Synthesis of chiral β-aminophosphine oxides *via* novel azaboretidinium bromide salts[1]

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The enamino(triphenyl)phosphonium salts $[Ph_3PCH{=}CMeNR^1R^2]^+ Br^-$ [where $R^1 = R^2 = (CH_2)_4$, $(CH_2)_5$; (*S*)-CHMePh; R^1 = H, R^2 = (*S*)-CHMePh; R^1 = H, R^2 = (*S*)-$(CH_2)_3$-CH(CH_2OH)] have been synthesised and have been shown to react with an excess of borane·tetrahydrofuran to give novel azaboretidinium salts—the first examples of four-membered C–B–N–C heterocycles. The structure of [(1*S*,3*R*,4*S*,1′*S*)-4-methyl-1-(1-phenylethyl)-1,2-azaboretidin-1-ium-2-uid-3-yl]triphenylphosphonium bromide has been established by X-ray crystallography. Borane does not result in any significant stereoselectivity in these reductions and the azaboretidinium salts are mixtures of diastereomers. In contrast, the similar reduction with (*R*)-(+)-monoisopinocampheylborane or (*S*)-(−)-monoisopinocampheylborane leads to single diastereomers in high yields when R^1 and R^2 are non-bulky; with sterically demanding groups the azaboretidinium salts are unstable and decompose on work-up. Heating these azaboretidinium salts with aqueous sodium hydroxide in methanol, or better, aqueous sodium hydroxide alone, results in the direct formation of the phosphine oxides, $Ph_2P(O)CH_2CHMeNR^1R^2$ which, in the case of compounds derived from Ipc_2BH_2, have an ee value of >75%. In some cases, particularly when R^1 and R^2 are bulky, the use of sodium hydroxide in methanol results in an appreciable amount of *rac*-$Ph_2PCH_2CHMe(OMe)$ as a by-product, but this can be avoided by carrying out the reactions in the absence of methanol.

Although several methods are described in the literature for the synthesis of P–N ligands[2–8] there are very few reported examples of chiral P–N compounds.[9–15] Transition metal complexes of chiral P–N ligands have recently found application as catalysts for asymmetric hydrogenation,[9] hydrosilylation of carbonyl compounds,[10] palladium-assisted substitution of allyl acetates[11] and conjugate addition of nucleophiles to α,β-unsaturated carbonyl compounds.[12]

Previous work carried out in our Department suggested the possibility that chiral β-aminophosphorus ligands may be conveniently prepared from enamino(triphenyl)phosphonium salts of the type $[Ph_3PCR^1{=}CR^2NR^3R^4]^+ X^-$ **1** by reduction of the double bond and modification of the triphenylphosphonium group. We have shown that trifluoromethanesulfonate (triflate) salts of type **1** (where R^1 = alkyl, aryl or CO_2R; R^2 = alkyl or aryl; R^3 = H; R^4 = Me, X = OSO_2CF_3) are available from the reactions of *N*-methylnitrilium triflate salts with triphenylphosphoranes[16,17] or, for R^1 = H, with trimethylsilylmethylidenetriphenylphosphorane.[18] Compounds where R^1 = H, R^2 = Me and X = Br are more conveniently prepared by the method of Schweizer and co-workers[19,20] from the reactions of primary or secondary amines with triphenyl(prop-2-ynyl)phosphonium bromide **2**.

We now describe the borane reduction of a number of enamino(triphenyl)phosphonium salts and the conversion of some of the novel azaboretidinium salts produced into enantiomerically pure β-aminodiphenylphosphine oxides with potential application as ligands for asymmetric catalysis.

Results and discussion

Our initial efforts were directed towards the synthesis of enamino(triphenyl)phosphonium salts of type **1** having a chiral group on the nitrogen atom, in the expectation that this might be used to exert stereocontrol in the reduction step. The synthesis from nitrilium triflate salts was clearly not suitable for this purpose, but Schweizer's route from **2** could easily be adapted by suitable choice of a chiral primary or secondary amine, although the compounds available by this route are restricted to those where R^1 = H and R^2 = Me.

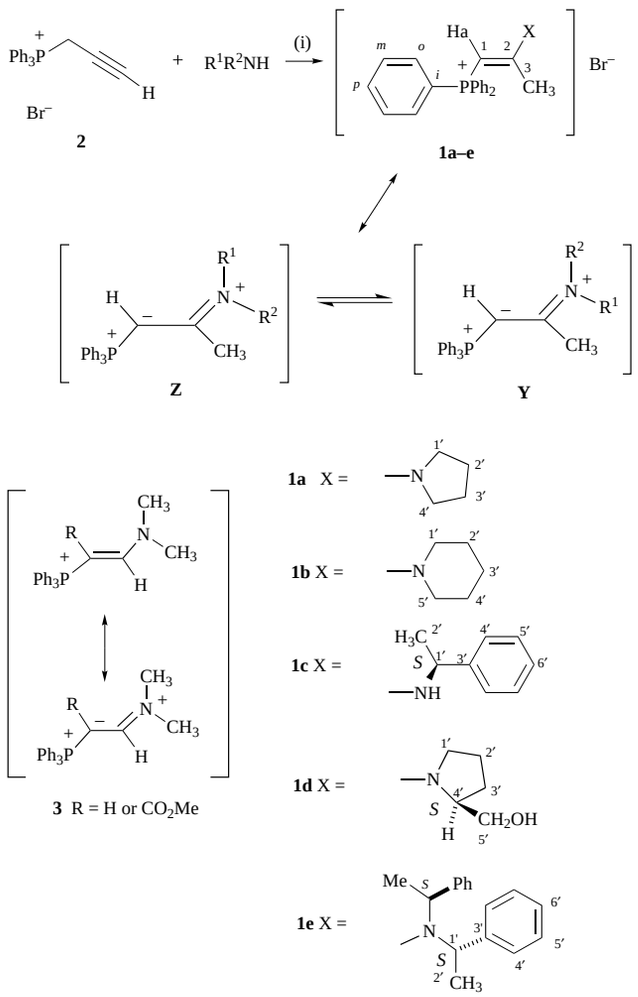
Compound **2** is easily prepared in good yield (70%) by reaction between triphenylphosphine and prop-2-ynyl bromide with hydrogen bromide (48% aq.) in dioxane.[21] The known reaction between **2** and piperidine[22] and the new reactions with pyrrolidine, (*S*)-(−)-1-phenylethylamine, (*S*)-(+)-pyrrolidine-2-methanol and (*S*,*S*)-*N*,*N*-bis(1-phenylethyl)amine were carried out by refluxing the reactants in acetonitrile to give the expected salts **1a**–**e** (Scheme 1) in the yields shown in Table 1. In each case the progress of reaction was conveniently followed by ^{31}P NMR spectroscopy and most of the products were isolated analytically pure without the need for recrystallisation. The physical and spectroscopic data for these compounds are given in Tables 1–3.† Similar reactions, including the reaction with (*R*)-(+)-1-phenylethylamine, have recently been reported by Palacios *et al.*[23]

An interesting observation from the ^{13}C NMR spectrum of **1a** is that the four C atoms of the pyrrolidine ring (C1′ and C2′) are non-equivalent. The C1′ and C2′ carbon atoms of the piperidine ring in **1b** are broadened suggesting non-equivalence in this compound also. The source of this non-equivalence is likely to be restricted rotation around the C2–N bond. This is most clearly shown for the compound **1d** which exists as two rotamers in a 1:2 ratio as demonstrated by the two sets of bands present in the ^1H, ^{13}C and ^{31}P NMR spectra (see Tables 2 and 3). We have not established the structure of the major rotamer, but it is expected to be **1dY** (where $R^1 = C^{1'}H_2$, $R^2 = C^{4'}HCH_2OH$) rather than **1dZ** (see Scheme 1) as in the latter there will be considerable steric interaction between the CH_2OH group and the methyl substituent C3. It is known from X-ray crystallographic studies[17] that enamino(triphenyl)phosphonium salts of type **1** have the *E*-configuration with the PPh_3 group *anti* to the amino substituent. It has also been established that in the solid state and, presumably, also in solution the nitrogen lone pair electrons are extensively delocalised so that the molecule exists predominantly in the zwitterion form shown in Scheme 1. This strengthens the C2–N bond resulting in

† The numbering in the NMR assignments and the discussion is as shown on the structures. The names in the Experimental section are given with the systematic IUPAC numbering systems.

Table 1 Physical data for enaminophosphonium salts **1a**–**e**

Comp.	Yield (%)	Mp (°C)	Molecular formula	Found (calc.) (%) C	H	N	Br	P	*m/z*, [(M^+ − Br)]
1a	90	230–231	$C_{25}H_{27}BrNP$	66.1 (66.4)	6.1 (6.0)	3.2 (3.1)	17.5 (17.7)	6.7 (6.8)	372
1b	75	232–233	$C_{26}H_{29}BrNP$	66.7 (66.9)	6.4 (6.2)	3.0 (3.0)	17.1 (17.2)	6.6 (6.6)	386
1c	76	251–252	$C_{29}H_{29}BrNP$	69.4 (69.3)	6.1 (5.8)	3.0 (2.8)	16.2 (15.9)	5.9 (6.2)	422
1d	78	197–198	$C_{31}H_{33}BrNOP$	64.9 (64.6)	6.0 (6.3)	2.9 (3.0)	16.6 (15.9)	6.4 (6.2)	402
1e	88	79–80	$C_{37}H_{37}BrNP$	73.1 (73.3)	6.1 (6.1)	2.4 (2.3)	13.2 (13.2)		526



Scheme 1 *Reagents and conditions:* (i) acetonitrile, reflux 1–2 h

restricted rotation around this bond with the possibility of having the rotamers **Y** and **Z**. A similar observation has been made previously by Bestmann *et al.*,[24] who showed that for the compound **3** the two N–CH_3 groups had distinctly different chemical shift values at room temperature. The rotational energy does depend upon the group bonded to the C1 atom and for the compounds **3** (R = Me, Et or Pr^n) only a single methyl signal is seen in each case.[24]

Attempts to hydrogenate the salt **1a** using 10% palladium on charcoal as a catalyst in methanol gave only unchanged starting material after a week at room temperature and 1 atm hydrogen. The zwitterionic character of **1a**–**e** suggested the possibility that an electrophilic reducing agent, such as borane, may be more appropriate for this reduction. Consequently, the reduction of **1c** was explored using an excess of BH_3·THF in THF solvent at room temperature. Monitoring by ^{31}P NMR spectroscopy showed that a clean reaction occurred over 3 h to give a single product, and after work-up a pale-yellow oil was isolated in 84% yield. It quickly became apparent from the spectroscopic evidence that this compound was not the expected reduction product, $(Ph_3PCH_2CHMeNHCHMePh)^+$ Br^-. Mass spectrometry showed the presence of boron, which was confirmed by ^{11}B NMR spectroscopy, and the ^1H, ^{13}C and ^{31}P NMR spectra indicated that it was an approximate 1 : 1 mixture of two diastereomers. Fortunately, it proved possible to separate these by recrystallisation from propan-2-ol and good crystals were obtained of the diastereomer **4cA** which was insoluble in propan-2-ol; the soluble diastereomer **4cB** was isolated as a slightly impure pale-yellow oil. The single crystal X-ray structure of **4cA** established that it was a novel azaboretidinium salt having the 1*S*,3*R*,4*S*,1′*S*-configuration (see ref. 1). The molecule is associated with half a molecule of propan-2-ol in the unit cell.‡

The similar reduction of the compounds **1a**,**b**,**d** and **e** using a large excess of BH_3·THF in dichloromethane gave the analogous products **4a**,**b**,**d** and **e**. The compounds *rac*-**4a** and *rac*-**4b**, which have a novel spiro structure, were obtained in good isolated yields as a racemic mixture in a clean reaction with no by-products. The reaction of **1d** (as a 2 : 1 mixture of rotamers) gave, in addition to the diastereomers *rac*-**4dA** and *rac*-**4dB**, appreciable amounts of the decomposition products **5** and **6** (see Scheme 2).

