Articles

Synthesis of Amine Derivatives of the Polyhedral Borane Anion $[B_{20}H_{18}]^{4-}$

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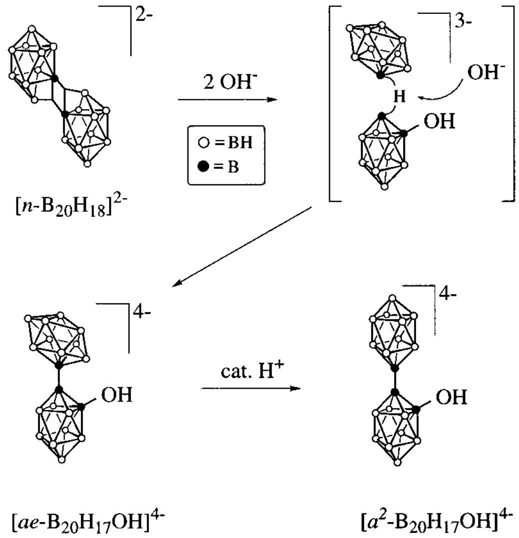
Ethylenediamine (en) reacts with the polyhedral borane anion $[n\text{-}B_{20}H_{18}]^{2-}$, in the presence or absence of strong nonnucleophilic auxiliary bases, to produce the $[ae\text{-}B_{20}H_{17}(en)]^{3-}$ anion. In either case, substitution is accompanied, to an approximately equal extent, by reduction of the starting material to form $[a^2\text{-}B_{20}H_{18}]^{4-}$. As found with similar substituted systems derived from this 20-boron structure, $[ae\text{-}B_{20}H_{17}(en)]^{3-}$ may be conveniently rearranged to the $[a^2\text{-}B_{20}H_{17}(en)]^{3-}$ anion. A more convenient synthesis of the known $[ae\text{-}B_{20}H_{17}NH_3]^{3-}$ ion, which employs acetonitrile as the source of the NH_3 ligand instead of liquid ammonia, is also described.

Introduction

The electrophilic polyhedral borane $[n\text{-}B_{20}H_{18}]^{2-}$ anion[1] has great potential as a precursor in reductive substitution reactions leading to new derivative chemistry. The $[n\text{-}B_{20}H_{18}]^{2-}$ anion consists of a pair of 10-boron-atom cages connected by a pair of three-center, two-electron bonds providing an electron-deficient region of the structure which is susceptible to attack by nucleophiles. The reductive substitution chemistry of this species with hydroxide and alkoxide ions, producing the $[B_{20}H_{17}OH]^{4-}$ and $[B_{20}H_{17}OR]^{4-}$ ions, respectively, was first elucidated three decades ago (Scheme 1).[2] Since that time, however, the potential of the $[n\text{-}B_{20}H_{18}]^{2-}$ ion to form new derivatives has remained virtually unexplored.

Recent interest in the production of new boron-rich, water-soluble species for application in boron neutron capture therapy[3] prompted our reexamination of the reductive substitution chemistry of the $[n\text{-}B_{20}H_{18}]^{2-}$ ion. Subsequently, the ammonia-substituted anions $[ae\text{-}B_{20}H_{17}NH_3]^{3-}$ and $[a^2\text{-}B_{20}H_{17}NH_3]^{3-}$ have been prepared[4] by the reaction of liquid ammonia with $[n\text{-}B_{20}H_{18}]^{2-}$ in the presence of a suitable base. Both of these isomeric ammonio derivatives, when encapsulated in small unilamellar liposomes, have been shown to be effective in the tumor-selective concentration of boron *in vivo*.[4] A more convenient synthetic method has now been discovered for the production of the isomeric $[B_{20}H_{17}NH_3]^{3-}$ anions which circumvents the use of liquid ammonia and instead uses acetonitrile as the source of the NH_3 ligand.

Scheme 1



The demonstrated success of the $[B_{20}H_{17}NH_3]^{3-}$ anions as potential neutron capture target species suggested the development of a more general method for the production of other amine-substituted derivatives of $[B_{20}H_{18}]^{4-}$. Ethylenediamine was selected as a useful substituent since it demonstrates the synthesis of an amine derivative which contains a free functional group capable of conjugation to organic substrates. Reported here are the results of our investigation of the synthesis of isomeric $[B_{20}H_{17}NH_2CH_2CH_2NH_2]^{3-}$ anions and further observations of related chemistry.

Experimental Section

Materials. Synthetic reactions were performed under nitrogen with Schlenk techniques. The polyhedral borane starting materials were prepared by published methods,[1,5] and $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ was dried over P_2O_5 under reduced pressure. Acetonitrile and THF were dried under nitrogen over CaH_2 and Na, respectively, and distilled prior to use. Ethylenediamine and ethanol were distilled over Na and magnesium ethoxide, respectively, and stored under nitrogen over 3A molecular sieves. Sodium hydride (95%), $Li[HNCH_2CH_2NH_2]$, potassium *tert*-butoxide (95%) and lithium diisopropylamide (LDA, 97%)

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(1) Chamberland, B. L.; Muetterties, E. L. *Inorg. Chem.* **1964**, *3*, 1450−1456. Hawthorne, M. F.; Pilling, R. L.; Stokely, P. F. *J. Am. Chem. Soc.* **1965**, *87*, 1893−1899.

