Substituted Monocarbon Carboranes Involving Thiol, Disulfide or Dimethyl Sulfide Ligands†

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New sulfur-substituted derivatives of *closo*- and *nido*-monocarbon carboranes have been synthesised for their potential application in ^{10}B neutron capture therapy of tumours. The compounds 7-Me_3N-4(6)-HS-*nido*-7-$CB_{10}H_{11}$ and 4,4′-, 6,6′- and 4,6′-S_2(7-Me_3N-*nido*-7-$CB_{10}H_{11}$)$_2$ were obtained by Friedel-Crafts substitution of 7-Me_3N-*nido*-7-$CB_{10}H_{12}$ with S_2Cl_2; high-temperature boron insertion and methylation of the products gave 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$ as a result of a cluster rearrangement process. Its structure has been confirmed by X-ray crystallography.

The synthesis of new boron compounds for application to the treatment of cancer through ^{10}B neutron capture therapy has become an urgent goal in the light of the resurgence of interest in this treatment.[1] The clinical success of Hatanaka,[2] who has treated over 100 patients suffering from glioma, with the disodium salt of undecahydromercaptododecaborate ion, $[^{10}B_{12}H_{11}(SH)]^{2-}$, has stimulated a search for other boron compounds which may have better tumour-localising properties.

The mechanisms by which $[B_{12}H_{11}(SH)]^{2-}$ or its oxidised derivative $[B_{12}H_{11}SSB_{12}H_{11}]^{4-}$ are transported through the blood stream and concentrated in tumour tissue are not understood, although plasma exchange has been observed in dogs,[3] and interactions with serum albumin has been observed by NMR spectroscopy.[4] Plasma proteins are probably responsible for its transportation through the body. Furthermore, the unsubstituted ion $[B_{12}H_{12}]^{2-}$ has little selective accumulation in tumours such as glioma, even though the blood–brain barrier is reduced in the region of the tumour. It is clear that although the nature of the interactions is uncertain, the thiol substituent is clearly implicated in the processes.

In a search for species with tumour-localising properties better than $[B_{12}H_{11}(SH)]^{2-}$, we have sought to synthesise thiol or disulfide derivatives of other stable boron clusters, in particular those of the monocarbon carboranes tridecahydro-7-carba-*nido*-undecaborate(1 –), [*nido*-7-$HCB_{10}H_{12}$]$^-$, and dodecahydro-1-carba-*closo*-dodecaborate(1 –), [*closo*-1-$HCB_{11}H_{11}$]$^-$. These are potentially useful species in that the carbon cluster atom increases the kinetic stability of the boron cluster, and simultaneously introduces a variety of substitution sites in the cluster the chemical properties of which still have to be explored. These clusters are still anionic and retain the possibility of aqueous solubility with appropriate cations.

Previous reactions to introduce thiol or disulfide substituents into boron cluster compounds have included the acid-catalysed nucleophilic thiolation of $[B_{12}H_{12}]^{2-}$ with *N*-methylthiopyrrolidone,[5] or of $[B_{10}H_{10}]^{2-}$ with tetramethylthiourea,[6] and the Friedel-Crafts reaction of 1,2-dicarbadodecaborane with S_2Cl_2.[7] It is the latter route which we found successful with monocarbon carboranes.

Experimental

Solvents and Intermediates.—Solvents were dried and purified by standard procedures. The compound 7-Me_3N-*nido*-7-$CB_{10}H_{12}$ was prepared by the literature method;[8] $Et_3N{\cdot}BH_3$ was purchased from Aldrich Chemical Co. and handled in a N_2-filled glove-box. All other reagents were used as received.

Spectra.—The NMR spectra were recorded on Bruker WM 250 and WH 360 spectrometers (^1H, 250 and 360; ^{11}B, 80.2 and 115.5 MHz) on solutions in CD_3CN. All chemical shifts were measured relative to the internal lock solvent and are quoted as positive to high frequency of the reference standards $SiMe_4$ or $Et_2O{\cdot}BF_3$. Mass spectra were obtained on an AEI MS9 mass spectrometer.

Preparation of 7-Me_3N-4(6)-HS-*nido*-7-$CB_{10}H_{11}$ *and* 4,4′-(6,6′ *and* 4,6′)-S_2(7-Me_3N-*nido*-7-$CB_{10}H_{11}$)$_2$.—Samples of 7-Me_3N-7-$CB_{10}H_{12}$ (0.5 g, 2.6 mmol) and $AlCl_3$ (0.347 g, 2.6 mmol) were suspended in dry CH_2Cl_2 (40 cm^3) in a two-necked round-bottomed flask (100 cm^3) fitted with a reflux condenser and dropping funnel, and flushed with dry nitrogen. The mixture was cooled to – 10 °C and a solution of S_2Cl_2 (0.176 g, 1.3 mmol) in CH_2Cl_2 (5 cm^3) added dropwise with stirring. The mixture was refluxed for 5 h until the starting carborane was no longer observed by thin-layer chromatography (TLC), cooled, and poured into water (100 cm^3). The yellow product **1** was filtered off, washed several times with water, and dried over NaOH. The organic layer was separated from the filtrate, washed with water, and evaporated *in vacuo* to give product **2** in low yield (*ca.* 5%). TLC of **1** on SiO_2, eluted with 10% MeCN–90% CH_2Cl_2, showed what appeared to be an isomer mixture in the approximate ratio 1:1:2, estimated from the chromatogram. The major isomer (R_f 0.43) was separated by column chromatography on SiO_2 to yield the disulfide (Found: C, 22.1; H, 8.9; N, 6.5; S, 14.1. $C_8H_{40}B_{20}N_2S_2$ requires C, 21.6; H, 9.1; N, 6.3; S, 14.4%). TLC of **2** on SiO_2, eluted with CH_2Cl_2, showed one major product (R_f 0.45) with some impurities. It was purified chromatographically on a column using SiO_2 to give 7-Me_3N-4(6)-HS-7-$CB_{10}H_{11}$ (Found: C, 21.6; H, 9.4; N, 6.2; S, 14.4. $C_4H_{21}B_{10}NS$ requires C, 21.5; H, 9.5; N, 6.3; S, 14.4%). The mass spectrum showed a group of ions with mass cut-off at *m*/*z* 225 corresponding to the ion $[^{11}B_{10}{}^{12}C_4{}^1H_{21}{}^{14}N^{32}S]^+$.

Reduction of Isomer Mixture S_2(7-Me_3N-7-$CB_{10}H_{11}$)$_2$ *by* $NaBH_4$.—To a suspension of an isomer mixture of S_2(7-Me_3N-7-$CB_{10}H_{11}$)$_2$ (1.0 g, 2.23 mmol) in a solution of 2% NaOH in

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† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1992, Issue 1, pp. xx–xxv.

