture

Trimethyl phosphite (0.09 g, 0.72 mmol) was added to a solution of dimethyl (*Z*)-3-benzyl-5-oxo-pent-3-en-1-ynylphosphonate **20c** (0.20 g, 0.72 mmol) in toluene (4 cm^3) at −78 °C and the mixture then allowed to warm to room temperature and monitored by NMR spectroscopy. This showed the gradual formation of the bisphosphonate **25**. A sample of this was isolated by chromatography and shown to be the same as the sample of **25** prepared and characterised earlier.

Reaction of dimethyl 5-methylfuran-2-carbonylphosphonate 1d with trimethyl phosphite

Trimethyl phosphite (6.2 g, 50 mmol) was added to a stirred sample of the phosphonate **1d** (4.36 g, 20 mmol) cooled to −78 °C under an atmosphere of dry nitrogen. The mixture was then allowed to warm to room temperature and the progress of the reaction monitored by ^{31}P NMR spectroscopy. When the reaction of **1d** was complete, the volatile components were removed under reduced pressure (40 °C at 0.005 mmHg) to give a residue, which contained the ylidic phosphonate **5d** [δ_P 53.0 ppm (d, J_{PP} 94) and 29.3 ppm (d, J_{PP} 94)] (*ca.* 88%), together with its decomposition products **6d** (*ca.* 8%) and **7d** (*ca.* 2%), and the ketone **20d** (*ca.* 2%). After decomposing the ylidic phosphonate **5d** by the addition of water, the products in the residue were isolated by column chromatography on silica gel using petroleum ether (bp 40–60 °C)–ethyl acetate mixtures as the eluent.

Dimethyl 5-oxo-hex-3-en-1-ynylphosphonate was isolated as a mixture of the *E* and *Z* isomers **20d** and **22d** (60 : 40) as a yellow oil; *m/z* (ESI) 203 (M + H^+. $C_8H_{12}O_4P$ requires 203).

(Z)-Isomer **20d** δ_P(109.3 MHz, $CDCl_3$) −3.8; δ_H(400 MHz, $CDCl_3$) 2.34 (3 H, s, Me), 3.80 (6 H, d, J_{PH} 12.2, POMe), 6.07 (1 H, dd, J_{HH} 12, J_{PH} 4.4, 3-H) and 6.54 (1 H, dd, J_{HH} 12, J_{PH} 1.2, 4-H); δ_C(100.63 MHz, $CDCl_3$) 30.5 (Me), 53.9 (x2)(d, J_{PC} 7, POMe), 87.4 (d, J_{PC} 296, C-1), 95.6 (d, J_{PC} 51, C-2), 116.3 (d, J_{PC} 6, C-3), 142.5 (d, J_{PC} 3, C-4) and 195.9 (C-5);

(E)-Isomer **22d** δ_P(109.3 MHz, $CDCl_3$) −4.0; δ_H(400 MHz, $CDCl_3$) 2.25 (3 H, s, Me), 3.77 (6 H, d, J_{PH} 12.2, POMe), 6.55 (1 H, dd, J_{HH} 16.3, J_{PH} 3.7, 3-H) and 6.68 (1 H, dd, J_{HH} 16.3, J_{PH} 1.0, 4-H); δ_C(100.63 MHz, $CDCl_3$) 31.1 (Me), 53.8 (x2)(d, J_{PC} 7, POMe), 85.5 (d, J_{PC} 297, C-1), 95.7 (d, J_{PC} 52, C-2), 119.47 (d, J_{PC} 7, C-3), 142.0 (d, J_{PC} 3, C-4) and 195.9 (C-5); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 1716 C=O, 1257 P=O, 1039 P–O.

Dimethyl 5-methylfuran-2-ylmethylphosphonate **7d**, from the hydrolysis of **5d**, was isolated as a colourless oil; δ_P(109.3 MHz,

$CDCl_3$) 26.7; δ_H(400 MHz, $CDCl_3$) 2.26 (3 H, d, J_{PH} 2, Me), 3.21 (2 H, d, J_{PH} 20.8, CH_2); δ_C(100.63 MHz, $CDCl_3$) 25.7 (d, J_{PC} 144, CH_2); *m/z* (ESI) 227.0424 (M + Na^+. $C_8H_{13}O_4PNa$ requires 227.0449).[21]

Tetramethyl 5-methylfuran-2-ylmethane-1,1-bisphosphonate **6d** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 19.0; δ_H(400 MHz, $CDCl_3$) 4.04 (1 H, t, J_{PH} 25.2, α-CH); δ_C(100.63 MHz, $CDCl_3$) 37.7 (t, J_{PC} 136, α-CH); *m/z* (ESI) 335.0427 (M + Na^+. $C_{10}H_{18}O_7P_2Na$ requires 335.0425).[21]

