Heteroaromatic Boron Compounds

VII. Synthesis and Aromaticity of 3,2-Borazaropyridines

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Derivatives of a new unusually stable monocyclic aromatic system,
3,2-borazaropyridine (IV), isoelectronic with pyridine, have been
synthesized by Raney-nickel desulphurization of various types of
borazarothienopyridines (V — VII). The 3,2-borazaropyridines are
very resistant towards hydrolytic ring-opening. The dipole moments,
pK_a-values, UV spectra and NMR spectra of 2,3-dimethyl-4-ethyl-3,2-
borazaropyridine (IVg) and 2,3-dimethyl-5-ethyl-3,2-borazaropyridine
(IVf) have been measured and compared with those of 2,3,4-tri-
methylpyridine (VIII) and 2,3,5-trimethylpyridine (IX). These
physical data confirm the aromatic nature of IV. VIII and IX could
be brominated with N,N-dibromoisocyanuric acid and nitrated with
potassium nitrate, when fuming sulphuric acid or fluorosulphonic
acid was used as a solvent. VIII reacted in the 5-position, while IX
was substituted in the 6-position. IVf and IVg *did not* undergo
electrophilic substitution under these conditions and were recovered
unchanged, except for the partial oxidation of the B — CH₃ group to
the B — OH group during attempted nitration. These results indicate
that 3,2-borazaropyridinium ions are even more deactivated towards
electrophilic substitution than the isoelectronic pyridinium ions. On
the other hand, IVa, IVb, IVf and IVg were nitrated in the 6-posi-
tion when fuming nitric acid in acetic anhydride-acetic acid was
used, while VIII and IX did not react. There is, however, evidence
that this reaction is not a simple electrophilic substitution.

Recently, Dewar and co-workers[1] obtained borazarene derivatives in low
yield starting from the difficultly available 14,16,18-tribora-13,15,17-
triazarotriphenylene (I). Hydrolysis of I gave bis-2-borazaryl ether (II), while
reaction with lithium alkyls gave B-alkyl derivatives of borazarene. Reduc-
tion of II with lithium aluminium hydride apparently led to borazarene (III).
However, Dewar *et al.*[1] found that borazarene itself, as well as its B — O- and
B-alkyl derivatives were very reactive and chemically unstable systems,
prone to polymerization and other reactions, in marked contrast to its poly-
cyclic analogues.[2-4] In many cases, the borazarenes could not be isolated in a
pure state, but were identified by their mass spectra and their UV and IR

spectra. There appears not to be any obvious theoretical reason for the instabil-
ity of borazarene, as it is isoelectronic with benzene itself. The results were also
surprising in view of the fact that Namtvedt and Gronowitz [5] found that a
derivative of 3,2-borazaropyridine (IVa), isoelectronic with pyridine, was
apparently very stable and definitely exhibited aromatic properties. In the
present paper, additional evidence for the great stability and the aromatic
properties of the 3,2-borazaropyridine system will be presented.

All 3,2-borazaropyridines were prepared through Raney-Nickel desulphuri-
zation of the three types of borazarothienopyridines (V − VII).[6,7] We have
studied the effect on the yield of different commercial Ra − Ni catalysts,
such as [LS-S-32], [LS-S-34], and [LS-S-35], as well as different solvents such
as dilute sodium hydroxide solution, conc. ammonia, methanol and ethanol.
We found that [LS-S-35] in methanol gave the best result. This catalyst has a
good desulphurization activity combined with a low hydrogenative effect.
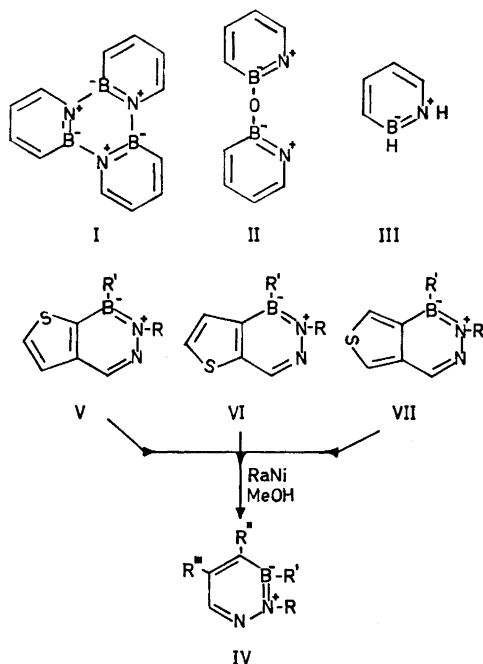
	R	R′	R″	R‴	Yield of IV
a	CH_3	OH	C_2H_5	H	49 %
b	CH_3	OH	H	C_2H_5	43 %
c	CH_3	OH	CH_3	CH_3	41 %
d	H	OH	H	C_2H_5	27 %
e	H	OH	C_2H_5	H	34 %
f	CH_3	CH_3	C_2H_5	H	44 %
g	CH_3	CH_3	H	C_2H_5	49 %

Scheme 1.

