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Syntheses and Characterization of (N→B)phenyl[N-arylaminodiacetate-O,O′,N]boranes and N-Arylaminodiacetic Acids

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ABSTRACT

The (N→B)phenyl[iminodiacetate-O,O′,N]borane **1** *is stable to hydrolysis, and the fact that the N-H proton has been shown to be more acidic than the α-protons to the carbonyl groups has led to the syntheses of N-substituted boron heterocycles. Thus, the reactions of compound* **1** *with 2,2,6,6-tetramethylpiperidine and aryl halides led to the syntheses of (N→B)phenyl[N-arylaminodiacetate-O,O′,N]boranes* **2–9**, *which were, in turn, hydrolyzed to afford the corresponding N-arylaminodiacetic acids* **10–17**. *All compounds studied in this work were characterized by ^{1}H, ^{13}C, and ^{11}B (for boron compounds) NMR, infrared, and mass spectroscopy.*

INTRODUCTION

We have been interested in the syntheses of bicyclic boron compounds derived from diethanolamines, iminodiacetic acids, and N-alkyl-N-(2-hydroxyethyl) glycines, as well as in studying the intramolecular N → B coordination [1–4]. The chemistry of the boron aminoacid derivatives has been little studied in spite of the high degree of hydrolytic stability and the fact that these derivatives are potentially useful for biological studies [2,5–10].

Recently, we reported the study of the reactivity of boron heterocycles derived from N-methylaminodiacetic acid and iminodiacetic acid with bases and alkyl halides [11].

We found that the boron heterocycles of N-methylaminodiacetic acid gave a mixture of α-alkylated compounds. No apparent reaction occurred on attempted alkylation of **1**, reported previously [1], because this compound decomposed readily to give phenylboronic acid and iminodiacetic acid. However, when lithium 2,6-dimethylpiperidide is used as the base, in the presence of tetramethylethylenediamine, the N-substituted boron heterocycles are obtained. This proved to be a new method for the synthesis of N-substituted boron heterocycles, which, in turn, can be hydrolyzed to give the corresponding N-substituted aminodiacetic acids. The latter are more expensive than iminodiacetic acid and only a few are commercially available. Moreover, several N-alkylamino acids have been found to be biologically active.

Consequently, a number of synthetic routes to N-alkylamino acids have been developed [12], but not for the syntheses of N-substituted aminodiacetic acids.

Our current interest in the use of boron heterocycles for the syntheses of new N-substituted aminodiacetic acids prompted us to extend these investigations to prepare N-aryl derivatives and also to modify the reaction conditions to improve the yields of both the boron heterocycles and the N-aryl aminodiacetic acids.

This article describes the syntheses and characterization by spectroscopic methods of

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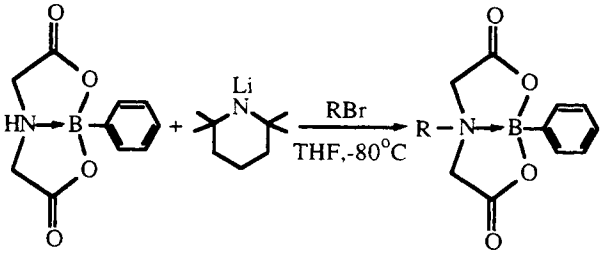


1

2 R=-Benzyl
3 R=-2-Methylbenzyl
4 R=-3-Methylbenzyl
5 R=-4-Methylbenzyl
6 R=-α-Methylbenzyl
7 R=-Phenethyl
8 R=-Phenacyl
9 R=-4-Chlorophenacyl

FIGURE 1 Synthesis of boron heterocycles **2–9**.

new (N→B)-phenyl[N-arylaminodiacetate-O,O',N]-boranes **3–9** and the corresponding N-arylaminodiacetic acids **11–17**.

Compound **2** has already been described in the literature [9,11]. Its ^{13}C NMR data were reported by us in a previous article [11], and its mass spectral data are given in this article. Compound **10** (cf. Table 1) is commercially available.

DISCUSSION

The reaction of (N→B)phenyl[iminodiacetate-O,O',N]borane **1** with lithium 2,2,6,6-tetramethylpiperidide and aryl halides led to (N→B)phenyl[N-arylaminodiacetate-O,O',N]boranes **2–9** (Figure 1). These compounds were obtained as white air-stable solids by recrystallization from methylene chloride/bexane.

The ^1H NMR spectra of compounds **2–9** exhibit the expected resonances (see Table I). These spectra clearly show the AB coupling pattern for the diastereotopic CH_2-COO protons, which indicates the presence of the intramolecular N→B coordination bond.