Reaction of dimethyl 5-phenylfuran-2-carbonylphosphonate 1e with trimethyl phosphite

To a solution of 5-phenylfuran-2-carbonyl chloride (0.5 g, 2.4 mmol) in dry toluene (30 cm^3), cooled to −78 °C under an atmosphere of dry nitrogen, was added trimethyl phosphite (1.0 g, 8 mmol). The mixture was then allowed to warm to room temperature and the progress of the reaction monitored by ^{31}P NMR spectroscopy. This showed the initial formation of the aroylphosphonate **1e** [δ_P ($CDCl_3$–PhMe) 0.4 ppm] which then reacted further. When the reaction was complete (*ca.* 12 h) volatile components were removed under reduced pressure (40 °C at 0.005 mmHg) and the residue analysed by NMR spectroscopy. This showed the aroylphosphonate **1e** had been converted into the ylidic phosphonate **5e** [δ_P ($CDCl_3$–PhMe) 53.9 (d, J_{PP} 84) and 27.9 (d, J_{PP} 84)] (*ca.* 60%), some of which had decomposed to give the bisphosphonate **6e** [δ_P 19.0 ppm] (*ca.* 40%). Decomposition the remaining ylide **5e** resulted in the formation of more bisphosphonate **6e** together with a limited quantity of the monophosphonate **7e**. Samples of these hydrolysis products were isolated by column chromatography on silica gel using petroleum ether (bp 40–60 °C)–ethyl acetate mixtures as the eluent.

Dimethyl 5-phenylfuran-2-ylmethylphosphonate **7e** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 26.1; δ_H(400 MHz, $CDCl_3$) 3.33 (2 H, d, J_{PH} 21, CH_2); δ_C(100.63 MHz, $CDCl_3$) 26.1 (d, J_{PC} 144, CH_2); *m/z* (ESI) 267 (M + H^+. $C_{13}H_{16}O_4P$ requires 267).[21]

Tetramethyl 5-phenylfuran-2-ylmethane-1,1-bisphosphonate **6e** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 18.8; δ_H(400 MHz, $CDCl_3$) 4.16 (1 H, t, J_{PH} 25.5, α-CH); δ_C(100.63 MHz, $CDCl_3$) 38.9 (t, J_{PC} 136, α-CH); *m/z* (ESI) 397.0564 (M + Na^+. $C_{15}H_{20}O_7P_2Na$ requires 397.0582).[21]

Reaction of dimethyl 1-methylpyrrole-2-carbonylphosphonate 1f with trimethyl phosphite

A solution of trimethyl phosphite (0.57 g, 4.6 mmol) and the phosphonate **1f** (0.5 g, 2.3 mmol) in dry toluene (20 cm^3) was heated at 60 °C for 48 h under an atmosphere of dry nitrogen. Volatile components were then removed *in vacuo* (50 °C at 0.005 mmHg) to give a residue that was shown by NMR spectroscopy to contain the ylidic phosphonate **5f** [δ_P 52.6 (d, J_{PP} 116) and 30.1 (d, J_{PP} 116)] together with one of its decomposition products, the bisphosphonate **6f**. The ylidic phosphonate was decomposed by the addition of water and samples of the resulting products isolated by column chromatography on silica gel using ethyl acetate–methanol mixtures as the eluent.

Dimethyl 1-methylpyrrol-2-ylmethylphosphonate **7f** (0.15 g), generated after the addition of the water, was isolated as a colourless oil; δ_P(109.3 MHz, $CDCl_3$) 27.4; δ_H(400 MHz, $CDCl_3$) 3.12 (2 H, d, J_{PH} 20, CH_2); δ_C(100.63 MHz, $CDCl_3$) 24.1 (d, J_{PC} 144, CH_2); *m/z* (ESI) 204.0779 (M + H^+. $C_8H_{15}NO_3P$ requires 204.0789).[21]

Tetramethyl 1-methylpyrrol-2-ylmethane-1,1-bisphosphonate **6f** (0.22 g) was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 20.0; δ_H(270 MHz, $CDCl_3$) 3.72 (1 H, br t, J_{PH} 25, α-CH); δ_C(100.63 MHz, $CDCl_3$) 36.1 (t, J_{PC} 133, α-CH); *m/z* (ESI) 334.0579 (M + Na^+. $C_{10}H_{19}NO_6P_2Na$ requires 334.0585).[21]

Reaction of dimethyl 1-phenylpyrrole-2-carbonylphosphonate 1g with trimethyl phosphite

A solution of trimethyl phosphite (1.90 g, 15 mmol) and the phosphonate **1g** (2.22 g, 7.95 mmol) in dry toluene (10 cm^3) was heated at 100 °C for 6 h under an atmosphere of dry nitrogen. ^{31}P NMR spectroscopy showed that *ca.* 50% of the starting materials had reacted and that the reaction had proceeded cleanly to give the ylidic phosphonate **5g** [δ_P 51.8 (d, J_{PP} 109) and 28.5 ppm (d, J_{PP} 109)] and some of its hydrolysis product **6g** [δ_P 20.1]. The mixture was subjected to column chromatography on silica gel using ethyl acetate–methanol mixtures as the eluent.

