quantity $D^{ion}(exp) = (D_{AB}^{exp} - D_{AB}^{cov})$ against $|\Delta\chi|$ and the continuous curve corresponding to the plot of $D^{ion}(cal)$, the last term of eq 31 against $|\Delta\chi|$, shows quite good agreement. The percentage error in the predicted bond energies based on eq 31 is only 6.8 for the parameters a and b equal to 1.768 and 9.381 when $\Delta\chi$ is expressed in electronvolts and the energy in kcal/mol. Equation 31 resembles that of Matcha[11] and gives similar behavior in the low- and high-value limits for $|\Delta\chi|$. The points in Figure 2 show that a proportionality to $|\Delta\chi|$ as given by Reddy et al.[12] (see eq 7) is not a good approximation, especially for polyatomic molecules.

The novel feature that has emerged in this work is a "rigorous" derivation of covalent binding energy within an electronegativity-based picture. While the derivation of the geometric mean–arithmetic mean results of eqs 25 and 26 have been mainly emphasized so far, the basic relations (22) and (23) directly give the covalent bond energy of the A–B bond in the AB_n molecule and the A–A bond energy, respectively, in terms of the χ and η parameters of the constituent atoms. An equation similar to eq 23 determining the bond energy of homonuclear diatomic molecules has recently been proposed[22] and is found to yield reasonably good results for the energy quantities. However, emphasis here has been on the calculation of the covalent contribution to heteronuclear bond energies from the corresponding homonuclear ones and also new formulation for the ionic contribution to the bond energy as given in eq 30.

(22) Ghanty, T. K.; Ghosh, S. K. *J. Phys. Chem.* **1991**, *95*, 6512–6514.

Concluding Remarks

The present work is concerned with a description of chemical binding in simple polyatomic molecules (AB_n type) through the electronegativity and hardness parameters of the constituent atoms. The key novel feature has been the prediction of the covalent contribution to bond energy using the concepts of bond electronegativity and bond hardness. For a heteronuclear diatomic molecule, the covalent contribution is shown to be given by an average of the geometric and arithmatic means of the bond energies of the corresponding homonuclear diatomics, while, for the covalent contribution to the A–B bond energies in polyatomic AB_n molecules, an n-dependent weighted average of A–A and B–B bond energies is predicted. This term along with a newly derived ionic term yields reasonably good estimates of bond dissociation energies. The present model also provides suitable schemes for obtaining the partial atomic charges. Further studies incorporating explicitly the effects of interaction between the charges as well as an extension to more complicated polyatomic molecules are in progress.

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Development of Carborane Synthons: Synthesis and Chemistry of (Aminoalkyl)carboranes

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A number of (aminoalkyl)-1,2-*closo*-dodecaboranes have been synthesized to provide carboranes with a functional group for covalent incorporation into structures of potential use in the treatment of cancer by boron neutron capture therapy (BNCT). (Phthalimidoalkyl)acetylenes reacted with decaborane to give the corresponding carboranes; removal of the phthalimido group under mild conditions using sodium borohydride in 2-propanol furnished the (aminoalkyl)carboranes which were isolated as their hydrochloride salts. An alternative approach involved the conversion of an (iodoalkyl)- or a ((tosyloxy)alkyl)carborane to the azido derivative which gave the amine on hydrogenation. An effective way of attaching a carborane moiety to thiouracil, which is selectively taken up in melanoma cells, is illustrated by the acylation of two of these amines with thiouracil-5-carboxylic acid.

Introduction

The development of carborane synthons with functional groups capable of covalent incorporation into a variety of different structures offers the potential for synthesizing boron compounds for use in the treatment of cancer by boron neutron capture therapy[1] (BNCT). Use of the amino function and its derivatives has already been described involving various boron cluster compounds,[2-5] but in the case of the highly lipophilic carboranes, only the less basic arylamines have been described. The synthesis of related (aminoalkyl)carboranes has been one of our objectives, but their formation has been greatly complicated by the fact that strongly basic amines do degrade the carborane cluster, converting the closo structure to its anionic nido counterpart.[6-8]

The first example of an aminoalkylcarborane was the reported synthesis of 1-((*N*,*N*-diethylamino)methyl) carborane by the reaction of equimolar amounts of (*N*,*N*-diethylamino)-2-propyne and decaborane in refluxing benzene.[9] However, the reported yield was only 4% and does raise questions regarding its structure. Preparation of bis(aminomethyl)carborane was described by the reaction of bis(halomethyl)carborane with aqueous ammonia, but the product from this reaction was shown conclusively to be the *nido*-carborane derivative.[10] More recently, (aminomethyl)-carborane was reported[11] to be formed by the action of hydrazine