Analysis of the product mixtures from the reaction of **1c** and **1d** showed no evidence that the chiral substituents on the nitrogen atom exert any stereocontrol in these reduction reactions as the diastereomeric products appear to be formed in an approximate 1 : 1 ratio in both cases. The salt **1e** derived from the C_2-symmetric amine $[(S)\text{-CHMePh}]_2NH$[25] similarly gave a 1 : 1 ratio of the diastereomers *rac*-**4eA** and *rac*-**4eB** upon reduction. In this last reaction the products **4eA** and **4eB** were obtained in very poor overall yield and the major products in this reaction were the decomposition products **5** and **7**. This implies that when the substituents on the nitrogen atom are bulky, as in **1d** and **1e**, the azaboretidinium salts obtained upon hydroboration are unstable and dissociate readily on work-up. The physical and spectroscopic data for the compounds *rac*-**4a**, **4b**, **4cA**, **4cB**, **4dA**, **4dB** and **4eA** plus **4eB** are shown in Tables 4–6. In the case of compounds **4c** and **4d** the diastereomers could be separated, but this was not possible in the case of compound **4e** as there was so little compound available.

As the presence of a chiral group on the nitrogen atom of **1** is insufficient to affect the facial selectivity using a simple borane complex for the hydroboration, an alternative strategy was to use a more bulky, chiral borane derivative in the hope that this would be selective. Attempts to use the bulky achiral borane

‡ The crystallographic data for this compound are reported in ref. 1 and atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, ref. 1, Issue 1.

Table 2 ^{1}H and ^{31}P chemical shifts for β-enaminophosphonium salts **1a**–**e**[a]

Comp.	δ_P[b]	δ_H (J/Hz)
1a	+16.1	1.85 (s, 3H, H3), 2.05 (m, 4H, H3′ and H2′), 3.40 (t, 2H, $^{3}J_{H-H}$ 6.2, H1′ or H4′), 3.55 (d, 1H, $^{2}J_{P-H}$ 14.6, H1), 3.60 (t, 2H, $^{3}J_{H-H}$ 6.2, H4′ or H1′) and 7.55–7.75 (m, 15H, Ph_3P)
1b	+16.1	1.60 (br s, 6H, H2′, H3′ and H4′), 1.80 (s, 3H, H3), 3.45 (br s, 4H, H1′ and H5′), 3.85 (d, 1H, $^{2}J_{P-H}$ 14.1, H1) and 7.45–7.70 (m, 15H, Ph_3P)
1c	+15.8	1.75 (d, 3H, $^{3}J_{H-H}$ 6.8, H2′), 1.90 (s, 3H, H3), 3.50 (d, 1H, $^{2}J_{P-H}$ 14.0, H1), 4.55 [apparent quintet (overlapping d of q), 1H, $^{3}J_{H-H}$ 6.8, $^{3}J_{NH-H}$ 4.2, H1], 7.20–7.90 (m, 20H, Ph_3P– and Ph) and 9.10 (apparent br t, 1H, $^{3}J_{NH-H}$ 4.2, NH)
1d	+16.2 +16.6	1.85 (s, 6H, H3), 1.90 (m, 1H, H3′$_a$), 1.95 (m, 4H, H2′), 2.05 (s, 6H, H3), 2.20 (m, 1H, H3′$_b$), 3.40 (m, 2H, H1′$_a$), 3.50–3.65 (m, 2H, H1′$_b$), 3.60 (d, 2H, $^{2}J_{P-H}$ 14.5, H1), 3.75–3.85 (m, 1H, H5′$_a$), 4.15–4.30 (m, 1H, H5′$_b$ and H4′), 5.10 (t, 1H, $^{3}J_{H-H}$ 6.5, OH), 5.20 (t, 1H, $^{3}J_{H-H}$ 6.5, OH) and 7.55–7.75 (m, 30H, Ph_3P)
1e	+15.8	1.90 (d, 6H, $^{3}J_{H-H}$ 7.1, H2′), 2.15 (s, 3H, H3), 3.60 (d, 1H, $^{2}J_{P-H}$ 13.4, H1), 5.25 (br m, 2H, H1′), 7.10–7.35 (m, 10H, Ph) and 7.55–7.75 (m, 15H, Ph_3P)

[a] All spectra were determined in $CDCl_3$. [b] 85% H_3PO_4 as external reference.

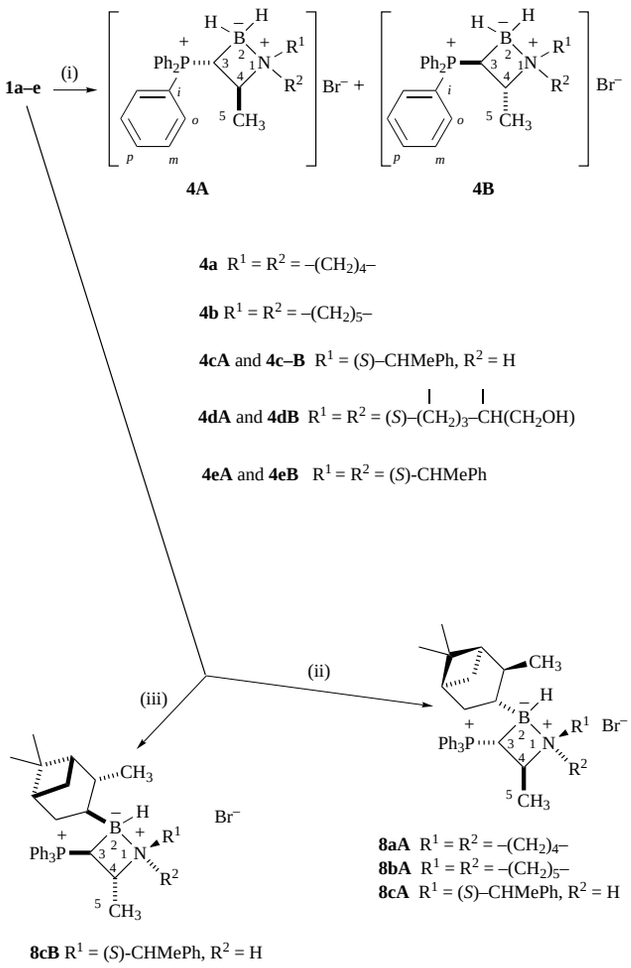
Table 3 ^{13}C chemical shifts and ^{31}P–^{13}C coupling constants for β-enaminophosphonium salts **1a**–**e**

	$\delta_C(CDCl_3)$ [$J(^{31}P-^{13}C)$/Hz]									
Comp.	1	2	3	1′	2′	*i*	*o*	*m*	*p*	Other bands
1a	57.5 [122.1]	162.5 [13.7]	22.0 [6.2]	49.0 [0.0] 49.1 [0.0]	24.4 [0.0] 25.0 [0.0]	123.5 [92.0]	132.5 [10.6]	130.0 [12.6]	133.5 [3.1]	
1b	59.5 [121.5]	163.6 [13.7]	22.4 [6.3]	48.5 [0.0] br. [0.0]	25.5 [0.0] br. [0.0]	123.5 [91.2]	133.0 [10.3]	130.5 [12.6]	134.0 [2.1]	23.5 (C3′)
1c	58.5 [122.0]	165.1 [13.7]	22.0 [6.2]	55.1 [0.0]	23.6 [0.0]	123.1 [91.0]	132.7 [10.4]	129.7 [12.5]	133.7 [2.8]	143.4 (C3′), 126.1 (C4′), 128.6 (C5′)
1d	57.2 [121.7] 59.7 [122.2]	162.6 [13.9] 163.5 [13.9]	22.5 [5.9]	49.1 [br.] 50.0 [br.]	27.1 [0.0] 27.8 [0.0]	123.1 [91.4] 123.3 [91.3]	132.8 [9.9] 132.9 [9.8]	129.9 [12.4]	133.5 [2.6]	22.1 and 23.1 (C3′), 61.8 and 61.9 (C4′), 62.6 br. (C5′)
1e	66.0 [118.7]	161.0 [11.8]	23.5 [7.3]	56.1 [br.]	17.5 [0.0]	122.5 [91.5]	132.5 [10.3]	130.0 [12.6]	133.9 [3.0]	138.9 (C3′), 128.7 (C4′), 127.8 (C5′), 132.4 (C6′)

Table 4 Physical data for the azaboretidinium bromide salts **4a**–**e** and **8aA**, **8bA** and **8cA**

				Found (calc.) (%)					
Comp.	Yield (%)	Mp (°C)	Molecular formula	C	H	N	Br	P	*m*/*z*, [(M^+ − Br)]
4a	89	159–160	$C_{25}H_{30}BBrNP{\cdot}0.5H_2O$	63.2 (62.9)	6.5 (6.1)	2.9 (3.1)	16.8 (17.0)	6.5 (6.8)	386
8aA	91	154–155	$C_{35}H_{46}BBrNP$	68.2 (67.8)	8.8 (8.0)	2.0 (2.3)			522
4b	78	236–237	$C_{26}H_{33}BBrNP{\cdot}0.5H_2O$	63.8 (63.8)	7.1 (6.8)	2.7 (2.9)	16.0 (16.3)	6.3 (6.3)	401
8bA	95	225–226	$C_{36}H_{48}BBrNP$	71.0 (70.1)	8.5 (7.8)	2.0 (2.3)			536
4cA	30	173–174	$C_{29}H_{32}BBrNP{\cdot}0.5H_2O$	66.6 (66.3)	6.6 (6.3)	2.7 (2.7)	14.9 (15.2)	5.6 (5.9)	436
8cA	86	159–160	$C_{39}H_{48}BBrNP$	72.1 (71.8)	7.8 (7.4)	2.0 (2.1)			572
4cB	38	Oil	$C_{29}H_{32}BBrNP$	68.6 (67.4)	6.8 (6.2)	3.1 (2.7)	16.1 (15.5)	6.2 (6.0)	436
4dA	28	Foam	$C_{26}H_{32}BBrNOP$	62.5 (62.9)	6.4 (6.4)	2.9 (2.8)	16.0 (16.1)		416
4dB	22	Oil	$C_{26}H_{32}BBrNOP$	62.0 (62.9)	6.1 (6.4)	2.5 (2.8)	15.9 (16.1)	5.9 (6.2)	416
4eA and **4eB**	2.5	Oil							541

9-BBN for the hydroboration of **1a** and **1c** failed to give any of the expected azaboretidinium salts and the starting materials were recovered unchanged. It is known that monoisocampheylborane ($IpcBH_2$) is less sterically demanding than either 9-BBN or $(Ipc)_2BH$ and it has been used with some success for the hydroboration of hindered prochiral *trans*-alkenes.[26] Consequently, (1*R*)-(+)-monoisopinocampheylborane, prepared *in situ* by the slow addition of a cold, dilute solution of (1*R*)-(+)-α-pinene in THF to $BH_3{\cdot}$THF in the same solvent at −5 °C,[27] was caused to react with the compounds **1a**–**c** in dichloromethane at room temperature and the reactions were monitored by ^{31}P NMR spectroscopy. In all successful reactions a milky appearance was observed after complete addition of the $IpcBH_2$ and this is another useful way of monitoring the



Scheme 2 *Reagents and conditions:* (i) BH_3·THF (1 M), dry CH_2Cl_2, −1 °C for 1 h then room temp. for 20 h; (ii) (1*R*)-(+)-α-pinene, BH_3·THF (1 M), dry CH_2Cl_2, −1 °C for 1 h then room temp. for 20 h; (iii) (1*S*)-(−)-α-pinene, BH_3·THF (1 M), dry CH_2Cl_2, −1 °C for 1 h then room temp. for 20 h

success of the reaction. Addition proceeded cleanly to give the expected azaboretidinium products, which are all insoluble in diethyl ether and can be easily obtained in an analytically pure state by a simple work-up procedure. The spectroscopic data and specific rotation values indicate that the compounds **8aA**, **8bA** and **8cA** are single diastereomers within the limits of the experimental data (see Scheme 2 and Tables 4–6). The similar reduction of **1d** and **1e** also gave single diastereomers although yields were low (<10%) and the major product isolated was the decomposition product **5** and the corresponding pinene–boron–amine complexes. When the asymmetric hydroboration of **1c** was repeated using (1*S*)-(−)-IpcBH$_2$ the other diastereomer **8cB** was obtained in high yield.