(2) Hawthorne; M. F., Pilling; R. L.; Garrett, P. M. *J. Am. Chem. Soc.* **1965**, *87*, 4740−4746.

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were purchased from Aldrich, opened and stored in a drybox, and used as supplied without further purification. The cation exchange resin used was Bio-Rad AG50W-X8, 50−100 mesh.

Physical Measurements. All ^{11}B NMR spectra were obtained with a Bruker AM-500 instrument at 160 MHz. Boron chemical shifts were externally referenced to $BF_3 \cdot Et_2O$ in C_6D_6; peaks upfield of the reference are designated as negative. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-360 spectrometer at 360 and 90.5 MHz, respectively, and externally referenced to TMS. Electrospray ionization mass spectra (ESI-MS) were obtained by injection of dissolved samples (50% CH_3CN/H_2O) into an ionspray source (typical flow 10 μL/min, orifice voltage 30 V) connected to a quadrupole mass spectrometer (PE Sciex API III, Perkin-Elmer, Norwalk, CT) which was scanned from *m/z* 50−500 (step size 0.1 dalton; scan speed 5 s). The mass spectrometer was operated in the negative ion mode using signals of the multiply charged ion series from a separate introduction of polypropylene glycol. Cyclic voltammograms were obtained with a Bioanalytical Systems Inc. CV-27 voltammograph using $[Et_4N][PF_6]$ as the supporting electrolyte in CH_3CN vs Ag/AgCl. HPLC measurements were carried out on a Beckman System Gold apparatus fitted with a reverse-phase C18 column and UV detector (λ = 292 nm utilized), using CH_3CN and 1 M aqueous Bu_4NBr as eluents.

$[Et_4N]_3[1\text{-}(2'\text{-}B_{10}H_9)\text{-}2\text{-}NH_2CH_2CH_2NH_2\text{-}B_{10}H_8]$, Designated $[Et_4N]_3$-[*ae*-$B_{20}H_{17}$(en)]. Solid $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ (4.0 g, 10 mmol) was added to a cooled stirred suspension of NaH (1.0 g, 40 mmol) in dry ethylenediamine (50 mL). The resulting mixture was stirred for 30 min while the bath temperature was maintained in the range 8−10 °C. The system was then allowed to warm up to 14 °C for another 30 min. The liquids were then removed *in vacuo* using a hot water bath. The solid residue was dissolved in absolute ethanol (approximately 120 mL). A saturated solution of dry Et_4NBr in absolute EtOH was then added to afford a precipitate. The resulting suspension was cooled overnight, and the precipitate was isolated by filtration, washed with absolute ethanol (3 × 25 mL), and dried *in vacuo*. The ^{11}B NMR spectrum of the isolated white solid in H_2O indicated an approximately 1:1 mixture of $[Et_4N]_3$[*ae*-$B_{20}H_{17}$(en)] and $[Et_4N]_4[a^2\text{-}B_{20}H_{18}]$. This solid was stirred twice with dry acetonitrile (120 mL), filtered, and dried *in vacuo* to yield 1.70 g (25%) $[Et_4N]_3$[*ae*-$B_{20}H_{17}$(en)] as a white solid. $^{11}B\{^1H\}$ NMR (ppm, H_2O): 11.1 (1B, apical B−B); 3.5 (1B, apical BH); −1.1 (1B, apical BH), −7.5 (1B, apical BH); −12.1 (1B, BN); −24.9, −26.0, −28.8 and −29.7 (total 15B, 1B−B + 14 equatorial BH). ESI-MS (*m/z*): 424 $\{[Et_4N][H][B_{20}H_{17}(en)]\}^-$; 296 $\{[H]_2[B_{20}H_{17}(en)]\}^-$; 147 $\{[H][B_{20}H_{17}(en)]\}^{2-}$. CV ($E_{p/2}$) + 60 mV. The compound was ion-exchanged to the sodium form Na_3[*ae*-$B_{20}H_{17}$(en)] in aqueous solution. ^{13}C NMR (ppm, D_2O): 37.32 (t, $^1J_{CH}$ = 136.23 Hz, $-CH_2NH_2$); 50.49 (t, $^1J_{CH}$ = 143.35 Hz, $BNCH_2-$).

