Boron-11 Nuclear Magnetic Resonance Study of the Reactions of 2-Functionalized Pyridines with Borane–Tetrahydrofuran and –Dimethyl Sulphide. Formation of Borinic Esters and N → B Bond Energy Differences in Five- and Six-membered Ring Borates

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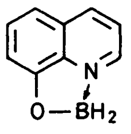
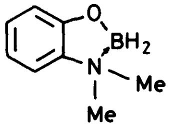
A ^{11}B n.m.r. study of the reactivity of 2-substituted pyridines containing carboxy, acyl, and hydroxy groups with borane–tetrahydrofuran (BH_3·THF) and BH_3·Me_2S showed that pyridines behave differently from their aliphatic analogues. The formation of stable borinic esters was observed. Variable-temperature n.m.r. data allowed us to calculate that five-membered B ← N co-ordinated heterocycles are 28 kJ mol^{-1} more stable than six-membered ones.

Reactions of 8-hydroxyquinoline,[1,2] *o*-(dimethylamino)phenol,[2] and several amino acids[3] with borane have been reported to lead to some of the few known examples of borinic esters, (**1**)—(**4**). However, reactions of aminoethanol derivatives[4] with boranes did not afford borinic derivatives; they gave only amino-alcohol(*N*–*B*)boranes [*e.g.* (**5**)], boric esters tris-(*N*–*B*)boranes [*e.g.* (**6**)], and (*N*–*B*)aminoethyl boric esters-(*N*–*B*)bisboranes [*e.g.* (**7**)].

In continuation of our studies of the factors that allow the synthesis of borinic bifunctional hydrides stabilized by internal co-ordination, we now report the reactions of pyridine analogues with BH_3·THF and BH_3·Me_2S. The 2-substituted pyridines studied contained carboxy, acyl, and hydroxy groups, and could in principle form five- or six-membered B ← N heterocycles. The products were investigated by ^{11}B n.m.r. measurements.



(**1**)



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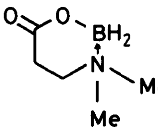

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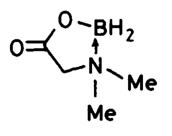
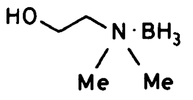


(**4**)



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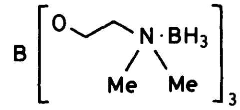
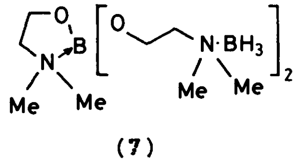


(**6**)