The ^1H NMR spectrum of compound **3** in DMSO-d_6 did not show the AB coupling pattern for the CH_2COO protons but instead a singlet signal at δ 4.2 with a chemical shift similar to these of the other bicyclic boron compounds (**2**, **4–9**).

However, after 24 hours, the spectra of **3** showed additional signals assigned to the N-arylaminodiacetic acid **11**, thus providing evidence that compound **3** is unstable in DMSO. Therefore, the spectra were obtained in CD_2Cl_2, which is a less polar solvent.

This spectrum showed the AB coupling pattern for the diastereotopic CH_2COO protons (see Table 1). The spectrum of compound **6** showed two AB coupling patterns for two diastereotopic $C\underline{H}_2$-COO protons. This can be explained to be attributable to the presence of a chiral carbon in the R group. The spectra of compounds **2–6** and **8** showed an unresolved pattern at δ 7.6 and 7.4 assigned to H (o) and H (m,p), respectively, for the B-phenyl group. In the case of compounds **7** and **9**, these signals are at δ 7.4, 7.5 and at 7.3, 7.4, respectively. The aromatic protons of the aryl groups show different coupling patterns (see Table 1), except for compound **2** where the signals are overlapped with those corresponding to the B-phenyl group and compound **4** where the signals of H (a) and H (e) are also overlapped with the signals of the B-phenyl group.

The $\delta(^{11}B)$ values (Table 1) confirm the tetrahedral environment of the ^{11}B nucleus, since they lie in the range reported previously for analogous boron heterocycles [1–4,11].

Table 2 shows that compounds **2–9** exhibit the expected ^{13}CNMR spectra.

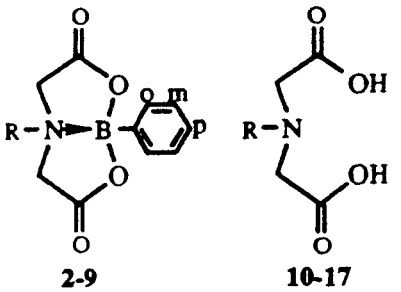
The assignments for C_1, C_2, C_o, C_m, and C_p for compounds **2–9** were achieved by comparison with the chemical shifts of bicyclic boron compounds reported by us previously [2,11]. The assignments for C_3 to C_{10} (N-R group): in compound **2** were deduced by comparison with the chemical shifts reported by us previously [11], while the assignments for compounds **3–9** were obtained using the ^{13}C-^1H HETCOR spectra, correlating the proton signals to the carbon signals. These spectra show the correlation between the proton signals of $C\underline{H}_2$-N from the R group and the signals due to C_3. In the case of compound **7**, the protons $C\underline{H}_2$-$C\underline{H}_2$-C_6H_5 show an unresolved pattern, which is correlated with carbon signals at δ 59.8 and 29.3 assigned to C_3 and C_4, respectively.

The spectra of compounds **3–6** exhibit the correlation of the proton signals of $C\underline{H}_3C_6H_4$ and C_6H_5 $CHC\underline{H}_3N$, respectively, with the signal assigned to C_{10}. The signals at δ 192.5 for **8** and 191.7 for **9** were assigned to C_4.

The carbons of the aromatic rings from the R groups exhibit the following correlations: for compound **3**, the signals of H (b–e) are correlated with C_6 to C_9, respectively; for compound **4**, the signal of H (c) is correlated with C_7 and H (d) with C_8. The assignments for C_5 and C_9 have been achieved by comparison with those given for compound **2**, because the signals of H (a, b) are overlapped with those of the B-Ph group. The spectrum of **5** shows correlations of H (a, b) with C_5 and C_9, and H (d, e) with C_6 and C_8. The spectra of compound **6** show the correlation of the double signal of H (a, e) with the signal at δ 128.6 assigned to C_5 and C_9. The assignment for C_6 to C_8 was achieved by comparison with the corresponding chemical shifts of compound **2**.

