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NMR Studies of 1,1-Diphenylboroxazolidone Derivatives of α-Aminoacids

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ABSTRACT

*A series of twelve 1,1-diphenylboroxazolidones (**1b–12b**) prepared from α-aminoacids and diphenylborinic acid were studied using one- and, in some cases, two-dimensional (HETCOR) NMR techniques. Interpretation of these spectra led to definitive assignment of all carbon, hydrogen, and boron resonances.*

INTRODUCTION

Boroxazolidones (also known as esters or mixed anhydrides of aminoacids and dialkyl or diarylborinic acids) are neutral complexes obtained by reaction of α-aminoacids with borinic acids. These compounds are characterized by a coordinating N → B bond, and their stability has been attributed to the formation of five-membered rings [1].

To our knowledge, spectroscopic analysis of these derivatives described in the literature includes ^{1}H NMR data on aspartic and glutamic derivatives [2], a systematic mass spectrometric study of all diphenyl derivatives of the essential α-aminoacids [3], and an X-ray diffraction study of the boroxazolidone derivative of proline [4]. Thus, the aim of this study is to perform a systematic NMR study (^{1}H, ^{13}C, and ^{11}B) of 12 boroxazolidones. These compounds have been shown to have practical applications due to their broad insecticidal, fungicidal, and herbicidal activity [5], as well as other applications as intermediates in asymmetric hydroboration [6] and in the synthesis of isoquinolines and isoindolines [7].

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RESULTS

The boroxazolidones described in this study (**1b–12b**) were prepared by reaction of glutamic acid (**1a**), lysine (**2a**), glycine (**3a**), isoleucine (**4a**), leucine (**5a**), methionine (**6a**), threonine (**7a**), aspartic acid (**8a**), phenyl-glycine (**9a**), tyrosine (**10a**), serine (**11a**), and proline (**12a**) with diphenyl-borinic acid. In all cases, the commercially available diphenylborinic acid ethanolamine complex was hydrolyzed with HCl previous to reaction [8].

The ^{13}C and ^{11}B NMR data of all compounds studied are summarized in Table 1, while the ^{1}H NMR data are included in the experimental section. In all cases, formation of the corresponding boroxazolidone was confirmed by the appearance of a signal between δ +3.0 and +6.7 in the ^{11}B NMR spectrum.

Observation of Table 1 shows that the carbonyl carbon in **1b–12b** shows chemical shifts in the range of δ 172–174. The aromatic carbon signals from the diphenylboronic group also show constant chemical shifts and can be assigned based on multiplicity and comparison with similar compounds [1]. Thus, the *ipso* to boron carbons are observed in all cases as broad signals in the range of δ 147–148, the *ortho* carbons appear around δ 131, the *meta* carbons around δ 127, and the *para* carbons between δ 126–127. With the exception of glycine, all boroxazolidone derivatives show diastereotopic signals for the aromatic carbons due to the existence of an asymmetric center at the 2 position. As expected, the main variations in chemical shifts are due to C-2 where the different substituents are introduced.

In general, the methodology used for the assignment of the ^{1}H and ^{13}C NMR spectra of all compounds includes assignment of the ^{1}H NMR spectrum based on selective homonuclear or het-

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TABLE 1 ^{13}C and ^{11}B NMR Data for Boroxazolidones **1b–12b** (ppm) in DMSO-d_6

