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The Use of Diazophosphonates in the Synthesis of Cyclic Ethers†

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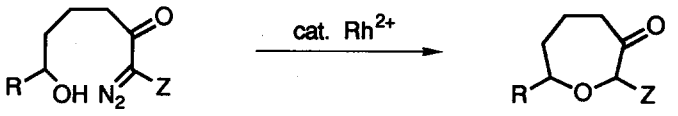
Abstract: *Two routes to cyclic ethers based on diazophosphonates are described. The first involves the rhodium(II) catalysed O-H insertion of 2-propanol followed by Wadsworth-Emmons reaction to give the enol ethers* ***3****, and deprotection and cyclisation to the cyclic enol ethers* ***5****. The second route involves the preparation of aldehyde and ketone phosphonates* ***9****, also by rhodium carbenoid O-H insertion reactions, followed by functional group interconversion. On treatment with sodium hydride the phosphonates* ***9*** *undergo intramolecular Wadsworth-Emmons reaction to give cyclic ethers* ***13****.*

The decomposition of diazocarbonyl compounds has been studied under thermal, photochemical, and, most commonly these days, transition-metal catalysed conditions,[1] and the inter- and intra-molecular reactions of the resulting carbenes or carbenoids by addition to a C=C bond or by C-H insertion are useful reactions in organic synthesis.[2] In contrast to the vast body of work on diazocarbonyl compounds and, in recent years particularly, their rhodium(II) catalysed decomposition, diazophosphonates have been much less widely studied. Thus α-diazo-β-keto alkylphosphonates undergo intramolecular C-H insertion on treatment with catalytic amounts of rhodium(II) acetate to give 2-phosphono cyclopentanone derivatives in a reaction entirely analogous to the corresponding α-diazo-β-keto carboxylic esters.[3] In addition to this work, Paquet and Sinaÿ have used a rhodium catalysed intermolecular O-H insertion reaction of diazo trimethyl phosphonoacetate to functionalise the primary O-H of a protected glucose derivative,[4] and similar O-H insertion reactions have been studied independently by Berchtold[5a] and Ganem.[5b] Our own interest in this area of chemistry is also concerned with rhodium carbenoid O-H insertion reactions, in particular the intramolecular version as a route to cyclic ethers.[6] Although much of our effort has involved the use of diazo β-keto esters (Scheme 1, Z = CO_2Me or CO_2Et), we have recently shown that diazo β-keto phosphonates can be cyclised similarly (Scheme 1, Z = $PO(OEt)_2$), and that the resulting 3-oxo-oxepane-2-phosphonates can be further elaborated by Wadsworth-Emmons olefination.[7,8]

† ***Dedicated to the memory of our friend and colleague Barrie C. Uff; 13 Feb 1937 - 19 Oct 1991***

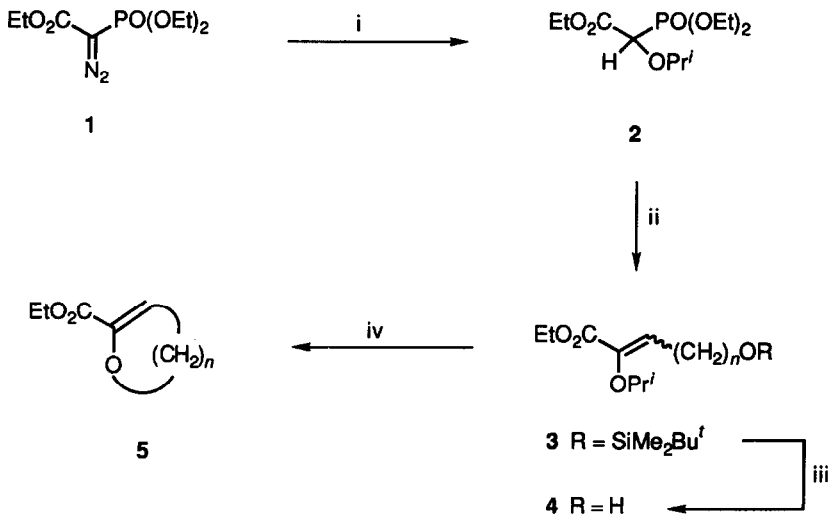


Scheme 1

We have now developed the chemistry of diazophosphonates, and report two further applications in cyclic ether synthesis using intermolecular rhodium carbenoid O-H insertion followed by (a) Wadsworth-Emmons olefination and acid catalysed cyclisation, or (b) intramolecular Wadsworth-Emmons reaction.[9]

RESULTS AND DISCUSSION

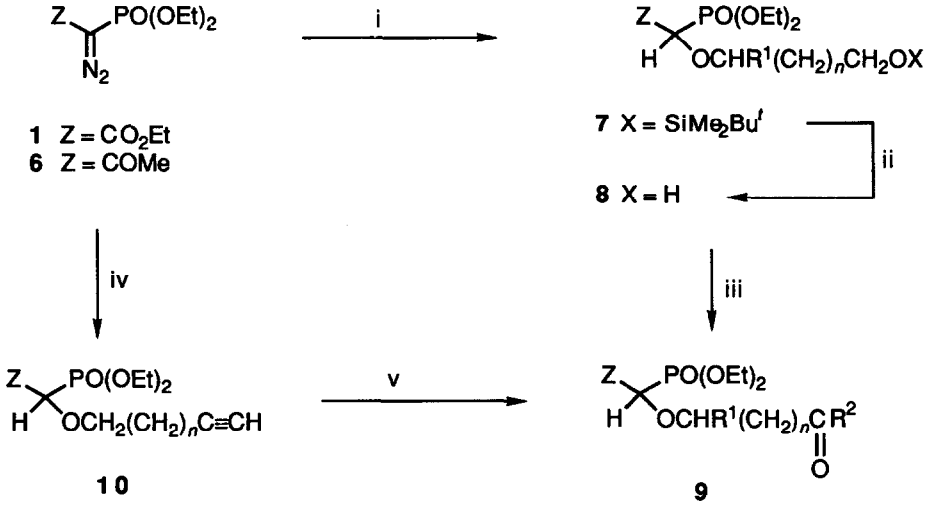
The starting material for the first route is triethyl diazophosphonoacetate **1** which on treatment with a catalytic amount of rhodium(II) acetate in refluxing 2-propanol is converted into the isopropyloxy derivative **2** by a formal O-H insertion of the resulting rhodium carbenoid. The phosphonate **2** undergoes Wadsworth-Emmons reaction (*cf.* ref. 5) with both 4-*tert*-butyldimethylsiloxybutanal and 5-*tert*-butyldimethylsiloxypentanal to give the enol ethers **3a** and **3b** in 50 and 76% yield respectively both as a 1:1 mixture of E- and Z-isomers. Deprotection of the silyl ethers **3** with aqueous acetic acid in tetrahydrofuran (THF) gave the corresponding alcohols **4**, which cyclised to the ethers **5** on treatment with camphorsulphonic acid (CSA) in refluxing benzene (Scheme 2). Although the dihydropyran **5a** is formed in only modest yield (47%), the cyclisation to the tetrahydro-oxepin **5b** proceeds in 81% yield.



Scheme 2 (**a**, n = 3; **b**, n = 4)

Reagents: i, ^{i}PrOH, cat. $Rh_2(OAc)_4$; ii, NaH, THF, 0°C; $^{t}BuMe_2SiO(CH_2)_nCHO$; iii, AcOH, H_2O, THF; iv, CSA, PhH, reflux.