$[Et_4N]_3[1\text{-}(1'\text{-}B_{10}H_9)\text{-}2\text{-}NH_2CH_2CH_2NH_2\text{-}B_{10}H_8]$, Designated $[Et_4N]_3$-$[a^2\text{-}B_{20}H_{17}(en)]$. Solid $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ (4.0 g, 10 mmol) was added to a stirred suspension of $Li[HNCH_2CH_2NH_2]$ (6.0 g, 92 mmol) in dry ethylenediamine (30 mL). The resulting mixture turned dark blue and slightly viscous and was stirred for 2.5 h at room temperature. The liquids were then removed *in vacuo* using a hot water bath, and the solid residue was dissolved in absolute ethanol (approximately 130 mL). A saturated solution of dry Et_4NBr in absolute EtOH was added to afford a precipitate. The resulting suspension was cooled overnight, and the precipitate was isolated by filtration, washed with absolute ethanol (3 × 25 mL), and dried *in vacuo*. The ^{11}B NMR spectrum of the resulting solid in H_2O indicated an approximately 1:1 mixture of $[Et_4N]_3$[*ae*-$B_{20}H_{17}$(en)] and $[Et_4N]_4[a^2\text{-}B_{20}H_{18}]$. This solid was refluxed for 24 h in 100 mL absolute ethanol, filtered, and dried *in vacuo*, whereby the ethylene diamine adduct $[Et_4N]_3$[*ae*-$B_{20}H_{17}$(en)] isomerizes to the corresponding a^2 isomer. The solid residue was stirred with 100 mL of anhydrous CH_3CN and filtered, leaving the bulk comprised of $[Et_4N]_4[a^2\text{-}B_{20}H_{18}]$ as an insoluble material. The resulting solution was evaporated to dryness and redissolved in a minimum amount of CH_3CN, and absolute ethanol was added until the solution turned cloudy. After overnight cooling, the mixture deposited additional $[Et_4N]_4[a^2\text{-}B_{20}H_{18}]$. The liquid phase was then transferred to a Schlenk flask containing 250 mL of THF. The resulting suspension was cooled overnight and the product, $[Et_4N]_3[a^2\text{-}B_{20}H_{17}(en)]$, was isolated as a white solid by filtration and dried *in vacuo* yielding 1.50 g (22%). $^{11}B\{^1H\}$ NMR (ppm, H_2O): 10.3 (2B, B−B); −5.2 (1B, apical BH); −7.3 (1B, apical BH); −12.2 (1B, BN); -25.1, −25.9 and −29.0 (total 15B, equatorial BH). ESI-MS (*m/z*): 538 $\{[Et_4N]_2[B_{20}H_{17}(en)]\}^{1-}$; 425 $\{[Et_4N][H][B_{20}H_{17}(en)]\}^{1-}$; 296 $\{[H]_2[B_{20}H_{17}(en)]\}^{1-}$; 147 $\{[H][B_{20}H_{17}(en)]\}^{2-}$. CV ($E_{p/2}$): +50 mV. The compound was ion-exchanged to the sodium form $Na_3[a^2\text{-}B_{20}H_{17}(en)]$ in aqueous solution. ^1H NMR (ppm, D_2O): 2.95 (d, $^3J_{HH}$ = 11.5 Hz, $\text{-}CH_2NH_2$); 2.96 (d, $^3J_{HH}$ = 11.5 Hz, $BNCH_2-$); −1.32 (br.s, 17H, BH). ^{13}C NMR (ppm, D_2O): 37.14 (t, $^1J_{CH}$ = 137.78 Hz, $-CH_2NH_2$); 46.33 (t, $^1J_{CH}$ = 143.21 Hz, $BNCH_2$). ESI-MS (*m/z*): 339 $\{[Na]_2[B_{20}H_{17}(en)]\}^-$; 318 $\{[H][Na][B_{20}H_{17}(en)]\}^-$; 295 $\{[H]_2[B_{20}H_{17}(en)]\}^-$; 147 $\{[H][B_{20}H_{17}(en)]\}^{2-}$.

$[Et_4N]_3[1\text{-}(2'\text{-}B_{10}H_9)\text{-}2\text{-}NH_3\text{-}B_{10}H_8]$, Designated $[Et_4N]_3$[*ae*-$B_{20}H_{17}NH_3$].[4] Solid $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ (2.0 g, 5 mmol) was added to a stirred suspension prepared from NaH (0.5 g, 20 mmol) in dry acetonitrile (50 mL) and absolute ethanol (2 mL). The mixture turned almost immediately into a greenish solution which was stirred at room temperature for 5 h. The apparatus was then opened to the atmosphere, 20 mL of ethanol and 25 mL of water were added, and the solution was stirred overnight at room temperature. The solvents were removed under reduced pressure using a hot water bath and the resulting solid residue was dissolved in ethanol (30 mL) under nitrogen. The product $[Et_4N]_3$[*ae*-$B_{20}H_{17}NH_3$] was then isolated via precipitation with a saturated solution of Et_4NBr in absolute ethanol as a white solid in 76% yield (2.45 g). It was identified by $^{11}B\{^1H\}$ NMR[4] and ESI-MS (*m/z*): 250 $\{[H]_2[B_{20}H_{17}NH_3]\}^-$; 125 $\{[H][B_{20}H_{17}NH_3]\}^{2-}$.

