Pergamon

Tetrahedron, Vol. 53, No. 33, pp. 11411-11424, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00722-9

Electrophilic Amination of Catecholboronate Esters formed in the Asymmetric Hydroboration of Vinylarenes

Frances I. Knight and John M.Brown*

The Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford, OX1 3QY, U.K.

Dario Lazzari and Alfredo Ricci

Dipartimento di Chimica Organica, Università degli Studi di Bologna,40136 Bologna, ITALY

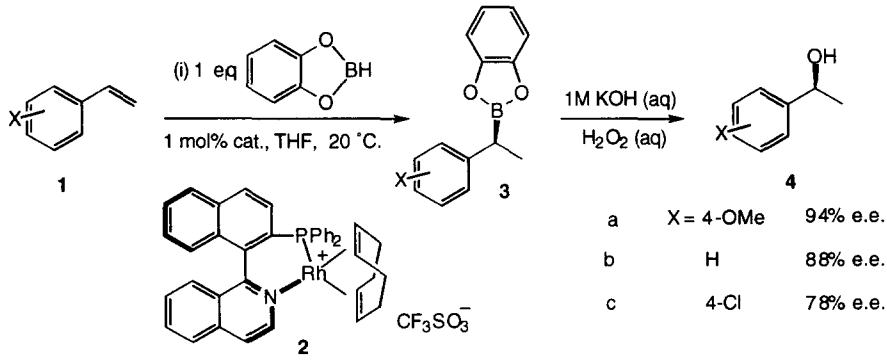
A. John Blacker

Zeneca Process Technology Department, PO Box A38, Leeds Rd. Huddersfield, Yorkshire HD2 1FF

Abstract : (*S*)-(4-Methoxyphenyl)-ethyl-1,3,2-benzodioxaborole, (*S*)-1-(4-chlorophenyl)ethyl-1,3,2-benzodioxaborole and (*S*)-1-indanyl-1,3,2-benzodioxaborole. intermediates in the catalytic asymmetric hydroboration of 4-chloro- and 4-methoxystyrene, were isolated as pure oils in 75%, 84% and 49% yield respectively. For the first example, amination with *N*-chloromagnesio-*N*-methyl-*O*-trimethylsilylhydroxylamine gave a mixture of (*S*)-1-(4-methoxyphenyl)-*N*-methylethylamine in 33% yield, 88% e.e. and (*S*)-1-(4-methoxyphenyl) ethanol in 31% yield, 86% e.e.. Related results were obtained in the other cases, and the steps of catalytic hydroboration and amination could be combined in a single sequence without isolation of the intermediate. Numerous variants were carried out in the amination procedure with only marginal improvements in chemoselectivity. An investigation of the mechanism was carried out using low temperature heteronuclear NMR on ^{13}C-1-(*S*)-1-(4-chlorophenyl)ethyl-1,3,2-benzodioxaborole. The dual pathway is a result of an irreversible and unselective initial step. © 1997 Elsevier Science Ltd.

Introduction

The asymmetric hydroboration of vinylarenes exemplified by **1**, catalysed by rhodium complex **2** and using catecholborane as the reactant, has been reported previously (Scheme 1). The normal oxidative workup of the intermediate catecholboronate esters **3** gives alcohols **4** in up to 95% e.e..[1] In common with other examples of catalysed asymmetric hydroboration,[2] only catecholborane is effective among commonly accessible hydroborating agents, and this limits the usefulness, since many of the common transformations of organoboranes do not work with boronate esters. We had hoped to extend the range to include amination and report here a systematic study of the reaction of benzylcatecholboronate esters with electrophilic aminating agents related to N-methyl-O-trimethylsilyl hydroxylamine.[3] In all cases a mixture of amine and alcohol was formed in comparable amounts. Since the completion of this work an alternative and general amination-selective procedure has been discovered.[4]

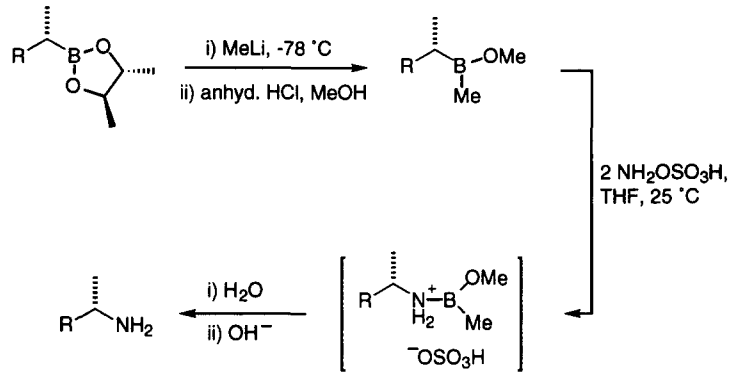


Scheme 1. Asymmetric hydroboration/oxidation catalysed by the Rh complex of (*S*)-1-(2-diphenylphosphino-1-naphthyl)isoquinoline

Discussion

A variety of aminating agents have been reacted with alkylboranes to prepare amines in previous work, including chloramine and hydroxylamine-*O*-sulphonic acid.[5] The 55-60% yields obtained implied that only two of the three alkyl groups on the organoborane were capable of migrating to nitrogen. The amination of organoboranes formed from relatively hindered alkenes could be achieved using hydroxylamine-*O*-sulphonic acid, and better results were achieved by changing the solvent from thf to diglyme.[6] Improved yields were obtained in specific cases by employing ammonium hydroxide and sodium hypochlorite (NH_2Cl in situ) as the reagent.[7] It was recognised early on that alkylboronate esters were unresponsive to these aminating agents but dialkylborinate esters were reactive, with selectivity for alkyl over methyl migration.[8] .

However, various monoalkylborate esters, such as $RBO_2(CH_2)_3$, did not react with hydroxylamine-*O*-sulphonic acid, although mixed dialkylborinite esters such as RR'BOR" were found to react with the more substituted R-group showing a significantly greater migratory aptitude. Multistep procedures proved necessary for applications in asymmetric synthesis,[9] as exemplified in Scheme 2 where the initial boronate ester was prepared by the Matteson protocol.[10]

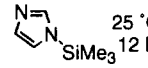
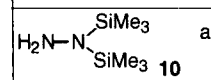
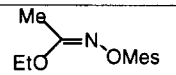


Scheme 2. An example of asymmetric amination via the alkylation of an alkylboronic ester.

Our objective was a one-pot synthesis of scalemic amines via catalytic hydroboration. Two of us[3] had had previous experience of the use of N-methyl-O-trimethylsilylhydroxylamine[11] and related electrophilic reagents for the amination of cyanocuprates, and the possibility that they would function as analogues of H_2O_2 provided a basis for the work.

Synthesis of aminating agents : It was decided to test these and related aminating agents in the hydroboration – amination reaction and thus a series of substituted hydroxylamines was synthesised by adaptations of the method by Wannagat (Table 1).[12] The free hydroxylamine was initially formed by reaction of the hydroxylamine hydrochloride salt with either lutidine, imidazole or triethylamine. This produced a sticky, white solid in all cases which was then stirred with trimethylsilylimidazole for the *N*-methyl silylhydroxylamine **5a** or a substituted chlorosilane for compounds **6**, **7** and **8**. Two equivalents of chlorotrimethylsilane were required for the preparation of the *bis*-trimethylsilyl derivative **9**.[13] The non-polar solvent allowed isolation of the required product as a colourless liquid, purified by distillation under reduced pressure. The synthesis of *bis*-trimethylsilylhydrazine was carried out following a modified version of the procedure by Wannagat[14], by refluxing an ethereal solution of hydrazine with chlorotrimethylsilane. The mixture was filtered and the filtrate distilled to give the product as a clear, colourless liquid in 28% yield. Two separate sets of resonances were observed in the ^1H NMR, which corresponded to a (presumably easily interconverting) mixture of the *bis*-1,1- and 1,2-trimethylsilylhydrazines

10a and **10b**. O-mesitylsulphonylhydroxylamine **11** was prepared from a stable commercially available imidate precursor, ethyl-O-mesitylsulphonylacetohydroxamate. The preparation by Tamura[15] was adapted for safety reasons such that 50% sulphuric acid in diethyl ether was used instead of 70% perchloric acid. These syntheses are summarised in Table 1.

