Synthesis of monohydroxy -methyl- and -ethyl-phosphines PPh$_2$CHROH

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Abstract

The preparation of α-hydroxyphosphines PPh$_2$CHROH with R = H (**a**), Ph (**b**) and Et (**c**), and β-hydroxyphosphines PPh$_2$CHR'HROH (**e**–**i**) has been achieved in high yield by reaction of HPPh$_2$ or LiPPh$_2$ with RCHO or the oxides of cyclohexene (**e**), limonene (**f**), styrene (**g**, **h**) and pinene (**i**). With the exception of styrene oxide, the reactions with the oxides are very regioselective, giving only one of the possible isomers. *Cis*- and *trans*-limonene oxides react with LiPPh$_2$ in different conditions selectively, giving *trans*-phosphino derivatives from commercial mixtures of limonene oxide.

1. Introduction

The preparation of functionalized phosphines has attracted considerable interest in recent years. These compounds are mainly used in the preparation of coordination and organometallic compounds to be tested as homogeneous catalysts. In particular, several water-soluble phosphines, sulphonated [1] or with alcohol groups [2], have been reported. For a number of reasons related to the control of the stereochemistry of the complex or the higher optical yields obtained in catalytic asymmetric synthesis, the greatest efforts have been made with polydentate phosphines [3].

Monodentate hydroxyphosphines have been prepared by a wide range of methods. They can be used directly in the syntheses of coordination compounds or as intermediates for further functionalizations

$$PPh_2H + CH_2O \longrightarrow PPh_2CH_2OH \quad [4a]$$

$$PPh_2(2\text{-}C_6H_4OPr^i) + HBr$$

$$\longrightarrow [HPPh_2(2\text{-}(C_6H_4OH))]Br + NaAc$$

$$\longrightarrow PPh_2(2\text{-}C_6H_4OH) \quad [4b]$$

$$CH_3PPh_2 + {}^nBuLi/TMDA \longrightarrow LiCH_2PPh_2$$

$$LiCH_2PPh_2 + (CF_3)_2C{=}O$$

$$\longrightarrow Ph_2PCH_2C(CF_3)_2OH \quad [4c]$$

$$PPh_3 + 2Li \longrightarrow LiPPh_2 + LiPh$$

$$LiPPh_2 + LiPh + ClCH_2CMe_2OH$$

$$\longrightarrow PPh_2CH_2CMe_2OH \quad [4d]$$

$$Ph_2PH + HC{=}CCROH \xrightarrow{\text{AIBN}} Ph_2PCH{=}CHROH \quad [2b]$$
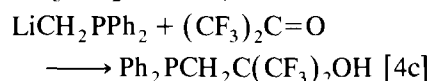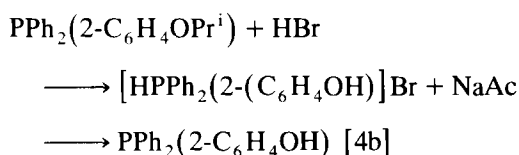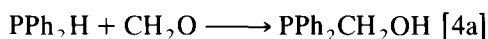
However, the β-hydroxyalkylation of nucleophiles is a general method for the synthesis of β-substituted alcohols. The epoxide-opening reaction shows high regioselectivity and stereoselectivity [5]. Generally, nucleophilic attack occurs at the least substituted carbon, with inversion of configuration. Theoretical studies corroborate the observed preference for inversion of configuration at the carbon attacked [6,7].

In this paper we report the preparation of α-hydroxyphosphines by the reduction of aldehydes by PR$_2$H (Eq. 1), and some β-hydroxyphosphines obtained by the epoxide-opening reaction (Eq. 2) and their use in the preparation of chiral monodentate functionalized phosphines. The great selectivity of the reaction allows the easy preparation of pairs of enantiomers. It has even been possible to separate selectively *trans* derivatives from mixtures of *cis* and *trans* limonene oxides.

$$PR_2H + R'CHO \dashrightarrow PR_2(CHR'OH) \quad (1)$$

$$R^1 \overset{O}{\underset{\triangle}{\wedge}} R^2 + LiPR_2^3 \longrightarrow R^1 \overset{HO}{\underset{\wedge}{\swarrow}} \overset{PR^3}{\underset{\diagdown}{}} R^2 \quad (2)$$

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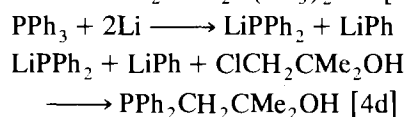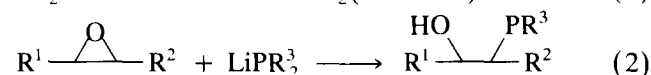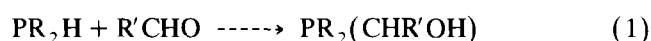
2. Results and discussion

2.1. α-hydroxyphosphines

The preparation of α-hydroxyphosphines PPh_2CH-ROH with R = H (a), Ph (b) and Et (c) was achieved by the method developed by Hellmann et al. [8]. The phosphines were prepared in quantitative yield by slowly adding the aldehyde RCHO to the neat secondary phosphine PPh_2H (Eq. 1). The reaction is highly exothermic and must be performed in an ice-bath to avoid an increase in the temperature which would favour oxygen-transfer reactions [9]. Under these conditions only products of a 1,2-carbonyl addition were observed. The phosphines were isolated as white solids on the addition of hexane to the mixture. The phosphine $PPh_2CHPhOH$ (b) is especially sensitive to air and must be handled with extreme care. Bubbling oxygen through $CHCl_3$ or acetone solutions of the phosphines leads quantitatively to the phosphine oxides.

