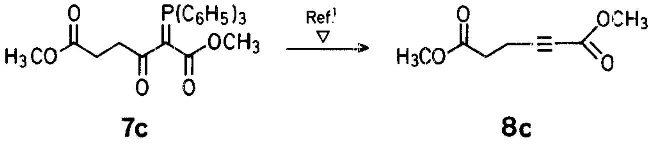
Synthesis of Dialkyl Hex-2-yne-1,6-dioates and Hept-2-yne-1,7-dioates

A. D. Abell, G. W. Heinicke, R. A. Massy-Westropp*

Department of Organic Chemistry, University of Adelaide, Adelaide 5001, Australia

The title compounds are prepared by flash vacuum pyrolysis of the corresponding phosphoranes, obtained from succinic or glutaric anhydrides and ethoxycarbonylmethylenetriphenylphosphorane.

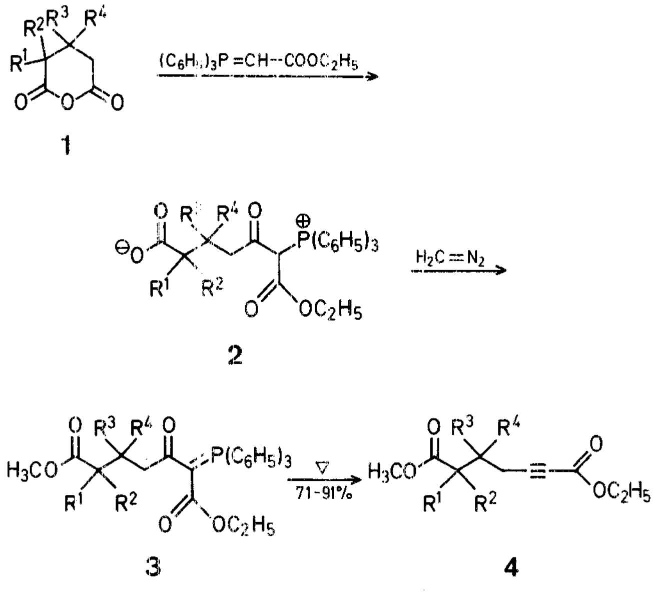
Few reports have appeared concerning the synthesis of dialkyl hex-2-ynedioates and hept-2-ynedioates. An early attempt at the preparation of dimethyl hex-2-ynedioate (**8c**) by pyrolysis of the phosphorane **7c**[1] (Schema **A**) was of little synthetic value both because of the low yield and the problem of isomerisation of the alkyne to the corresponding isomeric dienes. Dimethyl hex-2-ynedioate (**8c**) and two alkylated derivatives were prepared in low yields, by methods involving standard acetylene chemistry[2], for a study of their reactions with sodium methoxide. In particular, **8c** was prepared by oxidation and methylation of hex-2-yne-1,6-diol[3], a substrate which has also been employed for the synthesis of the corresponding *cis*- and *trans*-hex-2-ene-1,6-diols[4,5].



Scheme **A**

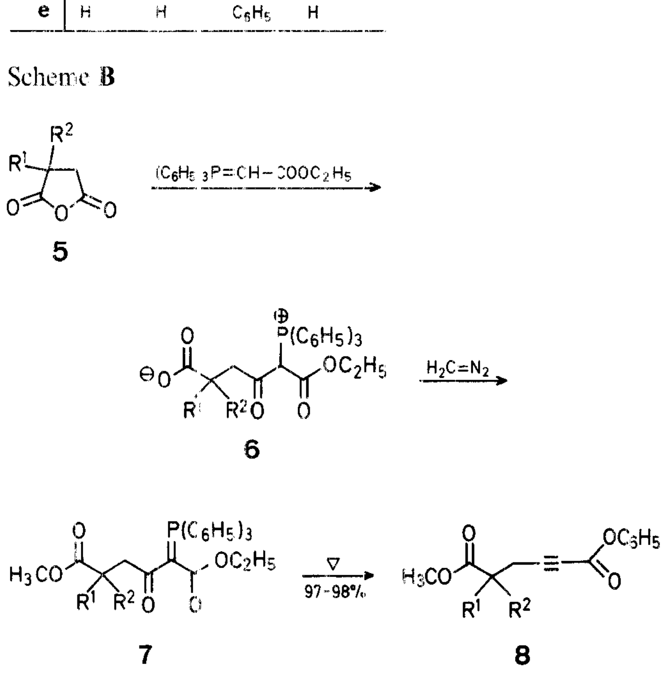
Acetylene derivatives are widely used in synthesis and, in a search for a general synthesis of functionalised alkynes, we have studied the pyrolysis of suitably substituted phosphoranes. In this paper we describe a short and efficient method for the preparation of dialkyl hex-2-yne-1,6-dioates and hept-2-yne-1,7-dioates from succinic and glutaric anhydrides.