Conversion of the azaboretidinium salts *rac*-**4a**,**b** and **4cA** to the phosphine oxides *rac*-**9a**,**b** and **cA** was initially carried out by heating the salts in a 30% w/w solution of sodium hydroxide in aqueous methanol and gave the expected products, together with *rac*-2-methoxy-1-(diphenylphosphinoyl)propane **10** and a small amount of triphenylphosphine oxide (see Scheme 3). Compound **10** has been fully characterised by spectroscopic

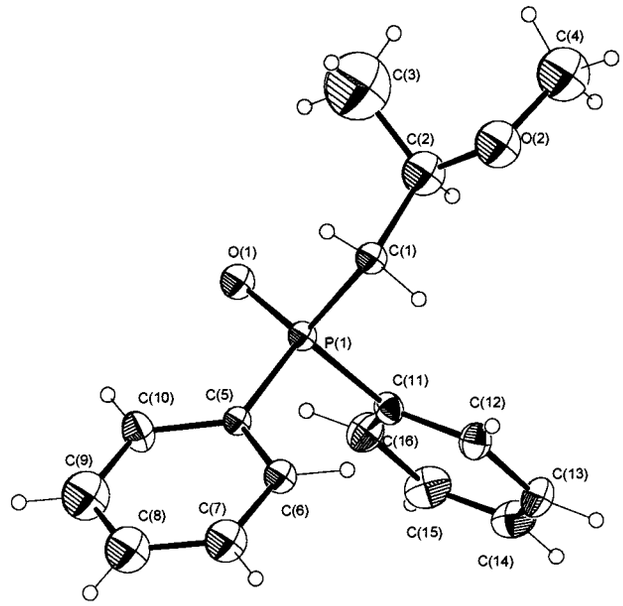
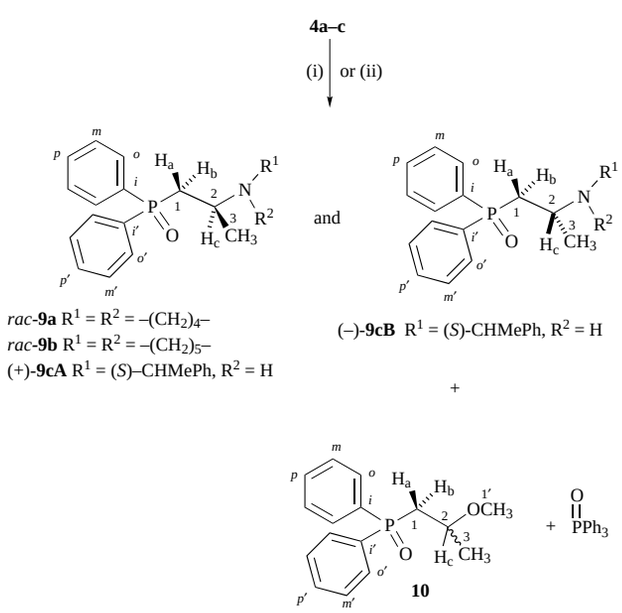


Fig. 1 X-Ray crystal structure of *rac*-2-methoxy-1-(diphenylphosphinoyl)propane **10**. The asymmetric unit includes a second, identical molecule, whose numbering scheme has been incremented by 20 relative to the above molecule. Selected bond lengths (Å) and angles (°): P(1)–O(1) 1.480(3)/1.477(3), P(1)–C(1) 1.807(4)/1.797(4), P(1)–C(5) 1.805(4)/1.810(5), P(1)–C(11) 1.798(4)/1.815(4); O(1)–P(1)–C(1) 114.4(2)/115.2(2), O(1)–P(1)–C(5) 112.1(2)/111.8(2), O(1)–P(1)–C(11) 111.2(2)/109.9(2), C(1)–P(1)–C(5) 105.2(2)/105.3(2), C(1)–P(1)–C(11) 106.9(2)/106.1(2), C(5)–P(1)–C(11) 106.6(2)/108.1(2).



Scheme 3 *Reagents and conditions:* (i) MeOH, NaOH aq. (30% w/w), reflux, 3 h; (ii) NaOH aq. (30% w/w), reflux, 3 h

methods and by X-ray crystallography (see Fig. 1). In the unit cell the molecules are orientated so that they form columns of approximately parallel P=O groups, in which the oxygen of one molecule is directed towards the phosphorus of its neighbour. The two molecules, which comprise the asymmetric unit, alternate within the column so that the alkyl substituent eclipses a phenyl group of an adjacent molecule. A structural database survey failed to identify any closely related molecules. This compound probably arises as a by-product of formation of **9** according to the mechanism proposed in Scheme 4. Its formation can be eliminated by carrying out the above reactions in aqueous sodium hydroxide alone without addition of methanol. The azaboretidinium salts are almost insoluble in cold sodium hydroxide solution, but on heating reaction pro-

Table 5 ^{1}H, ^{31}P and ^{11}B NMR spectroscopic data for the compounds **4a**–**e**, **8aA**, **8bA** and **8cA**[a]

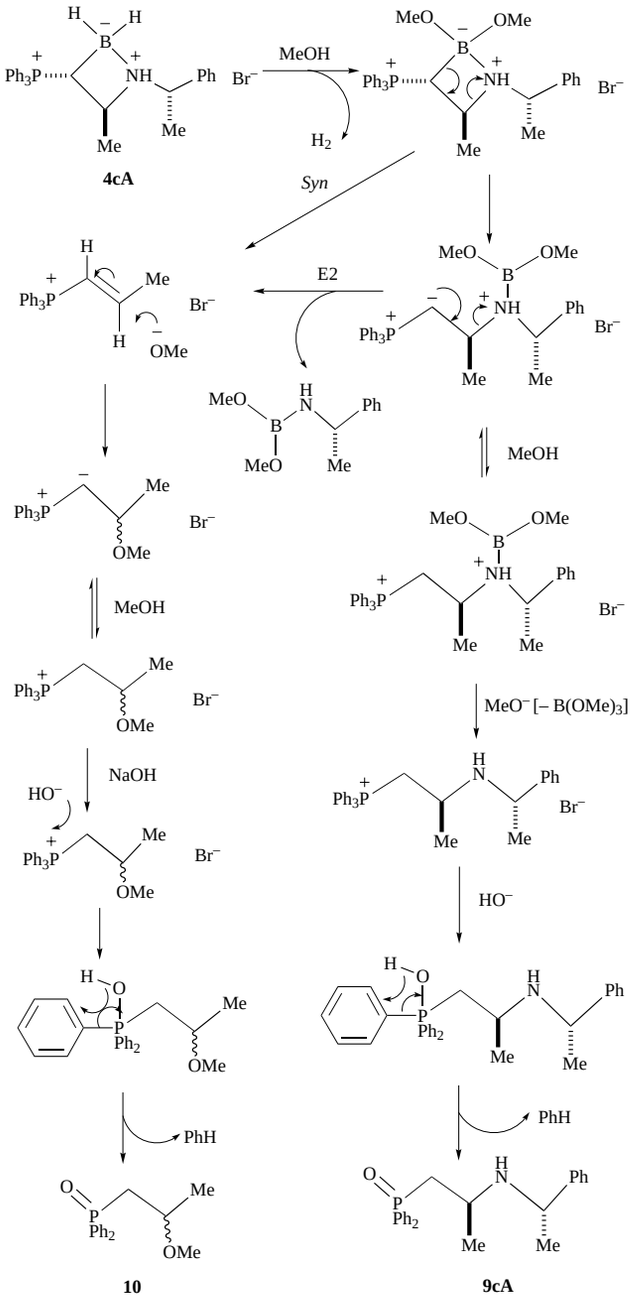
Comp.	δ_P[b]	δ_B[c]	δ_H(J/Hz)
4a	+30.1	−7.5	1.60 (d, 3H, $^{3}J_{H-H}$ 6.7, H5), 1.65–1.75 (m, 2H, H2′ or H3′), 1.80–1.95 (m, 2H, H3′ or H2′), 2.25–2.40 (m, 2H, H1′ or H4′), 2.55–2.70 (overlapping dt, 1H, $^{2}J_{Ha-Hb}$ 19.0, $^{3}J_{Ha\ or\ Hb-H}$ 9.1, H4′ or H1′), 2.80–2.95 (overlapping dt, 1H, $^{2}J_{Hc-Hd}$ 18.6, $^{3}J_{Hc\ or\ Hd-H}$ 9.3, H1′ or H4′), 3.10–3.25 (m, 2H, H4 and H3) and 7.55–7.75 (m, 15H, Ph_3P)
8aA	+29.8	−8.0	0.65–1.20 [m, 10H, (α-pinene moiety)], 1.50–1.60 [m, 4H, (α-pinene moiety)], 1.65 (d, 3H, $^{3}J_{H-H}$ 6.7, H9), 1.70–1.80 (m, 2H, H7 or H6), 1.85–1.95 (m, 2H, H6 or H7), 2.20–2.35 (m, 2H, H_a or H_b and H_c or H_d), 2.50–2.60 (overlapping dt, 1H, $^{2}J_{Ha-Hb}$ 19.0, $^{3}J_{Ha\ or\ Hb-H}$ 9.1, H_a or H_b), 2.80–2.95 (overlapping dt, 1H, $^{2}J_{Hc-Hd}$ 18.6, $^{3}J_{Hc\ or\ Hd-H}$ 9.3, H_c or H_d), 3.00–3.15 (m, 2H, H4 and H3) and 7.50–7.75 (m, 15H, Ph_3P)
4b	+30.2	−7.5	1.05–1.20 (m, 2H, H3′), 1.35–1.45 (m, 2H, H2′ or H4′), 1.50 (d, 3H, $^{3}J_{P-H}$ 6.2, H5), 1.60–1.70 (m, 2H, H4′ or H2′), 1.80–1.95 (m, 1H, $H1_a$′), 2.05–2.15 (m, 1H, $H1_b$′), 2.45–2.55 (overlapping dt, 1H, $^{2}J_{Ha-Hb}$ 16.4, $^{3}J_{Ha\ or\ Hb-H}$ 5.3, H1′), 2.55–2.65 (overlapping dt, 1H, $^{2}J_{Hc-Hd}$ 14.7, $^{3}J_{Hc\ or\ Hd-H}$ 4.7, H1′), 3.00–3.10 (m, 2H, H3 and H4) and 7.55–7.75 (m, 15H, Ph_3P)
8bA	+30.2	−8.1	0.70–1.20 [m, 10H, (α-pinene moiety)], 1.05–1.20 (m, 2H, H7), 1.35–1.45 (m, 2H, H6 or H8), 1.50 (d, 3H, $^{3}J_{P-H}$ 6.2, H10), 1.55–1.75 [m, 6H, (α-pinene moiety) and H8 or H6], 1.80–1.95 (m, 1H, H_b or H_a), 2.05–2.15 (m, 1H, H_c or H_d), 2.45–2.55 (overlapping dt, 1H, $^{2}J_{Ha-Hb}$ 16.4, $^{3}J_{Ha\ or\ Hb-H}$ 5.2, H_c or H_d), 2.60–2.70 (overlapping dt, 1H, $^{2}J_{Hc-Hd}$ 14.7, $^{3}J_{Hc\ or\ Hd-H}$ 4.7, H_c or H_d), 3.05–3.15 (m, 2H, H3 and H4) and 7.50–7.80 (m, 15H, Ph_3P)
4cA	+29.1	−8.2	1.12 (d, 3H, $^{3}J_{H-H}$ 6.5, H2′), 1.40 (d, 3H, $^{3}J_{H-H}$ 6.8, H5), 2.95–3.05 [m (overlapping), 2H, H3 and H4], 3.30–3.45 (dq, 1H, $^{3}J_{NH-H}$ 4.7, $^{3}J_{H-H}$ 6.5, H1′), 7.20–7.45 (m, 5H, Ph), 7.60–7.75 (m, 15H, Ph_3P) and 7.90 (d, 1H, $^{3}J_{NH-H}$ 4.7, NH)
4cB	+28.2	−8.0	1.45 (d, 3H, $^{3}J_{H-H}$ 6.4, H2′), 1.80 (d, 3H, $^{3}J_{H-H}$ 6.8, H5), 2.85–3.00 (m, 2H, H3 and H4), 3.15–3.30 (dq, 1H, $^{3}J_{H-H}$ 6.4, $^{3}J_{NH-H}$ 3.1, H1′), 7.20–7.45 (m, 5H, Ph), 7.60–7.75 (m, 15H, Ph_3P) and 8.65 (br s, 1H, NH)
8cA	+29.1	−5.2	0.60–1.14 [m, 10H, (α-pinene moiety)], 1.15 (d, 3H, $^{3}J_{H-H}$ 6.5, H11), 1.40 (d, 3H, $^{3}J_{H-H}$ 6.8, H10), 3.00–3.15 [m (overlapping), 2H, H3 and H4], 3.30–3.45 (dq, 1H, $^{3}J_{NH-H}$ 4.7, $^{3}J_{H-H}$ 6.5, H5), 7.20–7.45 (m, 5H, Ph), 7.60–7.75 (m, 15H, Ph_3P) and 7.85 (d, 1H, $^{3}J_{NH-H}$ 4.7, NH)
4dA	+29.5	−8.1	1.50 (d, 3H, $^{3}J_{H-H}$ 6.6, H5), 1.85 (m, 2H, H2′), 1.90 (m, 1H, $H3'_a$ or $_b$), 2.20 (m, 1H, $H3'_b$ or $_a$), 3.10–3.25 [m (overlapping), 2H, H4 and H3], 3.50 (m, 1H, $H1'_a$ or $_b$), 3.55 (m, 1H, $H1'_a$ or $_b$), 3.85 (m, 1H, $H5_a$), 4.20–4.35 (m, 2H, $H5'_b$ and H4), 5.15 (t, 1H, $^{3}J_{H-H}$ 6.6, OH) and 7.50–7.80 (m, 15H, Ph_3P)
4dB	+29.8	−8.0	1.10 (d, 3H, $^{3}J_{H-H}$ 6.6, H5), 1.75 (m, 2H, H2′), 1.85 (m, 1H, $H3'_a$ or $_b$), 2.10 (m, 1H, $H3'_b$ or $_a$), 3.00–3.15 [m (overlapping), 2H, H3 and H4], 3.35 (m, 1H, $H1'_a$ or $_b$), 3.45 (m, 1H, $H1'_a$ or $_b$), 3.75 (m, 1H, $H5_a$), 4.10–4.15 (m, 2H, $H5_b$ and H4), 5.15 (t, 1H, $^{3}J_{H-H}$ 6.6, OH) and 7.50–7.80 (m, 15H, Ph_3P)
4e	+27.4	−8.1	0.75 (d, 3H, $^{3}J_{H-H}$ 6.8, H5A), 1.10 (d, 3H, $^{3}J_{H-H}$ 6.8, H5B), 1.85 (d, 6H, $^{3}J_{H-H}$ 6.8, H2′A), 1.95 (d, 6H, $^{3}J_{H-H}$
(**A** + **B**)	+29.2		6.8, H2′B), 3.00–3.20 (m, 4H, H3 and H4), 3.45 (q, 1H, $^{3}J_{H-H}$ 6.8, H1′A), 3.70 (q, 1H, $^{3}J_{H-H}$ 6.8, H1′B) and 7.10–7.90 (m, 25H, Ph_3P and Ph)

