Table II. Atomic Positional Parameters and Isotropic Thermal Parameters for the $Mo_3O_2S_8^{2-}$ Anion in I

atom	x	y	z	β, Å²
Mo(1)	0.75923 (7)	0.42100 (7)	0.55684 (6)	5.35 (3)
Mo(2)	0.74439 (6)	0.22568 (6)	0.54167 (5)	4.26 (2)
Mo(3)	0.77221 (7)	0.04710 (6)	0.58339 (5)	4.91 (2)
S(1)	0.8193 (3)	0.5103 (3)	0.6329 (3)	8.9 (1)
S(2)	0.6983 (4)	0.4855 (3)	0.4690 (3)	10.6 (2)
S(3)	0.6677 (2)	0.3329 (2)	0.5938 (2)	6.17 (8)
S(4)	0.8576 (2)	0.3297 (2)	0.5341 (2)	5.98 (8)
S(5)	0.6716 (2)	0.1397 (2)	0.6074 (2)	4.83 (7)
S(6)	0.8706 (2)	0.1400 (2)	0.5571 (2)	6.19 (8)
S(7)	0.8873 (3)	-0.0318 (8)	0.6547 (2)	8.3 (1)
S(8)	0.7707 (3)	-0.0376 (2)	0.6813 (2)	7.3 (1)
O(1)	0.6880 (6)	0.2138 (6)	0.4624 (4)	6.5 (2)
O(2)	0.7266 (6)	-0.0132 (5)	0.5152 (4)	6.7 (2)

Table III. Bond Lengths (Å) and Selected Angles (deg) for $Mo_3O_2S_8^{2-}$

Mo(1)-Mo(2)	3.030 (1)	Mo(2)-S(6)	2.363 (2)
Mo(2)-Mo(3)	2.884	Mo(2)-O(1)	1.668 (4)
Mo(1)-S(1)	2.129 (2)	Mo(3)-S(5)	2.281 (2)
Mo(1)-S(2)	2.082 (2)	Mo(3)-S(6)	2.276 (2)
Mo(1)-S(3)	2.246 (2)	Mo(3)-S(7)	2.390 (2)
Mo(1)-S(4)	2.231 (2)	Mo(3)-S(3)	2.392 (2)
Mo(2)-S(3)	2.440 (2)	Mo(3)-O(2)	1.691 (4)
Mo(2)-S(4)	2.442 (2)	S(7)-S(8)	2.053 (3)
Mo(2)-S(5)	2.370 (1)		
Mo(1)-Mo(2)-Mo(3)	156.18 (2)	Mo(1)-S(2)-Mo(3)	80.45 (5)
S(1)-Mo(1)-S(2)	111.12 (9)	Mo(2)-S(5)-Mo(3)	76.63 (5)
S(3)-Mo(1)-S(4)	103.24 (6)		

course only analogous in a formal sense; the trimolybdates contain polymeric anions.[10] Furthermore, the synthesis starting from $MoO_2S_2^{2-}$ must involve a more complex stoichiometry.

The structure determination of I reveals the anion shown in Figure 1. Atomic positional and isotropic thermal parameters are given in Table II, and selected interatomic distances and bond angles are given in Table III. Do, Simhon, and Holm[5] have isolated the salt $(Bu_4N)_2Mo_3O_{2.55}S_{7.45}$ in 11% yield from the reaction of $Mo_8O_{26}^{4-}$ isomers with $(Me_3Si)_2S$ in acetonitrile. The single-crystal x-ray structural investigation of this compound revealed that it contained both $Mo_3O_2S_8^{2-}$ and $Mo_3O_3S_7^{2-}$ anions in an approximately 1:1.22 mole ratio. The structure and dimensions of the first of these are in satisfactory agreement with the present results. As shown in Figure 1, the presence of a disulfide ligand, S(7)-S(8), demonstrates that the molybdenum atoms have been partially reduced. Plausible assignments of oxidation states are VI-IV-VI and VI-V-V for Mo(1)-Mo(2)-Mo(3), respectively. Holm et al.[5] favor the first of these, but there is no compelling evidence in that direction. For example, we note that the anion could be viewed as a derivative of the Mo(V) species $Mo_2O_2S_6^{2-}$, with bidentate MoS_4^{2-} in place of S_2^{2-}. The dimensions of the MoS_4^{2-} moiety in $Mo_3O_2S_8^{2-}$ are close to those of the free tetrahedral anion, and the Mo(2)···Mo(3) separation of 2.884 Å is little changed from the Mo···Mo distance, 2.829 Å, in $Mo_2O_2S_6^{2-}$.[7]

