Reactions of Ylides formed from Trialkyl Phosphites with Dialkyl Acetylenedicarboxylates in the Presence of Carbon Dioxide

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The ylides (**2**) $\rightleftharpoons$ (**3**) formed from trialkyl phosphites and dialkyl acetylenedicarboxylates in the presence of carbon dioxide react with proton donors, such as phenol or diethylamine, to give stabilised ylides (**4**). With water, proton transfer within the stabilised ylide results in the formation of a quasiphosphonium salt (**6**) which can then cyclise to a 1,2-oxaphospholane (**7**) or dealkylate to give phosphonates (**5**). In some cases, hydrolysis of the ylide (**2**) $\rightleftharpoons$ (**3**) occurs to give phosphate and an acid (**9**). The formation of a furan (**12**) during the reaction of the ylide (**2**) $\rightleftharpoons$ (**3**) with 4-nitrobenzaldehyde has been investigated.

We have previously shown[1] by NMR spectroscopy and ^{13}C-labelling studies that trialkyl phosphites and dialkyl arylphosphonites react with acetylenedicarboxylic esters in the presence of carbon dioxide to form ylides (**3**) *via* the 2,5-dihydro-1,2-oxaphospholes (**1**). We have also shown that these ylides react with alcohols (ROH) to give the stabilized ylides (**4**; Z = OR) This could not be readily explained in terms of the ylide structure (**3**) and to explain the formation of the stabilised ylides (**4**; Z = OR) it was necessary to propose that the ylides (**3**) were in equilibrium with their precursors, the ketene ylides (**2**), and that the reaction of the alcohol proceeded *via* these ketene ylides.

We now report our studies of the reactions of several ylides (**2a–d**) $\rightleftharpoons$ (**3a–d**) with a number of other reagents and in most cases these also appear to proceed *via* the ketene ylide (**2**) rather than the ylide (**3**). Thus, for example, the addition of phenol to the trimethoxyphosphonium-ylide (**2a**) $\rightleftharpoons$ (**3a**) resulted in the formation of the stabilised ylide (**4a**; Z = OPh) despite the increased acidity of the phenol relative to the alcohols previously studied. In the presence of an excess of phenol, protonation and dealkylation of the stabilised ylide (**4a**; Z = OPh) does occur to give the corresponding phosphonate (**5a**; Z = OPh), but this reaction is rather slow. Even when a ten-fold excess of the phenol was present in the reaction mixture, the conversion of the stabilised ylide (**4a**; Z = OPh) into the phosphonate (**5a**; Z = OPh) took several hours. In contrast, the reaction of the stabilised ylide (**4a**; Z = OPh) with hydrogen chloride gas was immediate and led to the formation of the phosphonate (**5a**; Z = OPh) in essentially quantitative yield.

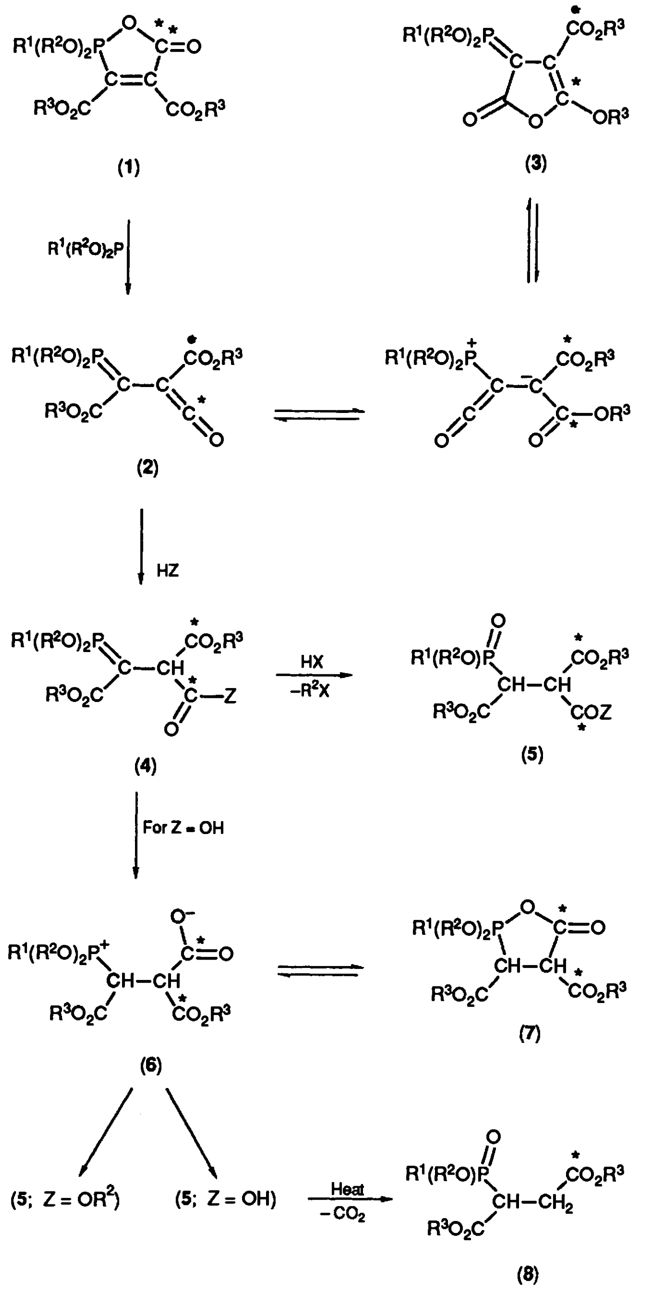
Interestingly, amines such as diethylamine were also found to undergo reaction with the ylides (**2**) $\rightleftharpoons$ (**3**) *via* the ketene ylide (**2**) to give amides. Thus the reaction of the trimethoxyphosphonium ylide (**2b**) $\rightleftharpoons$ (**3b**) with diethylamine led to the stabilised ylide (**4b**; Z = NEt_2). This was converted into the corresponding phosphonate (**5b**; Z = NEt_2) by the action of hydrogen chloride gas.

In contrast, the products formed on addition of water to the ylides (**2**) $\rightleftharpoons$ (**3**) depend on the ylide, the solvent used, and the quantity of water added. Thus, for example, the addition of 1 mol equiv. of water to the triethoxyphosphonium ylide (**2c**) $\rightleftharpoons$ (**3c**) in toluene resulted in the formation of the 1,2-oxaphospholane (**7c**) in essentially quantitative yield. This material was stable in solution in the absence of an excess of water, but it readily decomposed when additional water was added, or on exposure to anhydrous hydrogen bromide. In the latter case, the reaction proceeded very rapidly to give a mixture of the two diastereoisomers of the carboxylic acid (**5c**; Z = OH) as the major products. Confirmation that the carboxylic acid group was located on the β-carbon in the phosphonate (**5c**; Z = OH) was obtained by heating this material at 90 °C. This led to decarboxylation and the formation of the phosphonate (**8c**).

