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

Brian L. Booth, Nicholas J. Lawrence,* Robin G. Pritchard and Humayan S. Rashid

Chemistry Department, University of Manchester Institute of Science and Technology, Manchester, UK M60 1QD
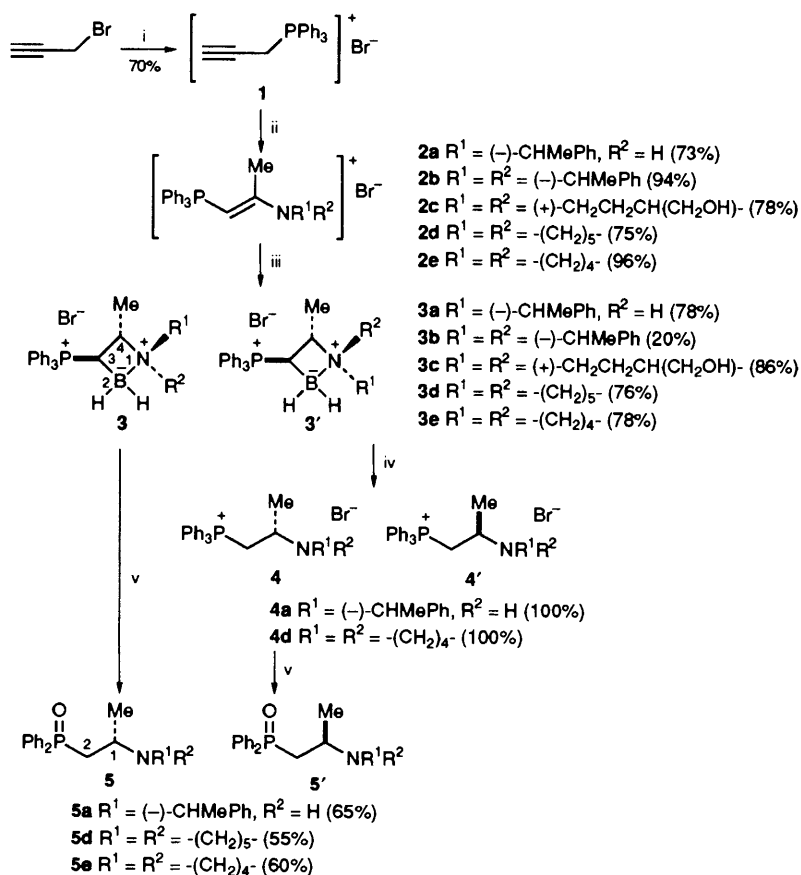
The title compound and related derivatives are synthesised from enamino(triphenyl)phosphonium salts and borane, and converted into β-aminophosphonium salts and β-aminophosphine oxides containing two chiral centres.

Enamino(triphenyl)phosphonium salts of the type [(E)-Ph₃PCH=CMeNR¹R²]⁺ 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 Pᴵᴵᴵᴵᴵᴵᴵᴵᴵᴵᴵ–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 BH₃·THF or BH₃·Me₂S 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†

2a R¹ = (–)-CHMePh, R² = H (73%)
2b R¹ = R² = (–)-CHMePh (94%)
2c R¹ = R² = (+)-CH₂CH₂CH(CH₂OH)- (78%)
2d R¹ = R² = -(CH₂)₅- (75%)
2e R¹ = R² = -(CH₂)₄- (96%)

3a R¹ = (–)-CHMePh, R² = H (78%)
3b R¹ = R² = (–)-CHMePh (20%)
3c R¹ = R² = (+)-CH₂CH₂CH(CH₂OH)- (86%)
3d R¹ = R² = -(CH₂)₅- (76%)
3e R¹ = R² = -(CH₂)₄- (78%)

4a R¹ = (–)-CHMePh, R² = H (100%)
4d R¹ = R² = -(CH₂)₄- (100%)

5a R¹ = (–)-CHMePh, R² = H (65%)
5d R¹ = R² = -(CH₂)₅- (55%)
5e R¹ = R² = -(CH₂)₄- (60%)

Scheme 1 Reagents and conditions: i, PPh₃, 48% HBr aq., 1,4-dioxane; ii, R¹R²NH (1 equiv.), MeCN, reflux (1 h), then room temp. (80 h); iii, BH₃·THF (5 equiv.), CH₂Cl₂, 0 °C (1 h) then room temp. (12 h); iv, PrⁱOH, 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 1S,3R,4S,1'S diastereoisomer; the 1R,3S,4R,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$_3$PCH=CHMe]$^+$ Br$^-$ (35%) and (Ph-MeCH)$_2$NBH$_2$ (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$_2$P(O)CH$_2$CHMeOMe (30–35% yield), which is presumably formed by an E2 elimination of the amine from **4**
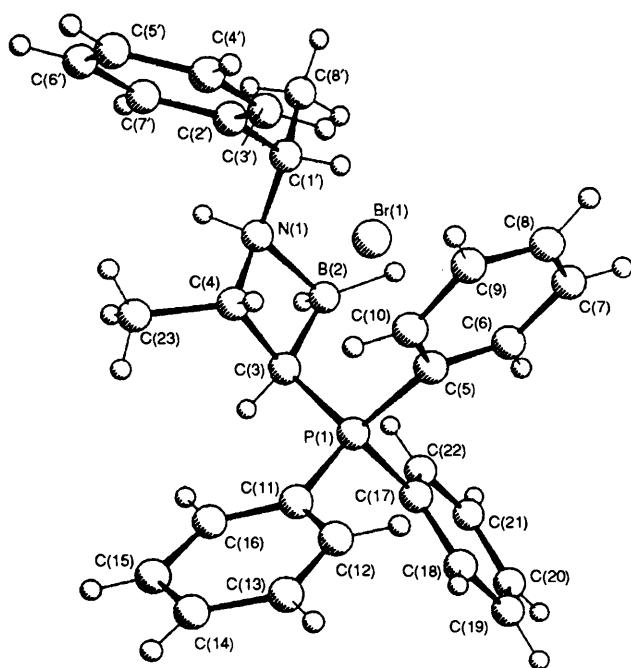
followed by attack of methoxide ion on the intermediate vinyl(triphenyl)phosphonium salt; the fact that this methyl ether is racemic seems to support this mechanism. Treatment of the pure diastereoisomer **3a** with 30% m/m aqueous NaOH gave a 93% yield of the pure diastereoisomer (1S,1'S) **5a**. Similar treatment of **3a'** also gave a 93% yield of the (1R,1'S) diastereoisomer (**5a'**) after chromatography.

