Tribromo- and Trifluoroborane Adducts of Some Pyrazines*

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Abstract

The trifluoro- and tribromoborane adducts of some methyl substituted pyrazines were synthesized and characterized. The 2:1 molecular adducts (*e.g.*, $C_4H_4N_2 \cdot 2BX_3$) could be isolated with unsubstituted, 2-methyl, 2,3-dimethyl, and 2,6-dimethyl pyrazines. The 1:1 molecular adducts could be isolated only with 2,6-dimethylpyrazine. The adducts were characterized by elemental analyses and infrared spectroscopy. The adducts were studied using ^{11}B-NMR and chemical shift assignments made. The chemical shift assignments and the different reactivities of the two nitrogen sites in 2,6-dimethylpyrazine are discussed.

Introduction

For some time the research on boron chemistry in this laboratory has been concerned with a study of molecular adducts in which a nitrogen atom is a Lewis base. Specifically, adducts have been synthesized and characterized in which boranes such as BH_3, BH_2Br, BH_2CN, BF_3, BCl_3 and BBr_3 have reacted with pyridine, and pyridine molecules with methyl, ethyl, amino, cyano, bromo, chloro, and fluorosubstituents in the 2-, 3-, and 4-positions [1–6]. Additionally, studies have been made on the products of the reaction of quinoline, isoquinoline and aniline with BH_3 [3] and BH_2Br [2].

Inasmuch as the above research was confined to Lewis bases which were nitrogen-heterocyclic compounds containing a single nitrogen atom, it was of interest to consider similar nitrogen-heterocyclic compounds containing two nitrogen atoms. A search of the literature revealed that each of the nitrogen atoms in 2,2′-bipyridine accept a borane molecule to form 2,2′-bipyridine(bis)borane [7]. It has also been reported that pyrazine forms adducts with one and two moles of triethylborane [8].

Accordingly, this research was undertaken to study the behavior of a six-membered ring containing two nitrogen atoms as potential donors. Thus, pyrazine, 2-methylpyrazine, 2,3- and 2,6-dimethylpyrazines were studied as Lewis bases with tribromo- and trifluoroborane.

Experimental

All reactions and transfers of chemicals were conducted in an atmosphere of dry nitrogen or in a glass high vacuum system. Infrared spectra were determined on a nujol mull of the adducts placed between sodium chloride plates using a Perkin-Elmer model 599 spectrometer. As a consequence of the adducts being sensitive to moisture, the samples for infrared analysis were prepared in a dry nitrogen atmosphere in a glove box and immediately transferred to the spectrometer.

^{11}B nuclear magnetic resonance spectra were obtained at 64.2 MHz on a Nicolet NT-200 wide bore spectrometer using $(CH_3O)_3B$ as an external reference. The tribromoborane adducts were synthesized as detailed below, whereas the trifluoroborane adducts were synthesized by the addition of BF_3 gas to a benzene solution of the appropriate pyrazine. The samples for analysis were withdrawn directly from the reaction flask without isolation or purification and the spectrum immediately taken. The ^{11}B chemical shifts for BBr_3 (+19.6 ppm) and BF_3 (–6.4 ppm) are sufficiently different from the shifts of the adducts to make purification unnecessary. Attempts to obtain spectra on the isolated compounds were unsuccessful due to poor solubility.

Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee, by the Schwarzkopf Microanalytical, Laboratory, Inc., Woodside, New York, or in this laboratory using an F & M Model 185 CHN Analyzer.

All of the nitrogen bases and boranes were obtained from the Aldrich Chemical Company, Milwaukee, Wisconsin. Pyrazine (99+%) was used without further purification. The 2,6-dimethylpyrazine (98%) was sublimed before use. The other bases, 2-methyl-

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pyrazine and 2,3-dimethylpyrazine were distilled prior to use. Tribromoborane was distilled under reduced pressure, the tribromoborane then being stored over mercury. Trifluoroborane etherate was freshly prepared by bubbling BF_3 gas through dry diethyl ether at 0 °C. NMR spectra taken on samples prepared with aged $BF_3 \cdot (OCH_2CH_3)_2$ showed the presence of a large peak at *ca.* −19.9 ppm assigned to BF_4^-. Dichloromethane was distilled from P_4O_{10} prior to use. Benzene and diethyl ether were distilled from sodium and benzophenone prior to use.

