Chemistry of Heterocyclic Compounds, Vol. 44, No. 8, 2008

SYNTHESIS AND SPECTRAL CHARACTERISTICS OF 2-ARYL-6-METHYL- AND 2-ARYL-6-BENZYL-4,8a-DIPHENYLPERHYDRO[1,3,2]DIOXABORININO-[5,4-*c*]PYRIDINES

Le Tuan Anh[1], K. B. Polyanskiy[2], J. A. Mamyrbekova[3], A. T. Soldatenkov[1], S. A. Soldatova[1], V. V. Kurilkin[1], and P. B. Terentiev[4]

Aryl-N-methyl- and aryl-N-benzyl-B-substituted 4,8a-diphenylperhydro[1,3,2]dioxaborinino[5,4-c]-pyridines, which are representatives of a new class of bicyclic compounds containing four heteroatoms, were synthesized from N-methyl- and N-benzyl-3-(α-hydroxybenzyl)-4-phenyl-γ-piperidols by cyclocondensation with arylboronic acids. The ^{1}H NMR and mass spectra of these compounds were examined as well as mass spectra of previously obtained analogs.

Keywords: N-alkyl-2,4,8a-triarylperhydro[1,3,2]dioxaborinino[5,4-*c*]pyridines, arylboronic acids, 3-(α-hydroxybenzyl)-4-phenyl-γ-piperidols, mass spectra.

We have previously reported the synthesis of perhydro[1,3,2]dioxaborinino[5,4-*c*]pyridines, which are representatives of a new class of compounds containing four heteroatoms, from N-methyldiol **1a** and a series of arylboronic acids **2a-f** [1, 2]. In the present work, we describe the synthesis of new N-methyl- and N-benzyl-2-aryl-4,8a-diphenylperhydrodioxaborninopyridines **2g-j** and **3a-d** from diol **1a** and N-benzyldiol **1b**, respectively, and arylboronic acids (Scheme 1) and examine the ^{1}H NMR and mass spectra of **2a-j** and **3a-d**. Products **2g-j** and **3a-d** were synthesized, similarly to **2a-f**, by the tandem diesterification of piperidols **1a** and **1b** with arylboronic acids upon heating these compounds in toluene at reflux. These products were separated by column chromatography. Their composition and structure were supported by elemental analysis and ^{1}H NMR spectroscopy (Tables 1 and 2) as well as the nature of their decomposition upon electron impact (Table 3).

The signal for H-4a provides the most useful information in the ^{1}H NMR spectra of **2g-i, 3a-b**. The triplet shape of this signal and large coupling constant (10.08-11.3 Hz) suggest, by analogy with similar characteristics for the cyclohexane system, that this proton has axial orientation relative to both *cis*-fused rings (this has been confirmed by X-ray diffraction structural data for **2a** [2]) as well as *trans* position relative to H-4 and H_e-5 protons. The axial orientation of H-4 proton is indicated by the broad half-height width of its unresolved signal.

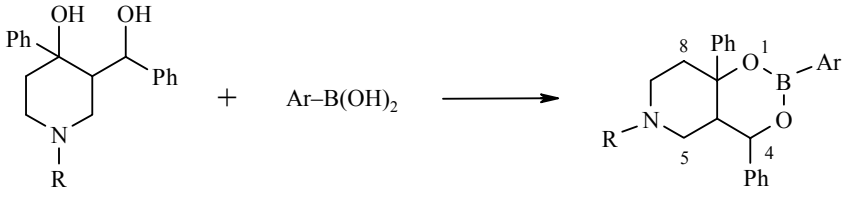
---

[1] Peoples' Friendship University of Russia, Moscow 117198, Russia; e-mail: ssoldatova@scu.pfu.edu.ru. [2]ChemBridge Corporation, Moscow 119048, Russia; e-mail: kirill198@post.ru. [3]Abobo-Adjame University, Abidjan, Côte D'Ivoire; e-mail: bekro2001@yahoo.com. [4]M. V. Lomonosov Moscow State University, Moscow 119899, Russia; e-mail: petr_terentev@mail.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1253-1259, August, 2008. Original article submitted October 26, 2007. Submitted after revision February 27, 2008.

