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$1\text{-}Me_2NH\text{-}2\text{-}CH_2Cl\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}$. An unusual product from the insertion reaction of Me_2NBCl_2 with Li_2 [$7\text{-}Me_3N\text{-}$*nido*$\text{-}7\text{-}CB_{10}H_{10}$]

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Abstract

The boron insertion reaction of Me_2NBCl_2 with $Li_2[7\text{-}Me_3N\text{-}$*nido*$\text{-}7\text{-}CB_{10}H_{10}]$ gave new neutral compound, $1\text{-}Me_2N(H)\text{-}2\text{-}CH_2Cl\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}$. The reaction is thought to proceed via a metathetical insertion of Me_2NBCl_2 into the *nido*-carborane dianion, accompanied by demethylation of the 7-trimethylamine group and methylene insertion into the B–N bond of the inserted reagent, with concomitant protonation of its nitrogen. Nucleophilic-displacement of dimethylamine by chloride ion and protonation of the $C\text{-}NMe_2$ group then gives the observed product, which was characterised by multinuclear NMR spectroscopy and X-ray crystallography.

Keywords: Boron; Carborane; Carbaborane; X-ray diffraction; Boron neutron capture therapy

1. Introduction

Selective substitution of borane clusters is important in the search for suitable boron-containing, tumour-seeking compounds for use in Boron Neutron Capture Therapy [1,2]. In a systematic study of substitution reactions, a series of two-substituted monocarbon carborane anions has been synthesised by the insertion of reagents "RBX_2", ($R = F$, Ph, *p*-Tol, $O(CH_2)_4Cl$, NMe_2; $X = Cl$, F) into $Li_3[$*nido*$\text{-}7\text{-}HCB_{10}H_{10}]$ [3]. The analogous reaction between RBX_2 and $Li_2[7\text{-}Me_3N\text{-}$*nido*$\text{-}7\text{-}CB_{10}H_{10}]$ produced neutral compounds of the form $1\text{-}Me_3N\text{-}2\text{-}R\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}$, where $R = H$, F, Ph, $O(CH_2)_4Cl$ and $O(CH_2)_4Br$ [4]. The recently reported [5] insertion of $^iPr_2NBCl_2$ into $Li_2[7\text{-}Me_3N\text{-}$*nido*$\text{-}7\text{-}CB_{10}H_{10}]$ yielded the unexpected product $1\text{-}Me_2N\text{-}2\text{-}^iPr_2N(H)CH_2\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}$ (**1**), whose crystal structure clearly indicated the loss of a methyl group from the trimethylamine ligand, and methylene insertion into the B–N bond with subsequent protonation of the di-isopropylamine nitrogen.

2. Results and discussion

We report here another rearrangement product from the insertion of Me_2NBCl_2 into $Li_2[7\text{-}Me_3N\text{-}$*nido*$\text{-}7\text{-}CB_{10}H_{10}]$ at ambient temperature. This product is $1\text{-}Me_2NH\text{-}2\text{-}CH_2Cl\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}$ (**2**), rather than either the expected $1\text{-}Me_3N\text{-}2\text{-}Me_2N\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}$ (**3**) or a rearranged product analogous to (**1**). The structure of (**2**) (see Fig. 1) was assigned on the basis of (a) its ^{11}B NMR spectra, which were consistent with a two-substituted CB_{11} cluster of effective C_s symmetry, and (b) its ^1H NMR spectrum, which contained two singlets, the relative intensities of which were 1:3, and not the 2:3 ratio expected for (**3**). The ^{11}B NMR spectra consisted of one singlet overlapping a doublet, and three doublets, with relative intensities 2:2:4:3, reading upfield. This pattern was consistent with an eleven-boron, twelve-vertex cluster with C_s symmetry, but the envelope of chemical shifts was narrow, as in the ^{11}B NMR spectra of $1\text{-}Me_2N\text{-}2\text{-}^iPr_2N(H)CH_2\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}$ and $1\text{-}Me_3N\text{-}2\text{-}Ph\text{-}$*closo*$\text{-}1\text{-}CB_{11}H_{10}$. The spectrum was assigned as follows: the singlet at δ −6.78 to B(2); the doublet at δ − 7.30 to B(12); the doublet at δ −12.36 to B(7, 11); the doublet at δ −14.63 to B(3, 6) and B(8, 10); and the final doublet at δ −15.38 to coincidence of the chemical shifts of the B(9) and B(4, 5)