The assignment of C_5 to C_{10} for compound **7**

TABLE 1 ^{1}H and ^{11}B NMR Data for Compounds **2–17**



2-9

10-17

2, 10 R= -CH_2-(a, b, c, e, d)

3, 11 R= -CH_2-(CH$_3$ at b; a, b, c, e, d)

4, 12 R= -CH_2-(CH$_3$ at a; a, b, c, e, d)

5, 13 R= -CH_2-(CH$_3$ at b; a, b, c, e, d)

6, 14 R= -CH(CH$_3$)-(a, b, c, e, d)

7, 15 R= -CH_2-CH_2-(a, b, c, e, d)

8, 16 R= -CH_2-CO-(a, b, c, e, d)

9, 17 R= -CH_2-CO-(Cl at b; a, b, c, e, d)

Compound	*CH_3-Bz*	*$PhCH_2N$*	*CH_2COO*	*C_6H_5 or C_6H_4*	*B-C_6H_5*	*$\delta(^{11}B)N\rightarrow B$*
2		3.8(s)	H_A: 4.4(d) H_B: 3.9(d) J_{AB} = 16.5	a, e: 7.6 (m) b–d: 7.4(m)	7.6(m) H(o) 7.4(m) H(m, p)	+12.5
3[f]	2.3(s)	3.7(s)	H_A: 3.9(d) H_B: 3.6(d) J_{AB} = 16.5	b: 7.15(d) c: 7.3(t) d: 7.26 e: 7.33(d) J = 7.3	7.6(m) H(o) 7.4(m) H(m, p)	+11.6
4	2.3(s)	3.7(s)	H_A: 4.4(d) H_B: 3.9(d) J_{AB} = 17.2	a, c: 7.4(b) c: 7.2(d) d: 7.3(t) J = 7.3	7.6(b) H(o) 7.4(m) H(m, p)	+12.2
5	2.3(s)	3.7(s)	H_A: 4.4(d) H_B: 3.9(d) J_{AB} = 17.2	a, e: 7.5(d) b, d: 7.2(d) J = 7.9	7.6(m) H(o) 7.4(m) H(m, p)	+12.3
6[g]		4.0(q) J_{AB} = 16.5	H_A: 4.62(d) H_B: 4.17(d) J_{AB} = 18.0 H_A: 4.60(d) H_B: 3.45(d)	a, e: 7.5(d) b–d: 7.4(m) J = 7.3	7.6(m) H(o) 7.4(m) H(m, p)	+12.2
7[g]		2.8(m)	H_A: 4.5(d) H_B: 4.3(d) J_{AB} = 17.2	a, e: 7.03(d) b–d: 7.18(m) J = 7.0	7.4(m) H(o) 7.3(m) H(m, p)	+11.9
8		4.5(s)	H_A: 4.6(d) H_B: 4.3(d) J_{AB} = 17.2	a, e: 7.49(d) b, d: 7.53(t) c: 7.63(t) J = 7.3	7.6(m) H(o) 7.4(m) H(m, p)	+12.9
9		4.5(s)	H_A: 4.6(d) H_B: 4.3(d) J_{AB} = 17.2	a, e: 7.6(d) b, d: 7.5(d) J = 8.6	7.5(m) H(o) 7.4(m) H(m, p)	+12.2
10		3.8(s)	3.4(s)	a–e: 7.35(s)		
11	2.3(s)	3.8(s)	3.4(s)	b–d: 7.2(b) e: 7.3(b)		
12	2.3(s)	3.8(s)	3.4(s)	a: 7.15(s) c: 7.17(d) d: 7.08(t) e: 7.22(d) J = 7.25		
13	2.3(s)	3.8(s)	3.4(s)	a, e: 7.22(d) b, d: 7.13(d) J = 7.9		
14[g]	1.5(d) J = 6.6	4.3(q) J = 6.6	H_A: 3.5(d) H_B: 3.2(d) J = 16.5	a–e: 7.4(s)		

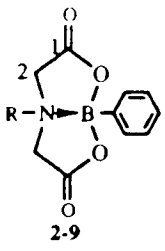
Continued

TABLE 1 Continued

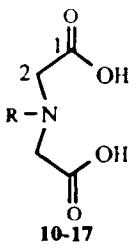
Compound	*CH_3-Bz*	*$PhCH_2N$*	*CH_2COO*	*C_6H_5 or C_6H_4*	*B-C_6H_5*	*$\delta(^{11}B)N\rightarrow B$*
15[h]		2.8(m)	3.2(s)	a, e: 7.5(d) b–d: 7.2(m) *J* = 7.0		
16		4.3(s)	3.5(s)	a, e: 8.0(d) b, d: 7.5(t) c: 7.6(t) *J* = 7.3		
17		4.3(s)	3.5(s)	a, e: 8.0(d) b, d: 7.6(d) *J* = 8.6		

$\delta(^1H)$ relative to $Si(CH_3)_4$; $\delta(^{11}B)$ relative to $BF_3 \cdot OC_2H_5$; solvent DMSO-d_6; [f]solvent CD_2Cl_2; [g]the CH_3CHN protons show a doublet at 1.3 and *J* = 6.6 Hz for compound **6**, and for compound **14**, a doublet signal at 1.5 with *J* = 6.6 Hz, and the chemical shift in the third column is given for CH_3 CHN; [h]the chemical shift in the third column is given for $-CH_2CH_2N$ protons; s: singlet; d: doublet; t: triplet; q: quartet; b: broad; m: unresolved pattern; and IJI: Hz.

