

Studies of the Reaction of Trivalent Phosphorus Compounds with Dialkyl Acetylenedicarboxylates in the Presence of Carbon Dioxide

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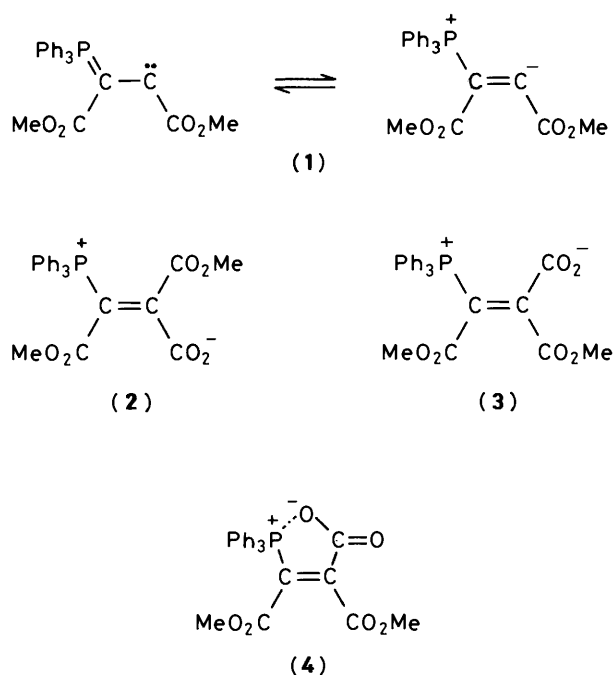
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Alkyl diphenylphosphinites react with dialkyl acetylenedicarboxylates in the presence of carbon dioxide to form 1,2-oxaphosphol-3-enes (**5**) which in the presence of excess phosphinite decompose to give di-ylides (**6**). The 1,2-oxaphosphol-3-enes (**5**) from dialkyl phenylphosphonites and trialkyl phosphites react with a further phosphorus component to give the ylides (**9**) which can readily be converted into dialkyl 1,2,2-tris(alkoxycarbonyl)ethylphosphonates (**11**). Studies using ^{13}C - and ^2H -labelled precursor provide evidence for rearrangement occurring *via* ketene intermediates.

The reaction of carbon dioxide with the 1:1 intermediate (**1**), formed in the reaction between triphenylphosphine and dimethyl acetylenedicarboxylate, has been known for many years.¹ On the basis of the evidence then available it was proposed that this CO_2 adduct was the betaine (**2**), although later evidence² suggested that some of the corresponding *cis* isomer (**3**) might also be formed. We have now shown that these proposed structures are inconsistent with the ^{31}P n.m.r. spectrum of the CO_2 adduct which shows the presence of only one signal at δ_{P} 0.3 p.p.m. This signal is at higher field than those expected for both betaines (**2**) and (**3**) and indicates a significant interaction between the phosphonium and carboxylate centres as shown in structure (**4**). We have also shown that it is possible to increase the covalent character in the bond between the carboxylate and phosphonium centres by progressively replacing the phenyl groups on the phosphorus by more electronegative substituents such as the methoxy group. Thus, for example, the reaction of methyl diphenylphosphinite with a molar equivalent of dimethyl acetylenedicarboxylate in the presence of carbon dioxide led to the formation of the oxaphospholene (**5a**) giving a high field signal in the ^{31}P n.m.r. spectrum at -40.9 p.p.m.

Although the oxaphospholene (**5a**) was very much more stable in solution than (**4**) it reacted readily with nucleophiles so that the addition of a second molar equivalent of methyl diphenylphosphinite led to the rapid formation of the 1,2-diphosphorane (**6a**) (see Scheme 1). Treatment of the diylide (**6a**) with hydrogen chloride gave the 1,2-bisphosphine oxide (**7**).

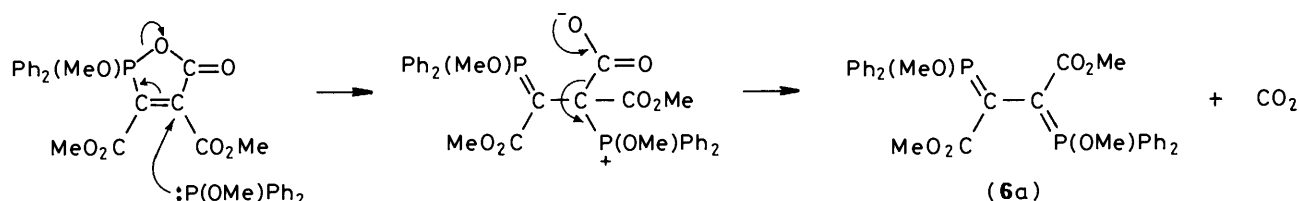
This susceptibility of the oxaphospholenes (**5**) to nucleophilic attack was found to increase as further phenyl groups on the phosphorus were replaced by alkoxy groups. Thus, during the preparation of the oxaphospholenes (**5b**) and (**5c**) from dimethyl phenylphosphonite it was necessary to keep the acetylenedicarboxylate in excess to prevent the initially formed oxaphospholenes from reacting further with the dimethyl phenylphosphonite. Interestingly, the ^{13}C n.m.r. spectra of the oxaphospholenes (**5b**) and (**5c**) were temperature dependent due to pseudorotation around the five co-ordinate phosphorus atom. Thus, in the oxaphospholene (**5c**) the two methoxy groups were observed as a doublet at δ_{C} 54.8 p.p.m. (J_{PC} 11 Hz) at 60°C , a broad ill-resolved signal at 26°C , and two doublets at δ_{C} 52.1 p.p.m. (J_{PC} 9) and δ_{C} 58.2 (J_{PC} 12) at -50°C . The difference in the values of J_{PC} in the two doublets observed at low temperature is consistent with the expected preferred conformation for the oxaphospholene (**5c**) in which one