The second diazophosphonate-based route to cyclic ethers involves the intramolecular Wadsworth Emmons reaction, which although it has been used for γ-lactones,[10,11] tetrahydropyridines,[12] cyclopentenones,[13] and various macro-cycles,[14,15] has not been applied to medium ring cyclic ether synthesis. The substrates **9** for the intramolecular Wadsworth-Emmons reaction were prepared by two routes from the diazophosphonates **1** and **6** as shown in Scheme 3. Thus rhodium carbenoid mediated O-H insertion reactions of mono *t*-butyldimethylsilyl protected diols gave the alkoxyphosphonates **7** in 61-83% yield. Deprotection of the silyl ethers followed by oxidation of the alcohols **8** with pyridinium dichromate (PDC) then gives the desired aldehydes **9a - 9g**. The ketone phosphonates **9h - 9j** were prepared by rhodium catalysed insertion into the O-H bond of commercially available terminal alkynols to give **10** followed by conversion to the methyl ketones by mercury(II) hydration of the triple bond. The ketones **9h - 9j** were not purified but cyclised directly as described below. Attempts to incorporate the synthetically useful CONMe(OMe) functionality, the so-called Weinreb amide,[16] were less successful. Although the diazo compound **11**, prepared from the commercially available phosphonate, underwent O-H insertion, the yields of the products **12** were rather poor, and the reaction sequence was not progressed.

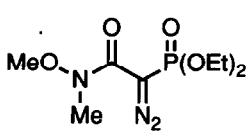


Scheme 3.

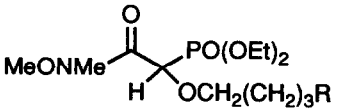
Reagents: i, $^tBuMe_2SiOCH_2(CH_2)_nCHR^1OH$, cat. $Rh_2(OAc)_4$, benzene, reflux; ii, AcOH; H_2O, THF; iii, PDC, CH_2Cl_2; iv, $HOCH_2(CH_2)_nC{\equiv}CH$, cat. $Rh_2(OAc)_4$, benzene, reflux; v, $HgSO_4$, H_2O, THF.

Key for Compounds in Scheme 3

Compound	*Z*	*n*	R^1	R^2	*Compound*	*Z*	*n*	R^1	R^2
7, 8, 9a	EtO_2C	1	H	H	**7, 8, 9f**	Ac	2	H	H
7, 8, 9b	EtO_2C	2	H	H	**7, 8, 9g**	Ac	3	H	H
7, 8, 9c	EtO_2C	3	H	H	**10a, 9h**	EtO_2C	1	H	Me
7, 8, 9d	EtO_2C	3	Me	H	**10b, 9i**	EtO_2C	2	H	Me
7, 8, 9e	EtO_2C	4	H	H	**10c, 9j**	EtO_2C	3	H	Me



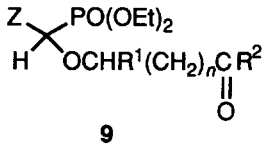
11



12a R = $CH_2OSiMe_2Bu^t$
12b R = C≡CH

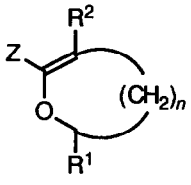
Treatment of the phosphonates **9** with sodium hydride in THF resulted in intramolecular Wadsworth-Emmons reaction and the formation of the cyclic ethers **13**. The cyclisations proceed in moderate yield (Table 1); the dihydrofuran **13a** and **13h** being formed in 50 and 23% yield respectively and the dihydropyrans **13b** (= **5a**), **13f**, and **13i** formed in 46, 46, and 40% yield. Of more interest to the general field of cyclic ether synthesis is the fact that the reaction works moderately well for 7-membered rings [**13c** (= **5b**), **13d**, **13g**, **13j**] with the yield of such cyclisations in the range 32-47%.

Table 1. Intramolecular Wadsworth-Emmons reactions



9

NaH, THF



13

9/13	*Z*	*n*	*R^1*	*R^2*	*Yield 13(%)*
a	EtO_2C	1	H	H	50
b	EtO_2C	2	H	H	46[a]
c	EtO_2C	3	H	H	43[b]
d	EtO_2C	3	Me	H	47
e	EtO_2C	4	H	H	—[c]
f	Ac	2	H	H	46
g	Ac	3	H	H	32
h	EtO_2C	1	H	Me	23[d]
i	EtO_2C	2	H	Me	40[d]
j	EtO_2C	3	H	Me	47[d]

Notes: [a]Product **13b** = **5a**; [b]Product **13c** = **5b**; [c]No 8-membered ring **13e** isolated; [d]overall yield from **10**.

EXPERIMENTAL

Commercially available solvents and reagents were used throughout without further purification, except for those detailed below which were purified as described. 'Light petroleum' refers to the fraction of petroleum ether boiling between 40°C and 60°C, and was distilled through a 36 cm Vigreux column before use. 'Ether' refers to diethyl ether; this, together with benzene and toluene, was dried where necessary by standing over sodium wire for several days. THF was distilled from potassium benzophenone ketyl under nitrogen prior to use. Dichloromethane was dried where necessary by distillation from phosphorus pentoxide. DMF was stirred for 15 h over barium oxide, decanted, and distilled under reduced pressure before storing over activated 4Å molecular sieves, under nitrogen. Compounds characterised by high-resolution mass spectrometry were chromatographically homogeneous.

General Procedure for the Preparation of t-Butyldimethylsiloxy-alkanols

A solution of t-butyldimethylsilyl chloride (5.00 g, 33 mmol, 1 equiv.) in DMF (20 ml) was added dropwise over 30 min to a stirred solution of the 1,n-diol (4 equivs.) and imidazole (5.65 g, 83 mmol, 2.5 equiv.) in DMF (45 ml). After stirring for 48 h at room temperature, ether (60 ml) and water (60 ml) were added. The aqueous layer was extracted with ether (3 x 50 ml) and the combined ethereal extracts washed with water (30 ml) and brine (50 ml) and then dried ($MgSO_4$). Evaporation of the solvent followed by Kugelrohr distillation of the residue yielded the desired mono-protected diol.

mono-protected TBDMS diol	yield	boiling point (approx.)
$HO(CH_2)_3OSiMe_2{}^tBu$	78%	110°C/6 mmHg
$HO(CH_2)_4OSiMe_2{}^tBu$	70%	120°C/6 mmHg
$HO(CH_2)_5OSiMe_2{}^tBu$	75%	140°C/6 mmHg
$HO(CH_2)_6OSiMe_2{}^tBu$	75%	150°C/4 mmHg

General Procedure for the Preparation of t-Butyldimethylsiloxy-alkylaldehydes

A solution of the mono-protected diol (11.5 mmol) in dichloromethane (10 ml) was added to a suspension of pyridinium chlorochromate (PCC) (3.70 g, 17 mmol) in dichloromethane (30 ml). After stirring for 90 min at room temperature, ether (20 ml) was added and the reaction mixture stirred for a further 30 min. The suspension was then filtered through a pad of silica under suction. The silica was washed with ether and the filtrate and washings were then combined. The solvent was removed by evaporation and the residue chromatographed on silica (light petroleum-ether) to yield the t-butyldimethylsiloxyalkylaldehyde derivative which was used immediately, without further purification or characterisation.

Triethyl phosphono-diazoacetate **1**

Triethyl phosphonoacetate (30 g, 0.134 mol) was added dropwise to a suspension of sodium hydride (80%, 4.42 g, 0.147 mol) in THF (400 ml) at 0°C. After stirring for 45 min, a solution of tosyl azide (26.4 g, 0.134 mol) in THF (50 ml) was added dropwise. The reaction was then left to stir for 1 h at 0°C and 2 h at room temperature. Ether (300 ml) and water (300 ml) were then added and the aqueous layer extracted with ether (3 x 200 ml). The combined ethereal extracts were washed successively with aqueous sodium hydroxide (5%, 200 ml), water (2 x 200 ml) and brine (200 ml) and then dried ($MgSO_4$). The solvent was removed by evaporation and the residue chromatographed on silica (ether) to yield the *title compound* **1** (20.94 g, 63%) which displayed identical spectral properties to those described in reference 17.