The phosphonates (**5c**; Z = OH) were also produced when a solution of the ylide (**2c**) $\rightleftharpoons$ (**3c**) in toluene was added slowly to a large excess of water. The large excess of water was found to be necessary to ensure that intramolecular dealkylation of the quasiphosphonium intermediate (**6c**) to give the phosphonates (**5c**; Z = OEt) was minimised.

The formation of the 1,2-oxaphospholane (**7c**) and the phosphonate (**5c**; Z = OH) can be rationalised as proceeding *via* a similar route to that previously proposed for the formation of the stabilised ylides (**5**; Z = OR)[1] and this has been supported by a ^{13}C-labelling study using the ylide [5-^{13}C, 4-^{13}C=O]-(**2c**) $\rightleftharpoons$ (**3c**). The sites of ^{13}C labelling are indicated (*) on the proposed reaction pathway shown in Scheme 1. Addition of water to the ketene ylide (**2c**) initially produces an ylide (**4c**; Z = OH) which contains a carboxylic acid group. Proton transfer therefore rapidly occurs to give the quasiphosphonium intermediate (**6c**) which can then either cyclise to give the 1,2-oxaphospholane (**7c**) or dealkylate to the phosphonate (**5c**; Z = OH). Intramolecular dealkylation of the intermediate (**6c**) results in the formation of the phosphonate (**5c**; Z = OEt).

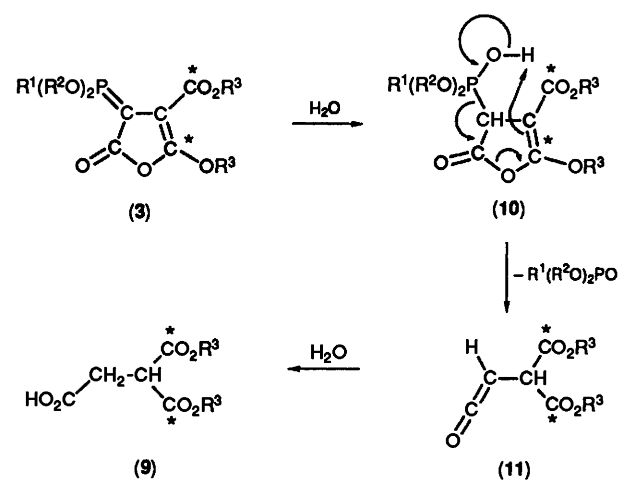
In contrast, the reaction of the ylide (**2a**) $\rightleftharpoons$ (**3a**) with an excess of water was found to follow a quite different route. Thus, addition of a solution of this ylide in toluene to an excess of water led to the formation of trimethyl phosphate and the carboxylic acid (**9a**). The formation of this latter material can only be satisfactorily explained by proposing that, in this particular case, the reaction proceeds *via* the major ylide component (**3a**) rather than the ketene ylide component (**2a**). For this to occur we must assume that the rate of attack on the ylide group in (**3a**) is fast relative to the rate of its interconversion to the ketene ylide (**2a**). This increased rate of attack by water at the trimethoxyphosphonium centre relative to that observed for the triethoxyphosphonium centre in (**3c**) can be explained by the reduction in steric hindrance around the phosphorus atom in the former case and its increased hydrophilicity. In the route proposed in Scheme 2, the addition of water across the ylide (**3a**) leads to the initial formation of



	R^1	R^2	R^3
a	MeO	Me	Et
b	MeO	Me	Me
c	EtO	Et	Et
d	Ph	Me	Me

Scheme 1.

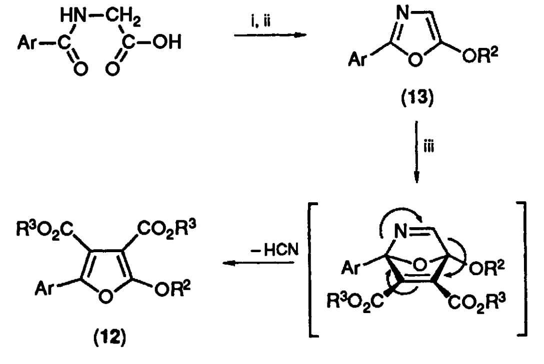
the phosphorane (**10a**). This then cleaves to give trimethyl phosphate and the ketene (**11a**), which then undergoes further reaction with water to give the carboxylic acid (**9a**). Support for this proposed route was provided by a labelling study involving the ^{13}C-labelled ylide [5-^{13}C, 4-^{13}C=O]-(**2a**) $\rightleftharpoons$ (**3a**) which confirmed that the two ester carbonyls in (**9**) were both isotopically labelled (*). We must therefore conclude that in the case of the ylide (**2a**) $\rightleftharpoons$ (**3a**), with an excess of water, the reaction proceeds *via* the major but usually less reactive ylide component (**3a**).



Scheme 2.

Under less vigorous conditions, the reaction of the ylide (**2a**) $\rightleftharpoons$ (**3a**) with water is more analogous to that of the corresponding ethoxy ylide (**2c**) $\rightleftharpoons$ (**3c**). Thus, for example, the slow addition of a 1 mol equiv. of water to a solution of the ylide (**2a**) $\rightleftharpoons$ (**3a**) in toluene led to the initial formation of the 1,2-oxaphospholane (**7a**). However, in this case the 1,2-oxaphospholane was less stable than the corresponding ethoxy system (**7c**) and considerable decomposition was observed resulting in phosphonate formation. If the addition of the water to the ylide (**2a**) $\rightleftharpoons$ (**3a**) is sufficiently slow, the final product from the reaction is the phosphonate (**5a**; Z = OMe) since intramolecular dealkylation of the intermediate (**6a**) is encouraged.

We have also investigated whether the ylides (**2**) $\rightleftharpoons$ (**3**) would undergo reaction with 4-nitrobenzaldehyde in a Wittig reaction.[2] Such a reaction would be expected to lead to the formation of trimethyl phosphate and an alkene. However, when a mixture of the ylide (**2a**) $\rightleftharpoons$ (**3a**) and 4-nitrobenzaldehyde was heated in a solvent such as chloroform or toluene, ^{31}P NMR spectroscopy indicated the formation of trimethyl phosphite and a phosphonate, rather than trimethyl phosphate. Furthermore, when the reaction was allowed to cool, a product was precipitated and this was identified as the furan (**12a**). The structure of this furan has been confirmed by the independent synthesis shown in Scheme 3. This approach, which is based on the addition of a dialkyl acetylenedicarboxylate to the appropriate oxazole (**13**), has been previously used for the preparation of a number of analogous systems.[3]

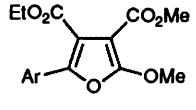


Ar = p-$NO_2C_6H_4$

Scheme 3. *Reagents:* i, R^2OH/H^+; ii, $PCl_5/CHCl_3$; iii, $R^3O_2C-C{\equiv}C-CO_2R^3$.