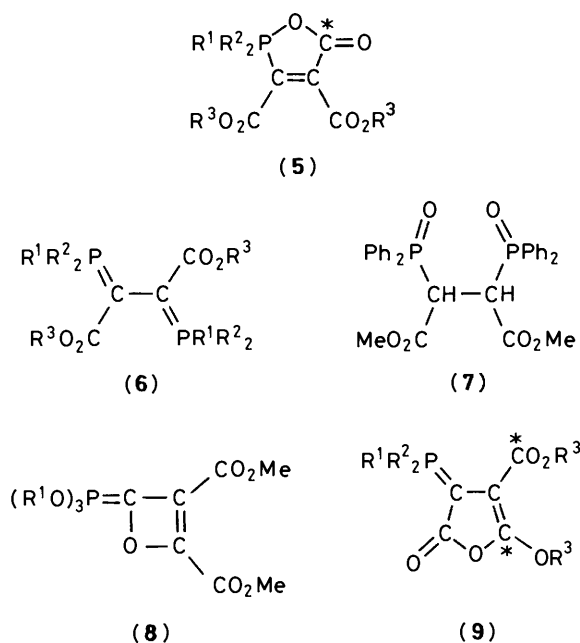
methoxy group adopts an apical position and the other adopts a radial position.³

The reactions of the oxaphospholenes (**5b**) and (**5c**) with phosphorus nucleophiles were found to proceed by a quite different route than that observed for the oxaphospholene (**5a**). Thus, addition of further dimethyl phenylphosphonite to the oxaphospholene (**5b**) led to the formation of equimolar quantities of a mono-ylide (δ_{P} 66.0) and dimethyl phenylphosphonate while addition of trimethyl phosphite to the oxaphospholene (**5c**) led to the formation of a different ylide (δ_{P} 46.7) together with the dimethyl phenylphosphonate. In neither case was there any sign of 1,2-diphosphorane formation as observed in the reactions of the oxaphospholene (**5a**).

Similar behaviour was also observed with the reaction of the oxaphospholenes (**5d**) and (**5e**) from trimethyl phosphite. Indeed, the increased susceptibility of these oxaphospholenes to nucleophilic attack meant that the reaction of equimolar quantities of trimethyl phosphite and dimethyl acetylenedicarboxylate in the presence of carbon dioxide resulted in a



Scheme 1.



	R ¹	R ²	R ³
a;	OMe	Ph	Me
b;	Ph	OMe	Me
c;	Ph	OMe	Et
d;	OMe	OMe	Me
e;	OMe	OMe	Et

mixture containing only about 14% of the oxaphospholene (**5d**). Most of the oxaphospholene (**5d**) had reacted further with trimethyl phosphite to give trimethyl phosphate and the ylide (δ_p 46.7), previously prepared by the action of trimethyl phosphite on the oxaphospholene (**5b**). The formation of the same ylide from both oxaphospholenes (**5b**) and (**5d**) clearly shows that the phosphorus atom in this ylide is derived from the trimethyl phosphite which is attacking the oxaphospholene. On the basis of the evidence originally available to us⁴ we proposed that the ylide had the structure (**8**; R¹ = Me), but subsequent work has revealed chemical behaviour which is inconsistent with this structure. Thus, for example, the addition of excess methanol to the ylide resulted in the formation of a new ylide exhibiting a temperature dependent ³¹P n.m.r. spectrum. The formation of such a stabilised ylide is inconsistent with the behaviour expected for the ylide (**8**; R¹ = Me). In order to help identify the true structure of the ylide, its synthesis was repeated using ¹³C-labelled carbon dioxide so that the progress of the carbon dioxide could be monitored throughout the course of the reaction.

The ³¹P n.m.r. spectrum of the CO₂ adduct (**5e**), prepared

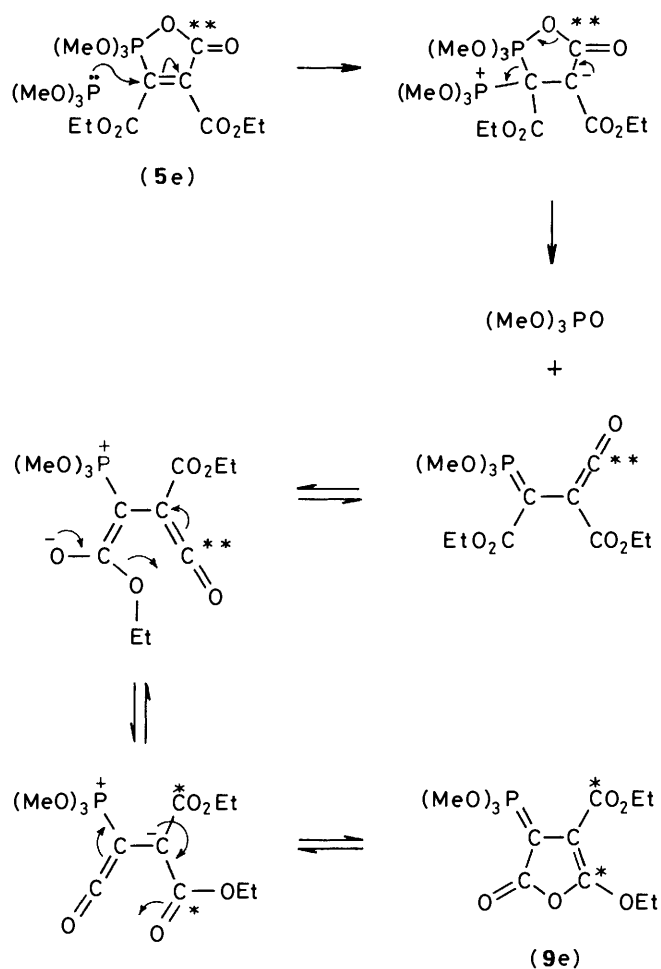
from 99% ¹³C-carbon dioxide, showed a doublet (J_{PC} 18 Hz) at δ_p -50.9 p.p.m., while the ¹³C n.m.r. signal for the labelled carbon was observed as a doublet (J_{PC} 18 Hz) at δ_c 158.7 p.p.m. This signal, although having a shift consistent with an ester carbonyl carbon exhibited no long range proton-carbon coupling as observed with the carbonyls of ethyl esters. The n.m.r. data was thus entirely consistent with the predicted incorporation of the carbon dioxide into the oxaphospholene ring as indicated (*) on the structure (**5e**).

