Diastereoselectivity in the Horner-Wittig Reaction: *X*-Ray Crystal Structure of 2-(1*RS*,2*SR*)-Diphenylphosphinoyl-1-phenylpropan-1-ol

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Ethyldiphenylphosphine oxide reacts with butyl-lithium and benzaldehyde to give the title compound which eliminates diphenylphosphinate ion in base to give *Z*-1-phenylpropene. The elimination is stereospecific and *syn*. The (1*RS*,2*RS*) isomer, prepared by sodium borohydride reduction of the corresponding ketone, gives *E*-1-phenylpropene.

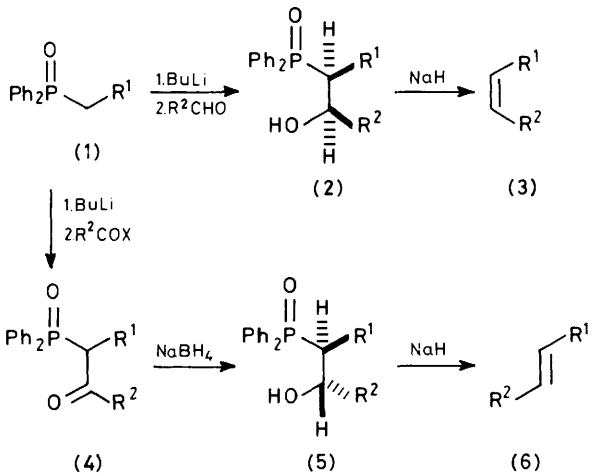
Stereoselectivity in the Wittig reaction can be achieved by careful choice of ylide structure or reaction conditions,[1] but it remains difficult to synthesise a pure *E* or *Z* isomer of a given olefin at will. The Horner [2] variant of the Wittig reaction normally allows isolation of the intermediate β-hydroxyphosphine oxides, *e.g.* (2): purification of single diastereoisomers of these crystalline compounds has led to syntheses of single geometrical isomers of trisubstituted alkenes,[3] dienes,[4] vinyl ethers,[5] allylic amines,[6] β,γ- and γ,δ-unsaturated ketals.[7]

We have reported [8] a method (Scheme 1) for the stereoselective synthesis of '*erythro*' (2) and '*threo*' (5) diastereoisomers of simple Horner-Wittig intermediates. We now describe the assignment of stereochemistry to the two series, including an *X*-ray crystal structure determination of (2; R^1 = Me, R^2 = Ph). Horner's assignments [9] of (2) and (5) (R^1 = R^2 = Ph) have recently been reassessed.[10]

Synthesis of Diastereoisomers (7) *and* (8).—Treatment of ethyldiphenylphosphine oxide (1; R^1 = Me) with butyllithium (BuLi) in dry tetrahydrofuran (THF) at 0 °C gave the red lithium derivative, which was treated with benzaldehyde at −78 °C. The resulting oil was most easily separated by flash chromatography [11] and gave pure *erythro* (7) and a much smaller amount of pure *threo* (8) adduct. The ratio was 88 : 12 and the yields (Scheme 2) are of isolated pure diastereoisomers.

Acylation [12] of the lithium derivative of (1; R^1 = Me) with ethyl benzoate or of the copper derivative with benzoyl chloride (a similar acylation of a phosphonate ester is known [13]), gave the ketone (9) whose reduction with sodium borohydride in ethanol was *threo* selective. Alternatively, *erythro* or mixed diastereoisomers could be converted into the *threo* isomer *via* oxidation to the ketone (9) with pyridinium dichromate (PDC) [14] in dimethylformamide (DMF) (91%) or in methylene chloride (68%), with sodium hypochlorite in acetic acid [15] (99%), or with barium manganate [16] in methylene chloride (79%). Separation of pure *threo* (8) adduct was again efficient by flash chromatography and gram quantities of each diastereoisomer could quickly be obtained by these methods. Attempted equilibration of the adduct mixture by a second treatment with BuLi after addition of benzaldehyde to the lithium derivative of the phosphine oxide (1; R^1 = Me) gave a roughly 2 : 1 mixture of adducts (7) and (8).