By varying the ester groups on the phosphite and on the acetylenedicarboxylate during the preparation of the ylide (**2**) $\rightleftharpoons$ (**3**) it was possible to produce a range of the furans (**12**). These showed that the R^2 group at C-2 of the furan was derived from the phosphite while the R^3 groups in the esters at C-3 and C-4 were derived from the acetylenic ester. Similar behaviour, leading to furan formation, was also observed in the reaction of 4-nitrobenzaldehyde with the dimethoxyphenylphosphonium ylide (**2d**) $\rightleftharpoons$ (**3d**) from dimethyl phenylphosphonite.

We have also shown that the reaction of the ^{13}C-labelled ylide [5-^{13}C, 4-^{13}C=O]-(**2a**) $\rightleftharpoons$ (**3a**)[1] with 4-nitrobenzaldehyde gives the labelled furan [2-^{13}C, 3-^{13}C=O]-(**12a**). It is interesting to note here that while the ^{13}C enriched carbon at C-5 in the ylide [5-^{13}C, 4-^{13}C=O]-(**2a**) $\rightleftharpoons$ (**3a**) is attached to an ethoxy group, the same ^{13}C labelled carbon has become attached to a methoxy group in the furan [2-^{13}C, 3-^{13}C=O]-(**12a**). Furthermore, the ethoxy group originally attached to C-5 in the ylide appears to migrate to the ester group at C-4 in the furan [2-^{13}C, 3-^{13}C=O]-(**12a**). To determine whether this migration of the ethoxy group occurs in an inter- or intramolecular manner, a mixture of the two ylides (**2a**) $\rightleftharpoons$ (**3a**) and (**2b**) $\rightleftharpoons$ (**3b**) was prepared and allowed to react with 4-nitrobenzaldehyde. The mixture of furans produced was then analysed by ^{13}C NMR spectroscopy, which suggested that only the furans (**12a**) and (**12b**) had been produced. This was confirmed by mass spectroscopy since only molecular ions corresponding to the furans (**12a**) (M^+ 363) and (**12b**) (M^+ 335) were observed from the mixture. There was no sign of any molecular ion at 349 arising from mixed ester products such as (**14**) and (**15**) which would have resulted from an intermolecular transfer of the alkoxy groups from C-5 in the mixture of the ylides (**2a**) $\rightleftharpoons$ (**3a**) and (**2b**) $\rightleftharpoons$ (**3b**).



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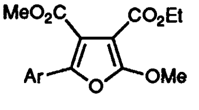
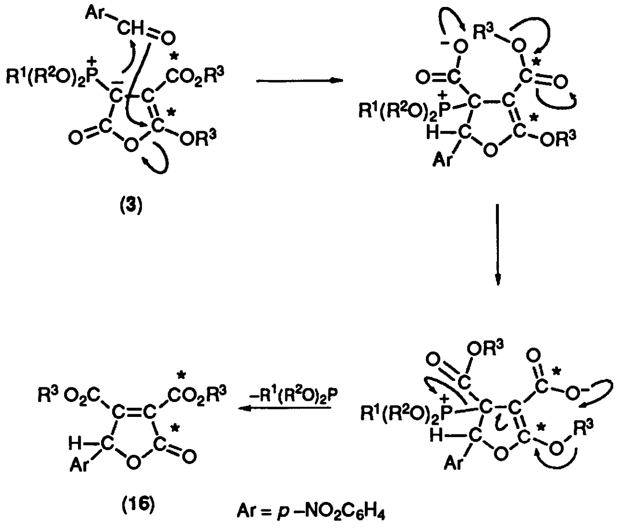


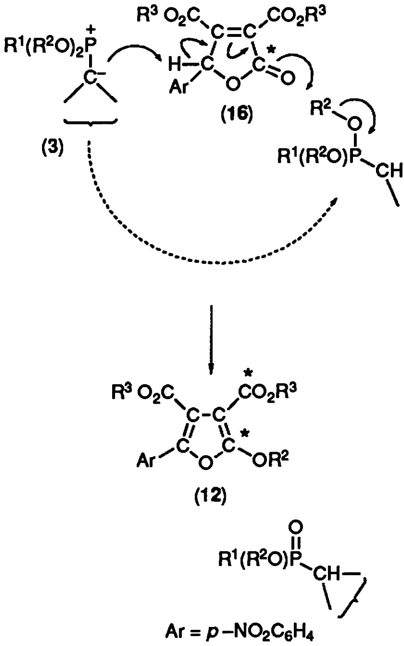
(15)

Ar = p-$NO_2C_6H_4$

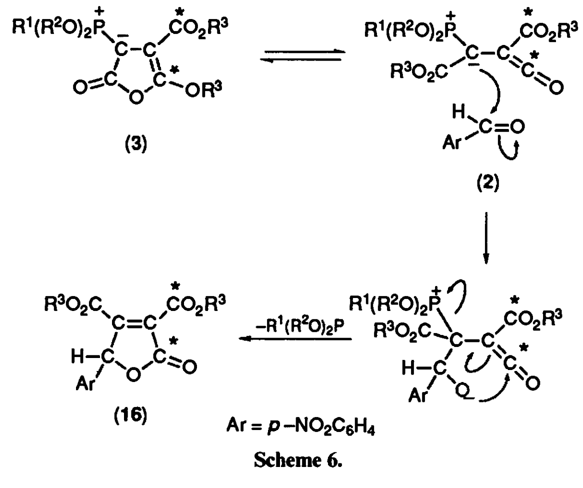
If the reaction of the ylide (**2**) $\rightleftharpoons$ (**3**) with 4-nitrobenzaldehyde to give the furan (**12**) occurs *via* (**3**) rather than (**2**), it is necessary to propose the mechanism indicated in Scheme 4. The initial reaction of the ylide with the 4-nitrobenzaldehyde leads to the dihydrofuranone (**16**) and it is probably the stability of this system which provides the driving force for the unexpected expulsion of the trivalent phosphorus component during the reaction. However, despite the stability of the dihydrofuranone (**16**), it does react further in the presence of the ylide (**2**) $\rightleftharpoons$ (**3**), undergoing deprotonation and subsequent alkylation to give the furan (**12**) (Scheme 5). This explains the formation of a phosphonate during the reaction and also the observation that the R^2 group at C-2 in the furan (**12**) is derived from the trivalent phosphorus component used to prepare the ylide (**2**) $\rightleftharpoons$ (**3**). The proposed reaction pathway also accounts for the intramolecular transfer of the R^3 group during the reaction and the observed ^{13}C labelling pattern (*) in the resulting furan. Despite this, however, Scheme 4 is not entirely satisfactory since it involves a two-stage intramolecular transfer of the ethoxy group *via* disfavoured six-[4] and seven-membered transition states. The need for such a step can be avoided, however, if the reaction of the ylide with 4-nitrobenzaldehyde is assumed to proceed *via* the ketene ylide (**2**) rather than the major ylide component (**3**). In these circumstances, the formation of the dihydrofuranone (**16**) is much more satisfactorily explained (Scheme 6). Moreover, this would be in line with our observations that the reactions of the ylides (**2**) $\rightleftharpoons$ (**3**) usually proceed *via* the



Scheme 4.