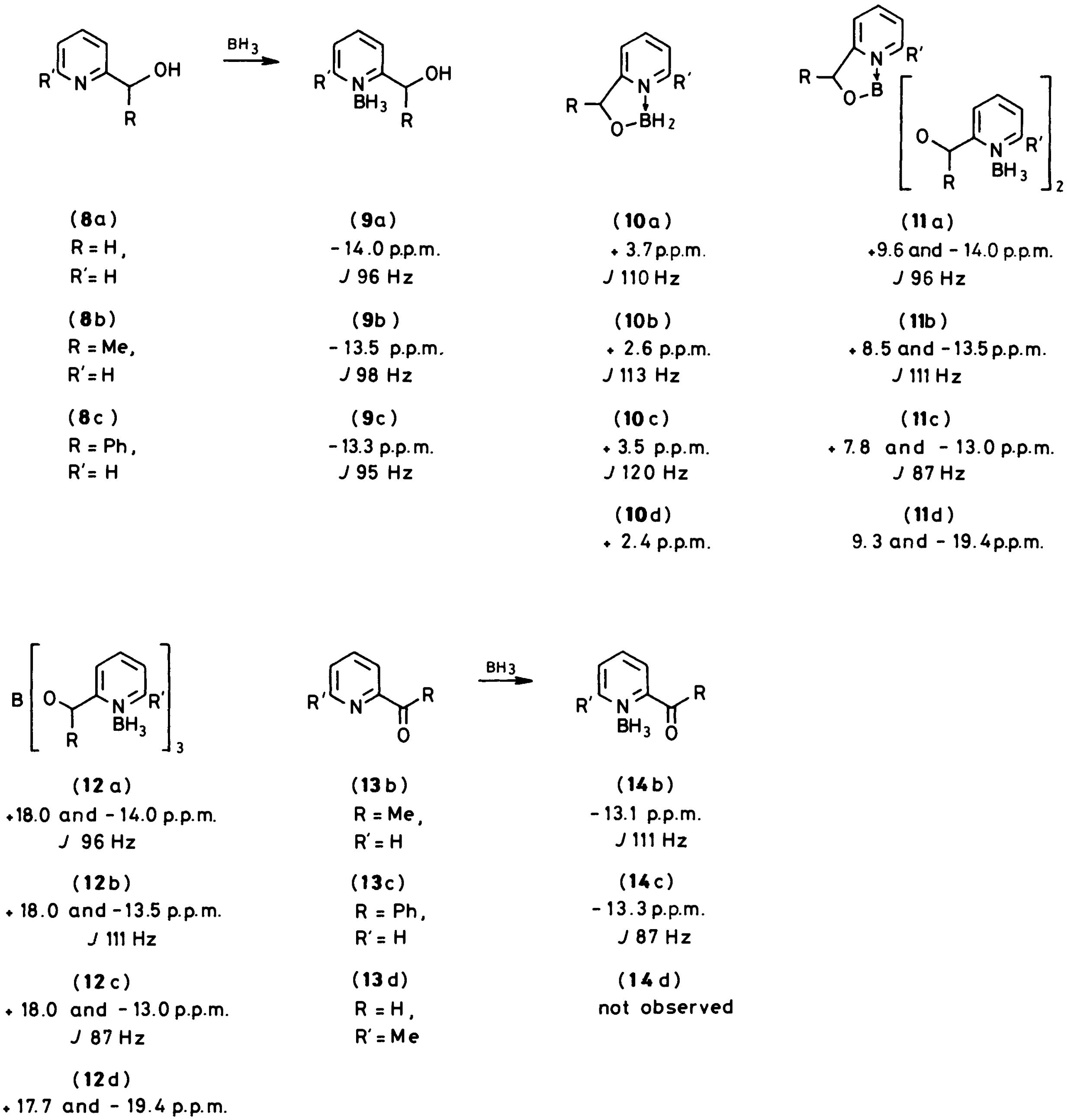


(**7**)

Results and Discussion

Reactions of the pyridylmethanols (**8a**—**c**) with BH_3·Me_2S (Scheme 1) gave initially the amine–boranes (**9a**—**c**), as evidenced by a ^{11}B signal around −13 to −14 p.p.m.[4,5] Further reaction gave the (2-pyridylmethoxo-*O*,*N*)boranes (borinic esters) (**10a**—**c**), showing signals at around +3.0 p.p.m.[2] The latter were transformed into the (*N*–*B*)-(2-pyridylmethyl) bis[(*N*–*B*)-(2-pyridylmethyl)borane] borates (**11a**—**c**) as shown by a ^{11}B n.m.r. singlet around +8.0 p.p.m.[4] and a quartet around −14 to −19 p.p.m. Reaction of the same substrates (**8a**—**c**) with BH_3·THF again gave the borinic esters (**10a**—**c**) and the N → B co-ordinated borates (**11a**—**c**), and also the tris-[(*N*–*B*)-(2-pyridylmethyl)borane] borates (**12a**—**c**) which gave signals around +18.0 (s) and −14.0 (q) p.p.m.[4,5] Thus addition of BH_3·THF (but not BH_3·Me_2S) to compounds (**11a**—**c**) causes rupture of the intramolecular N → B co-ordination; this reaction seems to depend on the N → B bond energy being less than that of the S → B bond. When the reaction was performed with the 2-acylpyridines (**13b** and **c**), with BH_3·Me_2S, a signal around −13.0 p.p.m. indicated the formation of the 2-acylpyridine–boranes (**14b** and **c**), which were transformed into the borinic esters (**10b** and **c**) (+3.0 p.p.m.)[2] by hydroboration of the carbonyl group, and then into the N → B co-ordinated borates (**11b** and **c**) (around +8.0 p.p.m.[4,5]). The analogous products were observed in the case of (**13d**) except for pyridine–borane (**14d**). As in the case of the pyridylmethanols, reaction of (**13b**—**d**) with BH_3·THF did not yield the pyridine–boranes (**14b**—**d**) but instead gave the borinic esters (**10b**—**d**), the N → B co-ordinated borates (**11b**—**d**), and the boric esters (**12b**—**d**) (Scheme 1).

