Carbon–Carbon Bond Forming Reactions *via* α-Phosphoryl-α-thio Carbocations

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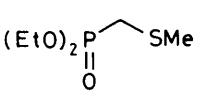
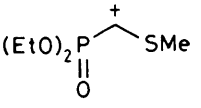
Diethyl chloro(methylthio)methylphosphonate (**3**) reacted with arenes and alk-1-enes in the presence of a Lewis acid to give the Friedel–Crafts product (**5**) and the ene product (**8**), respectively. The Pummerer rearrangement product (**4**) derived from diethyl (methylsulphinyl)methylphosphonate (**10**) also reacted with alk-1-enes in trifluoroacetic acid to give the products (**8**).

Despite current interest in the chemistry of the alkylthio or arylthio substituted alkylphosphonates (**1**),[1,2] there are few reports on the use of the cationic species (**2**) to accomplish carbon–carbon bond forming reactions.[3] Here we wish to describe the acid–promoted reactions of the chloride (**3**) and the trifluoroacetate (**4**) with arenes or terminal alkenes, which provide efficient routes to the aryl or alkenyl substituted methylthiomethylphosphonates (**5**) or (**8**).



(**1**)



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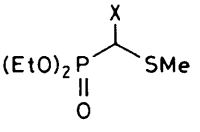


(**3**) X = Cl
(**4**) X = $OCOCF_3$

We first examined the reactions of diethyl chloro(methylthio)methylphosphonate (**3**) with aromatic compounds. When a benzene solution of (**3**) was treated with a stoicheiometric amount of stannic chloride ($SnCl_4$), the reaction proceeded smoothly at room temperature to give the Friedel–Crafts product (**5a**) (Ar = Ph) in 71% isolated yield. The reaction of electron rich aromatics such as anisole with (**3**) was carried out in dichloromethane by using equimolar amounts of both materials to afford the corresponding Friedel–Crafts products (**5**) in good yields. The results are summarized in the Table.† In general, $SnCl_4$ was superior to titanium tetrachloride ($TiCl_4$) as a Lewis acid for this reaction.

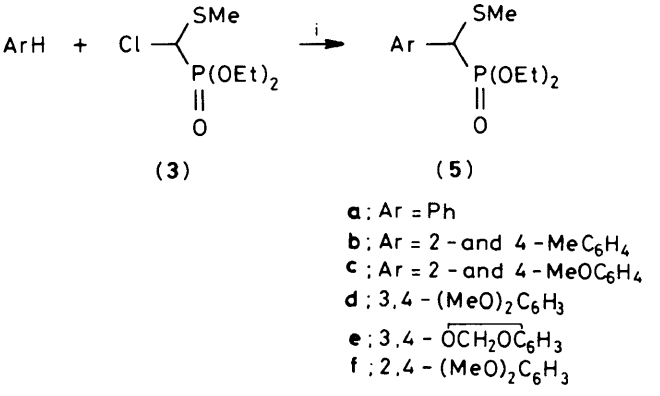
The chloride (**3**) also reacted with pent-1-ene (**6a**) in the presence of $SnCl_4$ to give the so-called 'ene' product (**8a**),[4] in 67% yield. The *E*:*Z* ratio of the alkenic bond was estimated to be 79:21 by ^1H n.m.r. spectroscopy (see the Experimental section). The most plausible mechanism for the formation of (**8a**) involves an attack of the double bond of the alkene (**6a**) on the carbon α to methylthio group of (**3**) followed by deprotonation of the resultant new cation (**7**). This regioselective alkene formation may be assisted by the lone pair electrons on the sulphur atom through a six-membered transition state. The reaction of (**3**) with allyltrimethylsilane was effected using $TiCl_4$ in place of $SnCl_4$ to afford the simple homoallylphosphonate (**9**) in 75% yield.