Ethyl 2-isopropyloxy-2-diethylphosphonoacetate **2**

A mixture of triethyl phosphono-diazoacetate **1** (7.0 g, 28 mmol), dirhodium tetraacetate (0.12 g, 0.28 mmol) and 2-propanol (50 ml) was refluxed for 10 h. The solvent was removed by evaporation and the residue chromatographed on silica (ethyl acetate-ether) to yield the *title compound* **2** (4.05 g, 51%), (Found: M+H$^+$, 283.1311. $C_{11}H_{23}O_6P$+H requires 283.1311); ν_{max} (film)/ cm^{-1} 2980, 2936, 1746, 1386, 1266, 1182, 1116, 1054, 1028 and 974 ; δ_H (250 MHz; $CDCl_3$) 1.20-1.38 (15 H, m, $OCH_2\underline{Me}$ and $\underline{Me}_2CH$), 3.74 (1 H, h, J 6.1, $Me_2C\underline{H}$), 4.16-4.34 (6 H, m, $OC\underline{H}_2Me$) and 4.38 (1 H, d, J 19.8, $OC\underline{H}P$); *m/z* (EI) 224 (MH^+-O-iPr, 14%), 197 (39), 167 (76), 152 (36), 111 (100), 65 (58) and 43 (79).

General Procedure for the Preparation of Enol Ethers **3**

A solution of triethyl isopropyloxy-phosphonoacetate **2** (6.9 mmol) in THF (5 ml) was added dropwise to a suspension of sodium hydride (80%, 0.22 g, 7.6 mmol) in THF (30 ml) at 0°C. After stirring for 20 min at 0°C, a solution of the t-butyldimethylsiloxyalkylaldehyde (6.9 mmol) in THF (5 ml) was added. The reaction was stirred for a further 1 h at 0°C and then allowed to warm to room temperature. Ether (50 ml) and water (50 ml) were added and the aqueous layer extracted with ether (3 x 50 ml). The combined ethereal extracts were washed with brine (75 ml) and then dried ($MgSO_4$). The solvent was removed by evaporation and the residue chromatographed on silica (light petroleum-ether) to yield the pure enol ether derivative as a mixture of E and Z isomers. The following compounds were prepared:

Ethyl 2-isopropyloxy-6-(t-butyldimethylsiloxy)hex-2-enoate **3a** (50%, E:Z ratio 1:1), (Found: M+H$^+$, 331.2305. $C_{17}H_{34}SiO_4$+H, 331.2305); ν_{max} (film)/ cm^{-1} 2956, 2928, 2856, 1720, 1642, 1370, 1258, 1148, 1104, 836 and 776; Z isomer: δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.89 (9 H, s, t-BuSi), 1.24 (6 H, d, J 6.1, $\underline{Me}_2CH$), 1.32 (3 H, t, J 7, $OCH_2\underline{Me}$), 1.60-1.67 (2 H, m, CH_2), 2.47 (2 H, q, J 7.6, CH_2), 3.64 (2 H, t, J 6.3, OCH_2), 4.14-4.29 (3 H, m, $OC\underline{H}_2Me$ and $Me_2C\underline{H}$) and 6.28 (1 H, t, J 7.6, =CH); E isomer: δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.89 (9 H, s, t-BuSi), 1.23 (6 H, d, J 6.1 $\underline{Me}_2CH$), 1.31 (3 H, t, J 7, $OCH_2\underline{Me}$), 1.59-1.67 (2 H, m, CH_2), 2.29 (2 H, q, J 7.6, CH_2), 3.64 (2 H, t, J 6.3, OCH_2), 4.06-4.29 (3 H, m, $OC\underline{H}_2Me$ and $Me_2C\underline{H}$) and 5.48 (1 H, t, J 7.7, =CH); *m/z* (EI): 273 (M^+-C_4H_9, 11%), 231 (32), 157 (M^+-$C_6H_{15}OSi$-C_3H_6, 100), 129 (22), 101 (28), 75 (98), 55 (31) and 43 (72).

Ethyl 2-isopropyloxy-7-(t-butyldimethylsilyloxy)hept-2-enoate **3b** (76%, E:Z ratio 1:1), (Found: M+H$^+$, 345.2461. $C_{18}H_{36}SiO_4$+H requires 345.2461); ν_{max} (film)/ cm^{-1} 2952, 2928, 2856, 1720, 1640, 1254, 1182, 1100, 836, 776 and 734; Z isomer: δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.89 (9 H, s, t-BuSi), 1.23 (6 H, d, J 6.1, $\underline{Me}_2CH$), 1.33 (3 H, t, J 7.2, $OCH_2\underline{Me}$), 1.46-1.55 (4 H, m, CH_2CH_2), 2.43 (2 H, q, J 7.4, CH_2), 3.61 (2 H, m, OCH_2), 4.01-4.26 (3 H, m, $OC\underline{H}_2Me$ and $Me_2C\underline{H}$) and 6.25 (1 H, t, J 7.6, =CH); E isomer: δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.89 (9 H, s, t-BuSi), 1.23 (6 H, d, J 6.1, $\underline{Me}_2CH$), 1.31 (3 H, t, J 7.2, $OCH_2\underline{Me}$), 1.45-1.55 (4 H, m, CH_2CH_2), 2.25 (2 H, q, J 7.5, CH_2), 3.61 (2 H, t, J 6.3, OCH_2), 4.01-4.26 (3 H, m, OCH_2Me and Me_2CH) and 5.47 (1 H, t, J 7.7, =CH); *m/z* (EI): 345 (MH^+, 17%), 303 (37), 287 (M^+-C_4H_9, 38), 245 (50), 171 (M^+-$OC_6H_{15}Si$-C_3H_6, 100), 75 (24) and 43 (30).

General Procedure for the Preparation of Hydroxy Enol Ether Derivatives **4**

A mixture of the enol ether **3** (4.4 mmol), THF (8 ml), water (4 ml) and glacial acetic acid (12 ml) was heated at 45-50°C for 30 min. After allowing to cool, dichloromethane (20 ml) and water (20 ml) were added. The aqueous layer was extracted with dichloromethane (3 x 20 ml) and the combined organic extracts washed successively with saturated sodium bicarbonate solution (5 x 25 ml) and brine (50 ml) and then dried ($MgSO_4$). The solvent was removed by evaporation and the residue chromatographed on silica (light petroleum-ether) to yield the respective hydroxy enol ether derivative.

Ethyl 2-isopropyloxy-6-hydroxyhex-2-enoate **4a** (79%), (Found: $M+NH_4^+$, 234.1705. $C_{11}H_{20}O_4+NH_4$ requires 234.1705); ν_{max} (film)/ cm^{-1} 3416, 2976, 2932, 1718, 1640, 1372, 1256, 1182 and 1106; Z isomer: δ_H (250 MHz; $CDCl_3$) 1.24 (6 H, d, *J* 6.2, $\underline{Me}_2CH$), 1.30-1.36 (3 H, m, $OCH_2\underline{Me}$), 1.65-1.75 (2 H, m, CH_2), 2.51 (2 H, q, *J* 7.6, CH_2), 3.61-3.66 (2 H, m, OCH_2), 4.18-4.31 (3 H, m, $OC\underline{H}_2Me$ and $Me_2C\underline{H}$) and 6.26 (1 H, t, *J* 7.8, =CH); OH not observed; E isomer: δ_H (250 MHz; $CDCl_3$) 1.23 (6 H, d, *J* 6.2, $\underline{Me}_2CH$), 1.30-1.36 (3 H, m, $OCH_2\underline{Me}$), 1.65-1.75 (2 H, m, CH_2), 2.33 (2 H, q, *J* 7.6, CH_2), 3.61-3.66 (2 H, m, OCH_2), 4.05 (1 H, heptet, *J* 6.1, $Me_2C\underline{H}$), 4.18-4.31 (2 H, m, OCH_2Me), and 5.43 (1 H, t, *J* 8.5, =CH); OH not observed; *m/z* (EI): 216 (M^+, 13%), 171 (M^+-OC_2H_5, 10), 157 (M^+-OC_3H_7, 100) and 82 (9).