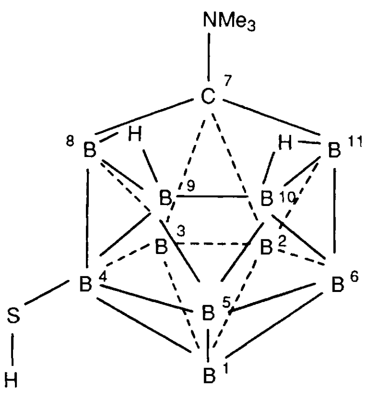


Fig. 1 Structure and numbering of 7-Me_3N-4-HS-*nido*-7-$CB_{10}H_{11}$

EtOH (20 cm^3) was added $NaBH_4$ (0.68 g, 17.8 mmol). The reaction mixture was stirred at 20 °C for 5–6 h, and poured into water. The clear solution was saturated with CO_2 to induce a precipitate which was extracted with Et_2O, the organic layer separated, washed with water, and solvent removed *in vacuo*. TLC of the product showed one major component of 7-Me_3N-4(6)-HS-7-$CB_{10}H_{11}$.

Preparation of $[NEt_3Me][1\text{-}Me_2N\text{-}2\text{-}HS\text{-}closo\text{-}1\text{-}CB_{11}H_{10}]$ *and* 1-Me_2N-7-Et_3N-*closo*-1-$CB_{11}H_{10}$.—A mixture of S_2(7-Me_3N-7-$CB_{10}H_{11})_2$ (2.0 g, 4.5 mmol) and $Et_3N{\cdot}BH_3$ (3.5 cm^3, 28.0 mmol) was heated at 200 °C for 4.5 h under a nitrogen atmosphere. A clear yellow mixture was obtained after vigorous gas evolution. After cooling to room temperature, the mixture was diluted with Et_2O, stirred, and the oily product separated from the organic layer. TLC on SiO_2, eluted with 10% MeCN–90% CH_2Cl_2, showed two major products and several minor components. The major products were separated by column chromatography on SiO_2 to yield $[NEt_3Me][1\text{-}Me_2N\text{-}2\text{-}HS\text{-}1\text{-}CB_{11}H_{10}]$ (R_f 0.3) (Found: C, 35.6; H, 10.6; N, 8.5; S, 9.4. $C_{10}H_{35}B_{11}N_2S$ requires C, 35.9; H, 10.6; N, 9.2; S, 9.6%) and 1-Me_2N-7-Et_3N-1-$CB_{11}H_{10}$ (R_f 0.73) (Found: C, 37.0; H, 10.6; N, 9.2. $C_9H_{31}B_{11}N_2$ requires C, 37.8; H, 10.9; N, 9.8%). The mass spectrum showed a group of ions with mass cut-off at *m*/*z* 288, corresponding to the ion $[^{11}B_{11}{}^{12}C_9{}^{1}H_{31}{}^{14}N_2]^+$.

Preparation of 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$.—The thiolated product of the previous reaction, $[1\text{-}Me_2N\text{-}2\text{-}HS\text{-}1\text{-}CB_{11}H_{10}]^-$ (0.5 g, 1.5 mmol), was shaken with Et_2O (5 cm^3) and dilute (1:3) hydrochloric acid (10 cm^3) until the solid had dissolved. The organic layer was separated, solvent removed by evaporation, and the solid dissolved in 5% aqueous potassium hydroxide (15 cm^3). The mixture was methylated with dimethyl sulfate (0.35 cm^3, 3.7 mmol) with stirring for 15 min. The white precipitate was filtered off and dried *in vacuo*. TLC on SiO_2, eluted with CH_2Cl_2, gave one major product, R_f 0.81. It was purified by column chromatography and recrystallised from aqueous MeCN (Found: C, 24.4; H, 13.0; N, 5.8; S, 9.1. $C_5H_{22}B_{11}NS$ requires C, 24.3; H, 13.0; N, 5.7; S, 9.0%). The mass spectrum showed a group of ions with a mass cut-off at *m*/*z* 249 corresponding to the ion $[^{11}B_{11}{}^{12}C_5{}^{1}H_{22}{}^{14}N^{32}S]^+$.

Crystallographic Determination of 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$.—Single crystals were grown by slow evaporation of a solution in CH_2Cl_2–hexane. X-Ray measurements were made on a specimen mounted in a thin-walled glass capillary using a CAD4 diffractometer and nickel-filtered Cu-Kα radiation (λ = 1.5418 Å) following previously published procedures.[9] The structure was solved by direct methods (SHELXS 86)[10] and developed and refined by full-matrix least squares. Non-hydrogens were refined anisotropically, hydrogens (which were experimentally located) isotropically. Crystal data and other experimental details are as follows.

Table 1 Fractional atomic coordinates ($\times 10^4$) for 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$

Atom	*x*	*y*	*z*
S	9019(1)	7250(1)	434(1)
N	8654(1)	5144(1)	858(2)
C(1)	8002(1)	5636(1)	1776(2)
C(2)	8250(3)	8016(2)	−1172(4)
C(3)	9773(3)	8044(3)	1951(4)
C(4)	9486(2)	4600(2)	1980(4)
C(5)	8093(3)	4609(2)	−659(4)
B(2)	8070(2)	6794(1)	1689(3)
B(3)	6953(2)	6226(2)	516(4)
B(4)	6756(2)	5295(2)	1843(4)
B(5)	7796(2)	5292(2)	3789(4)
B(6)	8625(2)	6220(2)	3662(3)
B(7)	6841(2)	7224(2)	1719(4)
B(8)	6024(2)	6290(2)	1832(5)
B(9)	6557(3)	5721(2)	3853(5)
B(10)	7711(3)	6282(2)	4982(4)
B(11)	7886(2)	7220(2)	3688(4)
B(12)	6615(3)	6900(2)	3786(5)

Table 2 Selected bond lengths (Å) and angles (°) for 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$