Scheme 5.



Scheme 6.

more reactive ketene ylide component (**2**). In view of the ease with which the furans (**12**) can be prepared from the ylides (**2**) $\rightleftharpoons$ (**3**), further studies in this area are in progress to assess the synthetic potential of this route for the synthesis of substituted furans.

Experimental

NMR spectra were obtained on JEOL FX100 and GSX270 spectrometers.

Dimethyl 1,2-*Bis*(*ethoxycarbonyl*)-2-(*phenoxycarbonyl*)*ethylphosphonate* (**5a**; Z = OPh).—A solution of trimethyl phosphite (0.5 g) in dry toluene (5 cm^3) was added dropwise to a solution of diethyl acetylenedicarboxylate (0.34 g) in dry toluene (10 cm^3) through which dry carbon dioxide was vigorously bubbled. Phenol (0.19 g, 1 mol equiv.) was added to the reaction mixture and after several minutes ^{31}P NMR spectroscopy indicated the formation of the stabilised ylide (**4a**; Z = OPh) in essentially quantitative yield [δ_P(toluene) 61.3 (major rotamer 65%), 59.3 (minor rotamer 35%)]. When the reaction was complete, hydrogen chloride gas was bubbled through the reaction mixture until the yellow colour of the solution had been discharged. Volatile components were then removed under reduced pressure (50 °C at 0.005 mmHg) to give an oil which was shown by NMR spectroscopy to be the phosphonate (**5a**; Z = OPh) as a mixture of its two diastereoisomers (Found: C, 50.65; H, 5.8; $C_{17}H_{23}O_9P$ requires C, 50.75; H, 5.76%); δ_P(toluene) 22.1 (44%) and 22.3 (56%); δ_P($CDCl_3$) 22.0, 22.1; δ_C($CDCl_3$) (major diastereoisomer) 13.3 (Me), 13.4 (Me), 44.1 (d, J_{PC} 131 Hz, α-CH), 50.2 (d, J_{PC} 4 Hz, β-CH), 53.2 (d, J_{PC} 7 Hz, POMe) (× 2), 61.6 (CH_2), 61.9 (CH_2), 120.7 (C-2, C-6), 125.7 (C-4), 128.9 (C-3, C-5), 150.0 (C-1), 164.9 (d, J_{PC} 3 Hz, CO_2Ph), 166.2 (d, J_{PC} 19 Hz, β-CO_2Et), and 166.6 (d, J_{PC} 5 Hz, α-CO_2Et); (minor diastereoisomer) 13.3 (Me), 13.4 (Me), 44.1 (d, J_{PC} 130 Hz, α-CH), 50.2 (d, J_{PC} 4 Hz, β-CH), 53.1 (d, J_{PC} 7 Hz, POMe), 53.2 (d, J_{PC} 7 Hz, POMe), 61.6 (CH_2), 62.0 (CH_2), 120.5 (C-2, C-6), 125.8 (C-4), 129.0 (C-3, C-5), 149.9 (C-1), 165.5 (d, J_{PC} 19 Hz, CO_2Ph), 165.8 (d, J_{PC} 3 Hz, β-CO_2Et), and 166.5 (d, J_{PC} 5 Hz, α-CO_2Et).

Dimethyl 1,2-*Bis*(*methoxycarbonyl*)-2-(N,N-*diethylcarbamoyl*)*ethylphosphonate* (**5b**; Z = NEt_2).—A solution of trimethyl phosphite (0.52 g) in dry toluene (5 cm^3) was added dropwise to a solution of dimethyl acetylenedicarboxylate (0.28 g) in dry toluene (10 cm^3) through which dry carbon dioxide was vigorously bubbled. Dry diethylamine (0.14 g, 1 mol equiv.) was then added and the reaction monitored by ^{31}P NMR spectroscopy. This showed that the reaction proceeded to give the stabilised ylide (**4b**; Z = NEt_2) in essentially quantitative yield [δ_P(toluene) 6.15 (major rotamer 80%), 59.4 (minor rotamer 20%)]. Volatile components were removed under reduced pressure (50 °C at 14 mmHg) and the resulting yellow oil taken up in dry toluene (5 cm^3). Hydrogen chloride gas was then bubbled through the solution until the colour had been discharged and volatile components were then removed under reduced pressure (50 °C at 0.005 mmHg). The residue, an oil, was shown to be the phosphonate (**5b**; Z = NEt_2), as a mixture of two diastereoisomers [δ_P(toluene) 22.9 (66%), 23.8 (33%)] in essentially quantitative yield. An analytically pure sample of the phosphonate (**5b**; Z = NEt_2) was obtained by chromatography on silica using light petroleum–ethyl acetate (50:50) as eluant (Found: C, 44.05; H, 7.05; N, 3.85. $C_{13}H_{24}NO_8P$ requires C, 44.19; H, 5.85; N, 3.96%); δ_P($CDCl_3$) 23.1 and 23.9; δ_C($CDCl_3$) (major diastereoisomer) 12.4 (Me), 13.7 (Me), 41.1 (CH_2), 42.6 (CH_2), 44.6 (d, J_{PC} 128 Hz, α-CH), 46.7 (β-CH), 52.9 (OMe, × 2), 53.3 (d, J_{PC} 7 Hz, POMe), 53.4 (d, J_{PC} 7 Hz, POMe), 164.7 (d, J_{PC} 1.5 Hz $CONEt_2$), 168.3 (d, J_{PC} 21 Hz, β-CO_2Me), and 168.6 (d, J_{PC} 6 Hz, α-CO_2Me); (minor diastereoisomer) 12.5 (Me), 13.6 (Me), 41.2 (CH_2), 42.4 (CH_2), 45.2 (d, J_{PC} 129 Hz, α-CH), 47.7 (β-CH), 52.8 (OMe), 52.9 (OMe), 53.4 (d, J_{PC} 7 Hz, POMe), 53.5 (d, J_{PC} 7 Hz, POMe), 164.9 (d, J_{PC} 17 Hz, $CONEt_2$), 167.7 (d, J_{PC} 1.5 Hz, β-CO_2Me), and 168.0 (d, J_{PC} 5 Hz, α-CO_2Me).