X-*Ray Crystal Structure Determination of* 2-(1RS, 2SR)-*Diphenylphosphinoyl-1-phenylpropan-1-ol.*—*Crystal data.* $C_{21}H_{21}O_2P$, M = 336.4, Monoclinic, space group $P2_1/c$; a = 9.859(1), b = 17.218(2), c = 11.421(1) Å, β = 111.41(1)°, U = 1805.0 Å^3, D_m = 1.24(1) g cm^{-3}, D_c = 1.24 g cm^{-3}, Z = 4, $F(000)$ = 712. Monochromatic (graphite) Cu-K_α radiation, λ = 1.5418$_2$ Å, μ = 13.2 cm^{-1}; specimen: cut rectangular block, 0.20 × 0.15 × 0.25 mm.



Scheme 1.

Structure determination. Accurate cell constants were determined from the setting angles of 15 strong reflections by a least-squares procedure with a Syntex $P2_1$ diffractometer. 3590 Independent reflections were measured by the ω/2θ scan technique with 2θ < 130°. After application of Lorentz and polarisation corrections, merging equivalent reflections yielded 3 084 unique reflections; 2 642 had $F_o > 3\sigma(F_o)$ and were treated as observed. No absorption corrections were applied.

Multisolution direct methods produced an *E*-map which showed the locations of all non-hydrogen atoms. The structure was refined by full-matrix least-squares methods to R = 0.084 whereupon the hydrogen atoms were located in a difference map. Subsequent refinement with non-hydrogen atoms anisotropic reduced the residual to a final value R = 0.043. In this model the thermal parameters of the methyl hydrogen atoms were constrained to be equal. Four intense reflexions (002, 100, 200 and $\bar{2}11$) suffered from extinction and were omitted. In the final cycle of refinement the quantity $w\Delta F^2$ was minimised (R_w = 0.044) where $w = 1/[\sigma(F_o) + 0.0004\ F_o^2]$. The final difference map showed no peaks >0.2e Å^{-3}. All calculations after the initial data processing were done with the program SHELX. Table 1 lists the final positional parameters of the non hydrogen atoms. Observed and calculated structure factors, anisotropic thermal parameters and fractional co-ordinates for the hydrogen atoms are listed in Supplementary Publication SUP 23758 (19 pp.).†

† For details of the Supplementary publications Scheme see Instructions for Authors (1984), *J. Chem. Soc., Perkin Trans. 1*, 1984, Issue 1.

Table 1. Atom co-ordinates ($\times 10^4$)

	x/a	*y/b*	*z/c*
C(1)	3 126(2)	7 286(1)	3 353(2)
C(2)	2 875(2)	7 970(1)	2 413(2)
C(3)	1 309(2)	8 270(2)	1 923(2)
O(1)	2 742(2)	7 506(1)	4 402(1)
C(1A)	2 261(2)	6 567(1)	2 761(2)
C(2A)	2 654(3)	6 148(1)	1 893(2)
C(3A)	1 923(4)	5 471(1)	1 371(3)
C(4A)	806(4)	5 206(2)	1 701(3)
C(5A)	403(3)	5 612(2)	2 551(3)
C(6A)	1 131(3)	6 296(1)	3 085(2)
P(1)	4 154(0.5)	8 737(0.3)	3 200(0.4)
O(2)	4 090(2)	8 903(1)	4 463(1)
C(1B)	3 751(2)	9 583(1)	2 210(2)
C(2B)	3 494(3)	9 558(2)	929(2)
C(3B)	3 209(3)	10 233(2)	226(3)
C(4B)	3 142(3)	10 927(2)	804(3)
C(5B)	3 414(4)	10 956(2)	2 061(3)
C(6B)	3 711(3)	10 285(1)	2 768(2)
C(1C)	5 952(2)	8 415(1)	3 345(2)
C(2C)	7 050(2)	8 453(1)	4 532(2)
C(3C)	8 456(3)	8 245(1)	4 699(2)
C(4C)	8 801(3)	7 994(1)	3 701(3)
C(5C)	7 726(3)	7 955(2)	2 520(3)
C(6C)	6 310(2)	8 160(1)	2 334(2)

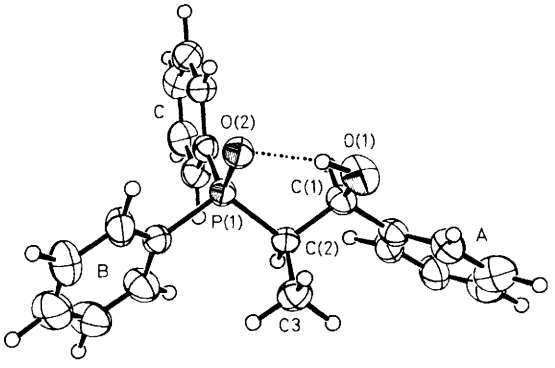


Figure 1. The observed conformation and atom numbering scheme for 2-(1*RS*,2*RS*)diphenylphosphinoyl-1-phenylpropan-1-ol. The intramolecular hydrogen bond is indicated by a dotted line

