SYNTHESIS AND STUDY OF AMINE-CARBOXYBORANES SUBSTITUTED ON THE BORON AND THEIR DERIVATIVES

doktori (PhD) értekezés

Berente Zoltán

Kossuth Lajos Tudományegyetem
Debrecen, 1999

List of abbreviations

BNCT	Boron Neutron Capture Therapy
Bu^t	*tert*-butyl, 1,1-dimethylethyl
4-CN-py	4-cyanopyridine
DABCO	1,4-diazabicyclo[2,2,2]octane
DMAP	4-dimethylaminopyridine
sym-DMEDA	*N,N'*-dimethylethylenediamine
Et	ethyl
HDL	high density lipoprotein
LDL	low density lipoprotein
Me	methyl
NBS	*N*-bromosuccinimide
Ph	phenyl
Phe	phenylalanine
pic	4-picoline, 4-methylpiridine
pip	piperidine, 1-azacyclohexane
Pr^i	isopropyl
py	pyridine
Q	quinuclidine, 1-azabicyclo[2,2,2]octane
THF	tetrahydrofurane
TMEDA	*N,N,N',N'*-tetramethylethylenediamine
TMPDA	*N,N,N',N'*-tetramethylpropylenediamine
TMS	tetramethylsilane

Legend

The boron-containing compounds throughout this thesis, except the "Summary of related literature", are marked with alphanumeric codes. Amine-borane complexes with specific substituents, but without regard to the amine, are referred to by numbers. If the amine is specified, a letter will be added to the number. Note: The letters denote one base of dibasic amines

A·BH_2COOH
1

A·BH_2COOMe
2

A·BH_2COOEt
3

A·BH_2COOPr^i
4

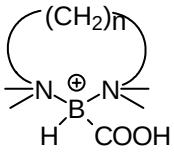
A·BH(Br)COOH
5

A·BH(Br)COOMe
6

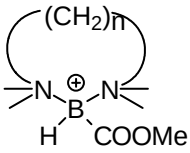
A·BH(Br)COOEt
7

A·BH(Br)$COOPr^i$
8

A·BBr_2COOH
9



10



11

A·BH(CN)COOH
12

A·BH(CN)COOMe
13

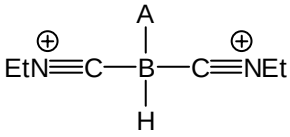
[$BH(CN)_2COOMe$](1–)
14

[$B(CN)_2(COOMe)_2$](2–)
15

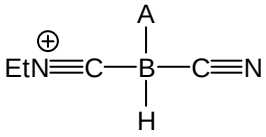
A·BH(NCAgCN)COOMe
16

A·BH(NC)COOMe
17

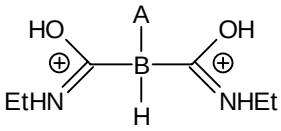
A·$BH(CN)_2$
18



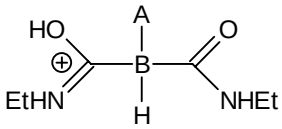
19



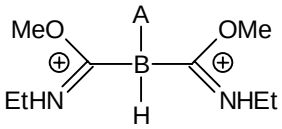
20



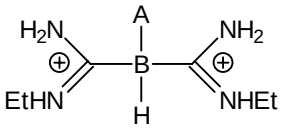
21



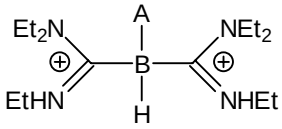
22



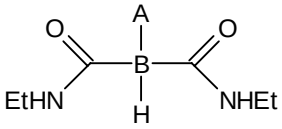
23



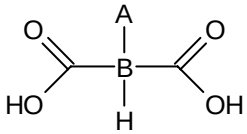
24



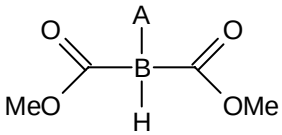
25



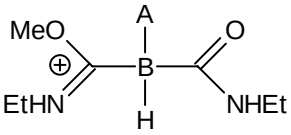
26



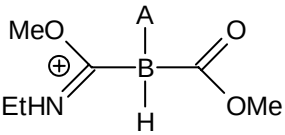
27



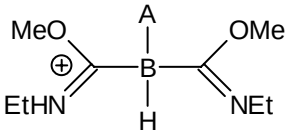
28



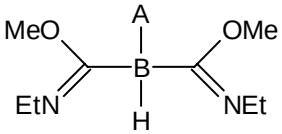
29



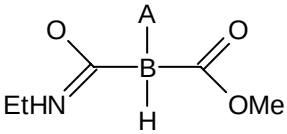
30



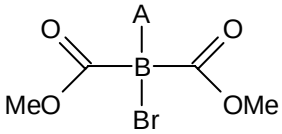
31



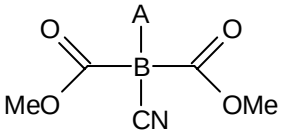
32



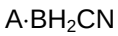
33



34



35



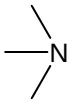
36

[A·BH$_2$CNEt](1+)
37

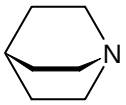
[A·BH$_2$C(OH)=NHEt](1+)
38

A·BH$_2$CONHEt
39

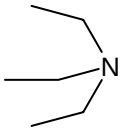
[A·BH$_2$C(OR)=NHEt](1+)
40



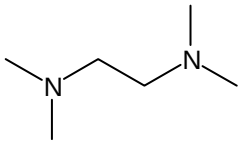
a



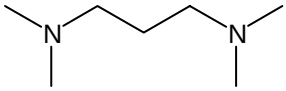
b



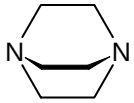
c



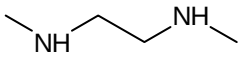
d



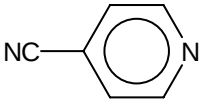
e



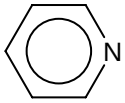
f



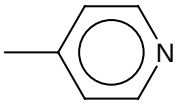
g



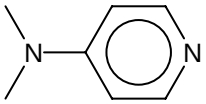
h



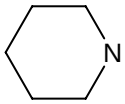
i



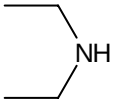
j



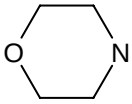
k



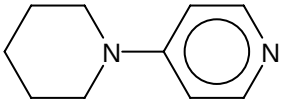
l



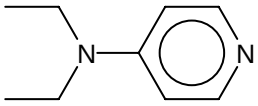
m



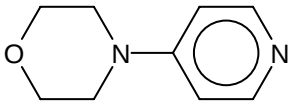
n



o



p



q

I. INTRODUCTION

The syntheses of the first representatives of amine-carboxyboranes (amine·BH_2COOH) were published in the late 1970's. Based on the isoelectronic relationship between $[\equiv C\text{-}N\equiv]^+$ and $[\equiv B\text{-}N\equiv]$ structural elements, amine-carboxyboranes were regarded as boron analogues of protonated α-amino acids and this concept, despite its shortcomings, has become widely accepted amongst the scientists in this area. Relying upon their structural similarity to biomolecules, the screening of biological and pharmacological activities of amine-carboxyboranes, as well as that of their precursors and some derivatives, began promptly. This quest has uncovered numerous valuable effects so far, and much effort is still being invested into the exploration of the mechanisms of these activities by studying the effect of these agents on relevant enzyme reactions and other processes at the molecular level. The promising biological activities of amine-carboxyboranes initiated the synthesis of a large number of their derivatives, however, the most of the compounds known so far are complexes of a broad variety of amines with carboxyborane bearing substituents on the carbonyl group, and only very few compounds have been synthesised with a substituent on the boron.

These proceedings, of course, arouse the interest of the boron chemistry research group at the Department of Inorganic and Analytical Chemistry at Lajos Kossuth University. However, they did not share the general opinion on analogy between amine-carboxyboranes and amino acids. Instead, they proposed that an analogy between amine-carboxyboranes and aliphatic carboxylic acids, based on the B—N ↔ C—C isoelectronic relationship (like in cases borazine ↔ benzene, hexagonal BN ↔ graphite, cubic BN ↔ diamond), would be more appropriate,

since this way the isoelectronic species possess the same charge. This concept seemed to be supported by experimental data (pK_a values, complexation studies and in a few cases X-ray data) and qualitative observations uncovered in the early studies of this new kind of compounds. With respect to all these, in the late 80's the group launched a long-term project with the purpose of setting up a library of amine-carboxyboranes bearing various substituents on the boron. Existence of such a library would allow a systematic comparison of amine-carboxyboranes and their derivatives substituted on the boron with carboxylic acids and their corresponding α-substituted derivatives in terms of physical chemical properties as well as carrying out biological structure-activity relationship studies among the new compounds.

The work described in this thesis, as a part of the project mentioned above, was aimed at the syntheses of hitherto unknown amine-cyanocarboxyboranes (amine·BH(CN)COOH), amine-dicarboxyboranes (amine·$BH(COOH)_2$) and their derivatives. We have chosen these substituents for the following reasons. First, earlier experiences in the literature make one conclude that amine-carboxyboranes substituted with an electron donating group on the boron may be less stable, because these substituents increase the hydridic character of the BH group. Second, these substituents were expected to turn amine-carboxyboranes into potential ligands in complexation studies with carboxylic groups of pK_a values higher than those of aliphatic carboxylic acids (4.5-5) but lower than those of unsubstituted amine-carboxyboranes (8-8.5). Third, the chemistry of cyanoboron compounds have considerable traditions in our laboratory, and as the literature on substitution reactions of amine-carboxyboranes was virtually non-existent at the time I joined the group, it seemed expedient to rely on the experience accumulated in that area. The synthetic strategy was the following: amine·BH_2COOH $\rightarrow$ amine·BH(Br)COOH $\rightarrow$ amine·BH(CN)COOH $\rightarrow$ amine·$BH(COOH)_2$. Earlier results of I. Lázár and Z. Kovács could be consulted in relation with the first step,

and the realisation of the third step was originally conceived by applying the standard method for B-CN $\rightarrow$ B-COOH transformations. However, as it often occurs on an unmapped area, this strategy had to be revised because of the long-winded failure with the second step and amine-dicarboxyboranes were finally prepared from amine-dicyanoboranes. In each reactions we strived to involve borane complexes of different types of amines (secondary and tertiary as well as pyridine-type ones), because, beyond the basicity of the amine, the presence or absence of a hydrogen on the nitrogen and especially the hybridisation of the nitrogen has major effect on the behaviour of the substituents on the boron, and thus, on the outcome of the reactions. Finally, it should be emphasised that enriching the inventory of the existing boron compounds was not at all the only purpose of the work, so we have been trying to uncover some characteristic features of the chemistry of these somewhat exotic compounds as well.

II. SUMMARY OF RELATED LITERATURE

Overview of the chemistry of amine-carboxyboranes and related compounds have been included in two review articles in the last years. Morin mentioned these compounds on the account that they were widely regarded as boron analogues of protonated amino acids,[1] whereas Carboni summarized the recent developments on the synthesis, reactivity and applications of these molecules as one type of amine borane complexes.[2] In the summary below, I wish to report the synthesis and biological activities of amine carboxyboranes and their derivatives in detail. Systematic study of chemical properties beyond the synthetic aspects is very scarce, so the characteristic features revealed so far will be mentioned together with the syntheses of the molecules. It should be pointed out at the beginning that amine-carboxyboranes and their derivatives mentioned below are solids (sometimes oils), which are stable as either neat substances or in most common solvents at room temperature or slightly elevated temperatures, despite the presence of B—H group(s) and carbonyl group adjacent to each other.

Those results achieved earlier in our laboratory, which are strongly related to my work will be cited in "Results and Discussion".

II.A. Synthesis of amine-carboxyboranes and their derivatives substituted on the carbonyl group

II.A.1. Synthesis of amine-carboxyboranes

Trimethylamine-carboxyborane, the first representative of amine-carboxyboranes was synthesized in 1976 by Spielvogel *et al.*[3] Since the attempts aimed at the direct hydrolysis of the cyano group adjacent to boron remained unsuccessful,[3,4] the authors applied $[Et_3O][BF_4]$ for the activation of the cyano group, and then hydrolyzed the thus formed [trimethylamine-(*N*-ethylnitrilium)dihydroboron(1+)] tetrafluoroborate into trimethylamine-carboxyborane in acidic aqueous solution.

The alkaline hydrolysis of the ethylnitrilium salt yielded the corresponding *N*-ethylamide, which could also be transformed into trimethylamine-carboxyborane.

$$A{\cdot}BH_2CN + [Et_3O][BF_4] \longrightarrow [A{\cdot}BH_2CNEt][BF_4] + Et_2O$$

$$[A{\cdot}BH_2CNEt][BF_4] + NaOH \longrightarrow A{\cdot}BH_2C(O)NHEt + Na[BF_4]$$

$$A{\cdot}BH_2C(O)NHEt + H_2O + HCl \longrightarrow A{\cdot}BH_2COOH + [EtNH_3]Cl$$

This procedure has become the most widely used method for the formation of carboxyl group on the boron.[3,5-12] Detailed studies revealed that a large number of amine-cyanoboranes readily undergoes the ethylation reaction and numerous ethylnitrilium salts were isolated[9,11,13-15]. In earlier syntheses the hydrolysis was performed at room temperature and it took days or even weeks to reach completion. The method has some limitations, e.g. it is not applicable to the preparation of carboxyboranes of secondary or primary amines, since though the corresponding *N*-ethylnitrilium salts are stable, their acidic hydrolysis leads to the rupture of the B—N bond.[5,16] A new, fast, high temperature hydrolysis of the *N*-ethylnitrilium salts was elaborated in our laboratory, which afforded the corresponding amine-carboxyboranes in high yield compared to earlier procedures.[13,14,17]

Other methods have also been applied for the activation of the cyano group in trimethylamine-cyanoborane. Miller hydrolyzed the $[Me_3N{\cdot}BH_2\text{-}NC\text{-}H_2B{\cdot}NMe_3]^+$ cation into $Me_3N{\cdot}BH_2COOH$ *via* the corresponding carboxamide.[18] $Me_3P{\cdot}BH_2COOH$ could be obtained by the same route.[19]

$$Me_3N{\cdot}BH_2I + CNBH_2{\cdot}NMe_3 \longrightarrow [Me_3N{\cdot}BH_2CNBH_2{\cdot}NMe_3]I$$

$$[Me_3N{\cdot}BH_2CNBH_2{\cdot}NMe_3]^+ + OH^- + H_2O \longrightarrow$$

$$\longrightarrow Me_3N{\cdot}BH_2C(O)NH_2 + 2\ H_2 + Me_3N + B(OH)_3$$

$$Me_3N{\cdot}BH_2C(O)NH_2 + H^+ + H_2O \longrightarrow Me_3N{\cdot}BH_2COOH + NH_4^+$$

Lázár *et al.* synthesized $Me_3N{\cdot}BH_2COOH$ by the hydrolysis of the $[Me_3N{\cdot}BH_2CN(Bu^t)]^+$ cation[20].

$$Me_3N{\cdot}BH_2CN + SbCl_5 \longrightarrow Me_3N{\cdot}BH_2CN{\cdot}SbCl_5$$

$$Me_3N{\cdot}BH_2CN{\cdot}SbCl_5 + Bu^tCl \longrightarrow [Me_3N{\cdot}BH_2CN(Bu^t)][SbCl_6]$$

$$[Me_3N{\cdot}BH_2CN(Bu^t)][SbCl_6] + 7\ KOH \longrightarrow$$
$$\longrightarrow Me_3N{\cdot}BH_2C(O)NH(Bu^t) + K[Sb(OH)_6] + 6\ KCl$$

$$Me_3N{\cdot}BH_2C(O)NH(Bu^t) + H_2O + H^+ \longrightarrow Me_3N{\cdot}BH_2COOH + [Bu^tNH_3]^+$$

Different approach could be used for the formation of carboxyl group on boron attached to phosphines. Imamoto *et al.* exchanged iodine directly to carboxylic acid group.[21]

$$(c\text{-}C_6H_{11})_3P{\cdot}BH_2I \xrightarrow[THF,\ -78°C]{LDBB,\ CO_2} (c\text{-}C_6H_{11})_3P{\cdot}BH_2COOH + \text{others}$$

A large number of amine-carboxyboranes has been synthesized in amine exchange reactions. This route can be applied to the synthesis of carboxyborane complex of any amine (A') which is either stronger base or less volatile than that in the starting complex (A), so amine-carboxyboranes not available *via* the ethylation route could be prepared this way. The most widely used starting material was $Me_3N{\cdot}BH_2COOH$,[22-29] but TMEDA[9,30] and *N*-Me-morpholine[31] complexes have also found application. It should be noted that deprotonation of the carboxyl group by the amines in excess was not reported.

$$A{\cdot}BH_2COOH + A' \longrightarrow A'{\cdot}BH_2COOH + A$$

II.A.2. Synthesis of amine-alkoxycarbonylboranes

The first representatives of amine-alkoxycarbonylboranes were synthesized by treating the [amine-(*N*-ethylnitrilium)hydroboron(1+)] cations with ethanol in the

presence of HCl.[8,32] Morse has prepared the intermediate amine-(*C*-alkoxy-*N*-ethylimidate)boranes also.[11,12]

$$[A{\cdot}BH_2CNEt][BF_4] + ROH \longrightarrow A{\cdot}BH_2C(OR)=NEt + H[BF_4]$$

$$A{\cdot}BH_2C(OR)=NEt + H_2O + H^+ \longrightarrow A{\cdot}BH_2C(O)OR + [EtNH_3]^+$$

During the last 15 years a remarkable repertoire has been developed for the esterification of the carboxylic group in amine-carboxyboranes.

Spielvogel *et al.*, probably with the amino acid analogy in mind, esterified the carboxylic group after its activation by dicyclohexyl-carbodiimide (DCC). Despite its shortcomings, i.e. 1-2 week reaction time, difficulties with isolation of the product from dicyclohexylurea (DCU) and very low yields with carboxyborane complexes of secondary and primary amines, other laboratories used this method also.[9,33,34]

$$A{\cdot}BH_2COOH + ROH + DCC \longrightarrow A{\cdot}BH_2COOR + DCU$$

Dallacker *et al.* have used *N,N'*-carbonyl-diimidazol (CDI) for the activation of the carboxylic group in the preparation of $Me_3N{\cdot}^{10}BH_2COOH$.[35]

$$Me_3N{\cdot}BH_2COOH + CDI \longrightarrow Me_3N{\cdot}BH_2C(O)X$$

$$Me_3N{\cdot}BH_2C(O)X \xrightarrow[X = 1\text{-imidazolyl}]{NaOEt\ /\ EtOH} Me_3N{\cdot}BH_2COOEt$$

A number of amine-alkoxycarbonylboranes was synthesized *via* the DMAP-catalyzed decomposition of carboxylic-carbonic anhydrides formed in the reaction between amine-carboxyboranes and alkyl carbonochloridates in the presence of Et_3N.[10,36]

$$A{\cdot}BH_2COOH + ClC(O)OR + Et_3N \longrightarrow A{\cdot}BH_2C(O)OCOOR + [Et_3NH]Cl$$

$$A{\cdot}BH_2C(O)OCOOR \xrightarrow{DMAP} A{\cdot}BH_2COOR + CO_2$$

The trimethylsilyl ester of $Me_3N{\cdot}BH_2COOH$ was synthesized by treating $Me_3N{\cdot}BH_2COOLi$ with Me_3SiCl.[33]

$$Me_3N{\cdot}BH_2COOH + n\text{-}BuLi \longrightarrow Me_3N{\cdot}BH_2COOLi$$

$$Me_3N{\cdot}BH_2COOLi + Me_3SiCl \longrightarrow Me_3N{\cdot}BH_2COOSiMe_3 + LiCl$$

Kovács found that the aliphatic tertiary amine complexes of methoxycarbonylboranes can also be conveniently prepared with good yields in methanol, in the presence of a cation exchange resin in H^+-form as a catalyst.[37]

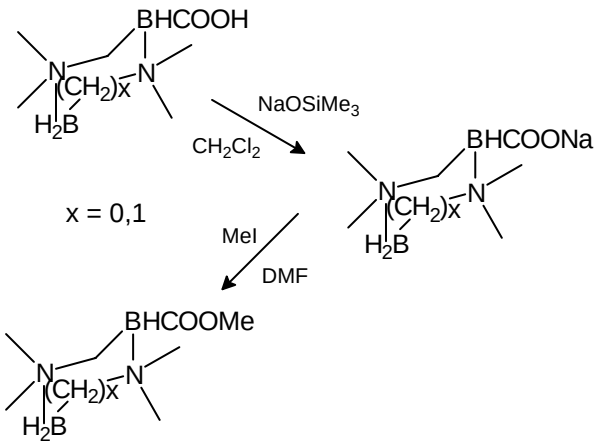
$$A{\cdot}BH_2COOH + MeOH \xrightarrow{\text{DOWEX AG 50 resin}} A{\cdot}BH_2COOMe + H_2O$$

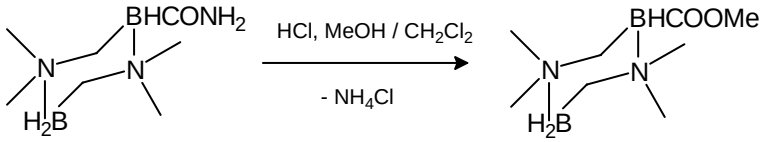
The most general method so far was found by Morse *et al.* They reacted amine-carboxyboranes with the corresponding trialkyl ortoformate in the presence of $Et_2O{\cdot}BF_3$.[38] The applicability of the method seems to be limited by the availability of the corresponding ortoformates only.

$$A{\cdot}BH_2COOH + HC(OR)_3 \xrightarrow{Et_2O{\cdot}BF_3 \,/\, CH_2Cl_2} A{\cdot}BH_2COOR + ROH + HCOOR$$

Ferrie and Miller applied two more esterification methods for carboxyl groups attached to boron in multipolar framework compounds. One was methylation of the

deprotonated carboxylic group with MeI and the other was nucleophilic substitution from amides.[19]





Amine exchange reaction has become widely used for the synthesis of amine-alkoxycarbonylboranes also, since the conditions necessary for the esterification caused side reactions, especially in the case of complexes of secondary or primary amines.[12,17,27,28,31,33,34]

$$A{\cdot}BH_2COOR + A' \longrightarrow A'{\cdot}BH_2COOR + A$$

II.A.3. Synthesis of amine-alkylcarbamoylboranes

Most of the known amine-*N*-ethylcarbamoylboranes were synthesized by the alkaline hydrolysis of the corresponding [amine-(*N*-ethylnitrilium)hydroboron(1+)] tetrafluoroborates.[3,5,9,11,12,39]

$$[A{\cdot}BH_2CNEt][BF_4] + NaOH \longrightarrow A{\cdot}BH_2C(O)NHEt + Na[BF_4]$$

Similarly, alkaline hydrolysis of $[Me_3N{\cdot}BH_2CN(Bu^t)][SbCl_6]$ yielded the corresponding alkylamide also.[20]

$$[Me_3N{\cdot}BH_2CNBu^t][SbCl_6] + 7\ KOH \longrightarrow$$
$$\longrightarrow Me_3N{\cdot}BH_2C(O)NHBu^t + K[Sb(OH)_6] + 6\ KCl$$

Amide groups on the boron are known to be formed from carboxylic groups also. Das *et al.* used DCC for this purpose,[25,26,34,40] and Lázár has also synthesized an amine-arylcarbamoylborane by this route.[9] However, the reaction takes 1-2 weeks, and the separation of the desired product from DCU is difficult.

$$A{\cdot}BH_2COOH + R'R''NH + DCC \longrightarrow A{\cdot}BH_2CONR'R'' + DCU$$

Morse *et al.* have formed the amide bond in acetonitrile in the presence of Ph_3P, probably *via* an active intermediate of the structure $[Me_3N.BH_2C(O)OPPh_3]^+$.[28]

$$Me_3N{\cdot}BH_2COOH + RNH_2 \xrightarrow{Ph_3P\ /\ CH_3CN} Me_3N{\cdot}BH_2C(O)NHR$$

In the same publication the synthesis of trimethylamine-phenylcarbamoylborane is reported in a reaction between the corresponding carboxyborane and phenyl isocyanate.[28]

$$Me_3N{\cdot}BH_2COOH + OCNPh \longrightarrow Me_3N{\cdot}BH_2C(O)NHPh + CO_2$$

Dallacker *et al.* readily produced ammonia-carbamoyl-^{10}B-borane from trimethylamine-carboxyborane *via* its 1-imidazolyl derivative.[35]

$$Me_3N{\cdot}BH_2C(O)X + 2\ NH_3 \longrightarrow NH_3{\cdot}BH_2C(O)NH_2 + Me_3N + XH$$
X = 1-imidazolyl

Amine exchange reactions have been applied for syntheses of a number of amine-*N*-ethylcarbamoylboranes.[27,39]

$$A{\cdot}BH_2COONHEt + A' \longrightarrow A'{\cdot}BH_2CONHEt + A$$

Morse *et al.* have obtained the cyclic dimer of *N*-ethylcarbamoylborane by the elution of $(EtO)_2P(O)CH_2NMe_2{\cdot}BH_2C(O)NHEt$ from a silica gel column, and they found it among the products of the thermal decomposition of morpholine·$BH_2CONHEt$ also. This substance can be a good starting material for the preparation of a large variety of amine-*N*-ethylcarbamoylboranes as it was demonstrated in one example.[41]

$$(EtO)_2P(O)CH_2NMe_2{\cdot}BH_2C(O)NHEt \xrightarrow[\text{silica gel; } CH_2Cl_2\text{-ether}]{} \overline{BH_2C(O)NH(Et)BH_2C(O)NH(Et)}$$

$$[BH_2C(O)NHEt]_2 + 2\ MeNH_2 \longrightarrow 2\ MeNH_2{\cdot}BH_2C(O)NHEt$$

II.A.4. Synthesis of peptide derivatives of amine-carboxyboranes

Spielvogel *et al.* coupled a number of amino acids and a dipeptide to amine-carboxyboranes. These dipeptide or tripeptide "analogues" in liquid ammonia undergo amine exchange and, if their ester group is sterically not hindered, amide formation. The coupling was carried out by applying Ph_3P and CCl_4 in acetonitrile in the presence of Et_3N.[42-46] It was noted also, that attempts aimed at the synthesis of $Me_3N{\cdot}BH_2COCl$ by $SOCl_2$ resulted in the formation of $Me_3N{\cdot}BH_2Cl$.[42]

$$\xrightarrow[Ph_3P\ /\ CCl_4]{}$$

$$Me_3N{\cdot}BH_2COOH + HCl{\cdot}NH_2CH(R)COOR' \xrightarrow[Et_3N\ /\ CH_3CN]{} Me_3N{\cdot}BH_2C(O)NHCH(R)COOR' + H_2O + HCl$$

$$Me_3N{\cdot}BH_2COOH + HCl{\cdot}NH_2CH_2C(O)NH_2CH_2COOEt \longrightarrow Me_3N{\cdot}BH_2C(O)NHCH_2C(O)NH_2CH_2COOEt + H_2O + HCl$$

$$Me_3N{\cdot}BH_2C(O)NHCH(R)COOMe + NH_3 \longrightarrow NH_3{\cdot}BH_2C(O)NHCH(R)COOMe + Me_3N$$

$$Me_3N{\cdot}BH_2C(O)NHCH(R)COOMe + NH_3 \longrightarrow NH_3{\cdot}BH_2C(O)NHCH(R)CONH_2 + MeOH + Me_3N$$

Amine exchange reactions were used in the synthesis of new dipeptide and tripeptide derivatives with various N-terminal groups also.[47]

$$Me_3N{\cdot}BH_2CO\text{-}NHCH(R)COOMe + A \longrightarrow A{\cdot}BH_2CO\text{-}NHCH(R)COOMe + Me_3N$$

It should be noted that all peptide analogues contain boron exclusively next to the *N*-terminal nitrogen.

II.A.5. Metal salts and complexes of amine-carboxyboranes

Amine-carboxyboranes are very weak acids, their pK_a values range between 8.14 and 8.94.[25,30] Deprotonation takes place on the carboxylic groups, since detailed complexation study showed that ammonia-carboxyborane did not undergo deprotonation on the nitrogen at pH≤11.[48]

Deprotonated amine-carboxyboranes readily form complexes with metals and syntheses of a number of such complexes in solid form have been reported. The authors described supposed structures for these complexes, however, none of them was verified by X-ray diffraction measurements.

A number of simple 1:1 complexes of trimethylamine-carboxylatoborane and divalent metal cations ($[Me_3N{\cdot}BH_2COOM]NO_3{\cdot}CH_3CN{\cdot}3CH_3OH$, M= Co, Ca, Zn)

were prepared in Morse's laboratory, along with a mixed Co(III) complex of the following composition: *cis*-$[Co(en)_2(Me_3N{\cdot}BH_2COO)_2]Cl{\cdot}2.5H_2O{\cdot}0.5CH_3OH$, where carboxylatoborane ligands were assumed to act as bidentate ligands in the former complexes and unidentate in the Co(III) complex.[49]

Spielvogel *et al.* obtained the binuclear copper complexes of $Me_3N{\cdot}BH_2COOH$ with compositions [tetrakis-μ-(trimethylamine-boranecarboxylato)-bis-(trimethylamine-carboxyborane)-dicopper(II)][50] and [tetrakis-μ-(trimethylamine-boranecarboxylato)-acetonitrile-dicopper(II)].[51] The carboxylatoborane ligands were assumed to act as bidentate ligands bridging the two different metal ions, whereas protonated amine-carboxyboranes were proposed to bind to one of the metal ions through a Cu—O bond and simultaneously to a carboxylate oxygen through an O···H···O bond.

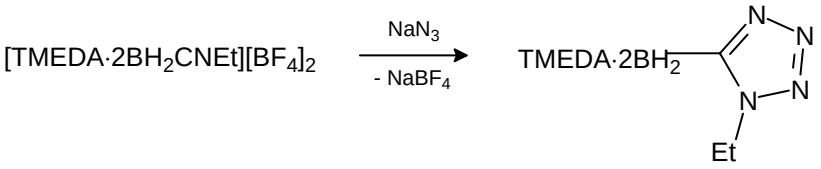
Norwood *et al.* reported the syntheses of two iron(III) and a chromium(III) complexes of composition $[M_3O(Me_3N{\cdot}BH_2COO)_6(solvent)_3]^+$, where trimethylamine-carboxylatoborane ligands acted as bridging bidentate ligands.[52]

The zinc complex of morpholine-carboxyborane was prepared from the sodium salt of the carboxyborane[52] on a cation exchange resin.[51]

II.A.6. Synthesis of miscellaneous amine-carboxyborane derivatives

As a result of his study of the reactivity of $[TMEDA{\cdot}2(BH_2CNEt)][BF_4]_2$ towards nucleophiles, Lázár has prepared a number of carboxylic acid derivatives[14]

$$[TMEDA{\cdot}2BH_2CNEt][BF_4]_2 + NaX \longrightarrow TMED{\cdot}2BH_2C(X)NEt + 2\ Na[BF_4]$$
$$X = CN, OEt, NH_2$$



Morse *et al.* synthesized the hydroxamic acid derivative of $Me_3N{\cdot}BH_2COOH$ by a method usual for the preparation of aliphatic hydroxamic acids. They also found

that, in contrast to the similar reactions with aliphatic carboxylic acids, the equilibrium is completely shifted towards the formation of the hydroxamic acid[53]

$$Me_3N{\cdot}BH_2COOH + NH_2OH{\cdot}HCl \longrightarrow Me_3N{\cdot}BH_2C(O)NHOH{\cdot}HCl + H_2O$$

II.B. Synthesis of derivatives of amine-carboxyboranes substituted on the boron

The preparation of the first representative of amine-carboxyborane derivatives substituted on the boron, Q·BH(Bzl)CONHEt was reported by Mills *et al*.[54] Although they mentioned that the corresponding carboxyborane could be observed spectroscopically, in their next paper, where they described the syntheses of a number of analogous amine-alkyl(*N*-ethylcarbamoyl)boranes,[55] the carboxamide→carboxylic acid transformation was not discussed at all.

$$A{\cdot}BH(R)CN + [Et_3O][BF_4] \longrightarrow [A{\cdot}BH(R)CNEt][BF_4] + Et_2O$$

$$[A{\cdot}BH(R)CNEt][BF_4] + NaOH \longrightarrow A{\cdot}BH(R)C(O)NHEt + Na[BF_4]$$

Later they reported that all attempts to hydrolyze amine-alkyl(*N*-ethylcarbamoyl)boranes remained unsuccessful, either in alkaline conditions due to unreactivity, or in acidic media due to decomposition. Spielvogel *et al*. had similar experience with $Me_3N{\cdot}BH(Me)CONHEt$, which was synthesized in the manner described above.[56] They assumed the decomposition to be the consequence of the increased hydridic character of the B—H hydrogen, due to the electron releasing effect of the alkyl substituent on the boron.