Compound	$B-C_6H_5$ *i*	*o*	*m*	*p*	C-1	C-2	C-3	C-4	C-5	C-6		^{11}B
	147.7	130.9	127.0	126.9								
1b[a]	147.2	130.8	127.9	125.9	174.0[b]	54.0	24.9[c]	29.7	173.8	—		+4.4
	148.1	131.0	127.1	126.0								
2b	147.7	130.9	127.0	125.9	174.4	55.2	29.4[c]	23.0	32.3[c]	41.0		+5.4
3b	147.4	130.9	127.0	126.3	172.4	42.9	—	—	—	—		+6.2
	147.8	131.2	126.9	125.9								
4b[a]	—	131.1	126.8	125.8	173.2	59.2	34.9	14.9	24.7	11.2		+3.6
	147.9	131.0	127.0	125.9								
5b	147.5	130.9	126.9	125.8	174.5	53.3	38.5[c]	23.8[c]	22.8	20.8		+5.6
	147.8	130.9	127.0	125.9								
6b[a]	147.3	130.8	126.9	125.8	173.9	53.5[c]	28.8	29.4[c]	14.1	—		+3.9
	147.8	131.3	127.0	125.9								
7b[a]	147.2	131.2	126.9	—	172.6	60.5	63.8[c]	20.6	—	—		+3.9
	147.4	131.0	127.0	126.0								
8b	146.9	—	126.9	125.9	173.3[b]	51.7	33.7	171.7	—	—		+4.9
									$C-C_6H_5$			
	147.8	131.2	127.2	126.1				*i*	*o*	*m*	*p*	
9b	147.6	131.1	127.0	126.0	172.7	58.9	—	134.3	129.2	128.3	128.5	+5.9
									$CH_2-C_6H_4OH$			
10b	148.1	131.3	127.1	126.0	173.7	57.1	34.4	*i'*	*o'*	*m'*	*p'*	
	147.3	130.9	127.0	125.9	175.0	57.3	37.5	127.1	130.3	115.4	156.3	+3.0
	147.7	131.0	126.9	125.9								
11b	147.3	130.9	—	—	172.3	57.3	58.7					+3.6
	147.6	131.2	127.1	126.1								
12b[a]	145.6	130.8	127.0	—	174.5	62.1[c]	27.3	24.8	50.0[c]	—	—	+6.7

[a]Confirmed by HETCOR.
[b]Confirmed by heteronuclear selective decoupling of NH_2 in the ^{13}C NMR spectrum.
[c]Confirmed by decoupling adjacent protons in the ^1H NMR spectrum.

eronuclear decoupling techniques, followed by correlation using HETCOR ^1H-^{13}C experiments, as described for **1b**.

Assignment of the ^1H NMR spectrum of **1b** was attained by homonuclear decoupling of the H-2 methine which induces changes at the signals at δ 2.04 and 1.84 (H-3 and H-3'). This was confirmed by irradiation of the signal at 2.46 (H-4) which gives rise to a pair of double doublets for H-3 and H-3'. This, in turn, allowed us to assign to the corresponding carbon signals from a bidimensional HETCOR spectrum the values shown in Table 1. Finally, assignment of the C-1 and C-5 carbonyl signals was attained by irradiation of the NH_2 group which shows that the multiplet at lower field in the ^{13}C coupled spectrum loses couplings and thus corresponds to C-1.

CONCLUSIONS

Unequivocal assignment of the ^1H and ^{13}C NMR spectra of 12 diphenylboroxazolidones (**1b–12b**) was attained by HETCOR and selective homonuclear and heteronuclear decoupling experiments. The existence of an asymmetric carbon at position 2 in all derivatives except for glycine is evidenced by the diastereotopic signals of the phenyl group in both the ^1H and ^{13}C spectra. In agreement with previous reports [7], heterocyclic five-membered rings are formed even in those cases where six- or seven-membered rings are possible (glutamic and aspartic acids).

EXPERIMENTAL

The ^{11}B NMR spectra were determined on a Jeol FX90Q spectrometer in DMSO-d_6 solution using $BF_3 \cdot OEt_2$ as an external reference. The ^1H and ^{13}C NMR spectra were obtained on a Jeol GSX-270 instrument in DMSO-d_6 using TMS as an internal reference. The IR spectra were measured on a Nicolet MX-1FT spectrophotometer using KBr. Melting points were determined on a Gallenkamp MFB-595 apparatus and are uncorrected.

L-Glutamic acid (**1a**), L-lysine (**2a**), L-glycine (**3a**), L-isoleucine (**4a**), L-leucine (**5a**), L-methionine (**6a**), L-threonine (**7a**), L-aspartic acid (**8a**), L-phenylglycine (**9a**), L-tyrosine (**10a**), L-serine (**11a**), and L-proline are commercially available products.