Reaction of 2-(β-hydroxyethyl)pyridine (**15**) with BH_3·THF or BH_3·Me_2S gave products with a signal at −14.0 p.p.m.,[4,5] corresponding to the amine–borane (**16**) and a triplet at +0.7 p.p.m.,[2] attributed to (**17**). The mixture was transformed into tris-[(*N*–*B*)-2-(β-hydroxyethyl)pyridineborane] borate (**18**). Basic hydrolysis of the boric esters (**12a**—**c**) and (**18**) led to the hydroxypyridine–boranes (**9a**—**c**) and (**16**) (−14·0 p.p.m.[4,5]).



(8a)
R = H,
R′ = H

(8b)
R = Me,
R′ = H

(8c)
R = Ph,
R′ = H

(9a)
− 14.0 p.p.m.
J 96 Hz

(9b)
− 13.5 p.p.m.
J 98 Hz

(9c)
− 13.3 p.p.m.
J 95 Hz

(10a)
+ 3.7 p.p.m.
J 110 Hz

(10b)
+ 2.6 p.p.m.
J 113 Hz

(10c)
+ 3.5 p.p.m.
J 120 Hz

(10d)
+ 2.4 p.p.m.

(11a)
+9.6 and − 14.0 p.p.m.
J 96 Hz

(11b)
+ 8.5 and − 13.5 p.p.m.
J 111 Hz

(11c)
+ 7.8 and − 13.0 p.p.m.
J 87 Hz

(11d)
9.3 and − 19.4 p.p.m.

(12a)
+18.0 and − 14.0 p.p.m.
J 96 Hz

(12b)
+ 18.0 and − 13.5 p.p.m.
J 111 Hz

(12c)
+ 18.0 and − 13.0 p.p.m.
J 87 Hz

(12d)
+ 17.7 and − 19.4 p.p.m.

(13b)
R = Me,
R′ = H

(13c)
R = Ph,
R′ = H

(13d)
R = H,
R′ = Me

(14b)
− 13.1 p.p.m.
J 111 Hz

(14c)
− 13.3 p.p.m.
J 87 Hz

(14d)
not observed

Scheme 1. Products from 2-pyridylmethanols and 2-acylpyridines, with ^{11}B n.m.r. data

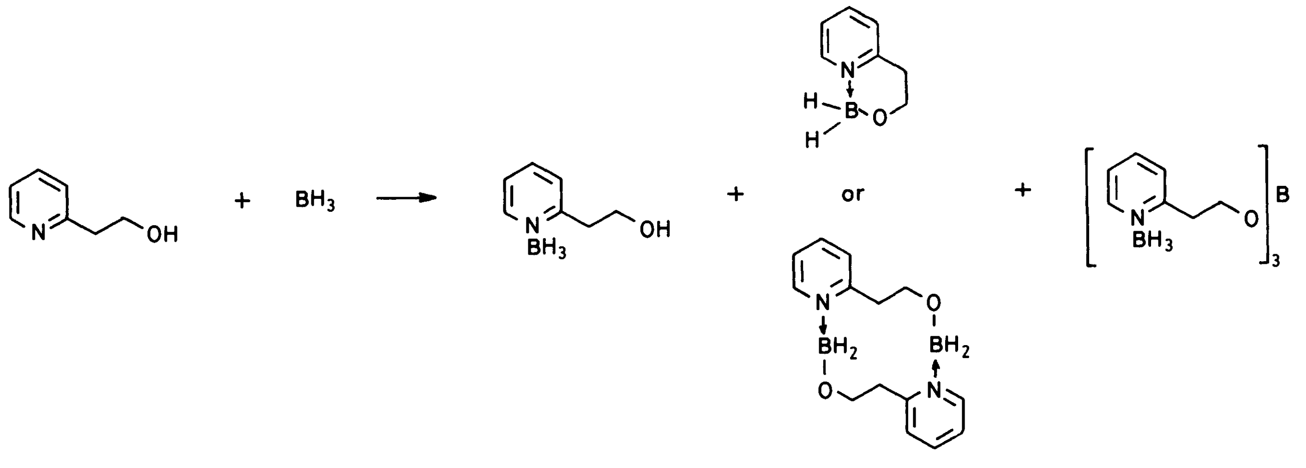
The pyridine-2-carboxylic acids (**19a** and **b**) gave exclusively the borinic esters (**20a** and **b**) (0.7 and 2.0 p.p.m.).[2] The fact that these compounds could be isolated and are fairly stable suggests that they may be used as reducing agents, in analogy to the boric ester derived from 8-hydroxyquinoline.[2,6]