Next we turned our attention to the trifluoroacetate (**4**) which is readily formed by the Pummerer rearrangement of diethyl (methylsulphinyl)methylphosphonate (**10**) with trifluoroacetic anhydride (TFAA).[5a] The reactions of alk-1-enes with compound (**4**) proved to be more efficient for the synthesis of the ene products (**8**) than with the chloride (**3**). Thus, when a solution of the sulphoxide (**10**) in trifluoroacetic acid was treated successively with TFAA (at 0 °C) and pent-1-ene (**6a**) (at room temperature), the ene product (**8a**) was obtained in 80% isolated yield. Similarly, the reactions with the alk-1-enes (**6b**—**e**) gave the corresponding ene products (**8b**—**e**) in good yields.‡ When the reaction of the sulphoxide (**10**) with the alk-1-ene (**6**)

Table. Preparation of diethyl aryl(methylthio)methylphosphonates (**5**)[a]

ArH	ArH: (3)	Lewis acid	Products	Yield (%)
Benzene	*b*	$SnCl_4$	(**5a**)	71
	b	$TiCl_4$	(**5a**)	66
	1:1	$SnCl_4$	(**5a**)	0
Toluene	*b*	$SnCl_4$	(**5b**)[c]	83
	1:1	$SnCl_4$	(**5b**)[c]	61
Anisole	1:1	$SnCl_4$	(**5c**)[d]	92
	1:1	$TiCl_4$	(**5c**)[d]	78
Veratrole	1:1	$SnCl_4$	(**5d**)	60
	1:1	$TiCl_4$	(**5d**)	Trace
1,3-Benzodioxole	1:1	$SnCl_4$	(**5e**)	87
	1:1	$TiCl_4$	(**5e**)	63
1,3-Dimethoxybenzene	1:1	$SnCl_4$		*e*
	1:1	$TiCl_4$	(**5f**)	65

[a] Reactions were carried out in CH_2Cl_2 unless otherwise noted. [b] Arene was used as the solvent. [c] Ratio of *p*- and *o*-isomers = 96:4. [d] Ratio of *p*- and *o*-isomers = 81:19. [e] A complex mixture of products was formed.



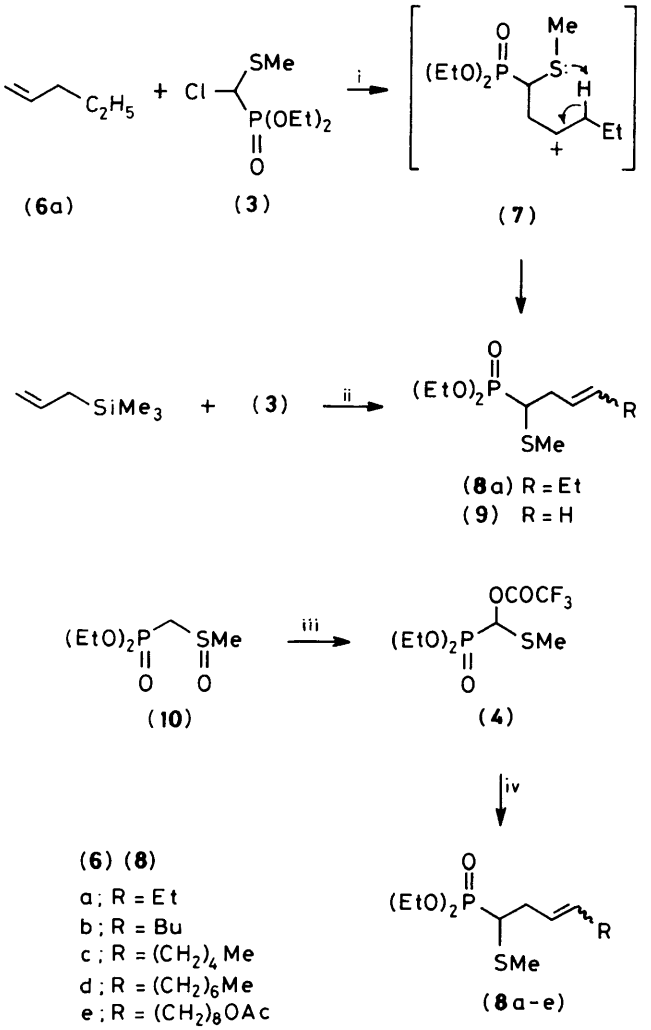
(**3**) (**5**)