Diphenylborinic acid was prepared from the corresponding ethanolamine complex, as described in the literature [8].

In all cases, equimolar amounts of diphenylborinic acid in (a) methanol, (b) ethanol, (c) methanol-water (5:1), or (d) ethanol-water (5:1) were mixed and heated for 5 hours and the solid product that formed was collected by filtration.

Diphenyl(glutamate-O,N)borane (**1b**). (a) 66% Yield; mp 169–170°C; IR ν_{max} (KBr): 3450, 3250, 3100, 1711 (C=O), 1433, 1252, 975, and 712 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.43 (dd, J = 11, 9 Hz, 1H, NH), 7.38 (d, J = 8 Hz, 4H, H *ortho*), 7.22 (2 t, J = 8, Hz, 4H, H *meta*), 7.16 (2 d, J = 7, 2H, H *para*), 6.77 (dd, J = 11, 9 Hz, 1H, NH'), 3.58 (quint, J = 5 Hz, 1H, H-2), 2.46 (t, J = 7 Hz, 2H, H-4), 2.04 (sext, J = 5 Hz, 1H, H-3), and 1.84 (sext, J = 7 Hz, 1H, H-3').

Diphenyl(lysinate-O,N)borane (**2b**). (d) 58% Yield; mp 192–193°C; IR ν_{max} (KBr): 3171, 3135, 2930, 1712 (C=O). 1631, 1433, 1291, 950, 762, and 703 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.46 (t, J = 7 Hz, 1H, NH), 7.44 (d, J = 7 Hz, 2H, H *ortho*), 7.39 (d, J = 7 Hz, 2H, H *ortho'*), 7.24 (2 t, J = 7 Hz, 4H, H *meta*), 7.16 (t, J = 7 Hz, 1H, H *para*), 7.14 (t, J = 7 Hz, 1H, H *para'*), 7.04 (t, J = 7 Hz, 1H, NH'), 3.50 (q, J = 5 Hz, 1H, H-2), 2.55 (quint, J = 6 Hz, 2H, H-6), 3.25 (b, 2H, NH_2), 1.85–1.65 (m, 1H, H-3), 1.65–1.50 (m, 1H, H-3'), and 1.50–1.20 (m, 4H, H-4,4',5,5').

Diphenyl(glycinate-O,N-borane) (**3b**). (d) 26% Yield; mp 242–245°C; IR ν_{max} (KBr): 3425, 3244, 3072, 1721 (C=O), 1600, 1433, 1302, 1220, 963, 750, and 704 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.38 (d, J = 7 Hz, 4H, H *ortho*), 7.22 (t, J = 7, 4H, H *meta*), 7.14 (t, J = 7 Hz, 2H, H *para*), 7.06 (bt, 2H, NH), and 3.43 (t, J = 6 Hz, 2H, H-2).