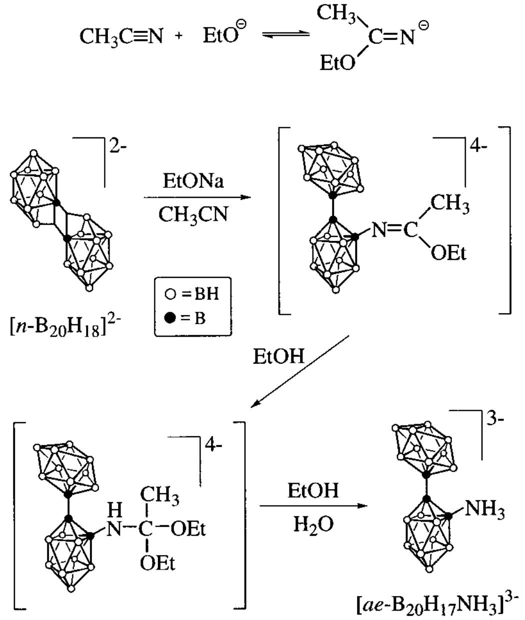
$K_4[1\text{-}(2'\text{-}B_{10}H_9)\text{-}2\text{-}OH\text{-}B_{10}H_8]$, Designated K_4[*ae*-$B_{20}H_{17}OH$].[2] Dry $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ (2.0 g, 5 mmol) was added to a solution of *t*-BuOK (2.37 g, 20 mmol) in dry ethylenediamine (25 mL). A precipitate was immediately formed, accompanied by a slight exotherm. This precipitate was removed by filtration, washed with absolute ethanol (3 × 20 mL) and dried *in vacuo* to yield 2.35 g K_4[*ae*-$B_{20}H_{17}OH$] as a white solid. This solid contains ethylenediamine, as confirmed by ^1H NMR. ESI-MS (*m/z*): 366 $\{K_3B_{20}H_{17}OH\}^-$.

$[Et_4N]_4[1\text{-}(1'\text{-}B_{10}H_9)\text{-}2\text{-}OCH_2CH_2OH\text{-}B_{10}H_8]$, Designated $[Et_4N]_4$-$[a^2\text{-}B_{20}H_{17}OCH_2CH_2OH]$. LDA (2.26 g, 20 mmol) was added to dry ethylene glycol (30 mL) under nitrogen at −10 °C. After approximately 1 min, the mixture turned into a maroon colored solution. The salt, $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ (2.0 g, 5 mmol), was added, and the mixture was allowed to warm to room temperature. After 30 min, all of the $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ had dissolved to produce a dark brown solution. After 2 h of stirring, a solution of Et_4NBr in EtOH (15 mL) was added to the reaction flask causing the immediate formation of a white precipitate. The mixture was heated between 80 and 90 °C for 24 h, causing the precipitate to dissolve. The system was cooled to room temperature, and the resulting white suspension was isolated by filtration under nitrogen and washed with absolute ethanol (3 × 20 mL). The ^{11}B NMR of the solid indicates a mixture of $[a^2\text{-}B_{20}H_{17}OCH_2CH_2OH]^{4-}$, [*ae*-$B_{20}H_{17}OCH_2CH_2OH]^{4-}$, and $[a^2\text{-}B_{20}H_{18}]^{4-}$. The mixture was suspended in anhydrous acetonitrile (50 mL), stirred for 30 min, and filtered under nitrogen. The filtrate was evaporated to dryness and dissolved in a minimum amount of anhydrous acetonitrile at room temperature, and the resulting solution was concentrated to about one-half of its original volume. Upon cooling in the refrigerator for several days, the concentrated solution deposited $(Et_4N)_4[a^2\text{-}B_{20}H_{17}OCH_2CH_2OH]$ as white powder. The yield was approximately 250 mg (6%). $^{11}B\{^1H\}$ NMR (ppm, D_2O): 14.1 (1B, B−B); 9.8 (1B, B−B); 4.2 (1B, B−O); −6.5 (1B, apical B−H); −8.3 (1B, apical B-H); −22.5, −23.2, −28.3 and −31.9 (total 15B, equatorial B−H). ESI-MS (*m/z*): 427 $\{(Et_4N)(H)_2(B_{20}H_{17}OCH_2CH_2OH)\}^-$; 297 $\{(H)_3(B_{20}H_{17}OCH_2CH_2OH)\}^-$.

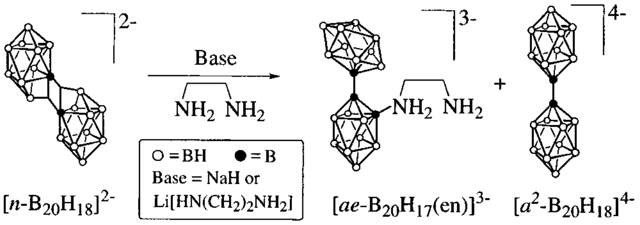
Results and Discussion

The synthesis of [*ae*-$B_{20}H_{17}(en)]^{3-}$ was initially attempted by treatment of $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ with an excess of $Li[HNCH_2CH_2NH_2]$ in dry acetonitrile. Rather than the expected product, this reaction furnished instead the previously described apical−equatorial ammonio derivative [*ae*-$B_{20}H_{17}NH_3]^{3-}$.[4] The formation of this compound presumably proceeds via the hydrolysis and/or solvolysis of an acetonitrile-containing intermediate formed in the first stage of the overall process. The ammonio derivative, [*ae*-$B_{20}H_{17}NH_3]^{3-}$, was identified by its characteristic $^{11}B\{^1H\}$ NMR[4] spectrum as well as by electrospray ionization

Scheme 2



Scheme 3



mass spectroscopy (ESI-MS). The mass spectrum of this ion contains two characteristic boron envelopes at *m/z* 250 and 125 corresponding to the $\{[H]_2[B_{20}H_{17}NH_3]\}^-$ and $\{[H][B_{20}H_{17}NH_3]\}^{2-}$ ions, respectively.

