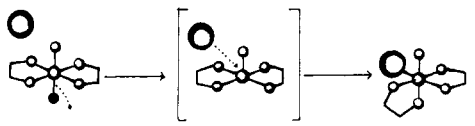

Figure 4. Proposed dissociative mechanism for the dehydration–anation of *trans*-$[CrF(en)_2(H_2O)]X_2$. The intermediate is a square-based pyramid; there is no rupture of the Cr–N(amine) bond, and the trans to cis isomerization is due to the entering anion X (● = water molecule).

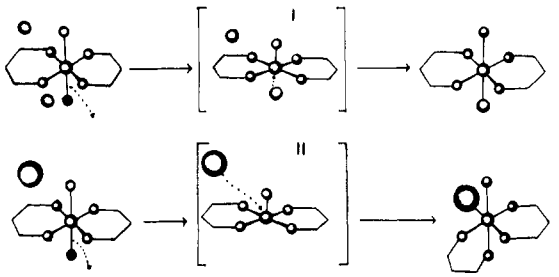

Figure 5. Proposed dissociative mechanism for the dehydration–anation of *trans*-$[CrF(tn)_2(H_2O)]X_2$. The intermediate is a square-based pyramid. There is no rupture of the Cr–N(amine) bond. When the entering anion, X^-, is small (Cl, Br), there is no trans to cis isomerization (I); when the entering anion is larger (I, S_2O_6), there is isomerization (II) (● = water molecule).

nonisomerization of the *trans*-$[CrF_2(aa)_2]Cl$ (aa = en, tn) series indicates that the trans to cis isomerization, in all the *trans*-$[CrF(en)_2(H_2O)]^{2+}$ salts and in the iodide and dithionate salts of *trans*-$[CrF(tn)_2(H_2O)]^{2+}$, occurs after and is due to the dehydration–anation process. In this case there is no rupture of the Cr^{III}–N(amine) bond.

Conclusions

The lack of X-ray structural data forces us to neglect the structural aspects of the solid-state transformation. Consequently, we are very limited in the interpretation of the results. But, taking into account all the experimental facts, especially the isomorphism, we can point out the following reasonable possibilities:

(a) E_a increases with the size of the anion (I > Br > Cl) due to the existence of less free space in the lattice, created by the packing of the anions, which are more or less similar in size with the voluminous *trans*-$[CrF(chxn)_2(H_2O)]^{2+}$ cation.

(b) E_a varies according to chxn > en > tn, possibly due to the different sizes of the amines and the isomerization process that occurs in many cases.

(c) Only in the chxn case may the isomerization be explained by the rupture of the Cr^{III}–N(amine) bond, while in the other two cases, the experimental data indicate one internal rearrangement of the pentacoordinate intermediate without rupture of the Cr–N(amine) bond.

(d) As a result of this, in the chxn case, E_a must correspond to two quasi-simultaneous processes: the dehydration and the Cr–N(amine) bond rupture. In contrast, in the en and tn cases, E_a corresponds only to the dehydration process, without rupture of the Cr–N(amine) bond. Consequently, E_a must be lower in the en and tn cases, compared with that in the chxn compounds. This is the experimental fact.

Contribution from the Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706

Boron Analogues of Choline. 2.[1] Efficient Syntheses of Boron Analogues of Choline, Acetylcholine, and Substituted Acetylcholines

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An efficient synthesis of isoelectronic and isostructural boron analogues of acetylcholine $[CH_3C(O)OCH_2CH_2N(Me_2)BH_3]$, benzoylcholine, (phenylacetyl)choline, and (phenoxyacetyl)choline from the reaction of the corresponding ester hydrochlorides with Et_4NBH_4 is described. The ester hydrochlorides are prepared from $Me_2NCH_2CH_2OH$ and the corresponding acid chlorides. Both reactions are very mild and give almost quantitative yields of products. A boron analogue of choline is similarly prepared from $Me_2NCH_2CH_2OH{\cdot}HCl$, which is in turn made efficiently from dimethylethanolamine and anhydrous HCl. ((Trimethylamine–boryl)carbonyl)choline is prepared by condensing trimethylamine–carboxyborane and the boron analogue of choline with dicyclohexylcarbodiimide. A boron analogue of suberoyldicholine is prepared from the reaction of the corresponding diester hydrochloride with $NaBH_4$.

We are interested in the synthesis and characterization of isoelectronic and isostructural boron analogues of biologically important molecules. These may be of use to probe fundamental biochemical events at the molecular level as welll as to provide entirely new classes of compounds of potential pharmacological value. Along these lines we have prepared some of the first examples of boron analogues of the α-amino acids[2-4] and their related precursors[5,6] and derivatives.[7,8] These analogues, typified by the protonated glycine analogue,[2] $H_3N{\cdot}BH_2CO_2H$, contain four-coordinate boron and possess appreciable air and hydrolytic stability. They have been found to possess significant pharmacological activity, in particular, antitumor,[9-11] antiarthritic,[12] and hypolipidemic[13,14] activity in animal model studies.