Other catalyst qualities caused over-reduction of the borazaropyridine systems. We found it most convenient to desulphurize $B-CH_3$ instead of $B-OH$ derivatives, since in the former case the progress of desulphurization could be followed by VPC. The yields varied between 27 and 49 %, and were in most cases greater than 40 %. The 3,2-borazaropyridines prepared and the yields obtained are given in Scheme 1. The $B-OH$ compounds were crystalline compounds, stable in air. The $B-CH_3$ compounds were liquids at room temperature, and could be distilled at normal pressure without decomposition. They were not completely stable in air, due to oxidation at the $B-CH_3$ bond. The purification of the $B-OH$ compounds caused some trouble due to the simultaneous formation of ethers, which could easily be observed in the NMR spectrum. This was especially observed for the nitro derivatives described below.

We also experienced some difficulties in obtaining good elementary analyses for some of the borazaropyridines. Different analytical laboratories obtained different non-reproducible results. This was also true for compounds, for which VPC data indicated that pure samples definitely had been obtained. The structures of the borazaropyridines were evident from the spectral data discussed below.

The 3,2-borazaropyridines are easily available compounds. Thus, Va—e and VIa—e are obtained in two steps [8] from the easily available 2,3-dibromothiophene. An improved method for the synthesis of 3-formyl-2-thiopheneboronic acid, the key intermediate for the preparation of V, starting from 2,3-dibromothiophene, has been worked out.

The fact that desulphurization and hydrogenation of V—VII stops at the borazaropyridine stage provides some evidence for the aromatic nature of this ring system. Especially striking is the transformation of VII to IVc, which includes an introduction of a formal double bond during the reductive operation.

In order to compare the properties of the 3,2-borazaropyridines with those of the isoelectronic pyridines, we have studied 2,3,4-trimethylpyridine (VIII) and 2,3,5-trimethylpyridine (IX), isoelectronic with IVf and IVg. The choice of VIII and IX instead of the true analogues 2,3-dimethyl-4-ethylpyridine and 2,3-dimethyl-5-ethylpyridine was based on the easier availability of VIII and IX, both of which are described in the literature, and the minor effect caused by the change of the ethyl to the methyl group. VIII was prepared in a four-step synthesis from 3-methyl-2,4-pentandione, according to Prelog et al.,[9] by reaction of the dione with cyanoacetamide to form 5-cyano-6-oxy-2,3,4-trimethylpyridine. Acid hydrolysis accompanied by decarboxylation yielded 6-oxy-2,3,4-trimethylpyridine, which via the 6-chloro derivative was transformed to VIII. IX was prepared according to Bohlmann et al.[10] through the reaction of 3,5-dimethylpyridine with methyllithium.

NMR SPECTRA

The structure of the 3,2-borazaropyridines followed from their NMR spectra, and the combined series of NMR spectra made it possible to make an unequivocal assignment of the ring-hydrogen bands. As expected from simple

Table 1. NMR spectral data for some 3,2-borazaropyridines in CDCl₃.

Compound	τ_4	τ_5	τ_6	τ_{NR}	τ_{OH}	τ_{CH_2}	τ_{CH_3}	J_{46}	J_{56}	J_{4-CH_3-5}
IVa	—	3.05	2.35	6.40	5.17	7.38	8.87	—	4.4	2)
IVb	3.67	—	2.52	6.40	4.25	7.55	8.85	2.3	—	1.0
IVc	8.02 (CH₃)	7.95 (CH₃)	2.58	6.43	5.02	—	—	—	—	0.8
IVc[a]	3.64	—	2.54	−0.30	2.54	7.58	8.88	2.2	—	1.2
IVe[a]	—	3.08	2.58	−0.10	2.58	7.58	8.97	—	4.3	—
IVf	—	3.09	2.24	6.27	9.30	7.45	8.88	—	4.6	b
X	3.35	—	—	6.40	5.08	7.37	8.83	—	—	1.0
Y	—	2.12	—	6.28	4.80	7.38	8.77	—	—	1.2

[a] Solvent DMSO.
[b] The coupling was not resolved.

Table 2. NMR spectral data for (a) 4-ethyl-2,3-dimethyl-3,2-borazaropyridine, and (b) 2,3,4-trimethylpyridine in different solvents.

(a)	τ_6	τ_5	τ_{N-CH_3}	τ_{CH_2}	τ_{CH_3}	τ_{B-CH_3}	J_{56}
CDCl₃	2.24	3.09	6.27	7.45	8.88	9.30	4.6
DMSO-d_6	2.20	3.02	6.33	7.50	8.93	9.33	4.6
(CD₃)₂CO	2.27	3.05	6.33	7.48	8.92	9.32	4.4
D₂SO₄	1.42	2.01	5.50	6.70	8.33	8.66	5.3
Pyridine-d_5	2.13	3.13	6.35	7.55	8.97	9.12	4.4

(b)	τ_6	τ_5	$\tau_{2,3,4-CH_3}$				J_{56}
CDCl₃	1.82	3.08	7.52; 7.78; 7.85				5.0
DMSO-d_6	1.88	3.05	7.58; 7.80; 7.88				4.8
(CD₃)₂CO	1.92	3.12	7.58; 7.80; 7.88				4.9
D₂SO₄	1.35	1.92	6.82; 6.97; 7.15				6.2
Pyridine-d_5	1.73	3.18	7.53; 7.93; 8.02				4.9

Table 3. NMR spectral data for (a) 5-ethyl-2,3-dimethyl-3,2-borazaropyridine, and (b) 2,3,5-trimethylpyridine in different solvents.