The formation of carboxylic group in amine-alkylboranes was attempted also *via* amine-alkyl[(*N*-ethylimino)alkoxymethyl]boranes, which were synthesized either by ethylation of amine-(*N*-ethylcarbamoyl)boranes by $[Et_3O][BF_4]$, or by nucleophilic addition to [amine-alkyl(*N*-ethylnitrilium)hydroboron(1+)] tetrafluoroborates.[57]

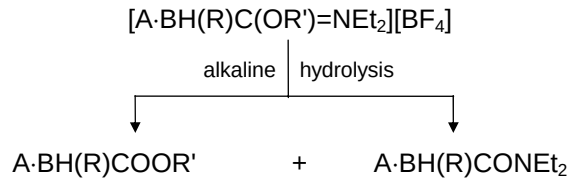
$$A{\cdot}BH(R)C(O)NHEt + [Et_3O][BF_4] \longrightarrow [A{\cdot}BH(R)C(OEt)NHEt][BF_4]$$

$$[A{\cdot}BH(R)C(OEt)NHEt][BF_4] + OH^- \longrightarrow A{\cdot}BH(R)C(OEt)=NEt$$

$$[A{\cdot}BH(R)CNEt][BF_4] + NaOR' \longrightarrow A{\cdot}BH(R)C(OR')=NEt$$

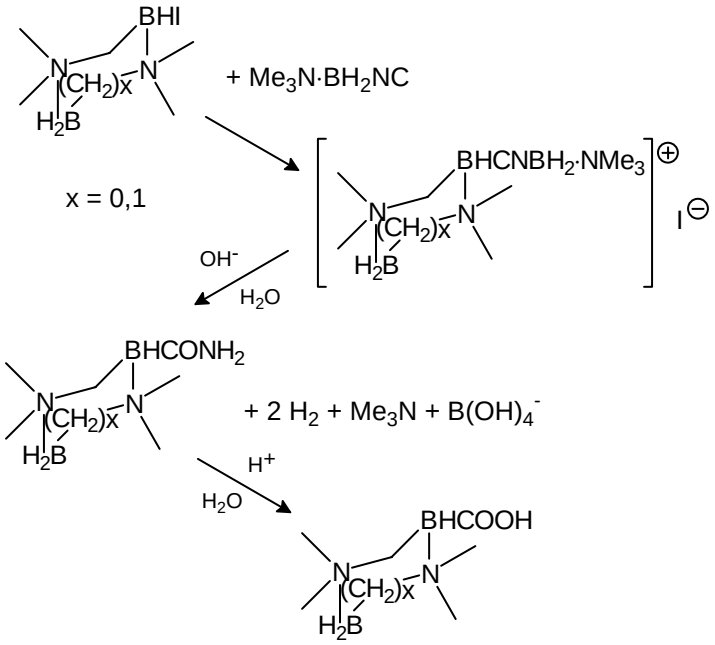
However, hydrolysis experiments in either acidic or alkaline media showed no reaction, in neutral water/MeCN solutions the products were the corresponding amides exclusively.[57]

Considering literature data, the authors suspected that alkylation of the lone pair on the nitrogen would promote the formation of ester group, and indeed, ester formation could be detected in varying ratios in alkaline hydrolysis of {amine-alkyl[(diethyliminiumylidene)alkoxymethyl]hydroboron(1+)} tetrafluoroborates.[57]



As a result of a detailed study of the reaction shown above, the authors reported the syntheses of four amine-alkyl(alkoxycarbonyl)boranes, and in the further hydrolysis experiments they rendered the formation of some Q·BH(Bu^i)COOH possible based on the appearance a new ν(CO) band in the IR spectrum of the reaction mixture.[58]

Miller formed carboxylic acid group on a few representatives of an uncommon type of amine-alkylboranes, i.e. multipolar framework heterocycles 1,1,4,4-tetramethyl-1,4-diazonia-2,5-diboratacyclohexane,[18] 1,1,3,3-tetramethyl-1,3-diazonia-2,4-diboratacyclopentane[19] as these ring systems are robust enough to withstand reasonable chemical processing. It should be noted that nucleophilic strength of aliphatic isonitriles were found not enough to carry out the substitution.


BHI
N
(CH2)x
N
H2B
+ Me3N·BH2NC
x = 0,1
BHCNBH2·NMe3
I
OH-
H2O
BHCONH2
+ 2 H2 + Me3N + B(OH)4-
H+
H2O
BHCOOH

II.C. Biological activities of amine-carboxyboranes and their derivatives

Considering their analogy to protonated α-amino acids, amine carboxyboranes and their derivatives have been submitted to biological activity screens which brought to light numerous promising effects. Due to these activities, syntheses of a large number of compounds are patented.[59-66]

The biological effects of these molecules have been studied in more and more detail in the last twenty years in order to disclose the relevant molecular processes behind these phenomena. Herewith I wish to present a brief summary of these efforts.

II.C.1. Antitumor (antineoplastic, anticancer) activities

Amine-carboxyboranes demonstrated significant antineoplastic activity against the growth of Ehrlich ascites carcinoma. The inhibition of protein synthesis by the boron derivatives in the tumor cells did not appear to be a mode of action that applied to the entire class of compounds,[67] though, considering the analogy with amino acids, the interference of these agents with protein synthesis could be expected.

Detailed mode of action studies involved examination of effects on growths of different tumor (e.g. $Tmolt_3$ human acute lymphoblastic T cell leukemia, L1210 lymphoid leukemia, HeLa-S^3 suspended cervical carcinoma, EH 118 MG glioma, SW480 human colorectal adenocarcinoma, TE418 human osteosarcoma, KB human epidermoid nasopharynx) cell lines *in vitro*, on tumors (P388 lymphocytic leukemia, Ehrlich ascites carcinoma and Lewis lung carcinoma) present in rodents *in vivo* and on activities of supposedly relevant enzymes. Generally, the optimum compound for each screen varied with the type of tumor cell. Based on the comparison of activities of amine-carboxyboranes with those of the corresponding amine-cyanoboranes, carboxy groups seemed to have little effect on activity.

$Me_3N{\cdot}BH_2C(O)$-Im proved to be exceptionally active, probably due to its high biological reactivity with tissue nucleophiles and enzymes.[27]

In a structure activity relationship study, the antineoplastic activity of carboxyborane complexes of cyclohexylamines and toluidines, where nitrogen is outside of the ring, were investigated. Besides a few minor differences they showed similar activity and mode of action in comparison with the carboxyborane complexes of heterocyclic amines.[29]

The copper complex [tetrakis-μ-(trimethylamine-boranecarboxylato)-bis-(trimethylamine-carboxyborane)-dicopper(II)] proved very efficient inhibitor of Ehrlich ascites growth in CF_1 male mice[50].

Peptide derivatives of amine-carboxyboranes proved to be weak antineoplastic agents, only those bearing short side-chains showed significant action[42]. Later the effect and mode of action of some peptide derivatives was studied in detail and $Me_3N{\cdot}BH_2CO$-Phe-OMe showed the most potent activity. The peptide derivatives showed some difference in action compared to the amine-carboxyboranes and their metal complexes.[44] A number of new peptide derivatives were synthesized to improve their delivery by increasing water solubility, however none except one had better activity.[47] The possible metabolites of $Me_3N{\cdot}BH_2CO$-Phe-OMe were studied also, and they afforded better activity than the parent compound.[45]

The conclusion of the mode of action studies can be drawn, that these agents inhibit key regulatory enzymes in nucleic acid synthesis[27,67] and the effect of these agents could be deduced to causing protein linked DNA breaks by inhibition of DNA topoisomerase II phosphorylation.[46,51,68,69]

II.C.2. Hypolipidemic activity

As betaine and choline have been implicated as cofactors in the liver for synthesis of cholesterol, the effect of amine-carboxyboranes and their derivatives on blood cholesterol levels have been also tested, and in certain cases considerable hypolipidemic activity was revealed.[23] It should be noted that positive correlation between antineoplastic and hypolipidemic effects of the same compounds in the

rodent screen is known in pharmacology.[40] *In vitro* enzymatic assays were performed also, and based on correlation analysis, the probable site of action of the amine-carboxyboranes and derivatives seemed to be in the early synthesis of lipids[23].

The ester derivatives of amine-carboxyboranes, particularly $Me_3N{\cdot}BH_2COOMe$, proved to be more effective hypolipidemic agents compared with the unsubstituted acids. These compounds inhibited the *de novo* synthesis of cholesterol and fatty acids. On the other hand, they accelerated the fecal excretion of cholesterol, too. Interestingly, lower drug doses afforded the higher magnitude of enzyme inhibition both *in vitro* and *in vivo*. Furthermore, $Me_3N{\cdot}BH_2COOMe$ reduced the cholesterol content of chylomicrons and LDL, with a significant elevation of HDL cholesterol contents, which is the desired combination of actions in the therapy of myocardial infarction and/or atherosclerosis.[8]

Carboxyborane complexes of heterocyclic amines showed similar modes of action, and the corresponding cyanoborane complexes were found virtually identical in activity.[70]

The copper complex also proved to be a potent hypolipidemic agent in rodents, however, its mode of action seemed to be somewhat different from that of either amine-carboxyboranes or standard therapeutic agents. It reduced cholesterol approximately equally in both the low-density and high-density lipoprotein fractions. It also reduced the appetites and increased the lipid excretion of CF_1 mice[71]. Later more metal complexes became involved in this study, and the calcium and chromium complexes showed the best and sodium and cobalt complexes the worst hypolipidemic activities. One mode of action of the metal complexes, unknown for amine-carboxyboranes, was to block the resorption of cholesterol from the intestine.[72]

Peptide derivatives of amine-carboxyboranes showed notable hypocholesterolemic activity and they proved to be more potent in triglyceride level suppression than the standard clofibrate[42]. In these studies the peptide derivatives seemed to be the

active agents, since in a comparative study $Me_3N{\cdot}BH_2CO$-Phe-OMe have outperformed its proposed metabolites.[45]

II.C.3. Antiinflammatory activity

While studying the metabolic effects of amine-carboxyboranes and derivatives on tumor cell metabolism, it was noted that the compounds interfered with oxidative phosphorylation processes of mitochondria, inhibited lysosomal enzymatic hydrolytic activities, and elevated cAMP levels. Such effects are known to be possessed also by commercially available anti-inflammatory agents (e.g., phenylbutazone, salicylates and indomethacin). This coincidence initiated the testing of these compounds for antiinflammatory activities, and numerous amine-carboxyboranes were found more potent, and much less toxic, than indomethacin.[32] Furthermore, they possess marked septic shock protective and pain blocking activity and they were found effective against induced edema and pleural effusion. Their supposed mode of action is blocking the release of chemical mediators (tumor necrosis factor-α and interleukins) from macrophages, thus reducing lysosomal hydrolytic and proteolytic enzymes in the affected cells and even the movement of macrophages to the sites of inflammation.[73,74] It should be noted that positive correlation between antineoplastic and antiinflammatory effects of the same compounds in the rodent screen is known in pharmacology.[40]

Selected complexes of carboxyborane and its ester and amide derivatives with heterocyclic amines were found equally active as antiinflammatory agents.[75]

The metal complexes and salts of amine-carboxyboranes also demonstrated significant antiinflammatory activity, but they were not as active as simple amine-carboxyboranes.[76]

The boron-containing peptides demonstrated antiinflammatory activity better than phenylbutazone, but were not as potent as indomethacin[42].

II.C.4. Antiosteoporotic activity

Studies on the effects of dietary boron (as borate) on mineral and hormonal metabolism showed that boron supplementation mimics the effects of estrogen therapy and may be affecting calcium and bone metabolism. Amine-carboxyboranes and derivatives also block the resorption of calcium from the bone, its release was decreased and the blood level remained high. These agents were found more active than calcitonin and the bisphosphonate standards. In a lactating rat model these compounds increased bone volume, bone weight, bone ash weight and density, while elevating bone and serum calcium levels.[77] In mode of action studies involving amine-carboxyboranes and their metal complexes there was no evidence that these agents would increase estrogen and/or testosterone levels. They rather slowed osteoporotic process by inhibiting calcium flux out of the bone, promoted bone mineralization by increasing calcium uptake by the cells and they improved the tensile strength of the bone as well by increasing collagen synthesis in bone cells. In addition, they seemed to act through regulation of the production and release chemical mediators initiating bone loss e.g. tumor necrosis factor-α and interleukins, which were shown to be involved in inflammatory processes also.[78-80]

II.C.5. Possible role of amine-carboxyboranes and their derivatives in Boron Neutron Capture Therapy (BNCT)

BNCT is based on the nuclear reaction between ^{10}B nuclei and thermal neutrons yielding high-energy α-particles. Since the effective range of α-particles is close to the diameter of human cells (≈10 μm), neutron irradiation will be lethal to those and only those cells which accumulate ^{10}B nuclei.

$$^{10}_{5}B + {}^{1}_{0}n \rightarrow {}^{4}_{2}\alpha + {}^{7}_{3}Li^{*}$$

$$^{7}_{3}Li^{*} \rightarrow {}^{7}_{3}Li + \gamma$$

These compounds seem applicable also for carrying ^{10}B to tumor cells for BNCT, and as carcinostatic agents, they would facilitate a two-fold attack on a neoplasm;

the direct inhibition of tumor growth by the boron compound could be coupled with concomitant use of neutron capture.

However, $Me_3N\cdot{}^{10}BH_2COOH$, $H_3N\cdot{}^{10}BH_2COOH$ and $H_3N\cdot{}^{10}BH_2CONH_2$,[35] as well as $NH_3\cdot BH_2COOH$, $MeNH_2\cdot BH_2CONHEt$, $Me_2NH\cdot BH_2COOMe$ and $Me_3N\cdot BH_2COOH$[81] did not show significant affinity towards tumor cells. Direct injection of ^{10}B-enriched amine-carboxyboranes into tumors resulted in much higher transient ^{10}B-concentrations and tumor/control quotients when introduced as peanut oil suspension in comparison with aqueous solutions[35]. In contrast, a compound named as "boromethylglycylphenylalanine" (probably $MeNH_2\cdot BH_2CO$-Phe) was reported to show tumor to normal ratio of 12.0 and tumor to blood ratio of 3.0.[82]

II.C.6. Studies on transport and disposition of amine-carboxyboranes and their derivatives in living systems

The uptake of trimethylamine-carboxyborane and three of its derivatives by cell layers was studied and the examined complexes ($Me_3N\cdot BH_2$-$^{14}COOH$ and $Me_3N\cdot BH_2$-$^{14}COOMe$ taken up by L-1210 leukemia cells[15] and $Me_nNH_{3-n}\cdot BH_2CO$-Phe-OMe (n=2,3) taken up by Caco-2 and HCT-8 epithelial cells[83]) exhibited passive transport. In a study on the epithelial transport of the dipeptide derivatives, it was found that boronated these compounds underwent metabolism (i.e. the ester group was hydrolyzed), though considerably slower than "traditional" dipeptide esters.[83]

The disposition and tissue distribution of these molecules were studied in rodents also, using radiolabelled materials. Both $Me_3N\cdot BH_2$-$^{14}COOH$ and $Me_3N\cdot BH_2$-$^{14}COOMe$ were found to rapidly distribute over the whole body, however most of the radioactivity was found finally in the urine and only marginal proportion of the labelled materials remained bound to DNA, RNA or proteins. The ester reached substantially higher transient concentrations in every organs except skin and carcass, probably due to its larger lipophilicity. It could be concluded from half-

lives that the ester undergoes rapid metabolism in the plasma, probably into the carboxylic acid.[15,84]

$Me_3N{\cdot}BH_2CO$-Phe-OMe (with ^{14}C-labelling universally distributed over the aromatic ring) was found to undergo rapid and extensive metabolism (ester hydrolysis following intravenuous or intraperitoneal, amide hydrolysis following per os administration) and the majority of the radioactivity was found in the skin and carcass.[85]

II.C.7. Toxicity of amine-carboxyboranes and their derivatives

Amine-carboxyboranes and their ester or amide derivatives are generally not or only slightly toxic, and regarding that their biological activities were studied in rodents at 8-20 mg/kg dosage, their therapeutic index (LD_{50}/therapeutic dosage) is relatively high. It should be noted that amine-cyanoboranes in general are considerably more toxic (typical $LD_{50} \leq$ 50-70).[6,50] LD_{50} values of amine-carboxyboranes and derivatives are summarized in Table 1.

Acute toxicity screens (based on organ weights, clinical chemistry, hematopoietic parameters and tissue morphology in rodents at 1, 2 or 5 times the therapeutic dosage) have been performed for the most effective complexes. $Me_3N{\cdot}BH_2COOMe$ and $EtNH_2{\cdot}BH_2COOH$ were found free of toxicity,[86] $Me_3N{\cdot}BH_2CO$-Phe-OMe showed test values slightly different from normal only at 5 times the therapeutic dosage[44], whereas the dicopper(II) complex of $Me_3N{\cdot}BH_2COOH$ showed slight toxicity in hepatic and kidney morphology.[87]

Table 1. LD_{50} values of various amine carboxyborane derivatives of composition $A{\cdot}BH_2COX$

A	X	LD_{50} (mg/body kg)	Ref.
Me_3N	OH	1800	6
Me_3N	OH	1800*	35
Me_2NH	OH	>200	67
$MeNH_2$	OH	>1000	67
NH_3	OH	>200	22
NH_3	OH	>1000	67
NH_3	OH	2500*	35
TMEDA/2	OH	>1000	32
py	OH	>200	32
Me_3N	OMe	225	8
Me_3N	OEt	>500	32
NH_3	NH_2	3500*	35
Me_3N	NHEt	320	6
TMEDA/2	NHEt	>1000	32
Me_3N	O(Cu)	39.2	71

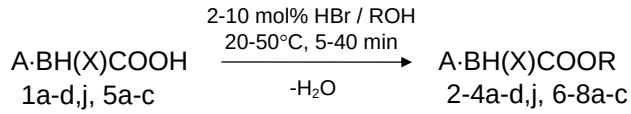
(* using ^{10}B-enriched compounds in $C_{57}BL/6J$ mice)

III. RESULTS AND DISCUSSION

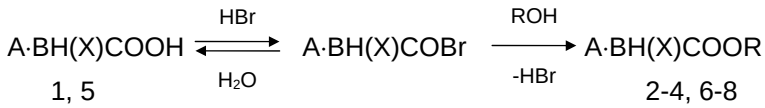
III.A. Synthesis of methyl, ethyl and isopropyl esters of amine-carboxyboranes

During the work with the purpose of extending the range of the existing amine-bromocarboxyboranes (5), an intriguing phenomenon was noticed, which finally lead to the elaboration of a new, efficient pathway for the esterification of amine-carboxyboranes and some of their derivatives substituted on the boron.

The bromination of $Et_3N{\cdot}BH_2COOH$ (1c) was attempted using bromine in methanol. The starting material (poorly soluble in methanol), was suspended in methanol and addition of bromine solution was started dropwise. Surprisingly, the first drop of the bromine solution caused the solid crystals dissolve in a few seconds, and after evaporation the major component of the residue was $Et_3N{\cdot}BH_2COOMe$ (2c), with very small amounts of $[Et_3NH]Br$ and $Et_3N{\cdot}BH(Br)COOMe$ (6c). It was clear that bromine cannot be the species responsible for the esterification reaction, as it is consumed by the bromination reaction. Since this reaction produces HBr, its possible activity was tested in the next step. When HBr (2-3 mole%) was added to the suspension of amine-carboxyboranes in methanol, ethanol or isopropanol a quick dissolution occurred and the ester formation reached an equilibrium state (which is near to the 100% conversion in the case of 0.2-0.4 M solutions) within a few minutes. The tetramethylethylenediamine complexes required somewhat longer reaction time. With amine-bromocarboxyboranes the reaction is also slower: in the presence of 10 mole% HBr at room temperature–50°C the esterification took 10-40 minutes.



Hydrogen iodide and iodine were found equally effective catalysts of the esterification, but in the presence of HCl the reaction is slower with orders of magnitude. It is supposed that the quick alcoholysis of the acid bromides (produced, presumably, in low equilibrium concentration) leads to the formation of the esters:



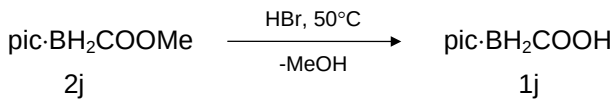
The existence of a similar equilibrium has also been detected with carboxylic acids and hydrogen halides and - in agreement with the usual order of reactivity of acid halides - the rate of alcoholysis of acid bromides and iodides (as well as the rate of their formation) is higher than that of the acid chlorides.[88]

Though acid halide derivatives of amine-carboxyboranes have not been prepared yet, and attempts to synthesize them have all failed[38,42], indirect evidences have been found for their existence earlier in our laboratory. Lázár has studied the reaction of amine-carboxyboranes with phosphorus tribromide in dichloromethane in the presence of triethylamine and examined the formation and stability of acid bromides at room temperature. Though acid bromides could not be separated, the corresponding esters and amides could be prepared in 40-60% yield by treating such mixtures with alcohols and amines. However, in agreement with literature[38,42] the production of amine-bromoborane and CO was detected in the absence of triethylamine.

The experimental conditions used for the preparation of the esters 2-4a-d,j and 6-8a-c are given in the Experimental section. Application of solutions more concentrated than those indicated is not advisable, due to the unfavourable shift of the equilibrium of the ester formation. After completion of the reaction the mixtures were kept over A4 molecular sieves for a few hours, which removed most of water and HBr, so to avoid a significant shift of the equilibrium towards the acid due to the increasing water-concentration upon evaporation of the mixtures. In addition, the employment of molecular sieves decreased the amount of the contaminants in many cases. In this way the percentage of the amine-carboxyborane in the crude products was fairly low (usually less than 1%) which could be easily removed by simple purification procedures, such as extraction with ether or pentane.

The anisochrony of the methylene protons, due to the presence of the chiral boron atom, resulted in the splitting of the O-CH_2 (7a,b), N-CH_2 (7c) and CH-$C\underline{H}_3$ (8a,b) bands ($\Delta\delta$ = 0.005-0.008 ppm) in the ^{1}H NMR spectra. Consequently, the configuration of the chiral boron atom, at least in these complexes, was stable on the NMR timescale.

The esters of amine-carboxyboranes could be easily hydrolyzed in aqueous HBr solution (pH≈2) at 70°C, employing N_2 stream bubbling through the mixture to continuously remove methanol, as it was demonstrated in the preparation of the hitherto unknown pic·BH_2COOH (1j) so the ester group can be applied as protecting group in further transformations.

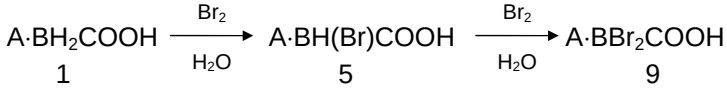


III.B. Halogenation reactions of amine-carboxyboranes

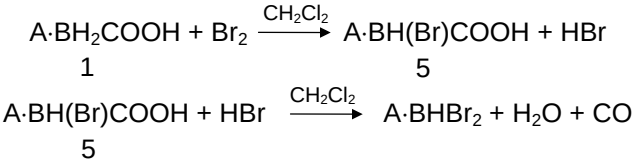
III.B.1. Bromination reactions of amine-carboxyboranes

The syntheses of amine-cyanocarboxyboranes and amine-dicarboxyboranes from amine-carboxyboranes were designed *via* amine-bromocarboxyboranes or their esters. The first representatives of amine-bromocarboxyboranes have been prepared in our laboratory. However, when I joined this project, only a limited number of amine-bromocarboxyboranes was known, so the purpose of the early phase of the work was extending the range of these supposedly key intermediates. Preliminary results showed that amine-bromocarboxyboranes are not stable in alkaline media and poorly soluble in most organic solvent, so it seemed expedient to synthesize their ester derivatives also.

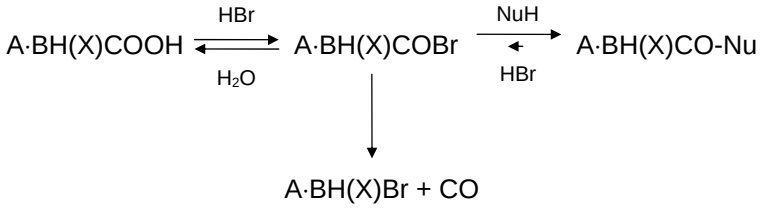
The first representatives of amine-bromocarboxyboranes were synthesized by Kovács in the reaction of amine-carboxyboranes and elemental bromine in water.



Unfortunately, this reaction was accompanied by decomposition *via* the rupture of the B—N bond. In certain cases, the product of the reaction was the twice brominated derivative (9) directly, and it was explained by the unfavourable relationship between the solubilities of 5 and 9. These observations initiated the testing of the reaction in different solvents. Kovács has found the complete decomposition of the B—N bond upon adding bromine to the solution of 1 in CH_2Cl_2. Based on the fact that the same decomposition took place upon adding HBr to the CH_2Cl_2 solution of 5, he concluded that the decomposition in the first reaction was caused by HBr formed in the bromination reaction.



We have then attempted the bromination of $Et_3N{\cdot}BH_2COOH$ in methanol as proton-acceptor solvent, and besides the bromination, the esterification also took place yielding $Et_3N{\cdot}BH(Br)COOMe$ directly. In a detailed study it was disclosed that esterification is accomplished in the presence of even a few mole% HBr, formed after adding a small portion of bromine (see II.A. chapter). This reaction was also accompanied by the decomposition of the B—N bond, and this decomposition was slowly proceeding even after the completion of esterification and the bromination. These observations lead to the assumption, that amine-carboxyboranes and amine-bromocarboxyboranes form acyl bromides in the presence of HBr. These acyl bromides can undergo nucleophilic substitution (affording carboxylic groups in water and methoxycarbonyl groups in methanol) in a reversible process, where the equilibrium is shifted overwhelmingly towards the formation of the carboxylic or methoxycarbonyl groups. On the other hand, acyl bromides can (and in the absence of nucleophiles or bases, like in CH_2Cl_2, they do completely) decompose *via* the loss of CO. Formation of acyl bromides from carboxylic acids upon the action of HBr[88], and decarbonylation upon the action of acids[89] are known from the literature.



In preliminary experiments ^1H and ^{11}B NMR monitoring showed that $Q{\cdot}BH(COOH)_2$ can be transformed into $Q{\cdot}BBr(COOMe)_2$ by bromine in methanol. The bromination is considerably slower than that of amine-carboxyboranes, it took 2.5 h at 50°C to reach complete consumption of bromine for $Q{\cdot}BH(COOH)_2$ in contrast to practically instantaneous reactions in the case of amine-carboxyboranes (1).

N-bromosuccinimide (NBS) has been successfully applied to bromination of amine-boranes[90] and α-bromination of carboxylic acids[91] as well. Furthermore, literature data implied that HBr will not accumulate during bromination by NBS, because reaction between HBr and NBS keeps the actual concentrations of both HBr and Br_2 at a low steady-state level during the bromination, where HBr is formed from the bromination reaction[92].

$$HBr + NBS \longrightarrow Br_2 + \text{succinimide}$$
$$Br_2 + R\text{-}H \longrightarrow R\text{-}Br + HBr$$

In our experiments NBS afforded a number of amine-bromocarboxyboranes from amine-carboxyboranes in $CHCl_3$ or in CH_2Cl_2 with better yields and purity than reactions between amine-carboxyboranes and bromine.

$$\underset{\textbf{1a-c}}{A{\cdot}BH_2COOH} \xrightarrow{NBS\ /\ CH_2Cl_2} \underset{\textbf{5a-c}}{A{\cdot}BH(Br)COOH}$$

By mistake, in an experiment where the solvent was commercial $CHCl_3$ (stabilized with ethanol), we observed that in the presence of alcohols the esterification also takes place besides bromination, similarly to reactions with bromine. Considering this observation, a number of amine-bromo(methoxycarbonyl)boranes was synthesized from amine-carboxyboranes using NBS in methanol.

$$\underset{\textbf{1a,b,e}}{A{\cdot}BH_2COOH} \xrightarrow{NBS\ /\ MeOH} \underset{\textbf{6a,b,e}}{A{\cdot}BH(Br)COOMe}$$

NBS was added as a solid in small portions, since it slowly reacts with methanol. The second portion was added minutes after the first one, while the esterification of the carboxyl group took place. Keeping this delay is expedient, since the esterification of amine-bromocarboxyboranes is considerably slower than that of

amine-carboxyboranes. The catalyst of the esterification is probably HBr formed from the bromination reaction, however, a possible explanation may be the generation of acyl hypobromites also[93], which would react with methanol affording the corresponding esters and HOBr and the latter may be able to maintain the catalytic cycle.

The synthesis of the bromo derivatives of pyridine base-carboxyboranes (pic·BH_2COOMe (2j) and DMAP·BH_2COOMe (2k)) failed either with bromine or NBS, although quick consumption of the brominating agents occurred even at -50 - -80 ^{O}C. Use of bromine in methanol resulted in decomposition accompanied by gas evolution on warming even when HBr was neutralized (pyridine-bases, $NaHCO_3$, NaOMe) at low temperature. No gas evolution was observed on using NBS in $CHCl_3$, but separation of the multicomponent reaction mixtures remained unsuccessful. A possible explanation for this remarkable instability of the target compounds may be that bromine is a better leaving group in py·BH(Br)COOR type complexes than in R_3N·BH(Br)COOR type complexes, probably due to the stronger electron donating property of amines with sp^2 hybride nitrogen towards boranes.

III.B.2. Attempts aimed at the synthesis of amine-iodocarboxyboranes and amine-iodo(methoxycarbonyl)boranes

Although the good leaving character of the bromine has been demonstrated in a number of reactions, some experiments aimed at the bromide→cyanide exchange has failed. It initiated the study of the possibilities to synthesize amine-iodocarboxyboranes or amine-iodo(methoxycarbonyl)boranes, which would be hitherto unknown types of compounds, because iodide is a better leaving group than bromide.

Reactions between Me_3N·BH_2COOH and iodine in water resulted in the complete decomposition of the B—N bond accompanied by effervescence. Application of thallium or copper salts intended to facilitate iodination, analogously to α-iodination of carboxylic acids[94], lead to the same result. The same reactions carried

out in water-methanol mixtures or methanol (for better dissolution) yielded $[Me_3NH]I$ and $Me_3N{\cdot}BH_2COOMe$. Attempted iodination of $pic{\cdot}BH_2COOH$ with I_2 in acetonitrile resulted in decomposition also.