Reagent	*Precursor*	*Base, Solvent*	*Silylating agent*	*Yield*
$MeNHOSiMe_3$ **5a**	MeNHOH.HCl	 ,pentane	 25 °C, 12 h,	57%
t-BuNHOSiMe3 **6**	t-BuNHOH.HCl	 ,pentane	Me_3SiCl	47%
$PhCH_2NHOSiMe_3$ **7**	PhCH2NHOH.HCl	 ,pentane	Me_3SiCl	92%
$MeNHOSiMe_2Bu^t$ **8a**	MeNHOH.HCl	 ,pentane	t-$BuMe_2SiCl$	50%
$Me_3SiNHOSiMe_3$ **9**	$NH_2OH.HCl$	Et_3N, pentane	Me_3SiCl	15%
 a **10**	H_2NNH_2	---, Et_2O	Me_3SiCl	28%
H_2N-OMes[b] **11**		50% aq H_2SO_4, Et_2O		used as Et_2O soln.

[a] *In equilibrium with the 1,2-disilylhydrazine;* [b] *Prepared in situ*

Isolation of catecholboronate esters : Following the previously described method, boronic esters **3a**, **3c** and **12** were prepared on a 1-4 gram scale by the catalysed hydroboration of 4-methoxystyrene, 4-chlorostyrene or indene respectively using catecholborane in thf. Isolation by short path distillation gave clear, colourless oils in 49 - 84% yield, analytically pure in the first two cases, which were stored in sealed vials under argon.Similar characteristics were observed in the NMR spectra of all three boronate esters. Thus, the ^{11}B NMR spectra all contained a broad resonance at ca. 34 ppm and the ^1H NMR CHB quartet was found at 3.03 and 3.01 ppm for **3a** and **3b** respectively and at 3.35 ppm for **12**. In all cases the absence of a resonance due to CHB in the ^{13}C NMR was due to broadening as a result of the proximity of the quadrupolar boron nucleus. The enantiomer excesses of the alcohols isolated after basic hydrogen peroxide workup were 86% [**3a**], 62% [**3b**] and 70% [**12**]. Before commencing amination studies it was confirmed that borane **3a** was unreactive towards H_2NOSO_3H in both toluene and acetonitrile.

Aminations of the isolated boranes : An initial reaction was carried out according to the procedure of Scheme 2. BuLi in thf at -78 °C was used to deprotonate the silylhydroxylamine **5**, and this lithiated species was added to the boronic ester **3a** at -78 °C. The reaction mixture was warmed to -20 °C and stirred for 1 h., then further warmed to room temperature. Workup and separation by acid extraction of the amine component produced an approximately 1 : 1 ratio of the *N*-methylamine **13a** to the alcohol **4a**, in 33% and 31% yields respectively.

Repeating the reaction at 0 °C and with inverse addition of the reagents, adding the aminating agent to the boronic ester, gave the same result although the ^1H NMR showed a slightly higher proportion of minor side products. Using 4-chlorophenylboronic ester **3b** gave the same product ratio of amine **13b** and alcohol **4b**. The competing formation of alcohol and amine indicates that the reagent can function both as an O-nucleophile and an N-nucleophile. In fact, the early studies of West on the NMR of the Li salt of **5** indicated rapid silyl transfer between the two heteroatoms.[11] It is interesting to note that amination was not observed with the conjugate base of $MeONH_2$. From these early results a systematic variation of solvent, base and silylating agent was conducted, key results being collected in Table 2 and Table 3, which typify a rather larger set of attempts. Almost all variations from the simple reaction conditions are ineffective, or diminish the proportion of amine in the reaction product, and conditions for the exclusion of alcohol from the product mixture were not found. The optimum reaction for ease of operation and work-up is probably Entry **2.**

Table 2. Effects of counterion, solvent and reaction conditions on the amination reaction of boranes with **5**; solvent thf unless otherwise stated.

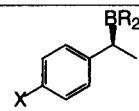
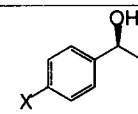
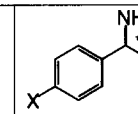
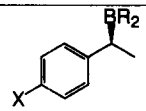
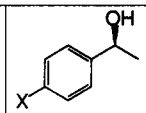
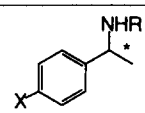
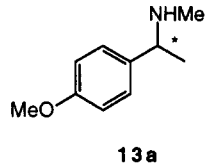
Entry	 (mmol)	MeNHOSiMe$_3$ (mmol)	Reagent (mmol)	 Yield (%)	 Yield (%)
1	X=OMe, (1.0)	1.0	KH,(0.9)	X=OMe, (42)	-
2	X=OMe, (1.0)	2.0	MeMgCl, (1.8)	X=OMe, (31)	X=OMe,(33)
3	X=Cl, (1.0)	2.0	MeMgCl, (1.8)	X=Cl, (24)	X=Cl,(24)
4	X=OMe, (1.0)	2.0	BuLi, (1.8)	X=OMe, (33)	X=OMe,(33)
			Solvent [all as entry **2,3**]		
5	X=OMe, (1.0)	2.0	thf:Et_2O = 1:1	X=OMe, (30)	X=OMe, (21)
6	X=OMe, (1.0)	2.0	^{t}BuOMe	X=OMe, (27)	X=OMe, (21)
7	X=OMe, (1.0)	2.0	Et_2O	X=OMe, (33)	X=OMe, (33)
8	X=Cl, (1.0)	2.0	Pentane	X=Cl, (45)	-
9	X=Cl, (1.0)	2.0	PhMe	X=Cl, (41)	X=Cl, (9)

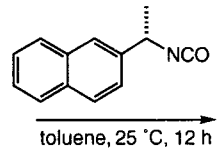
Table 3. Effect of reagent on the amination of boranes **13a** and **13b**. Reagents **5b** and **8b** were commercially available.

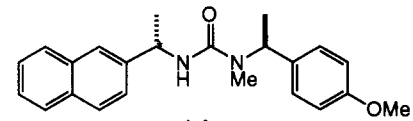
Entry	 (mmol)	$R^1NHOSiMe_2R^2$ Aminating Agent R^1, R^2, (mmol)	MeMgCl (mmol)	 Yield (%)	 Yield (%)
1	X=OMe, (0.50)	H, Me, (0.55) **5b**	0.45	X=OMe, (49)	-
2	X=Cl, (0.50)	H, Me, (0.55) **5b**	0.45	X=Cl, (45)	-
3	X=OMe, (0.5)	H, ^{t}Bu, (0.55) **8b**	0.45	X=OMe, (28)	X=OMe, (5)
4	X=Cl, (0.5)	H, ^{t}Bu, (0.55) **8b**	0.45	X=Cl, (26)	X=Cl, (6)
5	X=OMe, (1.0)	Me, ^{t}Bu, (1.0) **8a**	0.9	X=OMe, (21)	X=OMe, (25)
6	X=Cl, (1.0)	Me, ^{t}Bu, (1.0) **8a**	0.9	X=Cl, (28)	X=Cl, (31)
7	X=Cl, (1.0)	$PhCH_2$, Me, (1.2) **7**	1.2	X=Cl, (43)	-
8	X=OMe, (0.5)	^{t}Bu, Me, (1.2) **6**	0.9	X=OMe, (40)	-
9	X=Cl, (1.0)	^{t}Bu, Me, (1.2) **6**	1.15	X=Cl, (59)	-
10	X=OMe, (0.5)	2 $SiMe_3$ (1.0) **9**	0.9	X=OMe, (33)	-

Of all the modified reagents, the only ones which gave significant quantities of the amination product were the TBDMS ethers **8a** and **8b**, the latter being the only reagent where the product was biased in favour of the amine rather than the alcohol. For the rest, varying yields of secondary alcohol were obtained. Even the bis-TMS ether of hydrazine gave only alcohol after aqueous work-up, with no evidence for C-N bond formation. Finally the O-mesylate **11**, in the presence of DBU, gave amine as the predominant product but in very low isolated yield. It appeared that there was an intrinsic tendency to afford the product of boron migration to O in competition with boron migration to N, the former produced either concurrently or during aqueous workup when peroxidic species would be present.