The phosphine $PPh_2CHPhOH$ (b) has been obtained [10] using a similar reaction in hydrochloric acid and ether. It was characterized through intermediates as it is difficult to handle in air, but the melting point reported (186°C) is that of the oxide.

Analytical data and ^1H, ^{13}C and ^{31}P NMR spectra of the phosphines (a, b and c) are shown in Tables 1 and 2. ^1H NMR data of phosphines like $PPh_2CHPhOR$ have been reported [11]. The α-hydroxyphosphines b and c were obtained as racemic mixtures, as proved by the formation of two diastereomers on adding R-[{PPdCl(2-$C_6H_4CHCH_3NCH_2(2,6$-$Cl_2C_6H_4)$}$_2$] [12]. Each diastereomer showed the imine CH proton as a doublet, $J_{PH} = 5$–6 Hz, in the ^1H NMR spectrum. The signals could be assigned to the mononuclear palladium complex containing one phosphine and the cyclometallated ring see Eq. (3).
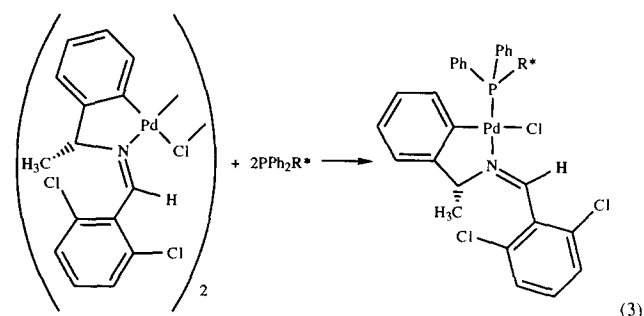

(3)

Table 1
Elemental analysis, optical rotations and mass spectra of phosphines and phosphine oxides

Phosphine and phosphine oxide		Elemental analyses % Exp. (Calc.)		Optical rotation $[\alpha]_D \pm 2°$	Melting point (°C)	Mass spectra
b	$C_{19}H_{17}OP$	C H	77.9(78.10) 5.8(5.82)		50–52	186(100), 183(27), 108(84), 107(56)
c	$C_{15}H_{17}OP$	C H	74.1(73.80) 7.0(6.96)		45–46	186(76), 183(19), 108(100), 107(66)
e	$C_{18}H_{21}OP$	C H	76.6(77.08) 7.6(7.39)		144–146	284(M^+, 44), 267(13), 229(13), 186(83), 183(64), 108(100)
(+)f	$C_{22}H_{27}OP$	C H	78.9(78.13) 8.0(7.98)	104(+)trans-f	115–117	338(M^+, 23), 243(15), 213(21), 186(65), 183(100), 108(69)
(−)f	$C_{22}H_{27}OP$	C H	77.6(78.13) 8.1(7.98)	−105(−)trans-f	116–118	
g	$C_{20}H_{19}OP$	C H	77.1(78.47) 6.2(6.21)	−36	oil	288(78), 287(100), 178(34), 167(21), 132(22)
h	$C_{20}H_{19}OP$	C H	76.9(78.47) 6.2(6.21)	123	92–94	288(100), 287(54), 183(78), 179(46, 108(36), 103(49)
i	$C_{22}H_{27}OP$	C H	77.2(78.07) 8.0(8.04)	−50	oil	320(23), 265(27), 252(11), 207(32), 186(42), 183(100)
(+)Of [a]	$C_{22}H_{27}O_2P$	C H	75.0(74.60) 7.6(7.62)	15	225–228	335(6), 271(24), 229(100), 203(90), 202(91), 201(82)
(−)Of [b]	$C_{22}H_{27}O_2P$	C H	75.4(74.60) 7.7(7.62)	−18	229–231	
Og	$C_{20}H_{19}O_2P$	C H	74.8(74.56) 6.0(5.90)	−25	128–130	304(43), 303(100), 201(51), 183(18), 179(29)
Oh	$C_{20}H_{19}O_2P$	C H	74.5(74.56) 6.0(5.90)	87	162–164	304(100), 303(91), 227(53), 202(85), 183(76), 180(81)
Oi	$C_{22}H_{27}O_2P$	C H	74.6(74.60) 7.4(7.62)	−41	145–147	336(15), 203(20), 202(100), 201(67), 155(19)

[a] (+)Of: oxide of (+)trans-f; [b] (−)Of: oxide of (−)trans-f.

2.2. β-hydroxyphosphines

The preparation of β-hydroxyamines by reaction of epoxides and ammonia has been widely used, but the analogous reaction between epoxides and secondary phosphines (Eq. 2) is relatively rare. However, β-hydroxyphosphines (e–i) have been obtained in good yield by reaction of PPh_2H with BuLi and different epoxides. The phosphine $PPh_2CH_2CH_2OH$ (d) was prepared by reaction of $BrCH_2CH_2OH$ and the red solution containing LiPh and $LiPPh_2$ obtained from PPh_3 and Li [13].

As an example, the preparation of a racemic mixture of trans-2-$PPh_2(C_6H_{10}OH)$ (e), previously reported by Issleib and Reischel [14], was performed at −78°C by dropwise addition of one equivalent of hexane solution of LiBu to a stirred mixture of PPh_2H and cyclohexene oxide in THF. The addition of each drop of LiBu produced an orange colour which disappeared immediately; and at the end of the addition the solution was yellow. After the addition at this temperature of 10% aqueous degassed NH_4Cl only a white solid containing the racemic mixture of trans-2-(diphenylphosphino)-cyclohexanol was finally obtained. No cis-2-(diphenylphosphino)cyclohexanol was detected by GC or ^{1}H or ^{13}C NMR spectroscopy.