Description of the Structure.—The ORTEP drawing in Figure 1 shows the atomic designations and the relative configurations of the two asymmetric carbon atoms. Thus the molecule is 2-(1*RS*,2*SR*)-diphenylphosphinoyl-1-phenylpropan-1-ol. Bond lengths and bond angles excluding hydrogen are listed in Tables 2 and 3. Figure 2 shows a packing diagram of the structure. The crystal is held together by Van der Waals forces but without much stabilization by stacking interactions between aromatic rings. An interesting feature of the structure is the P=O · · · H–O intramolecular hydrogen bond. The O · · · H and O · · · O separations are 1.92(3) and 2.738(4) Å respectively with an O · · · H–O angle of 161(2)°.

Identification of Diastereoisomers.—The n.m.r. spectra of *erythro* (2) and *threo* (5) diastereoisomers of these phosphine oxides are always distinct, correlate well with the established structures of (7) and (8), and can be used for identification (Table 1). One of the most characteristic features is the shape of the multiplet containing the aromatic protons of the Ph_2PO group. These resonate at lower field than those of C-phenyl

Table 2. Bond lengths (Å)

C(2)–C(1)	1.551(5)	O(1)–C(1)	1.433(3)
C(1A)–C(1)	1.515(5)	C(3)–C(2)	1.528(5)
P(1)–C(2)	1.821(4)	C(2A)–C(1A)	1.391(4)
C(6A)–C(1A)	1.377(4)	C(3A)–C(2A)	1.384(4)
C(4A)–C(3A)	1.367(5)	C(5A)–C(4A)	1.368(5)
C(6A)–C(5A)	1.398(4)	O(2)–P(1)	1.494(2)
C(1B)–P(1)	1.798(4)	C(1C)–P(1)	1.806(4)
C(2B)–C(1B)	1.391(4)	C(6B)–C(1B)	1.373(4)
C(3B)–C(2B)	1.383(4)	C(4B)–C(3B)	1.377(5)
C(5B)–C(4B)	1.363(5)	C(6B)–C(5B)	1.378(5)
C(2C)–C(1C)	1.394(4)	C(6C)–C(1C)	1.396(4)
C(3C)–C(2C)	1.375(4)	C(4C)–C(3C)	1.372(5)
C(5C)–C(4C)	1.380(5)	C(6C)–C(5C)	1.380(4)

Table 3. Bond angles (°)

O(1)–C(1)–C(2)	110.8(3)	C(1A)–C(1)–C(2)	112.9(2)
C(1A)–C(1)–O(1)	108.1(3)	C(3)–C(2)–C(1)	113.3(3)
P(1)–C(2)–C(1)	107.5(2)	P(1)–C(2)–C(3)	111.1(2)
C(2A)–C(1A)–C(1)	119.0(3)	C(6A)–C(1A)–C(1)	122.4(3)
C(6A)–C(1A)–C(2A)	118.6(3)	C(3A)–C(2A)–C(1A)	120.5(4)
C(4A)–C(3A)–C(2A)	120.5(4)	C(5A)–C(4A)–C(3A)	119.8(3)
C(6A)–C(5A)–C(4A)	120.3(4)	C(5A)–C(6A)–C(1A)	120.3(3)
O(2)–P(1)–C(2)	110.5(2)	C(1B)–P(1)–C(2)	108.9(2)
C(1B)–P(1)–O(2)	112.0(2)	C(1C)–P(1)–C(2)	107.6(2)
C(1C)–P(1)–O(2)	110.9(2)	C(1C)–P(1)–C(1B)	106.9(2)
C(2B)–C(1B)–P(1)	123.3(3)	C(6B)–C(1B)–P(1)	117.3(3)
C(6B)–C(1B)–C(2B)	119.4(3)	C(3B)–C(2B)–C(1B)	120.3(3)
C(4B)–C(3B)–C(2B)	119.1(4)	C(5B)–C(4B)–C(3B)	120.7(4)
C(6B)–C(5B)–C(4B)	120.3(4)	C(5B)–C(6B)–C(1B)	120.1(3)
C(2C)–C(1C)–P(1)	117.6(2)	C(6C)–C(1C)–P(1)	123.8(3)
C(6C)–C(1C)–C(2C)	118.6(3)	C(3C)–C(2C)–C(1C)	120.5(3)
C(4C)–C(3C)–C(2C)	120.6(3)	C(5C)–C(4C)–C(3C)	119.6(3)
C(6C)–C(5C)–C(4C)	120.7(3)	C(5C)–C(6C)–C(1C)	120.1(3)