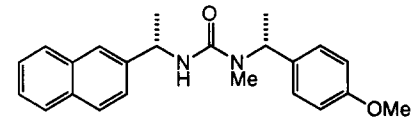


13a





14

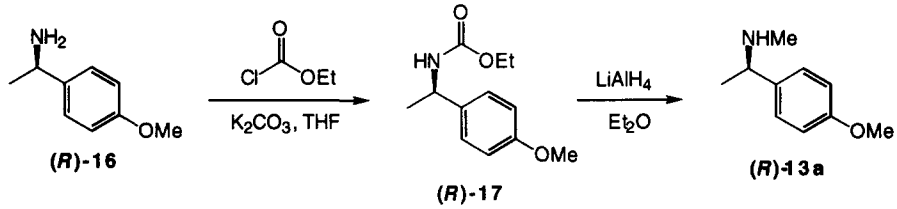


15

In several cases the enantiomer excess of the amine was measured by reaction with (*S*)-β-naphthylethyl isocyanate overnight to give the urea diastereomers **14** and **15** as a clear, colourless oil in 52-90% yield. In the ^{1}H NMR at 300MHz, the NCH_3 , OCH_3 (for the 4-OMe series) and $ArCHCH_3$ protons were distinct. For the amination of 4-methoxyphenylboronic ester **3a** using $MeNHOSiMe_3$ **5** and BuLi, the enantiomeric excess of the

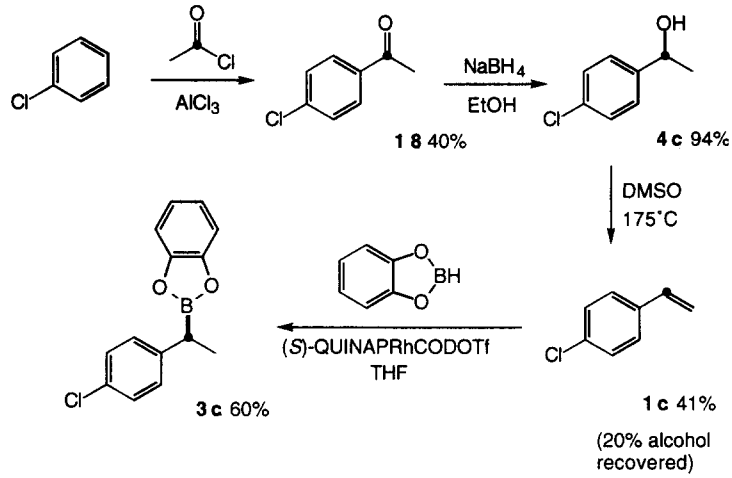
amine **13a** was found to be 88%. The absolute configuration was demonstrated to be *(S)*, like the corresponding hydroboration-derived alcohol **4a**, by synthesis of an authentic sample. Following the procedure of Ollis *et. al.*[16], amine **16** was resolved using (+)-tartaric acid and the amine *(R)*-**16** was obtained in 76% e.e. The specific rotation was $[\alpha]_D^{26}$ = + 27.4 (neat), in accord with the literature value of $[\alpha]_D^{26}$ = +36.0 for an enantiomerically pure sample of the *(R)*-amine. The resolved amine was then methylated following the procedure by Mariano[17], by conversion to the carbamate *(R)*-**17** by reaction with ethyl chloroformate and then reduction using lithium aluminium hydride to *(R)*-**13a.** The specific rotation was $[\alpha]_D^{23}$ = + 56.7 (neat). The sign of the rotation was in agreement with the literature value for an enantiomerically pure sample of the amine *(S)*-**13a**[18], but the value differed almost by a factor of ten and hence it appears that the intended value should be $[\alpha]_D^{26}$ = –68.4 and not $[\alpha]_D^{26}$ = –6.84 as reported. Comparison of the e.e.'s measured for the amine **13a** from different experiments shows that the aminations occurred with complete retention of configuration, irrespective of which base was used. Also, using the more substituted aminating agent **8** resulted in formation of 1-(4'-methoxyphenyl)-*N*-methylethylamine **5** without loss of enantioselectivity. Some configurational loss was observed for the alcohol component, formed in 40% e.e. - in contrast to the direct reaction of the boronic ester **3a** with basic hydrogen peroxide which gave 83% e.e. Finally, the enantiomeric excess of 1-aminoindane from amination of the indeneboronic ester was 68%.

It was confirmed that the same result as recorded above was observed in a one-pot reaction - a 1:1 mixture of amine and alcohol was obtained when hydroboration of 4-methoxystyrene was carried out in thf, and the borane reacted directly with an equivalent of hydroxylamine **5a** which had been pretreated with MeMgCl.



NMR Studies of the Amination Reaction

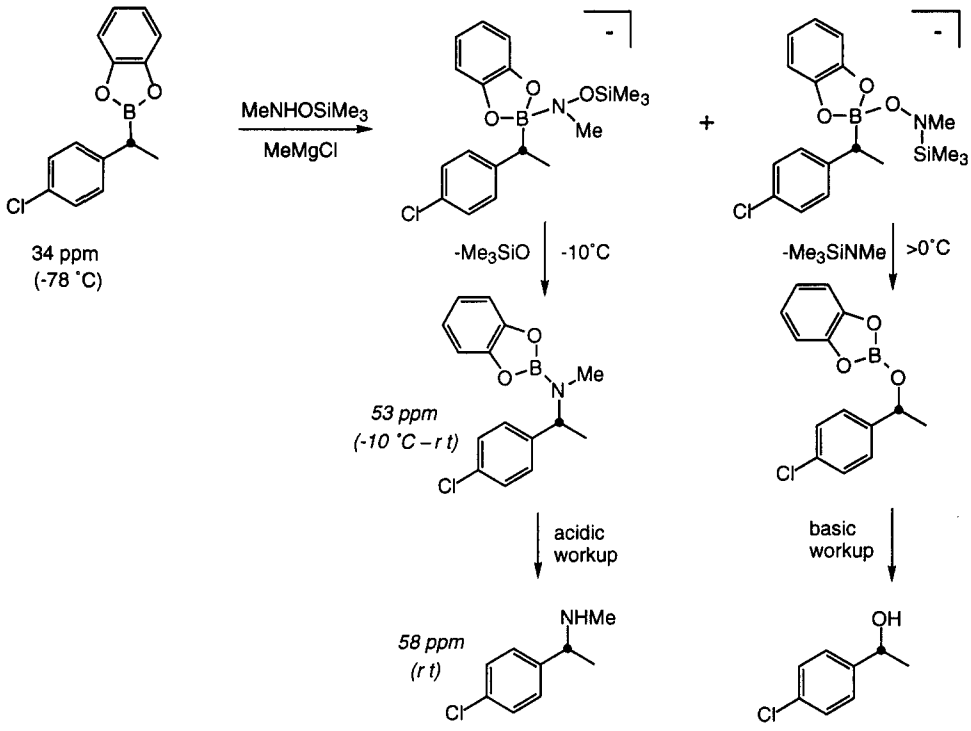
Synthesis of a ^{13}C labelled borane was carried out in an attempt to discover the reasons for the lack of chemoselectivity in the amination process.Beginning with 2 g of ^{13}C-1-acetic acid, reaction with thionyl chloride at 70°C for 2 h allowed the formation of ^{13}C-1-acetyl chloride which distilled off as a clear, colourless liquid. This was immediately used in the Friedel Crafts acylation[19] of chlorobenzene catalysed by aluminium trichloride which gave ^{13}C-1-4'-chloroacetophenone **18** in 40% yield based on the ^{13}C acetic acid, reduced with sodium borohydride in ethanol to give the alcohol **19** (94%). The ^{13}C NMR spectrum showed a peak at 69.5 ppm corresponding to C1. After many trial reactions dehydration was carried out using DMSO at 175 °C.[20] The reaction time was a critical factor, 15 h giving the best balance between conversion and polymerisation. But ^1H NMR showed the reaction to be only 50% complete and purification by column chromatography on neutral Al_2O_3 gave ^{13}C-1-(4'-chloro)styrene **1b** as a colourless liquid in 41% yield, and also permitted recovery of unreacted alcohol (20%). The ^{13}C NMR spectrum of (1-^{13}C)-**1b** showed a peak at 135.7 ppm corresponding to C1. Following the procedure described above for the unlabelled compound, (1-^{13}C)-**3b** was prepared as a colourless oil in 60% yield. The C-1 resonance at 24.7 ppm was considerably broadened by the quadrupole of the adjacent boron nucleus.