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(1) Barth, R. F.; Soloway, A. H.; Fairchild, R. G. *Cancer Res.* **1990**, *50*, 1061.
(2) Soloway, A. H.; Butler, D. N. *J. Med. Chem.* **1966**, *9*, 411.
(3) Davis, M. A.; Soloway, A. H. *J. Med. Chem.* **1967**, *10*, 730.
(4) Mizusawa, E. A.; Thompson, M. R.; Hawthorne, M. F. *Inorg. Chem.* **1985**, *24*, 1911.
(5) Sneath, R. L., Jr.; Wright, J. E.; Soloway, A. H.; O'Keefe, S. M.; Dey, A. S.; Smolnycki, W. D. *J. Med. Chem.* **1976**, *19*, 1290.
(6) Zakharkin, L. I.; Kalnin, V. N. *Tetrahedron Lett.* **1965**, *7*, 407.
(7) Hawthorne, M. F.; Wegner, P. A.; Stafford, R. C. *Inorg. Chem.* **1965**, *4*, 1675.
(8) Varadarajan, A.; Sharkey, R. M.; Goldgenberg, D. M.; Hawthorne, M. F. *Bioconjug. Chem.* **1991**, *2*, 102.
(9) Heying, T. L.; Ager, J. W.; Clark, S. L.; Mangold, D. J.; Goldstein, H. L.; Hillman, M.; Polak, R. J.; Szmanski, J. W. *Inorg. Chem.* **1963**, *2*, 1089.
(10) Zakharkin, L. I.; Grebennikov, A. V. *Izv. Akad. Nauk SSSR, Ser. Chim.* **1966**, 2019.
(11) Nakagawa, T.; Watanabe, H.; Yoshizaki, T. Japan Patent 7,031,940; *Chem. Abstr.* **1970**, *74*, 100213t.

0020-1669/92/1331-1955$03.00/0

upon (phthalimidomethyl)carborane. The authors claimed that they had isolated the compound as its hydrochloride salt but failed to provide supporting analytical documentation to justify the purported structure. Their conclusion was especially surprising in view of the fact that strongly basic amines[12] and hydrazine[13] per se, albeit in large excess and at reflux, does degrade the carborane moiety generating the hydrazinium salts of the corresponding *nido*-undecaborate structure.

In view of our interest, we undertook to confirm their observation, to synthesize other higher homologues of the (aminoalkyl)carboranes and their derivatives, and to determine the coexistence of the *closo*-carborane moiety in the same structure containing alkylamines. At the same time, this provided an opportunity to explore the stereoelectronic properties of the carborane nucleus and its effect upon nucleophilic displacement reactions.

Experimental Section

At the Australian Nuclear Science and Technology Organisation, ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-GX-400 Fourier transform spectrometer. In all cases the solvent was $(CD_3)_2SO$. Infrared spectra were run on a BioRad FTS-60 FTIR spectrometer, and samples were prepared as KBr disks. Mass spectra were recorded on a Vacuum Generator MM 12-12 quadropole FT mass spectrometer (matrix, PEG 200; collision gas, xenon) using an atom beam at 8 kV and 2 mA. At the Ohio State University, ^1H NMR were obtained at the Chemical Instrumentation Center and the College of Pharmacy using Bruker AM 500 and AC 250 spectrometers. IR spectra were obtained on an RFX40 FTIR spectrometer (Laser Precision Corp.). Mass spectra were obtained by use of a FG 70-2505 mass spectrometer and ionization through fast atom bombardment (FAB) using NBA (3-nitrobenzyl alcohol) or MB (Magic Bullit) as matrix compounds. Elemental analyses were performed either at the Microanalytical Unit, ANU, Canberra, ACT, or Galbraith Laboratories, Inc., Knoxville, TN. Melting points were determined on a Fisher-Johns apparatus and are uncorrected. TLC plates with Silica Gel 60 F-254 and Silica Gel 60 from E. Merck were used for TLC and column chromatography. 3-Butynyltosylate and other acetylenic compounds were obtained from Farchan Lab, Gainesville, FL.

1-(Phthalimidomethyl)-1,2-dicarba-*closo*-dodecaborane (1). *N*-Propargylphthalimide (25 g, 0.135 mol) and decaborane–acetonitrile adduct (27 g) were refluxed in toluene (550 mL) for 2 h. The cooled solution was filtered from a fine insoluble precipitate, the filtrate was evaporated under reduced pressure, and the residue was stirred with ethanol (120 mL) for 3 h until gas evolution had almost ceased. The resulting solid was collected, washed with a small amount of cold ethanol, and crystallized from toluene (120 mL). The product (27 g, 66%) was obtained as small lustrous crystals, mp 200–202 °C (lit.[11] mp 204–205 °C). IR (max, CO): 1775, 1724, (BH) 2580, 2600 cm^{-1}. ^1H NMR: δ 1.10–3.10 (b, BHs), 5.30 (bs, H1), 4.35 (s, H3), 7.95 (sym.m, arom). ^{13}C NMR δ 62.66, J_{CH} = 199.5, C1; 74.11, C2; 40.33, J_{CH} = 147.8, C3; 167.42, C4; 131.54, C5; 124.13, J_{CH} = 166.9, C6; 135.45, J_{CH} = 166.1, C7. (All J values are given in hertz throughout.) FAB-MS: m/z 303 (35%, M, negative mode).

