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Ring-Opening Reactions of Nonactivated Aziridines Catalyzed by Tris(pentafluorophenyl)borane

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The ring-opening reactions of nonactivated aziridines with amine nucleophiles are efficiently catalyzed by tris(pentafluorophenyl)borane leading to derivatives of *trans*-1,2-diamines in high yields. A mechanistic investigation of the reaction suggests that in situ formed $[(C_6F_5)_3B(OH_2)]\cdot H_2O$ catalyzes the opening through a Brønsted acid manifold.

Introduction

The chemistry of aziridines continues to attract the attention of the synthetic community.[1−6] In part, this interest is driven by the useful properties of aziridines centered around their ring-opening transformations.[7] The reactivity of aziridines as carbon electrophiles makes them versatile nitrogen-containing building blocks for the synthesis of biologically important compounds.[8−13] As well, biological properties of aziridine-containing molecules such as the azinomycins,[14−16] mitomycins,[17,18] FR-900482,[19−21] ficellomycin,[22−24] miraziridine,[25] maduropeptin,[26−29] and azicemicins[30−34] are of considerable interest.

Aziridines can be divided into two classes depending on the nature of the *N*-substituent (Figure 1).[35] Activated aziridines, such as *N*-tosyl and *N*-acyl aziridines, contain a strongly electronegative substituent that facilitates their ring-opening chemistry. Nonactivated aziridines, such as alkyl aziridines, do not have a substituent that is capable of stabilizing the anion resulting from the ring opening.

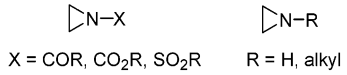

FIGURE 1. Activated and nonactivated aziridines.

There has been a great deal of interest in the ring opening of *N*-tosyl aziridines owing to their ease of preparation from olefins.[36−38] However, there have been comparably few reports on the ring opening of simple

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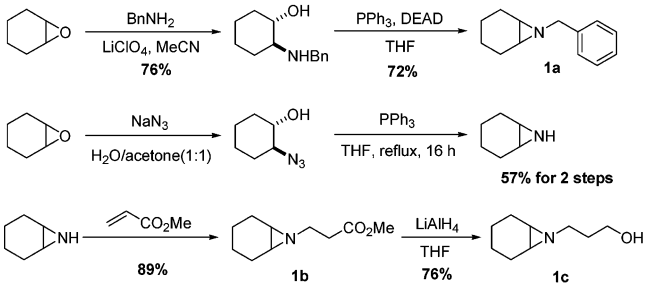
N-alkyl aziridines. Stoichiometric amounts of protic acids such as hydrochloric, sulfuric, triflic, and perchloric acid are known to promote the opening of *N*-alkyl aziridines.[39] Lewis acids known to catalyze the ring opening of *N*-alkyl aziridines with amines include $Yb(OTf)_3$[40−42] and $LiNTf_2$.[43] The reaction times in these examples tend to be long and catalyst loadings are high. The Lewis acids $Sn(OTf)_2$ or $Cu(OTf)_2$ have also been shown to open *N*-alkyl aziridines with aniline nucleophiles. Unfortunately, aliphatic amines do not work with these catalysts.[44] Recently, PBu_3 was shown to catalyze the ring opening of *N*-benzyl cyclohexene imine with aniline.[45] The enantioselective opening of various *N*-alkyl aziridines with $TMSN_3$ has been achieved with up to 94% ee.[46]

Tris(pentafluorophenyl)borane[47] ($B(C_6F_5)_3$) is a strong Lewis acid that has been extensively used as an activator in metallocene polymerization catalysis.[48] Recently, this molecule has found applications in synthetic transformations such as hydrosilation of alcohols,[49] enones,[50] carbonyl groups,[51] and imines,[52,53] stereoselective transformations of epoxides,[54,55] allylstannation of aromatic aldehydes,[56,57] allylation of secondary benzyl acetates,[58] cleavage of aryl and alkyl ethers with hydrosilanes,[59−61] and the aldol reaction.[62,63]

Results and Discussion

In the course of our work on the synthetic applications of functionalized aziridines,[64−66] we decided to examine the ring opening of nonactivated aziridines with amine nucleophiles. This method would provide a straightforward route to functionalized *trans*-1,2-diamines which are a biologically and synthetically important class of compounds.[8,67] Our studies required a range of alkyl aziridines (Scheme 1). *N*-Benzyl cyclohexene imine (**1a**), used in the majority of entries, was synthesized from cyclohexene oxide by ring opening with *N*-benzylamine followed by the Mitsunobu reaction to close the ring. *N*-Benzyl-2-phenylaziridine (**1e**) was synthesized in the same way from styrene oxide. Aziridine **1b** was synthesized by conjugate addition of cyclohexene imine to methyl acrylate. Aziridine **1d** was synthesized in a similar manner as **1b**, by conjugate addition of cyclohexene imine to methyl vinyl ketone**.** The reactions were run neat, no over-alkylation was observed, and high yields were obtained. This efficient methodology should facilitate rapid creation of diverse *N*-alkyl aziridines by using a wide range of commercially available, inexpensive α,β-unsaturated compounds. Aziridine **1c** was synthesized in 76% yield from **1b** by reduction with LAH.