C(2)–S	1.806(5)	C(3)–S	1.789(5)
B(2)–S	1.890(4)	C(1)–N	1.443(3)
C(4)–N	1.463(4)	C(5)–N	1.464(4)
B(2)–C(1)	1.730(5)	B(3)–C(1)	1.722(5)
B(4)–C(1)	1.727(5)	B(5)–C(1)	1.731(5)
B(6)–C(1)	1.729(5)	B(3)–B(2)	1.744(5)
B(6)–B(2)	1.751(5)	B(7)–B(2)	1.742(5)
B(11)–B(2)	1.750(5)	B(4)–B(3)	1.785(6)
B(7)–B(3)	1.782(6)	B(8)–B(3)	1.779(6)
B(5)–B(4)	1.772(6)	B(8)–B(4)	1.765(6)
B(9)–B(4)	1.765(6)	B(6)–B(5)	1.778(5)
B(9)–B(5)	1.761(6)	B(10)–B(5)	1.760(6)
B(10)–B(6)	1.766(5)	B(11)–B(6)	1.782(5)
B(8)–B(7)	1.774(6)	B(11)–B(7)	1.787(6)
B(12)–B(7)	1.774(6)	B(9)–B(8)	1.771(7)
B(12)–B(8)	1.776(7)	B(10)–B(9)	1.765(7)
B(12)–B(9)	1.760(6)	B(11)–B(10)	1.771(5)
B(12)–B(10)	1.768(7)	B(12)–B(11)	1.757(6)
C(3)–S–C(2)	99.3(3)	B(2)–S–C(2)	104.9(2)
B(2)–S–C(3)	103.1(2)	C(4)–N–C(1)	115.7(3)
C(5)–N–C(1)	115.7(3)	C(5)–N–C(4)	109.4(3)
B(2)–C(1)–N	116.4(2)	B(3)–C(1)–N	117.9(3)
B(3)–C(1)–B(2)	60.7(2)	B(4)–C(1)–N	123.3(3)
B(4)–C(1)–B(2)	110.6(2)	B(4)–C(1)–B(3)	62.3(2)
B(5)–C(1)–N	122.8(3)	B(5)–C(1)–B(2)	110.5(2)
B(5)–C(1)–B(3)	112.6(3)	B(5)–C(1)–B(4)	61.6(2)
B(6)–C(1)–N	117.4(3)	B(6)–C(1)–B(2)	60.8(2)
B(6)–C(1)–B(3)	111.8(2)	B(6)–C(1)–B(4)	112.1(3)
B(6)–C(1)–B(5)	61.8(2)	C(1)–B(2)–S	115.2(2)
B(3)–B(2)–S	118.8(2)	B(3)–B(2)–C(1)	59.4(2)
B(6)–B(2)–S	116.3(2)	B(6)–B(2)–C(1)	59.6(2)
B(6)–B(2)–B(3)	109.7(3)	B(7)–B(2)–S	127.3(2)
B(7)–B(2)–C(1)	108.0(3)	B(7)–B(2)–B(3)	61.5(2)
B(7)–B(2)–B(6)	110.8(3)	B(11)–B(2)–S	125.6(2)
B(11)–B(2)–C(1)	107.9(2)	B(11)–B(2)–B(3)	111.0(3)
B(11)–B(2)–B(6)	61.2(2)	B(11)–B(2)–B(7)	61.5(3)
B(9)–B(12)–B(8)	60.1(3)	B(10)–B(12)–B(7)	108.8(3)
B(10)–B(12)–B(8)	108.1(3)	B(10)–B(12)–B(9)	60.0(3)
B(11)–B(12)–B(7)	60.8(3)	B(11)–B(12)–B(8)	108.7(3)
B(11)–B(12)–B(9)	108.7(3)	B(11)–B(12)–B(10)	60.3(3)

Crystal data. $C_5H_{22}B_{11}NS$, M_r = 248.23, monoclinic, space group $P2_1/n$, a = 13.41(1), b = 14.90(2), c = 7.78(1) Å, β = 104.29(2)°, U = 1476 $Å^3$, Z = 4, D_c = 1.12 g cm^{-3}, $F(000)$ = 524, μ = 16.1 cm^{-1}. 2816 Data were measured, of which 2507 were unique, and 2220 satisfied the criterion $F_o > 5\sigma(F_o)$.

Refinement. 251 Parameters, $w = [\sigma^2(F_o) + 0.000\,012F_o{}^2]^{-1}$,

$R = 0.040$, $R' = 0.052$. Final atomic positional parameters are given in Table 1, selected bond lengths and angles in Table 2.

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and remaining bond lengths and angles.

Calculations.—AM1 calculations[11] were performed using the MOPAC program[12] supplied by Dr. J. J. P. Stewart, on a DEC Vax model 11/785 computer system. Symmetry constraints were not applied, and full geometry optimisations were obtained. Graphic presentations of input parameters and optimised results were obtained using the INTERCHEM program.[13]

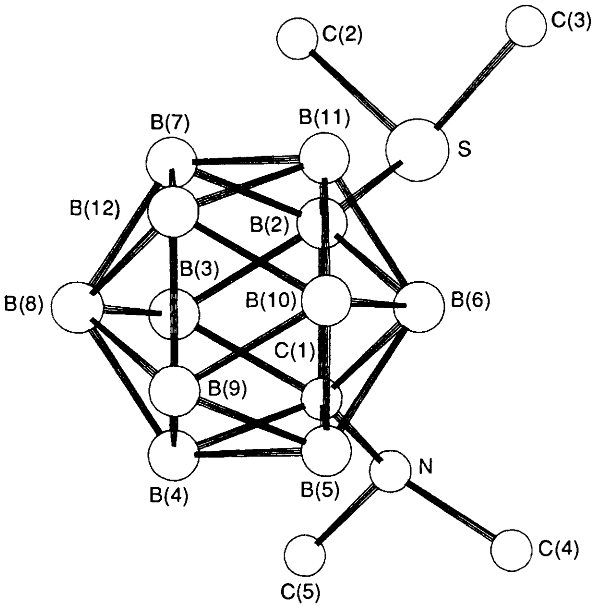


Fig. 2 Structure of 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$

Results and Discussion

Synthetic Reactions.—Although initial attempts to introduce a sulfur substituent (thiol or disulfide) into 7-Me_3N-7-$CB_{10}H_{12}$ by routes analogous to those for the preparation of $[B_{12}H_{11}(SH)]^{2-}$ or $[B_{10}H_9(SH)]^{2-}$ were unsuccessful, the electrophilic sulfur substitution was achieved using the reaction between S_2Cl_2 and 7-Me_3N-7-$CB_{10}H_{12}$ in the presence of $AlCl_3$. The major product of the reaction was an isomer mixture of 4,4′-, 6,6′- and 4,6′-S_2(7-Me_3N-7-$CB_{10}H_{11})_2$ in the approximate ratio 1:1:2, which was difficult to separate. The minor product of the reaction was 7-Me_3N-4(6)-HS-7-$CB_{10}H_{11}$. This reaction may be classified as an electrophilic substitution in the carborane cage, and occurs at the position of highest electron density. The disulfide isomer mixture was reduced with $NaBH_4$ to give 7-Me_3N-4(6)-HS-7-$CB_{10}H_{11}$, and its structure (Fig. 1) was established from NMR data.

When the isomer mixture (4,4′;6,6′;4,6′)-S_2(7-Me_3N-7-$CB_{10}H_{11}$) was treated with excess of $Et_3N{\cdot}BH_3$ at 200 °C, boron insertion[8,11] occurred in the cage with concomitant demethylation of the 7-Me_3N substituent to yield $[NEt_3Me]$-[1-Me_2N-2-HS-1-$CB_{11}H_{10}$], together with 1-Me_2N-7-Et_3N-1-$CB_{11}H_{10}$ as a by-product, whose structures were established from NMR data.