Ethyl 2-isopropyloxy-7-hydroxyhept-2-enoate **4b** (60%), (Found: M^+, 230.1518. $C_{12}H_{22}O_4$ requires 230.1513); ν_{max} (film)/ cm^{-1} 3416, 2976, 2932, 1718, 1640, 1370, 1248, 1180 and 1106; Z isomer: δ_H (250 MHz; $CDCl_3$) 1.23 (6 H, d, *J* 6.2, $\underline{Me}_2CH$), 1.33 (3 H, t, *J* 7.1, $OCH_2\underline{Me}$), 1.50-1.61 (4 H, m, CH_2CH_2), 2.46 (2 H, q, *J* 7.3, CH_2), 3.64-3.69 (2 H, m, OCH_2), 4.00-4.27 (3 H, m, OCH_2Me and $Me_2C\underline{H}$) and 6.25 (1 H, t, *J* 7.9, =CH); OH not observed; E isomer: δ_H (250 MHz; $CDCl_3$) 1.23 (6 H, d, *J* 6.2, $\underline{Me}_2CH$), 1.32 (3 H, t, *J* 7.1, $OCH_2\underline{Me}$), 1.50-1.61 (4 H, m, CH_2CH_2), 2.38 (2 H, q, *J* 7.3, CH_2), 3.64-3.68 (2 H, m, OCH_2), 4.00-4.27 (3 H, m, OCH_2Me and $Me_2C\underline{H}$) and 5.48 (1 H, t, *J* 8.1, =CH); OH not observed; *m/z* (EI) 230 (M^+, 10%), 171 (100), 142 (21), 115 (32), 97 (35), 70 (62), 55 (52), and 41 (30).

General Procedure for Cyclisation of Hydroxy Enol Ethers **5**

A mixture of the hydroxy enol ether **4** (2.2 mmol) and camphorsulphonic acid (0.05 g, 0.22 mmol) was heated under reflux in benzene **(CAUTION)** (15 ml) for 2 h. After allowing to cool, ether (20 ml) and water (20 ml) were added. The aqueous layer was extracted with ether (3 x 20 ml) and the combined ethereal extracts washed with brine (20 ml) and dried ($MgSO_4$). The solvent was removed by evaporation and the residue chromatographed on silica (light petroleum-ether) to yield the respective cyclic enol ether.

Ethyl 4,5-dihydropyran-2-carboxylate **5a** (47%), (Found: M^+, 156.0786. $C_8H_{12}O_3$ requires 156.0786); ν_{max} (film)/ cm^{-1} 2980, 2932, 1722, 1644, 1368, 1300, 1264, 1222, 1190, 1112, 1070, 1056 and 924; δ_H (250 MHz; $CDCl_3$) 1.32 (3 H, t, *J* 7.1, $OCH_2\underline{Me}$), 1.62-1.91 (2 H, m, 5-CH_2), 2.16-2.23 (2 H, m, 4-CH_2), 4.12 (2 H, t, *J* 4.2, 6-CH_2), 4.26 (2 H, q, *J* 7.1, $OC\underline{H}_2Me$) and 6.07 (1 H, t, *J* 4.1, 3-H); *m/z* (EI): 156 (M^+, 22%), 127 (M^+-C_2H_5, 13), 111 (M^+-OC_2H_5, 18), 83 (43), 55 (100), 43 (38) and 39 (23).

Ethyl 4,5,6,7-tetrahydro-oxepin-2-carboxylate **5b** (81%), (Found: M^+, 170.0943. $C_9H_{14}O_3$ requires 170.0943.); ν_{max} (film)/ cm^{-1} 2932, 1724, 1642, 1368, 1316, 1296, 1270, 1222, 1126, 1088, 1052 and 1036; δ_H (250 MHz; $CDCl_3$) 1.31 (3 H, t, *J* 7.0, $OCH_2\underline{Me}$), 1.62-1.72 (2 H, m, 5- or 6-CH_2), 1.86-1.95 (2 H, m, 6- or 5-CH_2), 2.26-2.33 (2 H, m, 4-CH_2), 4.02 (2 H, t, *J* 5.4, 7-CH_2), 4.23 (2 H, q, *J* 6.9, $O\underline{CH_2}Me$) and 6.39 (1 H, t, *J* 6.2, 3-H); *m/z* (EI); 170 (M^+,32%), 141 (22), 125 (15), 97 (41), 69 (22), 55 (100) and 41 (60).

Diethyl phosphono-N-methoxy-N-methylcarbamoyl-diazomethane **11**

A solution of diethyl (N-methoxy-N-methyl-carbamoylmethyl)phosphonate (Aldrich) (2.1 g, 8.8 mmol) in THF (15 ml) was added dropwise to a mixture of potassium hydride (0.42 g, 10.5 mmol) (prewashed with light petroleum) and tosyl azide (2.1 g, 10.5 mmol) in THF (60 ml) at 0°C. The mixture was stirred for 3 h at 0°C and then allowed to come to room temperature overnight. Ether (50 ml) and water (50 ml) were added and the aqueous layer extracted with ether (3 x 50 ml). The combined ethereal extracts were washed with brine (100 ml) and dried ($MgSO_4$). The solvent was removed by evaporation and the residue chromatographed on silica (ether-ethyl acetate) to yield the *title compound* **11** (0.83 g, 36%), (Found: $M+H^+$, 266.0906. $C_8H_{16}N_3O_5P$+H requires 266.0906); ν_{max} (film)/ cm^{-1} 2980, 2112, 1636, 1408, 1368, 1258, 1180, 1026 and 978; δ_H (250 MHz; $CDCl_3$) 1.34-1.40 (6 H, m, $OCH_2\underline{Me}$), 3.22 (3 H, s, NMe), 3.71 (3 H, s, NOMe) and 4.15-4.26 (4 H, m, $O\underline{CH_2}Me$); δ_C (62.9 MHz; $CDCl_3$) 16.2 (2 C, $OCH_2\underline{Me}$), 33.6 (NMe), 61.5 (OMe), 63.6 (2 C, $O\underline{CH_2}Me$), 163. (C=O), diazo carbon not observed; *m/z* (EI) 266 (MH^+, 100%), 234 (12), 197 (28), 177 (32), 137 (18), 109 (49), and 42 (33).

General Procedure for the Preparation of t-Butyldimethylsiloxy-alkyloxyphosphonates **7**

A mixture of diazo compound **1**, **6**[17] or **11** (20 mmol), the t-butyldimethylsiloxy mono-protected diol (20 mmol) and dirhodium tetraacetate (88 mg, 0.20 mmol) was refluxed for 6-8 h in dry benzene **(CAUTION)** (30 ml). The solvent was removed by evaporation and the residue chromatographed on silica (light petroleum-ether) to yield the respective *title compounds*.

Ethyl 2-(3-t-butyldimethylsiloxy)propyloxy-2-diethylphosphonoacetate **7a** (66%), (Found: $M+H^+$, 413.2124. $C_{17}H_{37}O_7PSi$+H requires 413.2124); ν_{max} (film)/ cm^{-1} 2928, 2856, 1748, 1258, 1118, 1054, 1026, 974, 838 and 778; δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me_2}Si$, 0.83 (9 H, s, t-BuSi, 1.25-1.33 (9 H, m, $OCH_2\underline{Me}$), 1.80 (2 H, m, *J* 6.2, CH_2), 3.53-3.76 (4 H, m, $O\underline{CH_2}$ and $\underline{CH_2}OSi$), 4.11-4.30 (6 H, m, $O\underline{CH_2}Me$) and 4.26 (1 H, d, *J* 22.2, OCHP); *m/z* (EI): 355 (M^+-C_4H_9, 57%), 297 (90), 269 (60), 195 (51), 167 (100), 147 (51) and 75 (84).