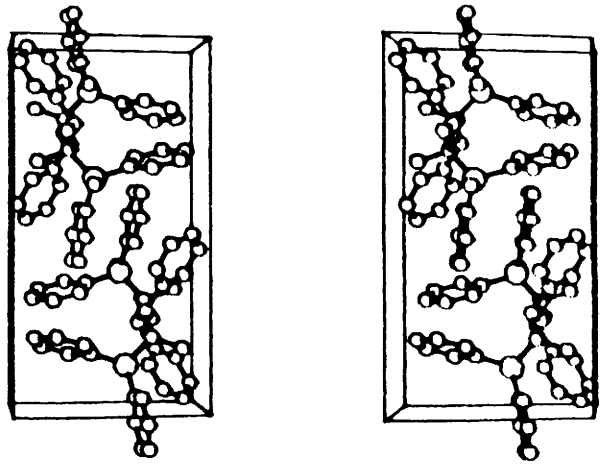
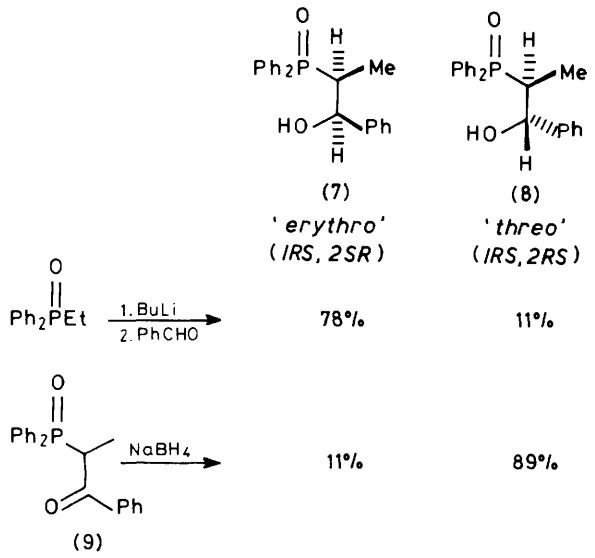


Figure 2. A view of the crystal packing along the *c*-axis. Hydrogen atoms are not depicted

groups and the *ortho* protons come at lowest field, around δ 8. In the *erythro* series (2) the *ortho* protons separate completely from the *meta* and *para* protons but in the *threo* series they overlap to some extent. This phenomenon has been observed in β-hydroxyalkylphosphine oxides with α-allyl, methoxy, methylthio, and phenylthio substituents.[17]

The series (2) and (5) with R^1 = alkyl and R^2 = phenyl show other characteristic features in their n.m.r. spectra, some or all of which can be used in any given case (Table 4),



Scheme 2.

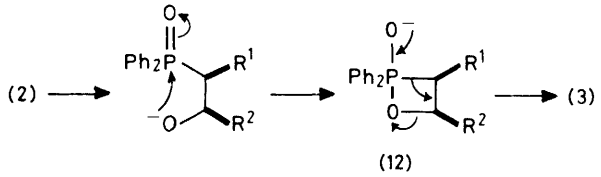
and are least apparent for (7) and (8). Coupling between the two protons on the main carbon skeleton (J_{AB}) is greater for the *threo* (*ca.* 7 Hz) than for the *erythro* (*ca.* 1 Hz) isomers. Coupling between the phosphorus atom and the α-H atom (J_{AP}) is greater for the *threo* (*ca.* 17 Hz) than for the *erythro* (*ca.* 10 Hz) isomers. Coupling is consistently observed between H_B and the hydroxy proton in the *threo* series (*J ca.* 5 Hz) but not in the *erythro* series ($J = 0$).

Completion of the Horner-Wittig Reaction.—We favour sodium hydride [8] in DMF at 50 °C or potassium hydroxide in dimethyl sulphoxide at 50 °C for the elimination step from adduct (2) to *Z*-alkene (3) or adduct (5) to *E*-alkene (6) though many other conditions may be used successfully.[2,10] *threo*-Adduct (8) gives *trans*-olefin (6; R^1 = Me, R^2 = Ph) stereospecifically in high yield, there being no trace of the *cis*-isomer by g.l.c.