SCHEME 1. Synthesis of Alkyl Aziridines



Both protic (HCl, H_2SO_4, TfOH) and Lewis acids ($Yb(OTf)_3$, $Cu(OTf)_2$, $BF_3{\cdot}OEt_2$) were reported to induce the aziridine ring-opening reaction. When applied to nonactivated aziridines, these protocols often suffer from high reaction temperatures, long reaction times, low functional group tolerance, and low selectivity. Recent advances in imine activation chemistry with $B(C_6F_5)_3$,[52,53] coupled with the fact that the pK_a values of the conjugate acid of aziridine and that of imine are close,[68] led us to consider $B(C_6F_5)_3$. We have found that catalytic amounts of $B(C_6F_5)_3$ in acetonitrile at 65 °C promoted exceptionally clean ring opening of *N*-benzyl cyclohexene imine with *N*-benzylamine to yield the corresponding *trans*-diamine. The reaction was performed on up to 2 mmol scale in technical grade acetonitrile without any special precautions to exclude water.

The ring opening was attempted with 10 mol % of $B(C_6F_5)_3$ at 65 °C in a range of solvents: toluene, diethyl ether, dichloromethane, and acetonitrile (Table 1).

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SCHEME 2. Proposed Structure of the Catalyst−Substrate Complex

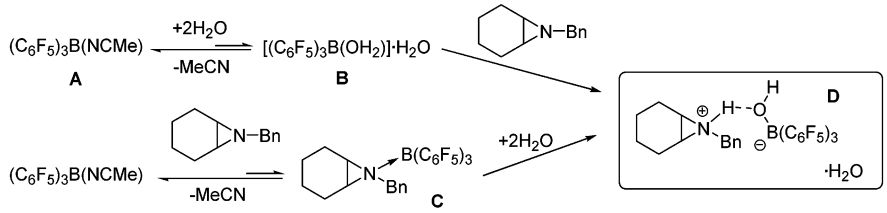


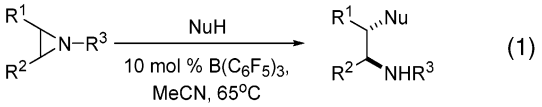
TABLE 1. Ring Opening of *N*-Benzyl Cyclohexene Imine (1a) with *N*-Benzylamine after 16 h

entry	solvent	$B(C_6F_5)_3$ (mol %)	*T* (°C)	additive	conv
1	Et_2O	10	35		0
2	PhMe	10	65		0
3	CH_2Cl_2	10	40		38
4	MeCN	0	rt		0
5	MeCN	0	65		11
6	MeCN	10	rt		30
7	MeCN	1	65		37
8	MeCN	10	65	4 Å molecular sieves[a]	42
9	MeCN	10	65	1 equiv of Proton Sponge	48
10	MeCN	10	65		100

[a] 100 to 200 mg of activated 4 Å molecular sieve beads per mL of solvent.

Of these, only acetonitrile gave complete conversion in 16 h. The reaction proceeded in dichloromethane, but at a slower rate. No conversion was observed in diethyl ether or toluene. When the reaction was run in acetonitrile at 65 °C without any catalyst, less than 20% conversion took place after 48 h. There was only 30% conversion after 16 h at room temperature with 10 mol % of catalyst and no conversion when the reaction was run at room temperature without the catalyst. Replacement of $B(C_6F_5)_3$ with BPh_3 in the reaction did not result in any increase in the amount of product produced over the background rate. When the reaction was performed with 4 Å molecular sieves or Proton Sponge[69] a much slower rate was observed. When 4 Å molecular sieves were added to the reaction there was less then 40% conversion after 16 h (Figure 2). This indicates that the presence of water is essential for the success of the reaction. When 1 equiv of Proton Sponge was added to the reaction there was less then 50% conversion after 16 h, suggesting that protic acidity plays a significant role in this process.

Various nucleophiles were used in the reaction (Table 2). Benzylamines worked best reacting in high yields within 24 h. Aniline reacted within 24 h (entry 2) while *N*-methyl aniline reacted within the same amount of time but the reaction required 2 equiv of the nucleophile (entry 4). When *n*-butylamine was used in the reaction, large amounts and long reaction times were required. The reaction with *tert*-butylamine did not go to completion, even after 48 h with 10 equiv of the nucleophile. No diastereoselectivity was observed when *(S)*-α-methylbenzylamine was used as the nucleophile, resulting in a 50:50 diastereomeric mixture (entry 5). Thiophenol reacted in 30 min at room temperature with only 5 mol % of the catalyst (entries 6 and 10). Although various conditions were attempted, we were unable to induce ring opening with alcohol nucleophiles. The reaction was attempted with benzyl alcohol and phenol and under reflux in methanol; however, even after 72 h, no ring-opened product was observed.



(1)

A number of alkyl aziridines were applied to the reaction. *N*-Benzyl cyclohexene imine (**1a**) was used in the majority of entries and was opened in excellent yields. Aziridine **1b** reacted with 2 equiv of the nucleophile in the lowest yield of 54% after 48 h (entry 7). Aziridine **1c** reacted under the same conditions (entry 8) to give a 97% yield of product. When aziridine **1d** was used (entry 9) no product was observed, presumably due to competing imine formation at the side chain ketone. Aziridine **1e** (entry 10) was opened with thiophenol to afford a single regioisomer. When cyclohexene imine was employed in the ring-opening reaction, no product was detected. In this case, the ^1H NMR indicated the presence of oligomerization and polymerization products, expected with *N*-unprotected aziridines.[40] *N*-Tosyl cyclohexene imine (**1f**), an activated aziridine, also underwent ring opening with *N*-benzylamine and 10 mol % of catalyst (entry 11). Under the same conditions *N*-Boc cyclohexene imine proved unreactive, resulting in less than 10% conversion after 48 h.

It was found that the diamine product of the reaction formed an adduct with $B(C_6F_5)_3$, which was inseparable from the diamine by column chromatography. Basic extraction with 10% aq NaOH or 10% aq NH_4OH failed to remove the catalyst from the product. Fortunately, by using the solid resin Amberlyst A-21 (loading: 1 mmol/g), the catalyst was completely separated from the diamine as seen by ^{19}F NMR and electron impact mass spectroscopy.