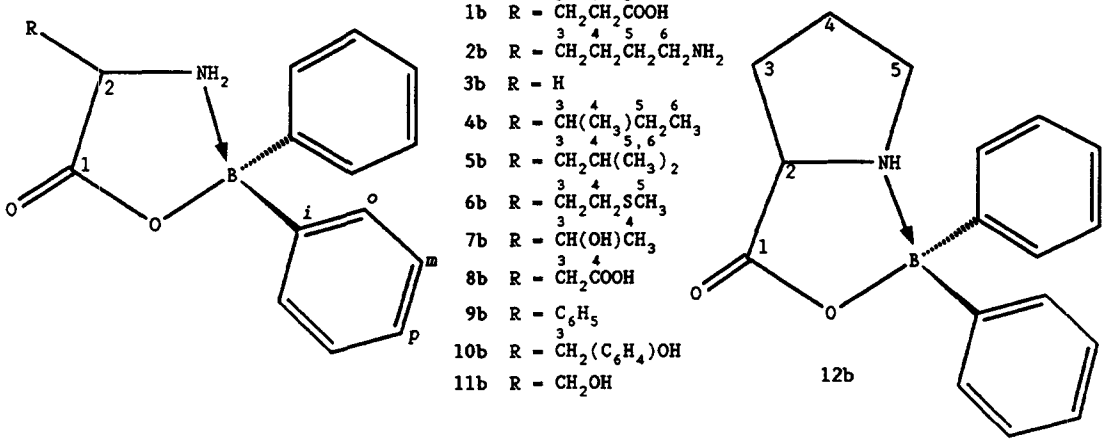
Diphenyl(isoleucinate-O,N)borane (**4b**). (b) 88% Yield; mp 221–223°C; IR ν_{max} (KBr): 3447, 3275, 3075, 2925, 1700 (C=O), 1437, 1267, 950, and 668 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.42 (d, J = 7 Hz, 4H, H *ortho*), 7.27 (dd, J = 12, 8 Hz, 1H, NH), 7.20 (t, J = 7 Hz, 4H, H *meta*), 7.12 (t, J = 7 Hz, 2H, H *para*), 7.14 (t, J = 7 Hz, 1H, H *para'*), 6.29 (dd, J = 12, 8 Hz, 1H, NH'), 3.46 (q, J = 6 Hz, 1H, H-2), 1.90–1.75 (m, 1H, H-3), 1.55–1.35 (m, 1H, H-5), 1.35–1.15 (m, 1H, H-5'), 0.94 (d, J = 7 Hz, 3H, CH_3 – 4), and 0.75 (t, J = 7 Hz, 3H, CH_3-6).

Diphenyl(leucinate-O,N)borane (**5b**). (b) 100% Yield; mp 171–174°C; IR ν_{max} (KBr): 3426, 3305, 3302, 1719 (C=O), 1641, 1437, 1266, 962, and 700 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.40 (d, J = 7 Hz, 4H, H *ortho*), 7.31 (bd, J = 12 Hz, 1H, NH), 7.21 (t, J = 7, 4H, H *meta*), 7.15 (td, J = 7, 2 Hz, 1H, H *para*), 7.12 (td, J = 7, 2 Hz, 1H, H *para'*), 6.69 (bd, J = 12 Hz, 1H, NH), 3.46 (q, J = 7 Hz, 1H, H-2), 1.90–1.76 (m, 1H, H-4), 1.64–1.45 (m, 2H, H-3), 0.85, and 0.82 (2 d, J = 7 Hz, 6H, CH_3-5,6).

Diphenyl(methionate-O,N)borane (**6b**). (d) 78% Yield; mp 222–224°C; IR ν_{max} (KBr): 3429, 3306, 2925, 1715 (C=O), 1640, 1537, 1437, 1275, 962, and 700 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.41 (d, J = 7 Hz, 4H, H *ortho*), 7.23 (2 t, J = 7 Hz, 4H, H *meta*), 7.15 (t, J = 7 Hz, 1H, H *para*), 7.13 (t, J = 7 Hz, 1H, H *para'*), 6.80 (t, J = 10 Hz, 1H, NH), 3.75–3.56 (m, 1H, H-2), 2.74–2.50 (m, 2H, H-4), 2.12–1.84 (m, 2H, H-3), and 1.98 (s, 3H, CH_3-5).

Diphenyl(threoninate-O,N)borane (**7b**). (d) 58% Yield; mp 202–203°C; IR ν_{max} (KBr): 3410, 3076, 2930, 1718 (C=O), 1642, 1433, 1274, 945, and 742 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.43 (d, J = 7 Hz, 4H, H *ortho*), 7.22 (2 t, J = 7, 4H, H *meta*), 7.16 (t, J = 7 Hz, 1H, H *para*), 7.14 (t, J = 7 Hz, 1H, H *para'*), 5.77 (t, J = 10 Hz, 1H, NH), 5.41 (d, J = 5 Hz, 1H, OH), 4.07 (m, 1H, H-3), 3.55 (sext, J = 4 Hz, 1H, H-2), and 1.19 (d, J = 7 Hz, 3H, CH_3-4).