a; Ar = Ph
b; Ar = 2- and 4-MeC_6H_4
c; Ar = 2- and 4-$MeOC_6H_4$
d; 3,4-$(MeO)_2C_6H_3$
e; 3,4-$OCH_2OC_6H_3$
f; 2,4-$(MeO)_2C_6H_3$

Scheme 1. *Reagent:* i, Lewis acid

† Kim and Oh noted that the reaction of (**3**) with toluene or anisole gave only a para-isomer.[3]

‡ The reaction of (**4**) with di- or tri-substituted alkenes gave unsatisfactory results.



Scheme 2. *Reagents:* i, $SnCl_4$; ii, $TiCl_4$; iii, $(CF_3CO)_2O$–CF_3CO_2H; iv, CH_2=$CHCH_2R$ (**6a**—**e**)–CF_3CO_2H

was carried out in dichloromethane in place of trifluoroacetic acid, only the trifluoroacetate (**4**) was obtained.

Finally, some chemical transformations of the products thus obtained are reported. Oxidation of the sulphide (**9**) with sodium metaperiodate followed by treatment of the resultant sulphoxide with a mixture of acetic anhydride and methanesulphonic acid[6] gave the (1*E*)-1-methylthiobuta-1,3-dienylphosphonate (**11**) and its stereoisomer (**12**) in 50 and 17% yields respectively. Furthermore, thermolysis of the sulphoxide obtained from (**8c**) afforded the (1*E*,3*E*)-nona-1,3-dienylphosphonate (**13**) (52%) along with a mixture of three stereoisomers of (**13**).

Experimental

^{1}H N.m.r. spectra were recorded on a JEOL JNM-PMX 60 (60 MHz) or a Varian XL-300 (300 MHz) spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Column chromatography was performed on silica gel 60 (Merck PF_{254} for p.l.c.) under pressure.

Diethyl Chloro(methylthio)methylphosphonate (**3**).—*N*-Chlorosuccinimide (4.4 g, 33 mmol) was added to a stirred solution of diethyl (methylthio)methylphosphonate[2a] (5.9 g, 30 mol) in carbon tetrachloride (50 ml) at 0 °C and the mixture was further stirred at room temperature for 3 h. The precipitated succinimide was removed by filtration and the filtrate was concentrated under reduced pressure to give, in an almost quantitative yield, the chloride (**3**)[5] as an oil; δ_H (60 MHz) 1.37 (6 H, t), 2.41 (3 H, s), 4.26 (4 H, quint), and 4.94 (1 H, d, J_{PH} 12 Hz). This compound was used without purification for further reactions.

General Procedure for the Preparation of Diethyl Aryl(methylthio)methylphosphonates (**5a**—**f**).—Stannic chloride (521 mg, 2 mmol) or titanium tetrachloride (379 mg, 2 mmol) was added to a solution of the chloride (**3**) (465 mg, 2 mmol) and arene (2 mmol) in dichloromethane (10 ml) at 0 °C and the mixture was stirred at room temperature for 30 min. The reaction was quenched by the addition of water (5 ml) and extracted with dichloromethane (3 × 10 ml), then dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed on silica gel [benzene–ethyl acetate (2:1)] to give the *phosphonates* (**5a**—**f**), whose physical data are as follows.