The sodium salt of the $[ae\text{-}B_{20}H_{17}NH_3]^{3-}$ ion has been previously reported[4] as one of the most promising water-soluble boron species for liposome-mediated tumor localization leading to boron neutron capture therapy (BNCT). Since this anion was previously prepared under more tedious conditions using liquid ammonia as solvent,[4] we decided to optimize the reaction conditions for the acetonitrile route to this species. Adjustments to the initial reaction conditions included the substitution of the original base by sodium ethoxide (prepared *in situ* from NaH and absolute EtOH in CH_3CN), as well as the introduction of water and ethanol following the initial reaction, in order to facilitate hydrolysis of the intermediate (Scheme 2; an analogous mechanism is proposed which employs ethylenediamine as the base/solvent). In this way $[ae\text{-}B_{20}H_{17}NH_3]^{3-}$ was isolated as its tetraethylammonium salt in 76% yield by precipitation from ethanol with a saturated solution of Et_4NBr in ethanol. This new procedure is much simpler than that used in the previously described route.[4]

The formation of $[ae\text{-}B_{20}H_{17}NH_3]^{3-}$ is in accord with the proposed mechanism of reductive substitution with hydroxide ion and $[n\text{-}B_{20}H_{18}]^{2-}$ shown in Scheme 1.[2] In the first step the polyhedral borane forms a complex with an electron donor (in the present case, an acetonitrile-derived adduct) which undergoes, in the presence of base, the loss of a proton postulated to be bridge-bound between the two B_{10}-cages.[6,7] We were, however, unable to isolate any acetonitrile-containing intermediates, presumably due to their rapid solvolysis to the ammonio derivative $[ae\text{-}B_{20}H_{17}NH_3]^{3-}$ (Scheme 2). Even under strictly anhydrous conditions, the ESI-MS of the initial reaction mixture does not exhibit peaks which correspond to ions derived from such an intermediate. The failure to detect an acetonitrile-containing intermediate, such as $[B_{20}H_{17}NCCH_3]^{3-}$, suggests the existence of the acetonitrile−ethoxide preequilibrium shown in Scheme 2. The reaction of the resulting nucleophile with $[n\text{-}B_{20}H_{18}]^{2-}$ would produce an easily hydrolyzed borane−imine intermediate that would lead directly to the $[ae\text{-}B_{20}H_{17}NH_3]^{3-}$ ion. The occurrence of $[B_{20}H_{17}NCCH_3]^{3-}$ as an intermediate is considered to be unlikely because its formation would not be predicted under the prevailing reaction conditions, and it would be expected to be an observable species since the single-cage functionalized borane $[2\text{-}B_{10}H_9NCCH_3]^-$ has been successfully isolated and characterized.[8]

Further investigations focusing on the preparation of the ethylenediamine derivative $[B_{20}H_{17}(en)]^{3-}$ were carried out using anhydrous ethylenediamine as the solvent. Two different bases have been identified as being suitable for the preparation of this compound in this solvent. However, the workup of each of the two reaction mixtures resulted in the isolation of a different isomer of $[B_{20}H_{17}(en)]^{3-}$ (*vide supra*). Moreover, in both cases the reaction between $[n\text{-}B_{20}H_{18}]^{2-}$ and ethylenediamine produces a mixture of compounds (Scheme 3), identified as $[ae\text{-}B_{20}H_{17}(en)]^{3-}$ and $[a^2\text{-}B_{20}H_{18}]^{4-}$, from which the desired product must be separated.

Sufficient data are not currently available to support a suitable explanation for the formation of the $[a^2\text{-}B_{20}H_{18}]^{4-}$ byproduct. It was established, however, that the formation of this anion also occurs in the absence of a strong base, since the dissolution of $[Et_3NH]_2[n\text{-}B_{20}H_{18}]$ in ethylenediamine produces soluble $[ae\text{-}B_{20}H_{17}(en)]^{3-}$ and deposits solid $[H_3NCH_2CH_2NH_3]_2[a^2\text{-}B_{20}H_{18}]$ after approximately 24 h at room temperature.

One possible explanation for the formation of $[a^2\text{-}B_{20}H_{18}]^{4-}$ is that an intermediate species, formed by coordination of an ethylenediamine molecule to $[n\text{-}B_{20}H_{18}]^{2-}$, can be further deprotonated by a base in two possible sites, as shown in Scheme 4. The abstraction of the intercage bridging hydrogen would result in the formation of the ethylenediamine adduct $[ae\text{-}B_{20}H_{17}(en)]^{3-}$. Another possibility would be a β-elimination process in the appended ethylenediamine moiety, which could lead to the formation, after rearrangement, of the $[a^2\text{-}B_{20}H_{18}]^{4-}$ species.