Elimination of diphenylphosphinate from *erythro* adducts (2) is more difficult to achieve with complete stereospecificity. With (2; $R^1 = R^2$ = Ph) it is almost impossible,[10] and when R^1 is capable of conjugation (e.g. allyl [18,19]) a *trans* double bond is formed, presumably by dissociation and recombination. However good yields of *Z*-alkene are formed from adduct (7) under a variety of conditions (Table 5). Sodium or potassium hydride, potassium hydroxide, or potassium t-butoxide give (3; R^1 = Me, R^2 = Ph) containing only a trace of *E*-isomer (g.l.c.). A polar solvent (DMF or DMSO) is important and the temperature should be high enough to cause rapid elimination (50—75 °C). At room temperature the ketone (4; R^1 = Me, R^2 = Ph) is formed, presumably by dissociation to benzaldehyde and a Cannizarro reaction. An excess of base is to be avoided as this causes dissociation to benzaldehyde and the anion of the phosphine oxide (1; R^1 = Me) and loss of stereospecificity.[10]

Treatment of adduct (7) with sodium hydride in THF at 25 °C or under reflux, potassium carbonate in DMF, DBU [6] in DMF, phase-transfer methods, or heating adduct (7) in benzene with silica gel gave no olefin of either geometry.

The formation of exclusively *trans*-olefin (6; R^1 = Me, R^2 = Ph) from adduct (8) and mostly *cis*-olefin (3; R^1 = Me, R^2 = Ph) from adduct (7) and the *X*-ray crystal structure determination of *erythro* stereochemistry for adduct (7) confirms that the elimination is *syn*-stereospecific. The loss of stereospecificity in elimination from adduct (7) results from a slower [10] elimination because R^1 and R^2 are eclipsed in the intermediate (12) and in the transition states leading to and from it.



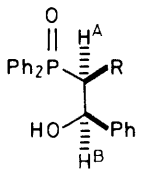
Experimental

General procedures have been described before.[4] Gas-liquid chromatograms were obtained with a Perkin-Elmer F11 flame-ionisation instrument using 15% Carbowax 20M on Chromosorb W (column 1) or 15% silicone grease PE380, 12 ft × ⅛ in (column 2).

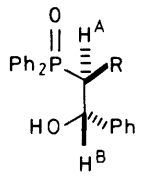
2-*Diphenylphosphinoyl*-1-*phenylpropan*-1-*ol* (7) and (8).—n-Butyl-lithium (2.9 ml of a 1.5M-solution in hexane) was added from a syringe to a stirred solution of ethyldiphenylphosphine oxide (1.0 g, 4.35 mmol) in dry THF (30 ml) at 0 °C. After 30 min the red solution was cooled to −78 °C and benzaldehyde (0.46 g, 4.35 mmol) added dropwise so that the solution remained at −78 °C. The pale yellow solution was allowed to reach room temperature over *ca.* 2 h and then water (20 ml) was added. The THF was removed under reduced pressure and brine (10 ml) added to the aqueous residue before extraction with dichloromethane (3 × 20 ml). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give an oil. Separation by flash column chromatography [11] (eluting with EtOAc and then acetone) gave two components. The first to elute was dried *in vacuo* to give the (1*RS*,2*SR*) diastereoisomer (7) (1.13 g, 78%) as rods, m.p. 168—170 °C (from acetone–light petroleum, b.p. 60—80 °C) (lit.,[4] m.p. 169—171 °C) (Found: C, 74.7; H, 6.4; P, 9.2. Calc. for $C_{21}H_{21}O_2P$: C, 75.0; H, 6.31; P, 9.23%); R_F 0.5 (EtOAc); $\nu_{max.}$ 3 260 (OH) and 1 160 cm^{-1} (P=O); δ_H ($CDCl_3$) 8.1—7.3 (10 H, m, Ph_2PO), 7.25 (5 H, br s, PhC), 5.25 (1 H, dd, J_{HH} 1, J_{HP} 9 Hz, C*H*OH), 4.65 (1 H, br s, OH), 2.55 (1 H, ddq, J_{HH} 1, $J_{HMe} = J_{HP}$ 7 Hz, PC*H*Me), and 1.0 (3 H, dd, J_{HMe} 7, J_{MeP} 16 Hz, PCH*Me*) (Found: M^+, 336.1278. Calc. for $C_{21}H_{21}O_2P$: *M*, 336.1279), *m*/*z* 337 (15%, *M* + 1), 336 (7), 230 (100, Ph_2POEt), and 202 (42, Ph_2POH). The second to elute was dried *in vacuo* to give the (1*RS*, 2*RS*) *adduct* (8) as needles (159 mg, 11%), m.p. 145—146 °C [from acetone–light petroleum (b.p. 60—80 °C)] (Found: C, 74.9; H, 6.25; P, 9.2. $C_{21}H_{21}O_2P$ requires C, 75.0; H, 6.31; P, 9.2%); R_F 0.4 (EtOAc), $\nu_{max.}$ 3 170 (OH) and 1 173 cm^{-1} (P=O); δ_H ($CDCl_3$) 7.9—7.4 (10 H, m, Ph_2PO), 7.25 (5 H, m, PhC), 5.55 (1 H, d, J_{HOH} 2 Hz, OH), 4.8 (1 H, dt, J_{HOH} 2, $J_{HH} = J_{HP}$ = 9 Hz, C*H*OH), 2.9 (1 H, ddq, J_{HMe} 7, $J_{HH} = J_{HP}$ = 9 Hz, C*H*Me), and 0.7 (3 H, dd, J_{HMe} 7, J_{MeP} 18 Hz, CH*Me*) (Found: M^+, 336.1291. $C_{21}H_{21}O_2P$ requires *M*, 336.1279), *m*/*z* 337 (83%, *M* + 1), 336 (5, M^+), 318 (35, *M* − H_2O), 230 (100, Ph_2POEt) and 202 (45, Ph_2POH).