We were unable to synthesize the analogous borinic compound with a six-membered ring derived from 2-pyridylacetic acid. This difficulty could be attributed to a solubility problem and/or to a lower stability of the resulting heterocycle.

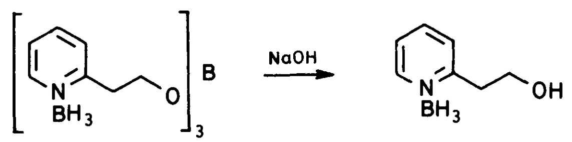
The foregoing results show that 2-pyridylmethanols and amino alcohols behave differently: borinic esters were never observed with amino alcohols. Furthermore, there is a marked difference in stability between five- and six-membered rings, as evidenced by formation of the esters (**11a**—**c**) with five-membered rings containing intramolecular N ⟶ B co-ordination from the pyridylmethanols (**8a**—**c**) with borane. Derivatives of type (**21**) are not formed from reactions of BH_3·THF or BH_3·Me_2S with 2-(β-hydroxyethyl)pyridine (**15**); thus the ring size factor seems to influence co-ordination. Comparison of structure (**11a**) with (**21**) suggests that the boron atoms would have similar acidities (in both cases they are bonded to three oxygen atoms) and also that the five-membered ring is more stable than a six-membered one.

Further evidence for the greater stability of N ⟶ B co-ordination in a five-membered ring was obtained from tris-[(*N*–*B*)-(2-pyridylmethyl)] borate (**22**) and tris-[(*N*–*B*)-2-(2-pyridyl)ethyl] borate (**23**). The ^{11}B n.m.r. spectrum of compound (**23**) showed a signal at + 17.1 p.p.m., which indicates that the equilibrium is shifted towards (**23a**). On the other hand, the signal at + 10.9 p.p.m. from (**22**) is evidence that in this case the equilibrium favours the cyclic form (**22b**).

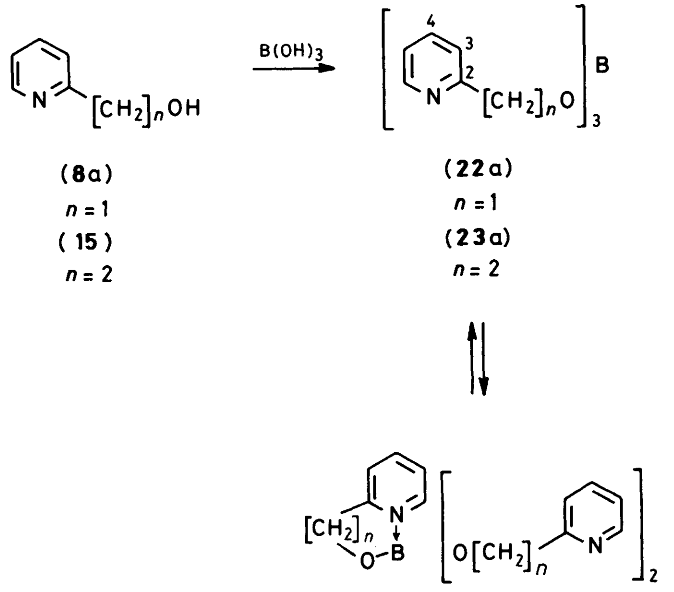
In order to determine quantitatively the difference in