The proposed mechanism shown in Scheme 4 for the formation of $[a^2\text{-}B_{20}H_{18}]^{4-}$ is generalized and highly speculative. We have not yet been able to identify any oxidized byproducts formed from the reduction of $[n\text{-}B_{20}H_{18}]^{2-}$ to $[a^2\text{-}B_{20}H_{18}]^{4-}$. The ^{11}B NMR of the product mixture contains only resonance due to $[a^2\text{-}B_{20}H_{18}]^{4-}$ and $[ae\text{-}B_{20}H_{17}(en)]^{3-}$, and no signals attributable to oxidized boron species are observed. Further analysis of the reaction mixture by distillation, ^1H NMR, and ESI-MS has failed to identify any oxidized organic products.

The mechanism proposed in Scheme 4 does not reflect the possible contribution of the free $-NH_2$ group of the ethylenediamine ligand to the formation of $[a^2\text{-}B_{20}H_{18}]^{4-}$. For example, no $[a^2\text{-}B_{20}H_{18}]^{4-}$ is observed in the syntheses of $[ae\text{-}B_{20}H_{17}NH_3]^{3-}$ or $[ae\text{-}B_{20}H_{17}NH_2CH_2CH_2CH_3]^{3-}$.[4] While the synthesis of $[ae\text{-}B_{20}H_{17}OCH_2CH_3]^{4-}$ is straightforward and is not ac-

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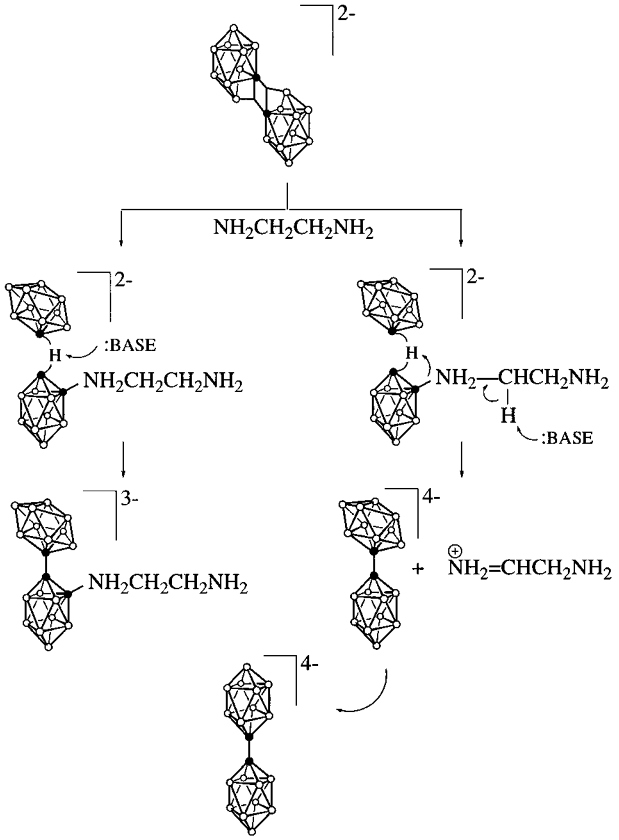
(6) Other protonated $[B_{20}H_{18}]^{4-}$ derivatives with a bridging hydrogen in this position have recently been structurally characterized; see ref 7 and see: Watson-Clark, R.; Knobler, C. B.; Hawthorne, M. F. *Inorg. Chem.* **1996**, *35*, 2963−66.

(7) Li, F.; Kane, R. R.; Shelly. K.; Knobler, C. B.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1996**, *118*, 6506−6507.

(8) Danan, D.; Mavunkal, I. J.; Bauer, J. A. K.; Knobler, C. B.; Hawthorne, M. F.; Shore, S. G. *Inorg. Chem.* **1994**, *33*, 6432−6434.

Scheme 4



companied by $[a^2\text{-}B_{20}H_{18}]^{4-}$ formation,[7] the synthesis of $[ae\text{-}B_{20}H_{17}OCH_2CH_2OH]^{4-}$ occurs with the production of a significant quantity of $[a^2\text{-}B_{20}H_{18}]^{4-}$. Thus, the presence of a terminal hydroxyl group in a presumably related ethylene glycol reaction also leads to $[a^2\text{-}B_{20}H_{18}]^{4-}$ formation.

During our preliminary attempts to identify suitable conditions for the separation of the product mixture obtained from the reaction of ethylenediamine and $[n\text{-}B_{20}H_{18}]^{2-}$ in the presence of $Li[HNCH_2CH_2NH_2]$, we discovered that when these products are transformed to the corresponding tetraethylammonium salts the *ae*-isomer of the ethylenediamine product can be easily rearranged to the corresponding a^2-isomer by heating to reflux in ethanol. Previous studies demonstrated that this type of isomerization takes place as an acid-catalyzed process,[4,5,9] and the fact that it can be simply achieved in boiling ethanol may indicate the occurrence of an alternative thermal rearrangement mechanism. Moreover, the mixture of the two polyhedral borane salts does not seem to have significant solubility in boiling ethanol and the system remains a suspension during the rearrangement process. The $[a^2\text{-}B_{20}H_{17}(en)]^{3-}$ salt obtained in this manner can then be separated from the mixture with anhydrous acetonitrile, in which it is soluble, whereas the $[a^2\text{-}B_{20}H_{18}]^{4-}$ salt remains essentially insoluble and is identifiable by its characteristic $^{11}B\{^1H\}$ NMR.[9]