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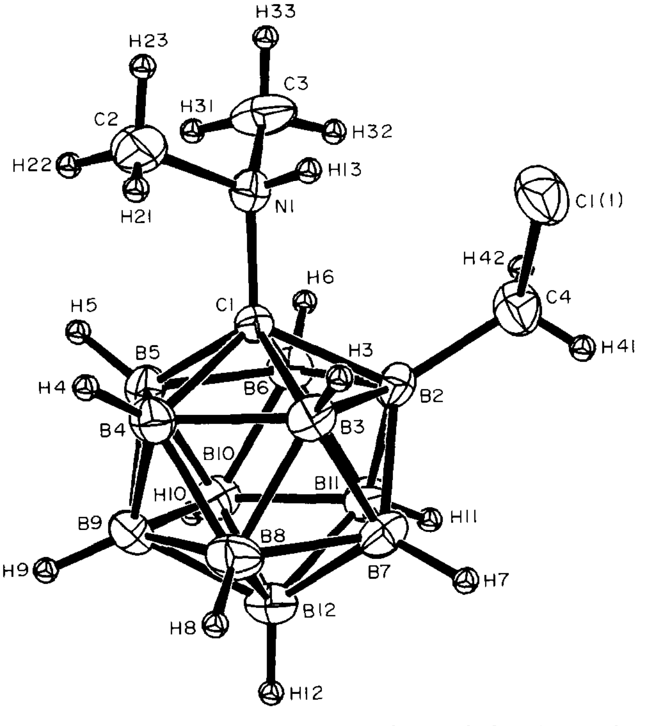
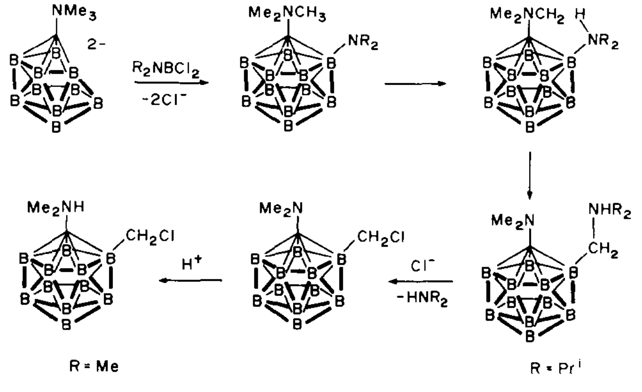


Fig. 1. Molecular structure of 1-Me_2NH-2-CH_2Cl-*closo*-1-$CB_{11}H_{10}$. Thermal ellipsoids are drawn at 40% probability.

resonances. The off-diagonal peaks of the $^{11}B-^{11}B$ COSY NMR spectrum confirmed this assignment. The structure was completely elucidated by an X-ray crystallographic study on a single crystal grown by slow evaporation of a 1,2-dichloroethane solution.

Structurally, the cage of (**2**) is similar to that in the previously reported structures of (**1**), 1-Me_2N-2-Me_2S-*closo*-1-$CB_{11}H_{10}$ (**4**) [6] and 1-Me_3N-*closo*-1-$CB_{11}H_{11}$ [7]. The most significant difference is the slight lengthening of the cage carbon–N(1) bond from 1.466 Å and 1.443 Å in (**1**) and (**4**), respectively, to 1.516 Å in (**2**). The longer bond length can be attributed to the quaternary nitrogen N(1) in (**2**), whereas in (**1**) and (**4**) this nitrogen is three-coordinate and does not carry the positive charge. The zwitterionic nature of (**1**) and (**4**) is maintained on the substituent at the B(2) position.

A rationalisation of the reaction mechanism is given in Scheme 1. Earlier, (**4**) was produced by a high-temperature insertion reaction, involving severe conditions that have been reported to demethylate the trimethylamine ligand [6,8]. The mild reaction conditions under which both (**1**) and (**2**) were produced unexpectedly also resulted in demethylation of the trimethylamine ligand. After the steps involving insertion of the RBX_2 reagent, demethylation, and methylene insertion, the reactions must follow differing paths. The presence of chloride in the solution is thought to give rise to nucleophilic displacement of dimethylamine in the reaction intermediate with the result that in (**2**) the amine group has been replaced by chlorine. However in the case of (**1**), the chloride does not displace the more sterically hindered, less volatile di-isopropylamine. After the loss of the amine from B(2), (**2**) maintains its zwitterionic nature by protonation at the only available site, i.e. the nitrogen bonded to the cage carbon atom (Scheme 1).