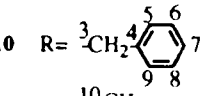
TABLE 2 ^{13}C NMR Data for Compounds **2–17**

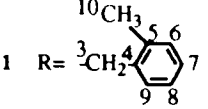


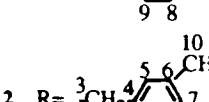
2-9

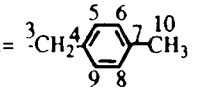


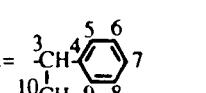
10-17

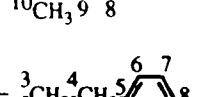
2, 10 R= 

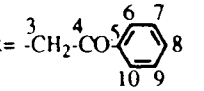
3, 11 R= 

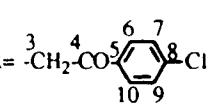
4, 12 R= 

5, 13 R= 

6, 14 R= 

7, 15 R= 

8, 16 R= 

9, 17 R= 

			R								*B-phenyl*		
Compound	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9	C_{10}	C_o	C_m	C_p
2	169.1	57.9	60.8	132.8	128.9	129.5	127.6	129.5	128.9	—	131.6	128.8	130.6
3[a]	168.0	58.5	58.6	132.5	138.6	130.8	128.0	127.6	130.2	19.8	132.8	128.8	130.9
4	169.1	58.0	60.9	138.2	130.2	132.2	127.6	128.7	128.9	20.9	132.8	128.6	130.4
5	169.1	57.9	60.7	139.1	129.4	127.5	131.5	127.5	129.4	20.7	132.8	127.6	128.9
6	169.8	59.6	65.7	135.0	128.6	129.5	129.5	129.5	128.6	15.1	132.4	127.7	128.9
	167.7	54.3	—	—	—	—	—	—	—	—	—	—	—
7	169.4	58.8	59.8	29.3	136.6	128.3	128.8	126.5	128.7	128.3	132.3	127.6	128.7
8	169.7	60.7	64.9	192.5	134.2	128.7	127.3	133.9	127.3	128.7	132.5	127.6	129.0
9	169.6	60.7	64.7	191.7	138.9	129.6	129.0	133.0	129.0	129.6	132.5	127.7	129.1
10	172.3	53.6	57.1	138.7	128.2	128.6	127.1	128.6	128.2	—	—	—	—
11	172.4	53.6	55.6	136.4	137.3	130.1	127.2	125.5	129.5	18.7	—	—	—
12	172.2	53.5	57.0	138.5	129.2	137.2	125.7	127.7	129.2	20.9	—	—	—
13	172.3	53.7	56.9	136.2	128.8	128.7	135.5	128.7	128.8	20.7	—	—	—
14[b]	172.5	65.1	71.6	148.7	138.6	138.4	138.4	138.4	138.6	26.2	—	—	—
15[b]	172.1	66.0	67.6	41.3	—	138.6	138.6	136.5	138.6	138.6	—	—	—
16	172.4	54.9	59.6	197.6	135.4	128.5	127.8	133.2	127.8	128.5	—	—	—
17	172.3	54.8	59.8	196.8	138.0	129.9	128.6	134.2	128.6	128.9	—	—	—

δ: (ppm): solvent DMSO-d_6: [a]solvent CD_2Cl_2: and [b]solvent D_2O.

TABLE 3 Infrared Data for Compounds **2–17**

Compound	*O-H*	*C-H Atom*	*C-Halif*	*C=O*	*B-O*	*N→B*
						1028
2		3066	2949	1778	1296	986
						1028
3		3014	2932	1768	1288	990
						1028
4		3014	2954	1770	1294	990
						1028
5		3014	2954	1770	1292	990
6		3054	2936	1768	1282	1026
						1026
7		3020	2940	1762	1244	992
				1752		1028
8		3016	2934	1684[a]	1238	988
				1764		1032
9		3018	2962	1694[a]	1302	954
10	3433	3100	2932	1640		
				1748		
11	3434	3002	2933	1606		
			2966	1728		
12	3432	3033	2933	1636		
				1732		
13	3418	3026	2926	1644		
14[b]		3017	2938	1640		
15[b]		3024	2930	1610		
				1716		
16	3432	3033	2942	1638		
				1668		
17	3434	3094	2994	1590		

ν(cm^{-1}), KBr, [a] ν_{CO} phenacyl group, and [b] N-arylaminodiacetate sodium salt.