Reaction of Hydrazine Hydrate with 1-(Phthalimidomethyl)-1,2-dicarba-*closo*-dodecaborane (1). Compound **1** (7.5 g, 0.025 mol) and hydrazine hydrate (3.1 g, 2 mol equiv) in ethanol (250 mL) were heated under reflux for 3.5 h. A white precipitate of phthalhydrazide began to separate after ca. 2 h. The reaction mixture was cooled to room temperature and then to 0 °C for 2 h; the solid was filtered, washed with a cold ethanol, and dried (3.4 g). Removal of the solvent under reduced pressure left a thick oil which, when dissolved in ethanol (20 mL), deposited a further amount of phthalhydrazide (0.38 g, total 93%) on standing overnight. The filtrate was evaporated under reduced pressure and redissolved in ethanol (12 mL) to which was added ethyl ether (15 mL) and petroleum ether (30 mL). On cooling, 1.40 g of crystals were deposited, mp 165–170 °C. Recrystallization from ethanol (6 mL), ethyl ether (6 mL) and petroleum ether (40 mL) gave the hydrazinium salt of (aminomethyl)-*nido*-dodecahydroundecaborate (**2**) (0.94 g), mp 170–173 °C (dec). Anal. Calcd for $C_3H_{20}N_3B_9$: C, 18.4; H, 10.2; N, 21.5. Found: C, 18.5; H, 10.0; N, 21.6. ^1H NMR: δ 1.87 (bs, H1), 2.65 (d, J = 13.3) and 2.85, (d, J = 13.3), H3, 6.32 (bs, $N_2H_5^+$). FAB-MS: m/z 33 (100%, $N_2H_5^+$, positive mode); m/z 162 (100%, M, negative mode).

The tetramethylammonium salt of the nido compound **2** was prepared by adding a 50% solution of tetramethylammonium bromide in water to an equimolar amount of hydrazinium salt in a small volume of water. The precipitate, which formed immediately, was twice recrystallized from ethanol–ethyl ether (2:1) to give the product, mp >230 °C. Anal. Calcd for $C_7H_{27}N_2B_9$: C, 35.6; H, 11.4; N, 11.8. Found: C, 35.7; H, 11.2; N, 11.6. ^1H NMR: δ 1.85, bs, H1; 2.64, d, J = 13.2 and 2.85, d, J = 13.2, H3; 3.10, s, Me's. FAB-MS: m/z 74 (100%, Me_4N^+, positive mode); 162 (100%, M, negative mode).

(((2-(Hydroxymethyl)benzoyl)amino)methyl)-*o*-carborane (3). A stirred suspension of **1** (2.60 g, 8.6 mmol) in 2-propanol (77 mL) and water (13 mL) was treated with sodium borohydride (1.63 g, 43 mmol). The solid dissolved after ca. 1 h; stirring was continued for 22 h. The separated crystals were collected and combined with the residue from evaporation of the solvent. The mixture was vigorously extracted with hot water (×2) and the dried product (2.45 g) was recrystallized from ethanol (932 mL) and water (11 mL) to give **3** (1.90 g, 66%), mp 188–192 °C. It was homogeneous by TLC (ethyl acetate/petroleum ether, 1:3), an analytical sample, mp 190–192 °C. Anal. Calcd for $C_{11}H_{21}NO_2B_{10}$: C, 43.0; H, 6.8; N, 4.6. Found: C, 42.7; H, 7.1; N, 4.2. IR (max, CO): 1631, (BH) 2578 cm^{-1}. ^1H NMR: δ 1.20–3.20, b, BHs; 5.11, bs, H1; 4.03, d, J = 6.6, H3; 4.63, d, J = 5.4, H4; 5.29, t, J = 5.4, OH; 9.10, t, J = 6.5, NH; 7.34–7.58, m (4 H), arom. ^{13}C NMR: δ 62.97, J_{CH} = 197.1, C1; 77.21, C2; 44.51, J_{CH} = 144.6, C3; 169.77, C4; 134.42, C5; 141.92, C10; 61.85, J_{CH} = 142.2, C11. FAB-MS: m/z 307 (78%, M, negative mode).