[a] All spectra were determined in $CDCl_3$. [b] 85% H_3PO_4 as external reference. [c] $BH_3{\cdot}Et_2O$ as external reference.

Table 6 ^{13}C chemical shifts and ^{31}P–^{13}C coupling constants for the azaboretidinium bromide salts **4a**–**e** and **8aA**, **8bA** and **8cA**

	$\delta_C(CDCl_3)$ [$J(^{31}P-^{13}C)$/Hz]							
Comp.	3	4	5	*i*	*o*	*m*	*p*	Other bands
4a	15.5	62.5	17.3	120.5	133.8	130.2	134.5	20.5, 59.6, 60.8
	[53.2]	[1.2]	[0.0]	[86.9]	[9.6]	[12.3]	[1.5]	
8aA	14.8	62.0	17.1	120.5	133.8	130.2	134.5	20.2, 20.4, 21.5, 23.5,
	(54.2)	(1.2)	(0.0)	(86.9)	(9.6)	(12.3)	(1.5)	23.6, 27.4, 27.5, 29.5,
								30.0, 37.4, 47.8, 59.6,
								60.7
4b	14.5	66.4	15.9	121.0	134.0	130.4	134.4	20.7, 21.7, 22.6, 50.9,
	[54.1]	[br.]	[0.0]	[87.2]	[9.6]	[12.2]	[2.5]	60.0
8bA	14.8	66.2	15.9	120.5	133.7	130.0	134.4	20.5, 20.6, 21.5, 21.7,
	(54.1)	(br.)	(0.0)	(87.2)	(9.8)	(12.1)	(1.8)	22.5, 23.5, 23.7, 27.5,
								27.6, 29.5, 30.0, 37.5,
								47.7, 50.7, 59.8
4cA	15.5	58.5	21.5	121.0	133.7	130.0	134.5	18.5, 65.7, 128.2, 128.5,
	[52.8]	[2.5]	[1.9]	[87.0]	[9.5]	[12.0]	[2.4]	129.0, 139.0
4cB	26.1	47.5	21.5	117.1	134.0	130.8	135.8	15.5, 56.8, 128.0, 128.4,
	[54.1]	[br.]	[br.]	[87.1]	[10.2]	[12.9]	[br.]	129.5, 138.4
8cA	15.1	58.4	21.5	121.0	133.7	130.0	134.5	18.5, 20.3, 21.1, 23.4,
	(56.8)	(2.4)	(1.9)	(87.0)	(9.6)	(12.0)	(1.9)	27.3, 27.4, 29.5, 30.1,
								37.5, 47.8, 65.9, 128.1,
								128.5, 129.0, 138.7
4dA	17.5	57.6	18.5	120.2	133.9	130.2	134.6	2.7, 27.6, 50.1, 57.3,
	[54.0]	[0.0]	[br.]	[87.3]	[9.4]	[12.2]	[2.4]	60.8, 61.9
4dB	25.5	57.2	19.5	120.0	133.6	130.0	134.6	8.7, 23.5, 50.0, 60.0, 69.8
	[54.2]	[0.0]	[0.0]	[87.3]	[9.4]	[12.2]	[2.4]	

ceeds cleanly to give good yields of the phosphine oxides *rac*-**9a**,**b** and **cB**, although some triphenylphosphine oxide is still produced under these conditions. The physical and spectroscopic properties of the compounds *rac*-**9a**,**b**,**cA** and **cB** are given in Tables 7–9. As expected, compound **9cB** has similar spectroscopic properties but the opposite specific rotation to that of **9cA**. Treatment of the pure diastereomers **8aA**, **8bA** and **8cA** obtained by reduction using $IpcBH_2$, with aqueous sodium hydroxide gave almost quantitative yields of the corresponding phosphine oxides (+)-**9aA**, (+)-**9bA** and (−)-**9cA** and no triphenylphosphine oxide formation was observed in these cases. The specific rotation of **9cA** obtained from **8cA** is almost identical to that obtained from the oxidation of **4cA** and this establishes that the hydroboration using (*R*)-(+)-monoisopinocampheylborane occurs by attack on the *si*-face of **1c** and, conversely, (*S*)-(−)-monoisopinocampheylborane must react



Scheme 4 Proposed mechanism for the formation of **10** and **9cA** from **4cA**

with the *re*-face to give **9cB**. Chiral GC analysis of compound (+)-**9bA** shows an ee value of 75% and we assume that in this case, and also the reaction of **1a** with (*R*)-(+)-IpcBH$_2$ the major product has the *S*-configuration, but we have been unable to establish this unequivocally.

In summary, provided that the substituents on nitrogen are non-bulky, the combination of reduction of an enamino-(triphenyl)phosphonium salt with either of the antipodes of IpcBH$_2$, followed by treatment with 30% w/w aqueous sodium hydroxide provides a rapid and quite versatile method for the synthesis of optically pure β-aminophosphine oxides in three steps from readily available triphenyl(prop-2-ynyl)phosphonium bromide.

Experimental

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AC300 spectrometer. *J* Values are given in Hz. The ^{11}B (64 MHz) and ^{31}P (81 MHz) spectra were recorded on a Bruker AC 200 instrument with $H_3B{\cdot}OEt_2$ and H_3PO_4 (85%) as standards respectively. Optical rotations ($[\alpha]_D$) were measured using an Optical Activity Ltd. AA-1000 polarimeter and are given in units of 10^{-1} deg cm^2 g^{-1}. Chiral GC analysis was carried out using a G-TA (trifluoroacetyl γ-cyclodextrin 30 m × 0.25 mm column). Low resolution mass spectra were recorded on a Kratos MS 45 instrument and fast atom bombardment (FAB) spectra were measured on a VG update AEI-M5902 instrument using a matrix of *p*-nitrobenzyl alcohol.