Scheme 3. Synthesis of 1-^{13}C-labelled borane **3b**.

It was hoped that further information would be obtained on monitoring the amination of the labelled boronic ester by ^{13}C NMR. Thus the silylhydroxylamine **5a** was dissolved in thf at -78 °C in an 8 mm NMR tube and a spectrum obtained which showed two resonances at 41 and -2 ppm, due to the NMe and $SiMe_3$ carbons respectively. The Grignard reagent was added and this was consumed immediately since the peak at -18 ppm, corresponding to MeMgCl, was absent. There was little or no change in the chemical shift of the methyl carbons of the aminating agent, however. Still at -78°C, addition of the labelled boronic ester resulted in a large number of broad resonances in the ^{13}C spectrum between 25 and 40 ppm, corresponding to various labelled species . The high field shift and broadening of the peaks indicated that the ^{13}C-enriched atom was still bonded to boron. At -10°C, a sharp peak at 53 ppm appeared and grew further as the temperature was increased to 25 °C to become the largest signal. A number of smaller peaks between 40 ppm and 60 ppm were also present. The shift and absence of broadening suggested that the ^{13}C labelled carbon was now bonded to nitrogen. Furthermore, the appearance of this peak coincided with the observation of a new resonance at 27 ppm in the ^{11}B NMR spectra, which was also associated with amination. A non-aqueous workup procedure was performed since the ^{11}B VT NMR study had suggested that the alcohol was being formed during the workup and it was hoped that the absence of water would prevent this. This was indeed correct and the addition of glacial acetic acid caused all the resonances between 40 and 60 ppm to disappear and a new peak at 58 ppm to appear. The latter shift coincided with that of the C-1 carbon of the amine, within experimental error. The series of broad peaks between 25 and 40 ppm were still present at this stage although the alcohol, whose C-1 carbon resonates at 69 ppm, was not observed. Further, it was possible to obtain amine free from alcohol, albeit in low yield. On proceeding to "normal" workup conditions of aqueous base, the expected mixture of amine and alcohol was formed. These results indicate that the reaction proceeds as indicated in Scheme 4. An irreversible but unselective addition of nucleophile to the boron centre (possibly accompanied by ring-opening of the catecholborane entity) gives a pair of intermediates, one of which will proceed to form amidoboronate and the other to form boronate ester. The rearrangement to form amidoboronate proceeds at a significantly lower temperature than does the rearrangement involving migration to oxygen. Despite this, efforts to form the amine selectively are defeated by the intrinsic lack of specificity of the initial step.

In conclusion, this work demonstrates the feasibility of converting catecholboronate esters into amines with retention of configuration. The synthetic utility is compromised by competitive formation of the corresponding alcohol and despite extensive efforts, this could not be averted. It is fortunate that the problem has been solved by a related approach which relies on the prior transformation of catecholboronate esters into trialkylboranes.[4]



Scheme 4. Observations of borane amination by ^{13}C NMR. In the intermediates the catechol may be part dissociated from boron.

Acknowledgments.

We thank LINK Asymmetric Synthesis and Zeneca plc for a Studentship in support of FIK, and the EC Human Capital and Mobility programme for a Network Grant (CTRX-009267) which enabled DL to visit Oxford. Johnson-Matthey provided a helpful loan of Rh salts.

Experimental.

General: NMR spectra were recorded on Varian Gemini 200, Brüker AC 200, AM250, WH 300 and AM500 spectrometers. Combustion analyses were carried out by Mrs V. Lamburn in the Dyson Perrins Laboratory. Mass spectra were obtained by Drs R Proctor and R Aplin within the department. I.r. spectra were recorded on a Perkin Elmer PE 1750 Fourier Transform spectrophotometer. UV Spectra were recorded on a Perkin Elmer Lambda 2 spectrometer Specific rotations were measured on a Perkin Elmer PE 241 polarimeter using a thermostatically jacketed cell. Melting points were recorded on a Reichert-Koffler block and are uncorrected.

Chiral capillary gas chromatography was carried out on a Fisons 8000 series machine using a 25m permethylated β-cyclodextrin in a BP10 stationary phase (Cydex-B™) column.
Bis-Trimethylsilylhydrazine **10**[15], *N*-methyl-*O*-trimethylsilylhydroxylamine **5**[13], *N,O-Bis*-trimethylsilylhydroxyl amine **9**[14], 1-(4-Chlorophenyl)-*N*-methylethylamine **13c**, 1-(4-Methoxyphenyl)-*N*-methylethylamine **13a**, 1-(4-methoxy)-phenylethylamine **16** and *(R)*- *N*-methyl- 1-(4-Methoxyphenyl)ethylamine *(R)*-**13a**[16,17] were prepared directly or by simple adaptation of literature procedures.