Attempted Equilibration of Adducts (7) *and* (8).—n-Butyl-lithium (2.9 ml; 1.5M in hexane) was added dropwise from a syringe to a stirred solution of ethyldiphenylphosphine oxide (1.0 g, 4.35 mmol) in dry THF (30 ml) at 0 °C. After 30 min the solution was cooled to −78 °C and benzaldehyde (460 mg, 4.35 mmol) added at that temperature. The solution was allowed to warm to 10 °C over 20 min and then cooled again to −70 °C before n-butyl-lithium (2.9 ml; 1.5M in hexane)

Table 4. N.m.r. spectra of adducts (10) and (11)



(10) *erythro*



(11) *threo*

R	*erythro* H_A (δ)	J_{AP} (Hz)	H_B (δ)	J_{BP} (Hz)	J_{AB} (Hz)	*threo* H_A (δ)	J_{AP} (Hz)	H_B (δ)	J_{BP} (Hz)	J_{AB} (Hz)
Me	5.25	9	2.55	7	1	4.8	9	2.9	9	9
Et	5.3	9	2.45	7	1	5.1	17	2.65	7	7
Pr^n	5.25	10	2.45	7	1	5.05	17	2.75	—	7
Pr^i	5.35	9	2.65	9	2	5.35	22	2.7	10	7
Bu^n	5.3	9	2.45	7	1	5.0	17	2.7	—	7
Bu^t	5.3	10	2.45	6	1	5.1	19	2.8	12	6

Table 5. Completion of the Horner-Wittig reaction on *erythro* adduct (7)

Base	Equivalents of base to (7)	Solvent	Temp. (°C)	Yield [a] of Alkene *Z*	*E*
KOH	1	DMSO	50	81	4
KH	1	DMF	50	81	4
$KOBu^t$	1	DMF	75	74	4
NaH	2	DMF	25	*b*	*b*
NaH	1	DMF	50	74	3
NaH	2	DMF	50	71	4
NaH	4	DMF	50	68	10
$KOBu^t$	2	THF	25	Starting material	
NaH	2	THF	Reflux	and ketone (4;	
NaH	35	THF	25	R^1 = Me, R^2 = Ph)	
K_2CO_3	2	DMF	100		
K_2CO_3	4	DMF	80		
Silica	—	Benzene	Reflux		
DBU	1	DMF	50	No reaction	
NaOH	*c*	CH_2Cl_2	25		
NaOH	*d*	CH_2Cl_2	Reflux		
NaOH	*e*	CH_2Cl_2	Reflux		

[a] Yields quoted as % isolated and distilled. [b] Ketone (4; R^1 = Me, R^2 = Ph) formed. [c] With benzyltrimethylammonium chloride. [d] With tetra-n-butylammonium iodide. [e] With benzyl trimethylammonium hydroxide.