This may be compared with the boron insertion reaction[14]

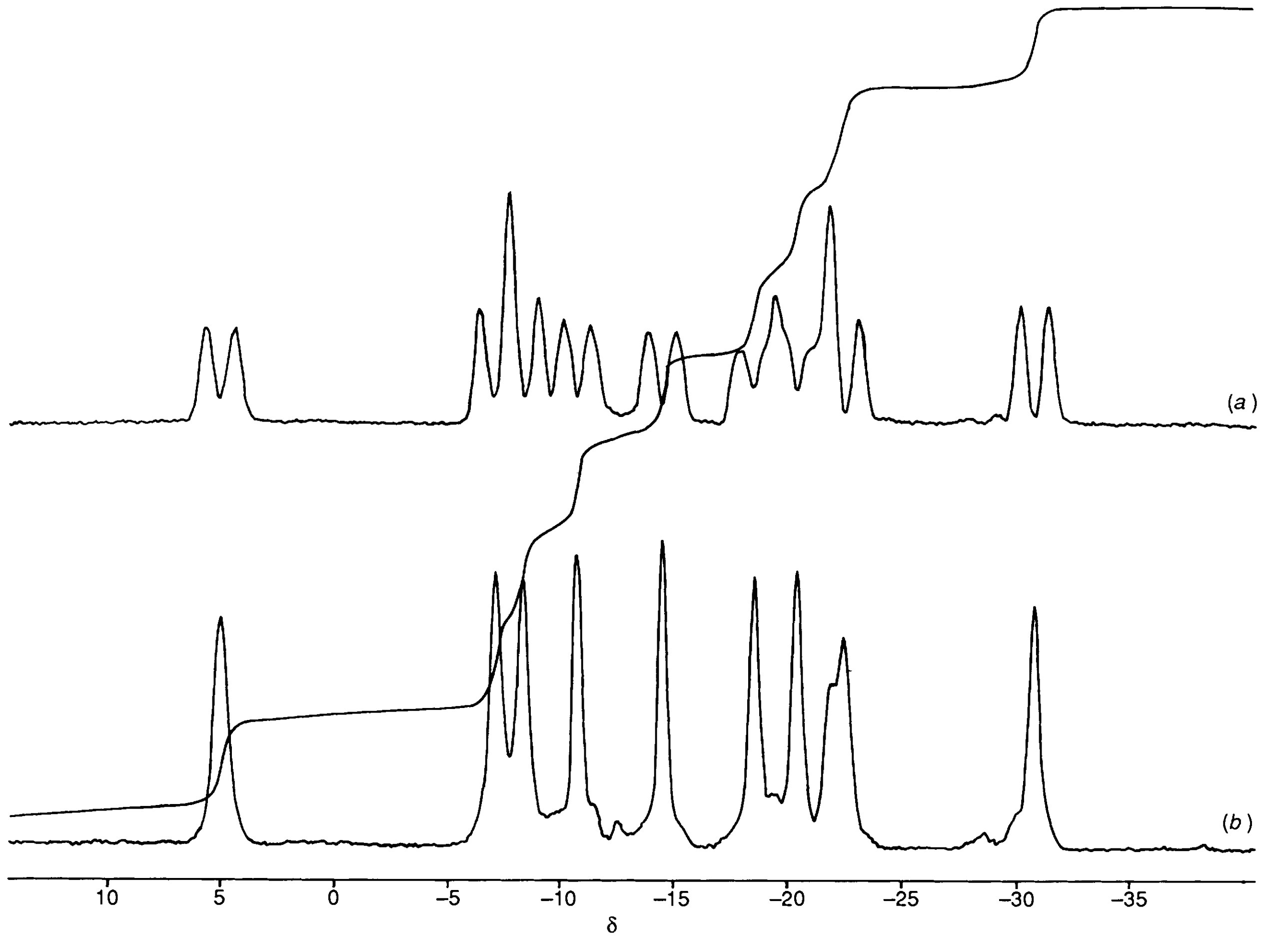


Fig. 3 NMR spectra of 7-Me_3N-4-HS-*nido*-7-$CB_{10}H_{11}$: (*a*) ^{11}B and (*b*) ^{11}B-{^1H broad band}

between *nido*-[7-$CB_{10}H_{13}$]$^-$ and $Et_3N{\cdot}BH_3$ at 180 °C which yielded *closo*-[1-$CB_{11}H_{12}$]$^-$, and the thermal decomposition of [$BH_2(NMe_3)_2$]$^+$[7-$CB_{10}H_{13}$]$^-$ which gave a lower yield of the same *closo* anion through a boron insertion reaction,[15] but also yielded the side-products 2-, 7- and 12-Me_3N-1-$CB_{11}H_{11}$ in the ratio 3:1:10 respectively. Insertion of isotopically labelled $Et_3N{\cdot}^{10}BH_3$ took place to give the label in B(2) of the resulting pseudo-icosahedral products [1-$CB_{11}H_{12}$]$^-$ and 1-Me_3N-1-$CB_{11}H_{11}$.[15] Insertions of $Et_3N{\cdot}BH_3$ on substituted *nido*-carboranes resulted in several different reactions. With 7-Me_3N-8-$PhCH_2$-7-$CB_{10}H_{11}$ a regiospecific cage rearrangement occurred to give 1-Me_3N-7-$PhCH_2$-1-$CB_{11}H_{10}$ as the only isomer.[15] With 4-Cl-7-Me_3N-7-$CB_{10}H_{11}$, boron insertion was accompanied by substituent removal, and the product was [NEt_3Me]$^+$[7-Me_2N-7-$CB_{11}H_{11}$].[16] In the present work, it is clear that boron insertion is accompanied by a structural rearrangement, since the expected isomer would have had the thiol substituent at B(7). The substituent was in this position only in the by-product.

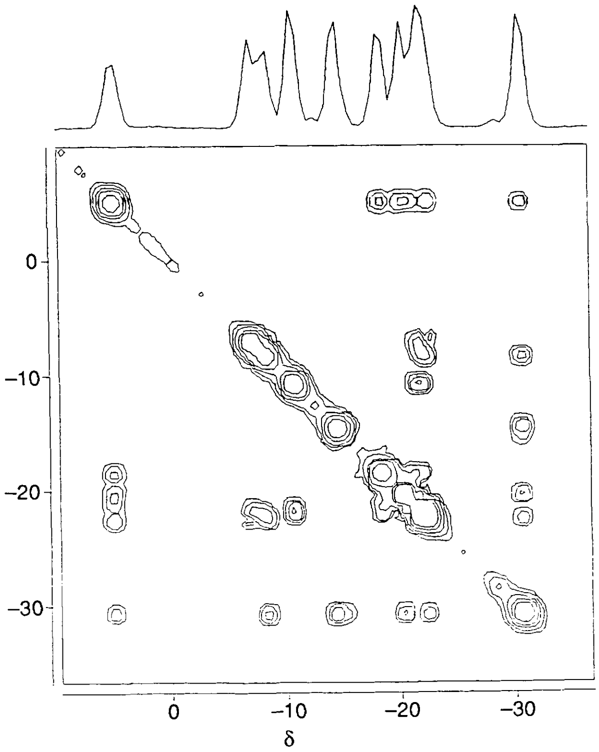


Fig. 4 ^{11}B–^{11}B COSY NMR spectrum of 7-Me_3N-4-HS-*nido*-7-$CB_{10}H_{11}$

The position of substitution of the *closo*-thiol was further confirmed by methylation with Me_2SO_4 in base, which resulted in 1-Me_2N-2-Me_2S-1-$CB_{11}H_{10}$, and whose structure (Fig. 2) was established unambiguously from NMR and single-crystal X-ray data.

NMR Spectra.—The position of substitution in the thiol and disulfide substituted *nido* derivatives was established through one-dimensional ^{11}B (115.5 MHz) and ^1H (360 MHz) and two-dimensional correlation spectroscopy (COSY) ^{11}B–^{11}B NMR spectra.