Treatment of the ¹³C-labelled oxaphospholene (**5e**) with further trimethyl phosphite led to the formation of an ylide (δ_p 46.8) and trimethyl phosphate. Surprisingly, the phosphorus signal from the ylide was observed to have triplet character although this was subsequently shown to be due to a doublet (J_{PC} 22 Hz) bisected by a singlet. This was explained by the ¹³C n.m.r. spectrum which showed two sites of equal labelling in the ylide. Only one of these signals showed coupling to phosphorus, that at δ_c 153.7 (J_{PC} 22 Hz), the other being observed as a singlet at δ_c 162.8. Both these signals showed long range J_{CH} coupling to the ethyl groups derived from the diethyl acetylenedicarboxylate.

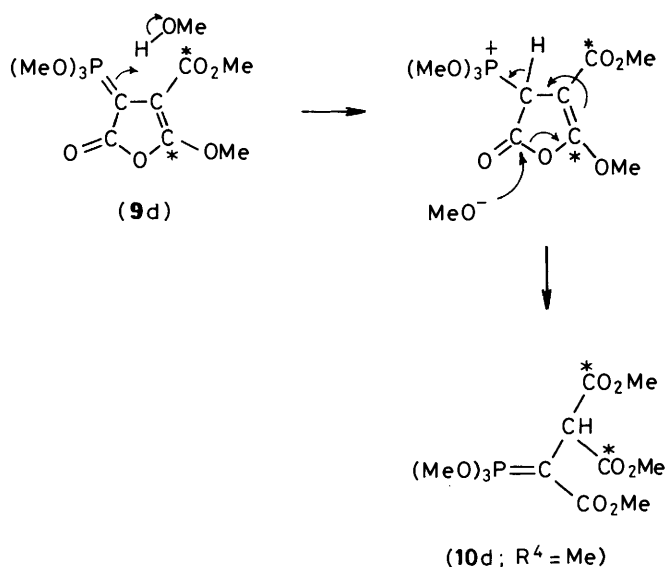
To identify those sites in the ylide adjacent to the sites of labelling, the ¹³C n.m.r. signals from the non-enriched carbons were analysed. However, only one carbon atom, that giving a signal at δ_c 86.6 showed $^1J_{CC}$ coupling (89 Hz) to the ¹³C labelled sites. Moreover, the signal from this carbon atom was observed in the phosphorus decoupled ¹³C n.m.r. spectrum as a clean doublet. The absence of any signal intensity at the centre of this doublet indicates that in all molecules of the ylide there is a ¹³C label adjacent to this carbon atom. This can only occur if the carbon atom, giving a signal at δ_c 86.6, is adjacent to both sites of labelling within the ylide. This information together with other n.m.r. data available enabled the ylide to be identified as (**9e**) with the sites of ¹³C-labelling as indicated (*). A possible mechanism for the formation of the ylide (**9e**) accounting for the observed labelling pattern is shown in Scheme 2. The change in the site of attack from C-4 in the oxaphospholene (**5a**) to C-3 in the oxaphospholenes (**5b**—**e**) probably reflects greater covalent character of the P—O bonds in the Δ^3 -oxaphospholene rings of (**5b**—**e**). Attack at C-3 would also be facilitated by the reduced bulk of the phosphonite and phosphite molecules relative to the methyl diphenylphosphinite.

The stabilised ylide formed on reaction of the ylide (**9d**) with methanol was thus identified as (**10d**; R⁴ = Me), the temperature dependent nature of the n.m.r. spectra of the latter ylide being due to restricted rotation about the bond to the α -ester group. This was confirmed by warming a sample of (**10d**; R⁴ = Me) whereupon the two ³¹P n.m.r. signals broadened and then coalesced. Attempts to isolate the stabilised ylide (**10d**; R⁴ = Me) by chromatography on silica or alumina, or treatment of the ylide with hydrogen chloride both led to protonation and dealkylation to give a phosphonate (**11d**; R⁴ = Me) whose structure was confirmed by an independent synthesis.

Two approaches to the synthesis of the phosphonate (**11d**; R⁴ = Me) were investigated. In the first, the monobromo derivative of trimethyl phosphonoacetate was allowed to react

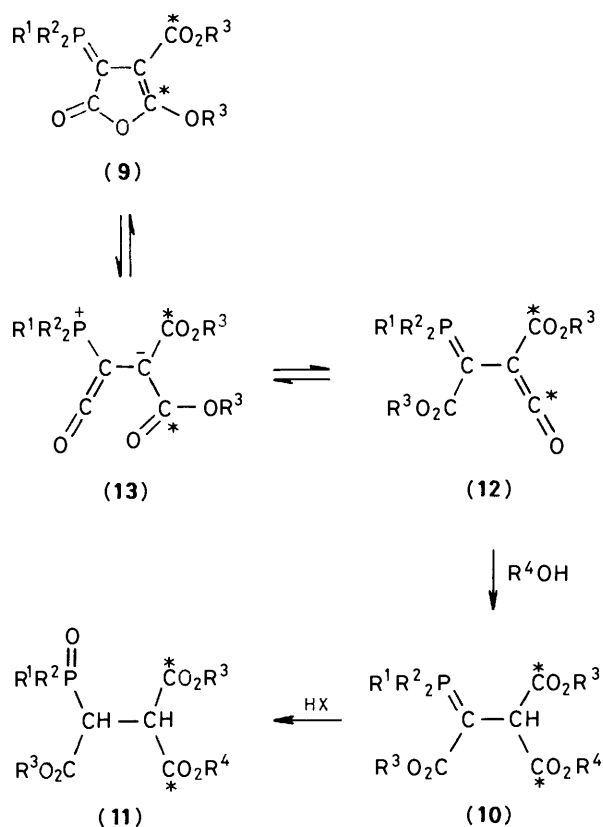


Scheme 2.