Pyrazine(bis)trifluoroborane

In a typical synthesis, 1.0 g (12.5 mmol) of pyrazine was dissolved in 50 ml of anhydrous dichloromethane. The solution, in a flask, was immersed in a stream of dry nitrogen gas and frozen in liquid nitrogen. To this, 3.16 ml (25.0 mmol) of $BF_3 \cdot (C_2H_5)_2O$ was injected by a syringe through a rubber septum. The etherate froze as a top layer in the reaction flask. The contents of the reactor were allowed to warm slowly to room temperature with stirring. A crystalline white solid formed. The reaction mixture was stirred for about three hours after which the solid was collected on a vacuum filter and washed with a little (*ca.* 10 ml) of dichloromethane under a nitrogen atmosphere in a glove box. The solid was crushed and then dried under a vacuum to give a 88.7% yield of white crystals, $C_4H_4N_2 \cdot (BF_3)_2$, (m.p. 126–8 °C (dec)). *Anal.* $C_4H_4N_2 \cdot (BF_3)_2$; Calc.: C, 22.27; H, 1.87; N, 12.99; B, 10.02; F, 52.85%. Found: C, 21.95; H, 1.87; N, 12.32; B, 10.14; F, 52.31%. IR spectra: 3217(m), 3150(s), 3106(s), 3085(m), 1591(m), 1492(s), 1445(s), 1050(m), 1000(m), 780(s), 770(m), 652(s), 629(w) cm^{-1}.

Pyrazine(bis)tribromoborane

In a typical preparation, 1.0 g (12.5 mmol) of pyrazine was dissolved in 50 ml of dichloromethane. The reaction flask was placed in liquid nitrogen and evacuated after the solution had frozen. To the resulting solid was added 2.4 ml (25.0 mmol) of tribromoborane. The reaction flask and its contents then were allowed to warm slowly to room temperature with stirring. Upon attaining room temperature, a crystalline yellowish solid was obtained. Stirring was continued for about three hours. The solid was collected on a vacuum filter in a glove box filled with nitrogen gas. The product was crushed and dried in a vacuum. The yellow crystals, $C_4H_4N_2 \cdot (BBr_3)_2$ (m.p. 122–4 °C (dec)), were obtained in 68.2% yield. *Anal.* $C_4H_4N_2 \cdot (BBr_3)_2$; Calc.: C, 8.27; H, 0.69; N, 4.82%. Found: C, 7.90; H, 0.77; N, 4.63%. IR Spectra: 3102(s), 3058(m), 3042(m), 1430(s), 1173(s), 1117(s), 696(s), 678(s), 648(w), 635(w) cm^{-1}.

2-Methylpyrazine(bis)trifluoroborane

A procedure similar to that used to prepare pyrazine(bis)trifluoroborane was used to synthesize 2-methylpyrazine(bis)trifluoroborane in 85.7% yield. The product, $(CH_3)C_4H_3N_2 \cdot (BF_3)_2$, is a white crystalline solid melting at 107–109 °C (dec). *Anal.* $(CH_3)C_4H_3N_2 \cdot (BF_3)_2$; Calc.: C, 26.14; H, 2.63; N, 12.19; B, 9.41%. Found: C, 25.11; H, 3.07; N, 11.65; B, 9.32%. IR spectra: 3262(w), 3177(w), 3141(w), 3100(m), 1613(m), 1545(w), 1497(m), 1318(w), 1273(w), 1080(w), 1006(w), 797(sh), 755(w), 728(w), 650(s), 630(w) cm^{-1}.

2-Methylpyrazine(bis)tribromoborane

In a manner similar to that described for the preparation of pyrazine(bis)tribromoborane, 2-methylpyrazine(bis)tribromoborane was isolated in 86.3% yield as a greenish-white crystalline product (m.p. 115 °C (dec)). *Anal.* $(CH_3)C_4H_3N_2 \cdot (BBr_3)_2$; Calc.: C, 10.09; H, 1.02; N, 4.71%. Found: C, 9.35; H, 1.50; N, 4.37%. IR spectra: 3130(sh), 3100(m), 3063(m), 3038(w), 1638(m), 1607(s), 1490(sh), 1188(s), 1156(s), 1124(s), 1094(w), 1060(sh), 1040(w), 1022(w), 1003(sh), 876(s), 823(m), 720(s), 685(sh), 658(s) cm^{-1}.