Ring-opening of an epoxide, which generally occurs under basic or neutral conditions, usually involves an S_N2 mechanism. Since primary substrates undergo S_N2 attack more readily than secondary, asymmetrical epoxides are attacked in basic conditions at the least substituted carbon, with inversion at that carbon. Therefore attack of the phosphide ion at asymmetrical epoxides like limonene, styrene and pinene oxides might be highly regioselective.

Limonene oxide is usually a mixture of cis- and trans-1,2-epoxides [15]. The reaction of the phosphide ion with the mixed cis and trans epoxides gave two isomers of the phosphine which were very difficult to separate. However, it is possible to test the reactivity of the two (+)-limonene oxides separately, using commercial samples of the pure cis- and trans-(+)-limonene

oxides (Eqs. 4 and 5). The reaction performed at −78°C with trans-(+)-limonene oxide, as in the case of $PPh_2(C_6H_{10}OH)$, gave a white solid containing only one phosphine isomer (+)trans-f (Eq. 4). However, with cis-(+)-limonene oxide the reaction took place at −10°C and, after hydrolysis, two different phosphine isomers, cis-f and cis-f', were obtained as an oil (Eq. 5). The phosphine in lower proportion, cis-f' (30%), was the product of the less favoured attack at the methyl-substituted carbon. Proton and carbon NMR data especially of the carbon atoms 7 and 8 (Table 2) confirm these assignments. However, stereoisomers other than (cis-f') proposed (Eq. 5) cannot be identified with the data available. The α_D value of the mixture was −30 ± 2°.

(+) trans-limonene
1S, 2R, 4R

(4)
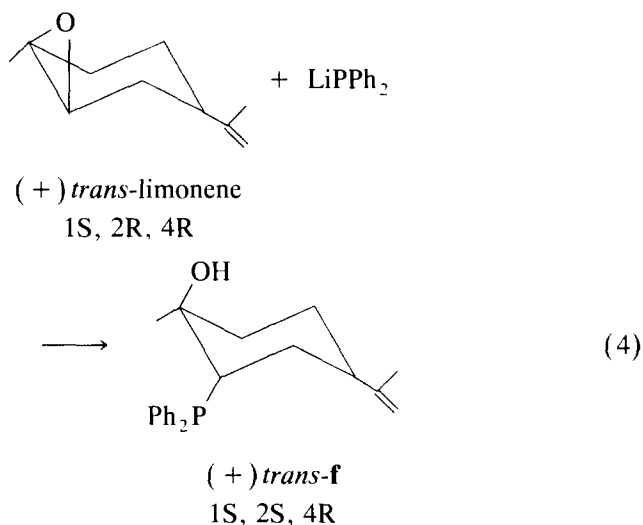
(+) trans-f
1S, 2S, 4R

Taking advantage of the different reactivities of the two isomers, it is possible to perform the reaction of a commercial mixture of one equivalent of (+)cis- and (+)trans-isomers (assumed to be 1:1 but ^{1}H NMR suggests a greater proportion of the trans-isomer) at −78°C with 0.5 equivalents of PPh_2H and LiBu. After hydrolysis, only one (+)trans-f isomer was obtained. The same reaction performed with the commercial mixture of (−)cis- and (−)trans-isomers gave only one isomer, (−)trans-f
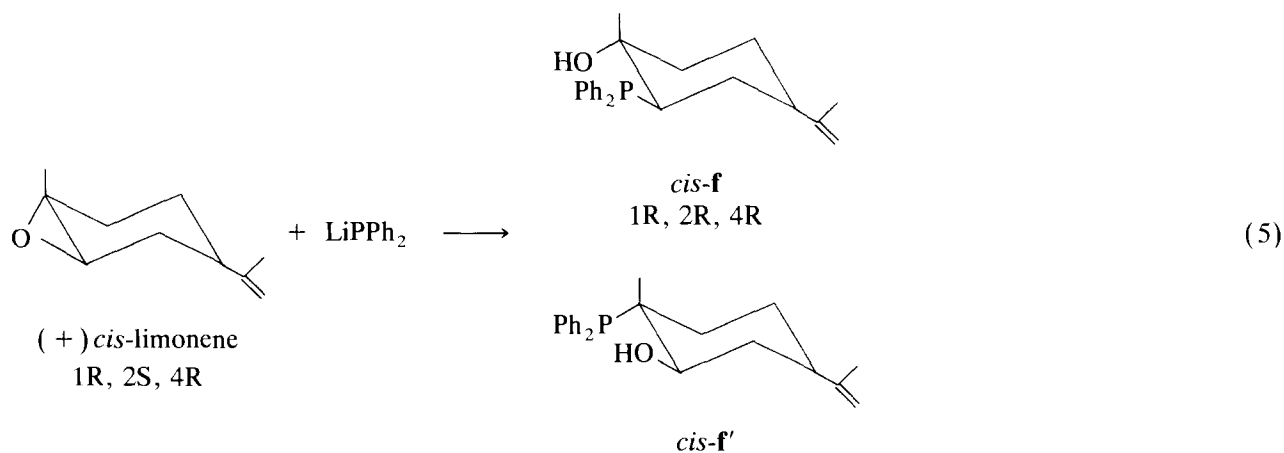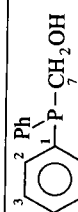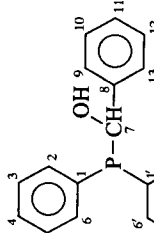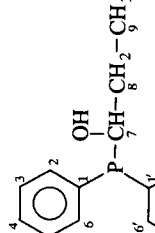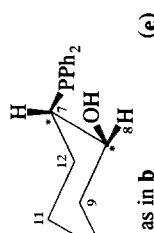