Scheme 3.

with dimethyl sodiomalonate. In the second, the monobromo derivative of dimethyl malonate was allowed to react with the sodium salt of trimethyl phosphonacetate. However, in both cases considerable difficulties were encountered due to the preferential formation of tetramethyl ethane-1,1,2,2-tetracarboxylate. For the former reactions, conditions were eventually established which gave a modest yield of the phosphonate (11d;



Scheme 4.

$R^4 = \text{Me}$) and this was shown to be identical to the product formed from the stabilised ylide (10d; $R^4 = \text{Me}$).

It is worth noting that, the difficulties experienced with the preparation of the phosphonate (11d; $R^4 = \text{Me}$) via the malonate routes clearly indicate the advantages of the 'CO₂ route' to such systems. This latter route can be carried out both rapidly and conveniently and gives high yields. We have also shown that it offers considerable flexibility in the nature of the ester groups present as, for example, in the preparation of the phosphonate (11; $R^1 = R^2 = \text{OPr}^i$, $R^3 = \text{Me}$, $R^4 = \text{Et}$).

Although at first sight the formation of the stabilised ylide (10d; $R^4 = \text{Me}$) and the phosphonate (11d; $R^4 = \text{Me}$) from the ylide (9d) would appear to proceed by the route indicated in Scheme 3, the use of deuterium labelled methanol showed this not to be the case. Thus when the phosphonate (11d; $R^4 = \text{Me}$) prepared using [²H₄]methanol was investigated it was found that two of the carboxylic ester methoxy groups had been equally labelled. This suggested that the methanol had been incorporated into a β-ester group. Further evidence for the incorporation of the alkoxy group from the alcohol in one of the β-esters in the stabilised ylides (10) comes from the use of alcohols other than methanol (*i.e.* where $R^4 \neq R^3$). In such cases the resulting phosphonates (11; $R^4 \neq R^3$) were formed as a mixture of two diastereoisomers clearly indicating the presence of two chiral centres in the molecule. This was confirmed by treating the ¹³C-labelled ylide [5-¹³C, 4-¹³C=O]-(9e) with methanol and then hydrochloric acid to convert it into the corresponding phosphonate [2-¹³C=O]-(11e; $R^4 = \text{Me}$). ¹³C N.m.r. spectroscopy showed as expected that two of the ester carbonyl groups in each diastereoisomer were labelled and that the β-carbon in each isomer was adjacent to both these sites of labelling. Moreover in each diastereoisomer one β-ester carbonyl carbon showed long-range coupling to ethyl while the other showed long-range coupling to methyl. To explain these

observations it is necessary to propose that the reactions of the ylides (**9**) with alcohols actually proceed *via* their precursors, the more reactive ylides (**12**), which we must consider to be in equilibrium with (**9**) (see Scheme 4). Indeed, some of the signals in the ^{13}C n.m.r. spectrum of the ylide do sharpen on cooling confirming the presence of an exchange process. We must also conclude that the intramolecular rearrangement of the intermediate (**13**) is sufficiently rapid to ensure that it plays little direct part in the reaction with the alcohol.

Further reactions of the ylides (**9**) will be described in a later paper.

Experimental

N.m.r. spectra were obtained on JEOL FX100 and GSX270 spectrometers.

1,2-Bis(methoxycarbonyl)-1-(triphenylphosphonia)ethylene-2-carboxylate (4).—This material was obtained using a previously reported procedure; $\delta_{\text{P}}(\text{CDCl}_3)$ 0.3.

2-Methoxy-3,4-bis(methoxycarbonyl)-2-diphenyl-1,2-oxaphosphol-3-en-5-one (5a).—Methyl diphenylphosphinite (0.32 g) in dry benzene (1 cm^3) was added dropwise to a solution of dimethyl acetylenedicarboxylate (0.23 g) in dry benzene (4 cm^3) through which dry carbon dioxide was vigorously bubbling. The solvent was removed from the reaction product under reduced pressure (40 °C at 16 mmHg) and the residue was shown by ^{31}P n.m.r. spectroscopy to be (**5a**) in essentially quantitative yield. Recrystallisation from a hexane-acetone mixture gave the pure product as a white crystalline solid, m.p. 131–132 °C (decomp.) (Found: C, 59.45; H, 4.9. $\text{C}_{20}\text{H}_{19}\text{O}_7\text{P}$ requires C, 59.73; H, 4.76%). For ^{31}P and ^{13}C n.m.r. data see Table.