Ethyl 2-(4-t-butyldimethylsiloxy)butyloxy-2-diethylphosphonoacetate **7b** (78%), (Found: $M+H^+$, 427.2281. $C_{18}H_{39}O_7PSi$+H requires 427.2281); ν_{max} (film)/ cm^{-1} 2952, 2932, 2856, 1748, 1258, 1100, 1026, 978, 836 and 776; δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me_2}Si$), 0.82 (9 H, s, t-BuSi), 1.23-1.33 (9 H, m, $OCH_2\underline{Me}$), 1.53-1.67 (4 H, m, CH_2CH_2), 3.47-3.66 (4 H, m, $O\underline{CH_2}$ and $\underline{CH_2}OSi$), 4.11-4.30 (6 H, m, $O\underline{CH_2}Me$) and 4.26 (1 H, d, *J* 22.8, OCHP); *m/z* (EI): 369 (M^+-C_4H_9, 39%), 241 (20), 167 (74), 139 (93), 109 (96) and 75 (100).

Ethyl 2-(5-t-butyldimethylsiloxy)pentyloxy-2-diethylphosphonoacetate **7c** (80%), (Found: M+H$^+$, 441.2437. $C_{19}H_{41}O_7PSiP$+H requires 441.2437); ν_{max} (film)/ cm^{-1} 2932, 2856, 1750, 1258, 1122, 1056, 1030, 976, 838 and 776; δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.85 (9 H, s, t-BuSi), 1.25-1.69 (15 H, m, $OCH_2\underline{Me}$ and $CH_2CH_2CH_2$), 3.42-3.66 (4 H, m, $OC\underline{H}_2$ and $C\underline{H}_2OSi$), 4.11-4.29 (6 H, m, $OC\underline{H}_2Me$) and 4.25 (1 H, d, J 21.5, OCHP); δ_C (62.9 MHz; $CDCl_3$) -5.3 ($SiMe_2$), 14.2 ($COOCH_2\underline{Me}$), 16.4 (2 C, $POCH_2\underline{Me}$), 22.2 ($OCH_2CH_2\underline{C}H_2$), 18.4 ($\underline{C}Me_3$), 29.3 ($SiOCH_2\underline{C}H_2$), 32.4 ($OCH_2\underline{C}H_2$), 61.7 ($COO\underline{C}H_2Me$), 63.0 ($SiOCH_2$), 63.5 (2 C, $PO\underline{C}H_2Me$), 73.0 (OCH_2), 76.9 (d, J 157, OCHP), 167.6 (C=O); m/z (EI): 383 (M^+-C_4H_9, 2%), 201 (13), 189 (16), 147 (65), 69 (100) and 41 (41).

Ethyl 2-(1-methyl-5-t-butyldimethylsiloxy)pentyloxy-2-diethyl-phosphono-acetate **7d** (85%), (Found: M+H$^+$, 455.2594. $C_{20}H_{43}O_7PSi$+H requires 455.2594); ν_{max} (film)/ cm^{-1} 2932, 2856, 1750, 1258, 1178, 1164, 1056, 1028, 974, 838 and 776; δ_H (250 MHz; $CDCl_3$) 0.0 (6 H,s, $\underline{Me}_2Si$), 0.89 (9 H, s, t-BuSi), 1.16-1.66 (18 H, m, Me, $CH_2CH_2CH_2$ and $OCH_2\underline{Me}$), 3.46-3.62 (3 H, m, OCH and OCH_2), 4.18-4.28 (6 H, m, $OC\underline{H}_2Me$) and 4.42 (1 H, d, J 19.8, OCHP); m/z (CI) 455 (MH^+, 100%), 397 (52), 241 (31), and 167 (6).

Ethyl 2-(6-t-butyldimethylsiloxy)hexyloxy-2-diethylphosphonoacetate **7e** (61%), (Found: M+H$^+$, 455.2594. $C_{20}H_{43}O_7PSi$+H requires 455.2594); ν_{max} (film)/ cm^{-1} 2932, 2856, 1750, 1258, 1102, 1052, 1026, 976, 838 and 776; δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.84 (9 H, s, t-BuSi), 1.25-1.34 (9 H, m, $OCH_2\underline{Me}$), 1.44-1.63 (8 H, m, $CH_2CH_2CH_2CH_2$), 3.44-3.63 (4 H, m, OCH_2 and CH_2OSi), 4.14-4.29 (6 H, m, $OC\underline{H}_2Me$) and 4.25 (1 H, d, J 21.4, OCHP); m/z (EI): 397 (M^+-C_4H_9, 3%), 241 (3), 167 (12), 118 (41), 90 (74), 63 (100), 51 (21) and 39 (84).

Diethyl 1-(4-t-butyldimethylsiloxy)butyloxy-2-oxopropanephosphonate **7f** (83%), (Found: M+H$^+$, 397.2175. $C_{17}H_{37}O_6PSi$+H requires 397.2175); ν_{max} (film)/ cm^{-1} 2952, 2932, 2856, 1736, 1254, 1094, 1032, 982, 838 and 776; δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.84 (9 H, s, t-BuSi), 1.27-1.35 (6 H, m, $OCH_2\underline{Me}$), 1.42-1.57 (4 H, m, CH_2CH_2), 2.38 (3 H, s, Ac), 3.53-3.63 (4 H, m, OCH_2 and CH_2OSi) and 4.10-4.19 (5 H, m, $OC\underline{H}_2Me$ and OCHP); m/z (EI): 339 (M^+-C_4H_9, 6%), 187 (8), 147 (16), 105 (75), 75 (100) and 41 (20).

Diethyl 1-(5-t-butyldimethylsiloxy)pentyloxy-2-oxopropanephosphonate **7g** (67%), (Found: M+H$^+$, 411.2330. $C_{18}H_{39}O_6PSi$+H requires 411.2332); ν_{max} (film)/ cm^{-1} 2932, 2856, 1256, 1100, 1052, 1030, 974, 836, 778 and 732; δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.89 (9 H, s, t-BuSi), 1.30-1.49 (12 H, m, $OCH_2\underline{Me}$ and $CH_2CH_2CH_2$), 2.31 (3 H, s, Ac), 3.53-3.62 (4 H, m, OCH_2 and CH_2OSi) and 4.08-4.23 (5 H, m, $OC\underline{H}_2Me$ and OCHP); m/z (CI) 411 (MH^+, 100%), 353 (11), 325 (8), 297 (52), 211 (10), and 167 (15).

Diethyl 1-(N-methoxy-N-methyl-carbamoyl)-1-(5-t-butyldimethylsiloxy)-pentyloxy-methanephosphonate **12a** (32%); ν_{max} (film)/ cm^{-1} 2936, 2856, 1672, 1470, 1386, 1256, 1164, 1096, 1052, 978, 836 and 776; δ_H (250 MHz; $CDCl_3$) 0.0 (6 H, s, $\underline{Me}_2Si$), 0.89 (9 H, s, t-BuSi), 1.30-1.71 (12 H, m, $CH_2CH_2CH_2$ and

$OCH_2\underline{Me}$), 3.21 (3 H, br s, NMe), 3.45-3.62 (4 H, m, OCH_2 and OCH_2Si), 3.78 (3 H, s, NOMe) and 4.16-4.27 (5 H, m, $OC\underline{H}_2Me$ and OCHP); satisfactory analytical data could not be obtained.