(+)cis-limonene
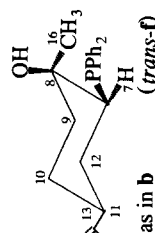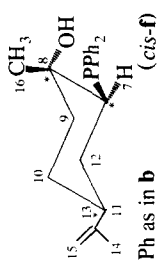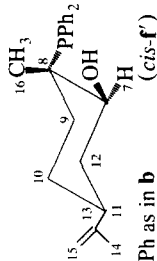1R, 2S, 4R

cis-f
1R, 2R, 4R

(5)

cis-f'
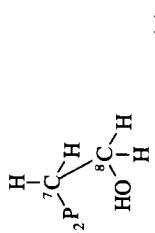
Table 2
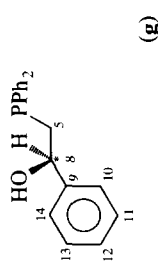^{1}H, ^{13}C and ^{31}P NMR data of phosphines and phosphine oxides

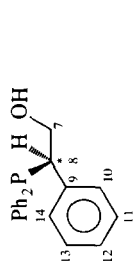| Phosphine–phosphine oxide	δ^{31}P [a]	δ^1H	δ^{13}C
(a)	−11.7	OH: 2.55 s broad; 7: 4.3 (d), J_{P-H} = 7.96 Hz; Ph: 7.2–7.4 m	1: 135.7 (d), J = 11.7; 2, 6: 133.3 (d), J = 17.4; 3, 5: 128.7 (d), J = 6.5; 4: 129.0; 7: 62.8 (d), J = 13.2
Rac-(b)	4.2	OH: not observed; 7: 5.5 (d), J_{P-H} = 2.1 Hz; Ph: 7.1–7.7 m	2, 6, 2', 6': 135.1 (m); 3, 5, 3', 5', 4, 4', 9, 10, 11, 12, 13: 129.4 (m); 7: 76.3 (d), J = 6.2
Rac-(c)	−6.5	OH: not observed; 7: 4.4 (m); 8: 1.6 (m); 9: 1.06 (t), J_{P-H} = 6.7; Ph: 7.3–7.6 m	1: 136.2 (d), J = 10; 1': not observed; 2, 6: 134.4 (d), J = 18.4; 2', 6': 133.2 (d), J = 17.4; 3, 5, 3', 5': 128.4; 4: 129.1; 4': not observed; 7: 74.1 (d), J = 15.5; 8: 28.6 (d), J = 20.0; 9: 11.0 (d), J = 13.5
(d)	−23.0	7: 3.72 (2H, dd), J_{P-H} = 7.3, J_{H-H} = 7.9; 8: 2.35 (2H, t), J_{H-H} = 7.7; OH: not observed; Ph: 7.26–7.40 (10H, m)	1: 137.8 (d), J = 11.9; 2, 6: 132.4 (d), J = 18.5; 3, 5: 128.3 (d), J = 4.5; 4: 128.1; 7: 31.7 (d), J = 12.6; 8: 59.5 (d), J = 23.6
(e)	−7.6	2, 6: 7.45 (2H, m); 2', 6': 7.52 (2H, m); 3, 4, 5: 7.32–7.37 (6H, m); 7: 2.34 (1H, m); 8: 3.47 (1H, m); 9a: 2.08 (1H, m); 9b: 1.40 (1H, m); 10a, 12a: 1.71 (2H, m); 10b, 11b: 1.20 (2H, m); 11a: 1.62 (1H, m); 12b: 0.90 (1H, m); OH: 2.68 (1H, b)	1: 138.4 (d), J = 15.2; 1': 137.3 (d), J = 16.4; 2, 6: 134.0 (d), J = 20.7; 2', 6': 132.5 (d), J = 18.3; 3, 5: 128.0 (d), J = 7.3; 3', 5': 127.9 (d), J = 6.7; 4: 128.5; 4': 127.6; 7: 43.5 (d), J = 12.5; 8: 71.9 (d), J = 13.8; 9: 35.1 (d), J = 6.7; 10: 24.2; 11: 25.8 (d), J = 5.3; 12: 27.0 (d), J = 3.6
(trans-f)	−9.7	2, 6: 7.55 (2H, m); 2', 6': 7.70 (2H, m); 3, 4, 5: 7.29–7.34 (6H, m); 7: 2.88 (1H, m); 9a, 10b: 1.62 (2H, m); 9b: 2.16 (1H, m); 10a: 1.72 (1H, m); 11: 2.16 (1H, m); 12a: 1.86 (1H, m); 12b: 1.35 (1H, m); 14: 1.41 (3H, s); 16: 1.08 (3H, s); 15E: 4.62 (1H, s); 15Z: 4.56 (1H, s)	1, 1': not observed; 2, 6: 135 (d), J = 21.2; 2', 6': 133.2 (d), J = 20.0; 3, 5: 128.6; 3', 5': 128.4; 4: 129.5; 4': 129.1; 7: 42.7 (d), J = 13.8; 8: 72.9 (d), J = 20.1; 9: 36.3 (d), J = 5.2; 10: 26.4; 11: 39.1 (d), J = 6.6; 12: 29.7 (d), J = 3.2; 13: 148.8; 14: 21.1; 15: 109.1; 16: 29.4 (d), J = 10.0

(cis-f) — Ph as in **b**; -13.7

1H: 2, 6: 7.48 (2H, m); 2', 6': 7.54 (2H, m); 3, 4, 5: 7.33 (6H, m); 7: 2.58 (1H, m), $J_{H-H} = 3.5$, $J_{P-H} = 13$; 9a: 1.84 (1H, m); 9b: 1.64 (1H, m); 10a: 1.28 (1H, m); 10b: 1.75 (2H, m); 11: 2.05 (1H, m); 12b: 1.10 (1H, m); 14: 1.61 (3H, s); 15E: 4.62 (1H, s); 15Z: 4.58 (1H, s); 16: 1.37 (3H, s)