Dimethyl 2,3-Bis(diphenylphosphinoyl)butane-1,4-dioate (7).—To the oxaphospholene (**5a**) (0.25 g) in benzene (3 cm^3) was added methyl diphenylphosphinite (0.13 g). ^{31}P N.m.r. spectroscopy showed the rapid formation of 1,2-bis(methoxycarbonyl)ethane-1,2-bis(methoxydiphenylphosphorane) (**6a**) in essentially quantitative yield; $\delta_{\text{P}}(\text{CDCl}_3)$ 64.1, 65.1 (J_{PP} 16 Hz), 65.7 (J_{PP} 16 Hz), and 66.4. The diphosphorane (**6a**) was converted into the corresponding bis(diphenylphosphinoyl) system (**7**) in essentially quantitative yield by treatment with concentrated hydrochloric acid. A pure sample of (**7**) (m.p. 197 °C) was obtained by reverse phase h.p.l.c. using methanol-water (60:40) as eluant (Found: C, 66.15; H, 4.9. $\text{C}_{30}\text{H}_{28}\text{O}_6\text{P}_2$ requires C, 65.93; H, 5.16%); $\delta_{\text{P}}(\text{CDCl}_3)$ 30.3; $\delta_{\text{C}}(\text{CDCl}_3)$ 48.40 (X of AA'X, W^* 91 Hz), 51.7 (s), 128.0 (t, J_{PC} 6 Hz), 128.6 (t, J_{PC} 6 Hz), 130.6 (X of AA'X, W 124 Hz), 131.1 (t, J_{PC} 5 Hz), 131.9 (t, J_{PC} 5 Hz), 131.9 (X of AA'X, W 127 Hz), and 168.2 (s); $\delta_{\text{H}}(\text{CDCl}_3)$ 2.88 (6 H, s), 4.67 (2 H, d, J 4.4 Hz), 7.29–7.44 (4 H, m), 7.52–7.56 (2 H, m), 7.56–7.65 (2 H, m), and 7.95–8.03 (2 H, m).

2,2-Dimethoxy-3,4-bis(ethoxycarbonyl)-2-phenyl-1,2-oxaphosphol-3-en-5-one (5c).—Dimethyl phenylphosphonite (0.28 g) in dry benzene (1 cm^3) was added dropwise to a solution of diethyl acetylenedicarboxylate (0.56 g) in dry benzene (3 cm^3) through which dry carbon dioxide was vigorously bubbling. Following the addition, the ^{31}P n.m.r. spectrum of the reaction mixture showed essentially quantitative formation of (**5c**). The solvent and excess acetylenic ester were removed from the reaction mixture by heating under reduced pressure (60 °C at 0.005 mmHg) to give (**5c**) in a good state of purity (for n.m.r. data see Table). Further attempts to purify the oxaphospholene (**5c**) were unsuccessful and led to decomposition.

The corresponding oxaphospholene (**5b**) from dimethyl acetylenedicarboxylate was also prepared (for n.m.r. data see Table).

(2,3-Dihydro-5-methoxy-4-methoxycarbonyl-2-oxofuran-3-ylidene)dimethoxyphenylphosphorane (9b).—Dimethyl phenylphosphonite (1.04 g) in benzene (5 cm^3) was added slowly to a solution of dimethyl acetylenedicarboxylate (0.43 g) in benzene (5 cm^3) through which dry carbon dioxide was vigorously bubbling. ^{31}P N.m.r. spectroscopy indicated the formation of both dimethyl phenylphosphonate (δ_{P} 22.0) and the ylide (**9b**) (for n.m.r. data see Table) in essentially quantitative yield.

(2,3-Dihydro-5-methoxy-4-methoxycarbonyl-2-oxofuran-3-ylidene)trimethoxyphosphorane (9d).—(a) A solution of trimethyl phosphite (0.43 g) in dry toluene (1 cm^3) was added dropwise to a solution of dimethyl acetylenedicarboxylate (0.25 g) in dry toluene (1.5 cm^3) through which dry carbon dioxide was being vigorously bubbled. The toluene was then removed under reduced pressure. ^{31}P N.m.r. spectroscopy showed an essentially quantitative yield of the phosphorane (**9d**) (for n.m.r. data see Table) together with an equimolar quantity of trimethyl phosphate. (b) To a solution of (**5c**) in deuteriochloroform was added trimethyl phosphite (1 mol equiv.). N.m.r. spectroscopy showed the essentially quantitative formation of the phosphorane (**9d**) together with an equimolar quantity of dimethyl phosphonate.

(2,3-Dihydro-5-ethoxy-4-ethoxycarbonyl-2-oxofuran-3-ylidene)trimethoxyphosphorane (9e).—The ylide (**9e**) was prepared from diethyl acetylenedicarboxylate using the same procedure as described for the preparation of the ylide (**9d**); $\delta_{\text{P}}(\text{CDCl}_3)$ 46.8; $\delta_{\text{C}}(\text{CDCl}_3)$ 14.1, 14.7, 47.8 (d, J_{PC} 250 Hz), 55.5 (d, J_{PC} 6 Hz), 59.4, 66.9, 86.6 (d, J_{PC} 15 Hz), 153.7 (d, J_{PC} 22 Hz), 162.8, and 164.3 (d, J_{PC} 25 Hz).

[1,2,2-Tris(methoxycarbonyl)ethylidene]trimethoxyphosphorane (10d).—The product from the reaction above, containing the ylide (**9d**) and trimethyl phosphate, was dissolved in deuteriochloroform (1 cm^3) and methanol (1 molar equivalent) was added. ^{31}P N.m.r. indicated the rapid formation of the stabilised ylide (**10d**) in quantitative yield (for n.m.r. data see Table). The passage of hydrogen chloride gas into the solution of the ylide (**10d**) resulted in the formation of the phosphonate (**11d**) which was identified by comparison with an authentic sample.