(a)	τ_6	τ_4	τ_{N-CH_3}	τ_{CH_2}	τ_{CH_3}	τ_{B-CH_3}	J_{46}	J_{4-CH_2-5}
CDCl₃	2.27	3.15	6.32	7.52	8.82	9.33	2.4	1.0
DMSO d_6	2.35	3.22	6.38	7.55	8.88	9.37	2.6	1.0
(CD₃)₂CO	2.29	3.20	6.33	7.50	8.82	9.33	2.5	1.2
D₂SO₄	1.40	1.67	6.48	7.60	9.07	9.45	2.3	1.0
Pyridine-d_5	2.18	3.22	6.37	7.62	8.92	9.35	2.2	1.1

(b)	τ_6	τ_4	$\tau_{2,3,5-CH_3}$
CDCl₃	1.88	2.85	7.57 (1); 7.77 (2)
DMSO d_6	1.93	2.77	7.63 (1); 7.82 (2)
(CD₃)₂CO	1.95	2.82	7.63 (1); 7.80 (2)
D₂SO₄	1.47	1.47	6.88 (1); 7.10 (2)
Pyridine	1.75	2.97	7.60 (1); 7.90 (1); 7.95 (1)

electron-density considerations, the 6-hydrogen resonance (*ortho* to the pyridinic hydrogen) occurs at the lowest field, while the 4-hydrogen resonance (*ortho* to the boron atom) occurs at the highest field (*cf.* Tables 1 − 3). A characteristic long-range coupling of about 1 c/s between the 5-methylene group and the 4-hydrogen was also observed. A corresponding coupling from a 4-methylene group to the 5-hydrogen was much smaller, and was not resolved. No long-range coupling between the 5-side chain and the 6-hydrogen could be observed.

It has been suggested [11],[12] (for review *cf.* Ref. 13) that the magnitude of the *ortho* side chain coupling constants appears to be related to the bond-order of the aromatic bond involved. These results therefore indicate a much higher bond-order of the 4 − 5 than the 5 − 6 bond, the resonance structure indicated in formulae IV thus being of greater importance than the other Kekulé type structure of 3,2-borazaropyridine.

The chemical shifts of IVf and IVg and their pyridine analogues VIII and IX have been studied in more detail in several solvents (Tables 2 − 3). A comparison of the chemical shifts of the two 3,2-borazaropyridines and the corresponding pyridines shows very similar shifts for the 5-hydrogens, while both the 4- and 6-hydrogen resonances of the borazaropyridines are shifted 0.3 − 0.4 ppm upfield. However, the over-all similarity indicates that as in the pyridines, ring-current effects, due to the aromatic nature of the rings, contribute to the
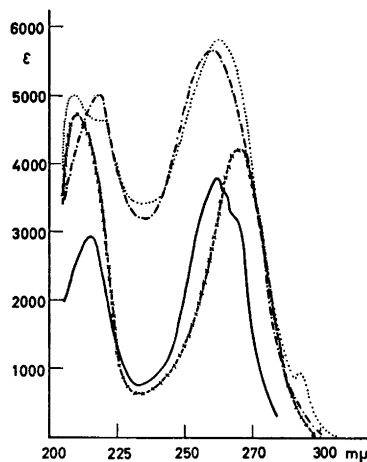

Fig. 1. UV spectra of compounds IVg (·····); IVf (-·-·-·); 2,3,4-trimethylpyridine, VIII (−); and 2,3,5-trimethylpyridine, IX (× − ×).

shifts in the same way. Changing from a B − CH$_3$ to a B − OH group causes an upfield shift of about 0.5 ppm of the 4-hydrogen resonance, and about 0.2 ppm of that from the 6-hydrogen, due to the + M − effect of the OH group. Shifts of similar magnitude are observed in phenols.[14] Protonation of IVg and VIII causes a large downfield shift of both the 5- and 6-hydrogen resonances, and a similar observation is made upon protonation of IVf and IX. The increase of J_{56} in IVg and VIII upon protonation has also been previously observed in pyridine-like heterocycles.[15],[16] A detailed comparison of NMR parameters with MO calculations will be given in a subsequent paper.

UV SPECTRA

The similarity of the UV spectra of the boron-nitrogen heterocycles with those of the isoelectronic parent compounds has been used by Dewar [2] as a main argument for their aromaticity.

The similarity of the UV spectrum of IVa and that of 3-hydroxypyridine has been pointed out earlier.[5] We have now compared the UV spectrum of IVg with that of IX, and the spectrum of IVf with that of VIII, and have found them to be very similar (Fig. 1). IVg shows absorption maxima at 210 mμ (ε 5000) and 262 mμ (ε 5800), while for IX, the maxima are at 210 mμ (ε 4700) and 270 mμ (ε 4100). The corresponding values for IVf are 218 mμ (ε 5200) and 260 mμ (ε 5830), and for VIII, 215 mμ (ε 2940), 267 mμ (ε 3800), and 269 mμ (ε 3580). Thus, UV spectra show the similar $\pi - \pi^*$ transitions of borazaropyridines and pyridines, confirming the aromatic nature of the former.