was added as before. The yellow-green solution was kept at −70 °C for 15 min, allowed to warm to 0 °C and then quenched with saturated aqueous ammonium chloride (20 ml). The THF was removed under reduced pressure and brine (15 ml) added before extraction with dichloromethane (3 × 20 ml). The combined organic extracts were dried ($MgSO_4$) and separated by column chromatography (46 × 3.2 cm Kieselgel 60 column, 70—230 mesh, eluting with EtOAc–EtOH, 99 : 1) to give the (1*RS*, 2*SR*) adduct (7) (809 mg, 55%) and the (1*RS*, 2*RS*) adduct (8) (368 mg 25%). This sequence was repeated with a 96 h delay before, quenching the anion, but the yield and isomer ratios were the same.

Z-1-*Phenylprop*-1-*ene*.—Sodium hydride (60 mg; 80% dispersion in oil, 2.0 mmol) was added in one portion to a stirred solution of the (1*RS*, 2*SR*) adduct (7) (336 mg, 1.0 mmol) in dry DMF (25 ml). The clear solution was warmed to 50 °C for *ca.* 1 h by which time a white solid had precipitated. The solution was cooled and the precipitate dissolved by the addition of water (20 ml). The solution was diluted with brine (20 ml) and extracted with ether (3 × 30 ml). The organic phases were combined, washed with water (3 × 40 ml), dried ($MgSO_4$), and the solvent was removed under pressure. Bulb-to-bulb distillation (Kugelrohr apparatus) gave the alkene (82 mg, 75%), b.p. 63—65 °C/20 mmHg (lit.,[20] b.p. 64.5 °C/20 mmHg), R_F 0.75 (EtOAc) $\nu_{max.}$ (liquid film) 1 445, 913, 805, 769, and 702 cm^{-1} (C–H out-of-plane deformation), δ_H (CCl_4) 7.2 (5 H, br s, Ph), 6.4 (1 H, dq, J_{HMe} 2, J_{HH} 11 Hz, PhC*H*), 5.7 (1 H, dq, J_{HMe} 7, J_{HH} 11 Hz, C*H*Me), and 1.85 (3 H, dd, *J* 2, 7 Hz, Me).[21] G.l.c. analysis (column 1 and 2) showed that the product contained *ca.* 5% of the *E*-isomer. The aqueous residues were re-extracted with dichloromethane (3 × 30 ml), the extracts were dried ($MgSO_4$) and evaporated to dryness to give ethyldiphenylphosphine oxide (20 mg).

E-1-*Phenylprop*-1-*ene*.—In the same way, the (1*RS*, 2*RS*) adduct (8) (425 mg, 1.26 mmol) and sodium hydride (76 mg, 80% dispersion in oil, 2.52 mmol) gave, after distillation, the alkene (121 mg, 81%), b.p. 72—74 °C/20 mmHg (lit.,[20] b.p. 73.5 °C/20 mmHg), R_F 0.75 (EtOAc), $\nu_{max.}$ (liquid film) 1 445, 962 (C–H out-of-plane deformation), 736, and 694 cm^{-1}; δ_H (CCl_4) 7.2 (5 H, m, Ph), 6.3 (1 H, dq, J_{HMe} *ca.* 1, J_{HH} 16 Hz, PhC*H*), 6.1 (1 H, dq, J_{HMe} 6, J_{HH} 16 Hz, C*H*Me), and 1.85 (3 H, d, *J* 6 Hz, Me).[21] The *Z* isomer was not detected by g.l.c. (columns 1 and 2).

2-*Diphenylphosphinoyl*-1-*phenylpropan*-1-*one* (9).—We now prefer the two methods described here to those described previously.[12] *Method A.* n-Butyl-lithium (22 ml; 1.5M in hexane) was added dropwise to a stirred solution of ethyldiphenylphosphine oxide (6.9 g, 0.03 mol) in dry THF (70 ml) at 0 °C. After 30 min, the red solution was cooled to −78 °C and ethyl benzoate (4.51 g, 0.03 mol) was added dropwise. The pale yellow solution was allowed to warm to room temperature before saturated aqueous ammonium chloride (40 ml) was added. The solvent was removed under reduced pressure and the residue was diluted with brine (20 ml) and extracted with dichloromethane (3 × 30 ml). The organic extracts were dried ($MgSO_4$) and evaporated to dryness to give the ketone (9) as needles (6.6 g, 66%), m.p. 153—154 °C (from EtOAc) (lit.,[12] 152—154 °C), R_F 0.25 (EtOAc); $\nu_{max.}$ 1 670 (C=O), 1 445 (P–Ph), and 1 185 cm^{-1} (P=O); δ_H ($CDCl_3$) 8.0—7.2 (15 H, m, 3 × Ph), 4.6 (1 H, dq, J_{HH} 7, J_{HP} 15 Hz, CHP), and 1.6 (3 H, dd, J_{HH} 7, J_{HP} 16 Hz, Me).