The Lewis acidity of $B(C_6F_5)_3$ is comparable to that of BF_3.[70] In the absence of water, $B(C_6F_5)_3$ is known to react with acetonitrile to give a four-coordinate adduct $(C_6F_5)_3B$-(NCMe).[70] When exposed to water, $B(C_6F_5)_3$ can form stable adducts that have been structurally characterized in the solid state as the trihydrate, $[(C_6F_5)_3B(OH_2)]\cdot 2H_2O$,[71] or monohydrate, $(C_6F_5)_3B(OH_2)$.[72,73] When water is present in acetonitrile, an equilibrium exists between the acetonitrile adduct and an aqua species of the form

(69) *N*,*N*,*N*′,*N*′-Tetramethyl-1,8-naphthalenediamine.

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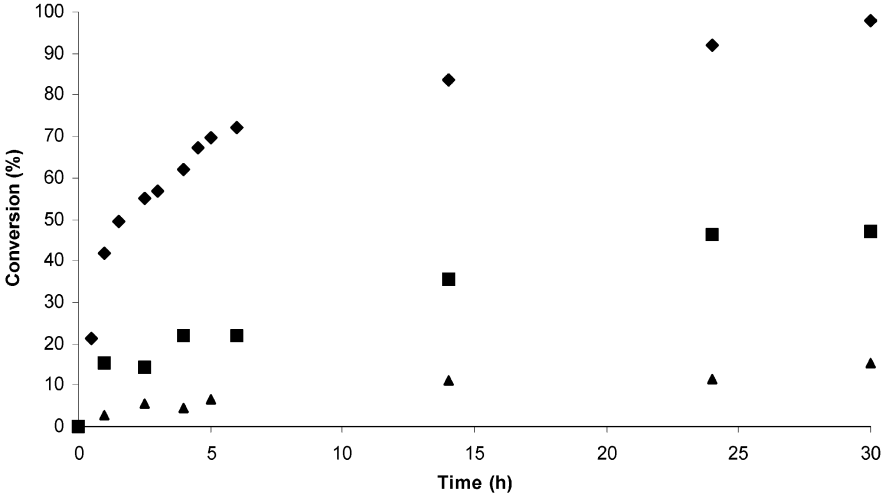


FIGURE 2. Conversion/time graph for ring opening of *N*-benzyl cyclohexene imine (**1a**) with *N*-benzylamine in acetonitrile at 65 °C: (▲) no catalyst, (■) 10 mol % of catalyst with 4Å molecular sieves, and (◆) 10 mol % of catalyst.

$[(C_6F_5)_3B(OH_2)]\cdot H_2O$.[74] This species is known to behave as a Brønsted acid[75] with a pK_a value estimated to be 8.4 in acetonitrile, comparable to HCl.[74]

We questioned whether the reaction proceeded through a Lewis acid or a Brønsted acid manifold. In an attempt to understand this system, we performed a series of NMR experiments to elucidate the structure of the catalyst precursor−substrate complex. When $B(C_6F_5)_3$ was dissolved in acetonitrile-d_3, ^{19}F NMR indicated formation of an adduct (Figure 3A). Addition of 2 equiv of water resulted in the appearance of peaks corresponding to the aqua species, $[(C_6F_5)_3B(OH_2)]\cdot H_2O$,[74] in a ratio of 1 to 0.18 for the acetonitrile and aqua adducts, respectively (Figure 3B). When 1 equiv of **1a** was added instead of water, a new set of peaks appeared in a ratio of 1 to 0.21 for the acetonitrile and aziridine adducts, respectively (Figure 3C). We attribute these peaks to a new adduct involving the coordination of $B(C_6F_5)_3$ to the aziridine nitrogen.

If 1 equiv of *N*-benzyl cyclohexene imine and 2 equiv of water are added to 1 equiv of $B(C_6F_5)_3$ in acetonitrile-d_3, a new set of peaks are obtained (Figure 3D). In this case, there is no equilibrium with the acetonitrile adduct, or any other species. Neither $[(C_6F_5)_3B(OH_2)]\cdot H_2O$ nor $(C_6F_5)_3B(NCMe)$ is detectable in the spectrum. Although close, the peaks also have ^{19}F chemical shifts that are different from the aziridine−$B(C_6F_5)_3$ adduct. The ^{1}H NMR spectrum of this complex (Figure 4D) is different from the aziridine ^{1}H NMR spectrum (Figure 4, top). The benzyl CH_2 and aziridine CH peaks are significantly shifted downfield. Also present is a broad water peak centered at 2.6 ppm. We believe that these data are consistent with formation of the aziridinium hydroxo-tris(pentafluorophenyl)borate adduct (Figure 5D), indicating that the reaction likely proceeds by a Brønsted and not the initially suspected Lewis acid activation. Furthermore, the ^{1}H NMR spectrum of the aziridine−$B(C_6F_5)_3$ adduct is also not consistent with any ring-opened product spectra as these should show diastereotopic benzylic protons. The corresponding spectra (Figure 4D) contain singlets for the benzylic protons, characteristic of the symmetrical aziridine-based structure.