The ^{11}B NMR spectrum of 7-Me_3N-4(6)-HS-7-$CB_{10}H_{11}$ **2** (Fig. 3) consisted of ten unique resonances which could be resolved on resolution enhancement, consistent with the absence of a plane of symmetry in the molecule. The substituted boron resonance occurred near δ −22.5 as a singlet which overlapped another boron resonance. Unambiguous assignment of

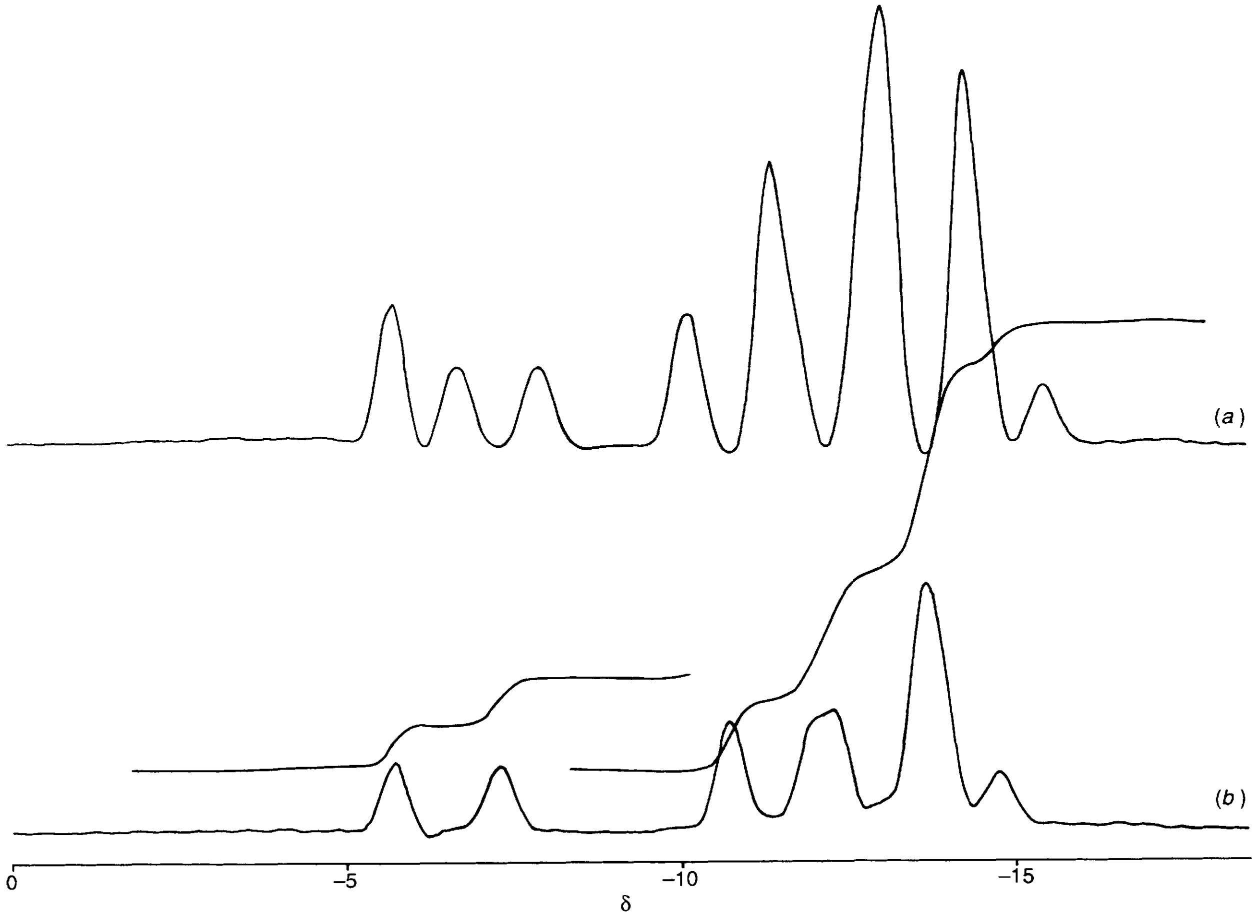


Fig. 5 NMR spectra of [1-Me_2N-2-HS-*closo*-1-$CB_{11}H_{10}$]$^-$: (*a*) ^{11}B and (*b*) ^{11}B-{^1H broad band}

Table 3 NMR data for 4,4′-$S_2(7\text{-}Me_3N\text{-}nido\text{-}7\text{-}CB_{10}H_{11})_2$ **1** and 7-Me_3N-4-HS-*nido*-7-$CB_{10}H_{11}$ **2**

Compound	Assignment	Relative intensity	$\delta(^{11}B)^a$	$\delta(^1H)^b$
1	5	1 BH	4.8	2.86
	3	1 BH	-7.6	2.70
	2	1 BH	-8.4	2.37
	8	1 BH	-11.2	2.52
	11	1 BH	-14.0	2.13
	4	1 B	-17.9	
	9	1 BH	-19.4	1.43
	10	1 BH	-20.8	1.31
	1	1 BH	-23.7	1.31
	6	1 BH	-31.2	0.48
	8,9	1 B-H-B		-2.95
	10,11	1 B-H-B		-3.42
	Me_3N	9 H		3.15
2	5	1 BH	4.9	2.86
	3	1 BH	-7.0	2.60
	2	1 BH	-8.4	2.36
	8	1 BH	-10.8	2.45
	11	1 BH	-14.6	2.11
	9	1 BH	-18.6	1.42
	10	1 BH	-20.4	1.35
	4	1 B	-21.8	
	1	1 BH	-22.3	1.31
	6	1 BH	-30.8	0.52
	8,9	1 B-H-B		-2.88
	10,11	1 B-H-B		-3.41
	Me_3N	9 H		3.14
	HS^c	1 H		-0.06

[a] Chemical shifts (δ) positive to high frequency of the reference $Et_2O{\cdot}BF_3$, to ±0.2 ppm obtained from $^{11}B\text{-}\{^1H\}$ NMR measurements. [b] Chemical shifts ±0.05 ppm; B–H shifts obtained from $^1H\text{-}\{^{11}B$ selective} measurements. [c] S–H removed on treatment with D_2O.

the resonances was obtained from the two-dimensional COSY spectrum (Fig. 4) and is presented in Table 3. The ^1H NMR spectrum of 7-Me_3N-4(6)-HS-7-$CB_{10}H_{11}$ **2** contained a singlet (relative intensity 9) at δ 3.14 due to the Me_3N substituent, and a singlet (relative intensity 1) at δ −0.06, which was removed when the sample was shaken with D_2O, and is consistent with the thiol (SH) hydrogen.

The ^{11}B and $^{11}B\text{-}\{^1H$ selective} NMR spectra of 4,4′-(4,6′- and 6,6′-)$S_2(7\text{-}Me_3N\text{-}7\text{-}CB_{10}H_{11})_2$ **1** showed a singlet (relative intensity 1) at δ −17.9, and although the poor solubility gave spectra whose quality precluded an unambiguous assignment, they are consistent with substitution at B(4) or B(6).