Diethyl methylthio(phenyl)methylphosphonate (**5a**):[2d] an oil; δ_H (60 MHz) 1.16 (3 H, t, *J* 7 Hz), 1.30 (3 H, t, *J* 7 Hz), 2.10 (3 H, s), 3.93 (1 H, d, J_{PH} 20 Hz, PCH), 4.13 (4 H, dq, J_{PH} 7, J_{HH} 7 Hz), and 7.15—7.65 (5 H, m).

Diethyl 2- *and* 4-*methylphenyl(methylthio)methylphosphonate* (**5b**): an oil (Found: C, 53.3; H, 7.4. $C_{13}H_{21}O_3PS{\cdot}0.25H_2O$ requires C, 53.2; H, 7.40%); δ_H (300 MHz) 1.18 (3 H, t, *J* 7.2 Hz), 1.31 (3 H, t, *J* 7.2 Hz), 2.09 [3 H (*p*-isomer; 96%), s, SMe], 2.13 [3 H (*o*-isomer; 4%), s, SMe], 2.34 [3 H (*p*-isomer), s, CMe], 2.38 [3 H (*o*-isomer), s, CMe], 3.83—4.24 (4 H, m), 3.92 (1 H, d, J_{PH} 20.9 Hz, PCH), 7.15 [2 H (*p*-isomer), br d, *J* 8.5 Hz], and 7.34 [2 H (*p*-isomer), dd, *J* 8.5, 2.0 Hz].

Diethyl 2- *and* 4-*methoxyphenyl(methylthio)methylphosphonate* (**5c**): an oil (Found: C, 50.1; H, 6.9. $C_{13}H_{21}O_4PS{\cdot}0.25H_2O$ requires C, 50.6; H, 7.0%); δ_H (300 MHz) 1.18 (3 H, t, *J* 7.2 Hz), 1.31 (3 H, t, *J* 7.2 Hz), 2.09 [3 H (*p*-isomer; 81%), s, SMe], 2.15 [3 H (*o*-isomer; 19%), s, SMe], 3.80 [3 H (*p*-isomer), s, OMe], 3.84 [3 H (*o*-isomer), s, OMe], 3.86—4.29 (4 H, m), 3.92 [1 H (*p*-isomer), d, J_{PH} 20.0 Hz, PCH], 4.65 [1 H (*o*-isomer), d, J_{PH} 20.1 Hz, PCH], 6.88 [2 H (*p*-isomer), br d, *J* 8.1 Hz], and 7.39 [2 H (*p*-isomer), dd, *J* 8.1, 2.0 Hz].

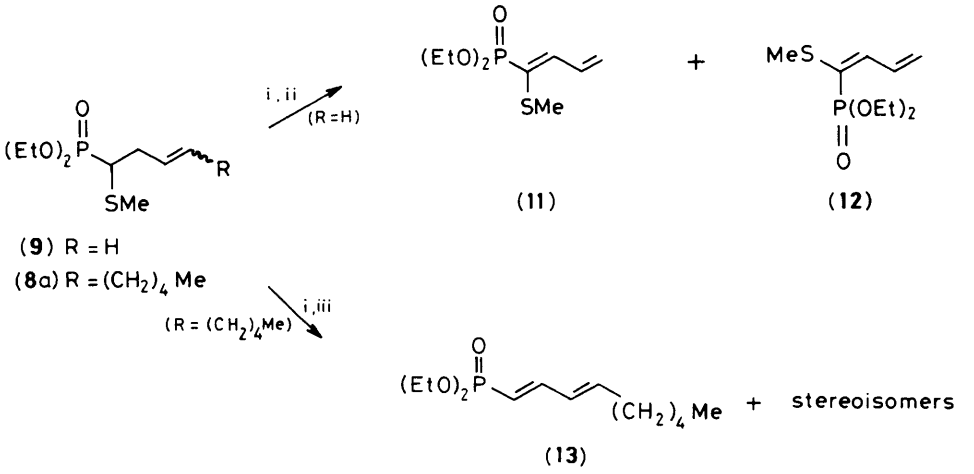
Diethyl 3,4-*dimethoxyphenyl(methylthio)methylphosphonate* (**5d**): an oil (Found: C, 49.5; H, 6.6. $C_{14}H_{23}O_5PS{\cdot}0.25H_2O$ requires C, 49.6; H, 7.0%); δ_H (60 MHz) 1.17 (3 H, t, *J* 7 Hz), 1.31 (3 H, t, *J* 7 Hz), 2.10 (3 H, s, SMe), 3.85 (1 H, d, J_{PH} 20 Hz, PCH), 3.86 (6 H, s, 2 × OMe), 4.13 (4 H, dq, J_{PH} 7, J_{HH} 7 Hz), and 6.6—7.1 (3 H, m).