[1,2-Bis(ethoxycarbonyl)-2-methoxycarbonylethylidene]trimethoxyphosphorane (10e).—The stabilised ylide (**10e**) was prepared from the ylide (**9e**) using the procedure used to prepare (**10d**). $\delta_{\text{P}}(\text{CDCl}_3)$ 59.5 (major rotamer), 58.0 (minor rotamer); $\delta_{\text{C}}(\text{CDCl}_3; -10^\circ\text{C})$ (major rotamer 70%) 13.4, 14.3, 39.8 (d, J_{PC} 232 Hz), 49.6 (d, J_{PC} 10 Hz), 51.6, 54.0 (d, J_{PC} 5 Hz), 57.8, 60.5, 169.2 (d, J_{PC} 20 Hz), 170.9, and 171.6; (minor rotamer 30%) 13.5, 14.0, 41.2 (d, J_{PC} 236 Hz), 48.8 (d, J_{PC} 10 Hz), 51.5, 54.1 (d, J_{PC} 6 Hz), 58.0, 60.6, 169.5 (d, J_{PC} 25 Hz), 170.6 (d, J_{PC} 2 Hz), and 171.2 (d, J_{PC} 3 Hz).

Dimethyl 1,2,2-Tris(methoxycarbonyl)ethylphosphonate (11d; R⁴ = Me).—(a) To a stirred solution of sodium hydride (1.18 g, 50%) in 1,2-dimethoxyethane (25 cm^3) at 20 °C was added methyl (dimethoxyphosphinoyl)acetate (4.5 g). When the evolution of hydrogen had ceased bromine (3.95 g) was added dropwise while ensuring that the reaction temperature did not exceed 20 °C. To the resulting suspension was then added, dropwise over a period of 1.5 h at 20 °C, a suspension of the dimethyl sodiomalonate prepared by the action of sodium hydride (50% in oil; 1.18 g) on dimethyl malonate (3.26 g) in 1,2-

* W = separation of outer lines of multiplet.

Table. N.m.r. data.^a

	(5a) ^b	(5b) ^c	(5c) ^b	(5c) ^d	(5d) ^e	(9b) ^c	(9d) ^c	(10d) ^c	
								major rotamer	minor rotamer
¹³ C									
α-C	150.1 (153)	151.9 (168)	150.6 (167)	151.8 (167)	150.9 (208)	48.9 (191)	47.9 (251)	36.7 (232)	41.3 (237)
β-C	141.5 (13)	139.2 (14)	139.3 (13)	137.4 (14)	135.7 (13)	85.5 (16)	85.1 (15)	49.5 (10)	48.7(9)
γ-C	159.1 (7)	158.6 (11)	158.5 (12)	159.1 (12)	156.8 (18)	154.2 (19)	153.8 (21)		
α-C=O	161.1 (27)	160.6 (28)	159.9 (28)	159.5 (28)	159.4 (32)	163.9 (19)	163.7 (26)	169.7 (20)	169.7 (26)
β-C=O	164.7 (14)	164.5 (13)	163.5 (13)	163.9 (13)	163.0 (13)	162.7	162.9	171.5 (2)	171.3 (2)
OR ³	53.0	52.7	61.3/13.2	62.1/13.4	51.3	50.1	50.5	49.5	49.9
OR ³	53.1	52.6	61.7/13.4	61.6/13.1	51.6	57.2	57.2	51.8 (× 2)	51.8 (× 2)
POMe	52.0 (7)	~ 53.0(br)	~ 53.0(br)		55.0 (12)	54.5 (7)	55.3 (6)		
PPh				58.2 (12)					
(C-1)	130.9 (163)	132.5 (194)	132.3 (193)	131.4 (192) ^f		125.8 (161)			
(C-2,6)	132.2 (11)	131.3 (12)	131.1 (12)	131.6 (10) ^f		131.1 (12)			
(C-3,5)	128.5 (17)	128.1 (18)	127.9 (17)	127.9 (17) ^f		128.3 (15)			
(C-4)	131.6 (4)	131.6 (3)	131.3 (4)	131.9 (4) ^f		133.1 (3)			
³¹ P	-40.9	-36.7	-37.0		-50.9	66.0	46.7	57.6 ^c	59.4 ^c

All samples were run as solutions in deuteriochloroform. ^a δ_c values in p.p.m. from Me₄Si (δ_c CDCl₃ = 77.0); J_{PC} in Hz in parentheses. δ_p values in p.p.m. from 85% phosphoric acid, positive values to lowfield. ^b 26 °C. ^c 20 °C. ^d -50 °C. ^e -10 °C, rotamer ratio 2:1. ^f Approximate couplings due to reduced solution at low temperature.

dimethoxyethane (25 cm³). After the reaction mixture had been allowed to stand for a short time it was filtered and the solvent removed under reduced pressure (50 °C at 16 mmHg) to leave an oil. Preparative layer chromatography on silica gel using ethyl acetate as the eluant enabled a sample of pure phosphonate (**11d**; R⁴ = Me) to be isolated (0.75 g, 9.6%), m.p. 76–77 °C (Found: C, 38.5; H, 5.35. C₁₀H₁₇O₉P requires C, 38.5; H, 5.5%); δ_p(CDCl₃) 21.3; δ_c(CDCl₃) 43.6 (J_{PC} 131 Hz), 49.4, 52.1, 52.25, 52.3, 52.9 (J_{PC} 7 Hz), 53.0 (J_{PC} 7 Hz), 166.2 (J_{PC} 3 Hz), 166.6 (J_{PC} 19 Hz), and 166.7 (J_{PC} 5 Hz).

(b) The mixture containing the phosphorane (**10d**) and trimethyl phosphite, previously prepared, was treated carefully with a few drops of concentrated hydrochloric acid and the mixture shaken. Volatile components were removed from the reaction mixture under reduced pressure (50 °C at 0.005 mmHg) to leave a viscous oil which was shown by ³¹P and ¹³C n.m.r. spectroscopy to be the phosphonate (**11d**; R⁴ = Me) in essentially quantitative yield (Found: C, 38.2; H, 5.2. C₁₀H₁₇O₉P requires C, 38.5; H, 5.5%).

The phosphonate (**11d**; R⁴ = Me) was also prepared by passing a solution containing the phosphorane (**10d**) down a short column of either alumina or silica gel.