Boron analogues of other important biologically active molecules such as neurotransmitters can be envisioned. In a previous com-

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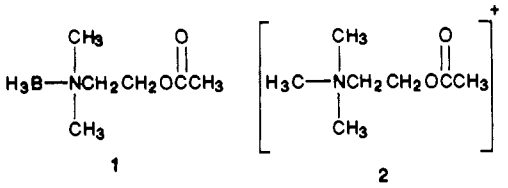
munication[1] we reported a remarkably facile synthesis of (2-acetoxyethyl)dimethylamine–borane (**1**), an isoelectronic and isostructural boron analogue of an important neurotransmitter, the acetylcholine (ACh) cation (**2**).



1 **2**

This boron analogue of ACh is a molecular species since the boron and nitrogen atoms bear canceling formal negative and positive charges, respectively. Although **1** belongs to a relatively well-known class of compounds, the amine–boranes, viewing the compound as an analogue of ACh suggests examination of its activity in novel areas. Thus this analogue may be useful in studies designed to probe the importance of the so-called "anionic" subsite of acetylcholinesterase and ACh receptors. In view of the potential interest in this area we have therefore prepared a number of additional examples of boron analogues of molecules related to ACh as well as a boron analogue of choline itself.[15]

Results and Discussion

A series of boron analogues of choline and its esters are prepared in good yields in two convenient steps shown in Schemes I and II.

Scheme I

$$\underset{\mathbf{3}}{Me_2NCH_2CH_2OH} + R\text{–}Cl \xrightarrow[0\ ^\circ C]{CH_2Cl_2 \text{ or ether}} \underset{\mathbf{4}}{}$$

4a, R = H
4b, R = CH_3CO
4c, R = C_6H_5CO
4d, $C_6H_5CH_2CO$

$$\underset{\mathbf{5}}{Me_2HN^+CH_2CH_2OR\ Cl^-}$$

5a, R = H (83%)
5b, R = CH_3CO (91%)
5c, R = C_6H_5CO (98%)
5d, R = $C_6H_5CH_2CO$ (89%)

$$\underset{\mathbf{3}}{Me_2NCH_2CH_2OH} + \underset{\mathbf{4e}}{C_6H_5OCH_2COCl} \xrightarrow[0\ ^\circ C]{\text{ether}} \underset{\mathbf{5a}\ (46\%)}{Me_2HN^+CH_2CH_2OH\ Cl^-} + \underset{\mathbf{6a}\ (45\%)}{Me_2NCH_2CH_2OCOCH_2OC_6H_5}$$

Scheme II

$$\underset{\mathbf{5}}{Me_2HN^+CH_2CH_2OR\ Cl^-} + Et_4NBH_4 \xrightarrow{CH_2Cl_2}$$

5a, R = H
5b, R = CH_3CO
5c, R = C_6H_5CO
5d, R = $C_6H_5CH_2CO$

$$\underset{\mathbf{1}}{H_3BN(Me_2)CH_2CH_2OR}$$

1a, R = H (40%)
1b, R = CH_3CO (85%)
1c, R = C_6H_5CO (17%)
1d, R = $C_6H_5CH_2CO$ (83%)

$$\underset{\mathbf{6a}}{Me_2NCH_2CH_2OCOCH_2OC_6H_5} + H_3B\cdot THF \xrightarrow{THF}$$

$$\underset{\mathbf{1e}\ (98\%)}{H_3BN(Me_2)CH_2CH_2OCOCH_2OC_6H_5}$$

Preparation of Precursor Hydrochlorides. *N,N*-Dimethylethanolamine (**3**) was allowed to react with the corresponding acid chlorides (**4b–d**) in either CH_2Cl_2 or anhydrous ether solvent at 0 °C to give the ester hydrochlorides (Scheme I). The yields of the ester hydrochlorides (**5b–d**) are almost quantitative in most cases. The protonated alcohol (**5a**) is similarly prepared in 83% yield from the alcohol **3** and dry HCl/ether solution at 0 °C. When a similar reaction is carried out with phenoxyacetyl chloride (**4e**) and **3** in ether at 0 °C, completely different types of products are obtained. (2-Hydroxyethyl)dimethylammonium chloride (**5a**) is separated as an insoluble solid (46% yield), and unprotonated ester (**6a**) is isolated from the mother liquor in 45% yield. The difference in reactivity of **4e** compared to that of the other acid chlorides used, **4b–d**, with **3** is not well-understood. All of these hydrochlorides are extremely hygroscopic, are purified by repeatedly washing with anhydrous ether under N_2, and are characterized by ^1H NMR and IR spectroscopy. These hydrochlorides have characteristic broad HN^+ stretches (2200 s, 2250 s, 2400 s cm^{-1}) in the IR spectra. In the ^1H NMR spectra the methyl proton resonances in the Me_2HN^+ moieties (2.74–2.94 ppm) are shifted downfield from the Me_2N absorption at 2.23 ppm of the unprotonated alcohol (**3**) as expected.