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Registry No. I, 123928-19-8; II, 116634-70-9; III, 123928-13-2; IV, 123928-14-3; $(NH_4)_2MoO_2S_2$, 16150-60-0; $[(n\text{-}Bu_4N)]_2MoOS_3$, 115564-39-1; $(Ph_4P)_2MoOS_3$, 83061-15-8.

Supplementary Material Available: Tables SI-SIII, listing crystallographic data, atomic positional parameters for tetrabutylammonium cations, and anisotropic temperature factors (4 pages); a table of calculated and observed structure factors (25 pages). Ordering information is given on any current masthead page.

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Synthesis and Characterization of Derivatives of Pyridine–Borane Adducts

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Syntheses for several amine·BH_2X (X = CN, C(O)NHR, C(S)NHR, C(CN)=NEt, COOR, COOH) adducts have been reported.[1] Primary interest in these compounds arises from their biological activity as antitumor,[2] antiinflammatory,[3] and antihyperlipidemic[4] agents. Pyridine–carboxyborane[5] was also shown to inhibit tumor growth in mice. Because of the interest in the biological activity of new borane adducts and because of difficulty in obtaining high yields of pyridine–carboxyborane, we undertook a study to isolate a variety of intermediates to attempt to determine which intermediates were isolable and under what conditions desired products are formed. This paper reports the isolation and characterization of new pyridine–borane derivatives and a method that improved the yield of pyridine–carboxyborane.

Experimental Section

All IR spectra were recorded on a Perkin-Elmer 1750 FT spectrometer. Samples were prepared as Nujol mulls between NaCl plates. The ^{11}B NMR spectra were obtained on a JEOL FX-90Q FT NMR spectrometer operating at 28.69 MHz; shifts were measured with respect to external $BF_3{\cdot}OEt_2$; ^1H NMR spectra were obtained on a Varian XL-300 spectrometer. All NMR results are reported in Table I. Elemental analyses were performed by MHW Laboratories, Phoenix, AZ 85018. All melting points are uncorrected.

Materials. Triethyloxonium tetrafluoroborate was prepared according to the procedure of Meerwein.[6] Approximately 1 M Et_3OBF_4 in CH_2Cl_2 was used as a fresh solution.

Safety Note. At no time was the $(BH_2CN)_x$ oligomer handled dry but manipulated as a solution due to potential explosion hazard.[7c,d]

Preparation of $C_5H_5N{\cdot}BH_2CN$ (1). To a solution of pyridine (39.55 g, 0.50 mol) in 100 mL of CH_2Cl_2 was added a solution of $(BH_2CN)_x$ oligomer[7a,b] (18 g, 0.46 mol) in 100 mL of CH_2Cl_2 at 10 °C during 30 min. The reaction mixture was brought to room temperature and stirring continued for 1 h. The ^{11}B NMR spectrum of the reaction mixture showed no unreacted $(BH_2CN)_x$ oligomer. The solution was washed with water twice and dried over Na_2SO_4. Solvent was removed, and the residue was subjected to vacuum (0.5 mmHg) for 24 h to remove any