The general reaction of the stabilised ylid, ethoxycarbonylmethylenetriphenylphosphorane with anhydrides **1**, **5**, **9** is known[6,7] to yield the corresponding acylated products **2**, **6**, **10**, which, on methylation with diazomethane, gave the desired phosphoranes **3**, **7**, **11**. Flash pyrolysis (500–540 °C in vacuo; quartz tube) of the phosphoranes gave the dialkyl hept-2-yne-1,7-dioates **4a–e** (Scheme **B**), dialkyl hex-2-yne-1,6-dioates **8a,b** (Scheme **C**), and the dialkyl 5-oxahept-2-yne-1,7-dioate **12** (Scheme **D**).



1-4	R1	R2	R3	R4
a	H	H	H	H
b	CH3	CH3	H	H
c	H	H	CH3	H
d	H	H	CH3	CH3
e	H	H	C6H5	H

Scheme **B**



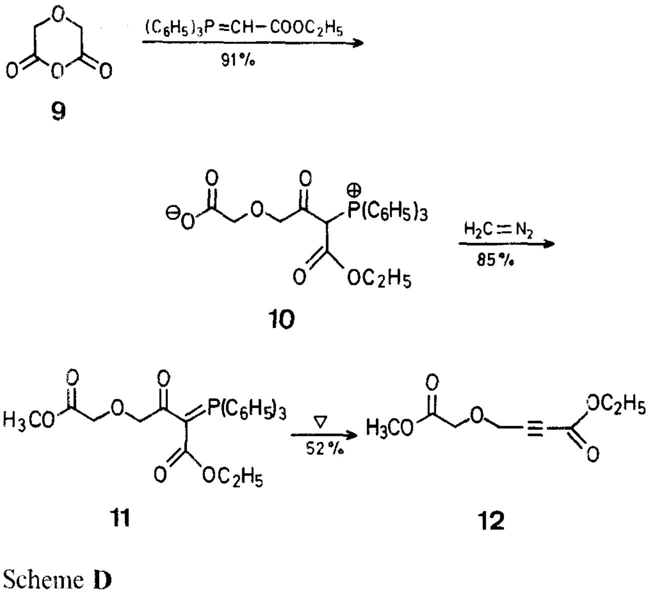
5-8	R1	R2
a	H	H
b	CH3	CH3

Scheme **C**

Table. Alkynes **4a**–**e**, **8a,b** and **12** prepared

Substrate	Tube temp. [°C]	Rate of heating of substrate flask [°C] over [min]	Vacuum [torr]	Product	b.p. (block) [°C]/torr	Yield [%]	Molecular Formula[a]	I.R. (Film) ν [cm]	¹H-N.M.R. (Solvent/TMS) ϱδ [ppm]
3a	520°	20–300° over 60	0.01	**4a**	74–76°/0.01	87	$C_{10}H_{14}O_4$ (198.2)	2250, 1745, 1715	CCl_4: 1.31 (t, 3H, J = 7 Hz); 1.68–2.18 (m, 4H); 2.46 (t, 2H, J = 6 Hz); 3.68 (s, 3H); 4.17 (q, 2H, H = 7 Hz)
3b	500°	20–250° over 20	0.008	**4b**	74–80°/0.02	78	$C_{12}H_{18}O_4$ (226.3)	2250, 1740, 1715	$CDCl_3$: 1.19 (s, 6H); 1.28 (t, 3H, J = 7 Hz); 1.66–2.01 (m, 2H); 2.16–2.51 (m, 2H); 3.69 (s, 3H); 4.21 (q, 2H, J = 7 Hz)
3c	530°	20–300° over 60	0.01	**4c**	71–73°/0.005	91	$C_{11}H_{16}O_4$ (212.3)	2250, 1740, 1710	CCl_4: 1.30 (t, 3H, J = 7 Hz); 1.06 (d, 3H); 2.36 (m, 4H); 3.67 (s, 3H); 4.21 (q, 2H, J = 7 Hz)
3d	540°	20–300° over 50	0.01	**4d**	57–60°/0.01	71	$C_{12}H_{18}O_4$ (226.3)	2230, 1740, 1705	CCl_4: 1.12 (s, 6H); 1.29 (t, 3H, J = 7 Hz); 2.30 (s, 2H); 2.43 (s, 2H); 3.61 (s, 3H); 4.15 (q, 2H, J = 7 Hz)
3e	510°	20–300° over 80	0.002	**4e**	87–89°/0.001	88	$C_{16}H_{18}O_4$ (274.3)	2310, 1730, 1702	$CDCl_3$: 1.34 (t, 3H, J = 7 Hz); 2.61–2.93 (m, 4H); 3.55 (m, 1H); 3.66 (s, 3H); 4.27 (q, 2H, J = 7 Hz); 7.32 (s, 5H)
7a	530°	20–300° over 40	0.02	**8a**	72–74°/0.005	98	$C_9H_{12}O_4$ (184.2)	2270, 1740, 1710	CCl_4: 1.28 (t, 3H, J = 7 Hz); 2.63 (s, 4H); 3.70 (s, 3H); 4.21 (q, 2H, J = 7 Hz)
7b	520°	20–300° over 40	0.005	**8b**	70–72°/0.01	97	$C_{11}H_{16}O_4$ (212.3)	2245, 1740, 1715	$CDCl_3$: 1.33 (s, 6H); 1.33 (t, 3H, J = 7 Hz); 2.64 (s, 2H); 3.76 (s, 3H); 4.29 (q, 2H, J = 7 Hz)
11	515°	20–300° over 60	0.008	**12**	72–74°/0.008	52	$C_9H_{12}O_5$ (200.2)	2245, 1750, 1710	$CDCl_3$: 1.27 (t, 3H, J = 7 Hz); 3.79 (s, 3H); 4.22 (s, 2H); 4.26 (q, 2H, J = 7 Hz); 4.46 (s, 2H)