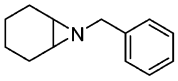
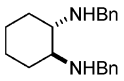
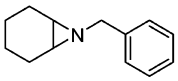
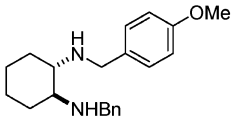
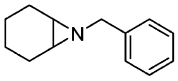
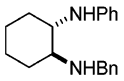
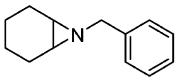
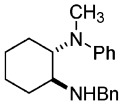
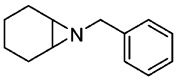
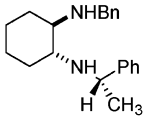
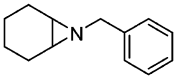
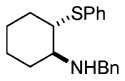
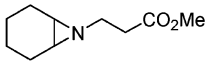
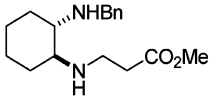
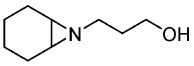
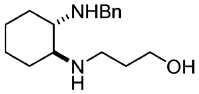
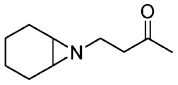
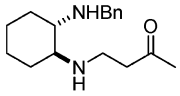
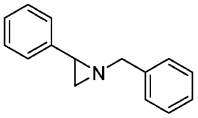
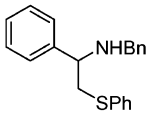
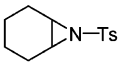
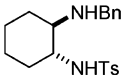
Therefore, we propose that in situ formed $[(C_6F_5)_3B(OH_2)]\cdot H_2O$ (Scheme 2, **B**) is the catalyst promoting the reaction through a Brønsted acid manifold. The aziridine is activated to ring opening by formation of an aziridinium adduct (Scheme 2, **D**), which is then opened by the nucleophile. When 4 Å molecular sieves are added to the reaction only the $B(C_6F_5)_3$−aziridine Lewis acid adduct (Scheme 2, **C**) can form. Since the rate of the reaction is higher than the background rate (entries 5 and 8, Table 1), this adduct must activate the aziridine toward ring opening. However, the poor equilibrium distribution retards the rate of the reaction. The Proton Sponge, added to the reaction, would trap the acidic $[(C_6F_5)_3B(OH_2)]\cdot H_2O$ acting in competition with aziridinium formation and retarding the reaction rate. We further attempted to elucidate the structure of complex **D** by comparison of its ^{1}H NMR spectra with another aziridinium ion prepared from triflic acid by literature methods. We hoped to see a correlation in the spectra between these two structures. Treating *N*-benzyl cyclohexene imine with 1 equiv of triflic acid in acetonitrile-d_3 produced a spectrum that was consistent with that of previously described aziridinium salts (Figure 5, bottom).[76] The NH^+ peak appears as a broad singlet at 6.2 ppm while the benzyl CH_2 and aziridine CH have shifted downfield to 4.2 and 3.4 ppm, respectively. As previously reported, the coupling constant between benzyl CH_2 and NH^+ protons is 6 Hz.[76] The ^{1}H NMR of the $B(C_6F_5)_3$−H_2O−aziridine complex (Figure 5, D) is consistent with these downfield trends. The sharpening of the aromatic region is similarly observed in both spectra. However, the benzylic splitting and NH_2^+ peak are not observed. We presume that

(74) Bergquist, C.; Bridgewater, B. M.; Harlan, C. J.; Norton, J. R.; Friesner, R. A.; Parkin, G. *J. Am. Chem. Soc.* **2000**, *122*, 10581−10590.

(75) Danopoulos, A. A.; Galsworthy, J. R.; Green, M. L. H.; Cafferkey, S.; Doerrer, L. H.; Hursthouse, M. B. *Chem. Commun.* **1998**, 2529−2530.

(76) Olah, G. A.; Szilagyi, P. J. *J. Am. Chem. Soc.* **1969**, *91*, 2949−2955.

TABLE 2. Ring Opening of Nonactivated Aziridines Catalyzed by $B(C_6F_5)_3$

Entry	Aziridine		Product		eq. NuH	T(°C)	Time	Yield
1		**1a**		**2a**	1.0	65	16 h	98%
2		**1a**		**2b**	1.2	65	16 h	99%
3		**1a**		**2c**	1.2	65	24 h	99%
4		**1a**		**2d**	2.0	70	24 h	84%
5		**1a**		**2e**	1.2	65	24 h	98%[a]
6		**1a**		**2f**	1.2	rt	30 min	98%[b]
7		**1b**		**2g**	2.0	65	48 h	54%
8		**1c**		**2h**	2.0	65	48 h	97%
9		**1d**		**2i**	2.0	65	16 h	0%
10		**1e**		**2j**	1.0	rt	30 min	95%[b,c]
11		**1f**		**2k**	1.2	65	12 h	99%

[a] Product isolated as a 50:50 diastereomeric mixture. [b] Reaction was run with 5 mol % of $B(C_6F_5)_3$. [c] Reaction was run in technical grade dichloromethane.

these differences are a result of a tighter association between the $(C_6F_5)_3B(OH_2)$ and aziridine components than when triflic acid is used. The disappearance of the benzylic splitting can be explained by rapid exchange between the aziridinium proton and the proton of the $[(C_6F_5)_3B(OH)]^-$ ion. This exchange causes both protons to appear in the broad water peak centered at 2.6 ppm, instead of the downfield NH^+ peak observed when triflic acid is used. Support for this suggestion is provided by the structural characterization of analogous ammonium hydroxoborate compounds[77,78] and an amino alcohol−$(C_6F_5)_3B(OH_2)$ adduct that we obtained from *N*-benzyl cyclohexene imine (Figure 6). All contain hydrogen bonds between the aziridinium ion and the $[(C_6F_5)_3B(OH)]^-$ anion.