Diethyl 3,4-*methylenedioxyphenyl(methylthio)methylphosphonate* (**5e**): an oil (Found: C, 48.5; H, 6.1. $C_{13}H_{19}O_5PS{\cdot}0.25H_2O$ requires C, 48.4; H, 6.1%); δ_H (60 MHz) 1.19 (3 H, t, *J* 7 Hz), 1.32 (3 H, t, *J* 7 Hz), 2.10 (3 H, s, SMe), 3.87 (1 H, d, J_{PH} 20 Hz, PCH), 4.13 (4 H, dq, J_{PH} 7, J_{HH} 7 Hz), 5.93 (2 H, s, OCH_2O), and 6.6—7.1 (3 H, m).

Diethyl 2,4-*dimethoxyphenyl(methylthio)methylphosphonate* (**5f**): an oil (Found: C, 50.1; H, 6.8. $C_{14}H_{23}O_5PS{\cdot}0.25H_2O$ requires C, 49.6; H, 7.0%); δ_H (60 MHz) 1.16 (3 H, t, *J* 7 Hz), 1.30 (3 H, t, *J* 7 Hz), 2.13 (3 H, s, SMe), 3.80 (6 H, s, 2 × OMe), 3.75—4.30 (4 H, m), 4.51 (1 H, d, J_{PH} 20 Hz, PCH), 6.3—6.6 (2 H, m), and 7.45—7.65 (1 H, m).

General Procedure for the Preparation of Diethyl (1-*Methylthioalk*-3-*enyl*)*phosphonates* (**8a**—**e**).—(*a*) By the same procedure as that described for the preparation of compounds (**5a**—**f**), the chloride (**3**) (465 mg, 2 mmol) was allowed to react with pent-1-ene (**6a**) (140 mg, 2 mmol) in the presence of stannic chloride (379 mg, 2 mmol) to give compound (**8a**).

(*b*) Trifluoroacetic anhydride (420 mg, 2 mmol) was added to



Scheme 3. *Reagents:* i, $NaIO_4$; ii, Ac_2O–$MeSO_3H$; iii, heat

a solution of diethyl (methylsulphinyl)methylphosphonate (**10**)[7] (428 mg, 2 mmol) in trifluoroacetic acid (2 ml) at 0 °C and the mixture was stirred at the same temperature for 30 min. Subsequently, the alk-1-ene (**6a**—**e**) (2 mmol) was added to the resultant solution containing the trifluoroacetate (**4**) at 0 °C and the mixture was stirred at room temperature for 1 h. Dichloromethane (10 ml) was added to the reaction mixture, then washed with saturated aqueous sodium hydrogen carbonate and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was chromatographed on silica gel [benzene–ethyl acetate (2:1)] to give the *phosphonates* (**8a**—**e**). The yields and physical data of new compounds thus obtained by the two methods are as follows.