Scheme 1.

Undoubtedly, there is a set of very unusual insertion reactions occurring between amino-BCl_2 reagents and Li_2[7-Me_3N-*nido*-7-$CH_{10}H_{10}$]. We are currently exploring these reactions and their mechanisms, and the results will be reported in a later paper [9].

3. Experimental details

3.1. General

All materials were reagent grade or better, and were used as received. 7-Me_2N-*nido*-7-$CB_{10}H_{12}$ was pre-

Table 1
Crystallographic data for 1-Me_2NH-2-CH_2Cl-*closo*-1-$CB_{11}H_{10}$

Formula	$B_{11}C_4H_{19}ClN$
Formula weight	235.56
Unit Cell	triclinic
Space Group	$P\bar{1}$
a, b, c Å	6.928(1), 7.971(1), 12.598(2)
α, β, γ deg	100.89(1), 96.61(2), 104.79(1)
V, Å^3	650.69
Z	2
$F(000)$	244
D_{calc}, g cm^{-3}	1.202
μ (Mo-Kα), cm^{-1}	2.20
hkl range	$h, -8$ to $+8$; $k, -9$ to $+9$; l, 0 to 14
Measured reflections	2487
Unique reflections	2280 (R_{int} = 0.014)
Observed reflections ($F > 4\sigma(F)$)	1603
No. of refined parameters	222
R	0.043
R_w	0.042
Weighting scheme	$1/[\sigma^2(F)+0.00057F^2]$
Max shift/esd in final LS cycle	0.07
Residual electron density, e Å^3	0.22 to −0.29
GOF	1.42

Table 2
Atomic coordinates for non-hydrogen atoms in 1-Me_2NH-2-CH_2Cl-*closo*-1-$CB_{11}H_{10}$

Atom	x	y	z
C(1)	0.3507(4)	0.0660(3)	0.7313(2)
B(2)	0.2184(5)	0.0263(4)	0.8367(2)
B(3)	0.0914(5)	0.0117(4)	0.7018(2)
B(4)	0.2321(5)	−0.0694(4)	0.6043(2)
B(5)	0.4513(5)	−0.1012(4)	0.6786(3)
B(6)	0.4417(5)	−0.0459(4)	0.8216(2)
B(7)	0.0056(5)	−0.1570(4)	0.7728(3)
B(8)	0.0139(5)	−0.2153(4)	0.6305(3)
B(9)	0.2382(5)	−0.2844(4)	0.6160(3)
B(10)	0.3656(5)	−0.2688(4)	0.7498(3)
B(11)	0.2224(5)	−0.1916(4)	0.8460(3)
B(12)	0.0964(5)	−0.3407(4)	0.7197(3)
N(1)	0.4618(3)	0.2589(3)	0.7373(2)
C(2)	0.6601(5)	0.3274(5)	0.8143(3)
C(3)	0.4941(7)	0.3021(5)	0.6290(3)
C(4)	0.2258(6)	0.1754(4)	0.9412(2)
Cl(1)	0.1963(1)	0.3820(1)	0.9133(1)

pared by the published method [8]. Me_2NBCl_2 was obtained from the low-temperature condensation of Me_2NH and BCl_3. NMR spectra were recorded on a Bruker AMX400 spectrometer (^1H, 400 MHz; ^{11}B, 128 MHz) in CD_3CN.