The ^{11}B NMR data for $[NEt_3Me]$[1-Me_2N-2-HS-*closo*-1-$CB_{11}H_{10}$] **3** and its methylated derivative 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$ **4** both clearly show 2-substituted *closo* structures with the B(2) shifts at δ −5.7 and −5.1 respectively (Figs. 5 and 6, and Table 4). The position of substitution is uniquely established as B(2) by the cross-terms in the ^{11}B–^{11}B COSY NMR spectra (Figs. 7 and 8). Although the shifts of the unique B(12) were similar (δ −7.3 and −8.7), those of B(9) changed from δ −14.7 for the anion **3** to δ −12.2 for the neutral methylated derivative **4**. In addition, the relative positions of B(7,11;3,6) and B(4,5;8,10) were inverted. Splitting of the symmetry-related B(3) and B(6) sites of **3**, also observed in the $^1H\text{-}\{^{11}B$, selective} NMR spectra, is possibly due to strong solvation. A related lowering of symmetry is also observed in the ^1H NMR spectra of **4**, in which the methyl groups of the Me_2N substituent are non-equivalent, possibly for a similar reason. The ^{11}B NMR data for 1-Me_2N-7-Et_3N-*closo*-1-$CB_{11}H_{10}$ **5** again show a *closo* structure, and the COSY spectrum (Fig. 9) is only interpretable on the basis of 7 substitution.

X-Ray Crystal Structure of 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$ **4**.—Bond lengths and selected angles are given in Table 2.

Table 4 NMR data for $[NEt_3Me]$[1-Me_2N-2-HS-*closo*-1-$CB_{11}H_{10}$] **3**, 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$ **4** and 1-Me_2N-7-Et_3N-*closo*-1-$CB_{11}H_{10}$ **5**

Compound	Assignment	Relative intensity	$\delta(^{11}B)^a$	$\delta(^1H)^b$
3	2	1 B	-5.7	
	12	1 BH	-7.3	1.65
	7,11	2 BH	-10.7	1.72
	$3,6^c$	1 BH	-11.9	1.75
		1 BH	-12.3	1.52
	4,5;8,10	2 BH	-13.7	1.99
		2 BH		1.40
	9	1 BH	-14.7	1.41
	$[(CH_3{}^dCH_2)_3NMe]^+$	9 H		1.23
	$[(CH_3CH_2{}^e)_3NMe]^+$	6 H		3.20
	$[Et_3NCH_3{}^f]^+$	3 H		2.82
	Me_2N	6 H		2.56
	HS	1 H		1.95?
4	2	1 B	-5.1	
	12	1 BH	-8.7	1.64
	9	1 BH	-12.2	1.58
	4,5;8,10	2 BH	-13.0	2.14
		2 BH		1.56
	3,6;7,11	2 BH	-13.7	2.08
		2 BH		1.67
	Me_2S	6 H		3.93
	Me_2N	3 H		2.70^g
		3 H		2.39
5	7	1 B	1.8	
	12	1 BH	-11.0	1.75
	2,3;4,6;5; and 8,11;9,10	9 B 2 H	-14.3	2.32
		3 H		2.00
		2 H		1.76
		2 H		1.43
	$(CH_3{}^hCH_2)_3N$	9 H		1.31
	$(CH_3CH_2{}^i)_3N$	6 H		3.26
	Me_2N	6 H		2.30

[a] Chemical shifts (δ) positive to high frequency of the reference $Et_2O{\cdot}BF_3$, to ±0.2 ppm from $^{11}B\text{-}\{^1H\}$ measurements. [b] Chemical shifts ±0.05 ppm to high frequency of the reference $SiMe_4$; B–H shifts obtained from $^1H\text{-}\{^{11}B$ selective} measurements. [c] Slight non-equivalence observed in ^{11}B and ^1H NMR spectra. [d] Triplet of 1:1:1 triplets [due to $J(^1H\text{-}^{14}N)$ coupling]. [e] Quartet. [f] Singlet. [g] Linewidth reduced on $^1H\text{-}\{^{11}B\}$ decoupling. [h] Triplet. [i] Quartet.

The molecular dimensions differ only slightly from those corresponding to the idealised C_s point group, and the carborane cage is little distorted from the ideal icosahedron, with an average B–C cage edge length of 1.728 Å and a mean B–B cage edge length of 1.762 Å, and range between 1.742(5) [B(7)–B(2)] and 1.787(6) Å [B(7)–B(11)]. These distances are similar to those which have been observed in $Ag[CB_{11}H_{12}]$,[17] 1-Me_3N-1-$CB_{11}H_{11}$,[18] and $[1\text{-}Me_2N\text{-}1\text{-}CB_{11}H_{11}]^-$.[19] The (Me)C–N distances of 1.463(4) and 1.464(4) Å are slightly shorter than those in 1-Me_3N-1-$CB_{11}H_{11}$ (1.516, 1.509 Å).[18] The observed cage C–N distance of 1.443(3) Å is substantially shorter than that in $Me_3NCB_{11}H_{11}$ (1.543 Å)[18] and this is reflected in the calculated bond index (see below). The distances of the Me_2S ligand [B–S 1.890(4); (Me)C–S 1.806(5) and 1.789(5) Å] are in the normal range for co-ordination to a boron cage,[20] and are consistent with distances in compounds in which the Me_2S group is not readily substituted by other ligands.

AM1 *Calculations*.—Calculations were performed on the *closo* compounds **3** and **4**, and on analogues of **2** (7-H_3N-4-HS-7-$CB_{10}H_{11}$ **6**) and **5** (1-H_2N-7-H_3N-1-$CB_{11}H_{10}$ **7**) partly to aid the interpretation of some of the experimental results, and selected data are presented in Table 5.

Heats of formation and ionisation potentials. The heats of formation of all species are comparable with those obtained