13C: 1, 1': 137.6, $J = 10$; 2, 6: 135.2 (d), $J = 21.1$; 2', 6': 132.7 (d), $J = 17.9$; 3, 5, 3', 5': 128.2 (m); 4: 129.0; 4': 128.7; 7: 47.1 (d), $J = 16.4$; 8: 72.7 (d), $J = 12.7$; 9: 41.6 (d), $J = 3.6$; 10: 28.6; 11: 45.5 (d), $J = 4.5$; 12: 32.5 (d), $J = 1.8$; 13: 148.8; 14: 20.9; 15: 108.6; 16: 24.1 (d), $J = 13.1$

(cis-f') — Ph as in **b**; 7.0

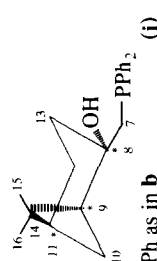1H: 2, 6: 7.62 (2H, m); 2', 6': 7.57 (2H, m); 3, 4, 5: 7.33 (6H, m); 7: 3.92 (1H, m); 9a: 1.28 (1H, m); 9b: 1.66 (1H, m); 10a: 1.56 (1H, m); 10b: 2.1 (1H, m); 11: 2.43 (1H, m); 12a: 1.72 (1H, m); 12b: 2.45 (1H, m); 14: 1.77 (3H, s); 15E: 4.77 (1H, s); 15Z: 4.78 (1H, d), $J = 5$
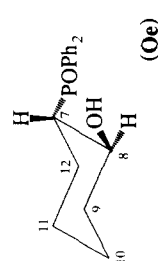
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(g) — -21.3

1H: OH: not observed; 7: 2.5 (2H, m); 8: 4.67 (1H, m); Ph: 7.1–7.8 (15H, m)

13C: 1: 138.3 (d), $J = 11.7$; 1': 137.8 (d), $J = 12.2$; 2, 6: 132.8 (d), $J = 21.8$; 2', 6': 132.4 (d), $J = 18.7$; 3, 5, 5': 128.2; 4, 4': 128.5; 7: 39.5 (d), $J = 13.9$; 8: 71.7 (d), $J = 16.9$; 9: 144.5 (d), $J = 5.8$; 10, 14: 125.6; 11, 13: 128.2, 12: 127.4

(h) — -8.1

1H: OH: not observed; 7: 3.8 (2H, m); 8: 3.9 (1H, m); Ph: 7.1–7.6 (15 H, m)

13C: 1, 1': not observed; 2, 6: 132.8 (d), $J = 20.5$; 2', 6': 132.2 (d), $J = 18.4$; 4, 4', 3, 5, 3', 5', 10, 11, 12, 13, 14: 124.7–128.5; 9: 137.2 (d), $J = 6$; 7: 63.9 (d), $J = 29.1$; 8: 47.6 (d), $J = 13.5$
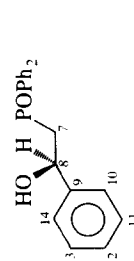
(i) — -24.4

1H: 2, 6: 7.50 (2H, m); 2', 6': 7.45 (2H, m); 3, 4, 5: 7.28, 7.34 (6H, m); 7: 2.61 (2H, d), $J_{H-P} = 4$ Hz; 9: 2.09 (1H, m); 10a: 2.12 (1H, m); 10b: 1.49 (1H, m); 11: 1.84 (1H, m); 12a: 1.89 (1H, m); 12b: 1.75 (1H, m); 13: 1.93 (2H, m); 15: 0.80 (3H, s); 16: 1.02 (3H, s)
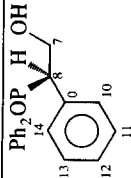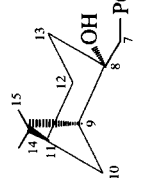
13C: 1, 1': not observed; 2, 6: 134.3 (d), $J = 19.7$; 2', 6': 133.1 (d), $J = 18.2$; 4: 129.4; 4': 128.7; 3, 5, 3', 5': 129.4 (m); 7: 45.8 (d), $J = 12.9$; 8: 76.5 (d), $J = 11.0$; 9: 53.4 (d), $J = 8.6$; 10: 27.4; 11: 40.7; 12: 25.2; 13: 32.6 (d), $J = 6.8$; 14: 38.2; 15: 23.4; 16: 27.2

(Oe) — 39.4

1H: OH: 5.27 (1H, b); 7: 2.52 (1H, m); 8: 3.81 (1H, m); 9a: 2.07 (1H, m); 9b: 1.39 (1H, m); 10a: 1.72 (1H, m); 10b: 1.12 (1H, m); 11a: 1.62 (1H, m); 11b: 1.23 (1H, m); 12a: 1.72 (1H, m); 12b: 0.93 (1H, m); Ph: 7.75 (2H, m); 7.69 (2H, m), 7.48 (4H, m), 7.55 (2H, m)

13C: 2, 6: 132.4 (d), $J = 8.8$; 2', 6': 131.1 (d), $J = 9.2$; 3, 5: 128.8, $J = 11.5$; 3', 5': 128.3, $J = 11.2$; 4: 132.2 (d), $J = 11.4$; 7: 43.7 (d), $J = 69.5$; 8: 69.5 (d), $J = 5.1$; 9: 35.3 (d), $J = 10.9$; 10: 24.0; 11: 25.5 (d), $J = 13.6$; 12: 26.6

(O(+)trans-f) — 34.3
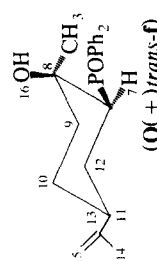
1H: 7: 2.89 (1H, m); 11: 2.37 (1H, m); 9a: 1.94 (1H, m); 9b: 1.70 (1H, m); 10a: 1.82 (1H, m); 10b: 1.58 (2H, m); 12a: 1.94 (1H, m); 14: 1.53 (3H, s); 16: 1.22 (3H, s); 15: 4.8 (1H, s); 15E, 15Z: 4.6 (1H, s); Ph: 7.84 (4H, m), 7.5 (6H, m)