Preparation of Boron Analogues of Ch, Ch Esters, and ACh. The hydrochlorides (**5a–d**) are reduced efficiently to the desired boron complexes (**1a–d**) by Et_4NBH_4[16] in CH_2Cl_2 as shown in Scheme II. The boron analogue of choline (**1a**) is obtained in 40% yield, which is low compared to that of other analoguues prepared under similar reaction conditions (Table I). The low yield in **1a** can be explained by several observations. The alcohol (**1a**) has been prepared by other workers by complexation routes of the alcohol (**3**) with $H_3B\cdot THF$[15] and $H_3B\cdot SMe_2$[15a] as shown in the two equations

$$\underset{\mathbf{3}}{Me_2NCH_2CH_2OH} + H_3B\cdot THF \xrightarrow{20\ ^\circ C}$$

$$\underset{\mathbf{1a}}{H_3BN(Me_2)CH_2CH_2OH}$$

$$\underset{\mathbf{3}}{Me_2NCH_2CH_2OH} + H_3B\cdot SMe_2 \xrightarrow{-35\ ^\circ C}$$

$$\underset{\mathbf{1a}}{H_3BN(Me_2)CH_2CH_2OH}$$

It was observed that, concurrently with complexation, partial alcoholysis of the BH_3 by the –OH group also occurred.[15] By using a BH_3 to alcohol ratio of 4:3, the corresponding borate ester (**7**) was prepared. Subsequent hydrolysis provided[15] **1a**. Moreover,

$$\underset{\mathbf{3}}{3Me_2NCH_2CH_2OH} + 4(H_3B\cdot THF) \xrightarrow{20\ ^\circ C}$$

$$\underset{\mathbf{7}}{B(OCH_2CH_2NMe_2\cdot BH_3)_3}$$

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Table I. Selected Physical and Spectral Data of Boron Analogues of Ch, ACh, and Related Derivatives

compd	analogues	mp, °C [bp, °C (torr)]	yield, %	IR ($CDCl_3$), cm^{-1}	^{11}B NMR ($CDCl_3/BF_3{\cdot}Et_2O$), ppm (J_{BH}, Hz)
1a	$Me_2NCH_2CH_2OH{\cdot}BH_3$		40	3510 (OH), 2370 (BH), 2270 (BH)	−9.0 (q, 98)
1b	$Me_2NCH_2CH_2OCCH_3{\cdot}BH_3$	89–90 (0.4)	85	2380 (BH), 2260 (BH), 1740 (CO)	−9.4 (q, 95)
1c	$Me_2NCH_2CH_2OCC_6H_5{\cdot}BH_3$	89–90	59	2380 (BH), 2260 (BH), 1720 (CO)	−9.2 (q, 95)
1d	$Me_2NCH_2CH_2OCCH_2C_6H_5{\cdot}BH_3$		83	2360 (BH), 2215 (BH), 1740 (CO)	−9.5 (q, 93)
1e	$Me_2NCH_2CH_2OCCH_2OC_6H_5{\cdot}BH_3$	47–48	98	2360 (BH), 2260 (BH), 1760 (CO)	−9.4 (q, 91)
9	$Me_2NCH_2CH_2OCBH_2NMe_3{\cdot}BH_3$	107–108	55	2370 (BH), 2260 (BH), 1660 (CO)	−9.4 (br)
11	$(Me_2NCH_2CH_2OCCH_2CH_2CH_2)_2{\cdot}2BH_3$	58–59	31	2370 (BH), 2260 (BH), 1730 (CO)	−9.3 (q, 105)

it was noted that **1a** is very soluble in H_2O.[15b] A moderate yield (52%) of **1a** was reported[15a] with the $Me_2S{\cdot}BH_3$ reaction. Considering that alcohol **1a** is soluble in H_2O and can form the borate ester (**7**) easily with excess reagents, a 40% yield of **1a** after aqueous workup is not surprising.

The boron analogue of acetylcholine (**1b**) is prepared in 85% yield by reaction of the ester hydrochloride with Et_4NBH_4. It can be purified by vacuum distillation. Reduction of **5b** with a twofold excess of $NaBH_4$ in refluxing THF for 6 days produced 74% of 1b whereas a 19% yield is obtaining when the reaction period was shortened to 1 day. The benzoylcholine analogue (**1c**) is prepared in 59% yield by complexing $Me_2NCH_2CH_2OCOC_6H_5$ (**6b**) with $BH_3{\cdot}THF$. When the ester hydrochloride (**5c**) was reacted with Et_4NBH_4, it produced a ca. 1:2 mixture (determined by a ^1H NMR spectrum of the mixture) of the desired product (**1c**) and a by product (**6b**). Only a 10% yield of **1c** was achieved

$$\underset{\textbf{5c}}{Me_2HN^+CH_2CH_2OCOC_6H_5\ Cl^-} + Et_4NBH_4 \xrightarrow{CH_2Cl_2} \underset{\textbf{1c}}{Me_2NCH_2CH_2OCOC_6H_5{\cdot}BH_3} + \underset{\textbf{6b}}{Me_2NCH_2CH_2OCOC_6H_5}$$

when a twofold excess of $NaBH_4$ in refluxing THF was used for 6 days; it produced a 3–4% yield of the byproduct $Me_2NCH_2CH_2OCOC_6H_5$. The phenylacetylcholine analogue (**1d**) is similarly prepared in 83% yield by reacting the corresponding ester hydrochloride with Et_4NBH_4. It was purified by column chromatography on a silica gel column with a CH_2Cl_2/pentane/CH_3OH (20:1:1) solvent mixture elution. The (phenoxyacetyl)choline analogue (**1e**) is prepared by complexation of the ester (**6a**) with $H_3B{\cdot}THF$. Attempts to purify **1a** and **1d** by vacuum distillation failed, producing decomposition products instead.