DIPOLE MOMENTS

The dipole moments of borazaro compounds have been some matter of controversy.[2] Recently, Dewar and Jones,[4] in order to explain the non-polarity of 10,9-borazaronaphthalene, suggested that the B$-$N σ-bond must be highly polar with its moment in a direction opposite to that due to the π-electrons. We found that the dipole moments of IVf and IVg also were very small (1.3 D and 1.2 D, respectively), and only about half of that of VIII (2.5 D) and IX (2.3 D). This indicates the B$-$N π-bond moment (which is opposed to the "pyridinic moment") must be larger than the B$-$N σ-bond moment. The dipole moments were determined according to the method of Hedestrand.[17] The low polarity of the alkylated borazaropyridines is also obvious from their boiling points. In spite of their higher molecular weight, their boiling point is lower than those of the trimethylpyridines.

BASICITIES

The 3,2-borazaropyridines show weak basic properties. Thus, IVf and IVg yield crystalline salts with anhydrous hydrogen bromide or hydrogen chloride in ether. These were, however, not as stable as those of VIII and IX, due to the weak base strength of IVf and IVg, and did not yield satisfactory analyses.

Potentiometric titration of IVf and IVg in 50 % ethanol$-$water with 0.1 N hydrochloric acid, as well as of the hydrochloride with 0.1 N sodium hydroxide, yielded pK_a-values of 2.5 and 2.3, respectively. Under the same conditions, VIII yielded a pK_a-value of 6.5 and IX of 6.3. The 3,2-borazaropyridines are thus about four powers of ten less basic than the corresponding pyridines. We suppose that the basic centre is the pyridinic nitrogen, and that the adjacent electron-attracting nitrogen diminishes the base strength, as for instance in pyridazine, which has a pK_a-value of 2.3 in water.[18]

HYDROLYTIC STABILITIES

The 3,2-borazaropyridines are extremely stable towards acid hydrolysis. Thus, the NMR spectra of IVf and IVg in conc. sulphuric acid did not change

during 50 h at 80°C. Also, the NMR spectra of the B−OH derivatives IVa and IVb in conc. sulphuric acid did not change after 5 h at 50°C. However, it is probable that the ether is immediately formed upon solution in conc. sulphuric acid, since when 30 % D_2SO_4 in D_2O was used with IVa, the appearance of a new N−CH_3 peak and ring-hydrogen resonances near those of IVa was observed, which we ascribe to the ether corresponding to IVa. IVa also showed good stability towards alkali. After standing for 24 h at room temperature in 1 N sodium hydroxide, 96 % of IVa could be recovered. After refluxing in 1 N sodium hydroxide for 1 h, 90 % of IVa was recovered. Additional evidence for the unusual hydrolytic stability of the 3,2-borazaropyridine ring was obtained during the attempted aromatic substitutions described below.

AROMATIC SUBSTITUTION

The 3,2-borazaropyridine system, especially when protonated, is strongly deactivated towards electrophilic substitution. Thus, no deuterium exchange was observed with IVf or IVg on heating with 98.3 % of D_2SO_4 at 80°C for 50 h. One of the strongest brominating agents known is N,N-dibromoisocyanuric acid (DBI) in fuming sulphuric acid (15 % SO_3) or in fluorosulphonic acid, introduced by Gottardi.[19-21] This author showed that 1,3-dinitrobenzene with this reagent yielded 1,3-dinitro-5-bromobenzene after 45 min at room temperature.[21] However, even after 24 h at room temperature, only starting material was recovered when IVf of IVg was subjected to these reaction conditions. VIII, on the other hand, yielded 59 % of 5-bromo-2,3,4-trimethylpyridine after 4 h reaction at room temperature. After 30 h, however, a 96 % yield of the bromo derivative was obtained. When excess of DBI was used, a 98 % yield of 5,6-dibromo-2,3,4-trimethylpyridine was obtained. The structure of the monobromo derivative was evident from its NMR spectrum, since the shift between the 5- and 6-hydrogen of VIII is large. According to Gottardi,[21] neither pyridine, nor pyridine-N-oxide is brominated under similar conditions.

Bromination of IX with DBI went even more smoothly. With fluorosulphonic acid as solvent, a yield greater than 80 % of 6-bromo-2,3,5-trimethylpyridine was obtained after 10 h. The structure is obvious from its NMR spectrum, as it is the low field doublet (at 1.87 τ) of IX which has disappeared, and not that at 2.83 τ. The small substituent shift, caused by bromine, is well known. It is interesting to note that IX is brominated faster in the 6-position than VIII in the 5-position, which is perhaps somewhat surprising in view of the known reactivities of pyridinic positions.

Plazek [22] has reported that alkyl pyridines can be nitrated with potassium nitrate in sulphuric acid containing 32 % of SO_3. We found that VIII, after about 5 h at 80−90°C, yielded 30 % of a mononitro derivative and 70 % starting material. Increasing the reaction time or using fluorosulphonic acid as solvent did not increase the yield. NMR indicates the mononitro compound to be 5-nitro-2,3,4-trimethylpyridine. IX, on the other hand, could be nitrated in high yield, both in fuming sulphuric acid and in fluorosulphonic acid, to 6-nitro-2,3,5-trimethylpyridine. Again, the NMR spectrum proved the structure of the isomer formed.