General Procedure for the Preparation of Hydroxyalkyloxy-phosphonates **8**

A mixture of the insertion product **7** (15 mmol), water (25 ml), THF (25 ml) and glacial acetic acid (70 ml) was heated at between 45-50°C for 1 h (the acetyl derivatives **7f**, **7g** were heated for only 20 min). After allowing to cool, dichloromethane (70 ml) and water (70 ml) were added. The aqueous layer was extracted with dichloromethane (3 x 50 ml) and the combined organic extracts washed successively with saturated sodium bicarbonate (5 x 50 ml) and brine (50 ml) and then dried ($MgSO_4$). The solvent was removed by evaporation and the residue chromatogaphed on silica (ethyl acetate-ether) to yield the *title compounds.*

Ethyl 2-(3-hydroxy)propyloxy-2-diethylphosphonoacetate **8a** (70%), (Found: $M+H^+$, 299.1260. $C_{11}H_{23}O_7P+H$ requires 299.1260); ν_{max} (film)/ cm^{-1} 3428, 2980, 2932, 1746, 1254, 1164, 1126, 1048, 1024 and 978; δ_H (250 MHz; $CDCl_3$) 1.29-1.43 (9 H, m, $OCH_2\underline{Me}$), 1.80-1.95 (2 H, m, CH_2), 3.77-3.83 (4 H, m, OCH_2 and $C\underline{H}_2OH$) and 4.14-4.35 (7 H, m, $OC\underline{H}_2Me$ and OCHP); OH not observed; *m/z* (EI): 299 (MH^+, 10%), 197 (32), 111 (53), 87 (100), 81 (31), 65 (46), 59 (31) and 41 (31).

Ethyl 2-(4-hydroxy)butyloxy-2-diethylphosphonoacetate **8b** (90%), (Found: $M+H^+$, 313.1416. $C_{12}H_{25}O_7P+H$ requires 313.1416); ν_{max} (film)/ cm^{-1} 3428, 2984, 2936, 1746, 1252, 1188, 1164, 1126, 1052 and 978; δ_H (250 MHz; $CDCl_3$) 1.29-1.38 (9 H, m, $OCH_2\underline{Me}$), 1.65-1.80 (4 H, m, CH_2CH_2), 3.57-3.70 (4 H, m, OCH_2 and $C\underline{H}_2OH$) 4.21-4.34 (6 H, m, $OC\underline{H}_2Me$) and 4.31 (1 H, d, *J* 18.8, OCHP); OH not observed; *m/z* (EI): 239 (M^+-OC_4H_9, 2%), 197 (22), 171 (22), 152 (27), 111 (31), 65 (31), 55 (76) and 43 (100).

Ethyl 2-(5-hydroxy)pentyloxy-2-diethylphosphonoacetate **8c** (83%), (Found: $M+H^+$, 327.1573. $C_{13}H_{27}O_7P+H$ requires 327.1573); ν_{max} (film)/ cm^{-1} 3436, 2936, 1746, 1256, 1186, 1164, 1126, 1054, 1026 and 980; δ_H (250 MHz; $CDCl_3$) 1.32-1.42 (9 H, m, $OCH_2\underline{Me}$), 1.44-1.70 (6 H, m, $CH_2CH_2CH_2$), 3.47-3.73 (4 H, m, OCH_2 and $C\underline{H}_2OH$) and 4.15-4.34 (6 H, m, $OC\underline{H}_2Me$) and 4.29 (1 H, d, *J* 21.6, OCHP); OH not observed; δ_C (62.9 MHz; $CDCl_3$) 13.8 ($COOCH_2\underline{Me}$), 16.1 (2 C, $POCH_2\underline{Me}$), 21.8 ($OCH_2CH_2\underline{C}H_2$), 28.8 ($HOCH_2\underline{C}H_2$), 32.0 ($OCH_2\underline{C}H_2$), 61.5 ($COO\underline{C}H_2Me$), 61.8 ($CH_2OH$), 63.4 (2 C, $PO\underline{C}H_2Me$), 72.8 (OCH_2), 76.3 (d, OCHP), 167.2 (C=O); *m/z* (EI): 239 (M^+-OC_5H_{11}, 5%), 197 (35), 152 (24), 111 (34), 75 (100), 69 (60), 55 (24) and 41 (74).

Ethyl 2-(1-methyl-5-hydroxy)pentyloxy-2-diethylphosphonoacetate **8d** (74%), (Found: $M+H^+$, 341.1729. $C_{14}H_{29}O_7P+H$ requires 341.1729); ν_{max} (film)/ cm^{-1} 3436, 2980, 2932, 1748, 1258, 1180, 1164, 1112, 1050, 1028 and 978 cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.52 (3 H, d, *J* 6.1, Me), 1.27-1.37 (9 H, m, $OCH_2\underline{Me}$), 1.46-1.59 (6 H, m, $CH_2CH_2CH_2$), 3.61-3.65 (3 H, m, OCH and $C\underline{H}_2OH$), 4.17-4.31 (6 H, m, $OC\underline{H}_2Me$) and 4.43 (1 H, d, *J* 19.4, OCHP); OH not observed; *m/z* (EI): 341 (M^+, 4%), 197 (64), 167 (71), 139 (71), 111 (100), 65 (79), 55 (88) and 41 (76).

Ethyl 2-(6-hydroxy)hexyloxy-2-diethylphosphonoacetate **8e** (90%), (Found: $M+H^+$, 341.1729. $C_{14}H_{29}O_7P+H$ requires 341.1729); ν_{max} (film)/ cm^{-1} 3436, 2932, 2864, 1738, 1250, 1184, 1166, 1128, 1056, 976 and 732; δ_H (250 MHz; $CDCl_3$) 1.29-1.69 (17 H, m, $OCH_2\underline{Me}$ and $CH_2CH_2CH_2CH_2$), 3.50-

3.69 (4 H, m, OCH_2 and CH_2OH), 4.15-4.33 (7 H, m, OCH_2Me and OCHP); OH not observed; *m/z* (EI): 239 (M^+-OC_6H_{13}, 8%), 224 (28), 197 (60), 152 (50), 111 (42), 83 (53), 65 (37), 55 (100) and 41 (84).

Diethyl 1-(4-hydroxy)butyloxy-2-oxopropanephosphonate **8f** (67%), (Found: $M+H^+$, 283.1310. $C_{11}H_{23}O_6P+H$ requires 283.1311); ν_{max} (film)/ cm^{-1} 3428, 2940, 1722, 1250, 1164, 1104, 1052 and 974; δ_H (250 MHz; $CDCl_3$) 1.32-1.39 (6 H, m, OCH_2Me), 1.66-1.75 (4 H, m, CH_2CH_2), 2.32 (3 H, s, Ac), 3.62-3.71 (4 H, m, OCH_2 and CH_2OH) and 4.13-4.26 (5 H, m, OCH_2Me and OCHP); OH not observed; *m/z* (CI): 281 (M^+-H, 100%), 263 (4), 220 (2), 195 (3), 172 (6), 156 (7), 144 (31) and 127 (48).

Diethyl (5-hydroxy)pentyloxy-2-oxopropanephosphonate **8g** (87%), (Found: $M+H^+$, 297.1470. $C_{212}H_{25}O_6P+H$ requires 297.1467); ν_{max} (film)/ cm^{-1} 3420, 2936, 1722, 1252, 1102, 1050 and 974; δ_H (250 MHz; $CDCl_3$) 1.31-1.39 (6 H, m, OCH_2Me), 1.44-1.73 (6 H, m, $CH_2CH_2CH_2$), 2.31 (3 H, s, Ac), 3.60 (2 H, t, *J* 6.3, OCH_2), 3.65 (2 H, t, *J* 6.1, OCH_2), and 4.13-4.27 (5 H, m, OCH and OCH_2Me), OH not observed; *m/z* (EI) 297 (MH^+, 35%), 254 (17), 211 (19), 193 (23), 167 (100), 139 (58). 111 (69), 81 (23), and 69 (44).

General Procedure for the Preparation of Alkyloxyaldehyde-phosphonates **9**

A solution of the alcohol **8** (3.07 mmol) in dichloromethane (5 ml) was added to a suspension of pyridinium dichromate (PDC) (1.73 g, 4.6 mmol) in dichloromethane (15 ml). After stirring for 20-24 h, ether (15 ml) was added and the mixture then stirred for a further 30 min. The reaction mixture was filtered through a pad of silica under suction. The silica was washed well with ether and the filtrate and washings were then combined. The solvent was removed by evaporation to give the crude aldehyde **9** which was used directly in the next step without further purification.