Preparation of ACh Analogues with Two Boron Atoms. Trimethylamine–carboxyborane (**8**) may be considered an isoelectronic boron–nitrogen analogue of a (substituted) acetic acid. Therefore, we desired to prepare the ester of **8** with the boron analogue of choline (**1a**). Trimethylamine–carboxyborane[3] (**8**)

$$\underset{\textbf{8}}{Me_3NBH_2COOH} + \underset{\textbf{1a}}{H_3B{\cdot}Me_2NCH_2CH_2OH} \xrightarrow[CH_2Cl_2]{DCC} Me_2NCH_2CH_2OCOBH_2NMe_3{\cdot}BH_3$$

9

is condensed with **1a** in the presence of dicyclohexylcarbodiimide (DCC) to prepare (2-(((trimethylamine–boryl)carbonyl)oxy)-ethyl)dimethylamine–borane (**9**) in 55% yield. The product is recrystallized from CH_2Cl_2/ether.

Boron Analogue of Suberoyldicholine. Suberoyldicholine has been studied for its effects on cholinergic excitation activity.[17] The boron analogue of suberoyldicholine (**11**) is prepared from the reduction of the diester dihydrochloride (**10**) with $NaBH_4$ in 31% yield. The diester dihydrochloride (**10**) is in turn prepared from

$$\underset{\textbf{3}}{2Me_2NCH_2CH_2OH} + ClCO(CH_2)_6COCl \xrightarrow[0\,°C]{ether} \underset{\textbf{10}}{Me_2HN^+CH_2CH_2OCO(CH_2)_6COOCH_2CH_2^+NHMe_2\ 2Cl^-}$$

$$\textbf{10} + NaBH_4 \xrightarrow{THF} \underset{\textbf{11}}{Me_2NCH_2CH_2OCO(CH_2)_6COOCH_2CH_2NMe_2{\cdot}2BH_3}$$

the reaction of *N,N*-dimethylethanolamine (**3**) and suberoyl chloride in 93% yield. All new compounds have been characterized by elemental analyses and IR and ^1H and ^{11}B NMR spectroscopy. Selected physical and spectral data of these compounds are given in Table I. The IR spectra exhibited characteristic strong B—H and C=O absorptions. The ^1H and ^{11}B NMR spectral data are consistent with the structures of these compounds. In **9**, the chemical shifts of two magnetically nonequivalent B atoms ($-BH_3$ vs. $-BH_2$) are very similar and their individual absorptions overlapped to give a broad signal at 9.4 ppm.

The boron–hydrogen bonds in these analogues possess appreciable hydrolytic stability. For example, samples of **1b** and **1c** in a 1:2 D_2O/THF solvent mixture, after about 8 days, lost only ca. 10% and 33%, respectively, of their BH_3 groups due to hydrolysis.

NMR Consideration. Acetylcholine and its analogues play very important roles in the transmission of the nerve impulse. Since conformational changes upon attachment to receptors may be of importance to understand the mechanism of action of these small molecules, detailed conformational studies of these compounds have been extensively undertaken. On the basis of X-ray[18–20] and NMR[21–24] studies, it was shown that choline and acetylcholine

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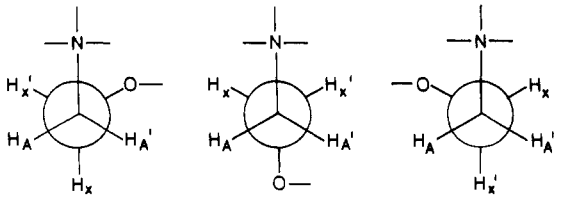
assume predominantly a gauche conformation in aqueous solution as well as in the solid state. Solution conformations of these compounds were assigned on the basis of analysis of AA'BB' multiplets of $-CH_2CH_2-$ resonances.

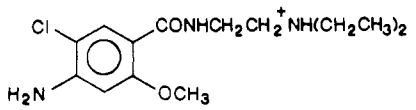
In the ^1H NMR spectra of all these boron analogues, an apparently perfect A_2X_2 system is observed for the $-CH_2CH_2-$ moiety as exemplified by the symmetrical 1:2:1 intensity distribution of the $-CH_2-$ triplets with $J = 6$ Hz. This implies that the two A protons are magnetically equivalent as are the two X protons. No observable difference exists in the free energy of gauche and trans conformations; hence, the population of each



conformer must be identical, $n_t = n_g = 0.33$. This conclusion is supported by the fact that spectra did not change upon decreasing the temperature to −60 °C.

Our results contrast with those reported[21-24] for acetylcholine, choline, and related compounds in D_2O, where an AA'BB' system with $J = 7$ Hz, $J' = 2.5$ Hz, and $n_g = 0.91$, $n_t = 0.09$ was observed. Due to rapid interconversion between gauche and trans rotameters, it is not possible to observe the individual coupling constants for these analogues in the NMR time scale. Instead, two time-averaged coupling constants are obtained.

The conformational behavior of metoclopramide and its protonated derivative **12** have been investigated[25] recently by ^1H NMR spectroscopy, and results similar to those of our studies were obtained in the observation of 1:2:1 symmetrical triplets ($J = 6$ Hz) for the $-CH_2-$ moieties.