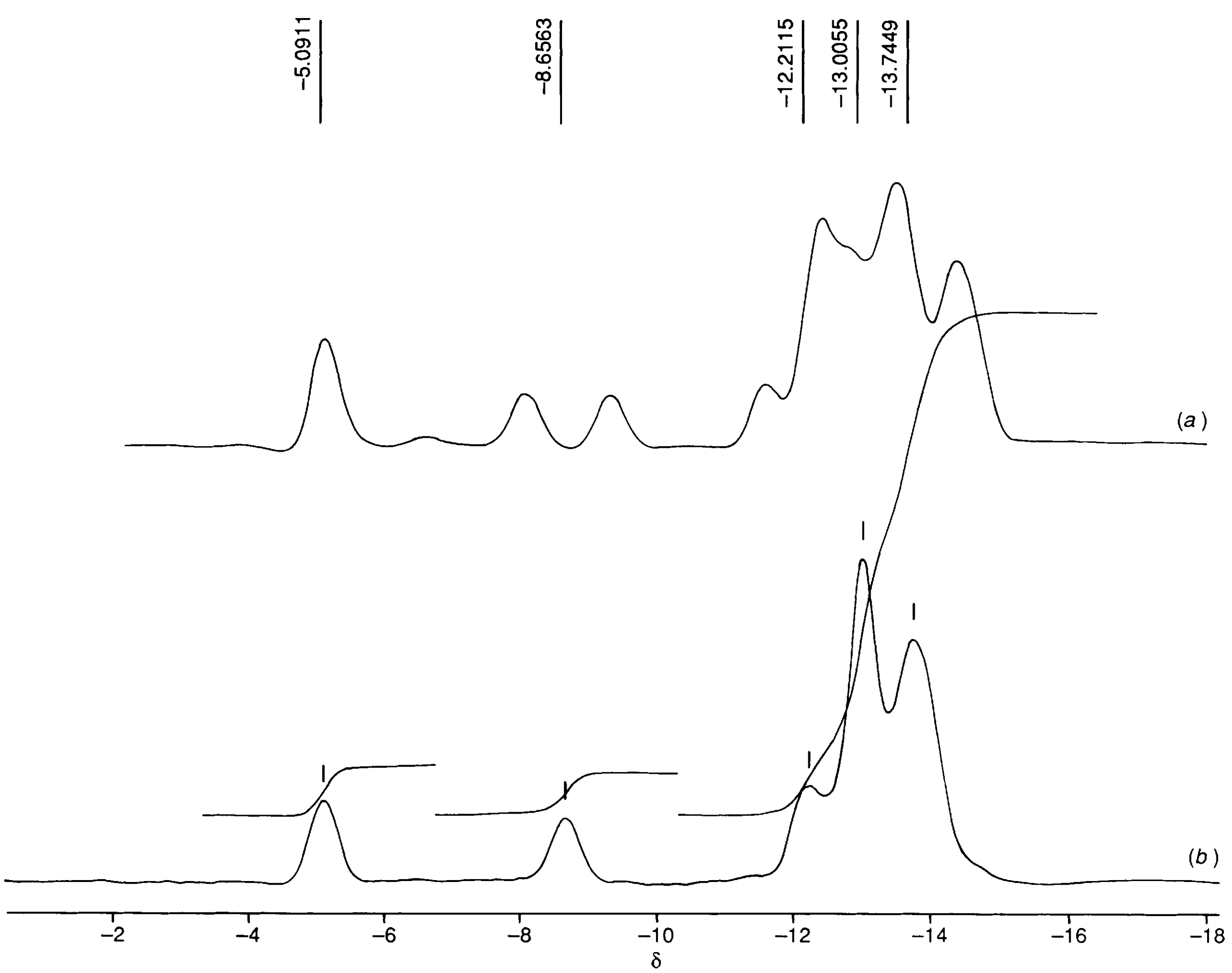


Fig. 6 NMR spectra of $1\text{-Me}_2\text{N-2-Me}_2\text{S-}$*closo*$\text{-1-CB}_{11}\text{H}_{10}$: (*a*) ^{11}B and (*b*) $^{1}\text{B-}\{^{1}\text{H}$ broad band$\}$

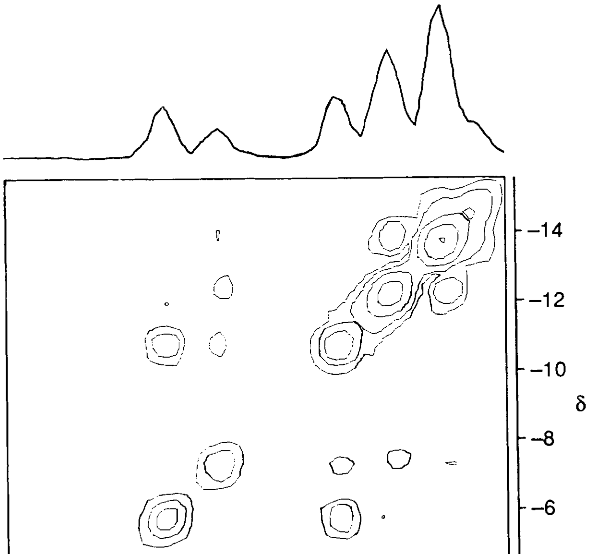


Fig. 7 ^{11}B–^{11}B COSY NMR spectrum of $[1\text{-Me}_2\text{N-2-HS-}$*closo*$\text{-1-CB}_{11}\text{H}_{10}]^-$

earlier for other monocarbon carborane derivatives. The values of three geometry-optimised rotamers of **3**, in which the thiol hydrogen was allowed to minimise in several orientations with respect to the $1\text{-Me}_2\text{N}$ substituent to torsion angles H–S–B–C of 162, 76 and 8° (Fig. 10), showed a slight preference for orienting the thiol hydrogen towards the Me_2N substituent, but the differences were too small readily to account for the non-equivalence in the NMR spectrum. All neutral species had high ionisation potentials suggesting good oxidative stability and hence are potentially useful compounds for neutron capture therapy, although that of the anionic derivative **3** was such that easy oxidation would be expected.

Optimised structures. The AM1 method has some deficiencies in predicting bond lengths in clusters, compared with *ab initio* methods.[21] Our own observations on substituted carboranes show that AM1 is better than minimum neglect of differential overlap (MNDO) in reproducing substituent effects,[22] and hence it has been applied in this work. The optimised geometries of **6** and **4** showed little distortion of the *nido*-carborane cage through the substitution with thiol. Similarly, in the *closo* compounds, little cage distortion was observed. Furthermore, the computed C–S distances of 1.816 and 1.819 Å, and the C–N distances 1.451 and 1.452 Å, agree with the experimental data. The computed cage C–N and B–S distances were 1.436 and 1.784 Å respectively, although the latter has only moderate correlation with experiment.

Bond indices. There is an excellent correlation between the calculated bond indices of adjacent boron atoms (indicating substantial bonding) and the observation of a correlation off-diagonal peak in the COSY NMR spectra. This is illustrated in Table 6 for the experimental data on compound **1** and

Table 5 AM1 Calculation results on 7-H_3N-4-HS-7-$CB_{10}H_{11}$ **6**, 1-Me_2N-2-Me_2S-1-$CB_{11}H_{10}$ **4**, rotamers of [1-Me_2N-2-HS-1-$CB_{11}H_{10}$]$^-$ **3a**–**3c** and 1-H_2N-7-H_3N-1-$CB_{11}H_{10}$ **7**

Compound	**6**	**4**	**3a**	**3b**	**3c**	**7**
ΔH_f/kcal mol^{-1}	−61.35	−108.81	−164.19	−164.80	−164.97	−152.57
Ionisation potential/eV	7.81	9.31	4.87	5.01	4.86	9.42
S–B						
Bond index	1.007	0.936	0.990	1.020	0.992	
s_σB–s_σB	0.021	0.022	0.024	0.023	0.022	
s_σS–p_σB	0.056	0.067	0.056	0.060	0.061	
p_σS–s_σB	0.316	0.241	0.313	0.318	0.315	
p_σS–p_σB	0.536	0.558	0.528	0.517	0.518	
p_πS–p_πB	0.074	0.042	0.068	0.096	0.071	
N–C						
Bond index	0.915	0.998	0.982	0.986	0.979	1.028
s_σN–s_σC	0.019	0.031	0.031	0.032	0.031	0.026
s_σN–p_σC	0.149	0.137	0.152	0.152	0.150	0.134
p_σN–s_σC	0.178	0.209	0.204	0.203	0.201	0.228
p_σN–p_σC	0.542	0.534	0.522	0.524	0.527	0.565
p_πN–p_πC	0.027	0.061	0.060	0.063	0.057	0.065

cal = 4.184 J, eV ≈ 1.60 × 10^{-19} J.