(Aminomethyl)-*o*-carborane Hydrochloride (4). A solution of **3** (2.0 g, 6.5 mmol) in glacial acetic acid (24 mL), water (6.0 mL), and concentrated HCl (6.0 mL) was heated on a steam bath for 2 h. The clear, colorless solution was evaporated under reduced pressure to dryness and the residue was stirred with chloroform (40 mL) for 2 h to remove the phthalide (**5**) (identified by TLC). The remaining solid (1.25 g) was taken up in acetone (200 mL), filtered, and concentrated to half its volume. The product slowly separated on cooling (1.04 g, 83%) (**4**), mp 220–280 °C (sublimes to the cool part of melting point tube outside the block). Anal. Calcd for $C_3H_{15}NB_{10}$·HCl: C, 17.2; H, 7.6; N, 6.7; Cl, 16.9. Found: C, 16.9; H, 7.6; N, 6.4; Cl, 17.0. IR (max, BH): 2579, 2595 cm^{-1}. ^1H NMR: δ 1.20–3.30, b, BHs; 5.43, bs, H1; 3.80, s, H3; 8.86, s, NH_3^+. ^{13}C NMR: δ 62.90, J_{CH} = 197.9, C1; 71.65, C2; 43.33, J_{CH} = 147.8, C3. FAB-MS: m/z 174 (100%, M + H, positive mode).

1-(3-Phthalimidopropyl)-1,2-dicarba-*closo*-dodecaborane (6). *N*-(4-Pentynyl)phthalimide[14] (28.8 g, 0.135 mol) and decaborane–acetonitrile adduct (27.0 g) were heated under reflux in toluene (500 mL) for 2.5 h. The solution was filtered from insoluble material, cooled, and filtered again. Removal of the solvent left a semisolid residue which was triturated with ethanol (60 mL) and allowed to stand overnight. The granular, pale cream colored product was collected, washed with a little ice-cold ethanol, and dried in air (26.5 g, 59%), mp 178–182 °C. For analysis a sample recrystallized from ethanol was obtained as almost colorless rods and prisms, mp 181.5–183 °C. Anal. Calcd for $C_{13}H_{21}NO_2B_{10}$: C, 47.1; H, 6.3; N, 4.2. Found: C, 47.2; H, 6.6; N, 4.0. IR (max, COs): 1714, 1764 (BH) 2585 cm^{-1}. ^1H NMR: δ 1.20–3.20, b, BHs; 5.12, bs, H1; 2.32, m, H3; 1.74, m, H4; 3.54, t, J = 6.7, H5; 7.84, m, arom. ^{13}C NMR: δ 64.22, J_{CH} = 197.1, C1; 76.95, C2; 34.89, J_{CH} = 129.9, C3; 29.07, J_{CH} = 130.7, C4; 37.51, J_{CH} = 139.0, C5; 168.91, C6; 132.70, C7; 124.00, J_{CH} = 170.0, C8; 135.30, J_{CH} = 164.9, C9. FAB-MS: m/z 331 (46%, M, negative mode).

(((2-(Hydroxymethyl)benzoyl)amino)propyl)-*o*-carborane (7). Compound **6** (2.85 g, 8.6 mmol) was reduced by the procedure used in preparing **3**. The dried product (2.70 g, 94%) was crystallized from ethanol (13 mL) and water (7 mL) to give **7** (2.02 g, 70%), mp 152–154 °C. Anal. Calcd for $C_{13}H_{25}NO_2B_{10}$·0.4H_2O: C, 45.6; H, 7.5; N, 4.1. Found: C, 45.9; H, 7.7; N, 4.2. IR (max, CO): 1613, (BH) 2569 cm^{-1}. ^1H NMR: δ 1.30–3.10, b, BHs; 5.19, bs, H1; 2.34, m, H3; 1.66, m, H4; 3.20, q, J = 6.3, H5; 4.58, d, J = 5.6, H6; 5.23, t, J = 5.7, OH; 8.38, t, J = 5.6, NH; 7.26–7.55, m, arom. ^{13}C NMR: δ 64.09, J_{CH} = 195.5, C1; 77.26, C2; 35.27, J_{CH} = 132.8, C3; 30.02, J_{CH} = 129.6, C4; 38.93, J_{CH} = 135.9, C5; 169.20, C6; 136.08, C7; 127.52, 128.09, 128.44, 130.57, 141.16, C12; 61.97, J_{CH} = 142.3, C13. FAB-MS: m/z 335 (100%, M).

(Aminopropyl)-*o*-carborane Hydrochloride (8). A solution of the compound **7** (3.0 g, 9 mmol) in glacial acetic acid (36 mL), water (9 mL), and concentrated hydrochloric acid (9 mL) was heated on a water bath for 3 h. After removal of the solvent the residue was left overnight and stirred with methylene chloride (50 mL) for 2 h. The finely crystalline hydrochloride was collected, washed with the same solvent, and air-dried (2.01 g, 94%), mp >300 °C with some sublimation from ca. 260 °C. An analytical sample was prepared from ethyl acetate–petroleum

(12) Hawthorne, M. F.; Young, D. C.; Garrett, D. M.; Owen, D. A.; Schwerin, S. G.; Tebbe, F. N.; Wegner, P. A. *J. Am. Chem. Soc.* **1968**, *90*, 862.