Triphenyl(prop-2-ynyl)phosphonium bromide was prepared by a previously described method.[17,19] Pyrrolidine, piperidine, (*S*)-(−)-1-phenylethylamine (ee 99%), and (*S*)-(+)-pyrrolidine-2-methanol (ee, 96%) were commercial samples used without further purification. (*S*,*S*′)-*N*,*N*-bis(1-phenylethyl)amine was prepared by the three step procedure reported by Hogeveen *et al.*[25] (1*R*)-(+)-Monoisopinocampheylborane was prepared by the addition of a solution of (1*R*)-(+)-α-pinene in dry THF to a cold solution of borane in the same solvent under an atmosphere of argon followed by stirring at 0 °C for 2 h.[27]

General procedure for reactions of triphenyl(prop-2-ynyl)-phosphonium bromide 2 with various amines

Triphenyl(prop-2-ynyl)phosphonium bromide **2** (1 mol equiv.) was dissolved in hot, dry acetonitrile (250 cm^3). After cooling the solution to room temperature, the amine (1 mol equiv.) was added dropwise to the vigorously stirred solution over a period of 10–15 min. The mixture was refluxed for 90 min and then stirred over a period of 70–80 h at room temperature. The reaction was monitored using ^{31}P NMR spectroscopy and TLC (hexane–Et_2O, 1 : 3). When no starting material was present, the white precipitate which had formed was filtered. The filtrate was concentrated under reduced pressure to give more white precipitate. The concentrated filtrate, a yellow–brown oil, was then dissolved in a small amount of hot dichloromethane, then ethyl acetate was added slowly whilst the mixture was warmed in a water bath until the solution became cloudy. The solution was allowed to cool at room temperature, then left in the freezer for 48 h to give a further crop of the white precipitate. The solids were combined and dried under vacuum to afford the desired product.

(a) With pyrrolidine. Reaction between **2** (15.0 g, 39.4 mmol) and pyrrolidine (2.80 g, 3.30 cm^3, 39.4 mmol) in acetonitrile (500 cm^3) gave 2-*methyl*-2-*pyrrolidinovinyl*(*triphenyl*)*phosphonium bromide* **1a** (16.0 g, 45.4 mmol, 90%); R_f 0.20 (hexane–Et_2O, 1 : 3).

(b) With piperidine. Compound **2** (7.62 g, 20.0 mmol) and piperidine (1.70 g, 1.20 cm^3, 20.0 mmol) in acetonitrile (250 cm^3) afforded 2-*methyl*-2-*piperidinovinyl*(*triphenyl*)*phosphonium bromide* **1b** (6.97 g, 15.0 mmol, 75%); R_f 0.25 (hexane–Et_2O, 1 : 3).

(c) With (*S*)-(−)-1-phenylethylamine. Reaction between (*S*)-(−)-1-phenylethylamine (6.35 g, 4.16 cm^3, 52.5 mmol) and **2** (20.0 g, 52.5 mmol) in acetonitrile (700 cm^3) gave 2-*methyl*-2-[N-(S)-(*phenylethyl*)*amino*]*vinyl*(*triphenyl*)*phosphonium bromide* **1c** (19.95 g, 39.74 mmol, 76%); R_f 0.27 ($CHCl_3$–MeOH, 9 : 1) $[\alpha]_{589}^{23}$ −42.4 (*c* 0.5 g in 100 cm^3 CH_2Cl_2).

(d) With (*S*)-(+)-pyrrolidine-2-methanol. Reaction between **2** (7.62 g, 20.0 mmol) and (*S*)-(+)-pyrrolidine-2-methanol (3.30 g, 20.0 mmol) in acetonitrile (250 cm^3) with exclusion of light gave a 1 : 2 mixture of rotamers of 2-*methyl*-2-[(S)-2-*hydroxymethyl-pyrrolidino*]*vinyl*(*triphenyl*)*phosphonium bromide* **1d** (7.52 g, 15.6 mmol, 78%); R_f 0.32 ($CHCl_3$–MeOH, 9 : 1); $[\alpha]_{589}^{23}$ +18.7 (*c* 0.80 g in 100 cm^3 CH_2Cl_2).

(e) With (*S*,*S*′)-*N*,*N*-bis(1-phenylethyl)amine. Compound **2** (0.85 g, 2.23 mmol) and (*S*,*S*′)-*N*,*N*-bis(1-phenylethyl)amine (0.50 g, 22.2 mmol) in acetonitrile (75 cm^3) gave a red oil, which was chromatographed (SiO_2, $CHCl_3$–MeOH, 9 : 1) to afford 2-*methyl*-2-[(*S*,*S*)-*N*,*N*-*bis*(*1-phenylethyl*)*amino*]*vinyl*(*triphenyl*)-*phosphonium bromide* **1e**, as an off-white foam (1.19 g, 1.96 mmol, 88%); R_f 0.15 ($CHCl_3$–MeOH, 9 : 1), $[\alpha]_{589}^{23}$ −112.0 (*c* 0.50 g in 100 cm^3 CH_2Cl_2).

Table 7 Physical data for phosphine oxides **9a–c**

Comp.	Yield (%)	Mp (°C)	Molecular formula	Found (calc.) (%) C	H	N	P	*m/z*, [(M − H)$^+$]
rac-**9a**	54[a] 87[b]	70–71	$C_{19}H_{24}NP{\cdot}0.5H_2O$	71.1 (70.8)	7.7 (7.8)	4.4 (4.3)	9.5 (9.6)	314
rac-**9b**	48[a] 80[b]	125–126	$C_{20}H_{26}NP$	73.1 (73.4)	7.9 (7.9)	4.2 (4.3)	9.4 (9.5)	328
rac-**9cA**	55[a] 79[b]	109–110	$C_{23}H_{26}NP$	75.7 (76.0)	7.0 (7.2)	3.8 (3.9)	8.2 (8.5)	364

[a] Using aq. methanolic NaOH. [b] Using aqueous NaOH.

Table 8 ^{1}H and ^{31}P NMR spectroscopic data for the phosphine oxides **9a–c**[a]

Comp.	δ_P[b]	δ_H(*J*/Hz)
rac-**9a**	+30.3	1.14 (d, 3H, $^3J_{H-Hc}$ 6.9. H3), 1.55–1.70 (m, 4H, H2′ and H3′), 2.15–2.30 (ddd, 1H, $^2J_{Ha-Hb}$ 15.4, $^3J_{Ha-Hc}$ 6.3, $^2J_{P-Ha}$ 14.5, H1$_a$), 2.30–2.40 (m, 2H, H1′ or H4′), 2.45–2.50 (m, 2H, H4′ or H1′), 2.60–2.75 (ddd, 1H, $^2J_{Hb-Ha}$ 15.4, $^3J_{Hb-Hc}$ 12.5, $^2J_{P-Hb}$ 9.5, H1$_b$), 2.90–3.05 (ddq, 1H, $^3J_{Hc-H}$ 6.9, $^3J_{Hc-Ha}$ 6.3, $^3J_{Hc-Hb}$ 12.5, H2), 7.30–7.45 (m, 6H, Ph) and 7.60–7.75 (m, 4H, Ph)
rac-**9b**	+30.9	1.05 (d, 3H, $^3J_{H-Hc}$ 6.7, H3), 1.15–1.45 (m, 6H, H2′, H3′ and H4′), 2.05–2.20 (ddd, 1H, $^2J_{Ha-Hb}$ 15.5, $^3J_{Ha-Hc}$ 6.3, $^2J_{P-Ha}$ 14.0, H1$_a$), 2.20–2.40 (m, 4H, H1′ and H5′), 2.50–2.65 (ddd, 1H, $^2J_{Hb-Ha}$ 15.5, $^3J_{Hb-Hc}$ 12.5, $^2J_{P-Ha}$ 9.9, H1$_b$), 3.00–3.20 (ddq, 1H, $^3J_{Hc-H}$ 6.7, $^3J_{Hc-Ha}$ 6.5, $^3J_{Hc-Hb}$ 12.5, H2), 7.30–7.50 (m, 6H, Ph) and 7.65–7.80 (m, 4H, Ph)
rac-**9cA**	+30.6	1.10 (d, 3H, $^3J_{H-Hc}$ 6.0, H3), 1.22 (d, 3H, $^3J_{H-H}$ 6.6, H2′), 1.80 (br, s, 1H, NH), 2.30–2.35 (ddd, 1H, $^2J_{Ha-Hb}$ 15.3, $^3J_{Ha-Hc}$ 5.8, $^2J_{P-Ha}$ 14.8, H1$_a$), 2.35–2.55 (ddd, 1H, $^2J_{Hb-Ha}$ 15.3, $^3J_{Hb-Hc}$ 12.1, $^2J_{P-Hb}$ 10.0, H1$_b$), 2.90–3.05 (ddq, 1H, $^3J_{Hc-H}$ 6.0, $^3J_{Hc-Ha}$ 5.8, $^3J_{Hc-Hb}$ 12.1, H2), 3.80 (q, 1H, $^3J_{H-H}$ 6.6, H4), 7.15–7.25 (m, 5H, Ph), 7.30–7.50 (m, 6H, Ph$_2$P) and 7.55–7.70 (m, 4H, Ph$_2$P)
rac-**9cB**	+31.9	1.12 (d, 3H, $^3J_{H-Hc}$ 6.0, H3), 1.35 (d, 3H, $^3J_{H-H}$ 6.6, H2′), 2.35–2.45 (ddd, 1H, $^2J_{Ha-Hb}$ 15.3, $^3J_{Ha-Hc}$ 5.8, $^2J_{P-Ha}$ 14.8, H1$_a$), 2.35–2.55 (ddd, 1H, $^2J_{Hb-Ha}$ 15.3, $^3J_{Hb-Hc}$ 12.1, $^2J_{P-Hb}$ 10.0, H1$_b$), 2.75 (br, s, 1H, NH), 3.00−3.10 (ddq, 1H, $^3J_{Hc-H}$ 6.0, $^3J_{HC-Ha}$ 5.8, $^3J_{Hc-Hb}$ 12.1, H2), 3.85 (q, 1H, $^3J_{H-H}$ 6.6, H4), 7.15–7.25 (m, 5H, H1′), 7.30−7.50 (m, 6H, Ph) and 7.55–7.70 (m, 4H, Ph)

[a] All spectra were determined in $CDCl_3$. [b] 85% H_3PO_4 as external reference.

Table 9 ^{13}C chemical shifts and ^{31}P–^{13}C coupling constants for phosphine oxides **9a–c**

Comp.	$\delta_C(CDCl_3)$ [$J(^{31}P-^{13}C)$/Hz][a] 1	2	3	*i* (*i*′)	*o* (*o*′)	*m* (*m*′)	*p* (*p*′)	Other bands
rac-**9a**	34.3 [70.5]	52.2 [1.9]	19.2 [3.0]	133.2 [98.9] *134.0* [*98.9*]	130.3 [9.2] *130.5* [*9.3*]	128.3 [11.9] *128.4* [*11.6*]	131.3 [2.9] *131.4* [*2.9*]	23.1, 23.4, 49.1, 49.4
rac-**9b**	33.1 [70.5]	54.7 [br.]	16.3 [4.9]	133.2 [99.3] *134.5* [*98.7*]	130.4 [9.1] *130.7* [*8.9*]	128.3 [11.7] *128.4* [*11.5*]	131.1 [3.1] *131.2* [*2.7*]	24.7, 25.9 (br), 49.1 (br)
rac-**9cA**	36.6 [69.5]	46.5 [2.3]	23.3 [7.2]	132.8 [98.7] *134.2* [*97.9*]	130.4 [10.2] *130.5* [*10.3*]	128.3 [11.5] *128.5* [*11.6*]	131.4 [3.2] *131.5* [*3.2*]	24.1, 55.4, 126.4, 126.7, 128.0, 146.0

[a] Shifts for *i*′, *o*′, *m*′ and *p*′ are given in italics.