Dimethyl [2-²H]-2-[²H₃]Methoxycarbonyl-1,2-bis(methoxycarbonyl)ethylphosphonate.—A deuteriated derivative of (**10d**) was first prepared by adding [²H₄]methanol (in excess) to a solution of the ylide (**9d**) and trimethyl phosphite in deuteriochloroform, prepared as previously described. Addition of several drops of concentrated hydrochloric acid resulted in the formation of the tetradeuteriated derivative of the phosphonate (**11d**; R⁴ = Me) which was identified spectroscopically by comparison with the non-deuteriated material. ¹³C N.m.r. spectroscopy showed the formation of equal quantities of the two diastereoisomers of the deuteriated phosphonate, the effects of deuteration being observed at δ_c 52.76 (OMe), 52.82 (OMe), and 49.4 (β-C).

Dimethyl 2-Ethoxycarbonyl-1,2-bis(methoxycarbonyl)ethylphosphonate (11d; R⁴ = Et).—This was prepared in essentially quantitative yield using the procedure previously described

for the preparation of (**11d**; R⁴ = Me) except that ethanol rather than methanol was added to the phosphorane (**10d**). N.m.r. spectroscopy showed the formation of equal quantities of the two phosphonate diastereoisomers. A pure sample of the phosphonate (**11d**; R⁴ = Et) was obtained by chromatography on silica using light petroleum–ethyl acetate (50:50) as eluant (Found: C, 40.8; H, 6.1. C₁₁H₁₉O₉P requires C, 40.5; H, 5.87%); δ_p(CDCl₃) 21.95 and 21.99; δ_c(CDCl₃) α-C, 44.3 (J_{PC} 131 Hz) (× 2); β-C, 50.4 (J_{PC} 1.5 Hz) (× 2); POMe, 53.5 (m) (× 4); Me, 52.79, 52.82, 52.95, 53.0; Et, 13.7 (× 2), 62.1, 62.2; β-CO₂Et, 166.4 (J_{PC} 3 Hz), 166.8 (J_{PC} 19 Hz); β-CO₂Me, 167.1 (J_{PC} 3 Hz), 167.6 (J_{PC} 19 Hz); α-CO₂Me, 167.7 (J_{PC} 4 Hz), and 167.6 (J_{PC} 4 Hz).

Dimethyl 1,2-Bis(ethoxycarbonyl)-2-(methoxycarbonyl)ethylphosphonate (11e; R⁴ = Me).—This was prepared in essentially quantitative yield from trimethyl phosphite and diethyl acetylenedicarboxylate using the procedure previously described for the preparation of (**11d**; R⁴ = Me). A pure sample of the phosphonate was obtained by chromatography on silica using light petroleum–ethyl acetate (50:50) as eluant (Found: C, 42.4; H, 6.35. C₁₂H₂₁O₉P requires C, 43.35; H, 6.22%); δ_p(CDCl₃) 22.06, and 22.10; δ_c(CDCl₃) α-C, 44.6 (J_{PC} 131 Hz) (× 2); β-C, 50.4 (× 2); POMe, 53.5 (m) (× 4); Et, 13.8 (× 4), 61.9 (× 2), 62.15, 62.2; Me, 53.0 (× 2); α-CO₂Et, 167.2 (J_{PC} 3 Hz), and 167.1 (J_{PC} 3 Hz); β-CO₂Et, 166.5 (J_{PC} 3 Hz) and 166.9 (J_{PC} 19 Hz); β-CO₂Me, 167.6 (J_{PC} 19 Hz), and 167.1 (J_{PC} 3 Hz).

Di-isopropyl 2-Ethoxycarbonyl-1,2-bis(methoxycarbonyl)ethylphosphonate (11; R¹ = R² = OPrⁱ, R³ = Me, R⁴ = Et).—Tri-isopropyl phosphite (4.16 g) in toluene (10 cm³) was added slowly to a solution of dimethyl acetylenedicarboxylate (1.24 g) in toluene (10 cm³) through which carbon dioxide was vigorously bubbling. ³¹P N.m.r. spectroscopy indicated a clean preparation of the ylide (**9**; R¹ = R² = OPrⁱ, R³ = Me) [δ_p(CDCl₃) 37.1] together with an equimolar quantity of tri-isopropyl phosphite. Dry ethyl alcohol (1 g) was added and the reaction allowed to stand until formation of the stabilised ylide (**10**; R¹ = R² = OPrⁱ, R³ = Me, R⁴ = Et) [δ_p(CDCl₃) 47.5 and 49.0] was complete (as monitored by ³¹P n.m.r. spectroscopy). The resulting mixture was then vigorously

shaken with a few drops of concentrated hydrochloric acid until the yellow colour of the solution had been discharged. Volatile components were removed under reduced pressure (50 °C at 14 mmHg) to give an oil which was shown by n.m.r. spectroscopy to be a mixture of tri-isopropyl phosphate and the phosphonate (**11**; $R^1 = R^2 = OPr^i$, $R^3 = Me$, $R^4 = Et$) in essentially quantitative yield. A sample of the pure phosphonate was obtained by reverse phase h.p.l.c. using a methanol-water mixture (60:40) as eluant (Found: C, 47.15; H, 7.05. $C_{15}H_{27}O_9P$ requires C, 47.10; H, 7.06%); $\delta_p(CDCl_3)$ 17.04 and 17.05; $\delta_c(CDCl_3)$ α -C, 45.98 (J_{PC} 131 Hz), and 45.95 (J_{PC} 131 Hz); β -C, 50.8; Me, 52.5, 52.6, 52.9, and 53.0; Et, 13.8 ($\times 2$), 62.1 and 62.2; Pr^iO , 23.5 (J_{PC} 5 Hz), 23.6 (J_{PC} 5 Hz), 23.9 (J_{PC} 3 Hz), and 24.0 (J_{PC} 3 Hz), 72.2 (m) ($\times 4$); α -CO₂Me, 168.1 (J_{PC} 5 Hz), and 168.2 (J_{PC} 5 Hz); β -CO₂Me, 167.2 (J_{PC} 2 Hz), and 168.0 (J_{PC} 19.5 Hz); β -CO₂Et, 166.6 (J_{PC} 2 Hz), and 167.3 (J_{PC} 19.5 Hz).