Table 3
Bond lengths (Å) for 1-Me_2NH-2-CH_2Cl-*closo*-1-$CB_{11}H_{10}$

C(1)–B(2)	1.731(4)	B(5)–B(6)	1.785(4)
C(1)–B(3)	1.715(4)	B(5)–B(9)	1.769(5)
C(1)–B(4)	1.729(4)	B(5)–B(10)	1.764(4)
C(1)–B(5)	1.717(4)	B(6)–B(10)	1.749(4)
C(1)–B(6)	1.729(4)	B(6)–B(11)	1.759(4)
C(1)–N(1)	1.516(3)	B(7)–B(8)	1.776(5)
B(2)–B(3)	1.791(4)	B(7)–B(11)	1.781(5)
B(2)–B(6)	1.800(4)	B(7)–B(12)	1.784(5)
B(2)–B(7)	1.771(4)	B(8)–B(9)	1.793(5)
B(2)–B(11)	1.769(4)	B(8)–B(12)	1.777(5)
B(2)–C(4)	1.584(4)	B(9)–B(10)	1.776(5)
B(3)–B(4)	1.781(4)	B(9)–B(12)	1.779(5)
B(3)–B(7)	1.770(4)	B(10)–B(11)	1.772(4)
B(3)–B(8)	1.774(5)	B(10)–B(12)	1.778(5)
B(4)–B(5)	1.790(5)	B(11)–B(12)	1.773(4)
B(4)–B(8)	1.763(5)	N(1)–C(2)	1.495(4)
B(4)–B(9)	1.758(4)	N(1)–C(3)	1.496(4)
		C(4)–Cl(1)	1.803(3)
B(3)–H(3)	1.05(3)	C(2)–H(21)	0.97(3)
B(4)–H(4)	1.04(3)	C(2)–H(22)	0.92(3)
B(5)–H(5)	1.06(3)	C(2)–H(23)	1.01(3)
B(6)–H(6)	1.11(3)	C(3)–H(31)	0.92(4)
B(7)–H(7)	1.07(3)	C(3)–H(32)	0.91(3)
B(8)–H(8)	1.09(3)	C(3)–H(33)	0.98(3)
B(9)–H(9)	1.07(3)	C(4)–H(41)	0.92(3)
B(10)–H(10)	1.03(3)	C(4)–H(42)	0.83(3)
B(11)–H(11)	1.05(3)		
B(12)–H(12)	1.06(3)		
N(1)–H(13)	0.84(3)		

3.2. Preparation of 1-Me_2NH-2-$ClCH_2$-*closo*-1-$CB_{11}H_{10}$

Treatment of 7-Me_3N-*nido*-7-$CB_{10}H_{12}$ (0.2 g, 1.1 mmol) with ^nBu Li (two equivalents) in THF (10 cm^3) at room temperature under an inert atmosphere gave a precipitate which redissolved immediately on addition of Me_2NBCl_2 (2 cm^3). After 30 min stirring at ambient temperature the volatiles were removed under vacuum and the residue was extracted with CH_2Cl_2. Chromatography of the extract on a silica gel column with CH_2Cl_2 as eluent afforded 1-Me_2NH-2-CH_2Cl-*closo*-1-$CB_{11}H_{10}$ (65 mg, 0.28 mmol, 25.6%), melting point = 200°C. Anal. Found: C, 22.8; H, 8.5; N, 5.7%. $C_4H_{19}N_1Cl_1B_{11}$ Calc.: C, 20.4; H, 8.1; N, 6.0%. ^{11}B NMR chemical shifts (ppm): −6.78 (1B, singlet); −7.30 (1B, doublet, $J(^{11}B–^1H)$ 143 Hz); −12.36 (2B, doublet, $J(^{11}B–^1H)$ 147 Hz); −14.63 (4B, doublet, $J(^{11}B–^1H)$ 109 Hz); −15.38 (3B, doublet, $J(^{11}B–^1H)$ 138 Hz). ^1H NMR chemical shifts (ppm): 3.35 (2H, singlet) (CH_2Cl); 2.97 (6H, singlet) (Me_2N). $^{11}B–^{11}B$