In the presence of amines containing sp^2 hybrid nitrogen, iodination of $pic{\cdot}BH_2COOMe$ with either I_2 or [py·I]Cl resulted in the formation of the corresponding [bis(amine)(methoxycarbonyl)hydroboron(1+)] cations, analogously to similar reactions with bromine[95]. Similarly, iodination of $TMEDA{\cdot}BH_2COOH$ by iodine in CCl_4, water or acetone yielded the cyclic $[TMEDA{\cdot}BH(COOH)]^+$ cation contaminated with more or less TMEDA·*n*HI.

$$pic{\cdot}BH_2COOMe + I_2 + 2\ pic \longrightarrow [(pic)_2BH(COOMe)]^+I^- + pic{\cdot}HI$$

$$TMEDA{\cdot}BH_2COOH + I_2 \longrightarrow Me_2\overline{NCH_2CH_2NMe_2}BH(COOH)]^+I^- + HI$$

These observations suggest that the B—I bond does exist, although with only a very short lifetime, and nucleophiles (amines, OH^-, OMe^-) readily expel the iodine. In the case of amines the product is a stable cationic compound, in the case of reactions in water and methanol the primary product of iodine displacement is presumably an amine complex of a hydroxy(carboxy)borane or methoxy(carboxy)borane, which contain too weak Lewis acids to remain stable.

III.C. Formation of cyano and isocyano group on the boron in the presence of methoxycarbonyl group

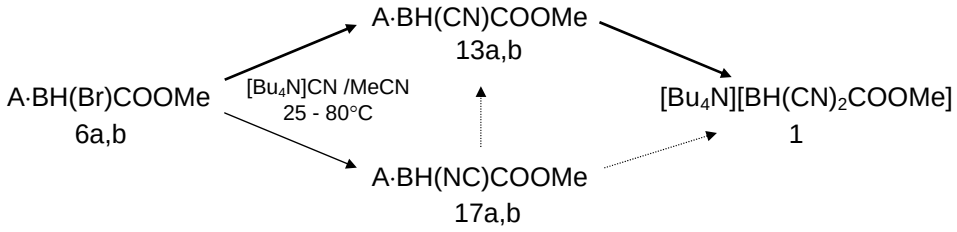
III.C.1. Synthesis of amine-cyano(methoxycarbonyl)boranes and amine-cyanocarboxyboranes

A considerable number of reactions have been attempted for the formation of amine-cyanocarboxyboranes (12). One group of these reactions was based on earlier examples for formation of B—CN bond. These experiments included reactions between A·BH_2COOR or A·BH(Br)COOR (R = H, Me) and $Hg(CN)_2$,[96,97] Me_3SiCN,[98,99] or AgCN.[100] Considering the ability of trityl cation to abstract hydride from boron,[101] reaction between A·BH_2COOMe and $[Ph_3C]CN$[102] was also attempted. On the other hand, a reaction between A·BH(Br)COOMe and acetone cyanohydrine, used for synthesis of α-cyano carboxylic acids,[103-105] was tested also, with regards to the supposed analogy between amine-carboxyboranes (1) and aliphatic carboxylic acids. Finally, encouraged by the success of NBS in bromination, reactions between A·BH_2COOMe and *N*-cyanosuccinimide[106] were given a try also. However, all these reactions failed under our conditions, i.e. the starting materials could be recovered, the rupture of the B—N bond took place, or there was no sign of the formation of the desired products in the multicomponent reaction mixtures.

The very first attempt for the synthesis of amine-cyanocarboxyboranes (12) was the reaction between amine-bromocarboxyboranes (5) and 1-5 M aqueous solutions of NaCN, but the starting material instantaneously decomposed with a vigorous effervescence. Similar, but somewhat slower decomposition was observed in the reaction between Me_3N·BH(Br)COOMe and methanolic solution of NaCN. After the role of OH^- and MeO^- species in the decomposition of amine-bromocarboxyboranes (5) and their esters was shown in relation with the study of C_nN_2B ring formation[14] and similar reasons lead to the failure of preparation of

amine-iodocarboxyboranes, it seemed expedient to return to this simple bromide→cyanide substitution on the boron, but in a polar aprotic solvent.

The reaction between amine-bromo(methoxycarbonyl)boranes (6) and tetrabutylammonium cyanide in acetonitrile was studied in detail. The reactions were monitored by recording ^{1}H and ^{11}B NMR spectra of small samples of the reaction mixtures, taken at various time intervals, evaporated to dryness and redissolved in $CDCl_3$. This monitoring showed that the starting material transformed into three products, which were later identified (with the help of the quantitative ^{13}C NMR and IR spectra of certain samples) as amine-cyano(methoxycarbonyl)borane (13), amine-isocyano(methoxycarbonyl)borane (17) and [(dicyano)hydro(methoxycarbonyl)borate(1-)] ion (14). The observations obtained in the monitoring of a number of reaction mixtures having different starting compositions and exposed to various temperatures can be summarized in the following scheme:

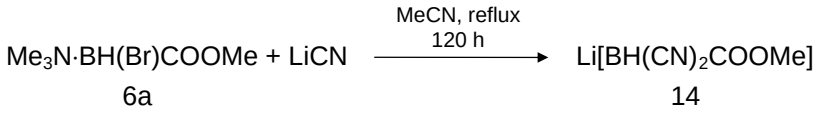


It was also observed that no substitution reaction took place in $CDCl_3$ as the NMR samples remained unchanged for at least two weeks. This experience well demonstrates the role of the polar aprotic solvent in the success of the reaction. It was found that the amine-expelling side reaction came into prominence at elevated temperatures (especially in the case of the Me_3N complexes) and to a somewhat less extent at larger excesses of $[Bu_4N]CN$. Amine→cyanide exchange on the boron has already been reported.[107,108] The largest proportion of Q·BH(CN)COOMe (88 mole%) was achieved after 96% conversion, when 1.5

molar equivalent of $[Bu_4N]CN$ was applied, though systematic optimization experiments may result in better yields of the desired product.

Q·BH(CN)COOMe possesses a much lower solubility in water than the side products, so it can be prepared in pure form after adding water to the evaporation residue of the reaction mixtures. Unfortunately, preparation of Me_3N·BH(CN)COOMe is not that straightforward, no solvent or mixture of solvents has been found to provide satisfactory separation neither in extraction nor in column cromatography so far, a few percent of either sideproduct remained as a contaminant after all purification attempts.

With the hope of a simpler preparation, the bromide→cyanide substitution in Me_3N·BH(Br)COOMe was attempted using another cyanide source, LiCN, and this reaction was monitored by ^1H and ^{11}B NMR also. Surprisingly, the evaporation residues of the samples could not be dissolved in $CDCl_3$, so the spectra were taken in D_2O. The desired reaction seemed to take place, but at similar reactant concentrations it was slower than that carried out with $[Bu_4N]CN$. The proportions of the side reactions were found different also: the formation of Me_3N·BH(NC)COOMe was undetectable, but the substitution of the amine to cyanide took place to a considerably greater extent. At the end, the reaction with LiCN was utilized for the formation of $Li[BH(CN)_2COOMe]$, which happened to crystallize with 4 molecules of acetonitrile.

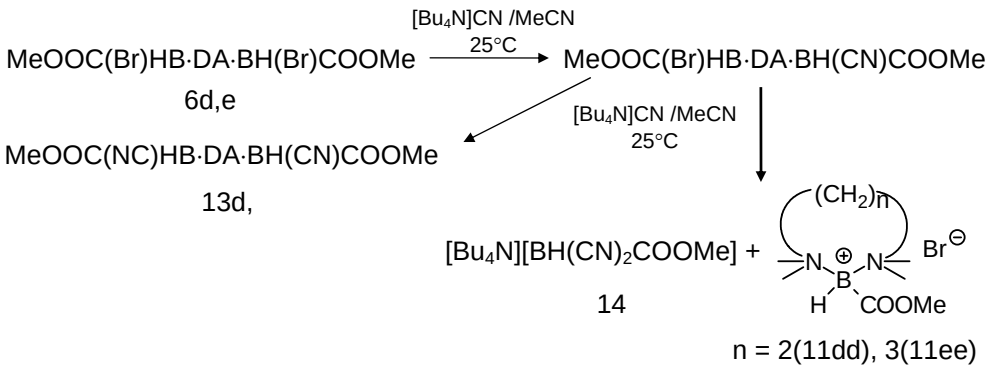


This anion can be the starting material for the synthesis of amine-dicyano(methoxycarbonyl)boranes ($A·B(CN)_2COOMe$) by the oxidation of the B—H hydrogen in the presence of the corresponding amines, analogously to the preparation of either amine-cyanoboranes from $Na[BH_3CN]$[109], where the oxidizing agent was the proton in amine hydrochlorides, or rather amine-dicyanoboranes (18) where B—H of $Li[BH_2(CN)_2]$ was oxidized by amine perbromides[110].

$$M[BH(CN)_2COOMe] + A{\cdot}HCl \xrightarrow{?} A{\cdot}B(CN)_2COOMe + MCl$$

$$M[BH(CN)_2COOMe] + A{\cdot}Br_2 + A \xrightarrow{?} A{\cdot}B(CN)_2COOMe + MCl$$

Bromide→cyanide substitution was attempted on the bis[bromo(methoxycarbonyl)borane] complexes of diamines (DA·2BH(Br)COOMe, DA = TMEDA (6d), TMPDA (6e)) and $[Bu_4N]CN$ also. The desired reaction could be observed, however, the formation of the $[BH(CN)_2COOMe(1–)]$ anion (14) was the favored process, parallel to the formation of cyclic [DA·BH(COOMe)(1+)] cations (11dd,ee). This increased proclivity to anion formation is probably due to the fact that diamines are weaker Lewis bases towards boranes (TMEDA·2BH_2COOR complexes were applied as starting materials for amine exchange reactions[30]), so cyanide readily expels it from the boron and the DA·BH(Br)COOMe complex left behind instantaneously transforms into the cyclic cation [DA·BHCOOMe(1+)] (11)[14].



Having synthesized $Me_3N{\cdot}BH(CN)COOMe$, however with some contamination, allowed the preparation of further two amine-cyano(methoxycarbonyl)boranes (amine = pic (13j), pic(13l)) *via* amine exchange reactions in refluxing acetonitrile with good yields, and it is certain that a series of more amine-cyano(methoxycarbonyl)boranes (13) can be synthesized this way in the future.

$$\underset{\textbf{13a}}{Me_3N{\cdot}BH(CN)COOMe} + A \xrightarrow[A = pic,\ pip]{MeCN\ reflux} \underset{\textbf{13j,l}}{A{\cdot}BH(CN)COOMe} + Me_3N$$

In preliminary experiments it was shown that $Q{\cdot}BBr(COOMe)_2$ also reacts with $[Bu_4N]CN$ in acetonitrile. The reaction is remarkably slower than that of Q·BH(Br)COOMe, probably because of the considerably larger steric hindrance of the boron, and after 50 % conversion it gave two products in ca. 1:1 ratio. These products were identified as $Q{\cdot}B(CN)(COOMe)_2$ and $[Bu_4N][B(CN)_2(COOMe)_2]$ by the ^1H and ^{11}B NMR spectra of the samples.

$$\underset{\textbf{34b}}{Q{\cdot}BBr(COOMe)_2} \xrightarrow[MeCN\ reflux]{[Bu_4N]CN} \underset{\textbf{35b}}{Q{\cdot}B(CN)(COOMe)_2} \xrightarrow[MeCN\ reflux]{[Bu_4N]CN} \underset{\textbf{15}}{[Bu_4N][B(CN)_2COOMe]}$$

$Me_3N{\cdot}BH(CN)COOMe$ and $Q{\cdot}BH(CN)COOMe$ were successfully hydrolyzed into the corresponding amine-cyanocarboxyboranes (12) in 1M HCl. In the case of the Q complex, acetone was added to the mixture until dissolution and it was evaporated when the reaction was complete. $Me_3N{\cdot}BH(CN)COOH$ - similarly to its methyl ester - is rather well soluble in water, finally it was obtained in crystalline form by deep-freezing and thawing the reaction mixture evaporated to third its volume.

$$\underset{\textbf{13a,}}{A{\cdot}BH(CN)COOMe} \xrightarrow[-\ MeOH]{1M\ HCl,\ 50°C} \underset{\textbf{12a,}}{A{\cdot}BH(CN)COOH}$$

The acidity constants of $Me_3N{\cdot}BH(CN)COOH$ and Q·BH(CN)COOH were found 5.91±0.02 and 5.75±0.02, respectively, as determined from the half-neutralization points of their potentiometric titration curves. These values are ca. 2.5 units lower than those of amine-carboxyboranes (1), and quite close to those common for aliphatic carboxylic acids. It can then be concluded that the strong electron releasing effect of the ≡B—N≡ unit towards the carboxylic group is compensated by a cyano group attached to the boron to a considerable extent.

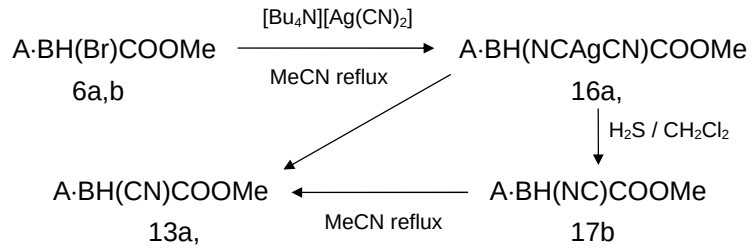
Esterification of amine-cyanocarboxyboranes (12) was unsuccessful using the method developed for amine-carboxyboranes (1) in our laboratory[17]: the –OMe group of the ester did not appear in the ^1H NMR spectrum of the evaporated samples of the reaction mixture even after an hour. It should be noted that this esterification method works the best for amine-carboxyboranes (1), and carboxylic groups with lower pK_a values (e.g. in A·BH(X)COOH, where X = Br (5), COOH (27)) require higher temperatures or larger quantities of catalyst for complete esterification.

III.C.2. Formation of isocyano group by nucleophilic substitution on the boron in amine-bromo(methoxycarbonyl)boranes.

Isocyano group adjacent to boron has been shown to be readily transformable into various functional groups.[111,112] Formation of isocyano group on the boron is carried out most commonly using silver cyanide for expelling halides or weak Lewis bases from the boron. Silver-carbon bond is cleaved (usually by H_2S or its salts) only after the formation of B—NCAg bond.[18,112,113] However, AgCN possesses very poor solubility in most solvents suitable for amine-bromocarboxyboranes (5) or amine-bromo(methoxycarbonyl)boranes (6). Therefore, in order to synthesize amine-isocyano(methoxycarbonyl)boranes (17), reactions between amine-bromo(methoxycarbonyl)boranes (6) and tetrabutylammonium dicyanoargentate were studied in acetonitrile, and they were monitored by ^1H and ^{11}B NMR, similarly to the study of bromide→cyanide

substitution. (It should be noted, that to our knowledge this reagent was prepared first in our laboratory in pure solid form.)

No reaction appeared to take place at room temperature for 4 h. In refluxing acetonitrile amine-bromo(methoxycarbonyl)boranes (6a,b) slowly transformed into the corresponding amine-cyano(methoxycarbonyl)boranes (13a,b) through an intermediate, which showed ^{1}H and ^{11}B NMR resonances very close to those observed earlier for amine-isocyano(methoxycarbonyl)boranes (17a,b) as contaminants, but the ^{11}B NMR signal was very broad ($\nu_{1/2}\approx330$ Hz). Although the signal did not show splitting due to B—H coupling, a B—H bond was probably present in the intermediate, because it is hard to imagine a reaction pathway between A·BH(Br)COOMe (6) and A·BH(CN)COOMe (13) involving a cleavage and then a formation of a B—H bond in acetonitrile. As the reaction proceeded towards the formation of amine-cyano(methoxycarbonyl)boranes (13a,b), the reaction mixture got darker and more viscous. Based on these observations and literature data[113] we supposed the intermediate to be A·BH(NCAgCN)COOMe (16), which was then somehow losing an AgCN parallel to the isomerization of B—NC bond to B—CN. The reaction mixture of the Q complex was evaporated at such a phase of the reaction when more than 90% of the boron was in the intermediate (probably 16b). The CH_2Cl_2 solution of the evaporation residue was then treated with gaseous H_2S and the black precipitate was filtered off, and evaporation of the filtrate afforded white solid, the main component of which could be identified as Q·BH(NC)COOMe by its characteristic IR band (2131 cm^{-1}) and ^{13}C NMR resonance (sharp peak near 170 ppm). It was contaminated with Q·BH(CN)COOMe and $[Bu_4N]Br$.



Q·BH(NC)COOMe did not appear to react with picoline even after 12 h reflux in acetonitrile, only some B—NC → B—CN isomerization could be observed by NMR monitoring. One can then conclude that isocyano group adjacent to boron is a poor leaving one, since picoline was not able to expel it, so Me_3N·BH(NC)COOMe, when it will be available in multigram scale, should be a good starting material for the syntheses of a series of amine-isocyano(methoxycarbonyl)boranes (17) *via* amine exchange reactions. This type of compounds have not been reported in the literature yet.

III.D. Synthesis of amine-dicarboxyboranes and related compounds from amine-dicyanoboranes

After the failure of a number of reactions aimed at the formation of B—CN group in the presence of B—COOR group, the synthetic pathway for the synthesis of amine-cyanocarboxyboranes and amine-dicarboxyboranes was redesigned to contain the formation of carboxyl group at the end of the synthetic sequence. Thus, in the early phase, the formation of two cyano groups on the boron was desirable.

III.D.1 Synthesis of amine-dicyanoboranes

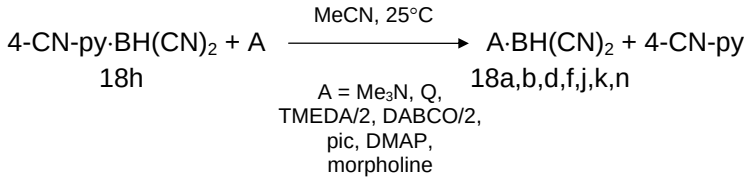
The first representatives of amine-dicyanoboranes ($A{\cdot}BH(CN)_2$, 18) were prepared in our laboratory[110] by oxidation of $Li[BH_2(CN)_2]$, which was in turn synthesized in the reaction of $(BH_2CN)_n$ oligomer and LiCN in methyl sufide, using amine perbromides in the presence of the corresponding amines.

$$Me_2S{\cdot}(BH_2CN)_n + LiCN \xrightarrow{Me_2S} Li[BH_2(CN)_2]$$

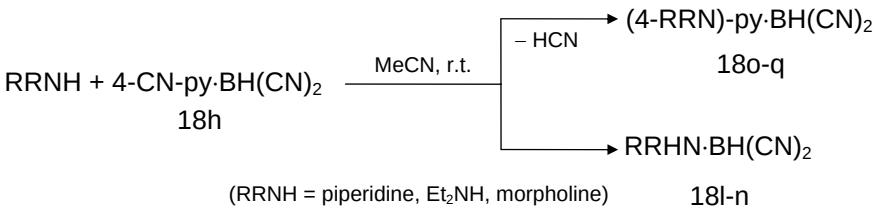
$$Li[BH_2(CN)_2] + A{\cdot}Br_2 + A \xrightarrow[A = 4\text{-CN-py , py}]{THF} A{\cdot}BH(CN)_2 + LiBr + A{\cdot}HBr \quad (18h,i)$$

Investigation of this reaction, originally established for pyridine and 4-CN-pyridine, was continued in order to obtain complexes of dicyanoborane with a broad variety of amines (further pyridine bases as well as secondary and tertiary alkylamines and diamines). Unlike 4-CN-pyridine and pyridine, many of these amines do not form isolable perbromides, therefore, reactions were carried out by adding the acetonitrile solution of $Li[BH_2(CN)_2]$ to a mixture of two equimolar amines and one equimolar bromine in acetonitrile. We found that these reactions lead to the formation of amine-dicyanoboranes as the most abundant products. ^{11}B (and sometimes ^{1}H) NMR monitoring of the reactions showed that the reactions, particularly those involving picoline and piperidine, were considerably slower than the formation of the pyridine and 4-CN-pyridine complex, and side reactions took

place. In the reaction involving piperidine 54% of $Li[BH_2(CN)_2]$ was consumed after 8 h at 50°C, whereas the reaction involving 4-cyanopyridine was complete in 30 min at 0°C. Based on the similar results starting from isolated amine perbromides (when it was feasible) and the reactivity order, showing the most nucleophilic amines being the most sluggish ones, amine perbromides are assumed to be the reactive species. It should be noted, that in the presence of DABCO, only the dinuclear complex $DABCO{\cdot}BH(CN)_2$ could be observed and isolated in a quite low yield. Attempts aimed at the isolation of amine-dicyanoboranes containing aliphatic amines from the reaction mixtures were inefficient on preparative scale. However, most of them could be obtained in multigram quantities with fairly good overall yields *via* $4\text{-CN-py}{\cdot}BH(CN)_2$ in base exchange reactions taking the advantage of low basicity of 4-CN-py towards $BH(CN)_2$ and the fact that the isolated yield of this complex could be improved to 88% by modification of the original procedure.

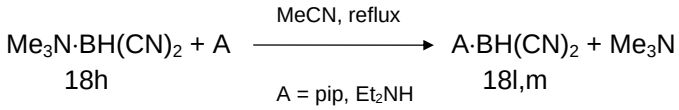


On the other hand, in analogous experiments involving secondary amines (i. e. piperidine, diethylamine and morpholine) aminodecyanation also took place on the aromatic ring, accompanied by the presence of an intensive blue color throughout the whole course of the reaction turning into rusty brown upon evaporation.



Landquist observed a resembling reaction, showing similar color changes, between 4-cyano-1-methyl-pyridinium iodide and methylamine or hydrazine in water[114]. Based on our observations, two of the four theoretical pathways[115] can be excluded: SN1 mechanism is hard to believe because the cyano group was stable in reactions with other amines, and benzyne mechanism is unlikely because 3-aminopyridine-borane complexes (product of the *cine*-substitution) were not detectable by ^{1}H NMR in the reaction mixtures. Of the remaining two options, radical mechanism (SNR1) seems less probable, as this mechanism, in the cases of dicyanopyridines[116], required photochemical induction and no substitution took place *via* thermal activation. Furthermore, these reactions usually resulted in hydrodecyanation predominantly over aminodecyanation, due to the efficient hydrogen donor character of the amine radicals, and we could not observe pyridine-dicyanoborane in the reaction mixtures. On the other hand, SNAr mechanism is favored to operate when: (a) the leaving group is one with strong *-I* effect, (b) there is a strong electron withdrawing group (here >NBH(CN)$_2$) situated ortho or para to the leaving group. Furthermore, SNAr reactions are catalyzed by strong bases[115]. Based on these considerations and resembling reactions in the literature[114,117], we assume that the mechanism of this aminodecyanation is, at least predominantly, SNAr, though our direct observations were not eligible to decide whether the colored species is radical or the corresponding Meisenheimer-complex.[115]

The proportions of aminodecyanation and base exchange reactions varied markedly from amine to amine, i.e., 4-(*N*-piperidino)-pyridine-dicyanoborane (18o) was isolated in 65% yield, 4-*N*,*N*-diethylaminopyridine-dicyanoborane (18p) was present in ca. 30 mol% besides 70 mol% $Et_2NH{\cdot}BH(CN)_2$ (18m), whereas formation of 4-(*N*-morpholino)-pyridine complex (18q) did not reach 10 mole %. The same experiments carried out in THF showed considerable suppression of aminodecyanation, probably due to the much lower polarity of the solvent, whereas the color changes were observed in THF as well. After all, piperidine and diethylamine complexes of dicyanoborane (18l,m) were synthesized from $Me_3N{\cdot}BH(CN)_2$ in base exchange reactions.



^{1}H NMR spectra of complexes of cyclic amines were not straightforward, their elucidation necessitated ^{13}C-^{1}H and ^{1}H-^{1}H correlation experiments. It can be concluded, that both in pip·BH(CN)$_2$ (18l) and morpholine·BH(CN)$_2$ (18n) the ring possesses a quite rigid chair conformation in solution with borane moiety in equatorial position, and this conformation is stable on the NMR timescale at room temperature. No other isomer could be observed in quantifiable amount. In contrast, the conformation of the piperidine ring in 4-(*N*-piperidino)-pyridine-dicyanoborane (18o), containing a "free" lone electron pair on the nitrogen, proved to be flexible in $CDCl_3$ solution (Fig. 1.).

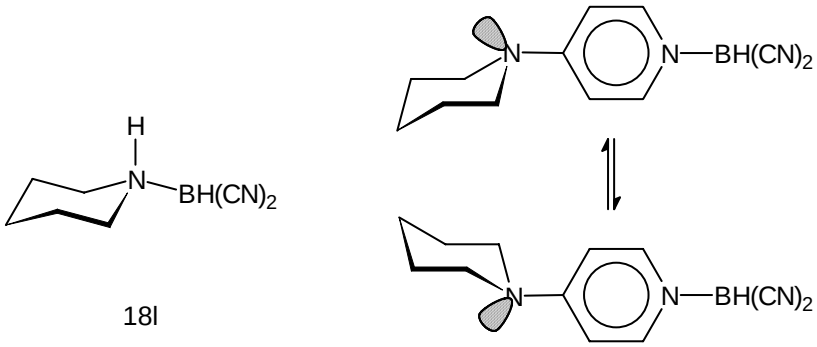


Figure 1. Complex formation on the nitrogen stiffens the flexible conformation of the piperidine ring

III.D.2. Ethylation of amine-dicyanoboranes

A number of [amine-bis(*N*-ethylnitrilium)hydroboron(2+)] tetrafluoroborates (19a,b,i,j) could be synthesized from amine-dicyanoboranes (18a,b,i,j) by $[Et_3O][BF_4]$, and each of them, except $[pic{\cdot}BH(CNEt)_2][BF_4]$ could be isolated, since they precipitated from the reaction mixtures.

$$\underset{\text{18a,b,i,}}{A{\cdot}BH(CN)_2} + 2\,[Et_3O][BF_4] \xrightarrow[A = Me_3N,\ Q,\ py,\ pic]{CH_2Cl_2,\ \text{reflux, 12-32h}} \underset{\text{19a,b,i,j}}{[A{\cdot}BH(CNEt)_2][BF_4]_2} + 2\,Et_2O$$

^{1}H NMR monitoring of the reaction mixtures, showing significant amounts of the starting material and/or the end-product besides the intermediate [amine-cyano(*N*-ethylnitrilium)hydroboron(1+)] cations (20) during the whole reaction period (even when only one molar equivalent of $[Et_3O][BF_4]$ was employed), led to the conclusion that the rates of the consecutive steps are surprisingly close to each other, and the isolation of the intermediates (20) does not seem feasible. The ethylation reaction of cyano groups in amine-dicyanoboranes (18) is considerably slower than that in the corresponding amine- cyanoboranes (36),[14] probably due to the strong electron-withdrawing effect of the cyano or *N*-ethylnitrilium group. Being a second-order reaction, the ethylation can be substantially accelerated by increasing the amount of $[Et_3O][BF_4]$. Though unreacted $[Et_3O][BF_4]$ does not give rise to contaminants during the preparation of their derivatives described below, in order to make the isolation of the bis(*N*-ethylnitrilium) salts easier, it is advantageous to apply $[Et_3O][BF_4]$ in low excess, as larger amounts prevent the precipitation of the product.

Analogous reactions were attempted with further amine-dicyanoboranes 18k-n also. ^{1}H and ^{11}B NMR monitoring showed that at the end of these reactions boron was detectable as BF_4^--ions and Lewis base complexes of BF_3 only, accompanied by intensive browning of the reaction mixtures. During the course of the reactions of 18k,l the expected twice ethylated products could be observed by ^{1}H NMR as

intermediates in low concentrations. As a comparison, the ethylation of amine-cyanoboranes **36g,k-m** was attempted under similar conditions. The reactions yielded the expected *N*-ethylnitrilium salts in rather fast reactions and without the appearance of considerable amounts of sideproducts. Thus, it can be concluded that ethylation failed in cases when the boron was simultaneously substituted with two cyano groups and an amine which was a strong Lewis base towards BHX_2.

Ethylation of diamine-bis(dicyanoboranes) ($DA{\cdot}2BH(CN)_2$, DA = DABCO, TMEDA) could not be carried out in homogeneous phase due to their poor solubility in every inert solvents we tested (chlorohydrocarbons, benzene, toluene), consequently the monitoring of the reactions were not feasible, and our attempts to isolate any ethylated product or solvolytic derivative remained unsuccessful.

III.D.3. Nucleophilic addition reactions of [amine-bis(*N*-ethylnitrilium)--hydroboron(2+)] cations

Water, methanol, ammonia and diethylamine readily add to [amine-bis(*N*-ethylnitrilium)hydroboron(2+)] tetrafluoroborates (19) to yield the corresponding bis(*C*-hydroxy-*N*-ethylimidate) (21), bis(*C*-methoxy-*N*-ethylimidate) (23), bis(ethylamidine) (24) and bis(triethylamidine) (25) derivatives, respectively, even in the presence of $[Et_3O][BF_4]$.

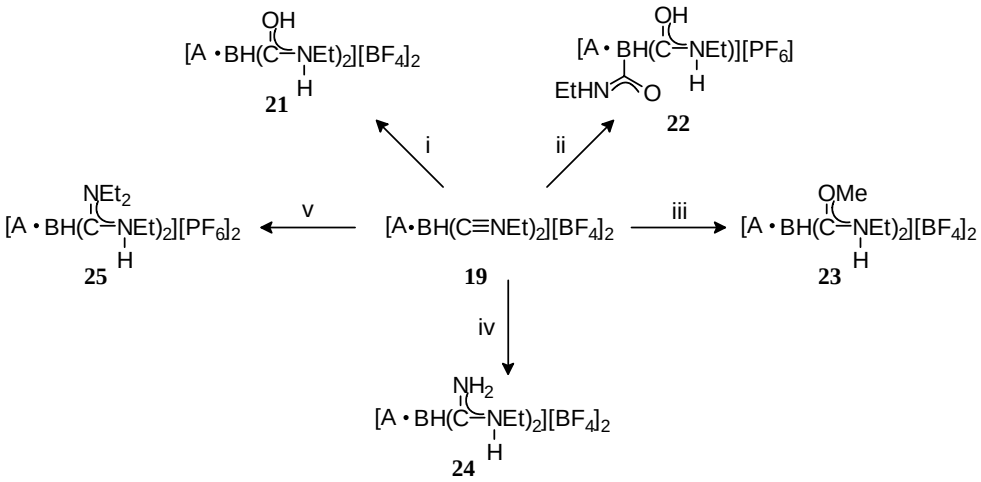


Figure 2. Nucleophilic addition reactions of [amine-bis(*N*-ethylnitrilium)hydroboron(2+)] (19) cations. See text for experimental details.

[Amine-bis(*C*-hydroxy-*N*-ethylimidate)hydroboron(2+)] (21) salts cannot be prepared from water, due to the strong acidity of the dication. Thus, their dissolution in water and then adding $NaPF_6$ results in the precipitation of [amine-*N*-ethylcarbamoyl(*C*-hydroxy-*N*-ethylimidate)hydroboron(1+)] hexafluorophosphates (22a,b,i,j) (Fig. 2., ii). [Amine-bis(*C*-hydroxy-*N*-ethylimidate)hydroboron(2+)] tetrafluoroborates (21a,b,i) were prepared after addition of water (two molar equivalents per *N*-ethylnitrilium group) to a vigorously stirred ethereal suspension of the bis(*N*-ethylnitrilium) salts (Fig. 2., i). Potentiometric titration proved these substances to be dibasic acids with $pK_{a1}<1$ and $pK_{a2}=3.1$-3.3 depending on the

amine. In other words, the amide group in amine-bis(*N*-ethylcarbamoyl)boranes is an extremely strong base, as the highest known corresponding pK_a values (those of the protonated acetamide and *N*-*n*-butylacetamide) are around –0.3.[118] The ease of the protonation of the amide group in such compounds is probably due to the strong electron releasing effect of the >N—B group towards the substituents on the boron.