13C: 2, 6: 131.6 (d), $J = 8.9$; 2', 6': 130.8 (d), $J = 8.8$; 3, 5: 128.6, $J = 11.2$; 3', 5': 128.4, $J = 11.1$; 4, 4': 131.7 (d), $J = 10.7$; 7: 43.7 (d), $J = 67.5$; 8: 72.7; 9: 37.5 (d), $J = 5.9$; 10: 25.5; 11: 39.1 (d), $J = 8.4$; 12: 28.0; 13: 146.6; 14: 21.8; 15: 110.6; 16: 26.7

(Og) — 27.9

1H: OH: 4.75 (1H, b); 7: 2.7 (2H, m); 8: 5.15 (1H, td), $J_{P-H} = 2.3$, $J_{H-H} = 10$; Ph: 7.3–7.8 (15H, m)

13C: 7: 39.1 (d), $J = 68.1$; 8: 69.2 (d), $J = 4.3$; 9: 143.7 (d), $J = 9.3$; 10, 14: 125.5; 11, 13: 128.8; 12: 127.6; 2, 6: 130.9 (d), $J = 9.3$; 2', 6': 130.4 (d), $J = 10.3$; 3, 5, 3', 5': 128.8 (m); 4, 4': 132.17

Table 2 (continued)

| Phosphine–phosphine oxide	$\delta^{31}P$ [a]	δ^1H	$\delta^{13}C$
(Oh)	28.4	OH: 3.1 (1H, b); 7: 4.2 (2H, dd), $J_{P-H} = 13$, $J_{H-H} = 6.2$; 8: 3.8 (1H, dt), $J_{P-H} = 10$, $J_{H-H} = 6.2$; Ph: 7.2–7.8 (15H, m)	Ph: 127.5–132.1; 7: 63.1; 8: 49.4 (d), $J = 65.7$
(Oi)	33.3	2, 6, 2', 6': 7.75 (4H, m); 3, 4, 5: 7.50 (6H, m); 7a: 2.66 (1H, dd), $J_{H-P} = 8.5$, $J_{H-H} = 15$; 7b: 2.84 (1H, dd), $J_{H-P} = 11.5$, $J_{H-H} = 15$; 9: 2.14 (1H, m); 10a: 2.07 (1H, m); 10b: 1.6 (1H, d, $J_{H-H} = 10$); 11: 1.79 (2H, m); 11, 13b: 1.79 (2H, m); 12a: 1.89 (1H, m); 12b: 1.68 (1H, m); 13a: 1.99 (1H, m); 15: 0.78 (3H, s); 16: 0.83 (3H, s)	2, 6: 130.9 (d), $J = 9.4$; 2', 6': 130.2 (d), $J = 9.6$; 3, 5: 128.8, $J = 5.2$; 3', 5': 128.6, $J = 5.1$; 4, 4': 131.7; 7: 41.9 (d), $J = 68.8$; 8: 76.7 (d), $J = 5.7$; 9: 52.5 (d), $J = 6.2$; 10: 27.1; 11: 40.3; 12: 25.2; 13: 33.0 (d), $J = 10.5$; 14: 37.5; 15: 23.0; 16: 26.7

Solvent is CH_2Cl_2.

With the asymmetric (+)styrene oxide, the reaction at −78°C gave an oil containing a mixture of the two possible phosphines (Eq. 6), 1-phenyl-2-(diphenylphosphino)ethanol (g) and 2-phenyl-2-(diphenylphosphino)ethanol (h), in a 7:3 ratio (^{31}P NMR spectrum). The greater amount of g is in accordance with the preferential nucleophilic attack of the phosphide ion at the least hindered carbon.

$$(6)$$
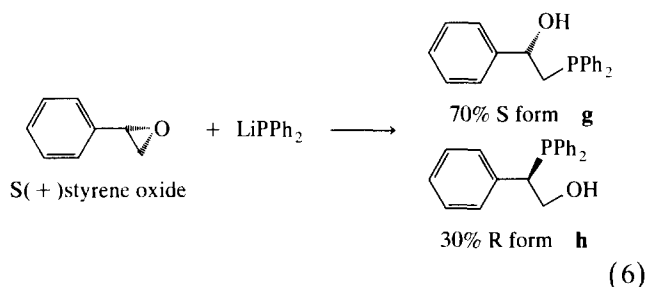
The separation of the two phosphines was best achieved through their oxides. The mixture of phosphines was dissolved in $CHCl_3$ and oxidized with H_2O_2. The organic layer contains the two oxides **Og** and **Oh**, which were separated by column chromatography. Reduction of the phosphine oxides proceeded in high yield without loss of optical purity [16] on heating dry toluene solutions of each oxide with $SiHCl_3$ and triethylamine.