(13) Grafstein, D.; Bobinski, J.; Dvorak, J.; Smith, H.; Schwartz, N.; Cohen, M. S.; Fein, M. M. *Inorg. Chem.* **1963**, *2*, 1120.

(14) Neumeyer, J. L.; Incho, H. H. German Patent 1,217,693; *Chem. Abstr.* **1966**, *65*, 8830h.

ether. Anal. Calcd for $C_5H_{19}NB_{10}$·HCl: C, 25.3; H, 8.5; N, 5.9; Cl, 15.0. Found: C, 25.2; H, 8.8; N, 5.6; Cl, 15.0. IR (max): 2575, 2593 (BH). ^{1}H NMR: δ 1.30–3.20, b, BHs; 5.27, bs, H1; 2.38, m, H3; 1.75, m, H4; 2.75, m, H5; 8.05, bs, NH_3^+. ^{13}C NMR: δ 64.26, J_{CH} = 197.9, C1; 76.74, C2; 34.35, J_{CH} = 133.1, C3; 27.84, J_{CH} = 130.3, C4; 38.67, J_{CH} = 143.9, C5. FAB-MS: m/z 202 (100%, M + H, positive mode).

1-(2-((*p*-Tolylsulfonyl)oxy)ethyl)-*o*-carborane (9). A solution of 3-((*p*-tolylsulfonyl)oxy)butyne (2.25 g, 10 mmol) in dry toluene (30 mL) was stirred with the decaborane–acetonitrile adduct (2 g) at 90 °C for 5 h. The mixture was cooled to room temperature and toluene was removed under reduced pressure. The residue was extracted in ethyl ether and the extract evaporated to dryness. The crude product was purified by column chromatography on silica gel using 4:1 hexane–ethyl acetate; compound **9** (2.21 g, 65%) was recrystallized from ethyl ether–hexane, mp 112 °C. Anal. Calcd for $C_{11}H_{22}O_3SB_{10}$: C, 38.5; H, 6.5; S, 9.4. Found: C, 38.5; H, 6.4; S, 9.6. ^{1}H NMR ($CDCl_3$): δ 2.47 (s, CH_3), 2.61 (t, $-CH_2-$, J = 6.1 Hz), 3.66 (bs, carborane CH) 4.10 (t, $-SO_2O-CH_2-$), 7.38 (d, aromatic H), and 7.77 (d, aromatic H). FAB-MS: m/z 343 (M^+). IR (max): 1180, 1360 ($-SO_2-$), 2575 and 1360 cm^{-1} (BH).

1-(2-Azidoethyl)-*o*-carborane (10). Procedure A. A mixture of **9** (340 mg, 1 mmol), sodium azide (275 mg, 5 mmol), and acetone (50 mL) was heated under reflux for 5 h. The mixture was cooled to room temperature, solvent was removed, and the residue was extracted with ethyl ether. The evaporation left a syrupy residue which was purified by column chromatography with silica gel and 6:1 hexane–ethyl acetate; compound **10** (150 mg, 70%) was obtained as colorless syrup. IR (neat): 2150 (N_3) and 2590 cm^{-1} (BH). ^{1}H NMR ($CDCl_3$): δ 2.47 (t, $-CH_2-$, J = 6.9 Hz), 3.48 (t, N_3-CH_2-) and 2.47 (bs, carborane C–H). FAB-MS: m/z 213 (M^+). Anal. Calcd for $C_4H_{15}N_3B_{10}$: C, 22.5; H, 7.1; N, 19.7. Found: C, 22.5; H, 7.2; N, 19.7.

Procedure B. A mixture of 1-(2-iodoethyl)-*o*-carborane[15] (**11**) (300 mg, 1 mmol), sodium azide (275 mg, 5 mmol), and acetone (50 mL) was heated under reflux for 3 h. The product from the reaction mixture was the azido compound **10** (160 mg, 75%), identical by IR and NMR with the sample obtained by procedure A.

1-(2-Acetamidoethyl)-*o*-carborane (13). A solution of **10** (210 mg, 1 mmol) in methanol (20 mL) containing acetic acid (120 mg) was hydrogenated at 25 °C for 18 h. Filtration and evaporation of the solvent gave the acetate salt, **12** (300 mg), of (aminoethyl)-*o*-carborane as a gummy material from which the acetamido derivative, **13**, was obtained as a crystalline solid by reaction with acetic anhydride in methanol. Compound **13** (240 mg, 98%) was obtained directly by hydrogenating **10** (210 mg) in methanol (20 mL) containing acetic anhydride (200 mg). Crystallization of **13** from ethyl ether–hexane yielded a product, mp 95 °C (sharp). ^{1}H NMR ($CDCl_3$) δ 5.85 (bs, NH), 3.70 (bs, carborane CH), 3.36 (dt, $N-CH_2-$), 2.45 (t, $-CH_2-$), and 1.98 ($COCH_3$). FAB-MS: m/z 230 (M + H$^+$). Anal. Calcd for $C_6H_{19}ONB_{10}$: C, 31.4; H, 8.3; N, 6.1. Found: C, 31.2; H, 8.0; N, 5.9.