2,3-Dimethylpyrazine(bis)trifluoroborane

A procedure similar to that described for the preparation of pyrazine(bis)trifluoroborane was followed to prepare 2,3-dimethylpyrazine(bis)trifluoroborane. A white crystalline product having a melting point of 102–106 °C (dec) was obtained in 67.3% yield. *Anal.* $(CH_3)_2C_4H_2N_2 \cdot (BF_3)_2$; Calc.: C, 29.57; H, 3.31; N, 11.49; B, 8.87%. Found: C, 29.86; H, 3.57; N, 11.27; B, 9.39%. IR spectra: 3280(sh), 3185(m), 3141(sh), 1633(m), 1610(w), 1509(s), 982(sh), 730(s), 608(s) cm^{-1}.

2,3-Dimethylpyrazine(bis)tribromoborane

A yield of 48.3% of 2,3-dimethylpyrazine(bis)-tribromoborane as a yellow crystalline solid (m.p. 110–115 °C (dec)) was obtained using a synthesis procedure similar to that used to prepare pyrazine(bis)tribromoborane. *Anal.* $(CH_3)_2C_4H_2N_2 \cdot (BBr_3)_2$; Calc.: C, 11.83; H, 1.32; N, 4.60; B, 3.55; Br, 78.71%. Found: C, 11.83; H, 1.49; N, 4.59; B, 4.06; Br, 78.47%. IR spectra: 3110(w), 1402(w), 1250(w), 1200(s), 1170(s), 1123(w), 1112(w), 1030(m), 998(m), 927(s), 867(w), 832(s) cm^{-1}.

2,6-Dimethylpyrazinetrifluoroborane

A procedure similar to that described for the preparation of pyrazine (bis)trifluoroborane was used to synthesize 2,6-dimethylpyrazinetrifluoroborane except benzene was used as a solvent in place of methylene chloride. A white crystalline adduct melting at 69–71 °C (dec) was obtained in 45.5% yield. *Anal.* $(CH_3)_2C_4H_2N_2 \cdot BF_3$; Calc.: C, 40.96;

H, 4.58; N, 15.92%. Found: C, 40.23; H, 4.65; N, 12.38%. IR spectra: 3288(s), 3152(sh), 3110(sh), 1640(s), 1495(w), 1320(w), 1307(sh), 1260(sh), 1245(sh), 860(sh), 818(w), 806(s), 768(m), 737(s), 722(m), 645(s) cm^{-1}.

2,6-Dimethylpyrazinetribromoborane

A procedure similar to that used to prepare pyrazine(bis)tribromoborane was employed to prepare 2,6-dimethylpyrazinetribromoborane except that the solvent methylene chloride was replaced by benzene. A 19.8% yield of the adduct, 2,6-dimethylpyrazinetribromoborane, was obtained as a yellow crystalline solid having a melting point of 112–117 °C (dec.). *Anal.* $(CH_3)_2C_4H_2N_2 \cdot BBr_3$; Calc.: C, 20.09; H, 2.25; H, 7.81%. Found: C, 19.56; H, 4.54; N, 7.64%. IR spectra: 3210(sh), 3090(sh), 1627(s), 1305(w), 1193(sh), 1150(sh), 997(sh), 880(w), 837(m), 829(m), 720(s), 710(s), 662(m) cm^{-1}.

2,6-Dimethylpyrazine(bis)trifluoroborane

A procedure similar to that described for the preparation of pyrazine(bis)trifluoroborane was used to synthesize 2,6-dimethylpyrazine(bis)trifluoroborane except that dry ether was used for the solvent and the $BF_3 \cdot O(CH_2CH_3)_2$ was used in molar excess (at least 8:1). The adduct was obtained as a white solid in 10.8% yield (m.p. 59–61 °C (dec)). *Anal.* Calc.: C, 29.57; H, 3.31; N, 11.49%. Found: C, 29.81; H, 3.93; N, 11.88%. IR spectra: 3090(m), 2180(w), 2110(w), 1655(s), 1635(sh), 1415(sh), 1265(w), 1195(sh), 1165(m), 880(w), 840(s), 740(s), 730(sh), 675(s) cm^{-1}.