(15) **(16)** **(17)** **(18)**



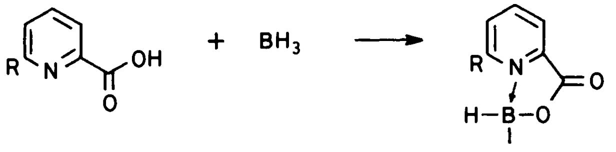
(18) **(16)**



(8a) n = 1 **(15)** n = 2

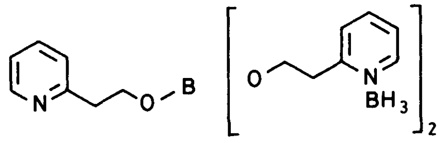
(22a) n = 1 **(23a)** n = 2

(22b) n = 1 **(23b)** n = 2



(19a) R = H **(19b)** R = CO2H

(20a) + 0.7 p.p.m. **(20b)** + 2.0 p.p.m.



(21)

stabilities between the five- and six-membered rings, ^{11}B variable-temperature n.m.r. measurements were performed. ^{11}B Chemical shifts of compound (**22**) were determined between 25 and 105 °C; the signal moved from +10.9 to +13.3 p.p.m., indicating that the concentration of the open form is increased at higher temperature. Compound (**23**) was examined between +25 and −70 °C. At low temperature the cyclic form is present, as evidenced by the shift of the signal from +17.1 to +15.2 p.p.m. These changes are good evidence of the existence of an equilibrium between the cyclic and open structures in the two compounds (**22**) and (**23**). Study of the ^{11}B chemical shift variation with temperature allowed us to calculate the equilibrium constant by using Eliel's equation.[7]

It has been reported that six-membered ring borinates from amino alcohols are less stable; this is attributed to greater steric difficulties associated with the formation of this ring. This factor favours formation of an equilibrium mixture of the simple ester and the chelate.[8]

In the case of the compounds studied here, it can be concluded that the five-membered B ⟵ N ring is favoured over the six-membered one by *ca.* 28 kJ mol^{-1}; the energy difference is attributed to ring stability (Scheme 2).

$$(\mathbf{22a}) \rightleftharpoons (\mathbf{22b})\ \Delta H = -21.50 \pm 0.4\ \text{kJ mol}^{-1}$$
$$\Delta S = -54.15 \pm 1.2\ \text{J mol}^{-1}\ \text{K}^{-1}$$

$$(\mathbf{23a}) \rightleftharpoons (\mathbf{23b})\ \Delta H = 7.61 \pm 0.4\ \text{kJ mol}^{-1}$$
$$\Delta S = 46.40 \pm 2.0\ \text{J mol}^{-1}\ \text{K}^{-1}$$

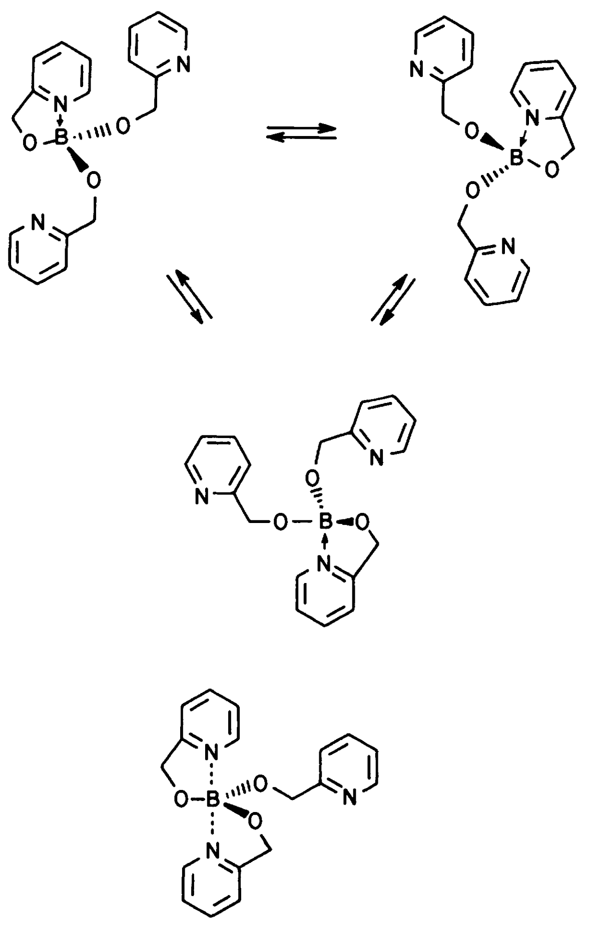
Scheme 2.