The apical-apical isomer of the ethylenediamine derivative, $[a^2\text{-}B_{20}H_{17}(en)]^{3-}$, was characterized by ^{11}B NMR and ESI-MS. The $^{11}B\{^1H\}$ NMR spectrum of this compound contains two singlets, corresponding to apical BH vertices at -5.2 and -7.3 ppm; these signals appear as doublets in the hydrogen-coupled spectrum and each corresponds to a single boron atom. Two broad singlets appear at 10.3 and -12.2 ppm and are attributed to the two apical boron atoms constituting the B−B bond between the two B_{10} cages, and to the boron atom connected to the ethylenediamine moiety, respectively. The remaining 15 equatorial BH vertices give rise to three upfield signals at -25.1, -25.9, and -29.0 ppm. The ^{11}B NMR spectrum of $[a^2\text{-}B_{20}H_{17}(en)]^{3-}$ is almost identical to that of the apical−apical ammonio derivative $[a^2\text{-}B_{20}H_{17}NH_3]^{3-}$.[4] This is not surprising since these compounds are closely related and significant differences in the boron chemical shifts would not be expected. Mass spectroscopy (ESI-MS) was also used in order to positively confirm the identity of the isolated product. The mass spectrum of $[a^2\text{-}B_{20}H_{17}(en)]^{3-}$ contained characteristic peaks at *m/z* 538, 425, 296, and 147 corresponding to the following anionic species: $\{[Et_4N]_2[B_{20}H_{17}(en)]\}^-$, $\{[Et_4N][H][B_{20}H_{17}(en)]\}^-$, $\{[H]_2[B_{20}H_{17}(en)]\}^-$, and $\{[H][B_{20}H_{17}(en)]\}^{2-}$, respectively. The tetraethylammonium salt of $[a^2\text{-}B_{20}H_{17}(en)]^{3-}$ was converted to the corresponding sodium salt by ion-exchange chromatograpy in order to facilitate the study of its ^1H and ^{13}C NMR spectra. Both types of spectra indicated the presence of two chemically nonequivalent methylene groups in the ethylenediamine ligand. The ^1H NMR spectrum contained two overlapping doublets at 2.95 and 2.96 ppm with $^3J_{HH} = 11.52$ Hz, corresponding to the two sets of methylene protons. The differences in the chemical shift of the two carbon atoms in the ^{13}C NMR spectrum of the a^2-isomer are more pronounced (the signals of the two atoms are ca. 9 ppm apart) since they are more strongly affected by the electron-withdrawing effect exerted by the positively charged nitrogen appended to the boron cage. A triplet at 37.14 ppm ($^3J_{CH} = 137.78$ Hz) was assigned to the carbon atom connected to the terminal NH_2 group, whereas the downfield triplet at 46.33 ppm ($^3J_{CH} = 143.21$ Hz) was attributed to the carbon atom connected to the positively charged nitrogen that is coordinated to the boron cage. The sodium salt of $[a^2\text{-}B_{20}H_{17}(en)]^{3-}$ was additionally characterized with ESI-MS. Its mass spectrum contained boron envelopes at *m/z* 339, 318, 295, and 147, attributed to the ionic species $\{[Na]_2[B_{20}H_{17}(en)]\}^-$, $\{[H][Na][B_{20}H_{17}(en)]\}^-$, $\{[H]_2[B_{20}H_{17}(en)]\}^-$, and $\{[H][B_{20}H_{17}(en)]\}^{2-}$, respectively.

It should be pointed out that the ^{11}B and ^{13}C NMR spectra of $[a^2\text{-}B_{20}H_{17}(en)]^{3-}$ indicate incomplete isomerization; both spectra contained small signals attributable to the *ae*- isomer. The a^2/*ae* isomer ratio was approximately 20:1 as estimated from the ^{11}B NMR spectra. This ratio remained essentially unchanged regardless of the duration of the thermal isomerization step (reflux in ethanol for up to 4 days). These facts indicate that the $a^2/ae\text{-}[B_{20}H_{17}(en)]^{3-}$ system probably achieves equilibrium between these two isomers during the thermal rearrangement.

Other bases such as lithium diisopropylamide (LDA), NaH, and *t*-BuOK were also used in the reaction between $[n\text{-}B_{20}H_{18}]^{2-}$ and ethylenediamine under the same conditions as those employed in the case of $Li[HNCH_2CH_2NH_2]$. The principal product of the reaction using LDA was the undesired $[a^2\text{-}B_{20}H_{18}]^{4-}$ ion according to the results obtained from the ^{11}B analysis of the reaction mixture. Application of *t*-BuOK unexpectedly resulted in the formation of the hydroxy derivative, $[ae\text{-}K_4B_{20}H_{17}OH]^{4-}$, in high yields, identified by its $^{11}B\{^1H\}$ NMR[2] and mass spectrum (see Experimental Section). Although the synthesis of this hydroxy derivative in aqueous media has been previously described,[2] this new method for its preparation has the advantage of yielding anhydrous products since the synthesis is carried out under strictly anhydrous conditions. The mechanism of the formation of the hydroxy product, $[ae\text{-}K_4B_{20}H_{17}OH]^{4-}$, under these conditions is presently unclear, although a possible explanation may involve formation of the intermediate adduct $[ae\text{-}K_4B_{20}H_{17}OC(CH_3)_3]^{4-}$, which

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(9) Hawthorne, M. F.; Pilling, R. L.; Stokley, P. F. *J. Am. Chem. Soc.* **1965**, *87*, 3704.

undergoes subsequent loss of 2-methyl-1-propene, presumably via a β-elimination step under the basic reaction conditions.