(2,3-*Dihydro*-5-*ethoxy*-4-*ethoxycarbonyl*-2-*oxofuran*-3-*ylidene*)*triethoxyphosphorane* (**3c**).—The ylide (**3c**) was prepared by the route previously reported for the preparation of the ylide (**3b**);[1] δ_P($CDCl_3$) 41.2; δ_C($CDCl_3$) 14.0, 14.6, 15.5 (d, J_{PC} 7 Hz), 49.2 (d, J_{PC} 248 Hz), 59.1, 65.4 (d, J_{PC} 6 Hz), 66.7, 87.0 (d, J_{PC} 15 Hz), 153.6 (d, J_{PC} 21 Hz), 162.7, and 164.2 (d, J_{PC} 25 Hz).

2,2,2-*Triethoxy*-3,4-*bis*(*ethoxycarbonyl*)-1,2-*oxaphospholan*-5-*one* (**7c**).—To a solution containing the ylide (**3c**) (0.36 g) in toluene (4 cm^3), prepared as previously indicated, was added water (not exceeding 1 mol equiv.). ^{31}P NMR spectroscopy indicated the conversion of the ylide (**3c**) into the 1,2-oxaphospholane (**7c**) in essentially quantitative yield. δ_P(toluene) −41.1; δ_P($CDCl_3$) −39.0; δ_C($CDCl_3$) 13.5, 13.6 (d, J_{PC} 1.5 Hz), 13.7, 50.4, 52.7 (d, J_{PC} 160 Hz), 61.2, 61.8, 64.1 (d, J_{PC} 12 Hz), 165.3 (d, J_{PC} 17 Hz), 167.1 (d, J_{PC} 21 Hz), and 168.1 (d, J_{PC} 6 Hz).

Diethyl 1,2-*Bis*(*ethoxycarbonyl*)*ethylphosphonate* (**8c**).—(*a*) A solution containing the ylide (**3c**) (0.36 g) in toluene (4 cm^3), prepared as previously indicated, was added dropwise to water (20 cm^3) with vigorous stirring. ^{31}P NMR spectroscopy indicated the formation of the two diastereoisomers of the phosphonate (**5c**; Z = OH) [δ_P($CDCl_3$) 19.7 and 19.9]. Removal of the volatile components under reduced pressure and subsequent heating under reduced pressure (90 °C at 16 mmHg) led to decarboxylation of the phosphonate (**5c**; Z = OH) to give the phosphonate (**8c**) in high yield. A sample of the phosphonate (**8c**) was isolated by chromatography on silica using light petroleum–ethyl acetate (50:50) as eluant (Found: C, 46.65; H, 7.5. $C_{12}H_{23}O_7P$ requires C, 46.45; H, 7.47%); δ_P($CDCl_3$) 21.8; δ_C($CDCl_3$) 13.9, 14.0, 16.16 (d, J_{PC} 6 Hz), 116.21 (d, J_{PC} 6 Hz), 31.4 (d, J_{PC} 3 Hz), 41.1 (d, J_{PC} 132 Hz), 61.0, 61.6, 62.8 (d, J_{PC} 6.5 Hz), 62.85 (d, J_{PC} 6.5 Hz), 168.1 (d, J_{PC} 6 Hz), and 171.0 (d, J_{PC} 19 Hz).

(*b*) Hydrogen bromide gas was passed into a cooled solution containing the 1,2-oxaphospholane (**7c**) in toluene prepared previously until the yellow colour of the solution had been discharged. Any excess of hydrogen bromide was quickly removed from the solution under reduced pressure and ^{31}P NMR spectroscopy indicated the formation of a mixture of the two diastereoisomers of the phosphonate (**5c**; Z = OH) [δ_P(toluene) 20.4 and 20.5]. The volatile components were removed under reduced pressure and the residue heated (90 °C at 16 mmHg) to bring about the decarboxylation of the phosphonate (**5c**; Z = OH). The identity of the product was confirmed to be the phosphonate (**8c**) by comparing the NMR spectra with those of the sample previously produced and characterised.

[5-^{13}C, 4-^{13}C=O]-2,2,2-*Triethoxy*-3,4-*bis*(*ethoxycarbonyl*)-1,2-*oxaphospholan*-5-*one* [5-^{13}C, 4-^{13}C=O]-(**7c**).—To a solution of [5-^{13}C, 4-^{13}C=O]-(2,3-dihydro-5-ethoxy-4-ethoxycarbonyl-2-oxofuran-3-ylidene-triethoxyphosphorane [5-^{13}C, 4-^{13}C=O]-(**3c**) (0.12 g), prepared by a previously reported method,[1] in deuteriochloroform (1.25 cm^3) was added small quantities of water (*ca.* 2 mg) until NMR spectroscopy indicated that the conversion of the ylide [5-^{13}C, 4-^{13}C=O]-(**3c**) [δ_C($CDCl_3$) 153.7 (d, J_{PC} 21 Hz), 162.8] into the 1,2-oxaphospholane [5-^{13}C, 4-^{13}C=O]-(**7c**) [δ_C($CDCl_3$) 165.5 (d, J_{PC} 17 Hz), 167.3 (d, J_{PC} 21 Hz)] was complete.

Diethyl [2-^{13}C=O]-1,2-*Bis*(*ethoxycarbonyl*)*ethylphosphonate*

[2-^{13}C=O]-(**8c**).—A solution containing the ylide [5-^{13}C, 4-^{13}C=O]-(**3c**) (0.24 g) in toluene (2.5 cm^3), prepared as previously indicated, was added dropwise to water (10 cm^3) with vigorous stirring. ^{13}C NMR spectroscopy indicated the formation of the two diastereoisomers of the phosphonate [2-^{13}C=O, 2-^{13}CO$_2$H]-(**5c**; Z = OH) [δ_C(CDCl$_3$) 167.0 (d, J_{PC} 2 Hz), 167.5 (d, J_{PC} 19 Hz), 167.5 (d, J_{PC} 2 Hz), and 168.0 (d, J_{PC} 19 Hz)]. Removal of the volatile components under reduced pressure and subsequent heating (90 °C at 16 mmHg) led to decarboxylation of the phosphonate [2-^{13}C=O, 2-^{13}CO$_2$H]-(**5c**; Z = OH) to give the phosphonate [2-^{13}C=O]-(**8c**) [δ_C(CDCl$_3$) 170.4 (d, J_{PC} 19 Hz)].