Table 4
Selected bond angles (°) for 1-Me_2NH-2-CH_2Cl-*closo*-$CB_{11}H_{10}$

B6–B2–B3	107.3(0.2)	B12–B7–B11	59.7(0.2)
B7–B2–B3	59.6(0.2)	B4–B8–B3	60.4(0.2)
B7–B2–B6	107.4(0.2)3	B7–B8–B3	59.8(0.2)
B11–B2–B3	107.4(0.2)	B7–B8–B4	108.2(0.2)
B11–B2–B6	59.0(0.2)	B9–B8–B7	108.0(0.2)
B11–B2–B7	60.4(0.2)	B10–B9–B8	107.7(0.2)
C1–B2–B3	58.3(0.2)	B8–B12–B7	59.8(0.2)
C1–B2–B6	58.6(0.1)	B9–B12–B7	108.3(0.2)
C1–B2–B7	104.0(0.2)	B9–B12–B8	60.6(0.2)
C1–B2–B11	103.7(0.2)	B11–B12–B7	60.1(0.2)
C4–B2–B3	124.3(0.2)	B11–B12–B9	108.0(0.2)
C4–B2–B6	118.6(0.2)	B3–C1–B2	62.6(0.2)
C4–B2–B7	125.6(0.3)	B4–C1–B2	114.0(0.2)
C4–B2–B11	122.2(0.2)	B4–C1–B3	62.3(0.2)
C4–B2–C1	123.6(0.2)	B5–C1–B2	114.6(0.2)
B4–B3–B2	108.7(0.2)	B5–C1–B3	114.4(0.2)
C1–B3–B2	59.1(0.2)	B5–C1–B4	62.6(0.2)
C1–B3–B4	59.3(0.2)	B6–C1–B2	62.7(0.2)
C1–B3–B7	104.8(0.2)	B6–C1–B3	114.2(0.2)
C1–B3–B8	104.9(0.2)	B6–C1–B4	113.7(0.2)
B5–B4–B3	107.8(0.2)	B6–C1–B5	62.4(0.2)
C1–B4–B3	58.5(0.2)	N1–C1–B2	116.2(0.2)
C1–B4–B5	58.4(0.2)	N1–C1–B3	115.6(0.2)
C1–B4–B8	104.8(0.2)	N1–C1–B6	119.6(0.2)
C1–B4–B9	104.6(0.2)	H13–N1–C1	109.6(2.3)
C1–B5–B4	59.0(0.2)	C2–N1–C1	114.4(0.2)
C1–B5–B9	104.6(0.2)	C2–N1–H13	104.8(2.3)
C1–B5–B10	104.3(0.2)	C3–N1–C1	114.8(0.2)
C1–B5–H5	117.9(1.4)	C3–N1–H13	103.7(2.3)
B3–B7–B2	60.7(0.2)	C1–N1–C2	108.5(0.3)
B8–B7–B2	108.9(0.2)	H21–C2–N1	102.5(0.2)
B8–B7–B3	60.0(0.2)	H31–C3–N1	108.9(0.2)
B11–B7–B2	59.8(0.2)	H41–C4–B2	111.8(2.1)
B11–B7–B3	107.9(0.2)	H42–C4–B2	115.0(2.4)
B12–B7–B3	107.7(0.2)	H42–C4–H41	100.6(3.0)
B12–B7–B8	59.9(0.2)	C11–C4–B2	115.5(0.2)

COSY correlations were observed between −6.78 and −12.36; −7.30 and −12.36, −14.63, −15.38, −12.36 and −14.63 and −15.38 ppm.

3.3. X-ray diffraction study

Crystal data are given in Table 1.

Direct methods in the program SHELXS-86 yielded a solution whose electron density map revealed the "CB_{11}" structure substituted at the one and two positions. These substituents were clearly not the expected NMe_3 and NMe_2 groupings, and included a heavy atom whose peak was somewhat more than twice the height of those of carbon and nitrogen. This was assumed to be a chlorine atom (on the basis that no other heavy atom had been present in the reaction mixture) and thus the substituents appeared to be CH_2Cl and NMe_2. Least-squares refinement with anisotropic atoms converged with $R = 0.089$. At this point a difference electron density map revealed chemically reasonable positions for all the hydrogen atoms at the highest 19 peaks in the map (0.68–0.36 e Å^{-3}), including the unambiguous location of a hydrogen on the NMe_2 group, suggesting a quaternary nitrogen. The cage hydrogens were refined with a common isotropic temperature factor. Full-matrix least-squares refinement converged to $R = 0.043$ and $R_w = 0.042$ {222 parameters, 1603 reflections, anisotropic (B, C, N, Cl) and isotropic (H) atoms, $w = 1/[\sigma^2(F) + 0.00056F^2]$, max. shift/error = 0.01}. The residual electron density was in the range 0.22 to −0.29 e Å^{-3}. Table 2 lists the final atomic coordinates for non-hydrogen atoms, and Tables 3 and 4 list selected bond lengths and angles, respectively. Atomic scattering factors for neutral atoms and anomalous dispersion corrections were taken from SHELX-76. All calculations were performed using the programs SHELXS-86 [10] SHELX-76 [11] and ORTEP-II [12] on a DEC VAX computer.

Tables of thermal parameters and hydrogen-atom coordinates, and complete lists of bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre.

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