Hydroboration of enamino(triphenyl)phosphonium salts with borane

General procedure. A solution of the phosphonium salt in the minimum amount of anhydrous dichloromethane was cooled in an ice–salt bath and stirred continuously under an atmosphere of argon. When the temperature of the solution had reached −1 to −2 °C, a cold solution of borane in tetrahydrofuran (1 M) was added dropwise to the vigorously stirred solution over a period of 25 min. The mixture was stirred at approximately −1 °C for 1 h, after which, the ice–salt bath was removed and the mixture was then stirred for a further 2 h at room temperature. The reaction was monitored using ^{31}P NMR spectroscopy. When the ^{31}P NMR spectrum showed that the reaction was complete, the flask was placed in an ice–salt bath, a condenser was fitted and anhydrous methanol (0.5 cm^3) was added dropwise until vigorous effervescence had stopped. Deionised water (5.0 cm^3) was added, again dropwise, until no more effervescence was observed. The ice–salt bath was removed, the mixture was allowed to warm to room temperature and aqueous hydrogen bromide (10%) was added dropwise until all the white precipitate had dissolved. The acidic solution was then neutralised using saturated aqueous sodium carbonate, and the product was then extracted with chloroform (3 × 40.0 cm^3). The combined extracts were dried over anhydrous $MgSO_4$, filtered, then concentrated under reduced pressure to afford an oil. Slow addition of ethyl acetate to the oil gave the product as a white precipitate, which was filtered.

Synthesis of 4a. Compound **1a** (5.0 g, 11.06 mmol) in dichloromethane (20 cm^3) and a 1 M solution of borane in tetrahydrofuran (50.0 cm^3, 50.0 mmol) gave [(2R,3S)- and (2R,3R)-3-*methyl*-4-*azonia*-1-*boranuidaspiro*[3.4]*octan*-2-*yl*]-*triphenylphosphonium bromide* **4a** (4.60 g, 9.87 mmol, 89%) as a white solid.

Synthesis of 4b. Reaction between **1b** (5.0 g, 10.73 mmol) in dichloromethane (20.0 cm^3) and 1 M solution of borane in tetrahydrofuran (50.0 cm^3, 50.0 mmol) gave {(2R,3S)- and (2R,3R)-(3-*methyl*-4-*azonia*-1-*boranuidaspiro*[3.5]*nonan*-2-*yl*}-*triphenylphosphonium bromide* **4b** (4.00 g, 8.33 mmol, 78%).

Synthesis of 4c. Compound **1c** (5.0 g, 9.96 mmol) dissolved in the minimum amount of dichloromethane (20.0 cm^3) was

caused to react with a 1 M solution of borane in tetrahydrofuran (50.0 cm^3, 50.0) to afford, after work-up, a viscous pale yellow oil which contained a 1:1 mixture of two diastereomers (**4cA** and **B**) (4.32 g, 8.39 mmol, 84%).

The oil was first dissolved in the minimum amount of dichloromethane, then ethyl acetate was added slowly until a fine white precipitate was formed. The solution was then left in the freezer for 24 h. The precipitate was filtered under reduced pressure, and then dried under vacuum. The concentrated filtrate was then dissolved in the minimum amount of dichloromethane, and ethyl acetate was added slowly until more white precipitate appeared. The solution was then left in the freezer for 48 h. The precipitate was filtered under reduced pressure, then dried under vacuum. This procedure was repeated until no further precipitate was obtained after leaving the flask in the freezer for six weeks. A ^1H NMR spectrum of the combined precipitates indicated a 7:3 mixture of diastereomers, about 85% pure. The precipitate was then recrystallised from propan-2-ol, by carefully dissolving it in the minimum amount of warm propan-2-ol, keeping the temperature of the propan-2-ol below 50 °C. The flask was left at room temperature for 2 days during which time small, needle-shaped, white crystals began to crystallise. The flask was then placed in the freezer and left undisturbed for another 7 days. The solid was filtered under reduced pressure to afford crystals suitable for X-ray determination and finally dried under vacuum to afford a pure single diastereomer, [(1S,3R,4S,1′S)-4-*methyl*-1-(1-*phenylethyl*)-1,2-*azaboretidin*-1-*ium*-2-*uid*-3-*yl*]*triphenylphosphonium bromide* **4cA** (1.53 g, 2.96 mmol, 30%); $[\alpha]_{589}^{23}$ −180.5 (*c* 0.29 g in 100 cm^3 CH_2Cl_2).

The remaining pale yellow oil was washed several times with chloroform, then dried under vacuum to afford a 9:1 mixture of diastereomers as a pale yellow viscous oil containing predominantly [(1S,3R,4R,1′S)-4-*methyl*-1-(1-*phenylethyl*)-1,2-*azaboretidin*-1-*ium*-2-*uid*-3-*yl*]*triphenylphosphonium bromide* **4cB** (1.95 g, 3.78 mmol, 38%); $[\alpha]_{589}^{23}$ +100.5 (*c* 0.31 g in 100 cm^3 CH_2Cl_2).

Synthesis of 4d. A solution of **1d** (5.0 g, 13.1 mmol) in the minimum amount of anhydrous dichloromethane (25.0 cm^3), on reaction with 1 M borane in tetrahydrofuran (65.0 cm^3, 65.0 mmol) gave, after work-up, a pale yellow oil (5.56 g, 11.2 mmol, 86%), which contained a 1:1 mixture of diastereomers **4dA**, **4dB** and two other minor products **5** and **6**.

It proved impossible to separate the mixture by fractional crystallisation using a variety of solvent systems, but the use of column chromatography (SiO_2, $CHCl_3$–MeOH, 8:2) and an extremely slow rate of solvent flow led to the successful separation of the diastereomers **4dA** and **4dB**, and **5** and **6**.

The first compound collected was (*R*)-(+)-1-borylpyrrolidine-2-methanol **6** (0.220 g, 1.95 mmol, 15%) as a colourless oil; R_f 0.80 ($CHCl_3$–MeOH, 8:2); $[\alpha]_{589}^{23}$ +10.5 (*c* 0.84 g in 100 cm^3 CH_2Cl_2); ν_{max}($CHBr_3$ mull)/cm^{-1} 3300m (br sharp, O–H, st. vib.), 2422m (B–H, st. vib.), 2346m (B–H, st. vib.), 1438s (B–N, st. vib.); δ_H($CDCl_3$, 300 MHz) 1.85 (m, 2H, H2), 1.90 (m, 1H, $H3_a$), 2.20 (m, 1H, $H3_b$), 3.50 (m, 1H, $H1_a$), 3.55 (m, 1H, $H1_b$), 3.85 (m, 1H, $H5_a$), 4.15–4.30 (m, 2H, $H5_b$ and H4) and 5.00 (t, 1H, $^3J_{H-H}$ 6.6, OH); δ_C($CDCl_3$, 75 MHz) 22.5 (C3), 27.6 (C2), 49.5 (C1), 61.5 (C4) and 62.6 (C5); δ_B($CDCl_3$, 64 MHz, $BH_3{\cdot}Et_2O$ ref.) −7.0; *m*/*z* (EI/CI) 130 [($M^+ + NH_3$), 100%].

The second set of fractions gave (E)-*prop*-1-*enyl*(*triphenyl*)-*phosphonium bromide* **5** (0.85 g, 2.22 mmol, 17%) as a white solid; R_f 0.70 ($CHCl_3$–MeOH, 8:2); mp 210–211 °C [Found: C, 65.5; H, 5.5; Br, 20.9; P, 8.0. *m*/*z* (FAB) 303 [($M^+ - Br^-$), 100%. Calc. for $C_{21}H_{20}BrP$: C, 65.8; H, 5.2; Br, 20.9; P, 8.1%, *M*, 383]; δ_H($CDCl_3$, 300 MHz) 2.25 (dt, 3H, $^3J_{H-Hb}$ 6.5, $^4J_{CH_3-Ha}$ 1.9, H3), 6.50–6.80 [ddq, 2H, $^3J_{H-H}$ 16.5 (*trans*), $^3J_{H-H}$ 6.5, $^2J_{P-Ha}$ 22.1, H1 and H2] and 7.65–7.90 (m, 15H, Ph_3P); δ_C($CDCl_3$, 75 MHz) 21.5 (d, C3, $^3J_{P-C}$ 20.1), 110.0 (d, C1, J_{P-C} 86.4), 159.4 (d, C2, $^2J_{P-C}$ 2.9), 118.0 (d, C*i*, J_{P-Ci} 90.7), 130.2 (d, C*m*, $^3J_{P-Cm}$ 12.7), 133.4 (d, C*o*, $^2J_{P-Co}$ 10.6) and 135.0 (d, C*p*, $^4J_{P-Cp}$ 3.1); δ_P($CDCl_3$, 81 MHz, 85% H_3PO_4 ref.) +19.2.

The third set of fractions contained a single diastereomer of {(2R,3S,4S)-5-[(S)-*hydroxymethyl*]-3-*methyl*-4-*azonia*-1-*boranuidaspiro*[3.4]*octan*-2-*yl*}*triphenylphosphonium bromide* **4dA** obtained as a white foam (1.85 g, 3.73 mmol, 28%); R_f 0.45 ($CHCl_3$–MeOH, 8:2); $[\alpha]_{589}^{23}$ −44.0 (*c* 0.91 g in 100 cm^3 CH_2Cl_2).

The final set of fractions contained the other diastereoisomer {(2S,3R,4S)-5-[(S)-*hydroxymethyl*]-3-*methyl*-4-*azonia*-1-*boranuidaspiro*[3.4]*octan*-2-*yl*}*triphenylphosphonium bromide* **4dB** as a pale yellow oil (1.46 g, 2.94 mmol, 22%); R_f 0.30 ($CHCl_3$–MeOH, 8:2); $[\alpha]_{589}^{23}$ +21.0 (*c* 0.62 g in 100 cm^3 CH_2Cl_2).

Synthesis of 4e. Reaction between **1e** (0.72 g, 1.19 mmol) in dichloromethane (12 cm^3) and 1 M borane in tetrahydrofuran (6.0 cm^3, 6.0 mmol) gave a pale yellow oil, which contained a 1:1 mixture of two diastereomers (**4eA** and **B**), and two other products **5** and **7** (0.69 g, 1.11 mmol, 92%).

The mixture was impossible to separate by fractional crystallisation using a variety of solvent systems, but separation was achieved by column chromatography (SiO_2, $CHCl_3$–MeOH, 8:2) using an extremely slow rate of solvent flow and collecting small fractions.

The first compound collected was (S,S′)-*N*,*N*-*bis*(1-*phenylethyl*)*aminoborane* **7** (0.192 g, 0.81 mmol, 68%) as an oil; R_f 0.82 ($CHCl_3$–MeOH, 8:2); $[\alpha]_{589}^{23}$ −29.5 (*c* 0.15 g in 100 cm^3 CH_2Cl_2); ν_{max}(neat)/cm^{-1} 2422m (B–H, st. vib.), 2346m (B–H, st. vib.) and 1438s (B–N, st. vib.); δ_H($CDCl_3$, 300 MHz) 1.25 (d, 6H, $^3J_{H-H}$ 6.7, H2), 3.50 (q, 2H, $^3J_{H-H}$ 6.7, H1) and 7.20–7.80 (m, 10H, Ph); δ_C($CDCl_3$, 75 MHz) 25.0 (C2), 55.5 (C1), 126.5 (C4), 126.5 (C3), 128.5 (C5) and 145.9 (C3); δ_B($CDCl_3$, 64 MHz, $BH_3{\cdot}Et_2O$ ref.) −7.1; *m*/*z* (FAB) 237 [(M^+), 50%].