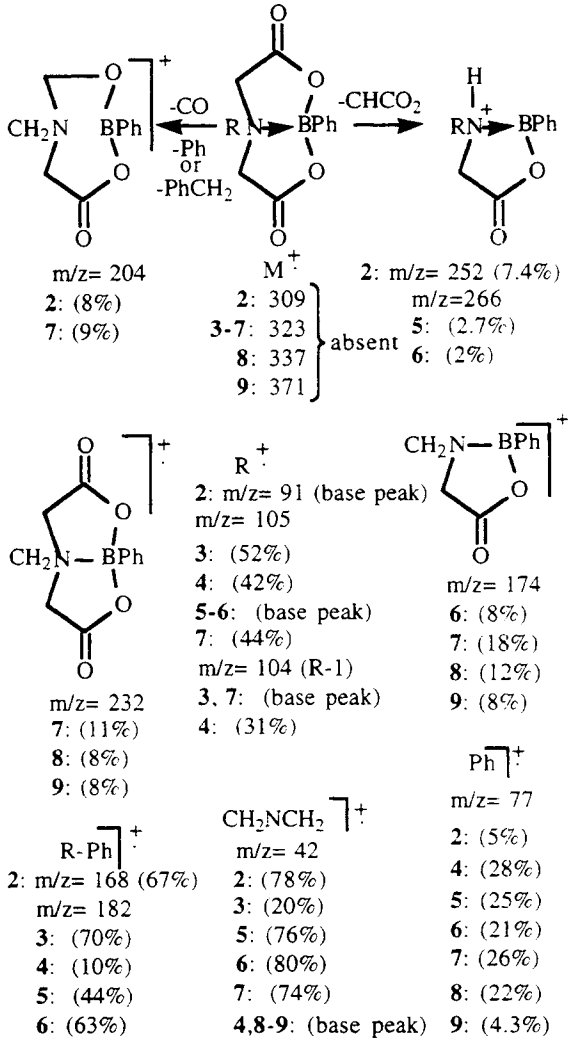


FIGURE 2 Mass spectral data of boron heterocycles **2–9**.

were achieved by comparison with those given for compound **2**.

The spectra of **8** show correlations between H (a, e), H (b, d), and H (c) with C_6, C_{10}; C_7, C_9; and C_8, respectively. For compound **9**, there is a correlation between the signal assigned to H (a, e) with the signal at δ 129.6 for C_6 and C_{10}, and the signal for H (b, d) is correlated with the signal at δ 129.0 for C_7 and C_9.

The IR spectra of the various compounds (see Table 3) show a band due to the carbonyl functions of the ester ($\nu \cong 1770$ cm^{-1}), a band due to the presence of the B-O group in the range of 1288–1302 cm^{-1}, and two bands due to the presence of the N→B group at 990 and 1028 cm^{-1}, these bands being also indicative of bicyclic compounds.

The 70 eV EI mass spectra of compounds **2–9** do not exhibit the molecular ion.

The following important fragment ions are observed. Spectrum of **2** exhibits a fragment ion at m/z = 252 (7.4%), and spectra of **5** and **6** exhibit a fragment ion at m/z = 266 with relative abundances of 2.7 and 2%, respectively, corresponding to the loss of the $-CHCO_2$ group from the molecular ion. Compounds **2** and **7** show the fragment ion at m/z = 204 with relative abundances of 8 and 9%, respectively, which correspond to the loss of CO and Ph (from **2**) and $PhCH_2$ (from **7**) (see Figure 2). The spectra show the corresponding base peak at m/z = 91 for compound **2**; m/z = 104 (R − 1) for compounds **3** and **7**; m/z = 42 for compounds **4**, **8**, and **9**; and m/z = 105 for compounds **5** and **6**. The fragment ion (C_2H_4N) at m/z = 42 is also observed for compounds **2** (78%), **3** (20%), **5** (76%), **6** (80%), **7** (74%). A fragment ion at m/z = 91 (17%) is also exhibited for compounds **5** (17%), **7** (84%), **8** (67%), and **9** (66%). Compounds **3** and **4** also show the fragment ion at m/z = 105 (52%) and (42%), respectively. The spectra of compounds **2** and **4–9** show the fragment ion at m/z = 77. Another radical ion observed for compounds **2–6** is apparent from the coupling between the R and Ph groups, for compound **2** at m/z = 168 and for compounds **3–6** at m/z = 182 with the following relative abundances: (70%), (10%), (44%), and (63%), respectively. The $[R - 1]^+$ fragment ion is also observed for compounds **4** (31%), **5** (12%), and **6** (11%).