Attempts to nitrate IVf and IVg under the same conditions did not lead to substitution. Only oxidation of the $B-CH_3$ group to the $B-OH$ group was observed, as IVf and IVa, and IVg and IVb, respectively, were recovered. Namtvedt and Gronowitz [23,24] found that borazarothienopyridines, such as V and VI, are nitrated in the boron-nitrogen containing ring in the 4- and 7-position, respectively, by nitric acid in acetic acid-acetic anhydride. The results of a preliminary investigation indicate this also to be the case of the 3,2-borazaropyridines, IVa, f, and g, all of which were nitrated in the 6-position, IVf and g with concomitant oxidation of the $B-CH_3$ group to $B-OH$, which made purification very difficult, and partial ether formation. The structures follow from consideration of chemical shifts in the NMR spectra. In the NMR spectra of the crude product, peaks in the aromatic region and N-methyl peaks ascribable both to the hydroxy derivative and the ether could be observed. Thus the crude product from the nitration of IVa showed two peaks at $1.95\ \tau$ and $2.12\ \tau$, with relative intensities of approximately 1:5, and peaks at $6.25\ \tau$ and $6.28\ \tau$, with the same relative intensities. In the same way, the NMR spectrum of the nitration product of IIb showed two 1:2:1 triplets at $3.16\ \tau$ and $3.35\ \tau$, with relative intensities of 1:2, and two sharp $N-CH_3$ resonances at $6.28\ \tau$ and $6.40\ \tau$, with the same relative intensities. Also the area of ethyl group resonance consisted of overlapping signals from two different ethyl groups, indicating the presence of two compounds. VIII and IX did not react under these conditions.

It seems reasonable that both bromination with DBI and nitration with potassium nitrate in strongly acidic media are electrophilic aromatic substitution reactions. It is also justified to assume that in these strongly acidic media, both pyridine and 3,2-borazaropyridines are completely protonated, even if the latter are about four powers of ten less basic. The results mentioned above therefore indicate that the 3,2-borazaropyridinium ions are less reactive than the isoelectronic pyridinium ions in electrophilic aromatic substitution.

Our results also indicate that the nitration in acetic anhydride — acetic acid is unlikely to be an electrophilic substitution reaction, but most probably proceeds *via* an addition — substitution — elimination mechanism, characteristic for borazaro derivatives.

Recently, Dewar and Logan [3] came to results opposite to ours concerning the reactivity of borazaro compounds relative to their parent compounds in electrophilic aromatic substitution. They determined the partial rate-factors (PRF) in the nitration of 10-methyl-10,9-borazarophenanthrene with nitric acid in acetic anhydride. At 0°C, reaction occurs in the 6- and 8-positions,[25] and is much more rapid than in phenanthrene (PRF for the 6-position of 10-methyl-10,9-borazarophenanthrene is 2.06×10^6; PRF for the 1-position of phenanthrene is 360). Dewar and Logan also claim that the high reactivity of the borazaro derivative may be predicted by simple MO calculations. However, the mechanism of the reaction has not been demonstrated by these authors, who assume it to be an electrophilic substitution reaction. As pointed out above, we have reason to believe, from the observed orientation in the reaction of borazarothienopyridines with fuming nitric acid in acetic anhydride-acetic acid, that this reaction is not a normal electrophilic substitution reaction. However, we agree with Dewar and Logan that in this specific

reaction, borazaro compounds are much more reactive than the corresponding parent compounds. However, we admit that the alternative explanation, assuming that in the electrophilic substitutions of the *free* bases, 3,2-borazaropyridines are more reactive than pyridines is not completely disproven.

The great stability and obvious aromaticity of the 3,2-borazaropyridines is in great contrast to the instability of the borazarenes found by Dewar *et al.*[1] Although it is well known that pyridine is more stable towards oxidation, and less reactive than benzene in electrophilic substitution, the difference between 3,2-borazaropyridines and the borazarenes appears much larger than expected. Further investigations of borazarenes in particular, as well as of 3,2-borazaropyridines, would therefore be of great interest.

EXPERIMENTAL

3-Formyl-2-thiopheneboronic acid. A solution of 96.8 g (0.40 mol) of 2,3-dibromothiophene in 400 ml of anhydrous ether was added under nitrogen in a slow stream and with vigorous stirring to 440 ml of 1.0 N ethereal ethyllithium cooled to − 75°C. After 5 min, 110.6 g (0.48 mol) of butyl borate was added in one portion through the wide-open dropping funnel, and the mixture was stirred at − 70°C for 3 h. 520 ml of 1.0 N ethereal ethyllithium was added in a slow stream, and 5 min after the addition was complete, 41.0 g (0.56 mol) of N,N-dimethylformamide in 50 ml of anhydrous ether was added dropwise with stirring. When the temperature of the mixture had risen to room temperature (after 2 h), it was cooled to − 10°C, 1300 ml of 1 N hydrochloric acid was added, and stirring was continued for 1 h at room temperature. The aqueous layer was extracted three times with ether, whereupon the combined ether phases were divided into two portions. Each of these portions was extracted three times with 200 ml 1 N sodium carbonate, and each aqueous extract immediately acidified with 4 N hydrochloric acid. After cooling, 35.0 g (56 %) of 3-formyl-2-thiopheneboronic acid was filtered off, which had the same physical properties as an authentic sample.[7]