2,6-Dimethylpyrazine(bis)tribromoborane

The synthesis of 2,6-dimethylpyrazine(bis)tribromoborane was performed similarly to that of pyrazine(bis)tribromoborane except a molar excess (at least 3:1) of tribromoborane was used. The resulting adduct was obtained as a yellow solid in 19.6% yield (m.p. 64–66 °C (dec)). *Anal.* Calc.: C, 11.83; H, 1.32; N, 4.60%. Found: C, 12.22; H, 2.05; N, 4.62%. IR spectra: 3210(s), 3090(sh), 1627(m), 1305(w), 1193(s), 1150(w), 977(m), 880(w), 837(m), 829(m), 720(s), 710(s), 662(m) cm^{-1}.

2,5-Dimethylpyrazine(bis)trifluoroborane

A stream of BF_3 gas was bubbled through a benzene solution of 2,5-dimethylpyrazine to yield a product presumed to be the adduct 2,5-dimethylpyrazine(bis)trifluoroborane. The resulting reaction mixture was analyzed directly by ^{11}B nmr spectroscopy, with no other characterization of the adduct. The bis adduct is presumed due to the results of the synthesis of the analogous 2,3-dimethylpyrazine adduct. Attempts to isolate the adduct were unsuccessful.

2,5-Dimethylpyrazine(bis)tribromoborane

A procedure similar to that described for the preparation of pyrazine(bis)tribromoborane was used to synthesize 2,5-dimethylpyrazine(bis)tribromoborane except benzene was used as the solvent. The resulting reaction mixture was analyzed by ^{11}B nmr spectroscopy, with no other characterization of the adduct. The bis adduct is presumed due to the results of the synthesis of the analogous 2,3-dimethylpyrazine adduct. Attempts to isolate the adduct were unsuccessful.

Results and Discussion

The location of an alkyl group on a heterocyclic ring has been related to the ^{11}B chemical shift for borane complexes of alkyl pyridines [9] and pyrazines [10]. The chemical shift of substituted pyridine complexes of borane and phenyl borane, compared to the unsubstituted pyridine, is nearly unaltered when there are alkyl groups meta to the nitrogen. Alkyl groups ortho to the nitrogen result in an upfield shift of the ^{11}B resonance upon complex formation [9]. A similar upfield shift in the ^{11}B resonance is observed also for 2-alkylpyridinetrihaloborane complexes [11]. The general trend in chemical shift is pyridine $\approx$ 3-alkyl $<$ 4-alkyl $<$ 2-alkylpyridine where an increase in chemical shift (upfield) is related to increased donor strength of the Lewis base.

Accordingly, it was of interest to learn whether a correlation could be found in trihaloborane complexes of alkylpyrazines in which the pyrazine ring is substituted at one or more sites. It was of interest also to learn whether any site selectivity exists in a molecule when the two nitrogen atoms are in different environments and if so, could the selectivity be determined using ^{11}B nmr chemical shifts.

The ^{11}B chemical shifts and available boron-nitrogen coupling constants for the trifluoroborane adducts are shown in Table I. For the unsubstituted pyrazine adduct, a single resonance at −18.3 ppm

TABLE I. ^{11}B NMR of Trifluoroborane Adducts of Substituted Pyrazines.

Substituent	$\delta^{11}B$ (ppm), $\lvert J \rvert$ $^{11}B-^{15}N$ (Hz)	
unsubstituted	−18.31, 7.0	
2-methyl	−15.6, 6.0	−18.3, 7.5
2,3-dimethyl	−18.26	
2,5-dimethyl	−18.25, 7.1	
2,6-dimethyl	−16.47, 5.1	−18.32, 6.6

TABLE II. ^{11}B NMR of Tribromoborane Adducts of Substituted Pyrazines.

Substituent	$\delta\,^{11}B$ (ppm), $\|J\|\,^{11}B-^{15}N$ (Hz)	
unsubstituted	−26.61, 2.8	
2-methyl	−25.86, 1.5	−26.36, 1.4
2,3-dimethyl	−26.53, 3.5	
2,5-dimethyl[a]		
2,6-dimethyl	−26.45, 3.6	

[a]Could not be observed.

is obtained. The addition of one methyl group to the ring results in two resonances in the nmr spectrum of the adduct, one at −18.3 ppm and another resonance downfield at −15.6 ppm.

