Synthesis and X-Ray Crystal Structure of (1*S*,3*R*,4*S*,1′*S*)-4-Methyl-3-triphenylphosphonium-1-[1′-methyl(methylphenyl)]-2-hydrido-2-borazetidinium Bromide—the First Example of a Four-membered C–B–N–C Heterocycle

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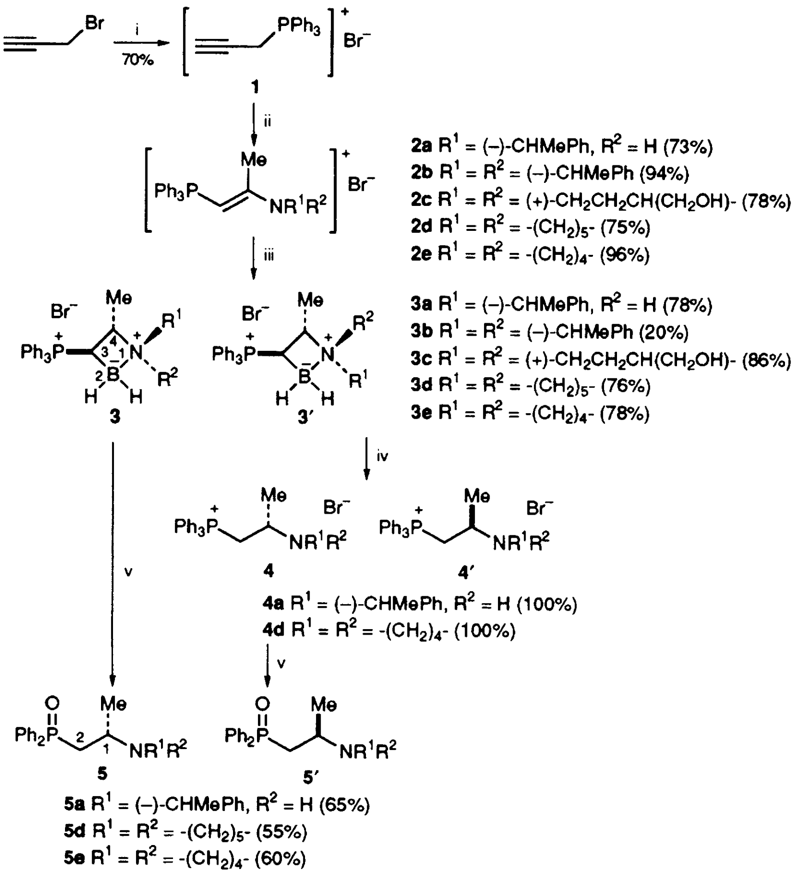
The title compound and related derivatives are synthesised from enamino(triphenyl)phosphonium salts and borane, and converted into β-aminophosphonium salts and β-aminophosphine oxides containing two chiral centres.

Enamino(triphenyl)phosphonium salts of the type [(*E*)-$Ph_3PCH{=}CMeNR^1R^2]^+\ X^-$ **2** are readily available either from the reactions of secondary amines with prop-2-ynyl(triphenyl)phosphonium bromide **1**[1] or from *N*-alkylnitrilium trifluoromethanesulfonate salts and trimethylsilylmethylidenetriphenylphosphorane.[2] Our interest in compounds of type **2** stems from the recognition that if the double bond could be reduced then the resultant β-aminophosphonium salts, particularly those bearing a chiral group on the nitrogen atom, could be useful precursors to a number of β-aminophosphine derivatives of potential value as asymmetric ligands. Relatively few bidentate P–N ligands have been reported;[3] nevertheless, chiral P^{III}–N ligands have found recent applications as catalysts for, *inter alia*, asymmetric hydrogenation reactions;[4] hydrosilylation of carbonyl compounds;[5] palladium-assisted substitution of allylic acetates;[6] and conjugate addition to α,β-unsaturated carbonyl compounds.[7]

Reaction between **1** and a number of primary and secondary amines in dry acetonitrile gave, as expected,[1] the salts **2a–e** in the yields shown in Scheme 1. Hydroboration of **2a–e** with a large excess of $BH_3{\cdot}THF$ or $BH_3{\cdot}Me_2S$ in dichloromethane at room temp. gave the novel borazetidinium salts **3a–e**. The hydroboration occurs with the expected regioselectivity—the nitrogen atom clearly directing the boron atom to the α-carbon atom, as is the case for simple enamines,[8,9] whilst the phosphonium group should activate the β-carbon to accept the partially nucleophilic hydrogen atom of the borane. The remarkable feature of the reaction was revealed when we isolated the products and showed them to be relatively stable boranes. The stability of the boranes is undoubtedly associated with the internal coordination of the amine and borane groups. This coordination *via* a four-membered ring has been invoked in previous studies of the hydroboration of enamines.[9] However, to our knowledge, this phenomenon has not been observed by X-ray diffraction.