Diphenyl(aspartate-O,N)borane (**8b**). (a) 17%



Yield; decomp. 275°C; IR ν_{max} (KBr): 3072, 2358, 1724 (C=O), 1590, 1434, 1392, 1298, 1222, 952, and 704 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.43 (d, J = 8 Hz, 4H, H *ortho*), 7.37 (t, 1H, NH), 7.22 (t, J = 7 Hz, 4H, H *meta*), 7.16 (t, J = 7 Hz, 1H *para*), 7.14 (t, J = 7 Hz, 1H, H *para'*), 6.80 (t, J = 11 Hz, 1H, NH'), 3.77 (sext, J = 6 Hz, 1H, H-2), and 2.78 (d, J = 6 Hz, 2H, H-3).

Diphenyl(phenylglycinate-O,N)borane (**9b**). (b) 29% Yield; mp 168–170°C; IR ν_{max} (KBr): 3450, 2925, 1718 (C=O), 1653, 1562, 1450, 1262, 963, 687, and 668 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.92 (dd, J = 12, 8 Hz, 1H, NH), 7.47, and 7.41 (2 d, J = 7 Hz, 4H, H *ortho*) 7.28 (s, 5H, H *aromatic*), 7.23 (t, J = 9 Hz, 4H, H *meta*), 7.14 (t, J = 9 Hz, 1H, H *para*), 7.12 (t, J = 9 Hz, 1H, H *para'*), and 4.74 (t, J = 8 Hz, 1H, H-2).

Diphenyl(tyrosinate-O,N)borane (**10b**). (b) 21% Yield; mp 149–150°C; ^1H NMR (DMSO-d_6) δ 9.34 (b, 1H, OH), 7.43, and 7.41 (2 d, J = 7 Hz, 4H, H *ortho*), 7.22 (t, J = 7 Hz, 2H, H *meta*), 7.20 (t, J = 7 Hz, 2H, H *meta'*), 7.17 (t, J = 7 Hz, 1H, H *para*), 7.14 (t, J = 7 Hz, 1H, H *para'*), 7.06 (d, J = 8 Hz, 2H, H-5), 6.72 (d, J = 8 Hz, 2H, H-6), 6.64 (t, J = 8 Hz, 1H, NH), 3.68–3.54 (m, 1H, H-2), 3.06 (dd, J = 14, 3 Hz, 1H, H-3), and 2.83 (dd, J = 14, 10 Hz, 1H, H-3').

Diphenyl(serinate-O,N)borane (**11b**). (c) 36% Yield; mp 259–260°C; ^1H NMR (DMSO-d_6) δ 7.4 (d, J = 7 Hz, 4H, H *ortho*), 7.21 (t, J = 7 Hz, 4H, H *meta*), 7.15 (t, J = 7 Hz, 1H, H *para*), 7.13 (t, J = 7 Hz, 1H, H *para'*), 6.28 (dd, J = 11, 8 Hz, 1H, NH), 5.25 (t, J = 5 Hz, 1H, OH), and 3.78–3.60 (m, 3H, H-2, 3,3').

Diphenyl(prolinate-O,N)borane (**12b**). (d) 100% Yield; mp 268–269°C; IR ν_{max} (KBr) 3431, 2925, 1719 (C=O), 1640, 1537, 1495, 1287, 937, and 709 cm^{-1}; ^1H NMR (DMSO-d_6) δ 7.93 (dd, J = 12, 7 Hz, 1H, NH), 7.49 (d, J = 8 Hz, 2H, H *ortho*), 7.45 (d, J = 8 Hz, 2H, H *ortho'*), 7.22 (t, J = 8 Hz, 4H, H *meta*), 7.16 (t, J = 7 Hz, 1H, H *para*), 7.13 (t, J = 7 Hz, 1H, H *para'*), 4.22 (q, 1H, H-2), 3.00 (sext, J = 5 Hz, 1H, H-5), 2.40, (sext, 1H, H-5'), 2.20–1.90 (m, 2H, H-3,3'), and 1.70 (quint, J = 7 Hz, 2H, H-4).

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