12

Conclusion

Isoelectronic and isostructural boron analogues of acetylcholine and choline have been prepared in a facile synthesis. Other boron choline ester analogues related to ACh have also been synthesized in high yield. The pharmacological properties of these compounds are under investigation and will be reported elsewhere. The boron analogue of ACh, in a preliminary study, has exhibited a relatively low toxicity ($LD_{50} > 750$ mg/kg in male mice).[26]

Experimental Section

General Considerations. IR spectra were recorded on a Perkin-Elmer 297 spectrometer. ^1H and ^{11}B NMR spectra were obtained on Varian EM 360A and JEOL-FX 90Q spectrometers, respectively. Elemental analyses were performed by Galbraith Labs., Inc., Knoxville, TN. The following compounds were purchased and used without further purification: $Me_2NCH_2CH_2OH$ (Alrich), C_6H_5COCl (Fisher), CH_3COCl (Eastman Kodak), $C_6H_5OCH_2COCl$ (Aldrich), $C_6H_5CH_2COCl$ (Aldrich), suberoyl chloride (Aldrich), $NaBH_4$ (Alfa), Et_4NOH (Alfa), BH_3·THF (Alfa), dicyclohexylcarbodiimide (Chemical Dynamics). Et_4NBH_4[16] and $Me_3N{\cdot}BH_2COOH$[3] were prepared by methods described previously.

Preparation of (2-Hydroxyethyl)dimethylammonium Chloride (5a). To a vigorously stirred solution of $Me_2NCH_2CH_2OH$ (133.71 g, 1.5 mol) in 100 mL of ether at 0 °C was added a cold solution of dry HCl (72 g, 2 mol) in 400 mL of ether dropwise over a period of 2 h. White fumes with some precipitation were produced immediately. The cloudy suspension was then stirred at ambient temperature for an additional 1 h, and the solvent was removed by filtration under a N_2 atmosphere. The extremely hygroscopic salt thus obtained was repeatedly washed with anhydrous ether and finally vacuum-pumped overnight to give a slightly pinkish salt (**5a**) (156.8 g, 83%). Suitable ^1H NMR and IR spectra of **5a** could not be obtained because of its extreme hygroscopic nature and insolubility in organic solvents.

Preparation of (2-Acetoxyethyl)dimethylammonium Chloride (5b). To a stirred solution of $Me_2NCH_2CH_2OH$ (17.83 g, 0.2 mol) in 100 mL of CH_2Cl_2 at 0 °C was added CH_3COCl (17.27 g, 0.22 mol) in 100 mL of CH_2Cl_2 dropwise from a dropping funnel over a period of 1 h. White fumes were produced immediately. The resulting solution (some precipitate that formed initially went into solution) was stirred at ambient temperature overnight, and the solvent was removed by vacuum. The white solid thus obtained was repeatedly washed with anhydrous ether and dried under vacuum overnight. The extremely hygroscopic ester hydrochloride (**5b**) (30.6 g, 91%) had the following spectral characteristics. IR (cm^{-1}, $CDCl_3$): ν_{HN^+} 2200 s, 2250 s, 2400 br s; ν_{CO} 1740 s. ^1H NMR($CDCl_3$): δ 2.1 (s, CH_3CO), 2.94 (s, $CH_3N^+CH_3$), 3.43 (dist t, CH_2N), 4.48 (t, CH_2O).

Preparation of (2-(Benzoyloxy)ethyl)dimethylammonium Chloride (5c). To a stirred solution of $Me_2NCH_2CH_2OH$ (17.83 g, 0.2 mol) in 200 mL of CH_2Cl_2 at 0 °C was added C_6H_5COCl (30.93 g, 0.22 mol) in 200 mL of CH_2Cl_2 dropwise over a period of 1 h. The resulting mixture was stirred overnight at ambient temperature. The solvent was removed under reduced pressure, and the white solid thus obtained was washed repeatedly with ether and then dried under vacuum. The white hygroscopic ester hydrochloride (**5c**) (42.5 g, 98%) had the following spectra data. IR (cm^{-1}, $CDCl_3$): ν_{HN^+} 2210 s, 2250 m, 2400 br s; ν_{CO} 1720 s. ^1H NMR ($CDCl_3$): δ 2.94 (s, $CH_3N^+CH_3$), 3.5 (dist t, CH_2N), 4.7 (dist t, CH_2O), 7.2–8.0 (m, aromatic).

Preparation of (2-(Phenylacetoxy)ethyl)dimethylammonium Chloride (5d). To a stirred solution of $Me_2NCH_2CH_2OH$ (8.91 g, 0.1 mol) in 150 mL of ether at 0 °C was added C_6H_5COCl (15.46 g, 0.1 mol) in 50 mL of ether dropwise. White fumes accompanied by a white precipitate were formed as the acid chloride was added. The suspension was stirred at room temperature for 5 h and filtered, and the hygroscopic solid was repeatedly washed with ether. The ether washings were concentrated and then kept in the freezer to collect additional product. The combined solid (21.7 g, 89%) was recrystallized from CH_2Cl_2/ether in the freezer to give a purplish solid (18.28 g, 75%); mp 122–128 °C dec. IR (cm^{-1}, CH_2Cl_2): ν_{HN^+} 2200–2500 br s); ν_{CO} 1740 s. ^1H NMR ($CDCl_3$): δ 2.74 (s, $CH_3N^+CH_3$), 3.3 (br m, CH_2N), 3.65 (s, CH_2), 4.43 (br m, CH_2O), 7.15 (s, aromatic).