[a] Satisfactory microanalyses obtained: C ±0.32, H ±0.34.



Scheme D

It should be noted that the closely related thermolysis of acylalkoxycarbonyl-alkylidenetriphenylphosphoranes to give acetylenes is well known[8].

Melting points are uncorrected and were determined with a Reichert apparatus. ¹H-N.M.R. spectra were recorded on a Varian T 60 spectrometer. I.R. spectra were recorded on a Jasco IRA-1 spectrometer.

1-Ethoxycarbonyl-2-oxoalkylidenetriphenylphosphoranes 3,7, and 11:

1-Ethoxycarbonyl-5-methoxycarbonyl-2-oxopentylidenetriphenylphosphorane (**3a**) is prepared by the method reported earlier[6]; m.p. 96–97°C (Lit.[6], m.p. 96–97°C).

1-Ethoxycarbonyl-4-methoxycarbonyl-2-oxobutylidenetriphenylphosphorane (**7a**) is prepared from **5a** by the method described[7]; m.p. 98–99°C (Lit.[7], m.p. 97–98°C).

1-Ethoxycarbonyl-5-methoxycarbonyl-5,5-dimethyl-2-oxopentylidenetriphenylphosphorane (**3b**) is prepared by methylation of 1-ethyl 6,6-dimethyl-3-oxo-2-(triphenylphosphonio)-heptanedioate[6] (**2b**; 600 mg, 1.22 mmol) dissolved in tetrahydrofuran (10 ml). with 20% excess of an ethereal solution of diazomethane at 20°C. The solvent is removed and the residue crystallised from ether/light petroleum; yield: 483 mg (79%); m.p. 92–94°C.

$C_{30}H_{33}O_5P$	calc.	C 71.41	H 6.59
(504.2)	found	71.57	6.40

I.R. (Nujol): ν = 1720, 1640, 1555 cm⁻¹.

¹H-N.M.R. (CDCl₃/TMS): δ = 0.65 (t, J = 7 Hz, 3H); 1.09 (s, 6H); 1.70–1.96 (m, 2H); 2.76–3.05 (m, 2H); 3.52–3.92 (m, 5H); 7.25–7.92 ppm (m, 15H).

1-Ethoxycarbonyl-5-methoxycarbonyl-4-methyl-2-oxopentylidenetriphenylphosphorane (**3c**) is prepared from 1-ethyl 5-methyl-3-oxo-2-(triphenylphosphonio)-heptanedioate (**2c**)[6] with diazomethane as described above for **2b**; yield: 89%; m.p. 102–103°C (ether/light petroleum).

$C_{29}H_{31}O_5P$	calc.	C 71.01	H 6.37
(490.2)	found	70.98	6.31

I.R. (Nujol): $\nu = 1725, 1650, 1545, 1100\ cm^{-1}$.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 0.67$ (t, $J = 7$ Hz, 3H; 1.92 (d, $J = 6$ Hz, 3H); 1.8–2.6 (m, 3H); 2.98 (m, 2H); 3.65 (s, 3H); 3.71 (q, $J = 7$ Hz, 2H); 7.20–7.83 ppm (m, 15H).

1-Ethoxycarbonyl-5-methoxycarbonyl-4,4-dimethyl-2-oxopentylidenetriphenylphosphorane **(3d)** is synthesized from 1-ethyl 5,5-dimethyl-3-oxo-2-(triphenylphosphonio)-heptanedioate **(2d)**[6] with diazomethane as described above for **2b**. The product is purified on a short silica gel column and is crystallised from ether/light petroleum to give **3d**; yield: 93%; m.p. 81–82°C.