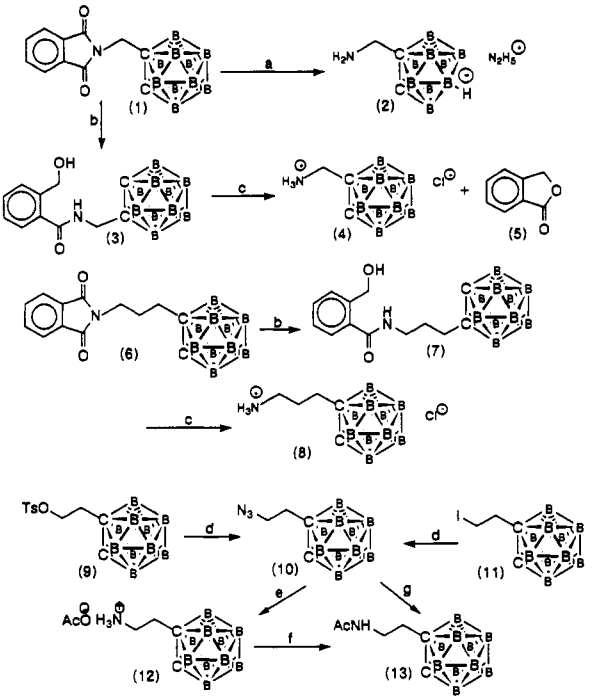
***N*^{1}-Phenyl-*N*^{3}-(*o*-carboranylmethyl)thiourea (14).** The reaction of molar equivalent amounts of **4**, triethylamine, and phenyl isothiocyanate and a catalytic quantity of DMAP in methylene chloride for 12 h gave a nearly theoretical yield of **14**. It was crystallized from aqueous ethanol, mp 178 °C (sharp). Anal. Calcd for $C_{10}H_{10}N_2SB_{10}$: C, 38.9; H, 6.5; N, 9.1. Found: C, 39.3; H, 6.4; N, 9.2. IR (max) (thioamide): 1540, (BH) 2576 cm^{-1}. ^{1}H NMR: δ 5.10, bs, H1; 4.44, d, J = 6.4, H3; 8.15, m, H4; 9.93, s, H6; 7.16, m, 7.36, m, arom. FAB-MS: m/z 309 (79%, M + H, positive mode).

***N*^{1}-Phenyl-*N*^{3}-(3-*o*-carboranylpropyl)thiourea (15).** *N*^{1}-Phenyl-*N*^{3}-(3-*o*-carboranylpropyl)thiourea was prepared by the same procedure described for **14**, using the amine hydrochloride, **8**. The product was purified by chromatography on silica gel using hexane–ethyl acetate (2:1) as the eluant and crystallized from aqueous ethanol, mp 145 °C. Anal. Calcd for $C_{12}H_{24}N_2SB_{10}$·0.25H_2O: C, 42.3; H, 7.2; N, 8.2. Found: C, 42.3; H, 6.8; N, 8.2. IR (max, thioamide): 1544, (BH) 2571 cm^{-1}. ^{1}H NMR: δ 5.21, bs, H1; 2.30, m, H3; 1.70, m, H4; 3.43, bs, H5; 7.75, bs, H6; 9.50, bs, H8; 7.12, m, 7.35, m, arom. FAB-MS: m/z 336 (100%, M, negative mode).

2-Thio-5-((carboranylmethyl)carboxamido)uracil (16). Thiouracil-5-carboxylic acid (0.86 g, 5 mmol), suspended in DMF (10 mL), was dissolved by the addition of *N*-methylmorpholine (0.56 mL, 5 mmol). The stirred solution was cooled to −20 °C and treated with isobutyl chloroformate (0.67 mL, 5 mmol). After 3 min a solution of **5** (1.05 g, 5 mmol) in DMF (5 mL), neutralized with *N*-methylmorpholine (0.56 mL), was added to the mixed anhydride and a total transfer was achieved with an additional 2 mL of DMF. After being stirred for 25 min, the mixture was allowed to warm to room temperature. After 90 min, the crystalline precipitate was filtered, washed with ice water, and dried (fraction 1, 0.55 g). The filtrate, collected before the water washings, was evaporated, and the solid residue was stirred with a mixture of ethyl acetate (30 mL) and water (30 mL) for 10 min, filtered, and dried (fraction 2, 0.77 g). A third fraction was obtained from the organic layer of the above filtrate which was washed with 1 N hydrochloric acid (2 × 10 mL), water, and sodium bicarbonate solution, dried ($MgSO_4$), and evaporated. The residue was suspended in a little cold ethyl acetate and collected (fraction 3, 0.16 g). The combined fractions were dissolved in methanol (80 mL); the solution was filtered and concentrated until crystals began to separate. After 16 h, the product was collected and dried (1.15 g, 77%), mp 340 °C. TLC (ethyl acetate): R_f 0.79. Anal. Calcd for $C_8H_{17}N_3O_2SB_{10}$·1.0CH_3OH: C, 30.1; H, 5.8; N, 11.7. Found: C, 29.7; H, 5.7; N, 11.6. IR (max, CO): 1693, (BH) 2586 cm^{-1}. ^{1}H NMR: δ 5.07, s, H1; 4.10, d, J = 6.8, H3; 8.01, s, H4; 9.20, t, J = 6.8, NH (amide). ^{13}C NMR: δ 63.02, J_{CH} = 197.1, C1; 77.01, C2; 43.93, J_{CH} = 145.0, C3; 162.14, J_{CNH} = 8.0, C4; 108.47, C5; 147.70, J_{CH} = 183.6, C6; 162.79, poorly resolved triplet, C7; 177.01, J_{CNH} = 8.7, C8; and 49.6q, J_{CH} = 139.1, MeOH. FAB-MS: m/z 326 (100%, M − H, negative mode).