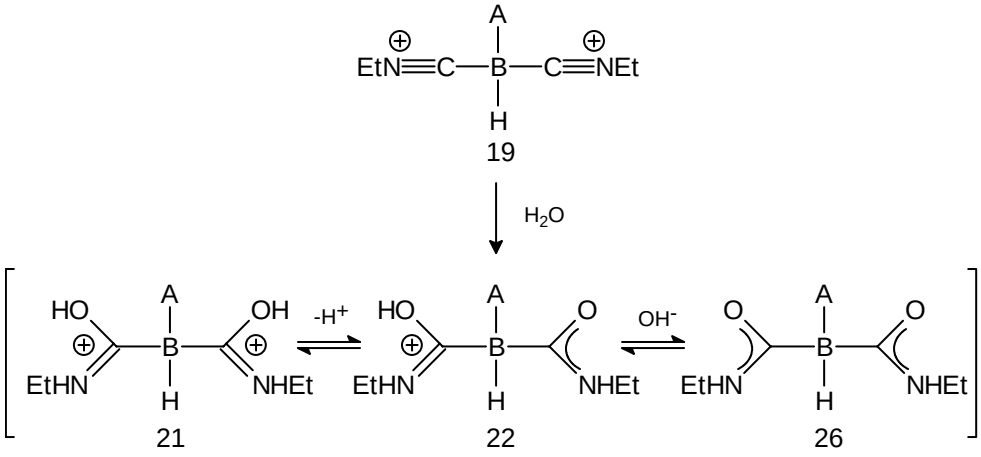
Dissolving the bis(*N*-ethylnitrilium) salts (19) in methanol yielded the corresponding bis(*C*-methoxy-*N*-ethylimidate) salt derivatives (23a,b,i,j) in minutes (Fig. 2., iii). Unlike aliphatic and aromatic alkylnitrilium salts, [amine-bis(*N*-ethylnitrilium)hydroboron(2+)] tetrafluoroborates (23) did not give orthoester in methanol even after days.

Both types of [amine-bis(amidinium)hydroboron(2+)] salts (24, 25) formed readily by dissolving the bis(*N*-ethylnitrilium) salts in liquid ammonia or diethylamine, respectively (Fig. 2., iv and v). The [amine-bis(triethylamidinium)hydroboron(2+)] cations were isolated as hexafluorophosphate salts (25b,i), since our attempts to crystallize the tetrafluoroborate salts (the primary products of the reactions) remained unsuccessful.

Only a limited number of compounds has been prepared so far with imidate or amidinium groups on the boron. Morse *et al.* have shown that such derivatives are stable intermediates in the transformation of [amine-(*N*-ethylnitrilium)dihydroboron(1+)] tetrafluoroborates into amine-carboxyboranes.[11] Sutton *et al.* have put considerable effort into the synthesis of amine-alkyl(carboxy)boranes *via* e.g. [amine-alkyl(*C*-alkoxy-*N*-ethylnitrilium)-hydroboron(1+)] cations,[58] but their attempts remained unsuccessful, similarly to those of Spielvogel *et al.*,[56] due to the presence of electron-donating alkyl group on the boron, which caused an increase in the hydridic character of the hydrogen attached to boron. Such compounds decomposed in acidic media instead of hydrolyzing into the corresponding carboxyborane complexes.

III.D.4. Hydrolytic behaviour of [amine-bis(C-hydroxy-*N*-ethylimidate)--hydroboron(2+)] cations and their deprotonated derivatives. Synthesis of amine-bis(*N*-ethylcarbamoyl)boranes and amine-dicarboxyboranes

The addition of water to [amine-bis(*N*-ethylnitrilium)hydroboron(2+)] cations (19) formally yield [amine-bis(*C*-hydroxy-*N*-ethylimidate)hydroboron(2+)] cations (21), or in other words, amine-boranes substituted with two protonated *N*-ethylamide groups. These compounds, as mentioned earlier, act as dibasic acids, so strong at the first base that they can be prepared only in once protonated form (22) from water. On further deprotonation with NaOH, they can be transformed into neutral amine-bis(*N*-ethylcarbamoyl)boranes (26), which can be readily extracted into dichloromethane.



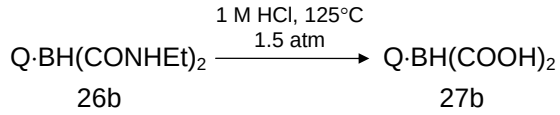
This way four amine-bis(*N*-ethylcarbamoyl)boranes (26a,b,ij) were prepared. Having synthesized the Me_3N complex, further amine-bis(*N*-ethylcarbamoyl)boranes can be prepared *via* amine exchange reactions, taking advantage of the volatility of Me_3N, and piperidine-bis(*N*-ethylcarbamoyl)borane (26l) was obtained this way. The range of amine-bis(*N*-ethylcarbamoyl)boranes probably can be extended by this route in the future to complexes of even much

weaker bases or such amines (e.g., secondary or primary ones), the dicyanoboranes (18) of which cannot be transformed into bis(*N*-alkylcarbamoyl)borane complexes. For historical reasons (i.e., for a longer period $Me_3N{\cdot}BH(CONHEt)_2$ was not available on preparative scale), synthesis of DMAP-bis(*N*-ethylcarbamoyl)borane (26k) *via* amine exchange reaction was accomplished starting from Q-bis(*N*-ethylcarbamoyl)borane (26b).

Amine-bis(*N*-ethylcarbamoyl)boranes (26) are fairly stable in alkaline solution even at elevated temperatures. For instance, $Q{\cdot}BH(CONHEt)_2$ could be quantitatively recovered after treatment with 1 M NaOH for 20 min at 120°C and 1.5 atm, and slow decomposition took place only in 50% NaOH close to its boiling point.

The aqueous solutions of 22 ⇌ 26 can be stored at room temperature for weeks at either 1M DCl or neutral solutions without any change in their NMR spectra. This behaviour is contrary to that of [amine-(*C*-hydroxy-*N*-ethylimidate)dihydroboron(1+)] cations (38), which, formed upon the hydrolysis of [amine-(*N*-ethylnitrilium)dihydroboron(1+)][tetrafluoroborates] (37) in acidic medium, slowly transform into amine-carboxyboranes (1).[3,5-12]

After numerous attempts it was found that $Q{\cdot}BH(CONHEt)_2$ can be transformed into $Q{\cdot}BH(COOH)_2$ in strongly acidic medium and at high temperature. The best yield (78%) was achieved by keeping the clear solution of the starting materials in a 125°C bath, at pH≈0 and 1.5 atm for 11 min when the first crystals of the product appeared in the mixture.



Under these conditions only one more of the existing amine-bis(*N*-ethylcarbamoyl)boranes, namely $pip{\cdot}H(CONHEt)_2$, transformed into the corresponding amine-dicarboxyborane (27l), all the other reactions resulted in the rupture of the B—N bond. There may be at least two explanations for this

experience. First, complexes with relatively weak B—N bonds (complexes of py, pic, Me_3N and probably other similar amines) are not stable in even less acidic solutions and lower temperatures, because of some kind of complexation competition between the proton and the borane moiety on the amine, and because the rupture of the B—N bond is irreversible in water. However, this is probably not the case for DMAP·BH$(CONHEt)_2$, since DMAP complexes (26k, 27k) could be readily prepared from Q complexes in amine exchange reactions, due to the considerably stronger B—N bonds in the products. The reason for the failure of the unexpectedly low stability of DMAP complexes towards acidic medium (see also the attempted acidic hydrolysis of DMAP·BH$(COOMe)_2$) may be the "too strong" electron donating property of DMAP through B—N bond, which results in an increased hydridic character of the hydrogen adjacent to boron. In other words, the B—H group in DMAP complexes is more susceptible towards an attack by an oxidating agent (here the proton). This assumption is supported by the findings of Funke and Mayr, who studied the kinetics and mechanism of the reactions between amine-boranes and carbenium ions. They concluded that BH_3 complexes of substituted pyridines, despite the lower basicities of the amines towards proton, are stronger hydride donors than trialkylamine complexes. Furthermore, they found that the reactivities of pyridine-boranes increased with the electron-donating ability of the substituents in pyridine, and found DMAP·BH_3 by far the strongest hydride donor of all studied complexes.[119] As a second explanation for the various hydrolytic behaviour of A·BH$(CONHEt)_2$ complexes, it is conceivable that for some subtle reasons pic, py, Me_3N and DMAP complexes are kinetically much more labile in acidic aqueous solutions than Q and pip complexes, however, literature data on hydrolysis kinetics of amine-boranes neither support nor disprove this hypothesis.

It should be noted, that both pip- and DMAP-dicarboxyborane (27k,l) could be obtained in amine exchange reaction carried out under conditions similar to those applied in analogous syntheses of amine-carboxyboranes (1) (large excess of the amine, without solvent or in small amount of acetonitrile), but these substances

required a different workup due to extensive salt formation, or in other words, deprotonation of amine-dicarboxyboranes by the amine applied in excess. This experience, which was not reported for any amine-carboxyboranes, is probably because amine-dicarboxyboranes, at least at their first base, are stronger acids than amine-carboxyboranes, presumably owing to the electron withdrawing effect of the carboxyl group. In agreement with these observations, the –COOH resonances in ^{1}H NMR (in DMSO-d_6 solution) can be found at lower fields for amine-dicarboxyboranes than those of amine-carboxyboranes.

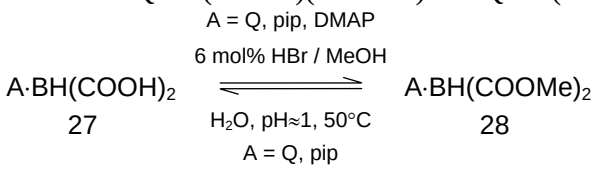
In conclusion, the range of available amine-dicarboxyboranes is rather narrow at the moment. As it was shown, the reason is that the vigorous conditions required for the formation of two carboxyl groups on the boron are unbearable to most amine-bis(N-ethylcarbamoyl)boranes. On the other hand, the applicability of amine exchange reactions is inherently poor, since B—N bonds are rather strong in all known amine-dicarboxyboranes. The huge difference between the conditions necessary for the hydrolysis of the amide group in amine-(N-ethylcarbamoyl)boranes (39) and amine-bis(N-ethylcarbamoyl)boranes (26) occurs probably due to the markedly different steric hindrance of the acyl carbons rather than electronic factors,[120] taking into account that - because of the presence of an amide group instead of a hydrogen on the boron - the electron density over the acyl carbon is probably less in bis-amides than in monoamides, so if electronic factors prevailed, the order of the rates should be reverse.

III.D.5. Esterification of amine-dicarboxyboranes and the hydrolysis of amine-bis(methoxycarbonyl)boranes

Amine-dicarboxyboranes (27) are relatively poorly soluble in organic solvents, and in order to facilitate their further transformations, which may require reactions in organic solvents, the preparation of their esters, or in other words, protecting the carboxylic group was attempted.

Similarly to amine-carboxyboranes (1), all known amine-dicarboxyboranes (27b,k,l) underwent esterification in methanol in the presence of a catalytic amount

(3 mol% relative to carboxyl groups) of HBr and the corresponding amine-bis(methoxycarbonyl)boranes (28) were obtained in practically quantitative yields. The reactions took somewhat longer times in comparison with those of amine-carboxyboranes (5-10 minutes in contrast to virtually instantaneous esterification), and the esters proved to be fairly sensitive to the careful application of molecular sieves; in one experiment incomplete drying and HBr removal before evaporation resulted in a 3:7 mixture of Q·BH(COOH)(COOMe) and Q·BH(COOMe)$_2$.



Amine-methoxycarbonylboranes underwent ester hydrolysis readily in acidic aqueous solutions (pH≈1) at 50°C employing constant N_2-bubbling through the reaction mixtures. Methyl esters of quinuclidine- and piperidine-dicarboxyboranes could be also hydrolyzed under similar conditions, and the corresponding amine-carboxyboranes were obtained after evaporation of the solvent and treatment with ether. DMAP·BH(COOMe)$_2$ is very poorly soluble in water, so its hydrolysis was attempted in acetonitrile:water=1:2 mixture at 40-50°C at pH≈1, and it resulted in the decomposition of the complex, probably for the same reason as described at the failure of the hydrolysis of DMAP·BH(CONHEt)$_2$ to DMAP·BH(COOH)$_2$. However, it seems likely that obtaining further amine-bis(methoxycarbonyl)boranes in a roundabout way would render the synthesis of the corresponding amine-dicarboxyboranes possible.

It should be noted that our experiments aimed at the alkaline ester hydrolysis of amine-bis(methoxycarbonyl)boranes were unsuccessful, e.g., ^{1}H NMR monitoring of the reaction showed that pip·BH(COOMe)$_2$ remained unchanged at pH>8 at 50°C for a couple of hours. Similar experience can be found in the literature for the attempted alkaline hydrolysis of Q·BH(Bu^i)COOEt.[58]

The difficulties of alkaline ester hydrolysis and the ease of acidic ester hydrolysis of A·BH(X)COOMe type compounds can be explained by one common reason: the

strong electron releasing effect of the ≡N—B≡ unit towards the methoxycarbonyl group on the boron hinders the alkaline hydrolysis by forming relatively large electron density over the acyl carbon and rendering the attack of OH^- more difficult, and on the other hand, the same effect advances acidic hydrolysis by promoting the protonation of the methoxycarbonyl group.

III.D.6. Hydrolytic behaviour of [amine-bis(*C*-methoxy-*N*-ethylimidate)--hydroboron(2+)] cations

As we have seen earlier, the known synthetic pathways allow the preparation of only a very limited number of amine-dicarboxyboranes. Hoping that ester groups can be hydrolyzed from yet unknown representatives of amine-bis(methoxycarbonyl)boranes as easily as it was carried out for Q- and pip-complexes, a synthetic pathway could be designed via [amine-bis(*C*-methoxy-*N*-ethylimidate)hydroboron(2+)] cations, taking into account that hydrolysis of *C*-alkoxy-*N*-alkylimidates in acidic media typically results in the formation of carboxylic acid esters (Fig. 3.).[121]

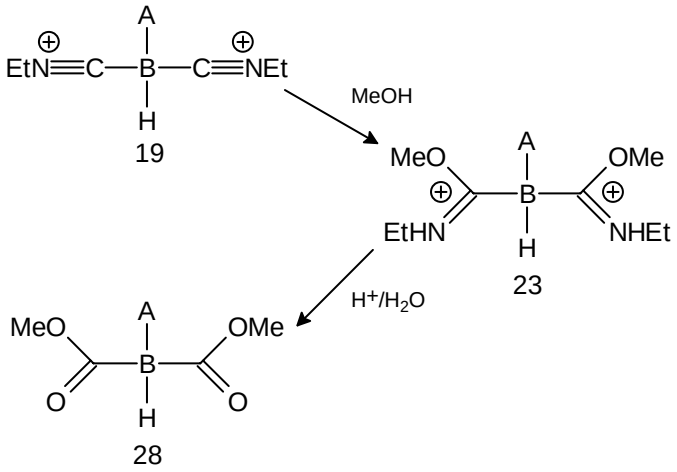
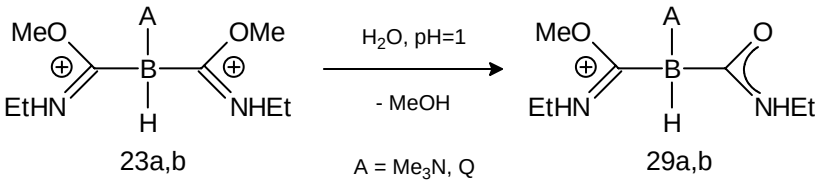


Figure 3. Expected reactions for the synthesis of amine-bis(methoxycarbonyl)boranes (28)

Furthermore, several amine-alkoxycarbonylboranes are known to be synthesized from [amine-(*N*-ethylnitrilium)dihydroboron(1+)] (37) cations *via* amine-(*C*-alkoxy-*N*-ethylimidate)dihydroboron(1+)] (40) species. It should be noted that hydrolysis of the py-complex was carried out in neutral medium, since at low pH the rupture of the B—N bond was observed.[11] Therefore, the hydrolyses of [amine-bis(*C*-methoxy-*N*-ethylimidate)hydroboron(2+)] cations 23a,b,i which were readily obtained by nucleophilic addition of methanol to the corresponding [amine-bis(*N*-ethylnitrilium)hydroboron(2+)] cations (19), were studied at various pH values.

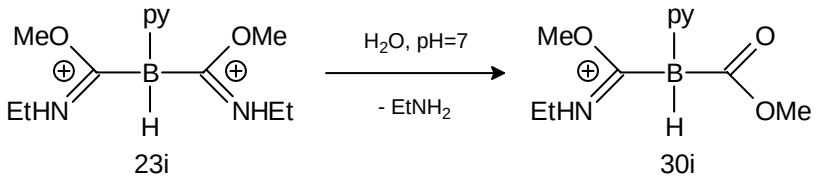
^{1}H NMR monitoring of the solutions of all the three complex cations 23a,b,i in 1 M HCl showed that the first step of hydrolysis was the appearance of methanol. In the case of the pyridine complex this was accompanied by formation of py·HCl and boric acid *via* the rupture of the B—N bond. In the cases of the other two complex cations, methanol was formed from one of the *C*-methoxy-*N*-ethylimidate groups on the boron leaving behind an [amine-(*N*-ethylcarbamoyl)(*C*-methoxy-*N*-ethylimidate)hydroboron(1+)] cation (29) and no other process was observed.



At room temperature, at pH=1-2, 60% conversion of the Q-complex cation was found after 5 days. At boiling point in 1 M HCl the reaction was complete within 3 min, but it was accompanied also by the rupture of the B—N bond and the same reactions took place in similar proportions in even 20% HCl near boiling point. The Me_3N-complex showed the same hydrolysis pattern with slightly more decomposition. Fortunately, the [amine-(*N*-ethylcarbamoyl)(*C*-methoxy-*N*-ethylimidate)hydroboron(1+)] cations (29) can be extracted into CH_2Cl_2, this way

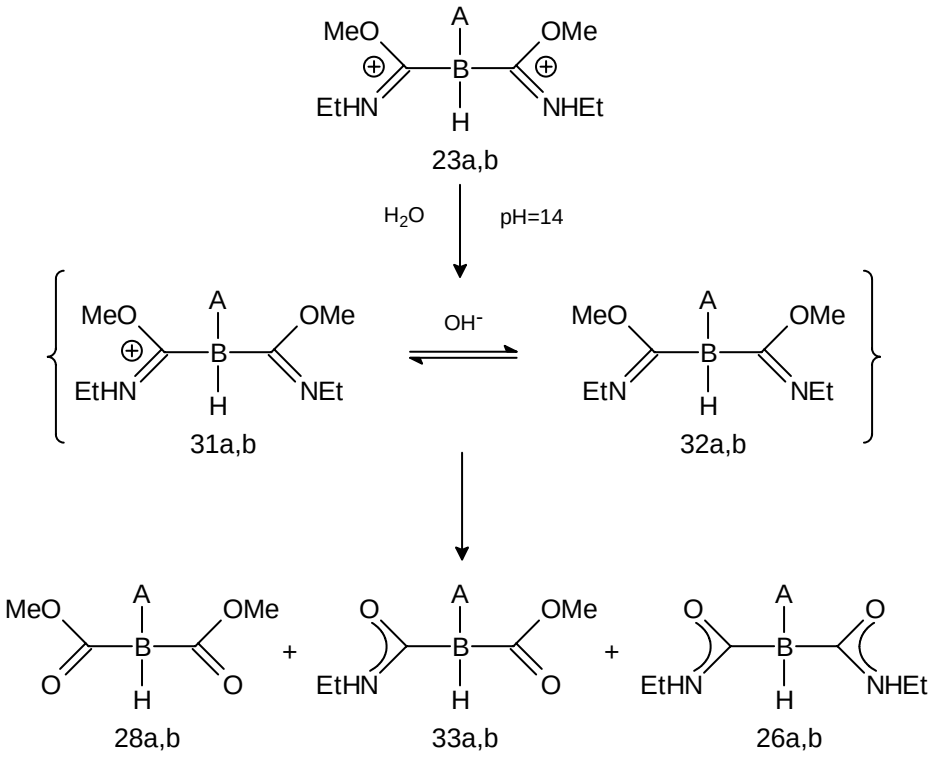
the tetrafluoroborate salt of the corresponding Q complex cation was obtained with good yield. After all, in contrast to *C*-methoxy-*N*-ethylimidate groups adjacent to carbon, this route is obviously unsuitable for the synthesis of amine-bis(methoxycarbonyl)boranes (28).

The hydrolyses of two [amine-bis(*C*-methoxy-*N*-ethylimidate)hydroboron(2+)] cations (23a,i) were studied in neutral aqueous solution also. In contrast to the observations obtained in acidic medium, the B—N bond in both complex cations proved stable even at temperatures close to the boiling point. The hydrolysis of the Me_3N complex cation 23a resulted in five major N-Me containing species in nearly equal proportions and a few minor ones by ^{1}H NMR, and all of them could be extracted into dichloromethane. During the hydrolysis of the py-complex cation 23i, the pH of the solution was decreasing. Therefore, the reaction was carried out by applying regular adjustment of the pH in order to keep it close to 7, and it resulted in the formation of three pyridine-containing species, the major component (70 mol%) of which could be identified as $\{py{\cdot}BH(COOMe)[C(OMe)NHEt]\}^+$ cation (30i) by ^{1}H NMR.



In 1 M NaOH the hydrolysis of [py-bis(*C*-methoxy-*N*-ethylimidate)-hydroboron(2+)] cation (23i) resulted in a mixture consisting of five pyridine-containing components. One of the two major components is probably the amine-bis(*N*-ethylcarbamoyl)borane (26i) and each seemed to be neutral by their ^{1}H NMR chemical shifts. The alkaline hydrolysis of Me_3N- and Q-complex cations lead to three-component mixtures. The components could be identified by ^{1}H NMR as amine-bis(*N*-ethylcarbamoyl)boranes (26) (25-40 mol%), based on the spectra of previously synthesized compounds, amine-bis(methoxycarbonyl)boranes (28) (20-

25 mol%) and "mixed" amine-(*N*-ethylcarbamoyl)(methoxycarbonyl)-
-boranes (33) (40-50 mol%). The yet unknown components were identified speculatively, using the integral ratios of observed signals and the chemical shifts and spectral patterns (e.g., the characteristic N-CH_2 signal of Q in the presence of a chiral boron) of known compounds. It is noteworthy, that *C*-methoxy-*N*-ethylimidate base (–C(OMe)=NEt) groups, did not seem to be present in $CDCl_3$ solution, as every *N*-CH_2 proton shared relatively strong (7-11 Hz) scalar couplings with NH-s in the amide region of ^{1}H NMR spectra. Although it seems obvious that –[C(OMe)-NHEt]$^+$ groups undergo deprotonation in alkaline aqueous solutions, the aforementioned observation may make one conclude that
–C(OMe)=NEt groups on the boron are not stable in these compounds, probably because of their proclivity to undergo nucleophilic substitution (see figure on the facing page). This is probably caused by the presence of an electron withdrawing substituent (here: –[C(OMe)-NHEt]$^+$) on the boron, since several amine-borane complexes are known in the literature with the composition A·BH(X)-C(OR)=NEt (X = H, alkyl) and those with alkyl group on the boron were observed to withstand hydrolysis in even relatively harsh conditions.[57]
In conclusion, –[C(OMe)-NHEt]$^+$ groups in these complex cations showed a hydrolysis pattern completely different from that observed for similar groups adjacent to carbon, and their transformation into methoxycarbonyl groups is not straightforward. In acidic media the transformation of [amine-bis(*C*-methoxy-*N*-ethylimidate)hydroboron(2+)] cations (23) into amine-bis(methoxycarbonyl)boranes (28) was not feasible, because the first step of the hydrolysis was the leaving of methanol. In neutral aqueous solution the hydrolysis of [py-bis(*C*-methoxy-*N*-ethylimidate)hydroboron(2+)] cation (23i) starts in a promising manner, but efforts should be invested into finding the way to the synthesis of py·BH$(COOMe)_2$. In alkaline media amine-bis(methoxycarbonyl)boranes (28) appear among the products of the hydrolysis, however, in only rather limited proportions.


MeO
A
OMe
B
EtHN
NHEt
H
23a,b
H2O
pH=14
OH-
MeO
A
OMe
B
EtHN
NEt
H
31a,b
MeO
A
OMe
B
EtN
NEt
H
32a,b
MeO
A
OMe
B
O
O
H
28a,b
+
O
A
OMe
B
EtHN
O
H
33a,b
+
O
A
O
B
EtHN
NHEt
H
26a,b

IV. EXPERIMENTAL SECTION

IV.A. Materials and methods

All reactions, except those involving water or noted otherwise, were performed under an oxygen and water free N_2 atmosphere using the general Schlenk techniques in flamed or oven dried glassware with absolutized solvents freshly distilled prior to use.

Acetone was distilled from a 1.5 m Raschig packed column. Acetonitrile was distilled from P_2O_5 after drying with CaH_2. Chloroform was distilled from P_2O_5 after shaking with cc. H_2SO_4 and drying with $CaCl_2$. Dichloromethane was distilled from CaH_2, then refluxed with $NaBH_4$/diglyme and fractionally distilled. Ethanol was distilled from $Mg(OCH_2CH_3)_2$. Ether was distilled from Na-benzophenone. Isopropanol was distilled from sodium. Methanol was distilled from $Mg(OCH_3)_2$. Methyl sulfide was dried with sodium, then fractionally distilled. Pentane was fractionally distilled. THF was distilled from Na-benzophenone. Water denotes twice distilled water.

Alcoholic HBr solutions were prepared by dropwise addition of concentrated aqueous HBr solution to P_2O_5 under vigorous stirring and dissolving the liberated HBr gas, after drying Granusic A (J. T. Baker), in the corresponding alcohol. Molecular sieves were activated by keeping under dynamic vacuum for 3 h at 220°C, and stored under dry N_2.

Ammonia was dried in a KOH-filled column before condensing. 4-Cyanopyridine and quinuclidine were recrystallized from ether. Diethylamine, picoline, pyridine and TMEDA were distilled from KOH. Morpholine was distilled from KOH, then from Na. Piperidine was distilled from CaH_2. NBS was recrystallized from water and dried in N_2 stream before use.

Bromine (Ferak), $[Bu_4N]I$ (Fluka), DABCO (Aldrich), DMAP (Janssen), 48% aq HBr solution (Fluka), $NaPF_6$ (Aldrich) and trimethylamine (Fluka) were used as received.

$[Bu_4N]CN$,[122] Cyanodihydroborane oligomer in methyl sulfide solution,[123] $DMAP{\cdot}BH_2COOMe$,[17] $Et_3N{\cdot}BH_2CN$,[17] $[Et_3O][BF_4]$,[124] $LiCN{\cdot}n$THF,[125] $Me_3N{\cdot}BH_2CN$,[109] $TMEDA{\cdot}2BH_2COOH$[14] and $TMPDA{\cdot}2BH_2COOH$[14] were prepared by known procedures. $Q{\cdot}BH_2CN$ was obtained anlogously to $Et_3N{\cdot}BH_2CN$.[17]

$Li[BH_2(CN)_2]$, 4-CN-py·$BH(CN)_2$, py·$BH(CN)_2$ and pip·$BH(CN)_2$ are already known[110], but their preparations have been considerably improved, and these newer syntheses are also included.

NMR spectra were recorded on a Bruker AM 360 instrument in 5 mm o.d. tubes at room temperature. ^1H (360.1 MHz) spectra were referred to internal DSS in D_2O and internal TMS in $CDCl_3$, acetone-d_6 and DMSO-d_6. ^1H NMR spectra of **19a,b,i** were recorded in CH_2Cl_2 without lock, and were referred to the solvent signal (5.32 ppm). Protons adjacent to boron generally gave distinguishable but broad signals, and their chemical shifts are omitted. ^{13}C (90.5 MHz) spectra were referred to solvent signals ($CDCl_3$: 77.0 ppm, acetone-d_6: 29.9 ppm, DMSO-d_6: 39.5 ppm) and DSS in D_2O as external reference. Ambiguities in assigning ^1H and ^{13}C signals were cleared with homonuclear decoupling and chemical shift correlation (^1H-^1H and ^{13}C-^1H) experiments. Carbons directly attached to boron could not be observed. ^{11}B (115.5 MHz) spectra were referred to $Et_2O{\cdot}BF_3$ in a capillary inserted into the tube. In cases when multiplicities could only be revealed by mathematical resolution enhancement, multiplets are marked "broad" and coupling constants are not given.

IR spectra were recorded on a Perkin Elmer Paragon PC 1000 FT-IR spectrometer.

Potentiometric titrations were carried out at 25±0.1°C using a Radiometer PH M 52 pH-meter referenced to a saturated calomel electrode. Approximate acidity constants were estimated from the half-neutralization pH.

The boron and bromine content of the samples was determined with acid-base titration in the presence of mannitol, or by using the Volhard method, respectively, after fusion with sodium hydroxide and potassium hydroxide. Analyses of BF_4 and PF_6 salts were performed in the presence of large excess of $CaCl_2$. LiCN·*n*THF was analyzed by the Liebig-Dénigès protocol[126].

Safety note. Dihydrocyanoborane oligomer was always handled in methyl sulfide solution, because explosions were experienced with neat $(BH_2CN)_n$.[127]

IV.B. Syntheses

IV.B.1. A·BH_2COOH (1a-c,e)

$Me_3N·BH_2COOH$ (1a)

$[Et_3O][BF_4]$ (60.7 g, 319.5 mmol) and $Me_3N·BH_2CN$ (25.78 g, 263.2 mmol) were dissolved on CH_2Cl_2 (180 ml). The solution was refluxed for 24 hours, then the solvent was evaporated. The solid residue was dissolved in water (110 ml), NaOH solution (70.5 ml 0.95 M) was added, and the solution was quickly warmed to 85°C and then kept at 85-90°C for 5 min. The mixture was then cooled to 30-40°C, its pH was adjusted to 2 with cc. HCl (≈1.5 ml) and ca. 100 ml water was evaporated. The viscous residue was extracted with CH_2Cl_2 (50 ml + 20×25 ml). The organic phase was dried over Na_2SO_4 and evaporated to dryness. The residue was stirred with ether (50 ml) overnight, the mixture was then filtered, the solid was washed with ether (2×30 ml) and dried in a N_2 stream.

Yield: 27.40g (89%). Anal. found (calcd for $C_4H_{12}BNO_2$): B, 9.31 (9.24)%. The spectroscopic data are in agreement with literature.[3]

Q·BH_2COOH (1b)

[Et_3O][BF_4] (7.73 g, 40.69 mmol) and Q·BH_2CN (6.08 g, 40.52 mmol) were dissolved in CH_2Cl_2 (180 ml). The solution was refluxed for 24 hours, then the solvent was evaporated. Ether (40 ml) was added to the oily residue and it was then evaporated after stirring. This treatment was repeated until solidification of the evaporation residue. The solid was then suspended in ether (70 ml), it was filtered off and then extracted eight times by the filtrate. The solid [Q·BH_2(CNEt)][BF_4] (5.55 g, 81%) was dried in a N_2 stream. The ethylnitrilium salt was dissolved in water (100 ml) and pH was adjusted to 2-3 using cc. HCl. The solution was quickly warmed to 80°C and then kept at 80-85°C for 8 min. The mixture was then cooled to room temperature, the crystalline product were filtered off, washed with water (3×6 ml) and dried in a N_2 stream.