The second set of fractions contained (*E*)-prop-1-enyl-(triphenyl)phosphonium bromide **5** (0.42 g, 1.10 mmol, 92%) and the final set of fractions were a 1:1 mixture of the diastereomers, {(3R,4S)-4-*methyl*-1,1-*bis*[(S)-1-*phenylethyl*]-1,2-*azaboretidin*-1-*ium*-2-*uid*-3-*yl*}*triphenylphosphonium bromide* **4eA** and {(3S,4R)-4-*methyl*-1,1-*bis*[(S)-1-*phenylethyl*]-1,2-*azaboretidin*-1-*ium*-2-*uid*-3-*yl*}*triphenylphosphonium bromide* **4eB** as a clear viscous oil (0.019 g, 0.030 mmol, 2.5%); R_f 0.24 ($CHCl_3$–MeOH, 8:2).

Hydroboration of enamino(triphenyl)phosphonium salts with (1*R*)-(+)-monoisopinocampheylborane

General procedure. A solution of the phosphonium salt in anhydrous dichloromethane (20.0 cm^3) was stirred continuously in an ice–salt bath under an atmosphere of dry argon. When the temperature of the solution had reached −7 to −5 °C, a cold solution of freshly prepared (1*R*)-(+)-monoisopinocampheylborane (10.0 mmol) in tetrahydrofuran was added *via* a narrow bore steel cannula to the vigorously stirred solution over 15 min. A milky white solution formed and the mixture was initially stirred at approximately −1 °C for 3 h, and then overnight at room temperature. The reaction was monitored using ^{31}P NMR spectroscopy. When the ^{31}P NMR spectrum showed that the reaction was complete the flask was placed in an ice–salt bath and bench chloroform (20.0 cm^3) was added dropwise until no effervescence was observed. Diethyl ether (30.0 cm^3) was added slowly to give the product as a white precipitate. The solvent layer was carefully removed *via* a narrow bore steel cannula and the precipitate was washed several times with diethyl ether (30.0 cm^3), then finally dried under vacuum to afford the product.

Synthesis of 8aA. Reaction between **1a** (1.0 g, 2.21 mmol) in dichloromethane (20 cm^3) and (1*R*)-(+)-monoisopinocampheylborane (10.0 mmol) in tetrahydrofuran gave, after work-up, {(2R,3S)-1-[(R)-*isopinocampheyl*]-3-*methyl*-4-*azonia*-1-*boranuidaspiro*[3.4]*octan*-2-*yl*}*triphenylphosphonium bromide* **8aA** (1.21 g, 2.01 mmol, 91%) as a fine, white solid; $[\alpha]_{589}^{26}$ −8.4 (*c* 0.86 g in 100 cm^3 CH_2Cl_2); ν_{max}($CHBr_3$ mull)/cm^{-1} 2432s (B–H, st. vib.), 2342m (B–H, st. vib.) and 1438s (B–N, st. vib.).

Synthesis of 8bA. A mixture of compound **1b** (1.0 g, 2.16 mmol) in dichloromethane (20.0 cm^3) and (1*R*)-(+)-monoisopinocampheylborane (10.0 mmol) in tetrahydrofuran reacted to afford {(2R,3S)-1-[(R)-*isopinocampheyl*]-3-*methyl*-4-*azonia*-1-*boranuidaspiro*[3.5]*nonan*-2-*yl*}*triphenylphosphonium bromide* **8bA** (1.26 g, 2.04 mmol, 95%) as a fine white solid; $[\alpha]_{589}^{24}$ −2.1 (*c* 2.13 g in 100 cm^3 CH_2Cl_2); ν_{max}($CHBr_3$ mull)/cm^{-1} 2432s (B–H, st. vib.), 2342m (B–H, st. vib.) and 1438s (B–N, st. vib.).

Synthesis of 8cA. Compound **1c** (1.0 g, 1.99 mmol) in dichloromethane (20.0 cm^3) was caused to react with (1*R*)-(+)-monoisopinocampheylborane (10.0 mmol) in tetrahydrofuran to give {(3R,4S,1′S)-2-[(R)-(+)-*isopinocampheyl*]-4-*methyl*-1-(1-*phenylethyl*)-1,2-*azaboretidin*-1-*ium*-2-*uid*-3-*yl*}*triphenylphosphonium bromide* **8cA** (1.12 g, 1.72 mmol, 86%) as a white solid; $[\alpha]_{589}^{23}$ −100.5 (*c* 0.39 g in 100 cm^3 CH_2Cl_2); ν_{max}($CHBr_3$ mull)/cm^{-1} 2432s (B–H, st. vib.), 2342m (B–H, st. vib.) and 1435s (B–N, st. vib.).

Hydrolysis of [(2*R*,3*S*)- and (2*R*,3*R*)-3-methyl-4-azonia-1-boranuidaspiro[3.4]octan-2-yl]triphenylphosphonium bromide 4a

(a) Using sodium hydroxide in methanol. A solution of **4a** (2.0 g, 4.29 mmol) in methanol (40.0 cm^3) was stirred vigorously and aqueous sodium hydroxide (30%, w/w, 10.0 cm^3) was added slowly. The mixture was stirred at room temperature for 3 h, then refluxed for 3 h. The reaction was monitored using ^{31}P NMR spectroscopy. When the ^{31}P NMR spectrum showed that the reaction was complete, the mixture was cooled to room temperature before extraction with chloroform (3 × 30 cm^3). The combined extracts were dried over anhydrous $MgSO_4$, then concentrated under reduced pressure and finally dried under vacuum to afford a white solid shown by ^{31}P NMR spectroscopy to contain three different phosphorus compounds (δ +30.3, +29.5 and +29.8 ppm). The mixture was successfully separated by column chromatography (SiO_2, EtOAc–CH_2Cl_2, 4:1).

The first compound separated was triphenylphosphine oxide (0.14 g, 0.50 mmol, 12%); R_f 0.40 (EtOAc–CH_2Cl_2, 4:1); mp 151–152 °C followed by *rac*-2-*methoxy*-1-(*diphenylphosphinoyl*)*propane* **10**, as a colourless oil (0.38 g, 1.39 mmol, 32%); R_f 0.20 (EtOAc–CH_2Cl_2, 4:1). On leaving the colourless oil dissolved in small amount of chloroform at room temperature over several months fine, needle-shaped crystals suitable for X-ray determination were obtained, mp 65–66 °C; $[\alpha]_{589}^{23}$ +0.4 [*c* 0.19 g in 100 cm^3 CH_2Cl_2 (AR)] (Found: C, 70.2; H, 6.7; P, 11.2. $C_{16}H_{19}O_2P$ requires C, 70.1; H, 6.9; P, 11.3%); ν_{max}($CHBr_3$ mull)/cm^{-1} 2356w (P–H, st. vib.), 2257w (P–H, st. vib.), 1181s (P=O, st. vib.) and 1088s (P=O, st. vib.); δ_H($CDCl_3$, 300 MHz) 1.25 (d, 3H, $^3J_{H–Hc}$ 6.1, H3), 2.25–2.40 (ddd, 1H, $^2J_{Ha–Hb}$ 15.3, $^3J_{Ha–Hc}$ 6.3, $^2J_{P–Ha}$ 14.4, H1$_a$), 2.60–2.75 (ddd, 1H, $^2J_{Hb–Ha}$ 15.3, $^3J_{Hb–Hc}$ 12.3, $^2J_{P–Hb}$ 9.4, H1$_b$), 3.10 (s, 3H, H3), 3.65–3.80 (ddq, 1H, $^3J_{Hc–H}$ 6.1, $^3J_{Hc–Ha}$ 6.3, $^3J_{Hc–Hb}$ 12.3, H2), 7.35–7.50 (m, 6H, Ph) and 7.65–7.80 (m, 4H, Ph); δ_C($CDCl_3$, 75 MHz) 21.0 (d, C3, $^3J_{P–C}$ 7.2), 37.5 (d, C1, $J_{P–C}$ 70.6), 56.0 (C1′), 72.0 (br s, C2), 128.2 (d, C*m*, $^3J_{P–Cm}$ 12.3), 128.9 (d, C*m*′, $^3J_{P–Cm'}$ 12.3), 130.5 (d, C*o*, $^2J_{P–Co}$ 9.4), 131.0 (d, C*o*′, $^2J_{P–Co'}$ 9.4), 131.5 (d, C*p*, $^4J_{P–Cp}$ 2.0), 131.7 (d, C*p*′, $^4J_{P–Cp'}$ 2.1), 133.1 (d, C*i*, $J_{P–Ci}$ 99.8) and 134.3 (d, C*i*′, $J_{P–Ci'}$ 99.3); δ_P($CDCl_3$, 81 MHz, 85% H_3PO_4 ref.) +29.6; *m*/*z* (FAB) 275 [(M + H)$^+$, 100%].

The final compound collected after eluting the column with a more polar solvent (MeOH–CH_2Cl_2, 8:2) was *rac*-2-*pyrrolidino*-1-(*diphenylphosphinoyl*)*propane* **9a** (0.72 g, 2.30 mmol, 54%) as an off-white solid; R_f 0.02 (EtOAc–CH_2Cl_2, 4:1); $[\alpha]_{589}^{23}$ +0.2 (*c* 0.21 g in 100 cm^3 CH_2Cl_2).

Crystal data for 10. $C_{16}H_{19}O_2P$, M = 274.28, triclinic, space group $P\bar{1}$, a = 8.608(3), b = 11.736(4), c = 15.925(5) Å, α = 76.71(3), β = 85.58(3), γ = 71.34(2)°, U = 1483.4(9) Å^3, Z = 4, D_c = 1.228 g cm^{-3}, $F(000)$ = 584, μ(Mo-Kα) = 0.181 mm^{-1}. A colourless needle shaped crystal (0.40 × 0.20 × 0.10 mm) was selected for X-ray measurements. Unit cell dimensions were determined from the setting angle of 25 accurately centred reflections ($6.0 < \theta < 11.5°$). 4583 Independent reflections were measured on a Siemens R3m/v diffractometer using graphite monochromated Mo-Kα radiation (λ = 0.710 73 Å, $2\theta < 50°$) with $\omega/2\theta$ scans. Data were collected at 233(2) K and the structure was solved by direct methods using SHELXS-86[28] and DIRDIF.[29] Refinement was by full-matrix least-squares methods on F^2 for all independent reflections. $wR2 = \{[\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]\}^{\frac{1}{2}} = 0.2997$ for all data, where $w = 1/[\sigma^2(F_o^2) + (0.0979p)^2 + 0.8577p]$, where $p = (F_o^2 + 2F_c^2)/3$. Conventional R [on F values for 3016 reflections with $F^2 > 2\sigma(F^2)$] = 0.067 goodness of fit = 1.082 on F^2 for 343 refined parameters. All atoms were refined anisotropically. Hydrogen atoms were constrained to chemically reasonable positions.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc.*, *Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/155.

(b) Using aqueous sodium hydroxide. A mixture of **4a** (1.0 g, 2.15 mmol) and aqueous sodium hydroxide (30%, w/w, 10.0 cm^3) was refluxed for 3 h. The mixture was then extracted with chloroform (3 × 30 cm^3) and the combined extracts were dried under vacuum to afford a white solid, which by ^{31}P NMR spectroscopy was a mixture of two phosphorus compounds (δ +30.3 and +29.8). This mixture was successfully separated by column chromatography (SiO_2, $CHCl_3$–MeOH, 9:1) to give triphenylphosphine oxide (0.07 g, 0.26 mmol, 12%) and **9a** (0.59 g, 1.88 mmol, 87%).