7,6-Dimethyl-7,6-borazarothieno[3,2-c]pyridine. 7-Hydroxy-6-methyl-7,6-borazarothieno[3,2-c]pyridine [7] (32.0 g, 0.19 mol), 400 ml of butanol, and 200 ml of benzene was refluxed for 6 h in a flask, fitted with a Dean-Stark trap. Excess butanol was distilled off, and the residue dissolved in 400 ml of anhydrous ether. This solution was cooled to − 10°C, and 300 ml of a 1 N solution of methylmagnesium iodide was added with stirring at such a rate that the temperature did not rise over 0°C. The reaction mixture was refluxed for 1 h, and after cooling poured onto 400 ml of 1 N hydrochloric acid and ice. The ether phase was separated, and the pH of the aqueous phase adjusted to 7 with solid sodium bicarbonate. The combined ether phases were dried over magnesium sulphate, the ether evaporated, and the residue distilled, yielding 23.7 g (75 %) of 7,6-dimethyl-7,6-borazarothieno[3,2-c]pyridine, b.p. 90 − 92°C/3 mmHg, m.p. 43.5 − 44°C after recrystallization from 50 % aqueous ethanol. NMR ($(CD_3)_2CO$): $\tau_2 = 2.53$ ppm; $\tau_3 = 2.12$ ppm; $\tau_4 = 1.65$ ppm; $\tau_{N-CH3} = 6.25$ ppm; $\tau_{B-CH3} = 9.10$ ppm. $J_{23} = 4.9$ c/s. [Found: C 50.94; H 5.98. Calc. for $C_7H_9BN_2S$ (164): C 51.27; H 5.53.]

5-Ethyl-3-hydroxy-2-methyl-3,2-borazaropyridine. 320 g Raney-Nickel (LS-S-35) was added to a stirred solution of 52.0 g (0.31 mol) of 7-hydroxy-6-methyl-7,6-borazarothieno [3,2-c]pyridine [7] in 1200 ml of methanol, and the mixture was heated to reflux for 3 h. An additional portion of 300 g of Raney-Nickel was added, and the mixture refluxed for 3 h. The nickel was filtered off, and washed carefully with methanol. The combined methanolic solutions were evaporated, leaving an oil, which was taken up in ether and washed with 100 ml of 1 N hydrochloric acid and water, and dried over magnesium sulphate. Evaporation of the ether yielded 24.2 g of the title compound, containing some starting material. Recrystallization from hexane yielded 18.4 g (43 %) of pure 5-ethyl-3-hydroxy-2-methyl-3,2-borazaropyridine in colourless crystals, m.p. 65 − 69°C. For NMR, see Table 1. [Found: C 52.64; H 7.68. Calc. for $C_6H_{11}BN_2O$ (138.0): C 52.23; H 8.03.]

5-Ethyl-3-hydroxy-3,2-borazaropyridine. Treatment of 5.0 g (0.033 mol) of 4-hydroxy-7,6-borazarothieno[3,2-c]pyridine [7] in 200 ml of methanol, with two 50 g portions in the

same way as described above, yielded 1.1 g (27 %) of the title compound, m.p. 106 – 110°C after recrystallization from hexane. NMR, see Table 1. [Found: C 49.03; C 6.58. Calc. for $C_5H_9BN_2O$ (123.95): C 48.45; H 7.32.]

4-Ethyl-3-hydroxy-3,2-borazaropyridine. Treatment of 5.0 g (0.033 mol) of 4-hydroxy-4,5-borazarothieno[2,3-c]pyridine [6] in 200 ml of methanol, with two 50 g portions of Raney-Nickel in the same way as described above, yielded 1.4 g (34.2 %) of the title compound, m.p. 109 – 112°C after recrystallization from hexane. NMR, see Table 1. [Found: C 48.14; H 6.83. Calc. for $C_5H_9BN_2O$ (123.95): C 48.45; H 7.32.]

2,4,5-Trimethyl-3-hydroxy-3,2-borazaropyridine. Treatment of 5.0 g (0.030 mol) of 7-hydroxy-6-methyl-7,6-borazarothieno[3,4-c]pyridine [7] in 200 ml of methanol, with two 50 g portions of Raney-Nickel in the same way as described above, yielded 1.87 g (41 %) of the title compound, m.p. 64 – 70°C after recrystallization from hexane. NMR, see Table 1. [Found: C 49.56; H 6.72. Calc. for $C_6H_{11}BN_2O$ (138.0): C 48.45; H 7.34.]

2,3-Dimethyl-5-ethyl-3,2-borazaropyridine. Method I. 8.0 g (0.058 mol) of 5-ethyl-3-hydroxy-2-methyl-3,2-borazaropyridine was reacted with butanol (230 ml), and the resulting boric ether dissolved in 290 ml of anhydrous ether, and reacted with 200 ml 1 N methylmagnesium iodide as described above for the preparation of 7,6-dimethyl-7,6-borazarothieno[3,2-c]-pyridine. Fractional distillation yielded 6.5 g (82 %) of the title compound, b.p. 177 – 180°C/760 mmHg. NMR, see Table 1. [Found: C 61.01; H 8.33. Calc. for $C_7H_{13}BN_2$ (136.0): C 61.82; H 9.63.]

2,3-Dimethyl-5-ethyl-3,2-borazaropyridine. Method II. Desulphurization of 10.0 g (0.061 mol) of 7-methyl-7,6-borazarothieno[3,2-c]pyridine [7] in 500 ml of methanol, with two 100 g portions of Raney-Nickel as described above, yielded 3.65 g (44 %) of the title compound, b.p. 177 – 180°C/760 mmHg, and with the same IR and NMR spectrum as the above sample.