X-ray quality crystals of the amino alcohol−$(C_6F_5)_3B(OH_2)$ adduct (*trans*-*N*-benzyl(2-hydroxycyclohexyl)ammonium hydroxotris(pentafluorophenyl)borate, **3**) were prepared by mixing stoichiometric quantities of *N*-benzyl cyclohexene imine and $B(C_6F_5)_3$ in toluene/pentane without any special precautions to exclude water. The resulting product was a *trans*-1,2-amino alcohol, formed upon ring opening of the aziridine by water (Figure 6). The $[(C_6F_5)_3B(OH)]^-$ ion is hydrogen bonded to the amine with an N−O distance of 2.806(4) Å and an N−H···O angle of

(77) Stibrany, R. T.; Brant, P. *Acta Crystallogr. Sect. C−Cryst. Struct. Commun.* **2001**, *57*, 644−645.

(78) Lancaster, S. J.; Rodriguez, A.; Lara-Sanchez, A.; Hannant, M. D.; Walker, D. A.; Hughes, D. H.; Bochmann, M. *Organometallics* **2002**, *21*, 451−453.

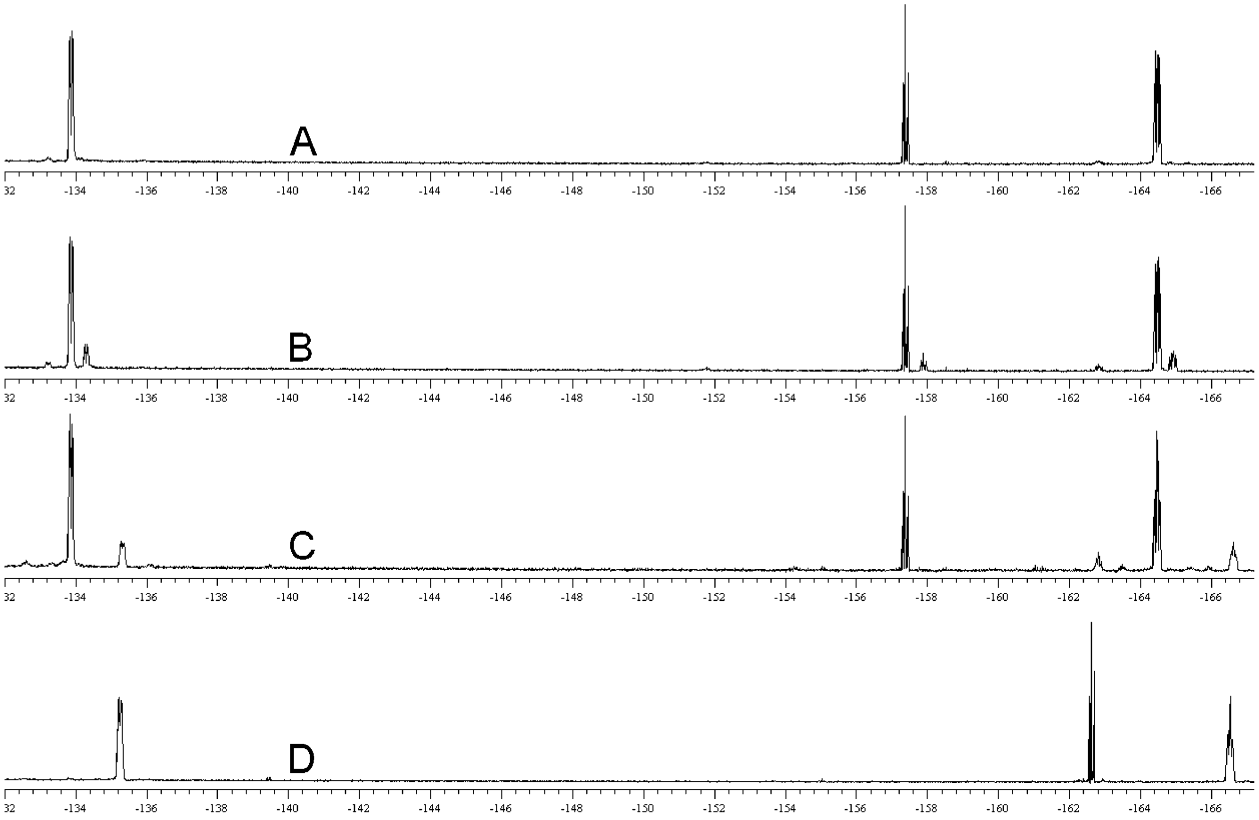


FIGURE 3. ^{19}F NMR of $B(C_6F_5)_3$ complexes in CD_3CN: (A) $(C_6F_5)_3B(NCMe)$ complex; (B) $B(C_6F_5)_3$ with 2 equiv of H_2O; (C) $B(C_6F_5)_3$ with 1 equiv of *N*-benzyl cyclohexene imine; and (D) $B(C_6F_5)_3$ with 2 equiv of H_2O and 1 equiv of *N*-benzyl cyclohexene imine.

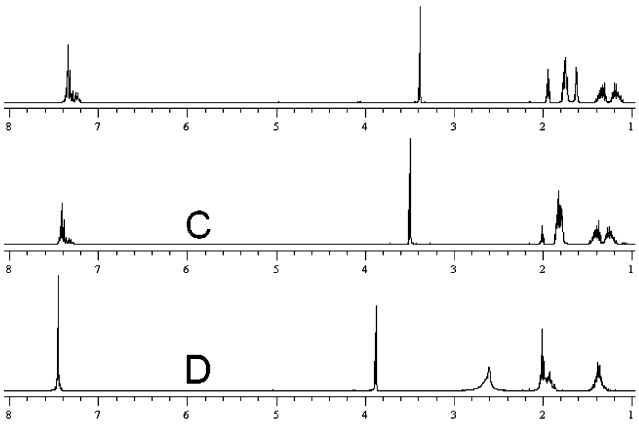


FIGURE 4. ^1H NMR of $B(C_6F_5)_3$ complexes in CD_3CN: top, *N*-benzyl cyclohexene imine; middle (C), $B(C_6F_5)_3$ with 1 equiv of *N*-benzyl cyclohexene imine; and bottom (D), $B(C_6F_5)_3$ with 2 equiv of H_2O and 1 equiv of *N*-benzyl cyclohexene imine.