The unreacted dimethyl 1-phenylpyrrole-2-carbonylphosphonate **1g** was isolated as a pale yellow oil.

Tetramethyl 1-phenylpyrrol-2-ylmethane-1,1-bisphosphonate **6g** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 20.1; δ_H(400 MHz, $CDCl_3$) 3.87 (1 H, t, J_{PH} 25.7, α-CH); δ_C(100.63 MHz, $CDCl_3$) 35.9 (t, J_{PC} 139, α-CH); *m/z* (ESI) 396.0735 (M + Na^+. $C_{15}H_{21}NO_6P_2Na$ requires 396.0741).[21]

Reaction of dimethyl thiophene-3-carbonylphosphonate 2a with trimethyl phosphite

Trimethyl phosphite (2.34 g, 19.0 mmol) was added dropwise to phosphonate **2a** (2 g, 9 mmol) at room temperature with stirring. The mixture was then heated at 100 °C under an atmosphere of dry nitrogen and the progress of the reaction monitored by ^{31}P NMR spectroscopy. This showed the initial formation of the ylidic phosphonate **14a** [δ_P 55.5 and 30.0 ppm (d, J_{PP} 90)] together with small quantity of the phosphate-phosphonate **18a**. After 12 h, the reaction was complete and the ylide had largely decomposed (>90%) to give either the rearrangement product **15a** (75%) or the hydrolysis product **16a** (15%). Decomposition of the remaining ylide by the addition of water led to the formation of both the bisphosphonate **16a** and the monophosphonate **17a**. Samples of the major reaction products were isolated by chromatography on silica gel using ethyl acetate–methanol mixtures as the eluent.

Dimethyl thiophen-3-ylmethylphosphonate **17a** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 28.8; δ_H(400 MHz, $CDCl_3$) 3.22 (2 H, d, J_{PH} 20.9, CH_2); δ_C(100.63 MHz, $CDCl_3$) 27.3 (d, J_{PC} 141, α-CH_2); *m/z* (ESI) 229.0059 (M + Na^+. $C_7H_{11}O_3PSNa$ requires 229.0064).[21]

Dimethyl 1-(dimethoxyphosphoryloxy)-1-(thiophen-3-yl)methylphosphonate **18a** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 2.0 (d, J_{PP} 32), 19.2 (d, J_{PP} 32); δ_H(400 MHz, $CDCl_3$) 5.72 (1 H, dd, J_{PH} 10 and 13, α-CH); δ_C(100.63 MHz, $CDCl_3$) 70.4 (dd, J_{PC} 176 and 7, α-CH); *m/z* (ESI) 352.9981 (M + Na^+. $C_9H_{16}O_7P_2SNa$ requires 352.9989).[21]

Tetramethyl thiophen-3-ylmethane-1,1-bisphosphonate **16a** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 20.8; δ_H(400 MHz, $CDCl_3$) 4.02 (1 H, t, J_{PH} 24.7, α-CH); δ_C(100.63 MHz,

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$CDCl_3$) 40.1 (t, J_{PC} 134, α-CH); *m/z* (EI) 314.0143 (M^+. $C_9H_{16}O_6P_2S$ requires 314.0143).[21]

Tetramethyl 1-(thiophen-3-yl)ethane-1,1-bisphosphonate **15a** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 24.7; δ_H(270 MHz, $CDCl_3$) 1.86 (3 H, t, J_{PH} 16, Me); δ_C(67.9 MHz, $CDCl_3$) 18.0 (t, J_{PC} 6, Me), 44.3 (t, J_{PC} 140, α-C); *m/z* (EI) 328.0299 (M^+. $C_{10}H_{18}O_6P_2S$ requires 328.0299).[21]