Preparation of 2-(Dimethylamino)ethyl Phenoxyacetate (6a). To a stirred solution of $Me_2NCH_2CH_2OH$ (8.91 g, 0.1 mol) in 150 mL of ether at 0 °C was added $C_6H_5OCH_2COCl$ (17.06 g, 0.1 mol) in 50 mL of ether dropwise. White fumes followed by precipitation of a white solid occurred as the reaction progressed. The suspension was stirred at room temperature for 5 h. The solid product $Me_2HN^+CH_2CH_2OH\,Cl^-$ (**5a**) was separated and repeatedly washed with ether (5.8 g, 46.18%). The ether portion was concentrated under reduced pressure to give the ester $Me_2NCH_2CH_2OCOCH_2OC_6H_5$ (**6a**; 10 g, 45%. IR (cm^{-1}, $CDCl_3$): ν_{CO} 1760 s. ^1H NMR ($CDCl_3$): δ 2.18 (s, CH_3NCH_3), 2.43 (t, CH_2N), 4.14 (t, CH_2O), 4.5 (s, CH_2OAr), 6.6–7.2 (m, aromatic).

Preparation of (2-Hydroxyethyl)dimethylamine–Borane (1a). To a stirred solution of $Me_2HN^+CH_2CH_2OH\,Cl^-$ (**5a**) (3.7 g, 0.03 mol) in 300 mL of CH_2Cl_2 was added solid Et_4NBH_4 (5 g, 0.034 mol) slowly. An initially vigorous evolution of H_2 gas took place. The mixture was stirred for 2 h at ambient temperature and then refluxed overnight. The cloudy solution was cooled, washed with 3 × 100 mL of H_2O, and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the colorless oily **1a** (1.2 g, 40.18%) was obtained. IR (cm^{-1}, CH_2Cl_2): ν_{OH} 3510 s; ν_{BH} 2370 s, 2270 s. ^1H NMR ($CDCl_3$): δ 2.6 (s, CH_3NCH_3), 2.87 (t, CH_2N) 3.53 (s, OH), 3.87 (t, CH_2O). ^{11}B NMR ($CDCl_3$, $BF_3{\cdot}Et_2O$): δ −9.0 (q, $J_{BH} = 98$ Hz). The spectral properties of **1a** matched well with the reported values.[15] An attempt to vacuum-distill **1a** was not successful. Anal. Calcd for $C_4H_{14}BNO$: C, 46.66; H, 13.70; N, 13.60. Found: C, 46.00; H, 12.50; N, 12.81.

Preparation of (2-Acetoxyethyl)dimethylamine–Borane (1b). To a stirred solution of the ester hydrochloride **5b** (3.80 g, 0.023 mol) in 300 mL of CH_2Cl_2 at room temperature was added solid Et_4NBH_4 (4.94 g, 0.034 mol, 50% excess) slowly. Initially, H_2 gas was evolved vigorously. When the reaction had subsided, it was refluxed for 3 h. The reaction mixture was then cooled, washed with water (3 × 100 mL), dried over $MgSO_4$, and concentrated and finally dried under vacuum. The product **1b**, a slightly yellowish liquid (2.8 g, 85% yield, pure by ^1H and ^{11}B NMR spectra) was distilled at reduced pressure to give a colorless liquid; bp 89–90 °C (0.4 torr). IR (cm^{-1}, CH_2Cl_2): ν_{BH} 2270 m, 2310 sh, 2380 s; ν_{CO} 1740 s. ^1H NMR ($CDCl_3$): δ 2.03 (s, CH_3), 2.62 (s, CH_3NCH_3), 2.98 (t, $J = 6$ Hz, CH_2N), 4.38 (t, $J = 6$ Hz, CH_2O). ^{11}B NMR

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($CDCl_3$, BF_3·Et_2O): δ − 9.42 (q, J_{BH} = 98 Hz). Anal. Calcd for $C_6H_{16}BNO_2$: C, 49.70; H, 11.12; N, 9.66; B, 7.46. Found: C, 49.63; H, 10.93; N, 9.32; B, 7.25.