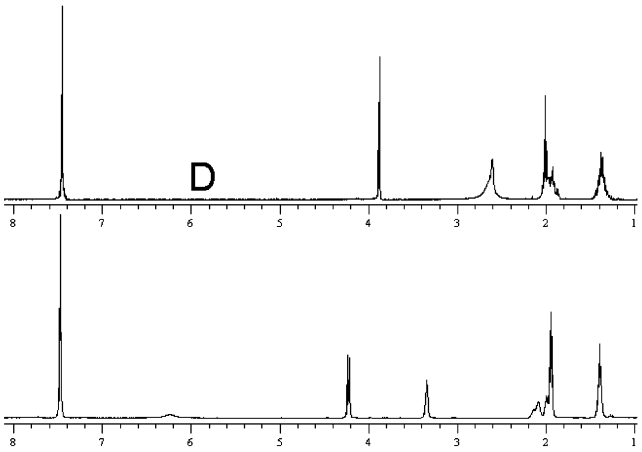


FIGURE 5. ^1H NMR in CD_3CN: top (D), $B(C_6F_5)_3$ with 2 equiv of H_2O and 1 equiv of *N*-benzyl cyclohexene imine; and bottom, *N*-benzyl cyclohexene imine with 1 equiv of TfOH.

145.1°. There is an internal hydrogen bond in the $[(C_6F_5)_3B(OH)]^-$ ion between one of the hydrogens of the water moiety and an aromatic fluorine atom, with an O−F distance of 2.810(3) Å and an O−H···F angle of 122(3)°. The C−F bonds vary from 1.345(4) to 1.376(5) Å, the C−C bonds vary from 1.362(6) to 1.393(5) Å, and the B−C bonds vary from 1.651(5) to 1.655(5) Å. The bond lengths contained in this structure are similar to those found in a number of other ammonium hydroxoborate compounds.[77,78]

In summary, a new process for the ring opening of nonactivated aziridines with catalytic amounts of $B(C_6F_5)_3$ in acetonitrile has been developed. The reaction proceeds with a variety of amines without any special precautions to exclude water, resulting in functionalized *trans*-diamines in high yields. NMR evidence suggests that in situ formed $[(C_6F_5)_3B(OH_2)]\cdot H_2O$ is the catalyst promoting the reaction through a Brønsted acid manifold. This unexpected scenario likely operates in other synthetically useful catalytic processes and is subject to ongoing investigations.

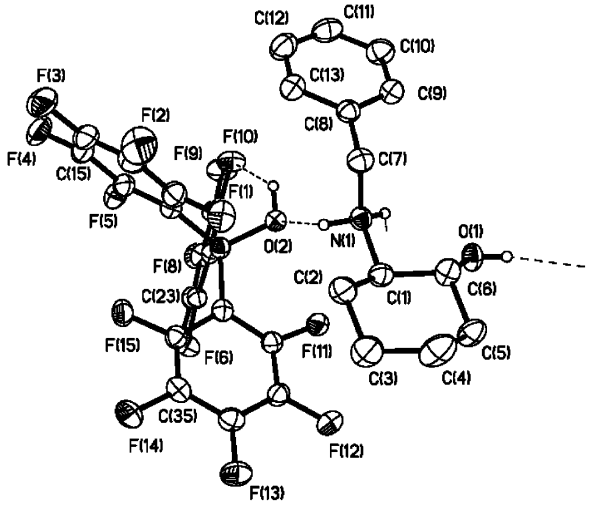


FIGURE 6. X-ray structure of amino alcohol−$(C_6F_5)_3B(OH_2)$ complex (**3**) showing 30% probability displacement ellipsoids. Selected bond lengths (Å) and angles (deg): B(1)−O(2) 1.498-(5), B(1)−C(11A) 1.654(5), B(1)−C(21) 1.655(5), B(1)−C(31) 1.651(5); O(2)−B(1)−C(31) 106.2(3), O(2)−B(1)−C(11A) 107.5-(3), O(2)−B(1)−C(21) 108.9(3).

Experimental Section

Representative Procedure for the Ring-Opening Reaction of Aziridines with Nucleophiles Catalyzed with $B(C_6F_5)_3$: *trans*-*N*,*N*′-Dibenzyl-1,2-cyclohexanediamine (2a). In a 15 × 100 mm^2 screw cap test tube, fitted with septum and magnetic stir bar, was placed *N*-benzyl cyclohexene imine (155 mg, 0.827 mmol), $B(C_6F_5)_3$ (42 mg, 0.083 mmol, 10 mol %), and 4 mL of degassed A.C.S. grade acetonitrile. No special precautions were taken to exclude water from the reaction. *N*-Benzylamine (108 μL, 1 mmol) was added via syringe and the solution was stirred under a stream of argon at 65 °C for 16 h; when TLC showed no remaining starting material. The solvent was removed in vacuo and to the residue was added 0.8 g of Amberlyst A-21 resin (1 g per mmol of product) and 5 mL of dichloromethane. The solution was stirred for 1 h then the resin was removed by filtration through a cotton plug. The solvent was removed in vacuo and the residue was purified by flash chromatography (R_f =0.3, SiO_2, 95:5 CH_2Cl_2/MeOH) to yield **2a** (238 mg, 0.808 mmol, 98%) as a clear oil that solidified to a white solid after standing.