Diethyl 1-methylthiohex-3-enylphosphonate (**8a**): [67%, method (*a*); 80% method (*b*)]; an oil (Found: C, 48.8; H, 8.1. $C_{11}H_{23}O_3PS{\cdot}0.25H_2O$ requires C, 48.8; H, 8.7%); δ_H (300 MHz) 0.99 (3 H, t, *J* 7.7 Hz, =CHCH$_2$*Me*), 1.35 (6 H, t, *J* 7.1 Hz), 2.05 (2 H, quint, *J* 6.8 Hz, =CHC*H*$_2$Me), 2.20—2.40 (1 H, m, PCH), 2.25 [3 H (*E*-isomer; 79%), s, SMe], 2.26 [3 H (*Z*-isomer; 21%), s, SMe], 2.52—2.73 (2 H, m, PCHC*H*$_2$), 4.12—4.27 (4 H, m), and 5.40—5.67 (2 H, m, CH=CH).

Diethyl 1-methylthio-oct-3-enylphosphonate (**8b**): [76%, method (*b*)]; an oil (Found: C, 51.9; H, 9.6. $C_{13}H_{27}O_3PS{\cdot}0.25H_2O$ requires C, 52.2; H, 9.3%); δ_H (60 MHz) 0.75—1.60 (7 H, m), 1.34 (6 H, t, *J* 7 Hz), 1.80—3.00 (5 H, m), 2.25 (3 H, s), 4.18 (4 H, dq, J_{PH} 7, J_{HH} 7 Hz), and 5.4—5.7 (2 H, m).

Diethyl 1-methylthionon-3-enylphosphonate (**8c**): [77%, method (*b*)]; an oil (Found: C, 53.65; H, 10.0. $C_{14}H_{29}O_3PS{\cdot}0.25H_2O$ requires C, 53.7; H, 9.50%); δ_H (60 MHz) 0.75—1.60 (9 H, m), 1.33 (6 H, t, *J* 7 Hz), 1.80—3.00 (5 H, m), 2.26 (3 H, s), 4.18 (4 H, dq, J_{PH} 7 Hz), and 5.4—5.7 (2 H, m).

Diethyl 1-methylthioundec-3-enylphosphonate (**8d**): [76%, method (*b*)]; an oil (Found: C, 55.9; H, 10.3. $C_{16}H_{33}O_3PS{\cdot}0.25H_2O$ requires C, 56.4; H, 9.90%); δ_H (60 MHz) 0.75—1.60 (19 H, m), 1.9—3.0 (5 H, m), 2.26 (3 H, s), 4.20 (4 H, dq, J_{PH} 7, J_{HH} 7 Hz), and 5.4—5.7 (2 H, m).

Diethyl 12-acetoxy-1-methylthiododec-3-enylphosphonate (**8e**): [70% method (*b*)]; an oil (Found: C, 55.25; H, 9.2. $C_{19}H_{37}O_5PS{\cdot}0.25H_2O$ requires C, 55.25; H, 9.15%); δ_H (60 MHz) 1.1—1.8 (18 H, m), 1.8—2.9 (5 H, m), 2.01 (3 H, s, COMe), 2.23 (3 H, s, SMe), 4.02 (2 H, t, *J* 7 Hz, C*H*$_2$OAc), 4.13 (4 H, dq, J_{PH} 7, J_{HH} 7 Hz), and 5.35—5.65 (2 H, m).

Diethyl 1-Methylthiobut-3-enylphosphonate (**9**).—By the same procedure as that described for the preparation of compound (**8a**) from (**3**) and (**6a**), the chloride (**3**) (465 mg, 2 mmol) was allowed to react with allyltrimethylsilane in the presence of titanium tetrachloride (379 mg, 2 mmol) to give the phosphonate (**9**)[1b] (75%) as an oil; δ_H (60 MHz) 1.34 (6 H, t, *J* 7 Hz), 2.24 (3 H, s), 2.4—3.0 (3 H, m), 4.18 (4 H, dq, J_{PH} 7, J_{HH} 7 Hz), 4.9—5.3 (2 H, m), and 5.55—6.30 (1 H, m).