The crowded pinene oxides showed different reactivity toward the phosphide ion. (−)α-pinene oxide did not react, even at reflux in THF with $LiPPh_2$ (Eq. 7). However (+)β-pinene oxide gave selectively only phosphine (i), corresponding to attack at the less hindered carbon (Eq. 8).

$$(7)$$

(−) α-pinene oxide
1R, 2R, 3S

$$(8)$$

(+) β-pinene oxide
1R, 2S

i
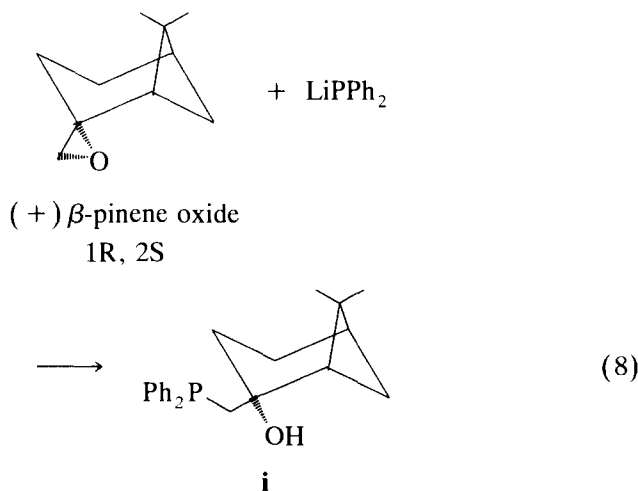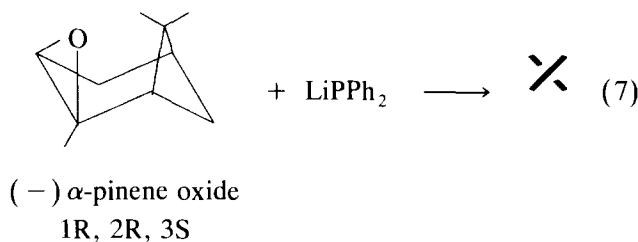
All these monohydroxophosphines are insoluble in water. The mass spectra of the phosphines and their oxides (Table 1) did not show any remarkable features. They all show the fragmentation pattern of the PPh_2 radical [17]. The molecular ion was not observed in the GC–MS spectra of the phosphine oxides. The ^{1}H, ^{13}C and ^{31}P NMR spectra of the phosphines are presented in Table 2. The ^{13}C spectra were tentatively assigned by estimation or comparison with published data [18]. The ^{1}H spectra were assigned with the help of two dimensional (H, C)–COSY experiments. The differentiation between *exo* and *endo* protons of the CH_2 groups of the rings was possible (xa and xb in Table 2), but not their complete assignation. However, a unique isomer was always observed with each phosphine. The difference between the $^1J_{PC}$ observed in the ^{13}C spectra of the phosphine (13–15 Hz) and the corresponding oxide (67–70 Hz) is large enough to use as a test of the oxidation state of the phosphorus derivative.

3. Experimental

^{1}H and ^{13}C NMR spectra were recorded on Gemini 200 or Unity 300 Varian instruments. ^{31}P NMR spectra were obtained with a Bruker WP80SY instrument (32.38 MHz). Chemical shifts for ^{1}H and ^{13}C NMR spectra were referred to Me_4Si. The reference for ^{31}P spectra was H_3PO_4 (85%) and $P(OMe)_3$ was used as secondary reference. All positive chemical shifts are downfield from the standard. All ^{31}P NMR spectra were proton decoupled. Solvents used were $CDCl_3$ for ^{1}H NMR, and CH_2Cl_2 or $CHCl_3$ with a 5 mm coaxial insert tube containing [$^2H_6$]acetone–$P(OMe)_3$ for ^{31}P spectra. ^{1}H/^{13}C COSY experiments were carried out on a Varian XL 500 instrument. IR spectra were recorded on a Nicolet 520 FT–IR instrument. Mass spectra were obtained with a Hewlett Packard 5890 chromatograph equipped with a 50 m Ultra-2 cross-linked 5% phenylmethyl silicone capillary column coupled to a Hewlett Packard 5971 A mass-selective detector. Elemental analyses were carried out at the Servei d'Anàlisis Elementals de la Universitat de Barcelona using an Eager 1108 microanalyzer. Optical rotation measurements were performed on a Perkin-Elmer 241MC polarimeter at 20°C with the sodium D-line.

All solvents were dried and purified by standard methods and purged with nitrogen before use. The phosphines Ph_2PCH_2OH (a) and $Ph_2PCH_2CH_2OH$ (d) were prepared as described in the literature [4a,13]. Commercial reagents from Fluka and Janssen were used without further purification. Standard techniques for the manipulation of air-sensitive compounds were used for the preparation of the phosphines. The phosphines must be stored under argon or nitrogen.

3.1. Preparation of $Ph_2PCH(Ph)OH$ (b) and Ph_2P-$CH(CH_2CH_3)OH$ (c)

Benzaldehyde (3.072 g, 16.5 mmol) or propionaldehyde (0.958 g, 16.5 mmol) was added dropwise to a Schlenk tube containing 2.69 g (15 mmol) of $HPPh_2$ at $-20°C$. The mixture was stirred until a white precipitate formed (15 min). The solid was filtered off, washed with small amounts of cold degassed ethanol and dried under vacuum. Yield: 4.12 g (94%) of **b** and 3.37 g (92%) of **c**.

3.2. Preparation of $Ph_2PC_6H_{10}OH$ (e)

To a solution of $HPPh_2$ (3.91 g, 21 mmol) and cyclohexene oxide (2.06 g, 21 mmol) in THF (20 ml) at $-78°C$, a 1.6 M hexane solution of ^nBuLi (13.1 ml, 21 mmol) was added dropwise. The mixture was stirred for 1 h, allowed to warm to room temperature and stirred for 2 h. The solution was cooled to 0°C and hydrolyzed by slow addition of 10% aqueous degassed NH_4Cl (100 ml). The aqueous layer was extracted with THF (3 × 10 ml) and the combined organic layer was dried over Na_2SO_4, filtered, and evaporated to dryness. The white precipitate obtained was recrystallized from THF/hexane. Yield **e**: 5.85 g (98%) of air-sensitive white crystals.