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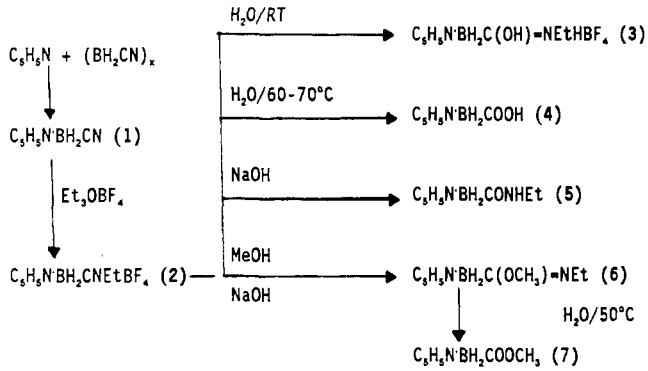
Table I. Spectral Data for Pyridine–Borane Derivatives[a]

compd	IR, cm^{-1}	^1H NMR ($CDCl_3$): δ, ppm	^{11}B NMR ($CDCl_3$): δ, ppm (J, Hz)
1	2419 and 2327 (BH), 2199 (C≡N), 1627 (C=C)	2.80 (q, br, BH_2), 7.78, 8.21, and 8.62 (m, C_5H_5N)	−14.7 (t, J_{BH} = 102)
2	2474 and 2440 (BH), 2314 (C≡NEt), 1625 (C=C)	1.53 (t, CH_2CH_3), 2.9 (br, BH_2), 4.09 (q, br, CH_2CH_3), 7.90, 8.34, and 8.67 (m, C_5H_5N)	−16.7 (t, br, BH_2), −0.46 (s, BF_4)
3	3229 and 3034 (NH and OH), 2385 (BH), 1625 (C=C), 1640 (C=N)	1.13 (t, CH_2CH_3) 3.24 (q, CH_2CH_3), 7.00 (NH/OH), 7.70, 8.13, and 8.49 (m, C_5H_5N)	−9.0 (t, br, BH_2), −0.42 (s, BF_4)
4	2405 and 2392 (BH), 1662 (C=O), 1625 (C=C)	2.80 (br, BH_2), 7.80, 8.27, and 8.52 (m, C_5H_5N)	−11.0 (t, J_{BH} = 98)
5	3321 (NH), 2399 and 2356 (BH), 1623 (C=C), 1593 and 1488 (amide bands I and II)	1.13 (t, CH_2CH_3), 3.31 (m, CH_2CH_3), 5.65 (br s, NH), 7.58, 8.01, and 8.65 (m, C_5H_5N)	−8.5 (t, J_{BH} = 95)
6	2385 and 2370 (BH), 1625 (C=C), 1619 (C=NEt)	1.16 (t, CH_2CH_3), 3.45 (m, CH_2CH_3 and OCH_3), 7.57, 8.01, and 8.57 (m, C_5H_5N)	−10.5 (t, J_{BH} = 100)
7	2405, 2392 (BH), 1662 (C=O), 1625 (C=C)	3.59 (s, OCH_3) 7.63, 8.07, and 8.60 (m, C_5H_5N)	−9.9 (t, J_{BH} = 96)

[a] s = singlet, t = triplet, q = quartet, m = multiplet, and br = broad.

Scheme I



traces of pyridine. The product (50 g, 92%) was isolated as a low-melting solid (32–34 °C) (lit.[8d] mp 34–35 °C). The ^1H NMR spectrum showed the compound to be sufficiently pure for further reactions.

Preparation of $C_5H_5N·BH_2CNEtBF_4$ (2). To 200 mL of a CH_2Cl_2 solution of **1** (50 g, 0.42 mol) was added a 1 M solution of Et_3OBF_4 (460 mL, 0.46 mol) and the new solution refluxed for 24 h under N_2 atmosphere. Solvent was removed, and the residue was subjected to dynamic vacuum (0.1 mmHg) for 48 h to remove volatile impurities. A pale yellow hygroscopic solid (melts at 27–30 °C) was obtained in 95% yield. The ^1H NMR spectrum (Table I) showed it to be sufficiently pure for further reactions.

Preparation of $C_5H_5N·BH_2C(OH)=NEtHBF_4$ (3). To 5.5 g (23.5 mmol) of nitrilium salt **2** at 5 °C, was added 10 mL of distilled water and the solution brought to room temperature while being stirred. After 3 h of stirring at room temperature, the solution was extracted with CH_2Cl_2 (4 × 40 mL) and the extract dried over Na_2SO_4. Solvent removal gave a thick mass, which was dissolved in a minimum amount of CH_2Cl_2; ether was added to give an opaque solution that cleared on warming. Cooling at 0 °C for 24–48 h gave a white crystalline material (2.36 g, 40% based on the amount of **2** used); mp 84–86 °C.