When the amine is chiral, as in **2a** and **2b**, an approximate 1 : 1 mixture of diastereoisomers **3** and **3′** is obtained. This lack of stereoselectivity in the reaction is not too surprising. Unlike the hydroboration of alkenes bearing an allylic chiral centre, *e.g.* alcohol[10] or silane,[11] where the selectivity is often high, there are few examples of stereoselective reactions with alkenes bearing an homoallylic chiral centre.[12] We have assigned the stereoisomers as having arisen from addition of the amine to either of the prochiral faces of the alkene. Spectroscopic data†



Scheme 1 *Reagents and conditions*: i, PPh_3, 48% HBr aq., 1,4-dioxane; ii, R^1R^2NH (1 equiv.), MeCN, reflux (1 h), then room temp. (80 h); iii, $BH_3{\cdot}THF$ (5 equiv.), CH_2Cl_2, 0 °C (1 h) then room temp. (12 h); iv, Pr^iOH, reflux; v, NaOH (30% m/m), MeOH

clearly indicate that these compounds possess a borane residue, and in the case of compound **3a** it was possible, by careful recrystallisation from propan-2-ol (see below), to isolate crystals of the 1*S*,3*R*,4*S*,1′*S* diastereoisomer; the 1*R*,3*S*,4*R*,1′*S* diastereoisomer **3a′**‡ could also be recovered in an almost pure state from the mother liquors as a pale yellow oil. A single-crystal X-ray determination on **3a** (Fig. 1) established that the compound was associated with half a molecule of propan-2-ol.§ The compound contains the novel C–B–N–C heterocyclic ring with two chiral carbon centres and a chiral nitrogen centre. The C–C and C–N bond lengths in the heterocyclic ring are as expected for single bonds (148 and 150 pm respectively) and are similar to those found for the C(4)–C(24) (149 pm) and N(1)–C(1′) (148 pm) bonds. The N–B and C–B bond lengths are 162 and 161 pm respectively and the N(1)–B(2)–C(3) bond angle is smaller (85°) than those for the atoms B(2)–N(1)–C(4) (90°) and B(2)–C(3)–C(4) (91°); the N(1)–C(4)–C(3) angle is 94°. The 4-membered ring is essentially planar with an N(1)–B(2)–C(3)–C(4) torsional angle of only 8°.

Attempts to improve the stereoselectivity in the hydroboration of **2** have not been successful. When the amine bears two large substituents on the nitrogen atom as in **2b**, the reaction with borane is not clean and cleavage of the N–C bond occurs to give [*E*-$Ph_3PCH{=}CHMe]^+$ Br^- (35%) and $(PhMeCH)_2NBH_2$ (30%), in addition to **3b** and **3b′**. The use of a more hindered borane, 9-BBN, which often leads to higher stereoselectivity in related reactions,[10] under similar conditions gave no reaction.

Upon heating the mixtures of diastereoisomers **3a**/**3a′** and **3e**/**3e′** in propan-2-ol they decompose to the corresponding reduction products **4**, but it proved impossible to separate the mixture of diastereoisomers in these cases. However, similar treatment of the pure **3a** gave a good yield of the pure diastereoisomer **4a**. We planned to convert the phosphonium salts to phosphine oxides by thermolysis of the corresponding triphenylphosphonium hydroxides.[13] Indeed, when either the compounds **3** or **4** are heated with 30% m/m aqueous NaOH solution in methanol the phosphine oxides **5a,d–e** can be isolated in the yields shown (see Scheme 1). The yields from this last reaction are only moderate. One of the major by-products is $Ph_2P(O)CH_2CHMeOMe$ (30–35% yield), which is presumably formed by an E2 elimination of the amine from **4** followed by attack of methoxide ion on the intermediate vinyl(triphenyl)phosphonium salt; the fact that this methyl ether is racemic seems to support this mechanism. Treatment of the pure diastereoisomer **3a** with 30% m/m aqueous NaOH gave a 93% yield of the pure diastereoisomer (1*S*,1′*S*) **5a**. Similar treatment of **3a′** also gave a 93% yield of the (1*R*,1′*S*) diastereoisomer (**5a′**) after chromatography.