2,2,2-*Trimethoxy*-3,4-*bis*(*ethoxycarbonyl*)-1,2-*oxaphospholan*-5-*one* (**7a**).—To a solution containing the ylide (**3a**)[1] (0.32 g) in toluene (4 cm^3) was added water (9 mg, 0.5 mol. equiv.). ^{31}P NMR spectroscopy indicated the formation of the 1,2-oxaphospholane (**7a**): δ_P(toluene) −38.4; δ_C(CDCl$_3$/toluene) 13.2, 13.3, 50.0 (d, J_{PC} 2 Hz), 52.1 (d, J_{PC} 159 Hz), 55.2 (d, J_{PC} 11 Hz), 60.9, 61.4, 164.3 (d, J_{PC} 19 Hz), 166.5 (d, J_{PC} 18 Hz), and 167.4 (d, J_{PC} 6 Hz).

Dimethyl 1,2-*Bis*(*ethoxycarbonyl*)-2-(*methoxycarbonyl*)*ethylphosphonate* (**5a**; Z = OMe).—To a solution containing the ylide (**3a**)[1] (0.32 g) in toluene (4 cm^3) was added water (18 mg). The mixture was shaken periodically over a period of an hour and then set aside. ^{31}P NMR spectroscopy indicated the eventual formation of the phosphonate (**5a**; Z = OMe). This was confirmed by comparing the ^{13}C NMR data with that from an authentic sample.[1]

3,3-*Bis*(*ethoxycarbonyl*)*propionic Acid* (**9a**).—A solution containing the ylide (**3a**)[1] (0.32 g) in toluene (4 cm^3) was added dropwise to water (20 cm^3) with vigorous stirring. Removal of the volatile components under reduced pressure (60 °C at 16 mmHg) gave an oil which was shown to contain only two major components, trimethyl phosphate and 3,3-bis(ethoxycarbonyl)propionic acid (**9a**). The trimethyl phosphate was removed by warming the mixture under reduced pressure (60 °C at 0.005 mmHg) to give the acid (**9a**); δ_H(CDCl$_3$; 270 MHz) 1.28 (6 H, t, J_{HH} 7 Hz, Me), 2.99 (2 H, d, J_{HH} 7 Hz, CH$_2$), 3.81 (1 H, t, J_{HH} 7 Hz, CH), 4.22 (2 H, q, J_{HH} 7 Hz, OCH$_2$), 4.22 (2 H, q, J_{HH} 7 Hz, OCH$_2$), and 11.57 (1 H, br s, CO$_2$H); δ_C(CDCl$_3$) 13.5 (Me, ×2), 32.5 (CH$_2$), 47.5 (CH), 61.3 (OCH$_2$, ×2), 168.2 (CO$_2$Et, ×2), and 172.8 (CO$_2$H, $^2J_{CH-2}$ 7 Hz, $^3J_{CH-3}$ 3.5 Hz).

[3-^{13}C=O]-3,3-*Bis*(*ethoxycarbonyl*)*propionic acid* (**9a**). A solution of [5-^{13}C, 4-^{13}C=O]-(2,3-dihydro-5-ethoxy-4-ethoxycarbonyl-2-oxofuran-3-ylidene)trimethoxyphosphorane[1] [5-^{13}C, 4-^{13}C=O]-(**3a**) (0.21 g) in toluene (2.5 cm^3) was added dropwise to water (20 cm^3) with vigorous stirring. Removal of the volatile components under reduced pressure (60 °C at 16 mmHg) gave an oil which was shown to contain [3-^{13}C=O]-3,3-bis(ethoxycarbonyl)propionic acid [3-^{13}C=O]-(**9a**); δ_C(CDCl$_3$) 47.7 (d, J_{CC} 58 Hz, C-3) and 168.3 (CO$_2$Et).

Dimethyl 2-*Methoxy*-5-(4-*nitrophenyl*)*furan*-3,4-*dicarboxylate* (**12b**).—(*a*) A mixture of *N*-(4-nitrobenzoyl)glycine (20 g), methanol (120 cm^3), and concentrated sulphuric acid (3 cm^3) was heated under reflux for 2 h and then allowed to cool. The reaction was worked up and the crystalline product recrystallised from methanol to give pure methyl *N*-(4-nitrobenzoyl)glycinate (18.7 g, 88%), m.p. 152–153 °C (lit.,[5] m.p. 148–151 °C) (Found: C, 50.55; H, 4.1; N, 11.8. Calc. for $C_{10}H_{10}N_2O_5$: C, 50.42; H, 4.23; N, 11.76%); δ_C([^{2}H$_6$]-DMSO) 41.3 (CH$_2$), 51.8 (MeO), 123.4 (C-3, C-5, ×2), 128.5 (C-2, C-6, ×2), 138.9 (C-1), 148.9 (C-4), 164.7 (C=O), and 169.7 (C=O).

Methyl *N*-(4-nitrobenzoyl)glycinate (2.5 g) phosphorus pentachloride (2.1 g) and alcohol-free chloroform (25 cm^3) were heated under reflux. After 72 h the resulting solution was cooled and aqueous potassium hydroxide added (20%; 100 cm^3). The mixture was extracted with benzene (4 × 50 cm^3), and the combined extracts were dried (MgSO$_4$), and evaporated under reduced pressure (16 mmHg at 50 °C) to give an orange solid. Recrystallisation of this solid from toluene gave 5-methoxy-2-(4-nitrophenyl)oxazole[6] (**13**; R^2 = Me) (1.7 g, 74%), m.p. 84 °C; *m/z* 200 (M^+) (Found: C, 54.65; H, 3.7; N, 12.7. $C_{10}H_8N_2O_4$ requires C, 54.55; H, 3.66; N, 12.73%); δ_C(CDCl$_3$) 58.8 (MeO), 101.0 (C-4), 124.0 (C-3′, C-5′), 125.6 (C-2′, C-6′), 132.7 (C-1′), 147.7 (C-4′), 150.1 (C-2), and 161.5 (C-5).

A suspension of 5-methoxy-2-(4-nitrophenyl)oxazole (**13**; R^2 = Me) (0.2 g) in dimethyl acetylenedicarboxylate (1.5 g) was heated at 120 °C for 16 h and then allowed to cool. The excess dimethyl acetylenedicarboxylate was removed under reduced pressure (50 °C at 0.005 mmHg) and the resulting solid recrystallised from toluene. The pure dimethyl 2-methoxy-5-(4-nitrophenyl)furan-3,4-dicarboxylate (40 mg, 13%) was isolated as a yellow solid, m.p. 179–181 °C (Found: C, 53.5; H. 3.8; N, 3.95. $C_{15}H_{13}NO_8$ requires C, 53.73; H, 3.91; N, 4.18%).