Labelling Studies using ^{13}C -Labelled Carbon Dioxide.—Enriched carbon dioxide (99% ^{13}C) was obtained from Aldrich at atmospheric pressure in a glass bulb (100 cm³) with breakseal. Reactions were carried out in a small glass separating funnel (40 cm³) with a glass stopcock. Reagents and solvents were introduced into the vessel *via* an injection septum at the top of the funnel while the labelled carbon dioxide was introduced by connecting the base of the funnel to the reservoir of labelled CO₂ and then opening the stopcock. The reaction vessel was filled with hydrogen prior to its attachment to the carbon dioxide reservoir to encourage the diffusion of the carbon dioxide from the reservoir to the reaction vessel. This mixing was aided by inserting a long needle attached to a gas-tight syringe through the septum and the barrel of the glass tap into the reservoir of CO₂. The labelled carbon dioxide could then be withdrawn into the syringe and reintroduced directly into the reaction vessel without removing the tip of the needle from the apparatus. Once the vessel had been charged with the labelled carbon dioxide the tap to the reservoir was closed. The acetylenic ester in deuteriochloroform was injected into the reaction vessel and the flask shaken gently until the solution had become saturated with carbon dioxide. The trivalent phosphorus compound was then introduced very slowly by injection using a long fine needle to restrict the flow of the phosphorus component as it was drawn into the reaction vessel. During the addition of the phosphorus component the contents of the reaction vessel were shaken to ensure rapid mixing of the reactants.

[5- ^{13}C ,4- $^{13}C=O$]-2,2-Dimethoxy-3,4-bis(methoxycarbonyl)-2-phenyl-1,2-oxaphospho-3-en-5-one [5- ^{13}C , 4- $^{13}C=O$]-(**5b**).—Using the apparatus and procedure previously described, dimethyl phenylphosphonite (0.25 g) in deuteriochloroform (1.5 cm³) was slowly added to an agitated solution of dimethyl acetylenedicarboxylate (0.22 g) in deuteriochloroform (1 cm³)

in an atmosphere of ^{13}C -enriched carbon dioxide (99% ^{13}C ; 40 cm³). The ^{31}P n.m.r. spectrum of the resulting solution showed an almost quantitative preparation of the labelled CO₂ adduct [5- ^{13}C ,4- $^{13}C=O$]-(**5b**) [δ_p -37.1 (d, J_{PC} 11 Hz); δ_c 158.5 (d, J_{PC} 11 Hz)].

[5- ^{13}C ,4- $^{13}C=O$]-2,2,2-Trimethoxy-3,4-bis(ethoxycarbonyl)-oxaphosphol-3-en-5-one [5- ^{13}C ,4- $^{13}C=O$]-(**5e**).—This was prepared using the apparatus and procedure previously described. Trimethyl phosphite (0.04 g) in deuteriochloroform (1.5 cm³) was slowly added to an agitated solution of diethyl acetylenedicarboxylate (0.22 g) in deuteriochloroform (1 cm³) in an atmosphere of ^{13}C -enriched carbon dioxide (99% ^{13}C ; 40 cm³). The ^{31}P n.m.r. spectrum of the resulting solution showed the major phosphorus product to be the labelled CO₂ adduct [5- ^{13}C ,4- $^{13}C=O$]-(**5e**) δ_p -50.9 (d, J_{PC} 18 Hz); δ_c 158.7 (d, J_{PC} 18 Hz).

[5- ^{13}C ,4- $^{13}C=O$]-Dihydro-5-ethoxy-4-ethoxycarbonyl-2-oxofuran-3-ylidenetrimethoxyphosphorane [5- ^{13}C ,4- $^{13}C=O$]-(**9e**).—This was prepared using the apparatus and procedure previously described. Trimethyl phosphite (0.17 g) in deuteriochloroform (1.5 cm³) was added slowly to an agitated solution of diethyl acetylenedicarboxylate (0.11 g) in deuteriochloroform (1 cm³) in an atmosphere of ^{13}C -enriched carbon dioxide (99% ^{13}C ; 40 cm³). The ^{31}P n.m.r. spectrum of the resulting solution showed the formation of equal quantities of trimethyl phosphate and the labelled ylide [5- ^{13}C ,4- $^{13}C=O$]-(**9e**) δ_p 46.8 (s) and 46.8 (d, J_{PC} 22 Hz), δ_c 153.7 (d, J_{PC} 22 Hz), and 162.8 (s).

Dimethyl [2- $^{13}C=O$]-2-Bis(ethoxycarbonyl)-2-(methoxycarbonyl)ethylphosphonate [2- $^{13}C=O$]-(**11e**; $R^4 = Me$).—The solution of the ^{13}C -labelled ylide [5- ^{13}C ,4- $^{13}C=O$]-(**9e**) was converted into the phosphonate [2- $^{13}C=O$]-(**11e**; $R^4 = Me$) using the procedure previously described. N.m.r. spectroscopy indicated the formation of equal quantities of the two diastereoisomers; δ_p 21.91 (d, 19.5 Hz), 21.91 (d, 3 Hz), 21.87 (d, 19 Hz), and 21.87 (d, 3 Hz); δ_c 167.3 (d, 19.5 Hz), 166.9 (d, 3 Hz), 166.6 (d, 19.5 Hz), 166.21 (d, 3 Hz), and 50.0 (C-2, d, J_{CC} 57 Hz).

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Received 5th May 1989; Paper 9/01902B