2-Thio-5-((carboranylpropyl)carboxamido)uracil (17). The same method and scale were used as described for **16** utilizing **8** as the amine hydrochloride. In this instance, the first precipitate was stirred with water for 30 min to give fraction 1 (0.55 g). When the residue from the filtrate (DMF) was then treated in the same way, no material remained undissolved. The organic layer was washed with acid and bicarbonate, dried, and concentrated under reduced pressure until crystals began to separate. These were collected after 30 min (fraction 2, 0.66 g). Both fractions were combined and dissolved in methanol (50 mL), and the solution was concentrated until crystallization. The product was separated after 16 h (0.88 g, 54%), mp 318–320 °C. TLC (ethyl acetate): R_f 0.66. Anal. Calcd for $C_{10}H_{21}N_3O_2SB_{10}$·0.25$CH_3OH$: C, 33.9; H, 6.1; N, 11.6. Found: C, 34.3; H, 5.7; N, 11.7. IR (max, COs): 1692, 1701 (BH) 2580 cm^{-1}. ^{1}H NMR: δ 5.19, bs, H1; 2.26, m, H3; 1.67, m, H4; 3.23, q, J = 6.5, H5; 7.96, s, H6; 8.67, t, J = 5.9, NH (amide). ^{13}C NMR: δ 64.13, J_{CH} = 197.1, C1; 77.16, C2; 35.21, J_{CH} = 132.3, C3; 30.29, J_{CH} = 130.0, C4; 38.67, J_{CH} = 140.7, C5; 162.20, J_{CNH} = 7.2, C6; 109.44, C7; 146.82, J_{CH} = 183.6, C8; 162.45, unresolved triplet due to J_{CNH}, C9; 176.84, J_{CNH} = 9.5, C10. FAB-MS: m/z 355 (100%, M, negative mode).

Scheme I



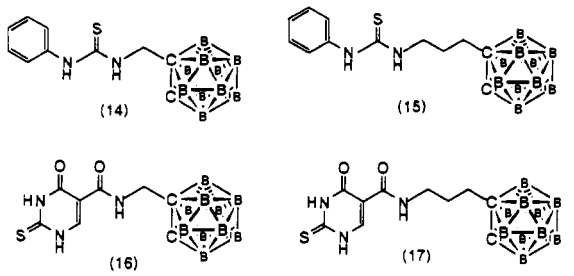
a) Hydrazine,EtOH,reflux,3.5h; b) $NaBH_4$,iPrOH,RT,20h; c) HCl,HOAc,95°,2h; d) NaN_3,acetone,reflux,5h; e) 5%Pd/C,MeOH,HOAc; f) MeOH,Ac_2O; g) 5%Pd/C,MeOH,Ac_2O.

Results and Discussion

On reinvestigation, the product from reaction of (phthalimidomethyl)carborane (**1**) with hydrazine was not the reported[11] (aminomethyl)carborane but was in fact the hydrazinium salt of the *nido*-dodecahydroundecaborate (**2**). This compound was formed by the removal of the phthalyl group and by the abstraction

(15) Zakharkin, L. I.; Brattsev, V. A.; Chapovskii, Y. A. *Zh. Obsch. Khim.* **1965**, *35*, 2160.

Scheme II



of a boron atom from the 3 or 6 position of the carborane cage.[12] Since these boron atoms are not equivalent, this may account for the observation that the methylene protons in the ^{1}H NMR spectrum appear as a pair of doublets at δ 2.85 and 2.65, J = 13.3 Hz. This nido anion was readily characterized as its tetramethylammonium salt.