(*b*) A solution containing (2,3-dihydro-5-methoxy-4-methoxycarbonyl-2-oxofuran-3-ylidene)trimethoxyphosphorane[1] (**3b**) (2.94 g) in dry toluene (25 cm^3) was heated under reflux with 4-nitrobenzaldehyde (0.82 g) for 0.5 h. The precipitate which formed on cooling was washed with cold toluene and then recrystallised from toluene to give the furan (**12b**) (1.13 g, 67%), m.p. 179–181 °C (Found: C, 53.5; H, 3.8; N, 4.1. $C_{15}H_{13}NO_8$ requires C, 53.73; H, 3.91; N, 4.18%).

(*c*) A solution containing (2,3-dihydro-5-methoxy-4-methoxycarbonyl-2-oxofuran-3-ylidene)dimethoxyphenylphosphorane[1] (**3d**) (0.25 g) in dry toluene (1 cm^3) was allowed to stand overnight with 4-nitrobenzaldehyde (60 mg). The precipitate which formed was filtered off and then recrystallised from toluene to give the furan (**12b**) (20 mg, 17%), m.p. 179–181 °C (Found: C, 53.5; H, 3.7; N, 4.2. $C_{15}H_{13}NO_8$ requires C, 53.73; H, 3.91; N, 4.18%). δ_H(CDCl$_3$; 270 MHz) 3.84 (3 H, s, OMe), 3.96 (3 H, s, OMe), 4.26 (3 H, s, 2-MeO), 7.73 (2 H, d, *J* 9 Hz, 2′-H, 6′-H), and 8.25 (2 H, d, *J* 9 Hz, 3′-H, 5′-H); δ_C(CDCl$_3$) 51.9 (OMe), 53.1 (OMe), 58.7 (2-OMe), 93.3 (C-3), 118.7 (C-4), 124.1 (C-3′, C-5′), 125.1 (C-2′, C-6′), 134.0 (C-1′), 138.8 (C-5), 146.7 (C-4′), 161.3 (C-2), 161.5 (C=O), and 164.2 (C=O).

Diethyl 2-*Methoxy*-5-(4-*nitrophenyl*)*furan*-3,4-*dicarboxylate* (**12a**).—(*a*) A suspension of 5-methoxy-2-(4-nitrophenyl)oxazole (**13**; R^2 = Me) (0.2 g) in diethyl acetylenedicarboxylate (2 g) was heated at 110 °C for 30 h after which the excess of diethyl acetylenedicarboxylate was removed under reduced pressure (50 °C at 0.005 mmHg). To the residue was added dry toluene (3 cm^3) and the resulting precipitate filtered off and recrystallised from toluene. The pure diethyl 2-methoxy-5-(4-nitrophenyl)furan-3,4-dicarboxylate (**12a**) (0.03 g, 9%) was isolated as a yellow crystalline solid, m.p. 170–172 °C (Found: C, 56.2; H, 4.8; N, 3.55. $C_{17}H_{17}NO_8$ requires C, 56.2; H, 4.71; N, 3.86%).

(*b*) The furan (**12a**) was also produced in the reaction of (2,3-dihydro-5-ethoxy-4-ethoxycarbonyl-2-oxofuran-3-ylidene)trimethoxyphosphorane[1] with 4-nitrobenzaldehyde using the procedure previously described for the preparation of the furan (**12b**). The product (**12a**) was isolated as a yellow crystalline solid (2.29 g, 79%), m.p. 170–172 °C (sublimes) (Found: C, 56.1; H, 4.8; N, 3.9. $C_{17}H_{17}NO_8$ requires C, 56.2; H, 4.71; N, 3.86%). δ_H(CDCl$_3$; 270 MHz) 1.33 (3 H, t, *J* 7 Hz, Me), 1.38 (3 H, t, *J* 7 Hz, Me), 4.25 (3 H, s, MeO), 4.30 (2 H, q, *J* 7 Hz, CH$_2$), 4.42 (2 H, q, *J* 7 Hz, CH$_2$), 7.74 (2 H, d, *J* 9 Hz, 2′-H, 6′-H), and 8.24 (2 H, d, *J* 9 Hz, 3′-H, 5′-H); δ_C(CDCl$_3$) 14.0 (Me), 14.2 (Me), 58.6 (OMe), 60.5 (CH$_2$), 62.1 (CH$_2$), 93.5 (C-3), 118.8 (C-4), 123.9 (C-3′, C-5′), 124.8 (C-2′, C-6′), 134.1 (C-1′), 138.3 (C-5), 146.4 (C-4′), 160.9 (C=O), 161.2 (C-2), and 163.7 (C=O).

Dimethyl 2-*ethoxy*-5-(4-*nitrophenyl*)*furan*-3,4-*dicarboxylate* (**12**; R^2 = Et, R^3 = Me). This compound was produced by the reaction of (2,3-dihydro-5-methoxy-4-methoxycarbonyl-2-oxofuran-3-ylidene)triethoxyphosphorane[1] with 4-nitrobenzaldehyde using the procedure previously described for the preparation of the furan (**12b**). The product (**12**; R^2 = Et, R^3 = Me) was obtained as a yellow crystalline solid (1.25 g, 54%), m.p. 147–148 °C (Found: C, 55.1; H. 4.2; N, 3.7. $\mathrm{C_{16}H_{15}NO_8}$ requires C, 55.02; H, 4.33; N, 4.01%); δ_H($\mathrm{CDCl_3}$; 270 MHz) 1.54 (3 H, t, *J* 7 Hz, Me), 3.83 (3 H, s, MeO), 3.96 (3 H, s, MeO), 4.61 (2 H, q, *J* 7 Hz, $\mathrm{CH_2}$), 7.72 (2 H, d, *J* 9 Hz, 2′-H, 6′-H), and 8.24 (2 H, d, *J* 9 Hz, 3′-H, 5′-H); δ_C($\mathrm{CDCl_3}$) 14.9 (Me), 51.7 (OMe), 53.0 (OMe), 68.8 ($\mathrm{CH_2}$), 93.8 (C-3), 118.4 (C-4), 123.9 (C-3′, C-5′), 124.9 (C-2′, C-6′), 134.0 (C-1′), 138.6 (C-5), 146.5 (C-4′), 160.9 (C-2), 161.5 (C=O), and 164.2 (C=O).