2,3-Dimethyl-4-ethyl-3,2-borazaropyridine. Method I. The procedure was identical with that for 2,3-dimethyl-5-ethyl-3,2-borazaropyridine (method I) given above. 8.0 g (0.058 mol) of 4-ethyl-3-hydroxy-2-methyl-3,2-borazaropyridine yielded 5.76 g (73 %) of the title compound, b.p. 72.0 – 73.5°C/15 mmHg. NMR, see Table 1. [Found: C 62.09; H 9.42. Calc. for $C_7H_{13}BN_2$ (136.0): C 61.82; H 9.63.]

2,3-Dimethyl-4-ethyl-3,2-borazaropyridine. Method II. The procedure was identical with that for 2,3-dimethyl-5-ethyl-3,2-borazaropyridine (method II) described above. 10.0 g (0.061 mol) of 4,5-dimethyl-4,5-borazarothieno[2,3-c]pyridine [7] yielded 4.1 g (49 %) of the title compound, b.p. 72 – 73°C/15 mmHg, with the same IR and NMR spectra as the above sample.

6-Bromo-2,3,5-trimethylpyridine. A solution of 4.75 g (0.0165 mol) of N,N-dibromo-isocyanuric acid in 10 ml of fluorosulphonic acid was added dropwise with stirring to 1.00 g (8.25 mmol) of 2,3,5-trimethylpyridine [10] in 10 ml of fluorosulphonic acid, and the mixture was stirred for 10 h at room temperature. It was carefully poured onto ice, and the precipitated isocyanuric acid filtered off. The aqueous solution was made alkaline with conc. potassium hydroxide solution. The alkaline solution was extracted with ether, and the combined ether phases dried over magnesium sulphate. Evaporation of the ether gave a crystalline residue, which was recrystallized from 50 % aqueous ethanol, yielding 1.51 g (91 %) of 6-bromo-2,3,5-trimethylpyridine, m.p. 68.0 – 68.5°C. NMR: $(CDCl_3)$ $\tau_4 = 2.75$ ppm; $\tau_{CH_3} = 7.53$; 7.65, 7.77 ppm. [Found: C 47.64; H 5.12; N 6.49; Br 40.49. Calc. for $C_8H_{10}BrN$ (200.1): C 48.02; H 5.04; N 7.00; Br 39.93.]

Changing the solvent to fuming sulphuric acid (15 % SO_3), and increasing the reaction time to 24 h gave 1.40 g (84 %) of 6-bromo-2,3,5-trimethylpyridine, with the same physical properties as the above sample.

5-Bromo-2,3,4-trimethylpyridine. A solution of 2.38 g (8.25 mmol) of N,N-dibromo-isocyanuric acid in 10 ml of fluorosulphonic acid was added dropwise with stirring to 1.00 g (8.25 mmol) of 2,3,4-trimethylpyridine, and the mixture was stirred for 40 h at room temperature. Work-up as described above yielded 1.59 g (96 %) of 2,3,4-trimethyl-5-bromopyridine, m.p. 67.0 – 68.0°C. NMR $(CDCl_3)$: $\tau_6 = 1.63$ ppm; $\tau_{CH_3} = 7.55$, 7.65 7.75 ppm. [Found: C 47.83; H 4.96; N 7.05; Br 39.63. Calc. for $C_8H_{10}BrN$ (200.1): C, 47.83; H 4.96; N 7.05; Br 39.63.]

5,6-Dibromo-2,3,4-trimethylpyridine. When 4.75 g (16.5 mmol) of N,N-dibromoiso-cyanuric acid in 10 ml of fluorosulphonic acid and 100 g (8.25 mmol) of 2,3,4-trimethyl-pyridine in 10 ml of fluorosulphonic acid were reacted for 30 h at room temperature and worked up as described above, 2.26 g (98 %) of the title compound, m.p. 94 – 96°C, was

obtained after recrystallization from 50 % aqueous ethanol. NMR (CDCl$_3$): $\tau_{CH3} = 7.53$ ppm (2), 7.75 ppm (1). [Found: C 34.54; H 3.48; N 5.09; Br 56.70. Calc. for C$_8$H$_9$Br$_2$N (278.99): C 34.44; H 3.25; N 5.02; Br 57.29.]

6-Nitro-2,3,5-trimethylpyridine. To a solution of 3.00 g (0.0248 mol) of 2,3,5-trimethylpyridine in 14 ml of fuming sulphuric acid (32 % SO$_3$), 5.0 g of potassium nitrate was added in small portions with stirring during 15 min (highly exothermic reaction). The mixture was stirred at 90°C for 7 h, poured onto ice, and made alkaline with conc. sodium hydroxide solution. The aqueous phase was extracted with ether, and the combined ether phases were dried over magnesium sulphate. Evaporation of the ether gave a crystalline residue, which was recrystallized from 50 % aqueous ethanol, yielding 3.1 g (75 %) of 6-nitro-2,3,5-trimethylpyridine, m.p. 77.3 − 78°C. NMR (CDCl$_3$): $\tau_6 = 2.42$ ppm; $\tau_{CH3} = 7.46$, 7.53, 7.62 ppm. [Found: C 58.21; H 6.21; N 16.21; O 19.31. Calc. for C$_8$H$_{10}$N$_2$O$_2$ (166.2): C 57.82; H 6.07; N 16.86; O 19.26.] When 14 ml of fluorosulphonic acid was used as solvent, 3.2 g (77 %) of 6-nitro-2,3,5-trimethylpyridine was obtained.