(S)-1-(4-Methoxyphenyl)ethyl-1,3,2-benzodioxaborole 3a

Following previous protocols, cycloocta-1,5-diene[*(S)*-1-(2-diphenylphosphino-1-naphthyl)isoquinoline] rhodium(I) trifluoromethanesulphonate **2** (16 mg, 0.02 mmol, 0.1 mol%) was placed in a Schlenk tube and backfilled with Ar. Dry, deoxygenated THF (15 ml) was added, followed by 4-methoxystyrene (3.00 g, 22.4 mmol). Catecholborane (2.10 ml, 22.4 mmol) was added dropwise with stirring and the solution was stirred for 1 h at rt. The solvent was removed *in vacuo* and the residue was purified by short path distillation producing **3a** as a colourless oil (4.26 g, 75%), b.p. 90° C (0.05 mm Hg); (Found: C, 70.98; H, 5.95. $C_{15}H_{15}O_3$ requires C, 70.90; H, 5.95%); υ_{max} (thin film) 2962, 1511, 1472, 1337 (B-O), 806 and 745; δ_H (300 MHz; $CDCl_3$) 7.35 (2H, d, *J* 8.6 Hz, Ar-H), 6.98 (2H, d, *J* 8.6 Hz, Ar-H), 7.30 (2H, m, Ar-H), 7.09 (2H, m, Ar-H), 3.86 (3H, s OCH_3), 3.03 (1H, q, *J* 7.4 Hz, C*H*CH_3) and 1.68 (3H, d, *J* 7.7 Hz, CHC*H*$_3$); δ_C (50 MHz; $CDCl_3$) 157.9 (C4), 148.3 (C1') , 135.4 (C1), 128.8 (C2 or C3), 122.7 (C2 or C3), 114.1 (C2'), 112.4 (C3'), 55.0 (OCH_3) and 16.0 (CH*C*H_3); δ_B (80 MHz; thf) 34.3 (br, s); *m/z* EI$^+$ 254 (M^+, 70%) and 239 (100). Similarly the enantiomer was prepared from cycloocta-1,5-diene[*(R)*-1-(2-diphenylphosphino-1-naphthyl)isoquinoline] rhodium(I)trifluoromethanesulphonate. **3a** (50 µl, 0.248 mmol) was syringed into a Schlenk tube filled with Ar. Dry, deoxygenated thf (0.5 ml) was added, followed by EtOH (0.5 ml), 1M KOH (aq) (0.5 ml) and H_2O_2 (aq) (0.5 ml, 30% solution). The solution was stirred for 1 h at rt, then extracted with Et_2O (3 × 2 ml). The organic layer was washed with 1M NaOH (aq) (2 × 2 ml), H_2O (2 ml) and brine (2 ml) and dried ($MgSO_4$). The solvent was removed *in vacuo* to give **4a** as a clear, colourless oil (28.7 mg, 73%). The e.e. of the alcohol, measured using a β-cyclodextrin chiral capillary g.c. column at 110 °C, was 86%, δ_H (300 MHz; $CDCl_3$) 7.29 (2H, d, J 8.6 Hz, Ar-H), 6.88 (2H, d, J 8.6 Hz, Ar-H), 4.81 (1H, q, *J* 6.4 Hz, C*H*CH_3), 3.77 (3H, s, OCH_3) and 1.45 (3H, d, *J* 6.4 Hz, CHC*H*$_3$); t_x : 67.97 and 73.68.

(S)-1-(4-Chlorophenyl)ethyl-1,3,2-benzodioxaborole 3c

Compound **3c** was similarly prepared from **2** (16 mg, 0.02 mmol, 0.2 mol%), 4-chlorostyrene (0.78 ml, 10.0 mmol) and catecholborane (0.70 ml, 10.0 mmol) and purified by short path distillation to give a clear, colourless oil (1.41 g, 84%), b.p. 190 °C (0.05 mm Hg); (Found: C, 65.27; H, 4.98; N, 9.04. $C_{14}H_{12}BO_2$ requires C, 65.05; H, 4.68%); δ_H (200 MHz; $CDCl_3$) 7.32 (4H, br, d, *J* 3.5 Hz, H2 and H3), 7.18 (4H, m, H2' and H3'), 3.01 (1H, q, *J* 7.5 Hz, C*H*CH_3) and 1.63 (3H, d, *J* 7.6 Hz, CHC*H*$_3$); δ_C (50 MHz; $CDCl_3$) 148.0 (C1'), 141.7 (C4), 131.5 (C1), 129.2 (C2 or C3), 128.7 (C2 or C3), 122.7 (C2'), 112.4 (C3') and 16.7 (CH*C*H_3); δ_B (80 MHz; thf) 34.5 (br, s); *m/z* EI$^+$ 258 (M^+, 70%), 223 (100, M^+-Cl) and 104 (80). Following the above procedure, for e.e. analysis **3c** (50 µl, 0.248 mmol) gave *(S)*-1-(4-Chlorophenyl)ethanol **213** (14 mg, 36%). The e.e., measured using a β-cyclodextrin chiral capillary g.c. column at 120° C, was 62%, δ_H (300 MHz; $CDCl_3$) 7.29 (4H, s, Ar-H), 4.84 (1H, q, *J* 6.6 Hz, C*H*CH_3), 2.4 (1H, br, OH) and 1.45 (3H, d, *J* 6.7 Hz, CHC*H*$_3$); t_x : 40.69 and 43.15.

(S)-1-(1-Indanyl)-1,3,2-benzodioxaborole 12

Compound **12** was similarly prepared from **2** (10 mg, 0.013 mmol, 0.1 mol%), indene (1.49 g, 12.9 mmol) and catecholborane (1.54 g, 12.9 mmol) and purified by short path distillation to give a colourless oil/gum (1.49 g, 49%), b.p. 220 °C (0.04 mm Hg); δ_H (200 MHz; $CDCl_3$) 7.27 (8H, m), 3.35 (1H, t, *J* 9.0 Hz, CHB), 3.13 (2H, dt, *J* 7.5 and 3.1 Hz, CH_2CH_2CHB) and 2.49 (2H, m, CH_2CHB); δ_C (50 MHz; $CDCl_3$) 148.5 (C1'), 144.3 and 143.8 (Ar-C), 126.5 (CH), 126.4 (CH), 124.9 (CH), 124.8 (CH), 122.9 (C2'), 112.7 (C3'), 33.1 (CH_2CHB) and 27.9 (CH_2CH_2CHB); δ_B (80 MHz; thf) 34.7 (br, s); *m/z* EI$^+$ 236 (M^+, 100%), 136 (40), 115 (100) and 91 (75). Following the above procedure for e.e. determination from **12** (50 µl, 0.248 mmol) gave (*S*)-1-indanol (13 mg, 39%). The e.e., measured by chiral shift NMR with Eu(hfc)$_3$, was 68%, δ_H (200 MHz; $CDCl_3$) 7.41 (1H, m, Ar-H), 7.26 (3H, m, Ar-H), 5.24 (1H, t, *J* 6 Hz, CHOH), 3.08 (1H, m), 2.82 (1H, m), 2.44 (1H, m) and 1.96 (1H, m).

General method of amination using *N*-methyl-*O*-trimethylsilyl-hydroxylamine 5

N-Methyl-*O*-trimethylsilylhydroxylamine **5** (270 µl, 1.78 mmol) and dry, deoxygenated thf (1 ml) were placed in a Schlenk tube at -78 °C. MeMgCl (593 µl, 1.61 mmol, 3M solution in thf) was added dropwise with stirring, followed by (*S*)-1-(4-methoxyphenyl)ethyl-1,3,2-benzodioxaborole **3a** (200 µl, 0.89 mmol) in thf (0.5 ml). The reaction solution was warmed to -20 °C and stirred for 1h, then allowed to warm to rt. 1M KOH (aq) (1 ml) was added, the solution was stirred for 5 min, then extracted with CH_2Cl_2 (3 × 5 ml). The organic layers were dried (Na_2SO_4) and the solvent was removed *in vacuo* to give a brown oil, which contained a mixture of compounds **4a** and **13a**. These were separated by dissolving the oil in 1M HCl (aq) (5 ml) and extracting the alcohol with Et_2O (3 x 5 ml). The acid layer was then basified to pH 2 with 1M KOH (aq) (6 ml) and extracted with CH_2Cl_2 (3 × 5 ml). The CH_2Cl_2 layer was dried (Na_2SO_4) and the solvent was removed *in vacuo* to give product as a yellow oil. The Et_2O layer was washed with 1M NaOH (aq) (3 × 5 ml) and H_2O (1 × 5 ml) to remove catechol, then dried (Na_2SO_4) and the solvent was removed *in vacuo* to give **13a** as an orange oil.