Preparation of (2-(Benzoyloxy)ethyl)dimethylamine–Borane (1c). Method a. To a solution of the ester hydrochloride **5c** (31.4 g, 0.13 mol) in 500 mL of CH_2Cl_2 at room temperature was added Et_4NBH_4 (21.82 g, 0.15 mol) with stirring. After the initially vigorous H_2 evolution had subsided, the reaction mixture was refluxed overnight. This was then cooled, washed with water (3 × 150 mL), dried over $MgSO_4$, and concentrated. The semisolid material (18 g) thus obtained contained a ca. 1:2 ratio of H_3B·$NMe_2CH_2CH_2OCOC_6H_5$ (**1c**) and $Me_2NCH_2CH_2OCOC_6H_5$ (**6b**) (by ^1H NMR). To this mixture was added ca. 300 mL of pentane, and this preparation was cooled in the freezer. The desired product **1c** separated out as a solid (4.8 g, 17%) and was purified by recrystalliation from CH_2Cl_2/pentane: white needles; mp 89–90 °C. IR (cm^{-1}, $CDCl_3$): ν_{BH} 2260 m, 2320 sh, 2380 s; ν_{CO} 1720 s. ^1H NMR ($CDCl_3$): δ 2.64 (s, CH_3NCH_3), 3.1 (t, J = 6 Hz, CH_2N), 4.6 (t, J = 6 Hz, CH_2O), 7.2–8.0 (m, aromatic). ^{11}B NMR ($CDCl_3$, BF_3·Et_2O): δ −9.17 (q, J_{BH} = 95 Hz). Anal. Calcd for $C_{11}H_{18}BNO_2$: C, 63.80; H, 8.76; N, 6.76; B, 5.22. Found: C, 64.02; H, 8.80; N, 6.70; B, 5.10. The pentane solutions were concentrated and vacuum pumped to give oily $Me_2NCH_2CH_2OCOC_6H_5$ (**6b**) (12.5 g, 48%). IR (cm^{-1}, neat): ν_{CO} 1720 s. ^1H NMR ($CDCl_3$): δ 2.23 (s, CH_3NCH_3), 2.58 (t, J = 6 Hz, CH_2N), 4.3 (t, J = 6 Hz, CH_2O), 7.1–8.0 (m, aromatic).

Method b. To a solution of **6b** (12.5 g, 0.065 mol obtained from method a) in 100 mL of dry THF was added 100 mL of BH_3·THF (0.1 mol), and the resulting mixture was refluxed overnight. The clear solution was cooled and concentrated to a thick liquid. Ca. 100 mL of pentane was added to precipitate the product **1c**. The crude product was purified (7.9 g, 59%) and characterized similarly by the method descried in (a).

Preparation of (2-(Phenylacetoxy)ethyl)dimethylamine–Borane (1d). To a stirred slightly yellowish solution of **5d** (21.7 g, 0.089 mol) in 450 mL of CH_2Cl_2 at 0 °C was added Et_4NBH_4 (14.21 g, 0.098 mol) slowly under N_2. The mixture was stirred at room temperature for 2 h and then refluxed overnight. The solution was cooled, washed with water (3 × 100 mL), dried over $MgSO_4$, and concentrated to give **1d** (16.3 g, 82.83%). IR (cm^{-1}, CH_2Cl_2): ν_{BH} 2215 s, 2360 s; ν_{CO} 1740 s. ^1H NMR ($CDCl_3$): δ 2.40 (s, CH_3NCH_3), 2.83 (t, J = 6 Hz, CH_2N), 3.54 (s, CH_2Ar), 4.30 (t, J = 6 Hz, CH_2O), 7.20 (s, aromatic). ^{11}B NMR ($CDCl_3$, BF_3·Et_2O): δ −9.5 (q, J_{BH} = 93 Hz). Attempted distillation of **1d** under reduced pressure (0.3 torr) at 110 −150 °C produced decomposition products (e.g., loss of B—H, C=O, groups, etc.). Finally the crude product was purified by column chromatography on a silica gel column eluted with CH_2Cl_2/pentane/CH_3OH (20:1:1). Anal. Calcd for $C_{12}H_{20}BNO_2$: C, 65.19; H, 9.12; N, 6.33. Found: C, 65.34; H, 8.93; N, 6.29.

Preparation of (2-(Phenoxyacetoxy)ethyl)dimethylamine–Borane (1e). To a stirred solution of **6a** (10 g, 0.045 mol) in 100 mL of dry THF under N_2 was added BH_3·THF (80 mL of a 1 M solution 0.08 mol). The mixture was then refluxed overnight and cooled, and the solvent was stripped off. The oily material was taken up in 300 mL of CH_2Cl_2, washed with water (3 × 100 mL), dried over $MgSO_4$, and concentrated to a brown oily product (**1e**; 10.5 g, 98.84%). The crude product was dried under vacuuum for several days and then kept in the freezer, whereupon it solidified. The product was purified by recrystallization from CH_3OH/hexane to give white plates; mp 47–48 °C. IR (cm^{-1}, $CDCl_3$): ν_{BH} 2260 s, 2360 s; ν_{CO} 1760 s. ^1H NMR ($CDCl_3$): δ 2.42 (s, CH_3NCH_3), 2.85 (t, J= 6 Hz, CH_2N), 4.38 (t, J = 6 Hz, CH_2O), 4.50 (s, CH_2CO), 6.66–7.35 (m, aromatic). ^{11}B NMR ($CDCl_3$, BF_3·Et_2O: δ −9.4 (q, J_{BH} = 91 Hz). Anal. Calcd for $C_{12}H_{20}BNO_2$: C, 60.79; H, 8.50; N, 5.91. Found: C, 60.58; H, 8.43; N, 5.79.