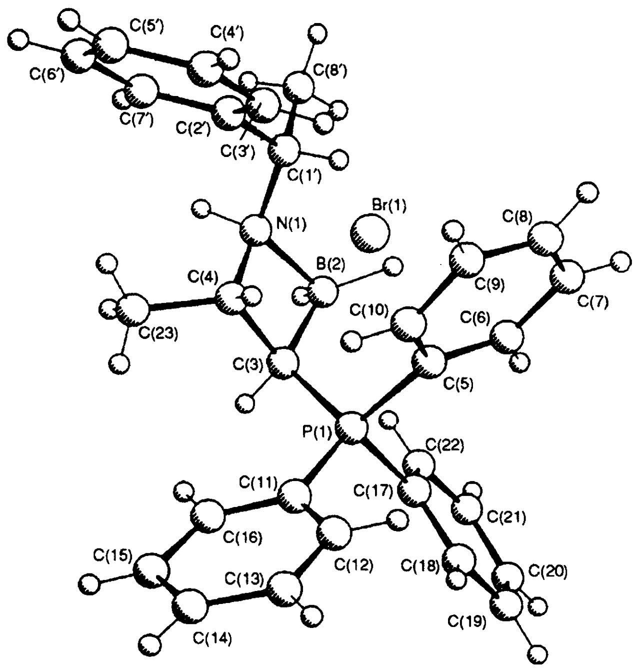


Fig. 1 X-ray structure of **3a**

In conclusion, this sequence represents a new method for the synthesis of β-aminophosphine oxides having both a chiral group on the nitrogen atom and at one of the carbon atoms bridging the nitrogen and phosphorus centres.

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Footnotes

† The reaction, in principle and assuming the normal *syn* addition of the boron and hydrogens atoms, can produce four possible stereoisomers. We assume that the minor isomer is the 1*R*,3*S*,4*R*,1′*S* isomer. The only uncertainty is the configuration of the N-1 centre, but it seems reasonable that the large α-methylbenzylamine group is placed *trans* to the methyl group, at C-4, thereby avoiding unfavourable 1,2 steric interactions. The structures of the related borazetidinium salts **3b** and **3c** are assigned by analogy.

‡ All compounds described in this paper were fully characterised by elemental analysis, ^1H, ^{13}C, ^{31}P, ^{11}B NMR spectroscopy and mass spectrometry. Typical data for compound **3a** are as follows: $[\alpha]_{546}^{26}$ −180.15 (*c* 0.29, CH_2Cl_2), mp 165–166 °C. FAB MS, *m*/*z* 436 [M − Br]$^+$ (100%); ν_{max}/cm^{-1} 3413 (NH), 2436 (BH); δ_H (300 MHz, $SiMe_4$ int. ref. $CDCl_3$) 1.12 (3H, d, J_{H-H} 6.5 Hz, CH_3), 1.41 (3H, d, J_{H-H} 6.7 Hz, CH_3), 2.95 (2H, m, CHN and CHP overlapping), 3.35 (1H, m, CH), 7.20–7.29 (3H, m, Ph), 7.41–7.44 (2H, m, Ph), 7.58–7.76 (15H, m, Ph_3P), 7.90 (1H, d, J_{H-H} 4.7 Hz, NH); δ_C ($CDCl_3$, 75 MHz) 15.8 (J_{P-C} 52.6), 18.7, 21.4 (J_{P-C} 1.8 Hz), 58.9 (J_{P-C} 2.5), 66.1, 121.2 (J_{P-C} 87.2), 128.3, 129.7 (J_{P-C} 12.1), 129.9, 133.6 (J_{P-C} 9.6), 134.0, 134.2 (J_{P-C} 2.5), 139.0; δ_P (85% H_3PO_4 ref.) +29.13; δ_B ($BH_3{\cdot}Et_2O$ ref.) −8.22.

§ *Crystal data*. $C_{30.5}H_{36}NBBrO_{0.5}P$: *M* = 546.3, trigonal, space group $P3_221$ (no. 154), *a* = 14.141(4), *c* = 24.497(8), *V* = 4242(4) Å^3 [from 20 reflections (15.1 ≤ 2θ ≤ 21.4°)], *Z* = 6, D_c = 1.283 g cm^{-3}, *T* = 233 K, colourless plate, μ = 15.13 cm^{-1}.

Data collection and processing: A crystal of **3a** having approximate dimensions of 0.30 × 0.20 × 0.05 mm was mounted on a glass fibre. All measurements were made on a Siemens R3m/v diffractometer with graphite-monochromated Mo-Kα X-radiation. The data were collected at a temperature of −40 ± 1 °C using the ω–2θ scanning technique to a maximum 2θ value of 46.1°. The structure was solved by direct methods using SHELXS-86[14] and DIRDIF.[15]

Full-matrix least-squares refinement using TEXSCAN[16] yielded final residuals of R = 0.058 and R' = 0.039 with $w = 1/[\sigma^2(F_o) + 0.03F_o^2]$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1

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