Yield: 5.55 g (81%). Anal. found (calcd for $C_8H_{16}BNO_2$): B, 6.33 (6.40)%. The spectroscopic data are in agreement with literature.[7]

Et_3N·BH_2COOH (1c)

[Et_3O][BF_4] (18.46 g, 97.2 mmol) and Et_3N·BH_2CN (13.56 g, 96.8 mmol) were dissolved in CH_2Cl_2 (50 ml). The solution was refluxed for 14 h, then the solvent was evaporated under reduced pressure. The remaining pale yellow oil was dissolved in water (50 ml), heated up quickly to mild boiling, then kept at this temperature for approx. 10 min, while white crystals appeared in the solution. The mixture was then cooled to room temperature, the crystals were filtered, washed with water (3×6 ml) and dried in a N_2-stream.

Yield: 10.87 g (71%). Anal. found (calcd for $C_7H_{18}BNO_2$): B, 6.72 (6.80)%. ^{1}H NMR ($CDCl_3$, δ): 1.15 (t, 9H, CH_3), 3.04 (q, 6H, CH_2). ^{11}B NMR ($CDCl_3$, δ): -17.2 (br). IR (KBr, cm^{-1}): 2401 ν(B-H), 1647 ν(C=O).

pic·BH_2COOH (1j)

A suspension of pic·BH_2COOMe (2.26 g, 13.74 mmol) in 0.01 M HBr (70 ml) was kept at 70-80°C employing N_2-bubbling through the mixture for an hour, during which time the solid melted and totally dissolved, then the solution was allowed to stand at room temperature overnight, while pic·BH_2COOH crystallized as colourless needles. The solid was filtered, washed with cold water and dried in a N_2-stream.

Yield: 1.652 g (80%). Anal. found (calcd for $C_7H_{10}BNO_2$): B, 7.07 (7.16)%. ^{1}H NMR ($CDCl_3$-DMSO-d_6, δ): 2.54 (s, 3H, CH_3), 7.46 (d, 2H, 3,5-CH), 8.39 (d, 2H, 2,4-CH). ^{11}B NMR ($CDCl_3$-DMSO-d_6, δ): -11.9 (br). IR (KBr, cm^{-1}): 2374, 2402 ν(B-H), 1650 ν(C=O).

IV.B.2. A·BH_2COOR (2-4a-d,j and 2e)

General procedure:

Amine-carboxyborane 1a-c,e,j (10.0 mmol, 5.0 mmol for 1d) was suspended in a calculated amount of alcohols to reach the concentration given below. A calculated amount of alcoholic HBr solution (0.5-1 M) was added to reach 3 mol% relative to carboxylic acid groups, and the mixture was kept at the given temperature for the given time. Molecular sieves (A4, 2.0 g) were then added at room temperature, which were filtered off after the given drying time and washed with the corresponding alcohol (3×2 ml). The filtrate was then evaporated to dryness (or in

the case of 3,4c to an oil with a constant weight). The crude products, if necessary, can be purified by the procedures given as follows:

A. The crude product was suspended in ether (20 ml), the suspension was filtered and the filter cake was extracted with the filtrate to a point when only a slowly settling residue remained. The extract was then evaporated to dryness in vacuum.

B. The same as procedure A, using *n*-pentane as the solvent.

C. Extraction was carried out as described in A. The extract was then filtered, the solid was washed with ether (2×3-4 ml) and dried in a N_2-stream.

D. The same as procedure C, using *n*-pentane as the solvent.

E. Ether (ca. 25-40 ml) was added to the crude product in portions until complete dissolution except some slowly settling residue. The mixture was then filtered and the filtrate was evaporated to solid.

F. The same as C, using n-pentane (20-35 ml) as the solvent, and evaporating the extract to a solid or in the case of 3,4c to a syrup with a constant weight.

Satisfactory analyses for boron were obtained: B±0.19

$Me_3N{\cdot}BH_2COOMe$ (2a)

Concentration: 0.25 M. Reaction time/temperature: 10 min/r.t. Drying time: 2 h. Purification method: F.

Yield: 87%. The spectroscopic data are in agreement with literature.[33]

$Q{\cdot}BH_2COOMe$ (2b)

Concentration: 0.25 M. Reaction time/temperature: 10 min/ r.t. Drying time: 2 h. Purification method: B.

Yield: 95 %. The spectroscopic data are in agreement with literature.[37]

$Et_3N{\cdot}BH_2COOMe$ (2c)

Concentration: 0.25 M. Reaction time/temperature: 15 min / r.t. Drying time: 2h. Purification method: F.

Yield: 86%. ^{1}H NMR ($CDCl_3$, δ): 1.15 (t, 9H, C-CH_3), 3.06 (q, 6H, N-CH_2), 3.52 (s, 3H, O-CH_3). ^{11}B NMR ($CDCl_3$, δ): −14.47 (t). IR (KBr, cm^{-1}): 2402 ν(B-H), 1666 ν(C=O).

$TMEDA{\cdot}2BH_2COOMe$ (2d)

Concentration: 0.25 M. Reaction time/temperature: 15 min / 50°C. Drying time: 2 h. Purification method: C.

Yield: 89%. ^{1}H NMR ($CDCl_3$, δ): 2.73 (s, 12 H, N-CH_3), 3.43 (s, 4H, N-CH_2), 3.54 (s, 6H, O-CH_3). ^{11}B NMR ($CDCl_3$, δ): −11.7 (br t). IR (KBr, cm^{-1}): 2398 ν(B-H), 1676 ν(C=O).

$TMPDA{\cdot}2BH_2COOMe$ (2e)

Concentration: 0.20 M. Reaction time/temperature: 10 min / r.t.. Drying time: 3h. Purification method: C.

Yield: 89%. ^{1}H NMR ($CDCl_3$, δ): 3.54 (s, 6H, OCH_3), 2.98 (m, 4H, NCH_2), 2.72 (s, 12H, NCH_3), 2.08 (m, 2H, $CH_2CH_2CH_2$). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 59.69 (NCH_2), 49.93 (OMe), 47.99 (NMe), 18.17 ($CH_2CH_2CH_2$). ^{11}B NMR ($CDCl_3$, δ): -11.2 (br t). IR (KBr, cm^{-1}): 2403 ν(B-H); 1670 ν(C=O).

$pic{\cdot}BH_2COOMe$ (2i)

Concentration: 0.25 M. Reaction time/temperature: 15 min / r.t. Drying time: 3 h. Purification method: D.

Yield: 94%. ^{1}H NMR ($CDCl_3$, δ): 2.53 (s, 3H, O-CH_3), 3.57 (s, 3H, C-CH_3), 7.40 (d, 2H, aromatic H), 8.41 (d, 2H, aromatic H). ^{11}B NMR ($CDCl_3$, δ): –11.1 (t). IR (KBr, cm^{-1}): 2384 ν(B-H), 1670 ν(C=O)

$Me_3N{\cdot}BH_2COOEt$ (3a)

Concentration: 0.25 M. Reaction time/temperature: 5 min / r.t. Drying time: 8 h. Purification method: B.

Yield: 91%. The spectroscopic data are in agreement with literature.[37]

Q·BH_2COOEt (3b)

Concentration: 0.25 M. Reaction time/temperature: 15 min / r.t. Drying time: 8h. Purification method: F.

Yield: 93%. ^{1}H NMR ($CDCl_3$, δ):1.22 (t, 3H, CH_2-*CH_3*), 1.78 (m, 6H, CH-*CH_2*), 2.03 (sept, 1H, $(CH_2)_3$-*CH*), 3.22 (m, 6H, N-CH_2), 4.00 (q, 2H, O-CH_2). ^{11}B NMR ($CDCl_3$, δ): –11.1 (t). IR (KBr, cm^{-1}): 2374 ν(B-H), 1668 ν(C=O).

$Et_3N{\cdot}BH_2COOEt$ (3c)

Concentration: 0.25 M. Reaction time/temperature: 5 min / r.t. Drying time: 8 h. Purification method: F.

Yield: 96%. ^{1}H NMR ($CDCl_3$, δ): 1.15 (t, 9H, N-CH_2-*CH_3*), 1.22 (t, 3H, O-CH_2-*CH_3*), 3.06 (q, 6H, N-CH_2), 4.02 (q, 2H, O-CH_2). ^{11}B NMR ($CDCl_3$, δ): –14.4 (t). IR (KBr, cm^{-1}): 2406 ν(B-H), 1668 ν(C=O).

TMEDA·$2BH_2COOEt$ (3d)

Concentration: 0.40 M. Reaction time/temperature: 15 min / 50°C. Drying time: 3 h. Purification method: A.

Yield: 91%. ^{1}H NMR ($CDCl_3$, δ): 1.23 (t, 6H, C-CH_3), 2.73 (s, 12 H, N-CH_3), 3.43 (s, 4H, N-CH_2), 4.03 (q, 4H, O-CH_2). ^{11}B NMR ($CDCl_3$, δ): −11.5 (br t). IR (KBr, cm^{-1}): 2364, 2390 ν(B-H), 1664 ν(C=O).

pic·BH_2COOEt (3i)

Concentration: 0.25 M. Reaction time/temperature: 5 min / r.t. Drying time: 3 h. Purification method: E.

Yield: 97%. ^{1}H NMR ($CDCl_3$, δ): 1.24 (t, 3H, CH_2-*CH_3*), 2.53 (s, 3H, C-CH_3), 4.07 (q, 2H, O-CH_2), 7.40 (d, 2H, aromatic H), 8.41 (d, 2H, aromatic H). ^{11}B NMR ($CDCl_3$, δ): – 10.9 (t). IR (KBr, cm^{-1}): 2406 ν(B-H), 1658 ν(C=O).

Me_3N·BH_2COOPr^{i} (4a)

Concentration: 0.25 M. Reaction time/temperature: 20 min / r.t. Drying time: 8h. Purification method: B.

Yield: 80%. ^{1}H NMR ($CDCl_3$, δ): 1.20 (d, 6H, CH-*CH_3*), 2.75 (s, 9H, N-CH_3), 5.08 (sept, 1H, O-CH). ^{11}B NMR ($CDCl_3$, δ): –9.4 (t). IR (KBr, cm^{-1}): 2386 ν(B-H), 1660 ν(C=O).

Q·BH_2COOPr^{i} (4b)

Concentration: 0.25 M. Reaction time/temperature: 20 min / r.t. Drying time: 8h. Purification method: B.

Yield: 96%. ^{1}H NMR ($CDCl_3$, δ): 1.19 (d, 6H, CH-*CH_3*), 1.77 (m, 6H, CH-*CH_2*), 2.03 (sept, 1H, $(CH_2)_3$-*CH*), 3.22 (m, 6H, N-CH_2), 5.04 (sept, 1H, O-CH). ^{11}B NMR ($CDCl_3$, δ): −11.0 (t). IR (KBr, cm^{-1}): 2360, 2386, 2400 ν(B-H), 1664 ν(C=O).

$Et_3N{\cdot}BH_2COOPr^i$ (4c)

Concentration: 0.25 M. Reaction time/temperature: 10 min / r.t. Drying time: 8h. Purification method: F.

Yield: 97%. ^{1}H NMR ($CDCl_3$, δ): 1.15 (t, 9H, CH_2-CH_3), 1.19 (d, 6H, CH-CH_3), 3.08 (q, 6H, N-CH_2), 5.05 (sept, 1H, OCH). ^{11}B NMR ($CDCl_3$, δ): −14.2 (t). IR (KBr, cm^{-1}): 2406 ν(B-H), 1662 ν(C=O).

TMEDA$\cdot 2BH_2COOPr^i$ (4d)

Concentration: 0.40 M. Reaction time/temperature: 30 min / 50°C. Drying time: 8 h. Purification method: E.

Yield: 97%. ^{1}H NMR ($CDCl_3$, δ): 1.20 (d, 12H, CH-CH_3), 2.73 (s, 12H, N-CH_3), 3.41 (s, 4H, N-CH_2), 5.05 (sept, 1H, O-CH). ^{11}B NMR ($CDCl_3$, δ): −11.4 (br). IR (KBr, cm^{-1}): 2368, 2400 ν(B-H), 1652, 1666 ν(C=O).

pic$\cdot BH_2COOPr^i$ (4i)

Concentration: 0.25 M. Reaction time/temperature: 20 min / r.t. Drying time: 8h. Purification method: E.

Yield: 96%. ^{1}H NMR ($CDCl_3$, δ): 1.21 (d, 6H, CH-CH_3), 2.52 (s, 3H, C-CH_3), 5.08 (sept, 1H, O-CH), 7.38 (d, 2H, aromatic H), 8.41 (d, 2H, aromatic H). ^{11}B NMR ($CDCl_3$, δ): −10.9 (t). IR (KBr, cm^{-1}): 2386, 2402 ν(B-H), 1656 ν(C=O).

IV.B.3. A·BH(Br)COOH (5a-c)

General procedure:

To a suspension of N-bromosuccinimide (1.03 g; 5.8 mmol) in CH_2Cl_2 (5 ml) a solution of the amine-carboxyborane (1a-c) (5.8 mmol) in CH_2Cl_2 (50 ml) was added (for dissolution gentle heating may be required). After 5 min. reaction time

the mixture was evaporated to dryness and the residue was taken up with pentane (10 ml), filtered, washed with cold (0°C) water (4x3 ml) and dried in a N_2 stream.

Me_3N·BH(Br)COOH (5a)

Yield: 0.93 g (81%). Anal. found (calcd for $C_4H_{11}BBrNO_2$): B, 5.46 (5.52)%, Br 40.70 (40.80)%. ^{1}H NMR ($CDCl_3$, δ): 2.92 (s, 9H, NCH_3). ^{11}B NMR ($CDCl_3$, δ): –5.6 (d). IR (KBr, cm^{-1}): 2476 ν(B-H), 1654 ν(C=O).

Q·BH(Br)COOH (5b)

Yield: 1.35 g (94%). Anal. found (calcd for $C_8H_{15}BBrNO_2$): B, 4.33 (4.36)%, Br 32.29 (32.23)%. ^{1}H NMR ($CDCl_3$, δ): 1.83 (m, 6H, C-CH_2), 2.11 (h, 1H, CH), 3.42 (m, 6H, NCH_2). ^{11}B NMR ($CDCl_3$, δ): –6.2 (d). IR (KBr, cm^{-1}): 2468 ν(B-H), 1646 ν(C=O).

Et_3N·BH(Br)COOH (5c)

Yield: 1.07 g (77%). Anal. found (calcd for $C_7H_{17}BBrNO_2$): B, 4.49 (4.54)%, Br, 33.59 (33.48)%. ^{1}H NMR ($CDCl_3$, δ): 1.26 (t, 9H, CH_3), 3.32 (m, 6H, CH_2). ^{11}B NMR ($CDCl_3$, δ): –6.4 (d). IR (KBr, cm^{-1}): 2492 ν(B-H), 1654 ν(C=O).

IV.B.4. A·BH(Br)COOMe (6a-e)

Me_3N·BH(Br)COOMe (6a)

1a (5.136 g, 43.91 mmol) was dissolved in distilled methanol (85 ml final volume). NBS (7.891 g, 44.33 mmol) was added to the solution in 15 portions. The second portion was added 5 min after the first one (ca. 5%) and subsequent portions were added when the pale yellow colour of the mixture disappeared. The temperature

was kept at 25°C by employing a cooling bath. The volatile parts were then evaporated *in vacuo*, the residue was triturated with ether which was then evaporated. The solid residue was suspended in 0.01 M HBr solution (25 ml) at 0°C, the product was filtered off, washed with 0.01 M HBr (2×10 ml) and dried in a N_2 stream.

Yield: 8.018 g (87%). Anal. found (calcd for $C_5H_{13}BBrNO_2$): B, 5.20 (5.15)%; Br, 37.9 (38.1)%. ^{1}H NMR ($CDCl_3$, δ): 2.91 (s, 9H, NCH_3), 3.62 (s, 3H, OCH_3). ^{11}B NMR ($CDCl_3$, δ): –5.4 (d). IR (KBr, cm^{-1}): 2474 ν(B-H), 1680 ν(C=O).

Q·BH(Br)COOMe (6b)

The reaction between 1b (3.180 g, 18.81 mmol) and NBS (3.363 g, 18.90 mmol) and the workup of the mixture was carried out analogously to that described for 6a.

Yield: 4.305 g (87%). Anal. found (calcd for $C_9H_{17}BBrNO_2$): B, 4.11 (4.13)%; Br, 30.61 (30.53)%. ^{1}H NMR ($CDCl_3$, δ): 1.84 (m, 6H, CCH_2), 2.11 (h, 1H, CH), 3.41 (m, 6H, NCH_2), 3.60 (s, 3H, OCH_3). ^{11}B NMR ($CDCl_3$, δ): –6.1 (d). IR (KBr, cm^{-1}): 2474 ν(B-H), 1686 ν(C=O).

Et_3N·BH(Br)COOMe (6c)

To a stirred solution of 2c (0.432 g; 2.49 mmol) in chloroform (15 ml) NBS (0.445 g; 2.50 mmol) was added, and after 10 min. the reaction mixture was extracted with cold (0^{o}C) water (4x10 ml). The organic layer was separated, dried over Na_2SO_4 and evaporated to obtain the product.

Yield 0.55 g (88%). Anal. found (calcd for $C_8H_{19}BBrNO_2$): B, 4.34 (4.29)%; Br, 31.75 (31.70)%. ^{1}H NMR ($CDCl_3$, δ): 1.25 (t, 9H, N-CH_2-*CH_3*), 3.32 (dq, 6H, N-CH_2), 3.61 (s, 3H, O-CH_3). ^{11}B NMR ($CDCl_3$, δ): –6.6 (d). IR (KBr, cm^{-1}): 2500 ν(B-H), 1682 ν(C=O).

TMEDA·2BH(Br)COOMe (6d)

To a suspension of 1d (0.62 g, 2.67 mmol) in methanol (10 ml) was added NBS (0.96 g, 5.39 mmol) over 30 min in small portions. After 30 min the precipitated crystals were separated on a filter, washed with methanol (3×4 ml) and dried in a N_2 stream.

Yield: 0.83 (74%). Anal. Calcd (found) for $C_{10}H_{24}B_2Br_2N_2O_4$: B, 5.18 (5.15)%; Br, 38.26 (38.57)%. ^{1}H NMR ($CDCl_3$, δ): 3.63 (s, 6H, OCH_3), 3.63, 3.45 (2×m, 3+1H, NCH_2) 3.02, 2.98, 2.97, 2.96 (4×s, 4×3H, NCH_3). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 55.97, 55.19 (NCH_2), 49.50 (OCH_3), 49.10, 48.77, 48.69, 47.72 (NCH_3). ^{11}B NMR ($CDCl_3$, δ): -7.0 (br d). IR (KBr, cm^{-1}): 2501 sh, 2484, ν(B-H); 1676 ν(C=O).

TMPDA·2BH(Br)COOMe (6e)

To a solution of 1e (0.63 g, 2.56 mmol) in methanol (12 ml) was added solid NBS (0.91 g, 5.12 mmol) in small portions over 30 min. The solution was evaporated to dryness and the residue was kept under high vacuum (<0.1 Hgmm) to afford a semisolid. It was then dissolved in dichloromethane (10 ml) and the succinimide was removed by extraction with aq HBr solution (7×3 ml 0.005 M). The CH_2Cl_2 layer was dried with Na_2SO_4, the solvent was evaporated with a N_2 stream and the residue was kept in vacuum to give a colorless oil of constant weight. Yield: 0.87 g (79%). Anal. Calcd (found) for $C_{11}H_{26}B_2Br_2N_2O_4$: B, 5.01 (4.86)%; Br, 37.01 (36.10)%. ^{1}H NMR ($CDCl_3$, δ): 3.62 (s, 6H, OCH_3), 3.25, 3.15, 2.99 (3×m, 1+2+1H, NCH_2), 2.95, 2.92 (2×s, 3+9H, NCH_3), 2.28, 2.19, 2.05 (3×m, 0.5+1+0.5H, $CH_2C\mathit{H}_2CH_2$). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 59.53, 59.13 (NCH_2), 49.39 (OCH_3), 47.99, 47.72, 47.48, 47.13 (NCH_3), 17.15 ($CH_2\mathit{C}H_2CH_2$). ^{11}B NMR ($CDCl_3$, δ): -6.4 (br). IR (neat, cm^{-1}): 2473 ν(B-H); 1674 ν(C=O).

IV.B.5. A·BH(Br)COOR (7,8a-c)

The procedure is the same as described in IV.B.2.

Me_3N·BH(Br)COOEt (7a)

Concentration: 0.25 M. Reaction time/temperature: 10 min / 50°C . Drying time: 2h. Purification method: D.

Yield: 79%. ^{1}H NMR ($CDCl_3$, δ): 1.26 (t, 3H, CH_2-*CH_3*), 2.91 (s, 9H, N-CH_3), 4.11 (dq, 2H, O-CH_2). ^{11}B NMR ($CDCl_3$, δ): –5.5 (d). IR (KBr, cm^{-1}): 2477 ν(B-H), 1675 ν(C=O).

Q·BH(Br)COOEt (7b)

Concentration: 0.25 M. Reaction time/temperature: 20 min / 50°C. Drying time: 2h. Purification method: E.

Yield: 90%. ^{1}H NMR ($CDCl_3$, δ): 1.24 (t, 3H, CH_2-*CH_3*), 1.83 (m, 6H, CH_2-*CH_2*), 2.10 (sept, 1H, $(CH_2)_3$-*CH*), 3.41 (m, 6H, N-CH_2), 4.09 (dq, 2H, O-CH_2). ^{11}B NMR ($CDCl_3$, δ): –6.1 (d). IR (KBr, cm^{-1}): 2492 ν(B-H), 1676 ν(C=O).

Et_3N·BH(Br)COOEt (7c)

Concentration: 0.25 M. Reaction time/temperature: 30 min / r.t. Drying time: 2h. Purification method: E.

Yield: 96%. ^{1}H NMR ($CDCl_3$, δ): 1.25 (t, 3H, O-CH_2-*CH_3*), 1.26 (t, 9H, N-CH_2-*CH_3*), 3.32 (dq, 6H, N-CH_2), 4.10 (q, 2H, O-CH_2). ^{11}B NMR ($CDCl_3$, δ): –6.5 (d). IR (KBr, cm^{-1}): 2498 ν(B-H), 1674, 1678, 1682 ν(C=O).

$Me_3N{\cdot}BH(Br)COOPr^i$ (8a)

Concentration: 0.25 M. Reaction time/temperature: 20 min / 50°C. Drying time: 8h. Purification method: B.

Yield: 87%. ^{1}H NMR ($CDCl_3$, δ): 1.22 (dd, 6H, CH-CH_3), 2.90 (s, 9H, N-CH_3), 5.09 (sept, 1H, O-CH). ^{11}B NMR ($CDCl_3$, δ): −5.3 (d). IR (KBr, cm^{-1}): 2476 ν(B-H), 1670 ν(C=O).

$Q{\cdot}BH(Br)COOPr^i$ (8b)

Concentration: 0.20 M. Reaction time/temperature: 25 min / 50°C. Drying time: 3h. Purification method: D.

Yield: 92%. ^{1}H NMR ($CDCl_3$, δ): 1.21 (dd, 6H, CH-CH_3), 1.83 (m, 6H, CH-CH_2), 2.10 (sept, 1H, $(CH_2)_3$-*CH*), 3.41 (m, 6H, N-CH_2), 5.07 (sept, 1H, O-CH). ^{11}B NMR ($CDCl_3$, δ): −6.1 (d). IR (KBr, cm^{-1}): 2484 ν(B-H), 1672, 1680 ν(C=O).

$Et_3N{\cdot}BH(Br)COOPr^i$ (8c)

Concentration: 0.25 M. Reaction time/temperature: 10 min / 50°C. Drying time: 8h. Purification method: E.

Yield: 94%. ^{1}H NMR ($CDCl_3$, δ): 1.22 (d, 6H, CH-CH_3), 1.26 (t, 9H, CH_2-CH_3), 3.32 (q, 6H, N-CH_2), 5.08 (sept, 1H, O-CH). ^{11}B NMR ($CDCl_3$, δ): −6.4 (d). IR (KBr, cm^{-1}): 2498 ν(B-H), 1674 ν(C=O).

IV.B.6. A·BH(CN)COOH (12a,b)

Me_3N·BH(CN)COOH (12a)

13a (72 mg, 0.46 mmol) was dissolved in water (2.0 ml), pH was adjusted to ≈1 using HCl (60 μl, 3 M). The solution was kept at 60°C for 9 h and a constant N_2 stream was bubbled through the mixture at a slow rate. (The volume of the mixture was kept nearly constant by regular refill.) The mixture was deep-frost overnight and after thawing the precipitated crystals were filtered off.

Yield: 32 mg (49%) Mw. by pH-metric assay (calcd.): 138.9 (142.0). ^{1}H NMR ($CDCl_3$, δ): 2.89 (s, 9H, NCH_3). ^{11}B NMR ($CDCl_3$, δ): −13.9 (d). IR (KBr, cm^{-1}): 2419 ν(B-H), 2210 ν(C≡N), 1662 ν(C=O).

Q·BH(CN)COOH (12b)

13b (195 mg, 0.938 mmol) was dissolved in water-acetone (10:3) mixture (6.5 ml), pH was adjusted to ≈1 using HCl (160 μl, 3 M). The solution was kept at 50°C for 80 min, then acetone and methanol were removed by bubbling N_2 through the mixture. The precipitated crystals were filtered, washed with 0°C water and dried in a N_2 stream.

Yield: 105 mg (58%) Mw. by pH-metric assay (calcd.): 196.1 (194.0). ^{1}H NMR ($CDCl_3$-DMSO-d_6, δ): 1.85 (m, 6H, CCH_2), 2.12 (h, 1H, CH), 3.36 (m, 6H, NCH_2). ^{11}B NMR ($CDCl_3$, δ): −14.9 (d).

IV.B.7. A·BH(CN)COOMe (13a,b,j,l)

Me_3N·BH(CN)COOMe (13a)

6a (1.007 g, 4.798 mmol) was added to the solution of $[Bu_4N]CN$ (1.927 g, 7.177 mmol) in acetonitrile and the mixture was stirred for 25 h at room temperature. The volatile components were then evaporated *in vacuo*, without warming the flask.

The residue was suspended in ether, and the insoluble parts were filtered off. The filtrate was a biphasic system which was then separated, the lower layer was extracted with ether (10×10 ml) and the washing portions were unified with the upper layer obtained after the filtering. This solution was then evaporated and the residue was triturated with pentane until solidification. The mixture was then filtered, and the product was washed with pentane (2×3 ml) and dried in a N_2 stream. (As determined by ^{11}B and ^{1}H NMR, the product was contaminated by 4-4-4 mol% $Me_3N{\cdot}BH(Br)COOMe$, $Me_3N{\cdot}BH(NC)COOMe$ and $[Bu_4N][BH(CN)_2COOMe]$)

Yield: 520 mg (70%) ^{1}H NMR ($CDCl_3$, δ): 2.90 (s, 9H, OCH_3), 3.61 (s, 3H, OCH_3). ^{11}B NMR ($CDCl_3$, δ): −13.6 (d) ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 48.77 (OCH_3), 51.90 (NCH_3), 128.9 (br q, BCN), 185.54 (br q, B*C*OOCH$_3$) IR (KBr, cm^{-1}): 2409, 2432 ν(B-H), 2208 ν(C≡N) 1689 ν(C=O).

Q·BH(CN)COOMe (13b)

6b (2.442 g, 9.322 mmol) was added to the solution of $[Bu_4N]CN$ (1.927 g, 7.177 mmol) in acetonitrile and the mixture was stirred for 25 h at room temperature. The volatile components were then evaporated *in vacuo*, without warming the flask. The residue was triturated with ether until solidification, and ether was then evaporated. The solid residue was stirred with water (10 ml) at 0°C, the insoluble product was filtered off, washed with 0°C water (3×5 ml) and dried in a N_2 stream.

Yield: 1.353 g (70%). ^{1}H NMR ($CDCl_3$, δ): 1.84 (m, 6H, CCH_2), 2.12 (h, 1H, CH), 3.33 (m, 6H, NCH_2), 3.59 (s, 3H, OCH_3). ^{11}B NMR ($CDCl_3$, δ): −14.6 (d). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 19.58 (CH), 24.03 (C*C*H$_2$), 48.93 (OCH_3), 50.84 (NCH_2), 128.7 (br, BCN), 186.2 (B*C*OOCH$_3$). IR (KBr, cm^{-1}): 2397 ν(B-H), 2204 ν(C≡N) 1688 ν(C=O).

pic·BH(CN)COOMe (13j)

13a (217 mg, 1.39 mmol) and picoline (0.70 ml, 0.67 g, 7.2 mmol) were dissolved in acetonitrile (1.4 ml). The solution was refluxed for 16 h, then evaporated to constant weight. The product was an oil.

Yield: 100 mg (90%). ^{1}H NMR ($CDCl_3$, δ): 2.63 (m, 6H, CCH_3), 3.59 (s, 3H, OCH_3), 7.65 (dd, 2H, 3,5-CH), 8.48 (dd, 2H, 2,6-CH). ^{11}B NMR ($CDCl_3$, δ): −14.5 (d). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 21.26 (CCH_3), 48.98 (OCH_3), 126.89 (3,5-CH), 128.7 (br, BCN), 146.05 (2,6-CH), 155.92 (*ipso*), 186.6 (B*C*OOCH_3). IR (KBr, cm^{-1}): 2397 ν(B-H), 2204 ν(C≡N) 1688 ν(C=O).

pip·BH(CN)COOMe (13l)

13a (132 mg, 0.846 mmol) was dissolved in piperidine (840 μl, ≈8.5 mmol) and acetonitrile (840 μl). The solution was refluxed for 6h and then evaporated to dryness. The resinous residue was triturated with ether until solidification, the insoluble product was filtered off, washed with ether and dried in a N_2 stream.

Yield: 95 mg (68%). ^{1}H NMR ($CDCl_3$, δ): 1.47 (m, 1H, 4-CH_2 ax), 1.70 (m, 2H, 3,5-CH_2 ax), 1.90 (m, 3H, 3,5-CH_2 eq + 4-CH_2 eq), 2.86 (m, 2H, 2,6-CH_2 ax), 3.32 (m, 2H, 2,6-CH_2 eq), 3.64 (s, 3H, OCH_3), 4.39 (br, NH). ^{11}B NMR ($CDCl_3$, δ): −16.6 (d). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 22.10 (4-CH_2), 24.27, 24.32 (3,5-CH_2), 49.42 (OCH_3), 49.92, 51.31 (2,6-CH_2), 129.2 (br, BCN), 188.5 (B*C*OOCH_3). IR (KBr, cm^{-1}): 3154 ν(N-H), 2396 ν(B-H), 2212 ν(C≡N), 1654 ν(C=O).

IV.B.8. A·BH(CN)$_2$ (18a,b,d,f,h-o)

Me_3N·BH(CN)$_2$ (18a)

Trimethylamine gas (~5 g; ~85 mmol) was bubbled through a stirred suspension of 18h (10.07 g; 60.00 mmol) in acetonitrile (40 ml) over 45 min at room temperature. During this period a Me_3N atmosphere of ~1000 Hgmm was maintained over the solution. The solvent was then evaporated *in vacuo*, and the residue was suspended in ether (35 ml). The product was collected on a filter, washed with ether (4×7 ml) and dried in a N_2 stream.

Yield: 6.840 g (93%). Anal. found (calcd for $C_5H_{10}BN_3$): B, 8.90 (8.79)%. ^{1}H NMR ($CDCl_3$, δ): 2.87 (s, NMe). ^{11}B NMR ($CDCl_3$, δ): -17.2 (d, J=110). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 51.55 (NMe). IR (KBr, cm^{-1}): ν(B-H), 2455; ν(C≡N), 2217.

Q·BH(CN)$_2$ (18b)

Quinuclidine (3.54 g; 31.8 mmol) was added to a stirred suspension of 18h (5.19 g; 30.9 mmol) in acetonitrile (20 ml) at room temperature. The mixture, which turned into a clear brown solution, was evaporated to dryness *in vacuo* after 30 min, and the residue was suspended in ether (20 ml). The product was collected on a filter, washed with ether (3×7 ml) and dried in a N_2 stream.