$C_{30}H_{33}O_5P$ calc. C 71.41 H 6.59
(504.2) found 71.21 6.57

I.R. (Nujol): $\nu = 1730, 1658, 1560\ cm^{-1}$.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 0.66$ (t, $J = 7$ Hz, 3H); 1.09 (s, 6H); 2.42 (s, 2H); 3.01 (s, 2H); 3.60 (s, 3H); 3.70 (q, $J = 7$ Hz, 2H); 7.30–7.87 ppm (m, 15H).

1-Ethoxycarbonyl-5-methoxycarbonyl-2-oxo-4-phenylpentylidenetriphenylphosphorane **(3e)** is prepared by reacting 3-phenylglutaric anhydride (1.9 g, 10 mmol) with ethoxycarbonylmethylenetriphenylphosphorane (3.5 g, 10 mmol) in dichloromethane (20 ml) at 35°C for 3 h, followed by methylation with an ethereal solution of diazomethane (25 ml, 12 mmol). The solvent is removed and the residue is chromatographed on a short silica gel column. Crystallisation from light petroleum/dichloromethane gives **3e**; yield: 4.64 g (86%); m.p. 129–130°C.

$C_{34}H_{33}O_5P$ calc. C 73.90 H 6.02
(552.6) found 73.77 5.85

I.R. (Nujol): $\nu = 1725, 1640, 1525\ cm^{-1}$.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 0.65$ (t, $J = 7$ Hz, 3H); 2.60 (m, 2H); 3.15 (m, 2H); 3.48 (s, 3H); 3.5–3.9 (m, 3H); 7.21–7.73 ppm (m, 15H).

1-Ethoxycarbonyl-4-methoxycarbonyl-4,4-dimethyl-2-oxobutylidenetriphenylphosphorane **(7b)** is prepared as follows: A solution of the anhydride **5b** (1 g, 10 mmol) and ethoxycarbonylmethylenetriphenylphosphorane (3 g, 10 mmol) in dichloromethane (15 ml) is treated intermittently with an ethereal solution of diazomethane (32 ml, 15 mmol) during 2 h at room temperature [in this case, the intermediate **6b** gives rise to enol lactones easily]. Preparative T.L.C. (ether) of the mixture gives **7b**: yield: 902 mg (22%); m.p. 125–126°C (ether/light petroleum).

$C_{29}H_{31}O_5P$ calc. C 71.01 H 6.37
(490.2) found 71.27 6.27

I.R. (Nujol): $\nu = 1735, 1658, 1545\ cm^{-1}$.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 0.64$ (t, $J = 7$ Hz, 3H); 1.13 (s, 6H). 3.18 (s, 2H); 3.35 (s, 3H); 3.66 (q, $J = 7$ Hz, 2H); 7.25–7.80 ppm (m, 15H).

1-Ethoxycarbonyl-3-(methoxycarbonylmethoxy)-2-oxopropylidenetriphenylphosphorane **(11)** is prepared as follows: A solution of diglycolic anhydride (**9**, 330 mg, 2.85 mmol) and ethoxycarbonylmethylenetriphenylphosphorane (990 mg, 2.85 mmol) in chloroform (10 ml) is allowed to stand at room temperature for 1 h. The product **10** crystallises from chloroform/light petroleum as colourless granules; yield: 1.17 g (91%); m.p. 176–178°C.

Methylation of **10** (543 mg, 1.17 mmol) in dichloromethane/tetrahydrofuran (1:5; 20 ml) with ethereal diazomethane (3 ml, 1.25 mmol) at 20°C, gives the required phosphorane **11**; yield: 473 mg (85%); m.p. 126–128°C (dichloromethane/light petroleum).

$C_{27}H_{27}O_6P$ calc. C 67.78 H 5.69
(478.1) found 68.04 5.71

I.R. (Nujol): $\nu = 1758, 1658, 1600, 1575\ cm^{-1}$.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 0.66$ (t, $J = 7$ Hz, 3H); 3.75 (S, 3H); 3.93–4.48 (m, 4H); 4.90 (s, 2H); 7.22–7.93 ppm (m, 15H).

Pyrolysis of Phosphoranes 3, 7, and 11; General Procedure:

The pyrolyses of the appropriate phosphoranes (0.4–1.2 mmol scale) is carried out under the conditions shown in the Table. The flask containing the phosphorane is connected to a quartz tube (400 × 30 mm). The system is evacuated, the tube heated to the required temperature and then the flask is heated as described. After the time shown, the product is collected from the trap (cooled with liquid nitrogen) and distilled (Table).

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