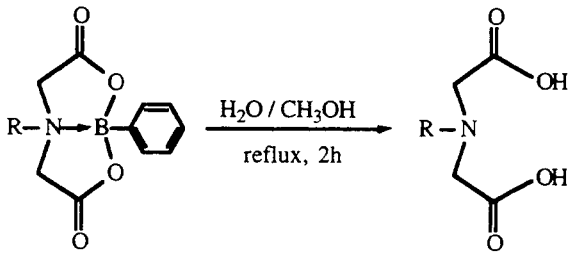


FIGURE 3 Synthesis of N-arylaminodiacetic acids.

The fragment ion at m/z = 174 is observed for compounds **6–9** with the following relative abundances: (8 %), (18%), (12%), and (8%), respectively, corresponding to the loss of CH_2CO_2 and the aromatic part of the R group. The fragment ion at m/z = 106 corresponding to R + **1** is exhibited for compounds **3** (10%), **4** (15%), **5** (45%), and **6** (16%). Compound **6** shows a fragment ion at m/z = 252 (18%) by the loss of $CHCO_2$ and CH_3 groups from the molecular ion. Compounds **7–9** show a fragment ion at m/z = 232 corresponding to the loss of $PhCH_2$ (11%), PhCO (8%), and p-ClC_6H_4CO (8%), respectively, from the molecular ion. Figure 2 shows the fragment ions proposed for compounds **2–9**.

Hydrolysis of compounds **2–5**, **8** and **9** gives the N-aryliminodiacetic acids **10–13**, **16** , and **17**, respectively, (Figure 3). Compounds **6** and **7** were shown to be stable to the hydrolysis under conditions shown in Figure 3. These compounds could be hydrolyzed with an aqueous solution of sodium hydroxide to give the N-aryliminodiacetate disodium salts **16** and **17**, respectively.

Table 1 shows the ^1H NMR spectra of compounds **10–17**, and they exhibit the expected resonances. These compounds show a single signal for $C\underline{H}_2$-COOH protons, except 14, which shows an AB coupling pattern due to the presence of a chiral carbon in the R group. The ^1H NMR spectra of **10–17** show the following coupling pattern for the aromatic protons: **10** and **14**, a single signal; **11**, two broad signals (H_{b-d} and H_e); **12**, a singlet (H_a), a triplet signal (H_d), and two doublets (H_c and H_e); **13** and **17**, two doublets (H_a, H_e and H_b, H_d); **15**, a doublet (H_a, H_e) and an unresolved pattern (H_b, H_d); **16**, a doublet (H_a, H_e) and two triplets (H_b, H_d, and H_c).

Table 2 shows the expected ^{13}C NMR spectra for compounds **10–17**. The assignments for C_1 to C_{10} were achieved in the same way as for compounds **2–9**.

Table 3 shows infrared data for compounds **10–17**.

The infrared absorption of the carbonyl functions are indicative of the presence of carboxylic acid groups.

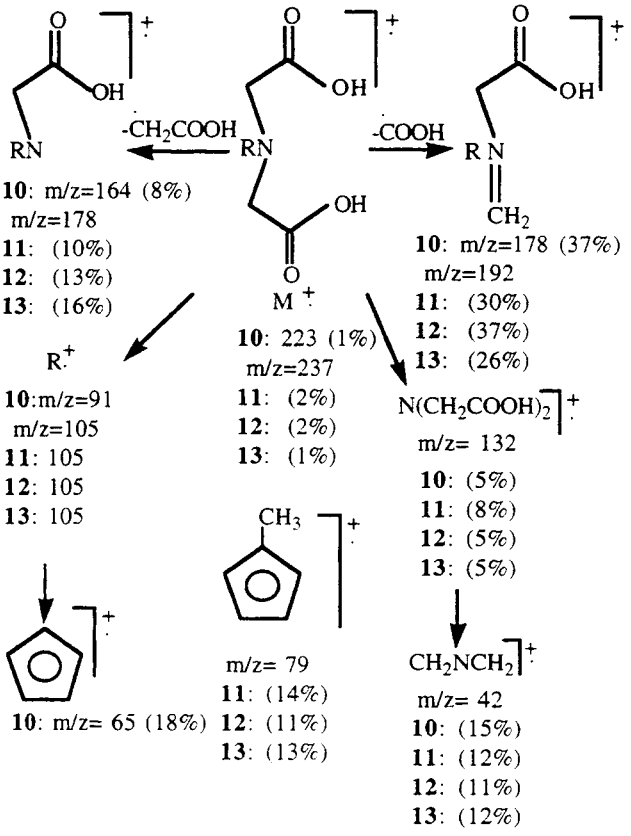


FIGURE 4 Mass spectra data for compounds **10** to **13**.