A series of experiments using sodium hydride as the base were performed in order to optimize the yield of the desired [*ae*-$B_{20}H_{17}$(en)]$^{3-}$. The ratio of the two reaction products [*ae*-$B_{20}H_{17}$(en)]$^{3-}$ and [a^2-$B_{20}H_{18}$]$^{4-}$ in each experiment was followed by HPLC, where the concentration of the base and the reaction temperature were the two experimental variables. The highest product/byproduct ratio was obtained with a slight excess of NaH (4.0 mol of NaH per mole of [Et_3NH]$_2$[*n*-$B_{20}H_{18}$], where the stoichiometric quantity should be 3.0 mol) and temperatures in the range 8−10 °C, slightly above the freezing point of the ethylenediamine solvent. Nevertheless, conversion of [*n*-$B_{20}H_{18}$]$^{2-}$ to the desired [*ae*-$B_{20}H_{17}$(en)]$^{3-}$ using this optimized procedure (see Experimental Section) does not exceed 25% (although the isolated yield is approximately 50%, since the byproduct [a^2-$B_{20}H_{18}$]$^{4-}$ is easily isolated and recycled). Another characteristic feature of the sodium hydride reaction is that the ethylenediamine derivative [*ae*-$B_{20}H_{17}$(en)]$^{3-}$ obtained with this base cannot be isomerized to the a^2-isomer by simple heating in ethanol as was observed with the product obtained from the Li[$HNCH_2CH_2NH_2$] preparation. It was also established that the *ae* to a^2 isomerization in boiling ethanol also took place when LDA was used as the base in the reaction of [Et_3NH]$_2$[*n*-$B_{20}H_{18}$] with ethylenediamine. Moreover, analogous isomerization takes place when the *ae* ammonia adduct [*ae*-$B_{20}H_{17}NH_3$]$^{3-}$, obtained from [*n*-$B_{20}H_{18}$]$^{2-}$ and Li[$HNCH_2CH_2$-NH_2] in acetonitrile, was heated in ethanol, but no isomerization took place under these conditions when the [*ae*-$B_{20}H_{17}NH_3$]$^{3-}$ obtained from reactions which employed NaH as the base. These facts suggest that lithium ions may play an important role in the mechanism of the thermal isomerization process. Although the thermal rearrangements in boiling ethanol were nominally carried out with the Et_4N^+ salts of [*ae*-$B_{20}H_{17}$(en)]$^{3-}$ and [*ae*-$B_{20}H_{17}NH_3$]$^{3-}$, there were some indications that the cation substitution was incomplete. However, deliberate attempts to facilitate the thermal isomerization of [*ae*-$B_{20}H_{17}NH_3$]$^{3-}$, obtained with NaH in acetonitrile, in boiling ethanol by the addition of lithium chloride proved to be unsuccessful.

The tetraethylammonium salt of [*ae*-$B_{20}H_{17}$(en)]$^{3-}$ was characterized by ^{11}B NMR and ESI-MS. The mass spectrum of this species contained essentially the same characteristic signals exhibited by the a^2-isomer. The ^{11}B{^{1}H} NMR spectrum of the *ae*-derivative, however, was quite characteristic of an apical−equatorial structure, since it contained three singlets (each for one boron atom) at +3.5, −1.1, and -7.5 ppm, which correspond to doublets in the proton-coupled spectrum and correspond to the unsubstituted apical BH vertices. The apical boron atom of the B−B bond connecting the two B_{10} cages gives rise to a broad singlet at 11.10 ppm, whereas the signal for the equatorial boron atom of the intercage bond overlaps with the upfield signal of the equatorial BH vertices, which appear in the range −24.9 to +29.7 ppm. The broad singlet for one boron atom at −12.1 ppm is attributed to the boron atom bonded to the ethylenediamine moiety. The sodium salt of [*ae*-$B_{20}H_{17}$(en)]$^{3-}$, obtained by ion-exchange, was characterized by ^{13}C NMR spectroscopy. The spectrum contains two triplets at 37.32 ppm ($^1J_{CH}$ = 136.23 Hz) and 50.49 ppm ($^1J_{CH}$ = 143.35 Hz), attributed to the $-CH_2NH_2$ and $-BNH_2CH_2-$ carbon atoms in the ethylenediamine moiety, respectively. These two triplets appear at a slightly lower field as compared to the ^{13}C NMR resonance obtained for [a^2-$B_{20}H_{17}$(en)]$^{3-}$. For comparison, under the same conditions (D_2O solvent) free ethylenediamine exhibits a single ^{13}C resonance at 42.84 ppm.

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