The 2,3-dimethyl- and 2,5-dimethylpyrazine adducts with trifluoroborane show a single resonance in the ^{11}B nmr spectra at −18.26 ppm and −18.25 ppm respectively, while the 2,6-dimethylpyrazine adducts give two resonances at −16.47 ppm and at −18.32 ppm. The coupling constants which were determined are of the expected magnitude [12] and probably negative [13].

The ^{11}B nmr data for the tribromoborane adducts are shown in Table II. The unsubstituted and 2,3-dimethylpyrazine adducts gave single resonances at *ca.* −26.6 ppm, while the 2-methylpyrazine adduct showed two resonances at −26.36 ppm and −25.86 ppm. The 2,6-dimethylpyrazinetribromoborane adduct gave only a single resonance at −26.45 ppm, even in the presence of a large excess of free tribromoborane. No adduct resonance could be observed for the reaction of 2,5-dimethylpyrazine with tribromoborane. The boron-nitrogen coupling constants are smaller than those of the trifluoroborane adducts, which is as expected for boron coordinated to the less electronegative bromine.

These chemical shift data suggest that, within a trihaloborane series, the upfield resonances result from a boron atom bonded to a nitrogen atom with a methyl group in the ortho position, while the downfield resonances result from a boron atom bonded to a nitrogen atom with a methyl group in the meta position. This conclusion is surprising for several reasons. First, other studies have shown that substitution of an alkyl group ortho to a pyridine [4] or pyrazine [10] nitrogen results in an upfield shift in the ^{11}B nmr. In this study, a downfield shift is observed upon methyl substitution in the meta position, while substitution in the ortho position leads to essentially no change in the chemical shift, compared with the unsubstituted pyrazine. Second, substitution of two methyl groups in the ortho position, as in 2,6-dimethylpyrazine adducts, should lead to a further upfield shift in the boron resonance of the adduct [10]. Again, a resonance essentially unchanged from that of the unsubstituted pyrazine is observed.

Any attempt to correlate the data in Tables I and II by assigning the upfield resonances to the boron bound to a nitrogen with a methyl group in the meta position leads to contradictions when the resonances due to the 2,3-dimethyl- and 2,5-dimethylpyrazine adducts are considered. The ^{11}B resonance in, for example, 2,3-dimethylpyrazine(bis)trifluoroborane is the same as the upfield resonance observed for the 2-methylpyrazine adduct. If the substitution of a methyl group were to shift the ^{11}B resonance downfield, the resonance for the 2,3-dimethylpyrazine adduct should reflect this. Similarly, the ^{11}B resonance for the 2,5-dimethylpyrazine adduct would be expected to be shifted downfield. Since this result is not observed it is concluded that the initial assignments are correct. Adducts of trihaloboranes with unsubstituted pyrazine give anomolous ^{11}B nmr spectra, where the observed resonances are upfield of the expected chemical shift.

There is no apparent selectivity of trifluoroborane for either nitrogen donor site in 2,6-dimethylpyrazine, whereas tribromoborane forms an adduct only at the nitrogen site with two adjacent methyl groups. The nitrogen at this site is expected to be a stronger electron donor and thus the trihaloborane preferentially reacts there (steric factors should not be a problem for the relatively small methyl group [4]). The strong Lewis acid tribromoborane withdraws electrons from the ring further decreasing the basicity of the other nitrogen. Trifluoroborane, a weaker Lewis acid, does not withdraw as many electrons from the ring and thus does not deactivate the second nitrogen as a donor.

In summary, the reaction of trifluoro- and tribromoborane with Lewis bases containing two nitrogen donor sites has been investigated. The two reaction sites are distinguished by the trihaloborane only in the case of the 2,6-dimethylpyrazine adduct where the nitrogen environments are unequivalent. No distinction was found in the 2-methylpyrazine adducts. The ^{11}B nmr chemical shift can be used only in the instance of the tribromoborane adduct with 2,6-dimethylpyrazine to determine site preference for adduct formation. Solution equilibrium and kinetic effects also may be factors, but were not addressed in this study.

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