(Z)- *and* (E)-*Diethyl 1-Methylthiobuta-1,3-dienylphosphonate* (**11**) *and* (**12**).—A solution of sodium metaperiodate (131 mg, 0.6 mmol) in water (2 ml) was added to a solution of (**9**) (140 mg, 0.6 mmol) in acetone (3 ml) and water (1 ml), and the mixture was stirred at room temperature for 15 h. The precipitated salts were removed by filtration and the filtrate was concentrated under reduced pressure. The resulting crude sulphoxide (130 mg, 0.5 mmol) was dissolved in dichloromethane (3 ml) containing acetic anhydride (60 mg, 0.6 mmol) and methanesulphonic acid (6 mg, 0.06 mmol), and the mixture was allowed to stand at room temperature for 15 h. The reaction mixture was concentrated under reduced pressure and the residue was chromatographed on silica gel [benzene–ethyl acetate (2:1)] to give compound (**12**) (17%), as an oil; δ_H (60 MHz) 1.33 (6 H, t, *J* 7 Hz), 2.33 (3 H, s), 4.12 (4 H, dq, J_{PH} 7.5, J_{HH} 7.5 Hz), 5.10—5.55 (2 H, m, =CH$_2$), 6.45 (1 H, dd, $J_{trans\text{-}PCCH}$ 42.0, J_{HH} 11.5 Hz, PC=CH), and 7.00—7.60 (1 H, m, C*H*=CH$_2$). The second eluate gave (**11**)[1b] in 50% yield as an oil; δ_H (60 MHz) 1.36 (6 H, t, *J* 7 Hz), 2.40 (3 H, s), 4.12 (4 H, dq, J_{PH} 7, J_{HH} 7 Hz), 5.4—5.8 (2 H, m, =CH$_2$), 6.6—7.3 (1 H, m, C*H*=CH$_2$), and 7.35 (1 H, dd, $J_{cis\text{-}PCCH}$ 17.5, J_{HH} 10.5 Hz, PC=CH).

(1E,3E)-*Diethyl Nona-1,3-dienylphosphonate* (**13**).—Compound (**8b**) (236 mg, 0.7 mmol) was oxidised with sodium metaperiodate (250 mg, 1.1 mmol) according to the procedure described for the preparation of (**11**) and (**12**). The resultant crude sulphoxide was dissolved in toluene (5 ml) containing sodium hydrogen carbonate (100 mg, 1.2 mmol) and the mixture was refluxed for 45 min. The salts were removed by filtration, the filtrate was concentrated under reduced pressure, and the residue was chromatographed on silica gel [benzene–ethyl acetate (2:1)] to give a mixture of three stereoisomers of (**13**) (12%). The second eluate gave the diene (**13**) in 52% yield as an oil (Found: C, 58.7; H, 9.9. $C_{13}H_{25}O_3P{\cdot}0.25H_2O$ requires C, 59.0; H, 9.7%); δ_H (300 MHz) 0.89 (3 H, t, *J* 6.8 Hz), 1.22—1.48 (6 H, m), 1.33 (6 H, t, *J* 7.1 Hz), 2.15 (2 H, q, *J* 6.8 Hz, =CHC*H*$_2$), 4.08 (4 H, dq, J_{PH} 7.1, J_{HH} 7.1 Hz), 5.57 (1 H, dd, J_{PH} 19.5, J_{HH} 17.2 Hz, PC*H*=CH), 6.07 (1 H, dt, *J* 15.0, 6.0 Hz, CH=C*H*CH$_2$), 6.15 (1 H, br dd, *J* 15.0, 9.0 Hz, C*H*=CHCH$_2$), and 7.08 (1 H, ddd, $J_{cis\text{-}PCCH}$ 20.6, J_{HH} 17.2, 9.0 Hz, PCH=C*H*).

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Received 2*nd June* 1986; *Paper* 6/1090