Hydrolysis of {(2*R*,3*S*)-1-[(*R*)-isopinocampheyl]-3-methyl-4-azonia-1-boranuidaspiro[3.4]octan-2-yl}triphenylphosphonium bromide 8aA

Compound **8aA** (0.50 g, 0.830 mmol) in chloroform (1.0 cm^3) and aqueous sodium hydroxide (30%, w/w, 5.0 cm^3) were refluxed for 3 h whilst stirring. The mixture was extracted with chloroform (3 × 30 cm^3) and the combined extracts were dried over anhydrous $MgSO_4$, filtered, then concentrated under reduced pressure and finally dried under vacuum to afford a pale yellow oil, which on treatment with diethyl ether (15.0 cm^3) gave a white precipitate. The precipitate was washed several times with diethyl ether (10.0 cm^3), dried under vacuum to finally afford (S)-(+)-2-*pyrrolidino*-1-(*diphenylphosphinoyl*)-*propane*-(+)-**9a** (0.252 g, 0.805 mmol, 97%) as a white solid; mp 70–71 °C; $[\alpha]_{589}^{26}$ +11.9 (*c* 2.64 g in 100 cm^3 CH_2Cl_2). The spectroscopic data were identical to those of the racemate reported previously.

Hydrolysis of {(2*R*,3*S*)- and (2*R*,3*R*)-(3-methyl-4-azonia-1-boranuidaspiro[3.5]nonan-2-yl}triphenylphosphonium bromide 4b

(a) With sodium hydroxide in methanol. Following the procedure described above a solution of **4b** (2.0 g, 4.17 mmol) in methanol (40.0 cm^3) was stirred vigorously with aqueous sodium hydroxide (30%, w/w, 10.0 cm^3) and the mixture was stirred at room temperature for 3 h, then refluxed for 3 h to afford a white solid after work-up. A ^{31}P NMR spectrum showed that the white solid contained three different phosphorus compounds (δ +30.9, +29.5 and +29.8). This mixture was successfully separated by column chromatography (SiO_2, EtOAc–CH_2Cl_2, 4:1) to give triphenylphosphine oxide (0.16 g, 0.575 mmol, 14%) followed by *rac*-2-methoxy-1-(diphenylphosphinoyl)propane **10** (0.42 g, 1.53 mmol, 37%). The final compound collected after eluting the column with a more polar solvent (MeOH–CH_2Cl_2, 8:2) was rac-2-*piperidino*-1-(*diphenylphosphinoyl*)*propane* **9b** (0.66 g, 2.02 mmol, 48%); R_f 0.02

(EtOAc–CH_2Cl_2, 4:1); $[\alpha]_{589}^{23}$ +0.1 (*c* 0.20 g in 100 cm^3 CH_2Cl_2) as an off-white solid.

(b) With aqueous sodium hydroxide. A mixture of **4b** (1.0 g, 2.08 mmol) and aqueous sodium hydroxide (30%, w/w, 10.0 cm^3) was refluxed for 3 h and then extracted with chloroform (3 × 30 cm^3). The combined extracts were dried over anhydrous $MgSO_4$, filtered, then concentrated under reduced pressure and finally dried under vacuum to afford a white solid containing two phosphorus compounds (δ +30.9 and +29.8). This mixture was successfully separated by column chromatography (SiO_2, $CHCl_3$–MeOH, 9:1) to give triphenylphosphine oxide (0.07 g, 0.25 mmol, 12%) and rac-2-*piperidino*-1-(*diphenylphosphinoyl*)-*propane* **9b** (0.56 g, 1.71 mmol, 80%).

Hydrolysis of {(2*R*,3*S*)-1-[(*R*)-isopinocampheyl]-3-methyl-4-azonia-1-boranuidaspiro[3.5]nonan-2-yl}triphenylphosphonium bromide 8bA

Reaction between **8bA** (0.50 g, 0.812 mmol) in chloroform (1.0 cm^3) and aqueous sodium hydroxide (30%, w/w, 5.0 cm^3) gave a pale yellow oil, which on treatment with diethyl ether (15.0 cm^3) gave (R)-(+)-2-*piperidino*-1-(*diphenylphosphinoyl*)*propane* (+)-**9bA** (0.260 g, 0.79 mmol, 98%) as a white solid; mp 125–126 °C; $[\alpha]_{589}^{26}$ +8.6 [*c* 0.33 g in 100 cm^3 CH_2Cl_2 (AR)]. The spectroscopic data were identical to those of the racemate **9b** reported previously. Chiral GC analysis of a solution of this compound in chloroform showed it to be a mixture of enantiomers with an ee value of 75%.

Hydrolysis of (1*S*,3*R*)-4-methyl-1-[(*S*)-phenylethyl]-1,2-azaboretidin-1-ium-2-uid-3-yl]triphenylphosphonium bromide 4cA

(a) With sodium hydroxide in methanol. Under the general conditions described a solution of **4cA** (1.0 g, 1.94 mmol) in methanol (20.0 cm^3) was heated with aqueous sodium hydroxide (30%, w/w, 10.0 cm^3) to afford a white solid after work-up. A ^{31}P NMR spectrum showed that the white solid contained a mixture of three different phosphorus compounds, having the following chemical shifts δ +30.6, +29.5 and +29.8. The mixture was successfully separated by column chromatography (SiO_2, EtOAc–CH_2Cl_2, 4:1) to give triphenylphosphine oxide (0.8 g, 0.278 mmol, 14%) followed by *rac*-2-methoxy-1-(diphenylphosphinoyl)propane **10** (0.42 g, 1.53 mmol, 37%). The final compound collected as a colourless oil after eluting the column with a more polar solvent (MeOH–CH_2Cl_2, 8:2) was [(2S,4S)-2-*methyl*-4-*phenyl*-3-*azapentyl*]*diphenylphosphine oxide* **9cA** (0.39 g, 1.07 mmol, 55%); R_f 0.02 [EtOAc–CH_2Cl_2, 4:1); $[\alpha]_{589}^{23}$ −150.2 (*c* 0.20 g in 100 cm^3 CH_2Cl_2).

Hydrolysis of {(3*R*,4*S*,1′*S*)-2-[(*R*)-(+)-isopinocampheyl]-4-methyl-1-(1-phenylethyl)-1,2-azaboretidin-1-ium-2-uid-3-yl}-triphenylphosphonium bromide 8cA

To **8cA** (0.50 g, 0.767 mmol) in chloroform (1.0 cm^3) was added aqueous sodium hydroxide (30%, w/w, 5.0 cm^3). The mixture was refluxed for 3 h whilst stirring to give, after work-up, [(2S,4S)-(−)-2-*methyl*-4-*phenyl*-3-*azapentyl*]*diphenylphosphine oxide* (−)-**9cA** (0.27 g, 0.74 mmol, 97%); $[\alpha]_{589}^{26}$ −162.3 (*c* 1.61 g in 100 cm^3 CH_2Cl_2). The melting point and spectroscopic data were identical to those of **9cA** reported previously.

Oxidation of [(1*S*,3*S*,4*R*,1′*S*)-4-methyl-1-(1-phenylethyl)-1,2-azaboretidin-1-ium-2-uid-3-yl]triphenylphosphonium bromide 4cB

Under similar conditions **4cB** (0.50 g, 0.971 mmol) on heating with aqueous sodium hydroxide (30%, w/w, 10.0 cm^3) gave a white solid, which contained two different phosphorus compounds (δ +30.6 and +29.8). This mixture was successfully separated by column chromatography (SiO_2, $CHCl_3$–MeOH, 9:1) to give triphenylphosphine oxide (0.04 g, 0.14 mmol, 15%) and [(2R,4S)-(+)-2-*methyl*-4-*phenyl*-3-*azapentyl*]-*diphenylphosphine oxide* (+)-**9cB** (0.26 g, 0.72 mmol, 74%); R_f 0.35 ($CHCl_3$–MeOH, 9:1); $[\alpha]_{589}^{26}$ +98.3 (*c* 0.15 g in 100 cm^3 CH_2Cl_2).

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References

1 Part of this work has been previously reported in B. L. Booth, N. J. Lawrence, R. G. Pritchard and H. S. Rashid, *J. Chem. Soc., Chem. Commun.*, 1995, 287.
2 G. K. Anderson and R. Kumar, *Inorg. Chem.*, 1984, **23**, 4064.
3 L. Dahlenburg, S. Kersten and D. Werner, *J. Organomet. Chem.*, 1991, **411**, 457.
4 T. J. Uriate, K. D. Tan and D. W. Meek, *Inorg. Chem.*, 1980, **19**, 79.
5 L. Sacconi, C. A. Mealli and F. Zanobini, *Inorg. Chem.*, 1975, **14**, 1380.
6 H. Werner, A. Hampp and B. Windmüller, *J. Organomet. Chem.*, 1992, **435**, 169.
7 L. D. Field and I. J. Luck, *Tetrahedron Lett.*, 1994, **35**, 1109.
8 D. J. Collins, S.-A. Mollard, N. Rose and J. M. Swan, *Aust. J. Chem.*, 1974, **27**, 2365.
9 H. Takahashi and K. Achiwa, *Chem. Lett.*, 1987, 1921.
10 W. R. Cullen, S. V. Evans, N. F. Han and J. Trotter, *Inorg. Chem.*, 1987, **26**, 514.
11 H. Kubota and K. Koga, *Tetrahedron Lett.*, 1994, **35**, 6689.
12 M. Kanai, K. Koga and K. Tomioka, *Tetrahedron Lett.*, 1992, **33**, 7193.
13 J. Barluenga, F. López and F. Palacios, *Synthesis*, 1989, 298.
14 V. G. Markl and B. Markl, *Tetrahedron Lett.*, 1981, **22**, 4459.
15 D. Cavalla and S. Warren, *Tetrahedron Lett.*, 1983, **24**, 295; D. Carvalla, W. B. Cruse and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1883.
16 M. I. K. Amer, B. L. Booth and P. Bitrus, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1673.
17 B. Beagley, P. Bitrus, B. L. Booth and R. G. Pritchard, *J. Chem. Soc., Perkin Trans. 1*, 1993, 1039.
18 P. Bitrus and B. L. Booth, *J. Chem. Res.*, 1993, 168.
19 S. DeVoe Goff, W. P. Murray and E. E. Schweizer, *J. Org. Chem.*, 1977, **42**, 200.
20 M. A. Caleago and E. E. Schweizer, *J. Org. Chem.*, 1978, **43**, 4207.
21 K. Eiter and H. Oegiger, *Justus Liebigs Ann. Chem.*, 1965, **62**, 682.
22 J. Barluenga, F. López and F. Palacios, *Tetrahedron Lett.*, 1988, **29**, 4863; J. Barluenga, F. H. Cano, M. C. Foces-Foces, F. López and F. Palacios, *J. Chem. Soc., Perkin Trans. 1*, 1988, 2329.
23 F. Palacios, D. Aparicio and J. Garcia, *Tetrahedron*, 1996, **52**, 9609.
24 H. J. Bestmann, P. Erlmann, H. Oechsner and G. Schmid, *Chem. Ber.*, 1984, **117**, 1561.
25 M. B. Eleveld, H. Hogeveen and E. P. Schudde, *J. Org. Chem.*, 1986, **51**, 3635.
26 H. C. Brown, P. K. Jadhav and A. K. Mandal, *J. Org. Chem.*, 1986, **51**, 3635.
27 H. C. Brown, N. Inoue, M. W. Rathke and K. R. Varma, *J. Am. Chem. Soc.*, 1966, **88**, 2870.
28 G. M. Sheldrick, in *Crystallographic Computing 3*, ed. G. M. Sheldrick, C. Kruger and R. Goddard, OUP, London, 1985, p. 175.
29 P. T. Beurskens, DIRDIF: Direct methods for Difference Structure—an automatic procedure for phasing extension and refinement of difference structure factors. Technical Report 1984/1, Crystallographic Laboratory, Toernooiveld, 6525 Ed. Nijmegen, Netherlands.

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