5-Nitro-2,3,4-trimethylpyridine. The procedure was identical with that described for 6-nitro-2,3,5-trimethylpyridine. From 3.0 g (0.0248 mol) of 2,3,4-trimethylpyridine, 1.95 g of 2,3,4-trimethylpyridine, b.p. 78 − 80°C/15 mmHg, and 1.33 g (32 %) of 5-nitro-2,3,4-trimethylpyridine, b.p. 135 − 136°C/15 mmHg, m.p. 66.5 − 67°C, were obtained upon fractionation. NMR (CDCl$_3$): $\tau_6 = 1.30$ ppm; $\tau_{CH3} = 7.38$, 7.55, 7.67 ppm. [Found: C 58.39; H 6.13; N 16.92. Calc. for C$_8$H$_{10}$N$_2$O$_2$ (166): C 57.82; H 6.07; N 16.86.]

Nitration of 5-ethyl-3-hydroxy-2-methyl-3,2-borazaropyridine. A solution of 0.43 ml fuming nitric acid ($d = 1.50$) in 6.0 ml of acetic anhydride was added dropwise to a solution of 0.69 g (5.0 mmol) of 5-ethyl-3-hydroxy-2-methyl-3,2-borazaropyridine in 25 ml of glacial acetic acid. The mixture was stirred at room temperature for 4 h, poured onto ice, and neutralized with 4 N sodium hydroxide solution. The pH was then adjusted to 4, and the aqueous phase extracted three times with ether. The combined ether phases were dried and evaporated, and the crystalline residue recrystallized from aqueous ethanol, yielding 0.72 g of a mixture of 5-ethyl-3-hydroxy-2-methyl-6-nitro-3,2-borazaropyridine and its anhydride, m.p. 126 − 127°C, which was further purified by chromatography on silica gel, using ether as eluent.

Nitration of 4-ethyl-3-hydroxy-2-methyl-3,2-borazaropyridine. 1.38 g (0.010 mol) of 4-ethyl-3-hydroxy-2-methyl-3,2-borazaropyridine in 50 ml of acetic acid was reacted with 0.85 ml of fuming nitric acid ($d = 1.5$) in 10 ml of acetic anhydride, and worked up as described above, yielding 1.0 g (73 %) of a mixture of 4-ethyl-3-hydroxy-2-methyl-6-nitro-3,2-borazaropyridine and its anhydride, m.p. 120°C, after recrystallization from aqueous ethanol. Chromatography as described above yielded the anhydride. [Found: C 41.04; H 5.02. Calc. for C$_8$H$_{10}$BN$_2$O$_3$ (169.0): C 40.72; H 5.13.]

Determination of acidity constants. For the potentiometric titrations,[26] a Radiometer pH-metre, type pHM26, combined with an autoburette, type ABU11, with a combination electrode, type GK2301B, from the same company was used. The cell was thermostated at 20.0°C. 3,2-Borazaropyridinium chlorides and collidinium chlorides were titrated with 0.100 N carbon dioxide-free sodium hydroxide in 50 % ethanol-water solutions, while the corresponding bases were titrated with 0.100 N hydrochloric acid in 50 % ethanol-water solutions. The measurements were carried out at different concentrations, varying from 2.55×10^{-4} mol to 4.16×10^{-4} mol in 20 ml of 50 % ethanol-water solution.

Dipole moment measurements. The dipole measurements were performed with a Dipolmeter, type DM01, from Wissenschaftlich Technischen Werkstätten GmbH, in a cell type DFL 2/s or DFL 2. The metre settings were calibrated with the aid of benzene and dibutylether, according to the directions in the instrument manual. The measurements were carried out in benzene solution at 25.0°C with weight per cent between 1.35 and 4.61. Indices of refraction of the solutions were determined with a Carl Zeiss Abbe type refractometer. The dipole moments were evaluated by the method introduced by Smith[27] and Guggenheim.[28] The slopes of the straight lines representing $\varepsilon_{12} - \varepsilon_1$ and $n_{12}^2 - n_1^2$ *versus* weight fraction of solute, k_1 and k_2, were obtained from the lines. For 2,3,4-trimethylpyridine, a value of 5.97 for k_1, and a value of 0.04 for k_2 was obtained. For 4-ethyl-2,3,dimethyl-3,2-borazaropyridine, the corresponding values were 1.42 and 0.02.

For 2,3,5-trimethylpyridine, a value of 4.91 for k_1, and a value of 0.04 for k_2 was obtained. For 5-ethyl-2,3-dimethyl-3,2-borazaropyridine, the corresponding values were 1.35 and 0.03.

NMR spectra were recorded with a Varian A-60 NMR spectrometer. Chemical shifts are given as τ values, tetramethylsilane serving as internal standard. Mass spectra were obtained with an LKB A-9000 combined gas chromatograph – mass spectrophotometer. IR spectra were recorded on a Perkin-Elmer 257 grating infrared spectrophotometer. The substances were analyzed on a Perkin-Elmer 9000 gas chromatograph, using a 5 % NPGS column, at temperatures between 90 and 120°C.

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