3.3. Preparation of (+) and (−)trans-$Ph_2PLimOH$ ((+)trans-f, (−)trans-f) and (+)cis-$Ph_2PLimOH$ (cis-f + cis-f')

3.3.1. (+)trans-f from a pure sample of (+)trans-limonene oxide

To a solution of $HPPh_2$ (1.117 g, 6 mmol) and (+)trans-limonene oxide (0.913 g, 6 mmol) in THF (5 ml) at $-78°C$, a 1.6 M hexane solution of ^nBuLi (3.8 ml, 6 mmol) was added dropwise. The mixture was stirred for 1 h and then allowed to warm to room temperature and stirred for 1 h. The mixture was then cooled to 0°C and hydrolyzed by slow addition of 10% aqueous degassed NH_4Cl (20 ml). The aqueous layer was extracted with THF (3 × 10 ml) and the combined organic layer was dried over Na_2SO_4, filtered and evaporated to dryness. The white precipitate obtained was recrystallized from THF/hexane. Yield (+)trans-f: 1.97 g (97%) of air-sensitive white crystals.

3.3.2. (cis)-f from a pure sample of (+)cis-limonene oxide

To a solution of $HPPh_2$ (1.117 g, 6 mmol) and (+)cis-limonene oxide (0.913 g, 6 mmol) in THF (5 ml) at $-78°C$, a 1.6 M hexane solution of ^nBuLi (3.8 ml, 6 mmol) was added dropwise. The mixture was allowed to warm to $-10°C$ and stirred for 2 h. The

mixture was then hydrolyzed by slow addition of 10% aqueous degassed NH_4Cl (20 ml). The aqueous layer was extracted with THF (3 × 10 ml) and the combined organic layer was dried over Na_2SO_4, filtered and evaporated to dryness. An air-sensitive viscous material was obtained containing two different phosphines cis-f (70%) and cis-f' (30%). Yield cis-f + cis-f': 1.72 g (85%).

3.3.3. (+)trans-f and (−)trans-f from cis/trans mixtures of (+) and (−)limonene oxides

To a solution of $HPPh_2$ (3.91 g, 21 mmol) and (+) or (−)limonene oxide (cis/trans mixtures (6.4 g, 42 mmol) in THF (20 ml) at $-78°C$, a 1.6 M hexane solution of ^nBuLi (13.1 ml, 21.0 mmol) was added dropwise. The mixture was stirred for 1 h and then hydrolyzed by slow addition of 10% aqueous degassed NH_4Cl (100 ml). The mixture was allowed to warm to room temperature and the THF layer separated. The aqueous solution was extracted with THF (3 × 10 ml) and the combined organic layer dried over Na_2SO_4, filtered, and evaporated to dryness. The white precipitate obtained was recrystallized from THF/hexane. Yields (+)trans-f: 6.88 g (97%); (−)trans-f: 6.53 g (92%) of air-sensitive white crystals.

3.4. Preparation of $Ph_2PCH_2CH(Ph)OH$ (g) and $Ph_2PCH(Ph)CH_2OH$ (h)

A 1.6 M hexane solution of ^nBuLi (20.6 ml, 33 mmol) was added dropwise by syringe over a 15 min period to a solution of R-(+) styrene oxide (3.964 g, 33 mmol) and $HPPh_2$ (6.15 g, 33 mmol), in 20 ml of THF at $-78°C$. The reaction mixture was worked up as described above for **e**, and a viscous material was obtained containing the two phosphines Ph_2PCH_2CH-(Ph)OH (**g**, 70%) and $Ph_2PCH(Ph)CH_2OH$ (**h**, 30%). The crude material was dissolved in 30 ml of $CHCl_3$, H_2O_2 (15%, 20 ml) was added and the mixture was stirred at room temperature for 1 h. The organic layer was separated and the aqueous solution was extracted with $CHCl_3$ (3 × 10 ml). The combined organic layer was dried over Na_2SO_4, filtered and evaporated to dryness. The resulting white solid was identified as a mixture of the oxides **Og** and **Oh**. Yield 9.85 g (97%).

Two of the mixture of oxides **Og** and **Oh** were dissolved in 10 ml of $CHCl_3$ and chromatographed on silica gel (Merck, 60, 230–400 mesh), using 90% $CHCl_3$/10% MeOH as eluent. Three bands were collected. The first band was identified as starting material (styrene oxide). The second band was collected and concentrated. Addition of hexane to the solution gave a white precipitate, which was filtered off and washed with hexane and dried under vacuum. The resultant white solid was identified as the oxide $Ph_2(O)PCH_2CH$-

(Ph)OH (**Og**). Yield 1.6 g (80%). The third band was worked up as described for the second band. The white solid obtained was identified as the oxide $Ph_2P(O)CH(PH)CH_2OH$ (**Oh**). Yield 0.3 g (15%).

3.4.1. Reduction of phosphine oxides with $HSiCl_3$

A solution of 1.53 g (5 mmol) of the oxide **Og** in 15 ml of warm toluene was added over a period of 10 min to a mixture of trichlorosilane (1.35 g, 10 mmol) and triethylamine (1.01 g, 10 mmol) in dry toluene (20 ml). The mixture was then refluxed for 2 h.

The reaction mixture was cooled in ice and 30 ml of 30% aqueous degassed NaOH was then added slowly with stirring. The mixture was stirred for 24 h until all the solids had dissolved. The organic layer was separated and the aqueous layer was extracted with toluene (3 × 10 ml). The combined organic solution was dried over Na_2SO_4, filtered and evaporated to dryness. The phosphine **g** appeared as a dense, air-sensitive oil. Yield 1.22 g (84%).

The phosphine oxide **Oh** was worked up as described for the oxide **Og**. The phosphine **h** was obtained as a white solid in similar yield.

3.5. Preparation of $Ph_2PPinOH$ (i)

The phosphine was prepared according to a procedure similar to that described above for **g** and **h** using (+)β-pinene oxide (3.9 g, 25.6 mmol). The phosphine **i** appeared a dense, air-sensitive oil. Yield 8.41 g (97%).

Acknowledgments

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