Yield: 5.206 g (96%). Anal. found (calcd for $C_9H_{14}BN_3$): B, 6.10 (6.18)%. ^{1}H NMR ($CDCl_3$, δ): 3.24 (m, 6H, N-CH_2), 2.19 (sept, 1H, CH), 1.91 (m, 6H, CCH_2). ^{11}B NMR ($CDCl_3$, δ): -18.5 (d, J=110). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 51.68 (NCH_2), 23.81 (C*C*H_2), 19.28 (CH). IR (KBr, cm^{-1}): ν(B-H), 2433; ν(C≡N), 2214.

TMEDA·2BH(CN)$_2$ (18d)

TMEDA (0.465 g; 4.00 mmol) was added to a solution of 18h (1.508 g; 9.04 mmol) in acetonitrile (5 ml), which was stirred for 20 h at room temperature to allow a white precipitate to fall out. The mixture was then concentrated to half its volume, filtered, and the product was washed with ether (2×5 ml) and dried in a N_2 stream.

Yield: 0.876 g (80%). Anal. found (calcd for $C_{10}H_{18}B_2N_6$): B, 8.74 (8.86)%. ^{1}H NMR (DMSO-d_6, δ): 3.43 (s, 4H, NCH_2), 2.84 (s, 12H, NCH_3). ^{11}B NMR (DMSO-d_6, δ): -18.0 (br d). ^{13}C {^{1}H} NMR (DMSO-d_6, δ): 54.22 (NCH_2), 48.75 (NCH_3). IR (KBr, cm^{-1}): ν(B-H), 2464; ν(C≡N), 2217.

DABCO·2BH(CN)$_2$ (18f)

DABCO (0.747 g; 6.66 mmol) was added to a stirred suspension of 18h (2.150 g; 12.80 mmol) in acetonitrile (7 ml). After 20 h stirring at room temperature, the mixture was filtered, the product was washed with ether (3×5 ml) and dried in a N_2 stream.

Yield: 1.297 g (85%). Anal. found (calcd for $C_{10}H_{14}B_2N_6$): B, 8.99 (9.01)%. ^{1}H NMR (DMSO-d_6, δ): 3.46 (s, 12H, NCH_2). ^{11}B NMR (DMSO-d_6, δ): -18.0 (br). ^{13}C {^{1}H} NMR (DMSO-d_6, δ): 48.37 (NCH_2). IR (KBr, cm^{-1}): ν(B-H), 2453; ν(C≡N), 2222.

4-CN-py·BH(CN)$_2$ (18h)

4-CN-pyridine (44.34 g; 425.9 mmol) was added to a solution of bromine (34.1 g; 213 mmol) in acetonitrile (125 ml) at 0°C. A solution of Li[$BH_2(CN)_2$] (15.280 g; 212.8 mmol) in acetonitrile (125 ml) was then added to the orange-colored solution at 0°C, which gave rise to a precipitate in 5 min. The stirred suspension was then allowed to warm to room temperature for 1 h. The mixture was evaporated *in vacuo* to a viscous slurry, and water (30 ml) and after trituration $Na_2S_2O_3$ solution

(10 ml 0.2 M) were added. The mixture was then evaporated *in vacuo* to a resin, which was treated with water (35 ml), the mixture was filtered at 0°C, the product was washed with 0°C water (3×25 ml) and dried in a N_2 stream.

Yield: 31.55 g (88%). Anal. found (calcd for $C_8H_5BN_4$): B, 6.36 (6.44)%. ^{1}H NMR (acetone-d_6, δ): 9.19 (m, 2H, 2(6)-CH), 8.59 (m, 2H, 3(5)-CH). ^{11}B NMR (acetone-d_6, δ): -18.0 (d, J=107). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 153.94 (2(6)-CH), 136.23 (3(5)-CH), 132.94 (4-CH), 120.11 (py-CN). IR (KBr, cm^{-1}): ν(B-H), 2451; ν(C≡N), 2252 (CCN), 2218 (BCN).

py·BH(CN)$_2$ (18i)

Procedure described for 18h (above) was followed using pyridine (7.592 g; 95.98 mmol) instead of 4-cyanopyridine, bromine (7.375 g; 46.15 mmol) in acetonitrile (25 ml) and Li[$BH_2(CN)_2$] (3.185 g; 44.36 mmol) in acetonitrile (30 ml). 8 ml water was used for the first and 20 ml for the second treatment and 4×5 ml for the washing.

Yield: 5.470 g (86%). Anal. found (calcd for $C_7H_6BN_3$): B, 7.51 (7.56)%. ^{1}H NMR ($CDCl_3$, δ): 8.74 (d, 2H, 2(6)-CH), 8.37 (tt, 1H, 4-CH), 7.93 (dt, 2H, 3(5)-CH). ^{11}B NMR ($CDCl_3$, δ): -18.9 (d, J=110). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 146.66 (2(6)-CH), 143.78 (4-CH), 127.47 (3(5)-CH). IR (KBr, cm^{-1}): ν(B-H), 2482; ν(C≡N), 2216.

pic·BH(CN)$_2$ (18j)

4-Picoline (0.589 g; 0.615 ml; 6.32 mmol) was added to a solution of 18h (0.980 g; 5.83 mmol) in acetonitrile (5 ml) at room temperature. After 1 h the solvent was evaporated *in vacuo*. The residual syrup was redissolved in CH_2Cl_2, and the solvent was evaporated. After repeating the redissolution-evaporation with CH_2Cl_2 the solid residue was suspended in ether, the suspension was filtered, the product was washed with ether (2×5 ml) and dried in a N_2-stream.

Yield: 0.865 g (95%). Anal. found (calcd for $C_8H_8BN_3$): B, 6.93 (6.89)%. ^{1}H NMR ($CDCl_3$, δ): 8.55 (d, 2H, 2(6)-CH), 7.65 (d, 2H, 3(5)-CH), 2.65 (s, 3H, CH_3). ^{11}B NMR ($CDCl_3$, δ): -19.1 (d, J=108). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 157.39 (4-C), 145.96 (2(6)-CH), 127.98 (3(5)-CH), 21.93 (CH_3). IR (KBr, cm^{-1}): ν(B-H), 2460, 2450; ν(C≡N), 2216.

DMAP·BH(CN)$_2$ (18k)

DMAP (0.754 g; 6.17 mmol) was added to a solution of 18h (0.992 g; 5.91 mmol) in acetonitrile (5 ml) at room temperature. After 0.5 h the mixture was evaporated *in vacuo* and the residue was suspended in ether (5 ml). The product was collected on a filter, washed with ether (3×5 ml) and dried in a N_2 stream. Yield: 1.085 g (99%). Anal. found (calcd for $C_9H_{11}BN_4$): B, 5.83 (5.81)%. ^{1}H NMR ($CDCl_3$, δ): 7.99 (d, 2H, 2(6)-CH), 6.72 (d, 2H, 3(5)-CH), 3.22 (s, 6H, NCH_3). ^{11}B NMR ($CDCl_3$, δ): -20.3 (d, J=103). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 156.02 (4-CH), 144.91 (2(6)-CH), 107.46 (3(5)-CH), 39.82 (NCH_3). IR (KBr, cm^{-1}): ν(B-H), 2431; ν(C≡N), 2212, 2208.

piperidine·BH(CN)$_2$ (18l)

Piperidine (1.98 g; 23.3 mmol) was added to a solution of 18a (0.966 g; 7.86 mmol) in acetonitrile (2 ml). The vessel was topped with a reflux condenser and placed into a 65°C bath for 4h. The atmosphere was purged with N_2 every 20 mins. The mixture was then evaporated *in vacuo*, the residue was treated with ether (6 ml). The white crystals were collected on a filter, washed with ether (2×4 ml) and dried in a N_2 stream.

Yield: 0.986 g (84%). Anal. found (calcd for $C_7H_{12}BN_3$): B, 7.24 (7.25)%. ^{1}H NMR ($CDCl_3$, δ): 5.39 (s, 1H, NH), 3.42 (m, 2H, eq NC*H*H), 2.74 (m, 2H, ax NCH*H*), 1.89 (m, 2H, eq NCH_2CH*H*CH_2), 1.6-1.8 (m, 3H, ax NCH_2C*H*HCH_2 and eq NCH_2CH_2C*H*H), 1.43 (m, 1H, ax NCH_2CH_2CH*H*). ^{11}B NMR ($CDCl_3$, δ): -21.6 (d, J=103). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 50.99 (NCH_2), 24.13 (NCH_2*C*H_2), 22.09 (NCH_2CH_2*C*H_2). IR (KBr, cm^{-1}): ν(N-H), 3112; ν(B-H), 2444; ν(C≡N), 2221.

$Et_2NH{\cdot}BH(CN)_2$ (18m)

Procedure described for 18l (above) was applied for diethylamine (1.84 g; 25.1 mmol) and 18a (1.032 g; 8.39 mmol) in acetonitrile (2 ml) for 5 h. 6 ml ether was used for the workup and 2×4 ml for the washing.

Yield: 1.020 g (89%). Anal. found (calcd for $C_6H_{12}BN_3$): B, 8.02 (7.89)%. ^{1}H NMR ($CDCl_3$, δ): 5.48 (br s, 1H, NH), 3.06 (m, 4H, NCH_2), 1.33 (t, 6H, CH_3). ^{11}B NMR ($CDCl_3$, δ): -22.8 (d, J=105). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 46.35 (NCH_2), 10.76 (CH_3). IR (KBr, cm^{-1}): ν(N-H), 3110; ν(B-H), 2455; ν(C≡N), 2225.

morpholine·$BH(CN)_2$ (18n)

Morpholine (2.25 g; 25.8 mmol) was added to a solution of 18h (3.475 g; 20.69 mmol) in acetonitrile (20 ml). After 30 min the non-transparent dark violet mixture was evaporated *in vacuo*, the residue was treated with ether (40 ml), the insoluble parts were filtered off and extracted six times with the filtrate. The solid on the filter was washed with dichloromethane (3×6 ml) and dried in a N_2 stream.

Yield: 2.704 g (87%). Anal. found (calcd for $C_6H_{10}BN_3O$): B, 7.10 (7.16)%. ^{1}H NMR (acetone-d_6, δ): 6.6 (br s, 1H, NH), 4.06 (m, 2H, eq OC*H*H), 3.81 (m, 2H, eq NC*H*H), 3.32 (m, 2H, ax NCH*H*), 2.98 (m, 2H, ax OCH*H*). ^{11}B NMR (acetone-d_6, δ): -20.9 (d, J=108). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 65.54 (OCH_2), 50.36 (NCH_2). IR (KBr, cm^{-1}): ν(N-H), 3119; ν(B-H), 2479; ν(C≡N), 2216.

4-(*N*-piperidino)-pyridine·$BH(CN)_2$ (18o)

Piperidine (0.591 g, 6.95 mmol) was added to a solution of 18h (1.130 g, 6.73 mmol) in acetonitrile (7 ml) at room temperature. The deep violet solution was evaporated to dryness after 0.5 h. The solid residue was suspended in ether, the suspension was filtered and extracted with ether (10×25 ml) then dried in a N_2 stream. The product was a violet solid which slowly turned into brown.

Yield: 0.993 g (65%). Anal. found (calcd for $C_{12}H_{15}BN_4$): B, 4.84 (4.78)%. ^{1}H NMR ($CDCl_3$, δ): 7.99 (d, 2H, 2(6)-CH), 6.77 (d, 2H, 3(5)-CH), 3.58 (m, 4H, 2'(6')-CH_2), 1.68-1.84 (m, 6H, 3'(5')- and 4'-CH_2). ^{11}B NMR ($CDCl_3$, δ): –20.3 (d, J=105). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 155.21 (4-C), 145.61 (2(6)-CH), 107.81 (3(5)-CH), 47.64 (2'(6')-CH_2), 25.27 (3'(5')-CH_2), 23.84 (4'-CH_2). IR (KBr, cm^{-1}): ν(B-H), 2464; ν(C≡N), 2212, 2208.

IV.B.9. $[A·BH(CNEt)_2][BF_4]_2$ (19a,b,i)

$[Me_3N·BH(CNEt)_2][BF_4]_2$ (19a)

A solution of 18a (3.504 g; 28.50 mmol) in dichloromethane (10 ml) was added to a stirred solution of $[Et_3O][BF_4]$ (13.597 g; 71.57 mmol) in dichloromethane (5 ml) and the mixture was refluxed for 30 h and vigorously stirred at room temperature overnight. The volatile components of the mixture were evaporated *in vacuo* and the residual viscous oil was triturated with ether. Repeated evaporation *in vacuo* resulted in the formation of a semisolid. It was transferred to a filter, and washed with a small amount of acetonitrile (2 ml).

Yield: 4.459 g (44%). Anal. found (calcd for $C_9H_{20}B_3F_8N_3$): B, 9.30 (9.14)%. ^{1}H NMR (CH_2Cl_2, δ): 4.21 (br, 4H, Et-CH_2), 3.05 (br, 9H, NCH_3), 1.57 (br, 6H, Et-CH_3).

$[Q{\cdot}BH(CNEt)_2][BF_4]_2$ (19b)

A solution of 18b (2.295 g; 13.11 mmol) in dichloromethane (7 ml) was added to a stirred solution of $[Et_3O][BF_4]$ (6.238 g; 32.84 mmol) in dichloromethane (2 ml) and the mixture was refluxed for 12 h and vigorously stirred at room temperature overnight. The precipitate was collected on a filter, washed with dichloromethane (2×6 ml) and then with ether (4×6 ml) and dried in a N_2 stream.

Yield: 4.680 g (88%). Anal. found (calcd for $C_{13}H_{24}B_3F_8N_3$): B, 8.12 (7.97)%. ^{1}H NMR (CH_2Cl_2, δ): 4.08 (q, 4H, Et-CH_2), 3.29 (br, 6H, NCH_2), 1.99 (br, 1H, CH), 1.81 (br, 6H, CCH_2), 1.44 (t, 6H, Et-CH_3).

$[py{\cdot}BH(CNEt)_2][BF_4]_2$ (19i)

A solution of 18i (3.920 g; 27.42 mmol) in dichloromethane (26 ml) was added to a stirred solution of $[Et_3O][BF_4]$ (13.270 g; 69.85 mmol) in dichloromethane (5 ml) and the mixture was refluxed for 25 h and stirred at room temperature overnight. The lower layer of the biphasic system formed in the reaction slowly transformed into a white solid, which was collected on a filter, washed with dichloromethane (3×15 ml) and then with ether (2×20 ml) and dried in a N_2 stream.

Yield: 9.265 g (90%). Anal. found (calcd for $C_{11}H_{16}B_3F_8N_3$): B, 8.83 (8.66)%. ^{1}H NMR (CH_2Cl_2, δ): 8.71 (br, 2H, 2(6)-CH), 8.44 (br, 1H, 4-CH), 7.90 (br, 2H, 3(5)-CH), 3.95 (br, 4H, Et-CH_2), 1.39 (br, 6H, Et-CH_3).

IV.B.10. {A·BH[C(OH)=NHEt]$_2$}[BF$_4$]$_2$ (21a,b,i)

{Me$_3$N·BH[C(OH)=NHEt]$_2$}[BF$_4$]$_2$ (21a)

Procedure described for 21i was carried out using water (87 mg, 4.83 mmol) and a suspension of 19a (0.427 g, 1.20 mmol) in ether (3 ml). In order to solidify the product, the ether was removed *in vacuo*, and the residue was partially redissolved in CH_2Cl_2 (3 ml), then evaporated to dryness. The solid product was collected on a filter using ether, washed with ether (2×2 ml) and dried in a N_2 stream.

Yield: 0.433 g (92%). Anal. found (calcd for $C_9H_{24}B_3F_8N_3O_2$): B, 8.38 (8.30)%. ^{1}H NMR (acetone-d_6, δ): 9.5 (br, OH), 6.2 (br, NH), 4.36 (m, 4H, Et-CH_2), 3.26 (s, 9H, NCH_3), 1.12 (t, 6H, Et-CH_3).

{Q·BH[C(OH)=NHEt]$_2$}[BF$_4$]$_2$ (21b)

Procedure described for 21i was carried out using water (63 mg, 3.50 mmol) and a suspension of 19b (0.355 g, 0.873 mmol) in ether (3 ml).

Yield: 0.360 g (95%). Anal. found (calcd for $C_{13}H_{28}B_3F_8N_3O_2$): B, 7.41 (7.32)%. ^{1}H NMR (acetone-d_6, δ): 3.40 (m, 4H, Et-CH_2), 3.19 (m, 6H, Q-NCH_2), 1.99 (sept, 1H, CH), 1.84 (m, 6H, Q-CCH_2), 1.16 (t, 6H, Et-CH_3).

{py·BH[C(OH)=NHEt]$_2$}[BF$_4$]$_2$ (21i)

Water (65 mg, 3.6 mmol) was added to a suspension of 19i (0.336 g, 0.897 mmol) in ether (3 ml). After 10 min vigorous stirring the ether was discarded and the residual syrup was solidified by keeping under vacuum. It was then suspended in ether (10 ml), the suspension was stirred, the insoluble parts were collected on a filter, washed with ether (2×2 ml) and dried in a N_2 stream.

Yield: 0.333 g (90%). Anal. found (calcd for $C_{11}H_{20}B_3F_8N_3O_2$): B, 8.02 (7.90)%. ^{1}H NMR (acetone-d_6, δ): 11.0 (br, OH) 8.81 (m, 2H, 2(6)-CH), 8.55 (tt, 1H, 4-CH), 8.07 (m, 2H, 3(5)-CH), 6.30 (br, NH), 3.36 (m, 4H, Et-CH_2), 1.08 (t, 6H, Et-CH_3).

IV.B.11. {A·BH[C(OH)=NHEt][C(O)NHEt]}[PF_6] (22a,b,i,j)

{Me_3N·BH[C(OH)=NHEt][C(O)NHEt]}[PF_6] (22a)

Procedure described for 22i was followed using 19a (0.360 g; 1.015 mmol) in water (1.8 ml) and $NaPF_6$ solution (5.50 ml, 0.40 M) and heating to 70°C. Yield: 0.255 g (70%). Anal. found (calcd for $C_9H_{23}BF_6N_3O_2P$): B, 3.03 (2.99)%. ^{1}H NMR (acetone-d_6, δ): 9.80 and 9.11 (2 br s, OH and NH), 3.50 (m, 4H, Et-CH_2), 2.87 (s, 9H, NCH_3), 1.22 (t, 6H, Et-CH_3). ^{11}B NMR (acetone-d_6, δ): -9.9 (d, J=105). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 52.92 (NCH_3), 35.94, 35.80 (Et-CH_2), 14.05 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H), 3413, 3242; ν(B-H), 2467, 2434; ν(C=N), 1646, 1560.

{Q·BH[C(OH)=NHEt][C(O)NHEt]}[PF_6] (22b)

Procedure described for 22i was followed using 19b (0.278 g; 0.683 mmol) in water (0.9 ml) and $NaPF_6$ solution (3.75 ml, 0.40 M).

Yield: 0.180 g (64%). Anal. found (calcd for $C_{13}H_{27}BF_6N_3O_2P$): B, 2.66 (2.62)%. ^{1}H NMR (acetone-d_6, δ): 3.43 (m, 4H, Et-CH_2), 3.23 (m, 6H, Q-NCH_2), 1.87 (m, 6H, Q-CCH_2), 1.18 (t, 6H, Et-CH_3) (the CH-septet coincides with the solvent signal). ^{11}B NMR (acetone-d_6, δ): -10.6 (d, J=105). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 53.11 (Q-NCH_2), 35.67 (Et-CH_2), 24.78 (Q-CCH_2), 20.14 (Q-CH), 14.02 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H), 3411; ν(B-H), 2441; ν(C=N), 1558.

{py·BH[C(OH)=NHEt][C(O)NHEt]}[PF_6] (22i)

19i (0.320 g; 0.854 mmol) was dissolved in water (1.6 ml) and $NaPF_6$ solution (4.70 ml, 0.40 M) was added. The precipitate was redissolved by heating to gentle boiling and dilution with water (2 ml). The clear solution was allowed to cool to room temperature for 3 h while the product crystallized as colorless needles. The mixture was then cooled to 0°C, the crystals were collected on a filter, washed with 0°C water (3×1 ml) and dried with air suction.

Yield: 0.215 g (66%). Anal. found (calcd for $C_{11}H_{19}BF_6N_3O_2P$): B, 2.87 (2.84)%. ^{1}H NMR (acetone-d_6, δ): 8.86 (d, 2H, 2(6)-CH), 8.57 (tt, 1H, 4-CH), 8.46 (br s, OH and NH), 8.10 (dd, 3(5)-CH), 3.36 (m, 4H, Et-CH_2), 1.07 (t, 6H, Et-CH_3). ^{11}B NMR (acetone-d_6, δ): -11.3 (d, J=101). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 149.95 (2(6)-CH), 145.53 (4-CH), 129.19 (3(5)-CH), 35.48, 35.35 (Et-CH_2), 14.18 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H), 3414, 3245; ν(B-H), 2415; ν(C=N), 1559.

{pic·BH[C(OH)=NHEt][C(O)NHEt]}(PF_6) (22j)

18j (0.560 mg, 3.567 mmol) was added to a solution of [Et_3O][BF_4] (1.825 g, 9.606 mmol) in CH_2Cl_2 (1.6 ml), and the mixture was refluxed for 18 h and then the volatile components were removed *in vacuo*, to yield a viscous oil. It was then dissolved in water (8 ml) and $NaPF_6$ solution was added (29 ml, 0.4 M). The mixture was warmed to 60°C and cooled to r.t. three times, then it was placed in an ice-water bath for 0.5 h. The white crystalline product was filtered, washed with 0°C water (3×2 ml) and dried by air suction.

Yield: 0.970 mg (69%). Anal. found (calcd for $C_{12}H_{21}BF_6N_3O_2P$): B, 2.77 (2.74)%. ^{1}H NMR (acetone-d_6, δ): 8.65 (d, 2H, 2(6)-CH), 8.40 (br, OH+NH), 7.90 (d, 2H, 3(5)-CH), 3.36 (m, 4H, Et-CH_2), 2.65 (s, 3H, pic-CH_3), 1.07 (t, 6H, Et-CH_3). ^{11}B NMR (acetone-d_6, δ): -10.3 (d, J=96). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 158.88 (4-C), 149.04 (2(6)-CH), 129.54 (3(5)-CH), 35.44 (Et-CH_2), 21.74 (pic-CH_3), 14.20 (Et-CH_3).

IV.B.12. {A·BH[C(OMe)=NHEt]$_2$}[BF$_4$]$_2$ (23a,b,i,j)

{Me$_3$N·BH[C(OMe)=NHEt]$_2$}[BF$_4$]$_2$ (23a)

Procedure described for 23i was carried out using 19a (0.482 g; 1.36 mmol). Yield: 0.533 g (94%). Anal. found (calcd for $C_{11}H_{28}B_3F_8N_3O_2$): B, 7.73 (7.74)%. ^{1}H NMR (acetone-d_6, δ): 9.94 (br, NH), 4.57 (s, 6H, OCH_3), 3.86 (m, 4H, Et-CH_2), 3.07 (s, 9H, NCH_3), 1.33 (t, 6H, Et-CH_3). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 63.36 (OCH_3), 53.11 (NCH_3), 41.20 (Et-CH_2), 13.70 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H), 3422; ν(B-H), 2471; ν(C=N), 1618.

{Q·BH[C(OMe)=NHEt]$_2$}[BF$_4$]$_2$ (23b)

Procedure described for 23i was carried out using 19b (0.525 g; 1.291 mmol). Yield: 0.580 g (95%). Anal. found (calcd for $C_{15}H_{32}B_3F_8N_3O_2$): B, 6.80 (6.89)%. ^{1}H NMR (acetone-d_6, δ): 9.85 (br, NH), 4.51 (s, 6H, OCH_3), 3.81 (m, 4H, Et-CH_2), 3.46 (m, 6H, Q-NCH_2), 1.94 (m, 6H, Q-CCH_2), 1.31 (t, 3H, Et-CH_3), (the Q-CH septet coincides with the solvent signal). ^{11}B NMR (acetone-d_6, δ): -0.3 (s, BF_4) -10.6 (br d, cation). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 63.09 (OCH_3), 53.22 (Q-NCH_2), 41.03 (Et-CH_2), 24.59 (Q-CCH_2), 19.98 (Q-CH), 13.63 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H), 3422; ν(B-H), 2476; ν(C=N), 1617.

{py·BH[C(OMe)=NHEt]$_2$}[BF$_4$]$_2$ (23i)

19i (1.020 g; 2.723 mmol) was dissolved in methanol (3 ml). After complete dissolution (~3 min) the volatile components were evaporated *in vacuo*. The residue was suspended in ether (5 ml), the suspension was filtered, the white crystals were washed with ether (3×5 ml) and dried in a N_2 stream.

Yield: 1.104 g (92%). Anal. found (calcd for $C_{13}H_{24}B_3F_8N_3O_2$): B, 7.26 (7.39)%. ^{1}H NMR (acetone-d_6, δ): 9.85 (br s, 2H, NH), 8.96 (d, 2H, 2(6)-CH), 8.69 (tt, 1H, 4-CH), 8.21 (dd, 2H, 3(5)-CH), 4.32 (s, 6H, OMe), 3.65 (m, 4H, Et-CH_2), 1.24 (t, 6H, Et-CH_3). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 149.71 (2(6)-CH), 147.03 (4-CH), 130.37 (3(5)-CH), 62.01 (OMe), 39.70 (Et-CH_2), 12.87 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H), 3422; ν(B-H), 2474; ν(C=N), 1628.

{pic·BH[C(OMe)=NHEt]$_2$}[BF_4]$_2$ (23j)

18j (0.506 g; 3.22 mmol) was added to a solution of [Et_3O][BF_4] (1.835 g; 9.66 mmol) in dichloromethane (2.5 ml) and the mixture was refluxed for 32 h, then the volatile components were removed *in vacuo*. Methanol (10 ml) was added to the residue, and after complete dissolution the solvent was evaporated *in vacuo*. The residue, solidified by treatment with ether (10 ml), was collected on a filter, washed with ether (2×10 ml) and dried in N_2 stream.

Yield: 1.268 g (88%). Anal. found (calcd for $C_{14}H_{26}B_3F_8N_3O_2$): B, 7.12 (7.16)%. ^{1}H NMR (acetone-d_6, δ): 9.77 (br s, 2H, NH), 8.74 (d, 2H, 2(6)-CH), 7.99 (d, 2H, 3(5)-CH), 4.30 (s, 6H, OMe), 3.64 (m, 4H, Et-CH_2), 2.69 (s, 3H, 4-CH_3), 1.24 (t, 6H, Et-CH_3). ^{11}B NMR (acetone-d_6, δ): -0.3 (s, BF_4), -10.3 (br d, cation). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 160.93 (4-C), 148.58 (2(6)-CH), 130.76 (3(5)-CH), 61.93 (OMe), 39.63 (Et-CH_2), 22.03 (4-CH_3), 12.86 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H), 3336; ν(B-H), 2476; ν(C=N), 1697.

IV.B.13. {A·BH[C(NH$_2$)=NHEt]$_2$}[BF$_4$]$_2$ (24a,b,i)

{Me$_3$N·BH[C(NH$_2$)=NHEt]$_2$}[BF$_4$]$_2$ (24a)

The procedure described for 24i was carried out using 19a (1.920 g; 5.413 mmol). Yield: 1.985 g (94%). Anal. found (calcd for $C_9H_{26}B_3F_8N_5$): B, 8.42 (8.34)%. ^{1}H NMR (acetone-d_6, δ): 8.38 (br, 1H, EtNH), 8.06 (br, 2H, NH$_2$), 3.50 (m, 4H, Et-CH$_2$), 3.02 (s, 9H, NCH$_3$), 1.31 (t, 6H, Et-CH$_3$). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 52.95 (NCH$_3$), 38.29, 38.12 (Et-CH$_2$), 12.75 (Et-CH$_3$). IR (KBr, cm^{-1}): ν(N-H) 3432, 3296, 3168; ν(B-H), 2457; ν(C=N), 1683, 1599.

{Q·BH[C(NH$_2$)=NHEt]$_2$}[BF$_4$]$_2$ (24b).

The procedure described for 24i was carried out using 19b (2.285 g; 5.619 mmol). Yield: 2.365 g (96%). Anal. found (calcd for $C_{13}H_{30}B_3F_8N_5$): B, 7.27 (7.36)%. ^{1}H NMR (acetone-d_6, δ): 8.52, 8.16, 8.12 (3 br s, NH), 3.44 (dq, 4H, Et-CH$_2$), 3.40 (m, 6H, Q-NCH$_2$), 1.94 (m, 6H, Q-CCH$_2$), 1.28 (t, 6H, Et-CH$_3$) (the Q-CH septet coincides with the solvent signal). ^{11}B NMR (acetone-d_6, δ): -0.24 (s, BF$_4$), -4.3 (br d, cation). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 53.03 (Q-NCH$_2$), 38.20, 38.07 (Et-CH$_2$), 24.64 (Q-CCH$_2$), 20.09 (CH), 12.78 (Et-CH$_3$). IR (KBr, cm^{-1}): ν(N-H) 3444, 3369, 3288, 3172; ν(B-H), 2463; ν(C=N), 1683, 1595.

{py·BH[C(NH$_2$)=NHEt]$_2$}[BF$_4$]$_2$ (24i)

19i (2.280 g; 6.085 mmol) was dissolved in liquid ammonia (~3 ml) in a -78°C bath and the stirred solution was refluxed for 0.5 h. The solvent was then allowed to evaporate moderately. The solid residue was kept under vacuum for 15 min, then suspended in ether (20 ml). The suspension was filtered, the product was washed with ether and dried in a N$_2$ stream. In order to solidify the evaporation residue, much longer time under vacuum and more thorough treatment with ether was required than in cases of raw 24a or 24b.

Yield: 2.387 g (96%). Anal. found (calcd for $C_{11}H_{22}B_3F_8N_5$): B, 7.79 (7.93)%. ^{1}H NMR (acetone-d_6, δ): 8.90 (d, 2H, 2(6)-CH), 8.57 (tt, 1H, 4-CH), 8.10 (m, 2H, 3(5)-CH), 3.43 (dq, 4H, Et-CH_2), 3.25 (br, NH), 1.25 (t, 6H, Et-CH_3). ^{11}B NMR (acetone-d_6, δ): -0.26 (s, BF_4), -5.8 (br d, cation). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 149.09 (2(6)-CH), 145.80 (4-CH), 129.22 (3(5)-CH), 37.96 (NCH_2), 12.81 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H) 3344, 3245, 3163; ν(B-H), 2445; ν(C=N), 1670, 1600.

IV.B.14. {A·BH[C(NEt$_2$)=NHEt]$_2$}[PF$_6$]$_2$ (25b,i)

{Q·BH[C(NEt$_2$)=NHEt]$_2$}[PF$_6$]$_2$ (25b)

Diethylamine (3 ml) was added to 19b (0.540 g; 1.328 mmol) and when the starting white solid completely transformed into a dense orange oil (inmiscible with diethylamine) (~0.5 h), the volatile components were removed *in vacuo*. The residue was dissolved in water (6 ml) and $NaPF_6$ solution (4.8 ml 0.40 M) was added and a pale orange amorphous semisolid precipitated. The mixture was allowed to stand at 5°C overnight while the product solidified. It was collected on a filter, washed with water (4×3 ml) and dried by air suction.