Method B. The lithium derivative was prepared as described for method A from ethyldiphenylphosphine oxide (1.0 g, 4.35 mmol) and butyl-lithium (3.19 ml; 1.5M in hexane). After 30 min the red solution was cooled to −60 °C and added dropwise through a double-ended needle to a stirred suspension of copper(I) iodide (910 mg, 4.78 mmol) in dry THF (25 ml) also at −60 °C. The dark reaction mixture was stirred for 1 h at −35 °C, cooled to −50 °C, and benzoyl chloride (613 mg, 4.35 mmol) was added dropwise. The reaction mixture was stirred for 1.5 h, and allowed to warm to room temperature overnight. Water (30 ml) was added, the reaction mixture was filtered through Hyflo, and the organic layer separated. The aqueous phase was extracted with chloroform (3 × 50 ml) and the combined organic extracts dried ($MgSO_4$) and evaporated to dryness to give the ketone (9) (1.2 g, 82.8%, from EtOAc).

Oxidation of the Alcohols (7) *and* (8) *to the Ketone* (9).—*Method A.* Pyridinium dichromate [14] (1.0 g, 2.66 mmol) was added to a stirred solution of mixed alcohols (7) and (8) (600 mg, 1.78 mmol) in dry dichloromethane (10 ml) at room temperature. The dark reaction mixture was stirred for 18 h and then filtered through a 5 cm bed of silica. The silica was washed with EtOAc, and the combined filtrates evaporated to dryness to give the ketone (9) (408 mg, 68%, from EtOAc).

Method B. Pyridinium dichromate [14] (500 mg, 1.34 mmol) was added to a stirred solution of the mixed alcohols (7) and (8) (300 mg, 0.89 mmol) in dry DMF (5 ml) at room temperature. The dark reaction mixture was stirred overnight and then poured into water (100 ml) and extracted with EtOAc (3 × 50 ml). The extracts were dried ($MgSO_4$) and evaporated to dryness to give the ketone (9) (270 mg, 91%, from EtOAc).

Method C. Sodium hypochlorite solution [15] (10% available chlorine; 2 ml) was added to a stirred solution of the mixed alcohols (7) and (8) (100 mg, 0.3 mmol) in glacial acetic acid (2 ml) at room temperature. After 1 h, the solution was cooled to 0 °C and saturated aqueous sodium bisulphite (10 ml) was added slowly. The mixture was extracted with dichloromethane (3 × 5 ml) and the organic extracts washed with 3M-NaOH, dried ($MgSO_4$), and evaporated to dryness to give the ketone (9) (98 mg, 99%, from EtOAc).

Method D. Barium manganate [16] (2.0 g) was added to a stirred solution of the mixed alcohols (7) and (8) (200 mg, 0.6 mmol) in dry dichloromethane (10 ml) at room temperature. The dark reaction mixture was stirred for 18 h and filtered through 'Hyflo'. The filter bed was washed with dichloromethane and the combined organic layers evaporated to dryness to give the ketone (9) (158 mg, 79%, from EtOAc).

Reduction of Ketone (9) *with Sodium Borohydride.*—Sodium borohydride (30 mg, 0.75 mmol) was added in one portion to a stirred solution of the ketone (9) (500 mg, 1.5 mmol) in ethanol (20 ml). The reaction mixture was heated under reflux for 3 h, cooled to room temperature, and a saturated aqueous ammonium chloride (10 ml) added. The ethanol was removed under reduced pressure and several drops of dilute HCl were added to the aqueous residue. Brine (15 ml) was added and the reaction mixture extracted with dichloromethane (3 × 30 ml). The extracts were dried ($MgSO_4$) and evaporated to give an oil which was separated by flash column chromatography (eluting with EtOAc and then with acetone) as above to give the (1*RS*, 2*SR*) adduct (7) (56 mg, 11%) and the (1*RS*, 2*RS*) adduct (447 mg, 89%) described above.

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