General Procedure for Intramolecular Wadsworth-Emmons Olefination Reaction of Phosphonate Aldehydes **9** *to give Cyclic Ethers* **13**

A solution of the aldehyde **9** (0.30 g, 0.93 mmol) in THF (100 ml) was added dropwise over 30 min to a suspension of sodium hydride (80%, 56 mg, 1.85 mmol) in THF (200 ml) at 0°C. After stirring for 2 h at 0°C, ether (200 ml) and water (200 ml) were added.The aqueous layer extracted with ether (2 x 200 ml) and the combined ethereal extracts washed with brine (200 ml) and then dried ($MgSO_4$). The solvent was removed by evaporation and the residue chromatographed on silica (light petroleum-ether) to yield the respective cyclic enol ethers **13**.

Ethyl 3,4-dihydrofuran-2-carboxylate **13a** (50%), (Found: M^+, 142.0630. $C_7H_{10}O_3$ requires 142.0630); ν_{max} (film)/ cm^{-1} 2980, 2924, 1726, 1628, 1378, 1320, 1266, 1210, 1174, 1124, 952, 936 and 738; δ_H (250 MHz; $CDCl_3$) 1.33 (3 H, t, *J* 7.2, OCH_2Me), 2.80 (2 H, dt, *J* 3.0, 9.8, 4-CH_2), 4.27 (2 H, q, *J* 7.2, OCH_2Me), 4.50 (2 H, t, *J* 9.8, 5-CH_2) and 5.97 (1 H, t, *J* 3.0, 3-H); *m/z* (EI) 142 (M^+, 10%),97 (23), 91 (24), 83 (15), 69 (40), 55 (43) and 41 (100).

Ethyl 4,5-dihydropyran-2-carboxylate **13b** (46%), same compound as **5a**, data given previously.

Ethyl 4,5,6,7-tetrahydro-oxepin-2-carboxylate **13c** (43%), same compound as **5b**, data given previously.

Ethyl 7-methyl-4,5,6,7-tetrahydro-oxepin-2-carboxylate **13d** (47%), (Found: M^+, 184.1099. $C_{10}H_{16}O_3$ requires 184.1099); ν_{max} (film)/ cm^{-1} 2972, 2928, 1728, 1644, 1372, 1318, 1268, 1222 and 1120; δ_H (250 MHz; $CDCl_3$) 1.30 (3 H, t, *J* 7.1, $OCH_2\underline{Me}$), 1.35 (3 H, d, *J* 6.4, Me), 1.50-1.92 (4 H, m, 5-CH_2, 6-CH_2), 2.21-2.30 (2 H, m, 4-CH_2), 3.85-3.93 (1 H, m, 7-H), 4.20 (2 H, q, *J* 7.1, $O\underline{CH_2}Me$) and 6.39 (1 H, t, *J* 5.9, 3-H); δ_C (62.9 MHz; $CDCl_3$) 14.3 (Me), 22.3 ($OCH_2\underline{Me}$), 24.0 (5-C), 26.1 (6-C), 38.2 (4-C), 60.9 ($O\underline{C}H_2Me$), 79.5 (7-C), 122.5 (3-C), 148.7 (2-C) and 164.6 (C=O); *m/z* (EI); 184 (M^+, 26%), 105 (24), 83 (34), 69 (24), 55 (100) and 41 (29).

2-Acetyl-4,5-dihydropyran **13f** (46%), (Found: M^+, 126.0681. $C_7H_{10}O_2$ requires 126.0681); ν_{max} (film)/ cm^{-1} 2932, 1698, 1684, 1626, 1356, 1290, 1276, 1260, 1220, 1078, 1046, 912 and 624; δ_H (250 MHz; $CDCl_3$) 1.81-1.88 (2 H, m, 5-CH_2), 2.21-2.28 (2 H, m, 4-CH_2), 2.28 (3 H, s, Ac), 4.09 (2 H, t, *J* 5.3, 6-CH_2) and 5.99 (1 H, t, *J* 4.3, 3-H); δ_C (62.9 MHz; $CDCl_3$) 20.8 (5-C), 21.5 (4-C), 25.3 (Me), 66.3 (6-C), 110.8 (3-C), 152.0 (2-C) and 194.8 (C=O); *m/z* (EI) 126 (M^+, 2%), 69 (25), 55 (29) and 41 (100).

2-Acetyl-4,5,6,7-tetrahydro-oxepin **13g** (32%),(Found: $M+H^+$, 141.0916. $C_8H_{12}O_2$+H requires 141.0916); ν_{max} (film)/ cm^{-1} 2932, 1698, 1684, 1626, 1356, 1310, 1264, 1250, 1220, 1120, 1082 and 612; δ_H (250 MHz; $CDCl_3$) 1.62-1.72 (2 H, m, 5-CH_2), 1.87-1.96 (2 H, m, 6-CH_2), 2.25-2.38 (2 H, m, 4-CH_2), 2.27 (3 H, s, Ac), 3.99 (2 H, t, *J* 5.3, 7-CH_2) and 6.27 (1 H, t, *J* 6.1, 3-H); δ_C (62.9 MHz; $CDCl_3$) 24.7 (5-C), 26.1 (MeCO), 26.3 (5-C), 31.4 (4-C), 72.7 (7-C), 120.0 (3-C), 156.8 (2-C) and 196.6 (C=O); *m/z* (CI) 158 (M+NH_4^+, 100%), 154 (97), 139 (13), 127 (35), and 87 (22).

General Method for the Preparation of Alkynyloxy Phosphonates **10**

A mixture of diazo compound **1** or **11** (8 mmol), the alkynol (8 mmol) and dirhodium tetraacetate (35 mg, 0.08 mmol) was refluxed for 2-5 h in benzene (**CAUTION**) (30 ml). The solvent was removed by evaporation and the residue chromatographed on silica (light petroleum-ether) to yield the respective phosphonates.

Ethyl 2-(3-butyn-1-oxy)-2-diethylphosphonoacetate **10a** (61%), (Found: $M+H^+$, 293.1154. $C_{12}H_{21}O_6P$+H requires 293.1154); ν_{max} (film)/ cm^{-1} 3280, 2980, 2936, 2908, 2116, 1744, 1392, 1368, 1264, 1186, 1162, 1128, 1056, 978 and 632; δ_H (250 MHz; $CDCl_3$) 1.24-1.39 (9 H, m, $OCH_2\underline{Me}$), 1.98 (1 H, t, *J* 2.6, C≡CH), 2.56 (2 H, dt, *J* 2.6, 6.9, ≡CCH_2), 3.65-3.85 (2 H, m, OCH_2), 4.21-4.36 (6 H, m, $O\underline{CH_2}Me$) and 4.40 (1 H, d, *J* 18.8, OCHP); *m/z* (EI) 293 (MH^+, 100%), 269 (23), 224 (71), 197 (62), 152 (48), 133 (44), 111 (65), and 83 (44).

Ethyl 2-(4-pentyn-1-oxy)-2-diethylphosphonoacetate **10b** (74%), (Found: $M+H^+$, 307.1311. $C_{13}H_{23}O_6P$+H requires 307.1311); ν_{max} (film)/ cm^{-1} 3284, 2980, 2112, 1746, 1264, 1196, 1164, 1128, 1024 and 976; δ_H (250 MHz; $CDCl_3$) 1.25-1.39 (9 H, m, $OCH_2\underline{Me}$), 1.81-1.91 (2 H, m, CH_2), 1.95 (1 H, t, *J* 2.7, C≡CH), 2.35 (2 H, dt, *J* 2.7, 6.9, ≡CCH_2), 3.59-3.78 (2 H, m, OCH_2) and 4.22-4.35 (7 H, m, $O\underline{CH_2}Me$ and OCHP); δ_C (62.9 MHz; $CDCl_3$) 14.1 ($COOCH_2\underline{Me}$), 15.0 ($OCH_2\underline{C}H_2$), 16.4 (2 C,

$POCH_2\underline{Me}$), 28.5 ($\underline{C}H_2C{\equiv}CH$), 61.8 ($COO\underline{C}H_2Me$), 63.7 (2 C, $PO\underline{C}H_2Me$), 68.8 ($C{\equiv}\underline{C}H$), 71.3 (OCH_2), 77.1 (d, *J* 157, OCHP), 83.5 ($\underline{C}{\equiv}CH$), 167.4 (C=O); *m/z* (CI) 307 (MH^+, 100%), 224 (34), 197 (23), 152 (33), 121 (15), 97 (13), and 67 (13).