Yield: 0.580 g (65%). Anal. found (calcd for $C_{21}H_{46}BF_{12}N_5P_2$): B, 1.63 (1.61)%. ^{1}H NMR (acetone-d_6, δ): 10.56 (br, NH), 4.20 (q, 4H, HNEt-CH_2), 4.13-3.91 (m, 8H, NEt-CH_2), 3.51 (m, 6H, Q-NCH_2), 2.15 (sept, 1H, Q-CH), 2.00 (m, 6H, Q-CCH_2), 1.6-1.4 (m, 18H, Et-CH_3). ^{11}B NMR (acetone-d_6, δ): -3.5 (d, J=110). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 54.08 (Q-NCH_2), 53.28, 46.67, 43.19 (Et-CH_2), 14.37, 14.05, 13.35 (Et-CH_3). IR (KBr, cm^{-1}): ν(N-H), 3417, 3299; ν(B-H), 2507; ν(C=N), 1631, 1579.

{py·BH[C(NEt$_2$)=NHEt]$_2$}[PF$_6$]$_2$ (25i)

Diethylamine (3ml) and acetonitrile (2 ml) were added to 19i (0.505g; 1.348 mmol) and the volatile components were removed *in vacuo* after 3.5 h stirring at r.t. Water (3 ml) and $NaPF_6$ solution (7 ml 0.4 M) were added and the mixture was vigorously agitated for 2 h. The solid precipitate was collected on a filter, washed with water and dried in a N_2 stream.

Yield: 0.465 g (54%). Anal. found (calcd for $C_{19}H_{38}BF_{12}N_5P_2$): B, 1.73 (1.70)%. ^{1}H NMR (acetone-d_6, δ): 9.14 (br, NH), 8.70 (m, 1H, 4-CH), 8.20 (m, 2H, 2(6)-CH), 7.56 (m, 2H, 3(5)-CH), 3.76 (q, 4H, HNEt-CH_2), 3.48-3.31 (m, 8H, NEt-CH_2), 1.35 (t, 6H, HNEt-CH_3), 1.19 (m, 12H, NEt-CH_3). ^{11}B NMR (acetone-d_6, δ): -9.0 (br d). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 146.6, 146.5 (4-C and 2(6)-CH), 129.99 (3(5)-CH), 48.87, 43.72, 41.96 (Et-CH_2), 15.11, 13.21, 11.39 (Et-CH_3).

IV.B.15. A·BH(CONHEt)$_2$ (26a,b,i-l)

Me$_3$N·BH(CONHEt)$_2$ (26a)

18a (1.050 g, 3.570 mmol) was added to the CH_2Cl_2 solution of [Et$_3$O][BF$_4$] (3.570g, 18.79 mmol in 6 ml), and after for 20 h reflux the volatile components were evaporated. The residue was dissolved in water (1.5 ml), the pH of the solution was adjusted to ≈11 by NaOH solution (1.9 ml, 9.5 M). The insoluble parts were filtered off and the filtrate was extracted with CH_2Cl_2 (1.0 ml) and the organic phase was discarded. The aqueous phase was then extracted with CH_2Cl_2 by continuous extraction. The CH_2Cl_2 phase was dried over $MgSO_4$ and evaporated.

Yield: 1.379 g (75%). ^{1}H NMR ($CDCl_3$, δ): 1.11 (t, 6H, Et-CH_3), 2.83 (s, 9H, NCH_3), 3.28 (m, 4H, Et-CH_2), 6.36 (br s, 2H, NH). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 15.11 (Et-CH_3), 32.50 (Et-CH_2), 51.64 (NCH_3). IR (KBr, cm^{-1}): ν(N-H), 3374, 3343; ν(B-H), 2374; amide I-II, 1603, 1576, 1527, 1496.

Q·BH(CONHEt)$_2$ (26b)

19b (2.435 g, 5.99 mmol) was dissolved in aqueous NaOH (15 ml, 1.0 M) and the solution (pH≈11) was extracted with CH_2Cl_2 by continuous extraction. The CH_2Cl_2 phase was dried over $MgSO_4$ and evaporated.

Yield: 1.453 g (91%). ^{1}H NMR ($CDCl_3$, δ): 1.10 (t, 6H, Et-CH_3), 1.75 (m, 6H, CCH_2), 2.00 (h, 1H, CH), 3.26 (m, 4H, Et-CH_2), 3.35 (m, 6H, NCH_2), 6.43 (br s, 2H, NH). ^{11}B NMR ($CDCl_3$, δ): –7.5 (d). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 15.11 (Et-CH_3), 20.07 (CH), 24.52 (C*C*H_2), 32.41 (Et-CH_2), 50.64 (NCH_2). IR (KBr, cm^{-1}): ν(N-H), 3340; ν(B-H), 2369; amide I-II, 1605, 1572, 1530, 1508.

py·BH(CONHEt)$_2$ (26i)

19i (845 mg, 2.26 mmol) was dissolved in aqueous NaOH (4.70 ml, 1.0 M) and the solution (pH≈11) was extracted with CH_2Cl_2 (4.0 ml) and the organic phase was discarded. The aqueous phase was then extracted with CH_2Cl_2 by continuous extraction. The CH_2Cl_2 phase was dried over $MgSO_4$ and evaporated.

Yield: 397 mg (75%). ^{1}H NMR ($CDCl_3$, δ): 1.11 (t, 6H, Et-CH_3), 3.29 (m, 4H, Et-CH_2), 6.40 (br s, 2H, NH), 7.64 (dd, 2H, 3,5-CH), 8.07 (dt, 1H, 4-CH), 8.80 (d, 2H, 2,6-CH). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 15.08 (Et-CH_3), 32.76 (Et-CH_2), 125.36 (3,5-CH), 140.92 (4-CH), 147.77 (2,6-CH). IR (KBr, cm^{-1}): ν(N-H), 3405, 3323, 3289; ν(B-H), 2408; amide II, 1582, 1526.

pic·BH(CONHEt)$_2$ (26j)

18j (337 mg, 2.14 mmol) was added to a CH_2Cl_2 solution of $[Et_3O][BF_4]$ (895 mg, 4.71 mmol in 2.2 ml) and the mixture was refluxed for 25 h. The volatile components were then evaporated, and the residue was dissolved in aqueous NaOH (7.20 ml, 1.0 M). The solution (pH≈11) was extracted with CH_2Cl_2 (5.0 ml) and the organic phase was discarded. The aqueous phase was then extracted with CH_2Cl_2 by continuous extraction. The CH_2Cl_2 phase was dried over $MgSO_4$ and evaporated.

Yield: 361 mg (68%). ^{1}H NMR ($CDCl_3$, δ): 1.11 (t, 6H, Et-CH_3), 2.52 (s, 3H, Pic-CH_3), 3.29 (m, 4H, Et-CH_2), 6.49 (br s, 2H, NH), 7.41 (dd, 2H, 3,5-CH), 8.61 (dd, 2H, 2,6-CH). ^{11}B NMR ($CDCl_3$, δ): −7.7 (br d). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 15.08 (Et-CH_3), 21.47 (Pic-CH_3), 32.76 (Et-CH_2), 126.11 (3,5-CH), 147.04 (2,6-CH), 153.86 (*ipso*-C).

DMAP·BH(CONHEt)$_2$ (26k)

DMAP (1.116 g, 9.13 mmol) was added to the acetonitrile solution of 26b (244 mg, 0.913 mmol in 10 ml), and the mixture was refluxed for 3 h. the volatile parts were then evaporated. The residue was suspended in ether (10 ml), the insoluble product was filtered, washed with ether (3×5 ml) and dried in a N_2 stream.

Yield: 211 mg (83%). ^{1}H NMR ($CDCl_3$, δ): 1.10 (t, 6H, Et-CH_3), 3.13 (s, 6H, NCH_3), 3.28 (m, 4H, Et-CH_2), 6.43 (br s, 2H, NH), 6.58 (dd, 2H, 3,5-CH), 8.14 (dd, 2H, 2,6-CH). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 15.38 (Et-CH_3), 32.71 (Et-CH_2), 39.72 (Pic-CH_3), 106.72 (3,5-CH), 146.98 (2,6-CH), 155.79 (*ipso*-C). IR (KBr, cm^{-1}): ν(N-H), 3317; ν(B-H), 2403; amide I-II, 1637, 1602, 1557, 1514.

pip·BH(CONHEt)$_2$ (26l)

26a (20.1 mg, 0.093 mmol) was dissolved in piperidine (1.0 ml) and the solution was kept at 80°C for 5h. The volatile parts were then evaporated *in vacuo*, the residue was suspended in ether (2 ml) and the suspension was filtered. The product was washed with ether (2×2 ml) and dried in a N_2 stream.

Yield: 20.9 mg (90%). ^{1}H NMR ($CDCl_3$, δ): 1.10 (t, 6H, Et-CH_3), 1.39 (m, 1H, 4-CH_2 ax), 1.60-1.85 (m, 5H, 3,5-CH_2 + 4-CH_2 eq), 2.67 (m, 2H, 2,6-CH_2 ax), 3.21-3.33 (m, 6H, Et-CH_2 + 2,6 CH_2 eq), 5.39 (br, 1H, pip-NH), 6.18 (br, 2H, EtNH). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 15.18 (Et-CH_3), 22.89 (4-CH_2), 24.97 (3,5-CH_2), 32.68 (2,6-CH_2), 50.01 (NCH_2). IR (KBr, cm^{-1}): ν(N-H), 3334, 3233; ν(B-H), 2402; amide I-II, 1604, 1511.

IV.B.16. A·BH(COOH)$_2$ (27b,k,l)

Q·BH(COOH)$_2$ (27b)

26b (893 mg, 3.34 mmol) was dissolved in aqueous HCl (13ml 1.0 M) in a flask connected to a mercury manometer and equipped with a teflon stopcock to avoid overpressure. The solution was heated in an oil bath (124-128°C) for 11 min, when the first crystals appeared in the mixture. The pressure in the flask was kept at ca. 1.5 atm over this period. After the appearance of the crystals the mixture was placed in an ice-water bath for 0.5 h. The precipitated crystals were filtered, washed with 0°C water (2×1.5 ml) and dried by air suction.

Yield: 557 mg (78%). ^{1}H NMR (DMSO-d_6, δ): 1.72 (m, 6H, CCH_2), 1.93 (h, 1H, CH), 3.27 (m, 6H, NCH_2), 10.64 (s, 2H, COOH). ^{11}B NMR (DMSO-d_6, δ): -9.9 (br). ^{13}C {^{1}H} NMR (DMSO-d_6, δ): 19.50 (CH), 23.65 (CCH_2), 49.50 (NCH_2). IR (KBr, cm^{-1}): ν_{assoc}(O-H), 2728, 2650; ν(B-H), 2446; ν(C=O), 1655, 1636.

DMAP·BH(COOH)$_2$ (27k)

DMAP (598 mg, 4.89 mmol) was added to the acetonitrile solution of 27b (103 mg, 0.483 mmol in 2 ml) and the solution was kept at 75-80°C for 2 h. The mixture was then evaporated to dryness, the residue was suspended in ether, and the suspension was filtered. The solid on the filter was thoroughly suspended in aqueous HCl (0.6 ml, 0.1 M), filtered, washed with water until the filtrate remained neutral (3×0.5 ml). The product was dried in a N_2 stream.

Yield: 86 mg (84%). ^{1}H NMR ($CDCl_3$, δ): 3.12 (s, 6H, NCH_3), 6.83 (d, 2H, 3,5-CH), 7.92 (d, 2H, 2,6-CH), 11.0 (br, 2H, COOH). IR (KBr, cm^{-1}): ν_{assoc}(O-H), 2719, 2586; ν(B-H), 2402; ν(C=O), 1644 (br).

pip·BH(COOH)$_2$ (27l)

a) 27b (40.0 mg, 0.15 mmol) was dissolved in piperidine (0.5 ml). The solution solidified in 5 min. It was then warmed to 70°C and kept at that temperature until it solidified again (25-30 min). The volatile parts were removed *in vacuo* and the residue was suspended in ether, and the suspension was filtered. The raw product was washed with 1M HCl (200 μl) and then water until the filtrate became neutral (2×200 μl). (The product is fairly well soluble in water.)

Yield: 11.6 mg (28%).

b) 26l (22 mg, 0.091 mmol) was dissolved in 1M HCl (0.7 ml, containing 0.2 ml D_2O) and the solution was kept close to boiling point for 9 min. The pH of th solution was adjusted to 11 by 5 M NaOH and it was extracted with CH_2Cl_2 (3×1 ml) to remove the starting material and piperidine (formed from decomposition). The aqueous phase was acidified to pH=1 by cc. HCl and it was extracted again with CH_2Cl_2 (5×1 ml). The organic phase was dried over $MgSO_4$ and evaporated. The residue was triturated with ether which was then evaporated.

Yield: 6 mg (24%).

^{1}H NMR (acetone-d_6, δ): 1.50 (m, 2H, 4-CH_2), 1.84 (m, 4H, 3,5-CH_2), 3.20 (m, 4H, 2,6-CH_2), 5.29 (br, 1H, pip-NH), 10.6 (br s, 2H, COOH). ^{13}C {^{1}H} NMR (acetone-d_6, δ): 23.38 (4-CH_2), 25.45 (3,5-CH_2), 50.31 (2,6-CH_2). IR (KBr, cm^{-1}): ν(N-H), 3198, ν_{assoc}(O-H), 2864, 2634; ν(B-H), 2381; ν(C=O), 1653, 1637.

IV.B.17. A·BH(COOMe)$_2$ (28b,k,l)

Q·BH(COOMe)$_2$ (28b)

Methanolic HBr solution (68 μl, 0.276 M) was added to the solution of 27b (67 mg, 0.31 mmol) in superdry methanol (2.5 ml). After 30 min stirring at r.t., A4 molecular sieves (125 mg) were added to the solution. After 3 h the molecular sieves were filtered off, and the filtrate was evaporated *in vacuo*.

Yield: 76 mg (100%). ^{1}H NMR ($CDCl_3$, δ): 1.80 (m, 6H, CCH_2), 2.05 (h, 1H, CH), 3.43 (m, 6H, NCH_2), 3.57 (s, 6H, OCH_3). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 20.01 (CH), 24.38 (C*C*H_2), 48.72 (OCH_3), 50.18 (NCH_2). IR (KBr, cm^{-1}):
ν(B-H), 2419; ν(C=O), 1680.

DMAP·BH(COOMe)$_2$ (28k)

The procedure described for 28b was applied to 27k (42 mg, 0.19 mmol) in superdry methanol (1.5 ml) using methanolic HBr (50 μl, 0.276 M) and A4 molecular sieves (22 mg).

Yield: 47 mg (100%). ^{1}H NMR ($CDCl_3$, δ): 3.15 (s, 6H, NCH_3), 3.59 (s, 6H, OCH_3), 6.61 (dd, 2H, 3,5-CH), 8.11 (dd, 2H, 2,6-CH). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 39.42 (NCH_3), 48.77 (OCH_3), 106.12 (3,5-CH), 147.00 (2,6-CH), 155.62 (*ipso*-C).

pip·BH(COOMe)$_2$ (28l)

The procedure described for 28b was applied to 27l (39 mg, 0.21 mmol) in superdry methanol (1.60 ml) using methanolic HBr (50 μl, 0.276 M) and A4 molecular sieves (60 mg).

Yield: 43 mg (96%). ^{1}H NMR ($CDCl_3$, δ): 1.40-1.55 (m, 1H, 4-CH_2 ax), 1.55-1.75 (m, 2H, 3,5-CH_2 ax), 1.86 (m, 3H, 3,5-CH_2 eq + 4-CH_2 eq), 2.93 (m, 2H, 2,6-CH_2 ax), 3.35 (m, 2,6-CH_2 eq), 3.61 (s, 6H, OCH_3). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 22.8 (4-CH_2), 25.5 (3,5-CH_2), 49.24 (OCH_3), 50.22 (2,6-CH_2). IR (KBr, cm^{-1}): ν(N-H), 3176; ν(B-H), 2434; ν(C=O), 1676, 1658.

IV.B.18. [Q·BH(CONHEt)-C(OMe)=NHEt][BF_4] (29b)

23b (31 mg, 0.066 mmol) was dissolved in 1 M HCl (0.5 ml) and the solution was kept at boiling point for 3 min. After cooling to r.t. it was extracted with CH_2Cl_2 (4×0.5 ml), the organic phase was dried over $MgSO_4$ and evaporated. The product was a pale yellow oil.

Yield: 15 mg (62%). ^{1}H NMR ($CDCl_3$, δ): 1.16 (t, 3H, amide Et-CH_3), 1.30 (t, 3H, imidate Et-CH_3), 1.87 (m, 6H, Q-CCH_2), 2.06 (h, 1H, CH), 3.0-3.5 (m, 6H, Q-NCH_2), 3.28 (m, 2H, amide Et-CH_2), 3.53 (m, 2H, imidate Et-CH_2), 4.37 (s, 3H, OCH_3), 7.05 (br, 1H, amide NH), 11.19 (br, 1H, imidate NH). ^{11}B NMR ($CDCl_3$, δ): −1.2 (s, $[BF_4]^-$), -12.4 (br d, complex). ^{13}C {^{1}H} NMR ($CDCl_3$, δ): 15.07 (amide Et-CH_3), 20.06 (imidate Et-CH_3), 20.14 (CH), 24.48 (Q-C*C*H_2), 32.35 (amide Et-CH_2), 48.34 (OCH_3), 49.90 (imidate Et-CH_2), 50.58 (Q-NCH_2).

IR (KBr, cm^{-1}): ν(N-H), 3398, 3237; ν(B-H), 2460; amide and imidate, 1637, 1576, 1535, 1487, 1465.

IV.B.19. Auxiliary reagents

$Li[BH_2(CN)_2]$

Methyl sulfide solution of $(BH_2CN)_n$ oligomer (125.0 ml 2.553 M; 319.1 mmol) was added to a stirred suspension of LiCN·0.03THF (11.60 g, 330.0 mmol) in methyl sulfide (125 ml) and the mixture was refluxed for 5 h. The insoluble parts were filtered off and extracted three times with the filtrate. The solvent was removed from the filtrate *in vacuo*. The semisolid residue was triturated with pentane (60 ml) which was then discarded, and the residue was kept under vacuum for 1 h. Upon treatment with pentane (80 ml) the residue completely solidified. It was collected on a filter, washed with pentane (2×80 ml) and dried in a N_2 stream. This product was used for the synthesis of **1a** and **1b** without further purification.

Yield: 22.82g (100%). ^{1}H NMR (D_2O, δ): 1.08 (q, $^1J_{HB}$=96). ^{11}B NMR (D_2O, δ): −42.14 (t, $^1J_{BH}$=96). ^{13}C NMR (D_2O, δ): 139.7 (q, $^1J_{CB}$=59).

The raw product can be purified through its dioxane adduct.[110] Note: The more THF the starting LiCN contains, the more tedious the removal of methyl sulfide becomes in the preparation.

$[Bu_4N][Ag(CN)_2]$

Acetonitrile solution of $[Bu_4N]I$ (3.520 g, 9.529 mmol in 12.5 ml) was added to finely ground AgCN (2.552 g, 19.06 mmol) suspended in acetonitrile (7.5 ml). After 30 min stirring at r.t. the mixture was filtered, the insoluble AgI was filtered off and washed with acetonitrile (25 ml). The filtrate was evaporated to dryness, the solid residue was suspended in ether, the suspension was filtered, washed with ether (2×5 ml) and dried in a N_2 stream.

Yield: 3.702 g (97%).

^{13}C NMR (quantitative) ($CDCl_3$, δ): 13.39 (4C, CH_3), 19.36 (4C, CH_3CH_2), 23.67 (4C, NCH_2CH_2), 58.57 (4C, NCH_2), 143.78 (2C, CN).

V. REFERENCES

1. C. Morin, *Tetrahedron*, 1994, 50, 12521.
2. B. Carboni and L. Monnier, *Tetrahedron*, 1999, 55, 1197.
3. B.F. Spielvogel, L. Wojnowich, M.K. Das, A.T. McPhail and K.D. Hargrave, *J. Am. Chem. Soc.*, 1976, 98, 5702.
4. C. Weidig, S.S. Uppal and H.C. Kelly, *Inorg. Chem.*, 1974, 13, 1763.
5. B.F. Spielvogel, J. Harchelroad F and P. Wisian-Neilson, *J. Inorg. Nucl. Chem.*, 1979, 41, 1223.
6. I.H. Hall, C.O. Starnes, B.F. Spielvogel, P. Wisian-Neilson, M.K. Das and L. Wojnowich, *J. Pharm. Sci.*, 1979, 68, 685.
7. B. Kemp, S. Kalbag and R.A. Geanangel, *Inorg. Chem.*, 1984, 23, 3063.
8. I.H. Hall, B.F. Spielvogel, A. Sood, F. Ahmed and S. Jafri, *J. Pharm. Sci.*, 1987, 76, 359.
9. I. Lázár, Ph.D. Dissertation, L. Kossuth University (Debrecen), 1988
10. B.F. Spielvogel, F.U. Ahmed and A.T. McPhail, *Inorg. Synth.*, 1989, 25, 79.
11. M. Mittakanti and K.W. Morse, *Inorg. Chem.*, 1990, 29, 554.
12. M. Mittakanti, M.R.M.D. Charandabi and K.W. Morse, *Inorg. Chem.*, 1990, 29, 3218.
13. B. Gyõri, I. Lázár and J. Emri, *J. Organomet. Chem.*, 1988, 344, 29.
14. B. Gyõri, Z. Berente and Z. Kovács, *Inorg. Chem.*, 1998, 37, 5131.
15. S.Y. Chen, B.S. Burnham, B.F. Spielvogel, A. Sood, S.D. Wyrick and I.H. Hall, *Appl. Organomet. Chem.*, 1996, 10, 279.
16. B. Gyõri, personal communication
17. B. Gyõri, Z. Berente, J. Emri and I. Lázár, *Synthesis*, 1995, 191.
18. N.E. Miller, *Inorg. Chem.*, 1991, 30, 2228.
19. D.J. Ferrie and N.E. Miller, *Synth. React. Inorg. Met.-Org. Chem.*, 1994, 24, 1139.
20. I. Lázár, J. Emri, B. Gyõri and Z. Kovács, *Polyhedron*, 1994, 13, 2599.
21. T. Imamoto and T. Hikosaka, *J. Org. Chem.*, 1994, 59, 6753.
22. B.F. Spielvogel, M.K. Das, A.T. McPhail, K.D. Onan and I.H. Hall, *J. Am. Chem. Soc.*, 1980, 102, 6343.

23. I.H. Hall, M.K. Das, J. Harchelroad F, P. Wisian-Neilson, A.T. McPhail and B.F. Spielvogel, *J. Pharm. Sci.*, 1981, 70, 339.

24. M.K. Das and P. Mukherjee, *J. Chem. Res.*, 1985, 66.

25. M.K. Das and P. Mukherjee, *J. Chem. Res.*, 1987, 368.

26. M.K. Das and P. Mukherjee, *J. Chem. Res.*, 1987, 2974.

27. C.K. Sood, A. Sood, B.F. Spielvogel, J.A. Yousef, B. Burnham and I.H. Hall, *J. Pharm. Sci.*, 1991, 80, 1133.

28. A. Sood, C.K. Sood, B.F. Spielvogel, I.H. Hall, O.T. Wong, M. Mittakanti and K. Morse, *Arch. Pharm. (Weinheim, Ger.)*, 1991, 324, 423.

29. B.S. Burnham, S.Y. Chen, A. Sood, B.F. Spielvogel and I.H. Hall, *Pharmazie*, 1995, 50, 779.

30. Z. Kovács, Ph.D. Dissertation, L. Kossuth University (Debrecen), 1991

31. M. Mittakanti and K.W. Morse, *Inorg. Chem.*, 1991, 30, 2434.

32. I.H. Hall, C.O. Starnes, A.T. McPhail, P. Wisian-Neilson, M.K. Das, J. Harchelroad F and B.F. Spielvogel, *J. Pharm. Sci.*, 1980, 69, 1025.

33. B.F. Spielvogel, F.U. Ahmed, G.L. Silvey, P. Wisian-Neilson and A.T. McPhail, *Inorg. Chem.*, 1984, 23, 4322.

34. M.K. Das, P. Mukherjee and S. Roy, *Bull. Chem. Soc. Jpn.*, 1990, 63, 3658.

35. F. Dallacker, T. Böhmel and W. Müllners, *Z. Naturforsch.*, 1985, 40, 344.

36. B.F. Spielvogel, F.U. Ahmed and A.T. McPhail, *Synthesis*, 1986, 833.

37. B. Gyõri, Z. Kovács, J. Emri and Z. Berente, *J. Organomet. Chem.*, 1994, 484, 225.

38. M. Mittakanti, D.A. Feakes and K.W. Morse, *Synthesis*, 1992, 380.

39. B.F. Spielvogel, F.U. Ahmed, K.W. Morse and A.T. McPhail, *Inorg. Chem.*, 1984, 23, 1776.

40. M.K. Das, P.K. Maiti, S. Roy, M. Mittakanti, K.W. Morse and I.H. Hall, *Arch. Pharm. (Weinheim, Ger.)*, 1992, 325, 267 and references therein.

41. M.R.M.D. Charandabi, D.A. Feakes, M.L. Ettel and K.W. Morse, *Inorg. Chem.*, 1991, 30, 2433.

42. A. Sood, C.K. Sood, B.F. Spielvogel and I.H. Hall, *Eur. J. Med. Chem.*, 1990, 25, 301.

43. M.C Miller III, S.D. Wyrick, I.H. Hall, A. Sood and B.F. Spielvogel, *J. Labelled Compd. Radiopharm.*, 1992, 31, 595.

44. I.H. Hall, E.S. Hall, M.C. Miller III, A. Sood and B.F. Spielvogel, *Amino Acids*, 1993, 4, 287.

45. M.C. Miller III, A. Sood, B.F. Spielvogel, R.P. Shrewsbury and I.H. Hall, *Met.-Based Drugs*, 1996, 3, 219.

46. M.C. Miller III, A. Sood, B.F. Spielvogel and I.H. Hall, *Anticancer Res.*, 1997, 17, 3299.

47. S. Karthikeyan, A. Sood, J. Tomasz, B.F. Spielvogel and I.H. Hall, *Amino Acids*, 1995, 8, 323.

48. K.H. Scheller, R.B. Martin, B.F. Spielvogel and A.T. McPhail, *Inorg. Chim. Acta*, 1982, 57, 227.

49. V.M. Norwood III and K.W. Morse, *Inorg. Chem.*, 1987, 26, 284.

50. I.H. Hall, B.F. Spielvogel and A.T. McPhail, *J. Pharm. Sci.*, 1984, 73, 222.

51. M.C. Miller III, A. Sood, B.F. Spielvogel and I.H. Hall, *Appl. Organomet. Chem.*, 1998, 12, 87.

52. V.M. Norwood III and K.W. Morse, *Inorg. Chem.*, 1986, 25, 3690.

53. V.M. Norwood III and K.W. Morse, *Inorg. Chem.*, 1988, 27, 302.

54. W.J. Mills, L.J. Todd and J.C. Huffman, *J. Chem. Soc., Chem. Comm.*, 1989, 900.

55. W.J. Mills, C.H. Sutton, M.W. Baize and L.J. Todd, *Inorg. Chem.*, 1991, 30, 1046.

56. A. Sood and B.F. Spielvogel, *Main Group Met. Chem.*, 1989, 12, 143.

57. C.H. Sutton, M.W. Baize, W.J. Mills and L.J. Todd, *Inorg. Chem.*, 1992, 31, 4911.

58. C.H. Sutton, M.W. Baize and L.J. Todd, *Inorg. Chem.*, 1994, 33, 4221 and references therein

59. B.F. Spielvogel, A.T. McPhail and I.H. Hall, 1982, U.S. Patent 4,312,989 (*Chem. Abstr.*, 1982, 97, 85322g)

60. A.T. McPhail, B.F. Spielvogel and I.H. Hall, 1985, U.S. Patent 4,550,186 (*Chem. Abstr.*, 1986, 104, 219142x)

61. B.F. Spielvogel, A.T. McPhail and I.H. Hall, 1986, U.S. Patent 4,587,359 (*Chem. Abstr.*, 1986, 105, 226985y)

62. B.F. Spielvogel, A.T. McPhail and I.H. Hall, 1986, Eur. Pat. 0 181 721 (*Chem. Abstr.*, 1987, 106, 18804g)

63. B.F. Spielvogel, A.T. McPhail and I.H. Hall, 1986, U.S. Patent 6,882,562 (*Chem. Abstr.*, 1987, 107, 96881q)

64. K.W. Morse, M.R.M.D. Charandabi, D.A. Feakes and M. Mittakanti, 1993, U.S. Patent 5,196,581 (*Chem. Abstr.*, 1993, 119, 117510h)

65. B.F. Spielvogel, A. Sood and I.H. Hall, 1993, WO Patent 93 05,795 (*Chem. Abstr.*, 1993, 119, 86052d)

66. B.F. Spielvogel, A. Sood and I.H. Hall, 1993, WO Patent 93 09,123 (*Chem. Abstr.*, 1993, 119, 203618f)

67. I.H. Hall, C.J. Gilbert, A.T. McPhail, K.W. Morse, K. Hassett and B.F. Spielvogel, *J. Pharm. Sci.*, 1985, 74, 755.

68. M.C. Miller III, A. Sood, B.F. Spielvogel and I.H. Hall, *Res. Commun. Pharmacol. Toxicol.*, 1996, 1, 245.

69. M.C. Miller III, A. Sood, B.F. Spielvogel, K. Bastow and I.H. Hall, *Met.-Based Drugs*, 1997, 4, 229.

70. I.H. Hall, A. Sood and B.F. Spielvogel, *Biomed. & Pharmacother.*, 1991, 45, 333.

71. I.H. Hall, J. Williams WL, J.G. Colleen, A.T. McPhail and B.F. Spielvogel, *J. Pharm. Sci.*, 1984, 73, 973.

72. I.H. Hall, B.F. Spielvogel, A. Sood, K.W. Morse, V.M. Norwood III and O.T. Wong, *Met.-Based Drugs*, 1994, 1, 329.

73. I.H. Hall, K.G. Rajendran, S.Y. Chen, O.T. Wong, A. Sood and B.F. Spielvogel, *Arch. Pharm. (Weinheim, Ger.)*, 1995, 328, 39.

74. M.E. Murphy, R.P. Shrewsbury, A. Sood, B.F. Spielvogel, A.L. Elkins and I.H. Hall, *Met.-Based Drugs*, 1995, 2, 257.

75. I.H. Hall, B.S. Burnham, S.Y. Chen, A. Sood, B.F. Spielvogel and K.W. Morse, *Met.-Based Drugs*, 1995, 2, 1.

76. I.H. Hall, K.G. Rajendran, S.Y. Chen, V.M. Norwood III, K.W. Morse, A. Sood and B.F. Spielvogel, *Appl. Organomet. Chem.*, 1994, 8, 473.

77. B.F. Spielvogel, A. Sood, B.R. Shaw and I.H. Hall, *In*: Current Topics in the Chemistry of Boron, 1994, The Royal Society of Chemistry, Cambridge, p. 193 and references therein.

78. K.G. Rajendran, A. Sood, B.F. Spielvogel, I.H. Hall, V.M. Norwood III and K.W. Morse, *Appl. Organomet. Chem.*, 1995, 9, 111.

79. K.G. Rajendran, S.Y. Chen, A. Sood, B.F. Spielvogel and I.H. Hall, *Biomed. & Pharmacother.*, 1995, 49, 131.

80. M.E. Murphy, A.L. Elkins, R.P. Shrewsbury, A. Sood, B.F. Spielvogel and I.H. Hall, *Met.-Based Drugs*, 1996, 3, 31.

81. B.F. Spielvogel, *Mol. Struct. Energ.*, 1988, 5, 329.

82. M. Takagaki, K. Ono, S. Masunaga, Y. Kinashi, T. Kobayashi, Y. Oda, H. Kikuchi and B.F. Spielvogel, *Kyoto Daigaku Genshiro Jikkensho*, 1994, 142. (*Chem. Abstr.*, 1994, 121, 296111q)

83. A.L. Elkins, J.G. Eley, M.C. Miller, I.H. Hall, A. Sood and B.F. Spielvogel, *Met.-Based Drugs*, 1996, 3, 277.

84. M.E. Hall, R.P. Shrewsbury, S.Y. Chen, A.L. Elkins, B.S. Burnham, B.F. Spielvogel and I.H. Hall, *Pharm. Sci.*, 1997, 3, 473.