^{13}C N.m.r. is not as sensitive as ^{11}B n.m.r. in detecting the equilibrium between the open and cyclic forms, as the C-4

Table. Chemical shifts (p.p.m.)

	^{13}C							^{11}B
Compd.	C-2	C-3	C-4	C-5	C-6	OCH_2	CH_2	
(**8a**)	161.1	122.1	137.0	120.7	148.2	64.5		
(**22**)[a]	160.7	122.0	137.4	120.4	146.1	65.2		+10.9
(**22**)[b]	160.7	122.3	138.0	120.2	145.1	65.4		+10.2[b]
(**9a**)	159.7	122.8	139.5	120.6	148.2	61.5		
(**15**)	159.6	123.7	136.5	121.3	148.6	61.3	40.8	
(**23**)[a]	159.5	123.6	136.0	121.2	149.0	62.5	40.2	+17.1
(**23**)[c]	159.2	123.9	136.0	121.3	147.0	61.1	38.9	+15.2
(**16**)	157.5	126.3	138.0	122.2	148.2	59.4	36.2	

[a] Room temperature; CD_2Cl_2 as solvent. [b] At −84 °C; CD_2Cl_2 as solvent. [c] At −73 °C; CD_2Cl_2 as solvent.



Scheme 3.

signals are only slightly shifted (0.6 p.p.m.) to low field in both cases when the temperature decreases. In all cases only one kind of signal is observed; this shows the existence of fluxional structures possibly passing through a pentaco-ordinate intermediate (Scheme 3).

Experimental

N.m.r. spectra were recorded with a JEOL FX90Q (^{11}B, ^{13}C) or a Varian EM-390 (^1H) spectrometer. Chemical shifts are given relative to BF_3•OEt_2 and Me_4Si, respectively. Mass spectra were obtained with a Hewlett-Packard 5985-A spectrometer, and i.r. spectra with a Nicolet MX-1FT spectrophotometer (KBr discs).

General Procedure for Reactions of 2-Acylpyridines, 2-Pyridylmethanols, and 2-Carboxypyridines with BH_3•THF *or* BH_3•Me_2S.—The amino ketone, amino alcohol, or amino acid was dissolved in THF and equimolecular amounts of borane were added dropwise at −78 °C. The course of the reaction was monitored by ^{11}B n.m.r.

2-*Hydroxymethylpyridine–borane* (**9a**) had m.p. 55—57 °C; δ_H(90 MHz; $CDCl_3$) 8.80 (1 H, d, *J* 6 Hz, H-6), 8.00 (1 H, t, *J* 5 Hz, H-4), 7.80 (1 H, d, *J* 5 Hz, H-3), 7.40 (1 H, t, *J* 6 Hz, H-5), and 5.05 (2 H, s, CH_2O); δ_B(28.7 MHz; THF) −14.0 (q, *J* 96 Hz); $\nu_{max.}$(KBr) 2 398 (B–H), 2 384 (B–H), 2 372 (B–H), and 1 059 cm^{-1} (B $\longleftarrow$ N); *m*/*z* 123 (3%, M^+), 124 (0.5, $M^+ + 1$), 122 (19), 119 (27), 121 (10), 120 (100), 92 (36), and 65 (15).