Preparation of $C_5H_5N·BH_2CO_2H$ (4). A 5.7 g (24.3 mmol) sample of **2** was dissolved in 10 mL of distilled water and the solution stirred for 15 min at 60–70 °C. The reaction mixture was cooled at 0 °C for a few minutes to give a white solid. After being filtered, the mother liquor was again heated at 60–70 °C for 15 min while being stirred; cooling gave additional precipitate. The combined material was recrystallized from hot water (60–70 °C) to give 1.37 g (41% based on the amount of **2** used) of acid; mp 120–122 °C dec (lit.[5] mp 115–116 °C).

Preparation of $C_5H_5N·BH_2CONHEt$ (5). A solution of 5.5 g (23.5 mmol) of **2** in 50 mL of CH_2Cl_2 was cooled in an ice–water bath, and a cold solution of 1 N NaOH was added slowly to pH 13.5. The reaction mixture was stirred for 45 min, during which time it attained room temperature. The organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (2 × 40 mL), and the combined organic solution was washed with water. Solvent removal after drying over Na_2SO_4 gave a light yellow solid, which was dissolved in CH_2Cl_2 (15 mL); hexane was added to give an opaque solution that cleared on warming. After several hours at room temperature white crystalline material was isolated (2.03 g, 52% based on the amount of **2** used); mp 92–94 °C. Anal. Calcd for $C_8H_{13}BN_2O$: C, 58.58; H, 7.99; N, 17.08. Found: C, 58.48; H, 8.13; N, 17.16.

Preparation of $C_5H_5N·BH_2C(OCH_3)=NEt$ (6). To a solution of **2** (11 g, 47 mmol) in CH_2Cl_2 (20 mL) was added 12 mL of methanol (6 equiv); the solution was stirred and kept for 24 h at room temperature. The solvent was removed under reduced pressure, and 100 mL of CH_2Cl_2 was added to the residue. The solution was washed with cold 1 N NaOH (3 × 40 mL) and cold water and dried over Na_2SO_4. Solvent removal gave a light yellow solid, which was dissolved in ether (30 mL). Hexane waas added until an opaque solution was obtained that became clear on warming. On standing for several hours at room temperature, the mixture yielded a white crystalline compound (6.3 g, 75% based on the amount of **2** used); mp. 72–74 °C. Anal. Calcd for $C_9H_{15}BN_2O$: C, 60.72; H, 8.49; N, 15.73. Found: C, 60.59; H, 8.45; N, 15.80.

Preparation of $C_5H_5N·BH_2COOCH_3$ (7). To 1.5 g (8.4 mmol) of **6** was added 10 mL of water and the solution stirred for 8 h at 50 °C. After cooling, the solution was extracted with CH_2Cl_2 (3 × 40 mL) and dried over Na_2SO_4. Solvent was removed and the impurity, **6**, was removed by using column chromatography (silica gel 70–230 mesh, 60 Å) with ether as eluant to give white solid (0.5 g, 40% based on the amount of **6** used); mp 41–43 °C. Anal. Calcd for $C_7H_{10}BNO_2$: C, 55.69; H, 6.68; N, 9.28. Found: C, 55.47; H, 6.61; N, 9.16.

Results and Discussion

Attempts to prepare pyridine–carboxyborane by the reported method[5] resulted in a smaller yield than reported (10% vs 29%), and extraction of the aqueous mother liquor with CH_2Cl_2 gave a small amount of impure $C_5H_5N·BH_2C(OH)=NEtHBF_4$ (**3**) as determined by its IR and ^1H NMR spectra. These results suggested that a systematic study designed to isolate precursors to the formation of carboxyboranes and similar derivatives would provide valuable information related to the mechanism of formation and the method necessary to produce pure product in high yield. Therefore, the reaction of nitrilium salt **2** with water, alkali, and methanol was investigated (Scheme I).