85. M.C. Miller III, R.P. Shrewsbury, A.L. Elkins, A. Sood, B.F. Spielvogel and I.H. Hall, *J. Pharm. Sci.*, 1995, 84, 933.

86. I.H. Hall, E.S. Hall, L.K. Chi, M.C. Miller III, K.F. Bastow, A. Sood and B.F. Spielvogel, *Appl. Organomet. Chem.*, 1992, 6, 229.

87. I.H. Hall, D.J. Reynolds, J. Chang, B.F. Spielvogel, T.S. Griffin and E.L. Docks, *Arch. Pharm. (Weinheim, Ger.)*, 1991, 324, 573.

88. M.F. Amsell, *In*: The Chemistry of Acyl Halides, Vol., 1972, Wiley-Interscience, New York, 204

89. J. Hine: Physical Organic Chemistry, 1962, McGraw-Hill, New York, p. 311

90. G. Jugie, J.P. Laussac and J.P. Laurent, *Bull. Soc. Chim. Fr.*, 1970, 2542.

91. C. Djerassi, *Chem. Rev.*, 1948, 43, 271.

92. J. Adam, P.A. Gosselain and P. Goldfinger, *Nature*, 1953, 171, 704.

93. M.S. Ramachandran, D. Easwaramoorthy, V. Rajasingh and T.S. Vivekanandam, *Bull. Chem. Soc. Jpn.*, 1990, 63, 2397.

94. C.A. Horiuchi and J.Y. Satoh, *Chem. Lett.*, 1984, 1509.

95. J. Emri, Z. Kovács and B. Gyõri, *Inorg. Chim. Acta*, 1995, 233, 119.

96. J. Emri and B. Gyõri, *J. Chem. Soc., Chem. Comm.*, 1983, 1303.

97. W.J. Mills, C.H. Sutton, E. Libby and L.J. Todd, *Inorg. Chem.*, 1990, 29, 302.

98. E.C. Evers, W.O. Freitag, J.N. Keith, W.A. Kriner, A.G. MacDiarmid and S. Sujishi, *J. Am. Chem. Soc.*, 1959, 81, 4493.

99. E.C. Evers, W.O. Freitag, W.A. Kriner, A.G. MacDiarmid and S. Sujishi, *J. Inorg. Nucl. Chem.*, 1960, 13, 239.

100. A. Meller, W. Maringgele and U. Sicker, *J. Organomet. Chem.*, 1977, 141, 249.

101. L.E. Benjamin, D.A. Carvalho, S.F. Stafiej and E.A. Takacs, *Inorg. Chem.*, 1970, 9, 1844.

102. H.E. Zieger and W. Shiming, *J. Org. Chem.*, 1994, 59, 3838.

103. A. Kleemann, P. Schalke and D. Arnoldi, 1979, DE,

104. P. Dowd, B.K. Wilk and M. Wlostowski, *Synth. Commun.*, 1993, 23, 2323.

105. B.K. Wilk, *Synth. Commun.*, 1993, 23, 2481.

106. R.W. Stephens and L.A. Domeier, *Synth. Commun.*, 1991, 21, 2025.

107. H. Nöth and H. Beyer, *Chem. Ber.*, 1960, 93, 928.

108. B.F. Spielvogel, F.U. Ahmed, M.K. Das and A.T. McPhail, *Inorg. Chem.*, 1984, 23, 3263.

109. P. Wisian-Neilson, M.K. Das and B.F. Spielvogel, *Inorg. Chem.*, 1978, 17, 2327.

110. B. Gyõri, J. Emri and I. Fehér, *J. Organomet. Chem.*, 1983, 255, 17.

111. J.L. Vidal and G.E. Ryschkewitsch, *Inorg. Chem.*, 1977, 16, 1673.

112. B. Gyõri, Z. Berente and I. Lázár, *Polyhedron*, 1998, 17, 3175 and references therein

113. J.L. Vidal and G.E. Ryschkewitsch, *Inorg. Chem.*, 1977, 16, 1898.

114. J.K. Landquist, *J. Chem. Soc., Perkin Trans. 1*, 1976, 454.

115. J. March: Advanced Organic Chemistry (4th ed.), 1992, Wiley-Interscience, New York, p. 641.

116. R. Bernardi, T. Caronna, G. Poggi and B.M. Vittimberga, *J. Heterocyclic Chem.*, 1994, 31, 903 and references therein.

117. A.D. Munno, V. Bertini, N. Picci, F. Iemma and M. Pocci, *Heterocycles*, 1998, 48, 1203.

118. B.C. Challis and J.A. Challis, *In*: Comprehensive Organic Chemistry, Vol. 2, 1979, Pergamon Press, Oxford, p. 996.

119. M.-A. Funke and H. Mayr, *Chem. Eur. J.*, 1997, 3, 1214.

120. B.C. Challis and J.A. Challis, *In*: Comprehensive Organic Chemistry, Vol. 2, 1979, Pergamon Press, Oxford, p. 1007.

121. D.G. Neilson, *In*: The Chemistry of Amidines and Imidates, Vol., 1975, Wiley, London, p. 422.

122. V. Fedij, E.A. Lenoir III, M.J. Suto, J.R. Zeller and J. Wemple, *Tetrahedron: Asymmetry*, 1994, 5, 1131.

123. B. Gyõri, Z. Kovács, J. Emri and I. Lázár, *Inorg. Chim. Acta*, 1994, 218, 21.

124. H. Meerwein, *Org. Synth.*, 1966, 46, 113.

125. K. Rossmanith, *Monatsh. Chem.*, 1965, 96, 1690.

126. C. Ayers, *In*: Comprehensive Analytical Chemistry, Vol.1B, 1960, Elsevier, Amsterdam, p. 235.

127. B. Gyõri, J. Emri and I. Fehér, *J. Organomet. Chem.*, 1984, 262, C7.

VI. SUMMARY

The work reported in this thesis was done in the framework of a long-term project aimed at the synthesis of hitherto unknown amine-cyanocarboxyboranes (12) and amine-dicarboxyboranes (27), with regards to the peculiar chemical behaviour and especially the promising biological and pharmacological activities of amine-carboxyboranes (1), the parent compounds. The preparation of the target compounds was attempted via amine-bromocarboxyboranes and their derivatives, the first representatives of which had been synthesized earlier in our laboratory.

In experiments aimed at extending the scope of their bromination reactions, amine-carboxyboranes (1) were observed to undergo extremely fast esterification in methanol in the presence of catalytic amounts of HBr. Based on this fact, a new, fast and high yield method has been elaborated for the syntheses of the methyl, ethyl and isopropyl esters of a number of amine-carboxyboranes (2-4). The method is suitable for the estrification of amine-bromocarboxyboranes (5) also. The reaction is supposed to proceed via acyl bromide intermediates. The exceptional rate of the reaction can be brought into connection with the unusual electron distribution, which is manifested also in high pK_a values, over the carboxylic groups involved.

By introduction of *N*-bromosuccinimide (NBS), $A{\cdot}BH_2COOR \rightarrow A{\cdot}BH(Br)COOR$ (R=H,Me) transformations, earlier carried out using elementary bromine, could be accomplished with much higher yield and purity for known compounds and this reagent allowed the preparation of numerous new complexes not available by the bromine route. A number of new amine-bromo(methoxycarbonyl)boranes (6) were prepared employing the one-pot reaction of amine-carboxyboranes with NBS in methanol, which affords the target molecules directly with high yield and purity.

This reaction, together with further observations, make one conclude that during the bromination an attack on the carbonyl group precedes the formation of the boron-bromine bond.

Reactions between amine-carboxyboranes and iodinating agents (I_2, $[C_5H_5N{:}I]Cl$ etc.) gave indirect evidence to the formation of B—I bond, but, due to their very short lifetime, our efforts to isolate the iodinated derivatives remained unsuccessful.

Bromide was expelled by cyanide from two amine-bromo(methoxycarbonyl)boranes (6a,b) in acetonitrile, using tetrabutylammonium cyanide as cyanide source, affording the corresponding amine-cyano(methoxycarbonyl)boranes (13a,b). The corresponding cyanocarboxyborane (12a,b) complexes have been obtained by acidic hydrolysis of the ester group and their approximate acidity constants were found around 5.8. Picoline- and piperidine-cyano(methoxycarbonyl)borane (13j,l) was prepared from trimethylamine-cyano(methoxycarbonyl)borane (13a) in amine exchange reaction.

Isocyano group was formed on the boron in reaction between amine-bromo(methoxycarbonyl)boranes (5) and tetrabutylammonium dicyanoargentate in acetonitrile.

The configuration of the chiral boron atom in each prepared asymmetric complexes were found stable on the NMR time scale.

Numerous amine-dicyanoboranes (13) have been prepared by base exchange reactions from 4-cyanopyridine-dicyanoborane (13h). In analogous experiments with secondary amines 4-cyanopyridine-dicyanoborane underwent aminodecyanation also, probably via SNAr mechanism, which demonstrates the strong electron-withdrawing effect of $>N{\cdot}BHX_2$ moiety towards the substituents on the nitrogen.

Amine-dicyanoboranes (13) have been transformed into [amine-bis(*C*-hydroxy-*N*-ethylimidate)hydroboron(2+)] (21), [amine-bis(*C*-methoxy-*N*-ethylimidate)-

hydroboron(2+)] (23), [amine-bis(amidinium)hydroboron(2+)] (24) and [amine-bis(triethylamidinium)hydroboron(2+)] (25) cations via [amine-bis(ethylnitrilium)hydroboron(2+)] tetrafluoroborates (19) by nucleophilic addition of water, methanol, ammonia and diethylamine, respectively. Amine-bis(*N*-ethylcarbamoyl)boranes (26) were obtained by deprotonation of [amine-bis(*C*-hydroxy-*N*-ethylimidate)hydroboron(2+)] cations (21), and futher representatives of 26 were obtained in amine exchange reactions. pK_a value corresponding to the protonation of the *N*-ethylamide group was found extremely high, which demonstrates the strong electron-donating effect of >N·BHX_2 moiety towards the substituents on the boron.

Under vigorous conditions two amine-bis(*N*-ethylcarbamoyl)boranes (26b,l) were hydrolyzed into amine-dicarboxyboranes (27b,l). Another amine-dicarboxyborane (27k) was prepared in amine exchange reaction. Carboxyl groups of these molecules were found more acidic than those of amine-carboxyboranes (1). Amine-dicarboxyboranes (27) were esterified using the method developed earlier for the preparation of amine-(methoxycarbonyl)boranes, and they could be recovered readily from their esters.

During seeking milder conditions for the synthesis of amine-carboxyboranes an unusual hydrolytic pattern was observed for *C*-methoxy-*N*-ethylimidate groups adjacent to boron.

VII. ÖSSZEFOGLALÁS

Az amin—karboxi-boránok (amin·BH_2COOH) elsõ képviselõi a 70-es évek második fele óta ismeretesek. A $[\equiv C\text{-}N\equiv]^+$ és [≡B-N≡] egységek közötti izoelektronos viszony alapján ezeket a molekulákat - pusztán elméleti alapon - a területen dolgozó kutatók széles köre a protonált α-aminosavak analógjainak tekintette. Ennek alapján az amin—karboxi-boránokat és származékaikat, mint biomolekulákkal rokon szerkezetû anyagokat, kiterjedt biológiai és farmakológiai hatásvizsgálatoknak vetették alá. Ezen kutatások számos nagyon ígéretes hatást hoztak napvilágra és a mai napig is komoly erõfeszítésekkel próbálják felderíteni a hatásmechanizmusukat. Ugyanakkor az eredményes biológiai hatásvizsgálatok nyomán megélénkültek az amin—karboxi-boránok különféle származékainak elõállítását célzó kutatások is. Mindazonáltal az eddig leírt vegyületek jobbára a karboxi-boránnak és annak karbonilcsoporton szubsztituált származékainak az aminok széles skálájával alkotott komplexei (A·$BH_2C(O)X$), és csak kevés bóron szubsztituált (A·BH(X)COOH) vegyület ismeretes.

A bórkémiai kutatásoknak ez az ága felkeltette a Kossuth Lajos Tudományegyetem Szervetlen és Analitikai Kémiai Tanszékén dolgozó bórkémiai kutatócsoport érdeklõdését is. Õk azonban az általánosan elterjedt szemlélettel szemben helyesebbnek gondolták az amin—karboxi-boránokat a karbonsavak analógjainak tekinteni. Ez a párhuzam a bórkémiában korábban ugyancsak elterjedt B—N ↔ C—C izoelektronos viszonyon alapult (lásd még bórazin ↔ benzol, hexagonális bór-nitrid ↔ grafit, köbös bór-nitrid ↔ gyémánt), és mind elméleti (az izoelektronosnak tekintett vegyületek töltése ilyenformán azonos), mind pedig tapasztalati oldalról (pK-értékek, komplexképzési sajátosságok és néhany röntgenszerkezet alapján) megalapozottabbnak tûnt. Mindezek alapján a

kutatócsoport a 80-as évek végétõl kísérletezni kezdett az amin—karboxi-boránok bóron szubsztituált származékainak, mint új típusú vegyületeknek az elõállításával. A munka hosszú távú célja egyrészt az volt, hogy az újonnan elõállított vegyületek kémiai tulajdonságait összehasonlítsák az analógnak tekintett karbonsavak, illetve α-szubsztituált karbonsavak megfelelõ származékaiéval, másrészt lehetõvé váljon az amin—karboxi-boránok ígéretes biológiai aktivitásával kapcsolatos szerkezet-hatás összefüggés-vizsgálatok kiterjesztése az addig ismert savszármazékokon túl a bóron szubsztituált származékokra is.

Ebbe a munkába kapcsolódtam be 1993-ban egyetemi hallgatóként. Célom az volt, hogy amin—karboxi-boránokból a laboratóriumban már kidolgozott brómozási eljárások alkalmazásával (esetleg továbbfejlesztésével) nyert amin—bromo-karboxi-boránokon vagy származékaikon (A·BH(Br)COOR) keresztül elõállítsam az eleddig ismeretlen amin—ciano-karboxi-boránok és karbonsavszármazékaik (A·BH(CN)COOR) több, lehetõleg különféle típusú aminokat tartalmazó képviselõjét, majd ezekbõl az - ugyancsak új típust képviselõ - megfelelõ amin—dikarboxi-boránokat és származékaikat ($A \cdot BH(COOR)_2$). A munka folyamán - ahogy ez ismeretlen területen gyakran elõfordul - némileg módosítani kényszerültünk ezt a stratégiát, és így végül az amin—dikarboxi-boránok elsõ képviselõit az elsõként ugyancsak ebben a laboratóriumban elõállított amin—diciano-boránokból kiindulva sikerült elõállítani. A munka célja természetesen nem elsõsorban az ismert bórvegyületek számának szaporítása volt, hanem lehetõségeinkhez mérten igyekeztünk feltárni ezeknek a szerves és szervetlen vegyületnek egyaránt tekinthetõ molekuláknak gyakran váratlan viselkedése mögött meghúzódó szabályszerûségeket is.

A kutatócsoportban korábban már dolgoztak ki eljárást az amin—karboxi-boránok (1) és metilésztereik (2) brómozására és elõállították az amin—bromo-karboxi-

boránok (5) és metilésztereik (6) elsõ képviselõit. Ezen reakciók akalmazhatósági körének kiterjesztésére irányuló vizsgálataink során észrevettük, hogy az amin—karboxi-boránok szokatlanul gyors reakcióban észterezõdnek metanolban katalitikus mennyiségû HBr jelenlétében már szobahõmérsékleten is. Erre a felismerésre alapozva új, az addig ismert eljárásokhoz képest gyors és jó hozamú módszert dolgoztunk ki különféle amin—karboxi-boránok metil-, etil- és izopropil-észtereinek (2-4a-e,i) elõállítására. Tekintettel arra, hogy a HCl katalitikus hatása nagyságrendileg kisebb, továbbá a laboratóriumban korábban vizsgált reakciók tapasztalataira is támaszkodva valószínûsíthetõ, hogy a reakció savbromid köztiterméken keresztül megy végbe. Amin—bromo-karboxi-boránok észteresítése (5 → 6-8a-c) esetében magasabb hõmérséklet és/vagy nagyobb mennyiségû katalizátor alkalmazására volt szükség, és a reakciót a komplex némi bomlása is kísérte. Amin—dikarboxi-boránok (27) észteresítésekor a reakció lassabb, mint amin—karboxi-boránok esetén, míg amin—ciano-karboxi-boránokat (12) ezzel a módszerrel nem sikerült észteresíteni. Ezek alapján valószínû, hogy a HBr-dal katalizált észteresítés az amin—karboxi-boránok esetén tapasztalt, az alifás karbonsavakéhoz képest is feltûnõen készséges lejátszódása a bórhoz kapcsolódó karboxilcsoport különösen nagy elektronsûrûségének (mely a szokatlanul magas pK-értékekben is megnyilvánul) a következménye.

Az amin—karboxi-boránok és észtereik (1,2)brómozására korábban használt elemi bróm helyett *N*-bróm-szukcinimidet (NBS) alkalmazva a már ismert vegyületeket jobb kitermeléssel és tisztábban sikerült elõállítani, valamint lehetõség nyílt további, bróm alkalmazásával a B—N kötés hasadása miatt csak rossz kitermeléssel, vagy egyáltalán nem elõállítható vegyületek preparálására is. Mindazonáltal a karboxi-borán sp^2 hibridizációjú nitrogént tartalmazó aminokkal képzett komplexeinek brómozása brómmal és NBS-del is a B—N kötés hasadását eredményezte. Kísérleti tapasztalataink azonban arra utalnak, hogy a

py·BH(Br)COOR típusú vegyületek valószínûleg léteznek, de nagyon rövid élettartamúak. Egy "kísérleti hiba" kapcsán észrevettük, hogy az amin—karboxi-boránok (1) reakciója NBS-del alkoholok jelenlétében a bóron lejátszódó brómozás mellett a karboxilcsoport észteresedéséhez is vezetett. Ez alapján egyszerû, jó kitermelést biztosító módszert dolgoztunk ki amin—bromo-(metoxi-karbonil)-boránok (6) elõállítására amin—karboxi-boránokból (1) egy lépésben. A reakció lefolyásának részletesebb vizsgálata és más brómozási reakciókban szerzett tapasztalataink alapján valószínûnek tûnik, hogy a bór-bróm kötés kialakulását (mind bróm, mind NBS alkalmazásakor) az amin—karboxi-boránok esetében megelõzi egy a karbonilcsoporton bekövetkezõ, még tisztázatlan átalakulás.

Tekintettel arra, hogy a brómatomot több különbözõ kísérletben nem sikerült cianocsoportra cserélni a bóron, megkíséreltük elõállítani az amin—karboxi-boránok és észtereik bóron jóddal szubsztituált származékait arra számítva, hogy a jód a brómnál jobb távozó tulajdonságú lesz. A kipróbált jódozószerek (I_2, $[C_5H_5N{:}I]Cl$ stb.) alkalmazásával azonban mindannyiszor a B—N kötés felhasadását tapasztaltuk. Az a tény, hogy (elsõsorban sp^2 hibrid N-atomot tartalmazó) aminok jelenlétében a jódozási reakciók (a hasonlóan végrehajtott brómozási reakciókkal analóg módon) [bisz(amin)-hidro-karboxi-bór](1+) kationok (10) képzõdéséhez vezettek, közvetve arra utal, hogy a bór-jód kötés átmenetileg létrejön, a kialakuló amin—jodo-karboxi-borán azonban rövid élettartamú, elkülönítésére irányuló kísérleteink ezért vallottak kudarcot.

Számos egyéb, a brómnak más csoportra történõ kicserélését célzó kísérlet végzõdött a kiindulási komplex elbomlásával. A laboratóriumban folyó más irányú kísérletek alapján levonható volt a következtetés, hogy a brómot már viszonylag kis egyensúlyi mennyiségben jelenlévõ nukleofilok (pl. OH^-, MeO^-) is kicserélik, a

létrejövõ, oxigéndonorral szubsztituált boránok aminkomplexei viszont nem stabilak, így az említett nukleofilok jelenlétében a kiindulási komplexek B—N kötései felhasadnak és a komplexek irreverzibilisen elbomlanak. Ezek alapján célszerûnek látszott a kívánt bromid→cianid szubsztitúciós reakció poláros aprotikus oldószerben történõ végrehajtása. Így végül acetonitrilben, cianidforrásként [tetrabutil-ammónium]-cianidot alkalmazva sikerült átalakítani két amin—bromo-(metoxi-karbonil)-boránt (6a,b) a megfelelõ amin—ciano-(metoxi-karbonil)-boránná (13a,b), amelyek új típust képviselnek. A reakciónak nem végterméke volt az amin—ciano-(metoxi-karbonil)-borán (13), ugyanis nagyobb cianidfölösleg mellett, vagy magasabb hõmérsékleten az amin cseréje is jelentõs mértékben végbement [diciano-hidro-karboxi-borát](1−) anion (14) képzõdése közben. A trimetil-amin—ciano-(metoxi-karbonil)-borán (13a) birtokában - az amin—ciano-boránokhoz, amin—karboxi-boránokhoz vagy savszármazékaikhoz hasonlóan - amincsere reakcióval minden bizonnyal igen nagy számú további amin—ciano-(metoxi-karbonil)-borán állítható majd elõ, példaként szintetizáltuk a piperidin— és a pikolin—ciano-(metoxi-karbonil)-boránt (13j,l). Az amin—ciano-(metoxi-karbonil)-boránokról az észtercsoportot savas közegben hidrolizáltuk. Az így kapott amin—ciano-karboxi-boránok (12) pK-értékei (5,8-5,9) - a cianocsoport elektronszívó hatásának következtében - már viszonylag közel esnek az egyszerû alifás karbonsavak pK-értékeihez, vagyis az ≡N-B≡ szerkezeti egységnek a bóron lévõ szubsztituensek felé mutatott elektronküldõ hatását egy a bórra elhelyezett cianocsoport képes jelentõs mértékben ellensúlyozni.

A reakció végterméke, a [diciano-hidro-(metoxi-karbonil)-borát](1−) anion (14) alkalmas kiindulási anyag lehet amin—diciano-(metoxi-karbonil)-boránok ($A{\cdot}B(CN)_2COOMe$) elõállítására.

A bromid→cianid cseréhez hasonló körülmények között, reagensként [tetrabutil-ammónium][diciano-argentát]-ot alkalmazva a bórhoz izocianocsoportot sikerült kapcsolni, és az így létrejövõ, új típust képviselõ amin—izociano-(metoxi-karbonil)-boránok (17) további, a bóron más (pl. tioformamido-, tetrazolil- stb.) csoportokkal szubsztituált amin—karboxi-boránok prekurzorai is lehetnek. A bromid→izocianid cserét kisebb részben az amin kiszorítása, nagyob részben az izocianocsoport cianocsoporttá történõ izomerizációja kísérte, mely utóbbi a hõmérséklet emelésével egyre nagyobb teret nyer. Elõkísérleteink alapján megalapozottnak látszik az a várakozás, hogy a trimetil-amin—izociano-(metoxi-karbonil)-boránból (17a), melynek tiszta formában történõ elõállítása még nem megoldott, nagy számban lesznek elõállíthatók további amin—izociano-(metoxi-karbonil)-boránok (17), és a megfelelõ karboxi-borán komplexek is.

Az amin—ciano-karboxi-boránok elõállításában mutatkozó nehézségek miatt az amin—dikarboxi-boránok (27) elõállítását az eredeti elképzeléseket megváltoztatva végül amin—diciano-boránokból (18) kiindulva valósítottuk meg. A laboratóriumban a 4-ciano-piridin—diciano-borán (18h) elõállítására korábban kifejlesztett eljárás egyszerûsítésével és hozamának lényeges növelésével lehetõség nyílt ebbõl az anyagból - mint a diciano-borán meglehetõsen gyenge komplexébõl - kiindulva nagy számú amin—diciano-borán (18a,b,d,f,j-o) elõállítása aminkicserélõdési reakcióval. A 4-ciano-piridin—diciano-borán és szekunder aminok hasonló körülmények között lejátszatott reakcióiban az amincsere mellett a piridingyûrû 4-es helyzetû szénatomján a szekunder amin minõségétõl függõ mértékben (10-90%-ban) 4-dialkilamino-piridin—diciano-boránokat (18o-q) eredményezõ aminodecianálódás is lejátszódott. Ez a meglehetõsen ritka típusú reakció az elméletileg lehetséges reakcióutak közül legvalószínûbben SNAr mechanizmus szerint játszódik le, és vélhetõleg az $>N\cdot BH(CN)_2$ molekularésznek a

nitrogénen lévõ szubsztituensekre gyakorolt erõs elektronszívó hatása teszi lehetõvé, hogy a szekunder aminok, mint erõs nukleofilok ne csak a bóron, hanem az aromás gyûrûn is támadhassanak.

A bórhoz kapcsolódó cianocsoportok karboxilcsoporttá alakítása - az alifás nitrilekétõl lényegesen eltérõ elektronellátottságuk miatt - erõs aktiválást igényel. Erre többféle eljárás közül a [trietil-oxónium][tetrafluoro-borátos] etilezés terjedt el leginkább. Az amin—diciano-boránok $[Et_3O][BF_4]$-tal két, egymástól rosszul elváló lépésben reagáltak [amin—bisz(etil-nitrílium)-hidro-bór](2+) kationok (19a,b,i,j) képzõdése mellett. A két egymást követõ etilezési reakció sebességei közötti kis különbség miatt az egyszeresen etilezett [amin—ciano-(etil-nitrílium)-hidro-bór](1+) kationok (20) elkülönítését - és hidrolízisükkel az amin—ciano-karboxi-boránok (12) elõállítását - nem sikerült megoldani.

Az [amin—bisz(etil-nitrílium)-hidro-bór](2+) kationok (19) aktivált C≡N kötéseire rendkívül könnyen addícionálódtak egyszerû nukleofilok, nevezetesen a víz, metanol, ammónia és dietil-amin, így gyors reakciókban, gyakran közel kvantitatív kitermeléssel képzõdtek a megfelelõ (rendre [amin—bisz(*C*-hidroxi-*N*-etil-imidát)-hidro-bór](2+) (21), [amin—bisz(*C*-metoxi-*N*-etil-imidát)-hidro-bór](2+) (23), [amin—bisz(*N*-etil-amidínium)-hidro-bór](2+) (24) és [amin—bisz(trietil-amidínium)-hidro-bór](2+)) (25) kationok tetrafluoroborátjai. A vízaddíció terméke vízben kétértékû, egybázisúként erõs savként viselkedik, ennek megfelelõen vízbõl még meglehetõsen savas közegben is csak egyszeresen pozítív töltésû kation (22) formájában preparálható. A második proton eltávolítását jellemzõ pK-értékek az amintól függõen 3,1-3,3 közé esnek, ami egyúttal azt is jelenti, hogy az amin—bisz(*N*-etil-karbamoil)-boránok (26) az egyik amidcsoportjukon rendkívül könnyen protonálódnak, ami szintén az ≡N-B≡

molekulaegységnek a bóron lévõ szubsztituensek felé irányuló erõs elektronküldõ hatásának következménye.

Az amin—(*N*-etil-karbamoil)-boránokban (39) az amidcsoport hidrolízise savas közegben viszonylag jó kitermeléssel amin—karboxi-boránok (1) képzõdéséhez vezet, már szobahõmérsékleten is. Az amin—bisz(*N*-etil-karbamoil)-boránok (26) amidcsoportjait azonban csak erõsebben savas közegben és magasabb hõmérsékleten tudtuk karboxilcsoporttá hidrolizálni, minden bizonnyal azért, mert a sztérikus gátlás - amely az amidcsoport hidrolízisének sebességét nagyban meghatározó tényezõ - ebben az esetben sokkal kifejezettebb, mint a monoamidok esetén. A hidrolízishez szükséges erélyes körülmények között a kevésbé stabilis komplexek B—N kötései irreverzibilisen felbomlottak, így hidrolitikus úton csupán két, kifejezetten erõs bázist tartalmazó amin—dikarboxi-boránt (27b,l) tudtunk elõállítani; ezek a vegyületek új típust képviselnek. A B—N kötés erõssége azonban tapasztalataink alapján nem az egyetlen tényezõ, amely behatárolja ennek a szintézisútnak az alkalmazhatóságát. A 4-dimetil-amino-piridin—bisz(*N*-etil-karbamoil)-boránt (26k) sem sikerült a megfelelõ dikarboxi-borán komplexszé átalakítani, noha ebben a komplexben a B—N kötés igen erõs. Más irányú kísérletekben szerzett tapasztalataink és irodalmi példák alapján az látszik valószínûnek, hogy az N—B egység elektronküldõ effektusa miatt a bóron lévõ hidrogén hidrides jellege kifejezettebb mint a többi hasonló komplex esetén, és így a hidrolízisnél alkalmazott erõsen savas közegben a proton képes redoxifolyamatban eltávolítani ezt a hidrogént. Ugyanakkor a 4-dimetil-amino-piridin—dikarboxi-boránt (27k) - éppen azért, mert a benne lévõ B—N kötés nagyon erõs - aminkicserélõdési reakcióval sikerült elõállítani kinuklidin—dikarboxi-boránból. Ezzel a módszerrel azonban nem szaporítható

jelentõsen az ismert amin—dikarboxi-boránok száma, mert a kinuklidinkomplex meglehetõsen stabilis és a kinuklidin nem eléggé illékony.

Az elõállított amin—dikarboxi-boránokat (27b,k,l) az amin—karboxi-boránokra kidolgozott módszerrel - igaz, hosszabb idõ alatt - sikerült metanolban katalitikus mennyiségû HBr jelenlétében észteresíteni. Mivel a bisz-észterekbõl (28b,k,l) a dikarbonsavakat - egy komplex (28k) kivételével - savas hidrolízissel könnyen sikerült visszanyerni, az észtercsoport valószínûleg az amin—dikarboxi-boránok esetén is jól használható lesz védõcsoportként.

Tekintettel arra, hogy az amidcsoport hidrolízisével csak meglehetõsen erélyes körülmények között, több tényezõ által behatárolva az amin—dikarboxi-boránoknak csupán két képviselõjét sikerült elõállítani, szerettünk volna kíméletesebb körülmények között is megvalósítható reakció utat találni olyan amin—dikarboxi-boránok elõállítására, amelyekbõl amincsere-reakcióval nagyszámú további amin—dikarboxi-borán preparálható. A szerves kémiai irodalom alapján ígéretesnek tûnt a már rendelkezésünkre álló [amin—bisz(*C*-metoxi-*N*-etil-imidát)-hidro-bór](2+) kationok (23) hidrolízise, amely várakozásaink szerint savas közegben a megfelelõ amin—bisz(metoxi-karbonil)-boránokhoz vezetett volna (28), és arra számítottunk, hogy a már ismert amin—bisz(metoxi-karbonil)-boránokhoz hasonlóan ezekbõl is könnyen kaphatnánk amin—dikarboxi-boránokat (27). A különbözõ pH-értékek mellett végrehajtott hidrolitikus kísérletek azonban azt mutatták, hogy a vizsgált csoportok hidrolízise savas, semleges és lúgos közegben egyáltalán nem, vagy csak igen alárendelt - a kémhatástól függõen más és más - mértékben vezet a kívánt termékhez (28), a reakciók jobbára az amin—bisz(*N*-etil-karbamoil)-boránok (26) illetve az amin—(metoxi-karbonil)-(*N*-etil-karbamoil)-boránok (33) képzõdése felé haladnak.