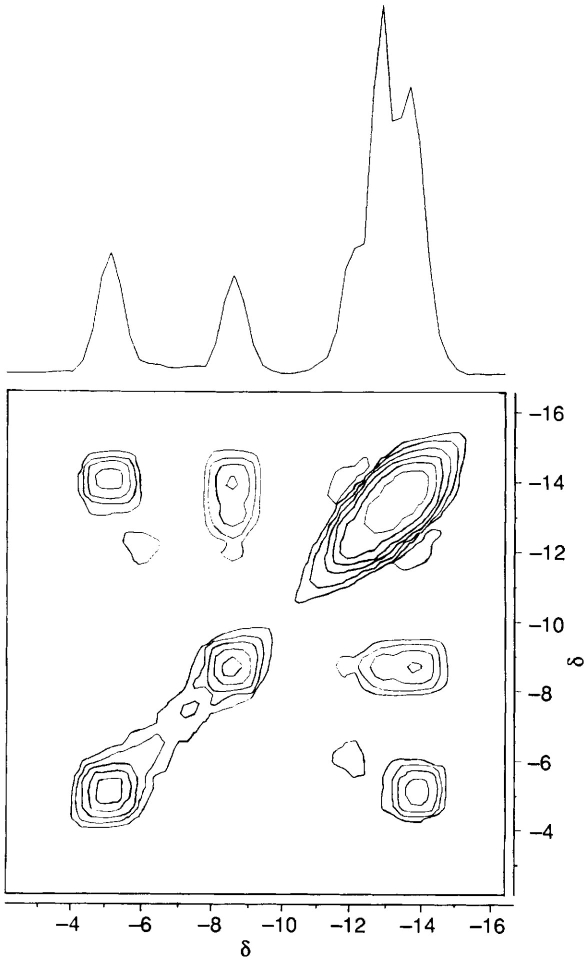


Fig. 8 ^{11}B–^{11}B COSY NMR spectrum of 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$

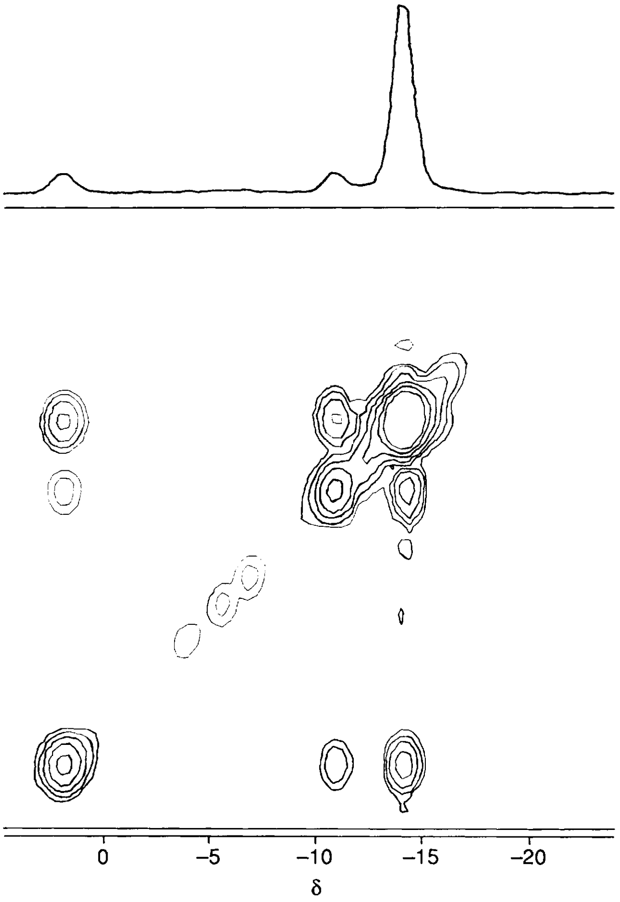
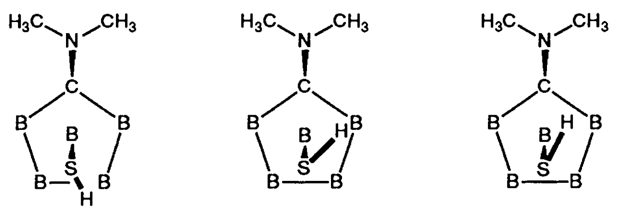


Fig. 9 ^{11}B–^{11}B COSY NMR spectrum of 1-Me_2N-7-Et_3N-*closo*-1-$CB_{11}H_{10}$

calculated indices for its analogue **6**. All correlations are observed for calculated bond indices >0.40, with the possible exceptions of B(2)–B(3) and B(1)–B(4) in which the sites are so close in shift that it would make observation of these cross-peaks very difficult. The bond indices for the cage C–N, B–S or B–N bonds, together with their resolution into σ and π components (Table 5) suggest that there is only a small contribution of π bonding in these bonds, and so the possibility of restricted rotation accounting for the observed non-equivalences in the NMR spectra of compounds **3** and **4** is small. However, the indices for **4** compared with those for **6** correlate well with the observed short C–N bond distance in **4**.



3a **3b** **3c**

Fig. 10 HS-Substituent orientation in rotamers of $[1\text{-}Me_2N\text{-}2\text{-}HS\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}]^-$ **3**. Geometry-optimised H–S–B–C torsion angles: **3a**, 162; **3b**, 76; **3c**, 8°

Table 6 Observed COSY correlations for $7\text{-}Me_3N\text{-}4\text{-}HS\text{-}7\text{-}CB_{10}H_{11}$ **2** and calculated bond indices for $7\text{-}H_3N\text{-}4\text{-}HS\text{-}7\text{-}CB_{10}H_{11}$ **6***

Position	Correlations	Bond indices
5	9, 10, 4, 1, 6	0.42, 0.43, 0.48, 0.52, 0.46
3	(2), (8), 4, 1	(0.44), (0.27), 0.57, 0.53
2	(3), (11), 1, 6	(0.44), (0.30), 0.57, 0.53
8	(3), (9), 4	(0.27), (0.40), 0.59
11	(2), (10), 6	(0.30), (0.40), 0.59
9	10, 5, 4	0.61, 0.42, 0.48
10	5, 6, 9	0.43, 0.48, 0.61
4	5, 3, 8, 9, (1)	0.48, 0.56, 0.59, 0.48, (0.40)
1	5, 3, 2, 6, (4)	0.52, 0.53, 0.52, 0.42, (0.40)
6	5, 2, 11, 10, 1	0.46, 0.56, 0.59, 0.48, 0.42

* Correlations that are not observed and their calculated bond indices are given in parentheses.

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