***N*-^{t}Butyl-*O*-trimethylsilylhydroxylamine 6**

Following the procedure described for **5** reaction of *N*-^{t}butylhydroxylamine hydrochloride (1.09 g, 8.71 mmol), imidazole (1.19 g, 17.4 mmol) and chlorotrimethylsilane (1.11 ml, 8.71 mmol) in pentane (8 ml) followed by short path distillation, produced **6** as a colourless liquid (0.574 g, 47%), b.p. 58 °C (50 mm Hg); (Found: M^++1, 162.13. $C_7H_{20}NOSi$ requires M^++1, 162.13); ν_{max} (thin film) 3238 (br, NH), 2960 (s), 1250 (s), 884 (s) and 842 (s); δ_H (300 MHz; $CDCl_3$) 4.56 (1H, br, NH), 1.06 (9H, s, $C(CH_3)_3$) and 0.12 (9H, s, $Si(CH_3)_3$); δ_C (50 MHz; $CDCl_3$) 55.2 ($C(CH_3)_3$), 26.5 ($C(CH_3)_3$) and -0.9 ($Si(CH_3)_3$); *m/z* CI$^+$ 162 (M^++1, 100%), 146 (20, M^+-CH_3) and 74 (50).

***N*-Benzyl-*O*-trimethylsilylhydroxylamine 7**

Following the procedure for *N*-Methyl-*O*-^{t}butyldimethylsilylhydroxylamine, reaction of *N*-benzylhydroxylamine hydrochloride (0.772 g, 4.84 mmol), imidazole (0.724 g, 10.6 mmol) and chlorotrimethylsilane (0.613 ml, 4.83 mmol) in pentane (0.5 ml), gave **7** as a clear, colourless liquid (0.872 g, 92%), (Found: M^++1, 196.12. $C_{10}H_{18}NOSi$ requires M^++1, 196.12); ν_{max} (thin film) 3255 (br, m, NH), 2958 (s), 1497 (m), 1455 (m), 1417 (m), 1249 (s), 1034 (m), 882 (s) and 842 (s); δ_H (200 MHz; $CDCl_3$) 7.33 (5H, m, C_6H_5), 5.25 (1H, br, NH), 4.02 (2H, br, CH_2Ph) and 0.12 (9H, s, $Si(CH_3)_3$); δ_C (63 MHz; $CDCl_3$) 137.0 (C1), 129.2 (C2 or C3), 128.2 (C2 or C3), 127.4 (C4), 58.7 (CH_2Ph) and -1.1 ($Si(CH_3)_3$); *m/z* CI$^+$ 196 (M^++1, 100%) and 91 (30).

N-Methyl-*O*-^{t}butyldimethylsilylhydroxylamine 8

Dry *N*-methylhydroxylamine hydrochloride (2.71 g, 32.0 mmol) was placed in a Schlenk tube with pentane (10 ml) and imidazole (6.62 g, 97.0 mmol) and the mixture was stirred for 12 h under Ar. ^{t}Butyldimethylsilyl chloride (3.52 g, 32.0 mmol) was added and the mixture stirred for a further 72 h. The solution was filtered and the solvent was removed *in vacuo* to give **8** as a clear, colourless liquid (2.60 g, 50%), (Found: M^++1, 162.13. $C_7H_{20}NOSi$ requires M^++1, 162.13); ν_{max} (thin film) 3400 (br, m, NH), 3273, 2956, 2931, 2896, 2858, 1473, 1254, 873, 838 and 780; δ_H (300 MHz; $CDCl_3$) 5.11 (1H, br, NH), 2.71 (3H, s, NCH_3), 0.92 (9H, s, $SiC(CH_3)_3$) and 0.11 (6H, s, $Si(CH_3)_2$); δ_C (63 MHz; $CDCl_3$) 41.5 (NCH_3), 26.1 ($SiC(CH_3)_3$) and -5.8 ($Si(CH_3)_2$); *m/z* CI$^+$ 162 (M^++1, 100%), 121 (10) and 104 (15).

In situ hydroboration - amination

Complex **2** (4.0 mg, 0.005 mmol, 1.0 mol%) and dry, deoxygenated thf (0.5 ml) were placed in an ampoule which was backfilled with Ar. 4-methoxystyrene (66 µl, 0.50 mmol) and catecholborane (53 µl, 0.50 mmol) were added and the solution was whirlimixed then left for 10 min, during which time the solution turned brown. *N*-methyl-*O*-trimethylsilylhydroxylamine (150 µl, 1.0 mmol) and thf (0.5 ml) were placed in a Schlenk tube and cooled to -78 °C. MeMgCl (298 µl, 0.9 mmol, 3.0 M solution in thf, ml, mmol) was added and the solution whirlimixed. The hydroboration solution was also cooled to -78 °C and added to the Schlenk tube, which was then warmed to -20 °C and stirred for 1 h. After warming to rt, the usual workup afforded 4'-methoxy-*N*-methyl-1-phenylethylamine **13a** (21 mg, 25%) and 4'-methoxy-1-phenylethanol **4a** (23 mg, 30%).

(*R*,*S*)- and (*S*,*S*)-1-[(1-Naphthyl)ethyl]-3-[4'-methoxy-*N*-methyl-α-methylbenzyl]urea

Following a prior procedure,[21] reaction of (*S*)-1-(1-naphthyl)ethylisocyanate (12.0 mg, 0.061 mmol) and racemic 1-(4-Methoxyphenyl)-*N*-methylethylamine **13a** (11 mg, 0.061 mmol), followed by purification by preparative tlc (Al_2O_3, pentane – Et_2O, 1 : 1) gave **14** and **15** together as a colourless oil (11 mg, 52%), (Found: C, 76.38; H, 6.87; N, 7.54. $C_{23}H_{26}N_2O_2$ requires C, 76.21; H, 7.23; N, 7.73%); ν_{max} (thin film) 3342 (br, s, NH), 3049 (s), 2793 (s) and 1620 (s, C=O); δ_H (500 MHz; $CDCl_3$) 8.22 (2H, d, *J* 8.5 Hz, Ar-H), 7.87 (2H, d, *J* 6.7 Hz, Ar-H), 7.79 (2H, d, *J* 7.9 Hz, Ar-H), 7.56 (2H, t, *J* 7.1 Hz, Ar-H), 7.48 (6H, m, Ar-H), 7.22 (2H, d, *J* 14.0 Hz, Ar-H), 7.20 (2H, d, *J* 13.9 Hz, Ar-H), 6.86 (2H, d, *J* 8.7 Hz, Ar-H), 6.83 (2H, d, *J* 8.7 Hz, Ar-H), 5.90 (2H, m, C*H*NH), 5.62 (2H, m, C*H*NCH_3), 4.63 (2H, m, NH), 3.81 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 2.54 (3H, s, NCH_3), 2.53 (3H, s, NCH_3), 1.68 (6H, d, overlap, *J* 6.7 Hz, $NHCHCH_3$), 1.49 (3H, d, *J* 7.0 Hz, NCH_3CHCH_3) and 1.46 (3H, d, *J* 7.0 Hz, NCH_3CHCH_3); δ_C (126 MHz; $CDCl_3$) 158.6 (Ar-C), 157.4 (Ar-C), 139.8 (Ar-C), 134.0 (Ar-C), 133.7 (Ar-C), 131.2 (Ar-C), 128.7 (CH), 128.2 (CH), 128.0 (CH), 126.3 (CH), 125.7 (CH), 125.2 (CH), 123.8 (CH), 122.2 (CH), 113.7 (CH), 55.2 (*C*HNH), 51.6 (*C*HNCH_3), 46.1 (OCH_3), 28.6 (NCH_3), 21.8 ($NHCHCH_3$) and 16.7 (NCH_3CHCH_3); *m/z* CI$^+$ 363 (M^++1, 70%), 229 (50), 135 (100).