The 70 eV EI mass spectra of compounds **10–13** exhibit the following fragmentations: the loss of COOH, the loss of CH_2COOH, and the loss of R (base peak), followed by the loss of two COOH groups. The fragmentation pattern proposed for compounds **10–13** is given in Figure 4. Compounds **14–17** show different fragmentation patterns compounds **14** and **15** exhibit the following important fragment ions: the base peak at m/z = 44 [CO], m/z = 18 [H_2O] with (92%) relative abundance for both compounds, m/z = 57 $[CH_3CH_2NCH_2]^+$ with the following relative abundances: (18%) and (10%); the fragment ion at m/z = 149 [$PhCHCH_3NCHO$] and [$PhCH_2CH_2NCHO$] with (3%) and (5%) relative abundances, respectively. Compound **14** also exhibits the following fragment ions; m/z = 60 (6%) $[(CH_3)_3NH]^+$, m/z = 43 (12%) [$NHCHCH_3$], and m/z = 41 (12%) $[NCCH_3]^+$.

Mass spectra of compounds **16** and **17** exhibit the following fragment ions: the base peak at m/z = 42 $[CH_2NCH_2]^+$, m/z = 88 $[CH_3NCH_2CO_2H]$ with relative abundances of (40%) and (47%), m/z = 60 $[(CH_3)_3NH]^+$ with (20%) and (17%), m/z = 58 $[(CH_3)_2NCH_2]^+$ with (20%) and (3%), m/z = 18 [H_2O] with (39%) and (85%), respectively. Compound **17** also shows the following fragment ions: m/z = 146 (32%) $[CH_2N(CH_2COOH)_2]^+$, m/z = 139 (10%) $[ClC_6H_4CO]^+$, and m/z = 75 (15%) $[NH_2CH_2CO_2H]^+$.

EXPERIMENTAL

NMR spectra were recorded on a Jeol GLX-270 spectrometer. All ^{1}H and ^{13}C chemical shifts are reported relative to TMS and ^{11}B relative to $BF_3OC_2H_5$, using DMSO-d_6 as solvent. Mass spectra were obtained with a Hewlett-Packard 59940-A instrument, and infrared spectra were determined on a Perkin-Elmer 16F PC FT-IR spectrometer. Melting points were taken in open capillary tubes on a Gallenkamp MFB-595 apparatus and are uncorrected. Solvents were dried by standard methods and distilled prior to use. Reagents were purchased from Aldrich Co. (Milwaukee, WI). The bicyclic organylboronate **1** was prepared as described previously [2].

The procedure outlined in the following paragraph is general for the preparation of compounds **2–9**.

Synthesis of (N → B)phenyl[N-benzylaminodiacetate-O,O',N]borane **2**

A solution of 3.1 mmol of *n*-butyllithium (2.5 M) in hexane was added dropwise to a stirred solution of 0.54 mL (3.1 mmol) of 2,2,6,6-tetramethylpiperidine in 10 mL of THF at 0°C. The solution was stirred 15 minutes at 0°C and 15 minutes at room temperature and then cooled with a Dry Ice acetone bath to −80°C. In another flask, a solution of 0.70 g (3.1 mmol) of (N→B)phenyl[iminodiacetate-O,O',N]borane **1** in 70 mL of THF was cooled to −80°C, and the first solution was transferred to this dropwise. The reaction mixture was stirred 2 hours at −80°C followed by addition of 0.38 mL (3.1 mmol) of benzyl bromide. The reaction mixture was stirred 4 hours at −80°C. After being warmed to room temperature, the solvent was evaporated under vacuum. The yellow solid was treated with CH_2Cl_2. The solution was filtered and the solvent was evaporated under vacuum. The remaining solid was recrystallized from dichloromethane/hexane to yield 0.35 g (35%) of compound **2**, mp 227–228°C.

(N→B)phenyl[N-(2-methylbenzyl)-aminodiacetate-O,O',N]borane **3**

The reaction of 0.50 g (2.28 mmol) of compound **1**, 0.9 mL (2.5M) of *n*-BuLi, and 0.30 mL (2.28 mmol) of 2-methylbenzyl bromide gave 0.21 g of compound **3** (33%), mp 215°C.