Reaction of dimethyl furan-3-carbonylphosphonate 2b with trimethyl phosphite

A solution of trimethyl phosphite (2.38 g, 19 mmol) and the phosphonate **2b** (1.90 g, 9.3 mmol) in dry toluene (30 cm^3) was heated at 100 °C for 12 h under an atmosphere of dry nitrogen. Volatile components were then removed *in vacuo* (50 °C at 0.005 mmHg). ^{31}P NMR spectroscopy showed the major products to be the ylidic phosphonate **14b** [δ_P($CDCl_3$) 53.6 ppm (d, J_{PP} 92) and 31.8 ppm (d, J_{PP} 92)] (*ca.* 45%) and its decomposition products **15b** (*ca.* 12%) and **16b** (*ca.* 22%). A small quantity of the phosphate-phosphonate **18b** (*ca.* 10%) had also been formed. After decomposing the ylide **14b** by the addition of water, the reaction products were isolated by column chromatography on silica gel using ethyl acetate–methanol mixtures as the eluent.

Dimethyl 1-(dimethoxyphosphoryloxy)-1-(furan-3-yl)methylphosphonate **18b** was isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 1.7 (d, J_{PP} 33) and 19.3 (d, J_{PP} 33); δ_H(400 MHz, $CDCl_3$) 5.62 (1 H, dd, J_{PH} 13 and 10, α-CH); δ_C(100.63 MHz, $CDCl_3$) 67.0 (dd, J_{PC} 180 and 6, α-CH); *m/z* (ESI) 337.0217 (M + Na^+. $C_9H_{16}O_8P_2Na$ requires 337.0218).[21]

Tetramethyl furan-3-ylmethane-1,1-bisphosphonate **16b** was isolated as a viscous pale yellow oil (found: C, 36.5; H, 5.4%. $C_9H_{16}O_7P_2$ requires C, 36.25; H, 5.41%); δ_P(109.3 MHz, $CDCl_3$) 21.2; δ_H(400 MHz, $CDCl_3$) 3.77 (1 H, t, J_{PH} ~24,[23] α-CH); δ_C(100.63 MHz, $CDCl_3$) 34.9 (t, J_{PC} 136, α-CH); *m/z* (ESI) 321.0263 (M + Na^+. $C_9H_{16}O_7P_2Na$ requires 321.0269).[21]

Tetramethyl 1-(furan-3-yl)ethane-1,1-bisphosphonate **15b** was isolated as a viscous pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 24.6; δ_H(270 MHz, $CDCl_3$) 1.73 (3 H, t, J_{PH} 16, Me); δ_C(69.7 MHz, $CDCl_3$) 16.2 (t, J_{PC} 6, Me), 39.4 (t, J_{PC} 136, α-C); *m/z* (EI) 312 (M^+. $C_{10}H_{18}O_7P_2$ requires 312).[21]

Reaction of dimethyl 2-(prop-2-ynyloxymethyl)furan-3-carbonylphosphonate 2c with trimethyl phosphite

To a solution of the phosphonate **2c** (3.0 g, 11 mmol) in dry toluene (30 cm^3) was added trimethyl phosphite (2.72 g, 22 mmol) and the mixture heated at 100 °C for 12 h under an atmosphere of dry nitrogen. Volatile components were then removed under reduced pressure (40 °C at 0.005 mmHg) and the residue analysed by ^{31}P NMR spectroscopy. This showed the formation of the ylidic phosphonate **14c** [δ_P($CDCl_3$) 52.1 ppm (d, J_{PP} 98) and 30.6 ppm (d, J_{PP} 98)] together with some of its hydrolysis product **16c**. A small quantity of the phosphate-phosphonate **18c** [δ_P($CDCl_3$) 19.3 ppm (d, J_{PP} 34) and 1.9 ppm (d, J_{PP} 34)] had also been formed. Column chromatography on silica gel using ethyl acetate–methanol mixtures as the eluent enabled a sample of *tetramethyl 2-(prop-2-ynyloxymethyl)furan-3-ylmethane-1,1-bisphosphonate* **16c** to be isolated as a pale yellow oil; δ_P(109.3 MHz, $CDCl_3$) 21.2; δ_H(400 MHz, $CDCl_3$) 3.97 (1 H, t, J_{PH} 24.6, α-CH); δ_C(100.63 MHz, $CDCl_3$) 34.9 (t, J_{PC} 136, α-CH); ν_{max}(CH_2Cl_2)/cm^{-1} 2957 cm^{-1} C≡C–H, 2853 cm^{-1} CH_2OCH_2, 1254 cm^{-1} P=O, 1031 cm^{-1} P–O; *m/z* (ESI) 389.0531 (M + Na^+. $C_{13}H_{20}O_8P_2Na$ requires 389.0531).[21]

X-Ray crystallography

Further details are provided within the ESI.† CCDC reference numbers 648419. For crystallographic data in CIF or other electronic format, see DOI: 10.1039/b717130g

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