Diethyl 2-*ethoxy*-5-(4-*nitrophenyl*)*furan*-3,4-*dicarboxylate* (**12c**). This compound was produced by the reaction of (2,3-dihydro-5-ethoxy-4-ethoxycarbonyl-2-oxofuran-3-ylidene)-triethoxyphosphorane with 4-nitrobenzaldehyde using the procedure previously described for the preparation of the furan (**12b**). The product (**12c**) was obtained as a yellow crystalline solid (1.16 g, 46.4%), m.p. 119–119.5 °C (Found: C, 57.0; H, 4.95; N, 3.7. $\mathrm{C_{18}H_{19}NO_8}$ requires C, 57.29; H, 5.08; N, 3.71%); δ_H($\mathrm{CDCl_3}$; 270 MHz) 1.34 (3 H, t, *J* 7 Hz, Me), 1.39 (3 H, t, *J* 7 Hz, Me), 1.55 (3 H, t, *J* 7 Hz, Me), 3.83 (3 H, s, MeO), 4.29 (2 H, q, *J* 7 Hz, $\mathrm{CH_2}$), 4.43 (2 H, q, *J* 7 Hz, $\mathrm{CH_2}$), 4.61 (2 H, q, *J* J Hz, $\mathrm{CH_2}$), 7.73 (2 H, d, *J* 9 Hz, 2′-H, 6′-H), and 8.23 (2 H, d, *J* 9 Hz, 3′-H, 5′-H); δ_C($\mathrm{CDCl_3}$) 14.0 (Me), 14.2 (Me), 14.9 (Me), 60.5 ($\mathrm{CH_2}$), 62.1 ($\mathrm{CH_2}$), 68.8 ($\mathrm{CH_2}$), 94.2 (C-3), 118.7 (C-4), 123.9 (C-3′, C-5′), 124.9 (C-2′, C-6′), 134.2 (C-1′), 138.3 (C-5), 146.4 (C-4′), 161.0 (C=O), 161.0 (C-2), and 163.8 (C=O).

Dimethyl 2-(4-*nitrophenyl*)-5-*isopropoxyfuran*-3,4-*dicarboxylate* (**12**; R^2 = $\mathrm{Pr^i}$, R^3 = Me). A solution of tri-isopropyl phosphite (1.46 g, 7 mmol) in dry toluene (6 $\mathrm{cm^3}$) was added dropwise to a solution of dimethyl acetylenedicarboxylate (0.5 g, 3.5 mmol) in dry toluene (55 $\mathrm{cm^3}$) through which dry carbon dioxide was vigorously bubbled. 4-Nitrobenzaldehyde (0.53 g, 3.5 mmol) was added and the reaction mixture heated under reflux for 5 h. The solvent was then removed under reduced pressure and, with time, the resulting oil crystallised. The crystals were washed with ether and then dried to give the furan (**12**; R^2 = $\mathrm{Pr^i}$, R^3 = Me) (0.51 g, 41%), m.p. 137.5–140 °C (Found: C, 56.4; H. 4.9; N, 3.7. $\mathrm{C_{17}H_{17}NO_8}$ requires C, 56.2; H, 4.72; N, 3.86%); δ_H($\mathrm{CDCl_3}$; 270 MHz) 1.51 (6 H, d, *J* 6 Hz, Me), 3.83 (3 H, s, MeO), 3.96 (3 H, s, MeO), 5.11 (1 H, septet, *J* 6 Hz, OCH), 7.73 (2 H, d, *J* 9 Hz, 2′-H, 6′-H), and 8.24 (2 H, d, *J* 9 Hz, 3′-H, 5′-H); δ_C($\mathrm{CDCl_3}$) 22.4 (Me), 51.7 (OMe), 53.0 (OMe), 78.3 (OCH), 95.1 (C-3), 118.2 (C-4), 124.0 (C-3′, C-5′), 125.0 (C-2′, C-6′), 134.1 (C-1′), 138.8 (C-5), 146.6 (C-4′), 160.7 (C-2), 161.6 (C=O), and 164.4 (C=O).

Study of the Mechanism of Formation of the Furans (**12**) *from the Ylides* (**3**).—Trimethyl phosphite (1 g) in dry toluene (5 $\mathrm{cm^3}$) was added dropwise to a solution of dimethyl acetylenedicarboxylate (0.28 g) and diethyl acetylenedicarboxylate (0.34 g) in dry toluene (10 $\mathrm{cm^3}$) through which carbon dioxide was bubbled vigorously. 4-Nitrobenzaldehyde (0.3 g) was then added and the mixture left at room temperature overnight. Approximately half the toluene was then removed using a rotary evaporator (60 °C at 20 mmHg) and, on cooling, a yellow solid (*ca.* 150 mg) precipitated. The ^{13}C NMR spectrum of this material was consistent with that of a mixture of diethyl 2-methoxy-5-(4-nitrophenyl)furan-3,4-dicarboxylate and dimethyl 2-methoxy-5-(4-nitrophenyl)furan-3,4-dicarboxylate. Mass spectroscopy gave M^+ 335 and 363.

Dimethyl [2-^{13}C, 3-^{13}C=O]-2-*methoxy*-5-(4-*nitrophenyl*)-*furan*-3,4-*dicarboxylate* [2-^{13}*C*, 3-^{13}C=O]-(**12b**). To a solution of [5-^{13}C, 4-^{13}C=O]-(2,3-dihydro-5-methoxy-4-methoxycarbonyl-2-oxofuran-3-ylidene)trimethoxyphosphorane[1] [5-^{13}C, 4-^{13}C=O]-(**3b**) (0.41 g) in toluene (2.5 $\mathrm{cm^3}$) was added 4-nitrobenzaldehyde (0.12 g). The mixture was heated under reflux for 1.5 h and on cooling a solid was precipitated. This was filtered off, recrystallised from toluene, and then dried. The product (0.06 g, 26%), m.p. 180 °C, was shown by NMR spectroscopy to be the furan [2-^{13}C, 3-^{13}C=O]-(**12b**) (Found: C, 53.9; H, 3.8; N, 4.2. $\mathrm{C_{14}{}^{13}CH_{13}NO_8}$ requires C, 53.87; H, 3.9; N, 41.17%); δ_C($\mathrm{CDCl_3}$) 93.1 (d, J_{CC} 90 Hz, C-3), 161.3 (C-2), and 161.5 (3-C=O).

Diethyl [2-^{13}C, 3-^{13}C=O]-2-*methoxy*-5-(4-*nitrophenyl*)*furan*-3,4-*dicarboxylate* [2-^{13}*C*, 3-^{13}C=O]-(**12a**). To a solution of [5-^{13}C, 4-^{13}C=O]-(2,3-dihydro-5-ethoxy-4-ethoxycarbonyl-2-oxofuran-3-ylidene)trimethoxyphosphorane[1] [5-^{13}C, 4-^{13}C=O]-(**3a**) (0.06 g) in deuteriochloroform (2.5 $\mathrm{cm^3}$) was added 4-nitrobenzaldehyde (60 mg). The mixture was set aside at room temperature overnight and the labelled furan which had been precipitated, was then filtered off and dried. This furan was shown by NMR spectroscopy to be [2-^{13}C, 3-^{13}C=O]-(**12a**); δ_C($\mathrm{CDCl_3}$) 161.1 (t, $^3J_{CH}$ 3 Hz, 3-C=O) and 161.4 (q, $^3J_{CH}$ 4 Hz, C-2).

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