(N→B)phenyl[N-(3-methylbenzyl)-aminodiacetate-O,O',N]borane **4**

A 0.50 g (2.28 mmol) amount of compound **1**, 0.91 mL (2.5 M) of *n*-Buli, and 0.31 mL (2.28 mmol) of 3-methylbenzyl bromide gave 0.25 g of compound **4** (34%), mp 223–225°C.

(N→B)phenyl[N-(4-methylbenzyl)-aminodiacetate-O,O',N]borane **5**

A 0.90 g (4.10 mmol) amount of compound **1**, 1.64 mL (2.5 M) of *n*-BuLi, and 0.76 g (4.10 mmol) of 4-methylbenzyl bromide gave 0.49 g of compound **5** (37%), mp 219–221°C.

(N→B)phenyl[N-(α-methylbenzyl)-aminodiacetate-O,O',N]borane **6**

One (1.00) g (4.56 mmol) of compound **1**, 1.83 mL (2.5 M) of *n*-BuLi, and 0.62 mL (4.56 mmol) of phenacyl bromide gave 0.47 g of compound **6** (32%), mp 263–265°C.

(N→B)phenyl[N-(phenethyl)aminodiacetate-O,O',N]borane **7**

One (1.00) g (4.56 mmol) of compound **1**, 1.83 mL (2.5 M) of *n*-BuLi, and 0.62 mL (4.56 mmol) of phenacyl bromide gave 0.39 g of compound **7** (27%), mp 209–211°C.

(N→B)phenyl[N-(phenacyl)aminodiacetate-O,O',N]borane **8**

0.50 g (2.28 mmol) of compound **1**, 0.91 mL (2.5 M) of *n*-BuLi, and 0.45 g (2.28 mmol) of phenacyl bromide gave 0.26 g of compound **8** (34%), mp 257–258°C.

(N→B)phenyl[N-(4-chlorophenacyl)-aminodiacetate-O,O',N]borane **9**

0.50 g (2.28 mmol) of compound **1**, 0.91 mL (2.5 M) of *n*-BuLi, and 0.53 g (2.28 mmol) of 4-chlorophenacyl bromide gave 0.25 g of compound **9** (30%), mp 225–226°C.

The procedure outlined in the following paragraph is general for the syntheses of compounds **10–13**, **16**, and **17**.

Synthesis of N-benzylaminodiacetic Acid **10**

A mixture of methanol/water (50:50) was added to 0.2 g (0.64 mmol) of (N→B)phenyl[N-benzylaminodiacetate-O,O',N]borane **2**. The reaction mixture was refluxed during 2 hours. The solvent was eliminated by vacuum distillation, and the solid obtained was recrystallized from acetone to yield 0.11 g of compound **10** (80%), mp 187–188°C.

N-(2-methylbenzyl)aminodiacetic Acid **11**

A 0.34 g (1.0 mmol) amount of compound **3** gave 0.20 g of compound **11** (80%) mp 189–191°C.

N-(3-methylbenzyl)aminodiacetic Acid **12**

A 0.15 g (0.46 mmol) amount of compound **4** gave 0.90 g of compound **12** (82%), mp 175–176°C.

N-(4-methylbenzyl)aminodiacetic Acid **13**

A 0.26 g (0.80 mmol) amount of compound **5** gave 0.19 g of compound **13** (0.79%), mp 198–200°C.

N-(phenacyl)aminodiacetic Acid **16**

A 0.16 g (0.47 mmol) amount of compound **8** gave 0.09 g of compound **16** (81%), mp 231–232°C.

N-(4-chlorophenacyl)aminodiacetic Acid **17**

A 0.10 g (0.40 mmol) amount of compound **9** gave 0.10 g of compound **17** (87%), mp 198°C.

The following procedure is general for the syntheses of compounds **14** and **15**.

Synthesis of N-(α-methylbenzyl)iminodiacetate Disodium Salt **14**

A solution of 0.05 g of sodium hydroxide in 5 mL of water was added to a stirred suspension of 0.2 g (0.62 mmol) of **6**. The solution was stirred 6 hours at room temperature, and the solvents were evaporated under vacuum. The white solid that resulted was treated with 10 mL of THF/MeOH (3:5). The solution was filtered and the solvents were evaporated under vacuum. The remaining solid was recrystallized from acetone to yield 0.11 g (63%) of compound **14**.

N-(phenethyl)iminodiacetate Disodium Salt **15**

From 0.15 g (0.46 mmol) of compound **7**, there was obtained 0.06 g of compound **15** (55%).

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