Preparation of (2-(((Trimethylamine–boryl)carbonyl)oxy)ethyl)dimethylamine–Borane (9). To a solution of Me_3N·BH_2COOH (**8**; 11.69 g, 0.1 mol) and H_3B·$NMe_2CH_2CH_2OH$ (**1a**) (12.60 g, 0.1 mol) in 450 mL of CH_2Cl_2 was added dicyclohexylcarbodiimide (22.69 g, 0.11 mol), and the resulting clear solution was stirred at ambient temperature for 4 days. The insoluble dicyclohexylurea was removed each day by filtering the reaction mixture. After 1 day ca. 70% of the reaction was complete (from the weight of insoluble urea) and the reaction was stopped after 4 days (ca. 90% completion). The clear solution was washed with water (3 × 100 mL), dried over $MgSO_4$ and concenrated to give 17.1 g of the crude ester (**9**), which was contaminated with some unreacted starting materials and byproduct. The crude semisolid material was dried under vacuum and washed with small amounts of ether to give 11.1 g (55%) of **9**. Finally the product was recrystallized from CH_2Cl_2/ether; mp 107–108 °C. IR (cm^{-1}, $CDCl_3$): ν_{BH} 2260 s, 2370 s; ν_{CO} 1660 s. ^1H NMR ($CDCl_3$): δ 2.6 (s, CH_3NCH_3), 2.7 (s, Me_3N), 3.0 (t, J = 6 Hz, CH_2N), 4.27 (t, J = 6 Hz, CH_2O). Anal. Calcd for $C_8H_{24}B_2N_2O_2$: C, 47.69; H, 11.98; N, 13.87. Found: C, 47.59; H, 11.89; N, 13.68.

Preparation of Bis(2-(dimethylamino)ethyl) Suberate Dihydrochloride (10). To a solution of suberoyl chloride (25 g, 0.118 mol) in 350 mL of ether at 0 °C was added *N,N*-dimethylethanolamine (23.40 g, 0.2625 mol) in 50 mL of ether dropwise. A white precipitate formed immediately as the reactants were mixed. The mixture was stirred overnight at ambient temperature, filtered, washed repeatedly with ether under N_2, and then finally vacuum pumped. The yield of diester dihydrochloride was 43 g (93.27%). The product **10** is not very soluble in CH_2Cl_2 and $CHCl_3$ solvents but soluble in water. IR (cm^{-1}, Nujol): ν_{HN^+} 2210 s, 2250 m, 2400 br; ν_{CO} 1730 s. ^1H NMR (D_2O): δ 1.4 (br m, CH_2), 2.41 (br m, CH_2), 2.98 (s, CH_3NHCH_3), 3.44 (m, CH_2), 3.86 (t, CH_2N), 4.4 (dist t, CH_2O).

Preparation of (2,2′-(Suberoyldioxy)diethyl)bis(dimethylamine–borane) (11). To a suspension of the diester dihydrochloride **10** (38.94 g, 0.1 mol) in 500 mL of THF was added $NaBH_4$ (15.15 g, 0.4 mol) followed by another 100 mL of THF. The suspension was stirred at ambient temperature for 1 h followed by refluxing for 4 days. The mixture was cooled and filtered, 200 mL of CH_2Cl_2 was added, and the mixture was repeatedly washed with water (3 × 200 mL). The organic portion was dried over $MgSO_4$ and concentrated to give a solid product (**11**; yield 10.50 g, 31%), mp 58–59 °C. IR (CH_2Cl_2): ν_{BH} 2370 s, 2310 sh, 2260 s; ν_{CO} 1730 s. ^1H NMR ($CDCl_3$): δ 1.4 (br m, CH_2), 2.23 (t, CH_2CO), 2.6 (s, CH_3NCH_3), 3.0 (t, J = 6 Hz, CH_2N), 4.32 (t, J = 6 Hz, CH_2CO). ^{11}B NMR ($CDCl_3$, BF_3·Et_2O): δ −9.26 (q, J_{BH} = 105 Hz). Anal. Calcd for $C_{16}H_{38}B_2N_2O_4$: C, 55.84; H, 11.13; N, 8.14. Found: C, 56.08; H, 11.41; N, 8.14.

BH Stability toward Hydrolysis. Samples of **1b** and **1c** were dissolved in a 1:2 D_2O/THF solvent mixture in an NMR tube. After 8 days, ca. 90% of the BH_3 group of **1b** and 67% of the BH_3 group of **1c** remained unhydrolyzed as monitored by ^{11}B NMR.

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Note Added in Proof. An isoelectronic and isostructural boron analogue of ACh of formula Me_3N·$BH_2CH_2OCOCH_3$ has been referred to (Sedlak, D. Ph.D. Thesis, University of München, 1982) in papers describing chemistry leading to Me_3N·$BH_2CH_2SCH_3$, an intermediate en route to this analogue: Biffar, W.; Nöth, H.; Sedlak, D. *Organometallics* **1983**, *2*, 579. Nöth, H.; Sedlak, D. *Chem. Ber.* **1983**, *116*, 1479.

Registry No. **1a**, 82879-04-7; **1b**, 100898-92-8; **1c**, 103935-67-7; **1d**, 103935-68-8; **1e**, 103935-69-9; **5a**, 2498-25-1; **5b**, 17210-49-0; **5c**, 2208-05-1; **5d**, 103960-48-1; **6a**, 103960-49-2; **8**, 60788-33-2; **9**, 103935-70-2; **10**, 28216-46-8; **11**, 103935-71-3; $C_6H_5OCH_2COCl$, 701-99-5; $Me_2NCH_2CH_2OCOC_6H_5$, 2208-05-1; Et_4NBH_4, 17083-85-1; $Me_2NCH_2CH_2OH$, 108-01-0; suberoyl chloride, 10027-07-3; choline, 62-49-7.