Although amine–cyanoboranes can be prepared by various methods,[8] pyridine–cyanoborane (**1**) was prepared from the reaction of $(BH_2CN)_x$ oligomer[7] with pyridine, because it provided a product that was obtained in a shorter period of time and with fewer purification problems. The nitrilium salt, $C_5H_5N·BH_2CNEtBF_4$ (**2**), was prepared according to a reported method;[5] however, only a 1:1.1 ratio of **1** Et_3OBF_4 was used instead of a 1:2 ratio.

A number of different products can be isolated depending on reaction conditions. Hydrolysis of **2** with cold water for 3 h followed by extraction and crystallization offered the hydrofluoborate salt of α-(hydroxyimine)borane, $C_5H_5N·BH_2C(OH)=NEtHBF_4$ (**3**). The IR spectrum shows an absorption at 1640 cm^{-1} for C=N, overlapping with the C=C absorption (1625 cm^{-1}) of the pyridine ring. From spectral data (Table I) it is clear that it is neither starting material, **2** (absence of C≡NEt absorption), acid **4**, nor carbamoyl derivative **5** (absence of C=O absorptions). However, if hydrolysis is continued for a longer time, acid formation begins. It is apparent, from the isolation of **3** from aqueous mother liquor, that **3** is a precursor to **4** and stable at room temperature for several hours. However, when **3** is crystallized from hot water, it forms the acid **4** by rapid hydrolysis.

Spielvogel et al.[5] have reported the synthesis of **4** from crude nitrilium salt **2** by hydrolyzing it with water at room temperature for 65 h. The solid product was combined with the residue obtained from solvent removal after the aqueous filtrate was extracted with CH_2Cl_2. Recrystallization from hot water gave them 29% yield of the acid **4**. However, in our hands the reported methodology resulted in a 10% yield of $C_5H_5N·B_2HCO_2H$ (**4**); extraction with CH_2Cl_2 of the aqueous solution obtained after initial precipitation of the product afforded an impure imine salt

3 (8%). When **2** was obtained as pure nitrilium salt (free from excess Et_3OBF_4 and volatile impurities) and hydrolyzed, the reaction products were exceptionally dependent on temperature and reaction times. For example, when **2** was hydrolyzed with boiling water for 60 min, boric acid was the only boron-containing product observed. However, when hydrolysis time was reduced to 5 min, a 12% yield of **4** was obtained apart from boric acid formation. At 40–50 °C for 30 min, there was no acid **4** formation but only imine **3** product. A systematic study using different reaction times and temperatures showed that hydrolysis of pure **2** at 60–70 °C for 15 min offers **4** in reasonably good yield (41%).

Cold alkaline hydrolysis of **2** gave **5**, whose IR and ^1H NMR data (Table I) are consistent with the anticipated structure. Characteristic absorptions of boranocarbamoyl at 1593 and 1488 cm^{-1} (amide I and II bands) were observed.

Reaction of **2** with methanol in CH_2Cl_2 followed by alkaline treatment gave $C_5H_5N{\cdot}BH_2C(OCH_3){=}NEt$ (**6**). The IR spectrum showed an absorption at 1620 cm^{-1} for C=N, overlapping with the C=C band at 1625 cm^{-1}. The ^1H NMR spectrum was consistent with the structure. For an acyclic imidate, the typical products of hydrolysis at low pH are an ester and amine.[9] Acidic hydrolysis of **6** with 0.5 N HCl did not proceed to the ester even at 50 °C for 6–8 h but formed a stable salt of imino ether. This may be due to greater basicity of the imino ether adjacent to a boron moiety, as was observed for boranocarbamoyl derivatives.[10] Under forced reaction conditions (100 °C) boric acid formation resulted. However, hydrolysis of **6** at neutral pH (50 °C, 8 h) gave a 40% yield of the ester $C_5H_5N{\cdot}BH_2COOCH_3$ **7**. The IR spectrum exhibited characteristic B–H and C=O absorptions, and the ^1H NMR spectrum was consistent with the structure (Table I).