Ethyl 2-(5-hexyn-1-oxy)-2-diethylphosphonoacetate **10c** (50%), (Found: $M+H^+$, 321.1467. $C_{14}H_{25}O_6P$+H requires 321.1467); ν_{max} (film)/ cm^{-1} 3280, 2980, 2112, 1746, 1260, 1164, 1128, 1098, 1052, 1026 and 976; δ_H (250 MHz; $CDCl_3$) 1.29-1.38 (9 H, m, $OCH_2\underline{Me}$), 1.65-1.77 (4 H, m, CH_2CH_2), 1.95 (1 H, t, *J* 2.6, $C{\equiv}CH$), 2.24 (2 H, dt, *J* 2.6, 6.9, ${\equiv}CCH_2$), 3.57-3.67 (2 H, m, OCH_2) and 4.19-4.34 (7 H, m, $OC\underline{H}_2Me$ and OCHP); δ_C (62.9 MHz; $CDCl_3$) 14.2 ($COOCH_2\underline{Me}$), 16.4 (2 C, $POCH_2\underline{Me}$), 18.0 ($OCH_2CH_2\underline{C}H_2$), 24.9 ($OCH_2\underline{C}H_2CH_2$), 28.4 ($\underline{C}H_2C{\equiv}CH$), 61.8 ($COO\underline{C}H_2Me$), 63.7 (2 C, $PO\underline{C}H_2Me$), 68.6 ($C{\equiv}\underline{C}H$), 72.4 (OCH_2), 77.0 (d, *J* 157, OCHP), 84.1 ($\underline{C}{\equiv}CH$), 167.5 (C=O); *m/z* (EI) 321 (MH^+, 25%), 224 (96), 197 (88), 152 (87), 111 (100) and 81 (63).

Diethyl 1-(N-methoxy-N-methyl-carbamoyl)-1-(5-hexyn-1-oxy)methane-phosphonate **12b** (30%), (Found: $M+H^+$, 336.1576. $C_{14}H_{26}NO_6P$+H requires 336.1576); ν_{max} (film)/ cm^{-1} 3284, 2980, 2936, 2112, 1670, 1442, 1388, 1258, 1166, 1124, 1052, 978 and 624; δ_H (250 MHz; $CDCl_3$) 1.30-1.39 (6 H, m, $OCH_2\underline{Me}$), 1.60-1.66 (4 H, m, CH_2CH_2), 1.93 (1 H, t, *J* 2.6, $C{\equiv}CH$), 2.23 (2 H, dt, *J* 2.6, 6.9, ${\equiv}CCH_2$), 3.26 (3 H, br s, NMe), 3.47-3.63 (2 H, m, OCH_2), 3.78 (3 H, s, NOMe) and 4.18-4.28 (5 H, m, $OC\underline{H}_2Me$ and OCHP); *m/z* (EI) 366 (MH^+, 19%), 304 (34), 179 (91), 139 (63), 111 (100), 81 (72), 65 (44), and 41 (44).

General procedure for the Preparation of Methyl Ketone Phosphonates **9h-9j**

A mixture of the alkynyloxy phosphonate **10** (0.5 g, 1.56 mmol), mercury (II) sulphate (36 mg, 0.12 mmol), THF (5 ml) and water (10 ml) was heated at 60°C for 1 h. Ether (20 ml) was added and the aqueous layer extracted with ether (3 x 20 ml). The combined ethereal extracts were washed with brine (50 ml) and dried ($MgSO_4$). The solvent was removed by evaporation to give the crude ketone phosphonate which was used directly in the next step without further purification.

General procedure for Intramolecular Wadsworth-Emmons Cyclisation Reaction of Ketones **9h-9j**

A solution of the methyl ketone phosphonate (**9h-9j**) (0.63 mmol) in THF (10 ml) was added dropwise over 20 min to a suspension of sodium hydride (80%, 21 mg, 0.69 mmol) in dry THF (50 ml) at 0°C. The reaction was allowed to come to room temperature overnight. Ether (50 ml) and water (30 ml) were added and the aqueous layer extracted with ether (3 x 30 ml). The combined ethereal extracts were washed with brine (200 ml) and then dried ($MgSO_4$). The solvent was removed by evaporation and the residue chromatographed on silica (light petroleum-ether) to yield the respective cyclic enol ethers **13h-13j**.

Ethyl 3-methyl-4,5-dihydrofuran-2-carboxylate **13h** (23%), (Found: M^+, 156.0786. $C_8H_{12}O_3$ requires 156.0786); ν_{max} (film)/ cm^{-1} 2980, 1714, 1658, 1374, 1332, 1266, 1174, 1140 and 1078; δ_H (250 MHz; $CDCl_3$) 1.34 (3 H, t, *J* 7.2, $OCH_2\underline{Me}$), 2.07 (3 H, t, *J* 1.6, Me), 2.77 (2 H, m, 4-CH_2), 4.28 (2 H, q, *J* 7.2, $OC\underline{H}_2Me$) and 4.34 (2 H, t, *J* 9.7, 5-CH_2); *m/z* (EI) 156 (M^+, 65%), 127 (100), 111 (53), 83 (33), 55 (94), and 43 (30).

Ethyl 3-methyl-4,5-dihydropyran-2-carboxylate **13i** (40%), (Found: M^+, 170.0940. $C_9H_{14}O_3$ requires 170.0943); ν_{max} (film)/ cm^{-1} 2976, 2932, 1714, 1640, 1370, 1284, 1228, 1208, 1194, 1152, 1094 and 1024; δ_H (250 MHz; $CDCl_3$) 1.34 (3 H, t, *J* 7.2, $OCH_2\underline{Me}$), 1.82-1.91 (2 H, m, 5-CH_2), 2.02 (3 H, t, *J* 1.1, Me), 2.15 (2 H, m, 4-CH_2), 4.01 (2 H, t, *J* 5.1, 6-CH_2) and 4.27 (2 H, q, *J* 7.1, $O\underline{CH_2}Me$); *m/z* (EI) 170 (M^+, 70%), 141 (100), 125 (32), 97 (35), 69 (49), 51 (63), and 41 (72).

Ethyl 3-methyl-4,5,6,7-tetrahydro-oxepin-2-carboxylate **13j** (47%), (Found: $M+H^+$, 185.1178. $C_{10}H_{16}O_3$+H requires 185.1178); ν_{max} (film)/ cm^{-1} 2932,1710, 1638, 1292, 1270, 1222, 1140, 1094, 1080, 1064 and 756; δ_H (250 MHz; $CDCl_3$) 1.31 (3 H, t, *J* 7.1, $OCH_2\underline{Me}$), 1.52-1.61 (2 H, m, 6-CH_2), 1.83-1.92 (2 H, m, 5-CH_2), 2.11 (3 H, s, Me), 2.32-2.37 (2 H, m, 4-CH_2), 3.86 (2 H, t, *J* 5.3, 7-CH_2) and 4.22 (2 H, q, *J* 7.1, $O\underline{CH_2}Me$); *m/z* (CI) 184 (M^+, 9%), 183 (83), 155 (45), 127 (100), 88 (22), and 68 (21).

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