Measurement of the E.e. of 1-(4-Methoxyphenyl)-*N*-methylethylamine from aminations

Following the general procedure, 1-(4-Methoxyphenyl)-*N*-methylethylamine **13a** from the amination experiment was reacted to give urea **14** + **15**, which was used without any purification. The e.e. was measured by integration of the 500 MHz ^{1}H NMR spectrum OCH_3, NCH_3 and $NHCHCH_3$ signals.

Resolution of 1-(4-Methoxyphenyl)ethylamine 16

Following the procedure by Ollis *et. al.*[16], using 4'-methoxy-1-phenylethylamine **16** (8.00 g, 0.053 mol) and (+)-tartaric acid (7.84 g, 0.054 mol) in MeOH (100 ml), gave *(R)*-4'-methoxy-1-phenylethylamine ***(R)*-16** (1.60 g, 20%), $[\alpha]_D^{26}$ +27.4 (neat), 76% e.e. (lit. value $[\alpha]_D^{26}$ +36.0 (neat), 100% e.e.).

***N*-Methylation of *(R)*-1-(4-Methoxyphenyl)ethylamine 16**

Following the procedure by Mariano[17], using (*R*)-4'-methoxy-1-phenylethylamine ***(R)*-16** (1.44 g, 9.50 mmol), ethyl chloroformate (1.32 ml, 1.50 g, 14.3 mmol) and K_2CO_3 (6.23 g, 0.046 mmol) in thf (9 ml), gave ***(R)*-17** (1.98 g, 94%) which was reduced with $LiAlH_4$ (0.614 g, 15.7 mmol) in Et_2O (20 ml) at 0 °C then the reaction was warmed to rt and stirred for 24 h to give ***(R)*-13a** (1.24 g, 84%), $[\alpha]_D^{23}$ +56.7 (neat), 76% e.e. (lit. value $[\alpha]_D^{26}$ -6.8 (neat)[see text].

^{13}C-1-(4-chloro)acetophenone 18

^{13}C-1-acetic acid (1.00 g, 16.4 mmol) and thionyl chloride (2.13 ml, 24.6 mmol) were placed in a flask equipped for distillation and flushed with argon. The mixture was heated to 70°C for 2 h, during which time ^{13}C-1-acetyl chloride distilled off as a clear, colourless liquid. The flask was then fitted to a reflux condenser with drying tube and chlorobenzene (2.00 ml, 19.7 mmol) and CH_2Cl_2 (2 ml) were added. $AlCl_3$ (2.62 g, 19.7 mmol) was added in 3 portions over a period of 30 min. The solution was then stirred at 100 °C for 20 min. The contents of the flask were then poured on to ice and the resulting solution basified with 1M NaOH to pH>7. The product was extracted with Et_2O, dried ($MgSO_4$) and the solvent removed *in vacuo* to yield **18** as an orange oil (1.03 g, 40%), Found: C, 62.35; H, 4.30. $C_{15}H_{15}O_3$ requires C, 62.39; H, 4.53%); ν_{max} (thin film) 1651 (s, C=O), 1588 (s), 1357 (m), 1244 (s) and 1094 (s); δ_H (300 MHz; $CDCl_3$) 7.90 (2H, dd, *J* 8.6 and 3.7 Hz, H2), 7.42 (2H, d, *J* 8.6 Hz, H3) and 2.58 (3H, d, *J* 6.1 Hz, CH_3); δ_C (63 MHz; $CDCl_3$) 197.3 (CO), 139.8 (C4), 127.4 (C4), 135.6 (d, *J* 53 Hz, C1) and 129.9 (C2 or C3), 129.0 (C2 or C3) and 26.5 (d, *J* 43 Hz, $COCH_3$); *m/z* CI$^+$ 173 (20, M^++NH_3), 155 (M^++1, 30%) and 140 (100, M^+-CH_3).

^{13}C-1-(4-Chlorophenyl)ethanol 4c

^{13}C-1-(4-chloro)acetophenone **18** (0.998 g, 6.61 mmol) was dissolved in EtOH (5 ml) and sodium borohydride (0.275 g, 7.27 mmol) added over 15 min. The suspension was stirred for a further 30 min then poured on to excess ice. The solution was acidified to pH 2 using 1M HCl and then extracted with Et_2O (2 × 10 ml). The organic layer was then dried ($MgSO_4$) and the solvent removed *in vacuo* to give **4c** as an orange oil (0.950 g, 94%), (Found: C, 61.36; H, 6.04. C_8H_9ClO requires C, 61.60; H, 5.76%); ν_{max} (thin film) 3339 (br, s, OH), 2974 (s), 1493 (s), 1094 (s), 1078 (s), 1015 (s) and 829 (s); δ_H (200 MHz; $CDCl_3$) 7.32 (4H, s, C_6H_4), 4.89 (1H, dq, *J* 143.8 and 6.4 Hz, C*H*OH), 2.18 (1H, br, OH) and 1.48 (3H, dd, *J* 6.3 and 4.5 Hz, CH_3); δ_C (50 MHz; $CDCl_3$) 144.2 (d, *J* 47.3 Hz, C1), 132.9 (C4), 128.5 (d, *J* 4.0 Hz, C2 or C3), 126.8 (d, *J* 2.8 Hz, C2 or C3), 69.5 (CHOH) and 25.1 (d, *J* 38.2 Hz, CH_3); *m/z* CI$^+$ 159 (M^+, 40%), 157 (M^+, 100%) and 140 (40).

^{13}C-1-(4-chloro)styrene 1c

^{13}C-1-(4-Chlorophenyl)ethanol **4c** (0.950 g, 6.03 mmol) was placed in a flask with DMSO (5 ml) and heated to 175 °C for 15 h.[22] The solution was cooled, then extracted with pentane (3 × 5 ml) and the organic phase was washed with H_2O (3 × 5 ml) and brine (1 × 5 ml), then dried (Na_2SO_4). The solvent was removed *in vacuo* and

^{1}H NMR showed the reaction to be only 50% complete. Purification by flash column chromatography (neutral Al_2O_3, pentane) yielded **1c** as a clear, colourless liquid (0.346 g, 41 %), and allowed recovery of some of the unreacted alcohol (0.165 g, 20%). (Found: C, 69.55; H, 5.09. $C_{15}H_{15}O_3$ requires C, 69.55; H, 5.05%); ν_{max} (thin film) 1607 (m, C=C), 1490 (s), 1392 (m), 1091 (s), 1013 (m), 985 (m), 911 (m) and 833 (s); δ_H (500 MHz; C_6D_6) 7.03 (2H, d, *J* 8.5 Hz, 3-H), 6.88 (2H, dd, *J* 8.5 and 8.5 Hz, 2-H), 6.35 (1H, ddd, *J* 154.6, 17.6 and 10.9 Hz, H_a), 5.41 (1H, dd, *J* 17.5 and 3.0 Hz, H_c) and 4.99 (1H, d, *J* 10.9Hz, H_b); δ_C (126 MHz; $CDCl_3$) 146.3 (C4), 135.7 (C*), 128.7 (C2 or C3), 127.4 (C2 or C3), 127.5 (d, *J* 78.6 Hz, C1) and 114.4 (d, *J* 70.0 Hz, CH_2); *m/z* CI$^+$ 141 (M^+, 40%), 139 (M^+, 100%) and 104 (15, M^+-Cl).