***trans*-*N*,*N*′-Dibenzyl-1,2-cyclohexanediamine (2a):** White solid, mp 34−35 °C (lit.[79] mp 36−37 °C), 98% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.18 (m, 5H) 3.86 (d, J = 13.2 Hz, 1H), 3.63 (d, J = 13.1 Hz, 1H), 2.24 (m, 1H), 2.13 (d, 2H), 1.70 (m, 1H), 1.20 (m, 1H), 1.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 141.0, 128.3, 128.0, 126.8, 60.9, 50.9, 31.5, 25.0. ESI 295 (M^+ + 1); EI-MS *m*/*z* (%) 294 (M^+, 10), 203 (29), 189 (27), 106 (42), 91 (100); HR-MS calcd for $C_{20}H_{26}N_2$ 294.209599, obsd 294.209710.

***trans*-*N*-Benzyl-*N*′-(4-methoxy-benzyl)-1,2-cyclohexanediamine (2b):** Clear oil, 99% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31−7.29 (m, 4H), 7.24−7.21 (m, 3H), 6.33 (m, 2H), 3.89 (d, J = 13.2 Hz, 1H), 3.83 (d, J = 13.0 Hz, 1H), 3.78 (s, 3H), 3.65 (d, J = 13.2 Hz, 1H), 3.59 (d, J = 13.0 Hz, 1H), 2.25 (m, 2H), 2.17−2.13 (m, 2H), 1.95 (s, 2H), 1.71 (m, 2H), 1.22 (m, 2H), 1.08−1.02 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.7, 141.3, 133.4, 129.3, 128.5, 128.2, 126.9, 113.9, 61.1, 60.9, 55.4, 51.1, 50.4, 31.7, 31.7, 25.2, 25.2. ESI 325 (M^+ + 1); EI-MS *m*/*z* (%) 324 (M^+, 5), 203 (34), 136 (37), 121 (100), 91 (68); HR-MS calcd for $C_{21}H_{28}N_2O$ 324.220164, obsd 324.220302.

***trans*-*N*-Benzyl-*N*′-phenyl-1,2-cyclohexanediamine (2c):** White solid, mp 72−73°C (lit.[44] mp 68−70°C), 99% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.25 (m, 4H), 7.22−7.18 (m, 1H), 7.12 (t, J = 7.9 Hz, 2H), 6.67 (t, J = 7.9 Hz, 1H), 6.62 (d, J = 7.9 Hz, 2H), 3.89 (d, J = 13.4 Hz, 1H), 3.65 (d, J = 13.4 Hz, 1H), 3.42 (d, 1H), 3.10 (d, 1H), 2.31 (td, 1H), 2.17−2.11 (m, 3H), 1.74−1.65 (m, 2H), 1.33−1.17 (m, 3H), 1.04−0.94 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.3, 140.8, 129.3, 128.4, 128.1, 126.9, 117.7, 114.1, 60.9, 57.5, 50.8, 32.5, 31.5, 25.0, 24.7. ESI 281 (M^+ + 1); EI-MS *m*/*z* (%) 280 (M^+, 40), 188 (52), 172 (28), 146 (47), 132 (37), 106 (81), 91 (100); HR-MS calcd for $C_{19}H_{24}N_2$ 280.193949, obsd 280.194107.

***trans*-*N*-Benzyl-*N*′-methyl-*N*′-phenyl-1,2-cyclohexanediamine (2d):** Clear oil, 84% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30−7.18 (m, 7H), 6.87 (d, J = 8.0 Hz, 2H), 6.72 (t, J = 7.2 Hz, 1H), 3.90 (d, J = 13.6 Hz, 1H), 3.67 (d, J = 13.4 Hz, 1H), 3.51 (td, 1H), 2.60 (td, 1H), 2.53 (s, 3H), 2.26−2.21 (m, 2H), 1.74−1.62 (m, 3H), 1.43−1.14 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.3, 140.8, 129.2, 128.5, 128.3, 126.9, 117.6, 114.8, 64.1, 56.8, 50.9, 31.8, 30.7, 27.0, 25.9, 24.7. ESI 295 (M^+ + 1); EI-MS *m*/*z* (%) 294 (M^+, 67), 187 (64), 146 (59), 120 (100), 107 (60), 91 (81); HR-MS calcd for $C_{20}H_{26}N_2$ 294.209599, obsd 294.209200.

***trans*-*N*-Benzyl-*N*′-(1-(*S*)-phenylethyl)-1,2-cyclohexanediamine (2e):** Isolated as a 50:50 mix of diastereomers as a clear oil, 98% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.15 (m, 10H), 3.94 (d, 1H), 3.89 (m, 2H), 3.83 (m, 1H), 3.66 (d, J = 1.8 Hz, 1H), 3.62 (d, J = 1.9 Hz, 1H), 2.35 (td, 2H), 2.22 (td, 2H), 2.15−1.88 (m, 8H), 1.33 (d, J = 6.7 Hz, 1H), 1.31 (d, J = 6.6 Hz, 1H), 1.21−1.07 (m, 4H), 1.05−0.81 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.6, 146.0, 141.4, 141.3, 128.5, 128.5, 128.4, 128.1, 128.0, 126.9, 126.8, 126.8, 126.7, 61.5, 61.4, 59.7, 57.9, 55.8, 54.4, 51.1, 50.9, 32.7, 31.7, 31.6, 31.6, 25.8, 25.4, 25.2, 25.0, 24.9, 24.0. ESI 309 (M^+ + 1); EI-MS *m*/*z* (%) 308 (M^+, 5), 217 (22), 203 (50), 189 (38), 120 (54), 105 (94), 91 (100); HR-MS calcd for $C_{21}H_{28}N_2$ 308.225249, obsd 308.224048.