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.

Received, 13th October 1994; Com. 4/06253A

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 1R,3S,4R,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, ^{1}H, ^{13}C, ^{31}P, ^{11}B NMR spectroscopy and mass spectrometry. Typical data for compound **3a** are as follows: [α]$_{546}^{26}$ −180.15 (c 0.29, CH$_2$Cl$_2$), 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$_3$P), 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$_3$PO$_4$ ref.) +29.13; δ$_B$ (BH$_3$·Et$_2$O 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/[σ^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

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

References

1 E. E. Schweizer, S. De Voe Goff and W. P. Murray, *J. Org. Chem.*, 1977, **42**, 200; M. A. Calcagno and E. E. Schwiezer, *J. Org. Chem.*, 1978, **43**, 4207.

2 B. L. Booth and P. Bitrus, *J. Chem. Res.*, 1993, (S) 168; M. I. K. Amer, B. L. Booth and P. Bitrus, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1673.

3 G. K. Anderson and R. Kumar, *Inorg. Chem.*, 1984, **23**, 4064; L. Dahlenburg, S. Kersten and D. Werner, *J. Organomet. Chem.*, 1991, **411**, 457; T. J. Uriate, K. D. Tan and D. W. Meek, *Inorg. Chem.*, 1980, **19**, 79; L. Sacconi, C. A. Mealli and F. Zanobini, *Inorg. Chem.*, 1975, **14**, 1380; H. Werner, A. Hampp and B. Windmüller, *J. Organomet. Chem.*, 1992, **435**, 169; L. D. Field and I. J. Luck, *Tetrahedron Lett.*, 1994, **35**, 1109; J. Barluenga, F. López and F. Palacios, *Synthesis*, 1989, 298; V. G. Markl and B. Merkl,

Tetrahedron Lett., 1981, **22**, 4459; R. J. Linderman and A. I. Meyers, *Tetrahedron Lett.*, 1983, **24**, 3043.

4 H. Takahashi and K. Achiwa, *Chem. Lett.*, 1987, 1921.

5 W. R. Cullen, S. V. Evans, N. F. Han and J. Trotter, *Inorg. Chem.*, 1987, **26**, 514.

6 H. Kubota and K. Koga, *Tetrahedron Lett.*, 1994, **35**, 6689.

7 M. Kanai, K. Koga and K. Tomioka, *Tetrahedron Lett.*, 1992, **33**, 7193.

8 G. B. Fisher, C. T. Goralski, L. W. Nicholson and B. Singaram, *Tetrahedron Lett.*, 1993, **34**, 7693; B. Singaram, C. T. Goralski and G. B. Fisher, *J. Org. Chem.*, 1991, **56**, 5691.

9 C. T. Goralski, B. Singaram and H. C. Brown, *J. Org. Chem.*, 1987, **52**, 4014.

10 W. C. Still and J. C. Barrish, *J. Am. Chem. Soc.*, 1983, **105**, 2487.

11 I. Fleming and N. J. Lawrence, *J. Chem. Soc., Perkin Trans. 1*, 1992, 3309.

12 D. A. Evans, J. Bartroli and T. Godel, *Tetrahedron Lett.*, 1982, **23**, 4577.

13 G. W. Fenton and C. K. Ingold, *J. Chem. Soc.*, 1929, 2342; J. Meisenheimer, J. Casper, M. Horing, W. Lauter, L. Lichtenstadt and W. Samuel, *Justus Leibigs Ann. Chem.*, 1926, **449**, 213; M. Zanger, C. A. Van der Werf and W. E. McEwen, *J. Am. Chem. Soc.*, 1959, **81**, 3806.

14 G. M. Sheldrick, in *Crystallographic Computing 3*, ed. G. M. Sheldrick, C. Kruger and R. Goddard, Oxford University Press, pp. 175–189.

15 P. T. Beurskens, DIRDIF: Direct methods for Difference Structures—an automatic procedure for phase extension and refinement of difference structure factors. Technical Report 1984/1 Crystallography Laboratory, Toernooiveld, 6525 Ed Nijmegen, 1984.

16 Molecular Structure Corporation TEXSCAN, TEXRAY Structure Analysis Package. MSC, 3200A Research Forest Drive, The Woodlands, TX 77381, 1985.