2-(β-Hydroxyethyl)pyridine–borane (**16**) showed δ_H(90 MHz; $CDCl_3$) 8.75 (1 H, d, *J* 6 Hz, H-6), 7.90 (1 H, t, *J* 7 Hz, H-4), 7.50 (1 H, d, *J* 7 Hz, H-3), 7.30 (1 H, t, *J* 7 Hz, H-5), 4.05 (2 H, t, *J* 7 Hz, CH_2O), and 3.40 (2 H, t, *J* 7 Hz, CH_2); δ_B(28.7 MHz; THF) −14.0 (q, *J* 90 Hz); $\nu_{max.}$(neat) 2 378 (B–H), 2 339 (B–H), and 1 052 cm^{-1} (N $\longrightarrow$ B); *m*/*z* 137 (0.2%, M^+), 134 (8), 122 (25), 107 (10), 106 (98), 105 (20), 104 (10), 94 (15), 93 (100), 92 (10), 80 (10), 79 (30), and 66 (20).

[2-Pyridylcarbonyloxy-*O*,*N*]borane (**20a**) had m.p. 161—162 °C; δ_H(90 MHz; C_2D_6SO) 9.2 (1 H, d, *J* 6 Hz, H-6), 8.60 (1 H, d, *J* 7 Hz, H-3), 8.50 (1 H, t, *J* 7 Hz, H-4), and 8.25 (1 H, t, *J* 7 Hz, H-5); δ_B(28.7 MHz; C_2D_6SO) 0.7 (t, *J* 118 Hz); $\nu_{max.}$(KBr) 2 418 (B–H), 1 355, and 1 053 cm^{-1} (N $\longrightarrow$ B); *m*/*z* 136 (0.3%, $M^+ + 1$), 135 (10, M^+), 134 (100), 133 (20), 107 (7), 106 (50), 105 (15), 79 (10), and 78 (62).

[6-Carboxy-2-pyridylcarbonyloxy-*O*,*N*]borane (**20b**) had m.p. 75—78 °C; δ_H(90 MHz; C_2D_6SO) 8.70 (2 H, m, H-5 and -3) and 8.30 (1 H, m, H-4); δ_B(28.7 MHz; C_2D_6SO) 2.0; $\nu_{max.}$(KBr) 2 452 (B–H) and 1 056 cm^{-1} (N $\longrightarrow$ B); *m*/*z* 178 (3%), 177 (1), 150 (3), 124 (10), 123 (100), 122 (10), 106 (10), 105 (93), 79 (10), 78 (30), 77 (55), 76 (25), 75 (10), and 46 (30).

Tris-[(N–B)-2-*pyridylmethyl*] *Borate* (**22**).—A solution of 2-pyridylmethanol (3.00 g, 27.0 mmol) in dry benzene (200 ml) was placed in a 250 ml flask equipped with stirrer and Dean–Stark trap. Boric acid (0.56 g, 9.1 mmol) was added and the mixture was kept under reflux for 8 h. Removal of the solvent *in vacuo* left compound (**22**) (3.30 g), δ_H(90 MHz; $CDCl_3$) 8.55 (1 H, d, *J* 6 Hz, H-6), 7.84 (1 H, t, *J* 6 Hz, H-4), 7.60 (1 H, d, *J* 6 Hz, H-3), 7.25 (1 H, d, *J* 6 Hz, H-5), and 4.95 (2 H, s, CH_2).

Tris-[(N–B)-2-(2-*pyridyl*)*ethyl*] *Borate* (**23**).—Compound (**23**) was prepared by the procedure described for (**22**). 2-(β-Hydroxyethyl)pyridine (3.00 g, 24.0 mmol) and boric acid (0.50 g, 8.1 mmol) gave (**23**) (3.2 g), δ_H(90 MHz; $CDCl_3$) 8.50 (1 H, d, *J*

4 Hz, H-6), 7.50 (1 H, t, J 6Hz, H-4) 6.90—7.20 (2 H, m, H-3 and -5), 4.00 (2 H, t, J 6 Hz, CH_2O), and 3.90 (2 H, t, J 6 Hz, CH_2).

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