***trans*-*N*-(2-(Phenylthio)cyclohexyl)benzenemethanamine (2f):**[45] Clear oil, 98% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35−7.20 (m, 10H), 3.91 (d, J = 13.1 Hz, 1H), 3.70 (d, J = 13.1 Hz, 1H), 2.94 (dd, 1H), 2.88 (s, 1H), 2.42 (td, J = 9.5, 4.0 Hz, 1H), 2.18 (m, 1H), 2.07 (d, 1H), 1.66 (m, 2H), 1.43−1.11 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 140.3, 133.6, 133.3, 128.9, 128.6, 128.3, 127.4, 127.0, 59.0, 53.6, 50.9, 33.5, 32.0, 26.3, 24.4. ESI 298 (M^+ + 1); EI-MS *m*/*z* (%) 297 (M^+, 8), 188 (37), 146 (60), 106 (93), 91 (100); HR-MS calcd for $C_{19}H_{23}NS$ 297.154428, obsd 297.155122.

***trans*-3-(2-*N*-Benzylamino-cyclohexylamino)propionic acid methyl ester (2 g):** Light brown oil, 54% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33−7.20 (m, 5H), 3.90 (d, J = 13.2 Hz, 1H), 3.63 (d, 1H), 3.62 (s, 3H), 3.00 (m, 1H), 2.71 (m, 1H), 2.47 (m, 2H), 2.19−2.07 (m, 4H), 1.82 (br s, 2H), 1.71 (m, 2H), 1.35−1.19 (m, 2H), 1.05−0.90 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.4, 141.2, 128.4, 128.3, 126.9, 61.6, 61.0, 51.6, 51.2, 42.4, 35.5, 31.8, 31.7, 25.2, 25.1. ESI 291 (M^+ + 1); EI-MS *m*/*z* (%) 291 (M^+ + H^+, 18), 290 (M^+, 13), 217 (21), 199 (27), 185 (62), 142 (37), 104 (72), 96 (63), 91 (100); HR-MS calcd for $C_{17}H_{26}N_2O_2$ 290.199428, obsd 290.198649. The compound was found to decompose when passed through either silica or alumina. Therefore, the compound contains small amounts of impurities.

***trans*-3-(2-*N*-Benzylamino-cyclohexylamino)propan-1-ol (2h):** Clear oil, 97% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.31−7.20 (m, 5H), 3.88 (d, J = 12.8 Hz, 1H), 3.82 (s, 1H), 3.70 (t, 2H), 3.63 (d, J = 13 Hz, 1H), 2.82−2.77 (m, 1H), 2.68−2.63 (m, 1H), 2.19−2.06 (m, 4H), 1.69−1.64 (m, 4H), 1.23−1.18 (t, 2H), 1.12−0.99 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ140.9, 128.4, 128.1, 126.8, 63.0, 62.1, 60.5, 50.9, 46.1, 32.2, 31.6, 31.4, 25.1, 24.8. ESI 263 (M^+ + 1). The compound was found to decompose when passed through either silica or alumina and over time even when stored at −20 °C. Therefore, the compound contains small amounts of impurities.

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***N*-[1-Phenyl-2-(phenylthio)ethyl]benzenemethanamine (2j):**[80] Clear oil, 95% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.15 (m, 15H), 4.36 (t, J = 7.2 Hz, 1H), 3.76 (s, 2H), 3.08 (d, J = 7.2 Hz, 2H), 1.63 (br s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 140.6, 140.2, 134.6, 132.4, 128.9, 128.7, 128.6, 128.2, 128.1, 127.6, 127.3, 127.1, 53.8, 53.5; ^{15}N NMR ($CDCl_3$, externally referenced to CH_3NO_2, 36 MHz) δ −340.4; ^{1}H, ^{15}N HMBC shows a strong correlation between ^{15}N and the ^{1}H peak at 4.36 ppm.

***trans*-2-(*N*-Benzylamino-cyclohexyl)-4-methylbenzenesulfonamide (2k):** White solid, mp 119−119.5 °C (lit.[40] mp 86.5−87.3 °C), 99% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.72 (d, J = 8.4 Hz, 2H), 7.34−7.17 (m, 7H), 5.42 (br s, 1H), 3.74 (d, J = 13.0 Hz, 1H), 3.56 (d, J = 13.0 Hz, 1H), 2.68 (td, J = 4.4 Hz, J = 10.0 Hz, 1H), 2.36 (s, 3H), 2.22 (td, 1H), 2.15−2.07 (m, 2H), 1.70−1.61 (m, 2H), 1.25−1.13 (m, 4H), 1.04−0.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.3, 140.3, 137.4, 129.7, 128.6, 128.2, 127.3, 127.1, 59.9, 57.7, 50.2, 33.0, 31.4, 24.8, 24.6, 21,7. ESI 359 ($M^+ + 1$). EI-MS m/z (%) 359 (M^+, 3), 203 (100), 186 (39), 91 (73); HR-MS calcd for $C_{20}H_{26}N_2O_2S$ 359.179325, obsd 359.178874.

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Supporting Information Available: Experimental procedures and spectral data for aziridines **1a**, **1b**, **1c**, **1d**, and **1e** and their precursors. This material is available free of charge via the Internet at http://pubs.acs.org.

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