^{13}C-1-(4-Chlorophenyl)ethyl-1,3,2-dioxaborole 3c

Following the procedure for the unlabelled compound, using ^{13}C-1-(4-chloro)styrene **1c** (567 mg, 4.06 mmol), **3c** was prepared as colourless oil (632 mg, 60%); δ_H (500 MHz; CD_2Cl_2) 7.31 (2H, s, 3-H), 7.30 (2H, d, *J* 3.5 Hz, 2-H), 7.23 (2H, m), 7.10 (2H, m), 3.00 (1H, dq, *J* 118.7 and 7.6 Hz, C*H) and 1.59 (3H, dd, *J* 7.6 and 3.8 Hz, C*HC*H*$_3$); δ_C (126 MHz; CD_2Cl_2) 148.5 (C4), 142.6 (d, *J* 39.9 Hz, C1), 131.7 (C1'), 129.7 (C2 or C3), 129.0 (C2 or C3), 123.2 (C2'), 112.8 (C3'), 24.7 (br, C*) and 16.9 (d, *J* 31.3 Hz, C*H$\underline{C}$H$_3$); *m/z* EI$^+$ 275 (M^++O_2, 15%), 140 (100) and 110 (60).

Amination of ^{13}C-1-(4-Chlorophenyl)ethyl-1,3,2-benzodioxaborole by ^{13}C NMR

N-Methyl-*O*-trimethylsilylhydroxylamine **5** (150 µl, 1.0 mmol) and dry, degassed thf (1.5 ml) were placed in an 8 mm NMR tube which had been previously backfilled with Ar. This was cooled to -78 °C and MeMgCl (298 µl, 0.9 mmol, 3.0 M solution in thf) was added. The solution was quickly whirlimixed, during which time CH_4 (20 ml) evolved. Keeping the sample at -78 °C, the ^{13}C NMR was obtained. ^{13}C-1-(4-Chlorophenyl)ethyl-1,3,2-dioxaborole **3c** (100 µl, 0.495 mmol) was added and again the ^{13}C NMR obtained. The solution was warmed to -10, 0, 10 and 25 °C and the ^{13}C NMR obtained at each temperature. Acetic acid (300 µl) and then H_2O (300 µl) was added, each time the solution was whirlimixed and the NMR obtained. This was followed by extraction into CH_2Cl_2 (2.0 ml) and then washing with 1M NaOH (aq) (1.0 ml), the ^{1}H NMR was obtained after both actions. The usual isolation procedure gave ^{13}C-1-(4-chlorophenyl)-*N*-methylethylamine (24 mg, 28%) and ^{13}C-1-(4-chlorophenyl)ethanol , (26 mg, 33%). ^{13}C-1-(4'-chlorophenyl)-*N*-methyl-1-ethylamine, δ_H (500 MHz; $CDCl_3$) 7.55 (2H, dd, *J* 8.5 and 6.7 Hz, 2-H), 7.42 (2H, d, *J* 8.5 Hz, 3-H), 4.13 (1H, dq, *J* 142.5 and 6.8 Hz, C*H), 2.45 (3H, d, *J* 3.9 Hz, NHC$\underline{H}_3$) and 1.82 (3H, dd, *J* 6.8 and 4.4 Hz, C*HC$\underline{H}_3$). δ_C (126 MHz; $CDCl_3$) 135.5 (C4), 134.3 (d, J 46.8 Hz, C1), 129.7 (C2 or C3), 129.3 (C2 or C3), 59.4 (C*), 31.7 (NHCH_3) and 20.1 (d, *J* 36.3 Hz, C*H$\underline{C}$H$_3$). *m/z* (CI$^+$) 173 (M^++1, 30%), 171 (M^++1, 100%), 157 (25) and 155 (80).

References

1. Brown, J. M.; Hulmes, D. I.; Layzell, T. P.*J. Chem. Soc., Chem. Commun.*, **1993**, 1673-1674; Valk, J. M.; Whitlock, G. A.; Layzell, T. P.; Brown, J. M. *Tetrahedron: Asymmetry* , **1995**, *6*, 2593-2596.
2. Schneyder, A.; Hintermann, L.; Togni, A., *Angew. Chem. Int. Ed.*, **1995**, *34*, 931; Wiesauer, C.; Weissensteiner, W. *Tetrahedron: Asymmetry* ,**1996**, *7*, 5-8; Hayashi, T.; Matsumoto Y.; Ito, Y.; *Tetrahedron : Asymmetry*, **1991**, *2*, 601; Burgess, K.; Ohlmeyer, M. J., *Chem. Rev.*, 1991, **91**, 1170.
3. Cassarini, A.; Dembech, P.; Lazzari, D.; Marini, E.; Reginato,G.; Ricci, A.; Seconi, G.*J. Org. Chem.*, **1993**, *58*, 5620, and refs. therein.
4. Fernandez, E; Hooper, M.W.; Knight, F. I.; Brown, J. M. *J.Chem. Soc. Chem. Commun.*, **1997**, 171.

5. Brown, H. C.; Heydkamp,W. R.; Breuer, E.; Murphy, W. S.*J. Am. Chem. Soc.*, **1964**, *86*, 3565.
6. Rathke, M. W.; Inoue, N.; Varma, K. R.; Brown, H. C. *J. Am. Chem. Soc.*, **1966**, *88*, 2870.
7. Kabalka, G. W.; Sastry, K. A. R.; McCollum, G. W.; Yoshioka, H. *J. Org. Chem.*, **1981**, *46*, 4296.
8. Brown, H. C.; Kim, K. W.; Cole, T. E.; Singaram, B.*J. Am. Chem. Soc.*, **1986**, *108*, 6761; Carboni B.; Vaultier, M. *Bull. Soc. Chim. Fr.* **1995**, *132*, 1003.
9. Brown, H. C.; Rangaishenvi, M. V.; Singaram, B. *J. Org. Chem.*, **1991**, *56*, 3286.
10. Matteson, D.S. *Acc. Chem. Res.* **1989**, *21*, 294.
11. Nowakowski, P.; West, R.*J. Am. Chem. Soc.*, **1976**, *98*, 5616; West, R.; Boudjouk, P.;. Matuszko, A. *J. Am. Chem. Soc.*, **1969**, *91*, 5184.
12 Smrekar, O.; Wannagat, U.*Monatsh. Chem.*, **1969**, *100*, 760.
13. Wannagat, U.; Smrekar, O. *Monatsh. Chem.*, **1969**, *100*, 750.
14. Wannagat, U.; Liehr, W.Z. *Anorg. Allg. Chem.*, **1958**, *297*, 129.
15. Tamura, Y.; Minamikawa, J.; Miki, Y.; Matsugashita, S.; Ikeda, M.*Tetrahedron Lett.*, **1972**, *40*, 4133
16. Ollis, W. D.; Rey, M.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans. I*, **1983**, 1009.
17. McQueney, M. S.; Lee, S.; W. H. Swartz, H. L. Ammon, P. S. Mariano and D. Dunaway-Mariano, *J. Org. Chem.*,1991, **56**, 7121.
18. Cervinka, O.; Fusek,J. *Coll. Czech. Chem. Comm.*, **1973**, *38*, 441.
19. For earlier Friedel-Crafts reactions with labelled acetyl chloride see : Smith, K. M.; Martynenko, Z.; Pandey, R. K.; Tabba, H. D. *J. Org. Chem* , **1983**, *48*, 4296-4302; Timm, U.; Merkle, U.; Meier, H. *Chem. Ber.*, **1980**, *113*, 2519-29; Xu, T.; Torres, P. D.; Beck, L. W.; Haw, J. F.*J. Am. Chem. Soc.*, **1995**, *117*, 8027-8.
20. Traynelis, V. J.; Hergenrother, W. L.; Livingston, J. R.; Valicenti, J. A.*J. Org. Chem.*, **1962**, *27*, 2377; Traynelis, V. J.; Hergenrother, W. L.; Hanson, H. T.; Valicenti, J. A.*J. Org. Chem.*, **1964**, *29*, 123.
21. Nabeya, A.; Endo, T.*J.Org.Chem.*, **1988**, *53*, 3358.

(*Received in UK* 12 *May* 1997; *accepted* 19 *June* 1997)