The ^{11}B NMR spectrum (Table I) of each compound consisted of a distinct triplet (except **2**, which was a very broad triplet, which collapsed to a singlet upon ^1H-decoupling. Only salts **2** and **3** showed another boron signal, but this was attributable to BF_4^-.

Since other amine·BH_2X adducts (X = CN, CONHR, COOR, CO_2H) including $C_5H_5{\cdot}BH_2CO_2H$ possess biological activity,[2-4] these compounds are being examined to determine the effect these functional groups have on the biological activity of the molecule.

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Convenient Small-Scale Method for the Insertion of Iron into Porphyrins

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The use of isotopes in the study of complex molecules is becoming increasingly important because of the rapid advance in NMR techniques. Isotope-edited 2D NMR experiments will allow assignment of complex spectra and direct observation of "odd" nuclei provide unique information about structure and bonding that is not otherwise accessible. In many cases, this strategy requires isotopic enrichment using expensive materials. Convenient and efficient preparative methods are therefore needed. In our ongoing studies of heme models and heme proteins using ^{57}Fe NMR,[1] we needed an efficient and mild small-scale insertion procedure for iron. In this note, we report a novel method for the incorporation of iron that is enriched in ^{57}Fe, the only NMR and Mössbauer active nucleus, into a number of heat-sensitive porphyrins, namely the "picket-fence" porphyrin[2] and some of the "basket-handle" porphyrins.[3]

Iron porphyrins are the prosthetic groups in many biological systems that are essential to the life processes. Well-known examples are the cytochromes, hemoglobin, and myoglobin. Several synthetic models have been designed and synthesized in order to study carbon monoxide and dioxygen binding[3-6] and electron transport.[7] A critical step in these syntheses is the insertion of the iron atom.[8] Only ferrous salts will react with porphyrins, but trace amounts of oxygen will oxidize the iron atom to the unreactive ferric state. A common solution to this problem is to use large excesses of ferrous salts. With isotopically enriched iron, this is however not possible. We therefore present a new route for insertion of iron into porphyrins using Fe_2O_3 as starting material that is based on in situ reduction of the ferric chloride. This method is quite convenient, mild, relatively fast, and easy to handle on a small scale. In contrast, a separate preparation of ferrous salts on a milligram scale for insertion into the reaction mixture is impractical.

A slight excess of iron (typically 1.7 times the molar amount of porphyrin) is used to make the insertion quantitative. The excess can easily be recovered after the reaction is complete. The iron oxide is dissolved in hot, concentrated hydrochloric acid, and the mixture is taken to almost dryness. Chlorobenzene is added, and the water is removed by azeotrope distillation. The ferric chloride is then reduced to ferrous chloride at 132 °C by the chlorobenzene, which acts both as a reagent and a solvent in the reaction.[9] After the reduction is complete, as judged by the change of color, the temperature is allowed to drop to a suitable level for the iron insertion, typically 70 °C, and the porphyrin is added, dissolved in chlorobenzene. It is of great importance that the reaction atmosphere is oxygen-free. The reaction mixture is therefore kept under a slight positive pressure of argon, and the porphyrin solution is degassed by three freeze–pump–thaw cycles, before entering the reaction flask.

^{57}Fe has been inserted into the following series of porphyrins in quantitative yield by this route: tetraphenylporphyrin, $\alpha,\alpha,\alpha,\alpha$-*meso*-tetrakis(*o*-pivalamidophenyl)porphyrin,[2] α-5,15-(2,2′-(nonanediamido)diphenyl)-α,α-10,20-bis(*o*-pivalamidophenyl)porphyrin, α-5,15-(2,2′-(decanediamido)diphenyl)-α,α-10,20-bis-(*o*-pivalamidophenyl)porphyrin, α-5,15-(2,2′-(dodecanediamido)diphenyl) α,α-10,20-bis(*o*-pivalamidophenyl)-porphyrin. Apart from tetraphenylporphyrin, these porphyrins will all isomerize at high temperature. The reaction time has been 4–16 h, and very little, if any, isomerization occurred.

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