A more recent and milder method for the removal of the phthalyl group has been reported.[16] This is a stepwise method, employing the reduction of the phthalimido moiety by sodium borohydride to an *o*-(hydroxymethyl)benzoyl derivative which is then hydrolyzed under acidic conditions to generate the amine hydrochloride in excellent yield. By use of this method the (phthalimidomethyl)- and (phthalimidopropyl)carboranes **1** and **6** were respectively converted to the corresponding (aminoalkyl)carborane hydrochlorides **4** and **8** (Scheme I).

An alternative route for the preparation of alkylamines is by the displacement of a (*p*-tolylsulfonyl)oxy group or a halide by the nucleophilic azide ion and its subsequent catalytic hydrogenation to the amine.[17,18] However, when either (chloromethyl) or (bromomethyl)carborane was subjected to such nucleophilic displacement by the azide moiety, starting material was recovered unchanged. Such a lack of reactivity of these halocarboranes is in sharp contrast to the reaction of the other alkyl halides but is in agreement with other studies whereby reactivity of the halides is enhanced following conversion to the nido analogue.[19] This has recently been described as being due to the unique stereoelectronic features of the carborane cage.[8] Support for this hypothesis is found in the fact that degradation of the cage to its nido structure significantly increases the reactivity and displacability of halogens and other leaving groups. Progressively insulating these leaving groups from the carborane moiety, by inserting methylenes, produces halocarboranes which understandably more closely resemble alkyl halides. As the first example, we synthesized 1-(2-((*p*-tolylsulfonyl)oxy)ethyl)-*o*-carborane (**9**) from commercially-available 3-butynyl tosylate and acetonitrile–decaborane complex. This carborane reacted readily with sodium azide in refluxing acetone displacing the tosyloxy function and yielding the corresponding azido structure (**10**). The same compound was also obtained from 1-(2-iodoethyl)-*o*-carborane (**11**).[15] This azido compound was hydrogenated in the presence of acetic acid over 5% Pd on charcoal and gave the corresponding amine salt (**12**) which was readily characterized as the crystalline 1-(2-(acetamido)ethyl)-*o*-carborane (**13**) (Scheme I). Compound **13** was obtained in nearly quantitative yield by performing the hydrogenation reaction of **10** in the presence of acetic anhydride. Higher homologues containing both the carborane and amino moieties were readily obtained by the insertion of additional methylene groups.

In addition to acylation as a means of characterizing the aminocarboranes, it has been possible to characterize these amines as their corresponding phenylthioureas (**14** and **15**) and as amide derivatives of the thiouracil-5-carboxylic acid (**16** and **17**) (Scheme II). The latter reactions provide a very effective way of attaching a carborane moiety to thiouracil. Such boron-containing structures may have potential for becoming selectively incorporated into melanoma cells.[20]

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(16) Osby, J. O.; Martin, M. G.; Ganem, B. *Tetrahedron Lett.* **1984**, *25*, 2093.
(17) Anisuzzaman, A. K. M.; Whistler, R. L. *J. Org. Chem.* **1972**, *37*, 1201.
(18) Whistler, R. L.; Anisuzzaman, A. K. M. *Carbohydr. Chem.* **1980**, *8*, 297.
(19) Zakharkin, L. I.; Grebennikov, A. V. *Izv. Akad. Nauk SSSR, Ser. Chim.* **1960**, *11*, 2019.
(20) Corderoy-Buck, S.; Wilson, J. G.; Gabel, D.; Tjarks, W.; Moore, D. E.; Chandler, A. *Proc. Aust.-Jpn. Workshop Malignant Melanoma, 4th* **1990**, 51.

Notes

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Preparation of Tin Nitride via an Amide Imide Intermediate[†]

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Introduction

Binary nitrides of most elements can be prepared under appropriate conditions. These compounds show an extraordinary range of physical and chemical properties, more so than the oxides which they resemble in some respects. The nitrides are classified[1] as ionic, mostly represented by groups I and II; covalent, mostly represented by groups III and IV; and interstitial, formed by many metals. As the names imply, the properties of these materials are somewhat predictable, particularly those of the ionic nitrides, which are salt-like, and of the interstitial nitrides, which can be considered as metals with expanded lattices containing nitrogen in interstitial positions. The covalent nitrides show a wider range of properties. Some of the latter are solids with very high melting points and low electrical conductivities (such as BN, AlN, and Si_3N_4) while others are volatile or can form the basis of polymeric networks (such as $(CN)_2$ or PN). In addition to these covalent nitrides, there are some that are semiconductors and have limited thermal stabilities (such as Cu_3N, Zn_3N_2, and Sn_3N_4). It is the latter that appeared to be of interest because of potential applications in the development of electronic devices. Tin nitride was selected for

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(1) Brown, B. R. In *Mellor's Comprehensive Treatise on Inorganic and Theoretical Chemistry*; Eldridge, A. A., Ed.; Longmans: London, 1964; Vol. 8, Supplement I, Part I, pp 150-239.

0020-1669/92/1331-1958$03.00/0