0009-3122/08/4408-1009©2008 Springer Science+Business Media, Inc.

The behavior of **2b-j** and **3b** upon electron impact in a mass spectrometer was also analyzed for identification of representatives of the new heterocyclic system. Since the ionization energy of Me_2O (10.0 eV), Me_3B (8.8 eV), and Me_3N (7.8 eV) drops in that order [4], we may assume that the positive charge upon formation of the molecular ions of these compounds would be localized predominantly on the nitrogen atom and peaks for nitrogen-containing compounds would predominate in the mass spectra (Table 4).

Scheme 1



1a, b **2a–j, 3a–d**

1a, 2a-R = Me; **1b, 3a–d** R = Bn; **2 a** Ar = Ph [1,2], **b** Ar = 4-Tol [1], **c** Ar = 3-Tol [2], **d** Ar = 2-Tol [2], **e** Ar = 2,4,5-$Me_3C_6H_2$ [2], **f** Ar = 3-$CF_3C_6H_4$ [2], **g** Ar = 4-$MeOC_6H_4$, **h** Ar = 4-NCC_6H_4, **i** Ar = 2-thienyl, **j** Ar = 3-F,4-ClC_6H_3; **3 a** Ar = Ph, **b** Ar = 4-Tol, **c** Ar = 3-Tol, **d** Ar = 3-F,4-ClC_6H_3

The mass spectra of all the compounds studied show rather strong molecular ion peaks (from 20 to 100%) (Table 3). The initial decomposition of the molecular ions shown in Scheme 2 involves breaking the C(5)–C(4a) bond in the nitrogen-containing ring to give predominantly ions *m/z* 71 and 70 or, to a lesser extent, boron-containing ions F_1–F_3, the peaks for which, as a rule, are three or four times lower in intensity than the nitrogen-containing ions. The second decomposition pathway for the molecular ions of compounds **2** and **3** involves opening of the boron-containing ring at the C(8a)–C(1) bond to give nitrogen-containing ions *m/z* 174 and 172, accompanied by migration of protons or the Ar radical to the nascent piperidine fragment and also the formation of F_4 ions with *m/z* 105 and 91. The peaks of the nitrogen-containing or hydrocarbon fragments are stronger in the decomposition of the molecular ion through pathway **B** than for the boron-containing fragments F_4. Such a fragmentation pathway is characteristic for all piperidine derivatives [5, 6].

Thus, the decomposition of the molecular ions formed in the electron impact ionization of all the bicyclic compounds studied **2b-j** and **3b** proceeds similarly. Both the structure and the electronic properties of the Ar substituent do not affect this process due to the considerable removal of Ar from the nitrogen atom, which is the site of localization of the positive charge, but do affect the intensity of many of the characteristic peaks.

TABLE 1. Characteristics of Compounds **2** and **3**

Compound	Empirical formula	Found, % / Calculated, %			mp °C	Yield, %
		C	H	N		
2g	$C_{26}H_{28}BNO_3$	75.23 / 75.55	6.90 / 6.83	3.50 / 3.39	92-94	89
2h	$C_{26}H_{25}BN_2O_2$	76.68 / 76.48	5.95 / 6.17	7.05 / 6.86	124-126	61
2i	$C_{23}H_{24}BNO_2S$	71.25 / 70.96	6.40 / 6.21	3.47 / 3.60	162-164	66
2j	$C_{25}H_{24}BClFNO_2$	69.15 / 68.91	5.37 / 5.55	3.37 / 3.21	88-90	62
3a	$C_{31}H_{30}BNO_2$	80.84 / 81.05	6.89 / 6.58	3.40 / 3.05	86-88	63
3b	$C_{32}H_{32}BNO_2$	80.90 / 81.19	6.90 / 6.81	2.82 / 2.96	90-92	72
3c	$C_{32}H_{32}BNO_2$	81.36 / 81.19	6.89 / 6.81	3.07 / 2.96	Oil	65
3d	$C_{31}H_{28}BClFNO_2$	72.51 / 72.75	5.83 / 5.51	2.59 / 2.74	Oil	60

Scheme 2

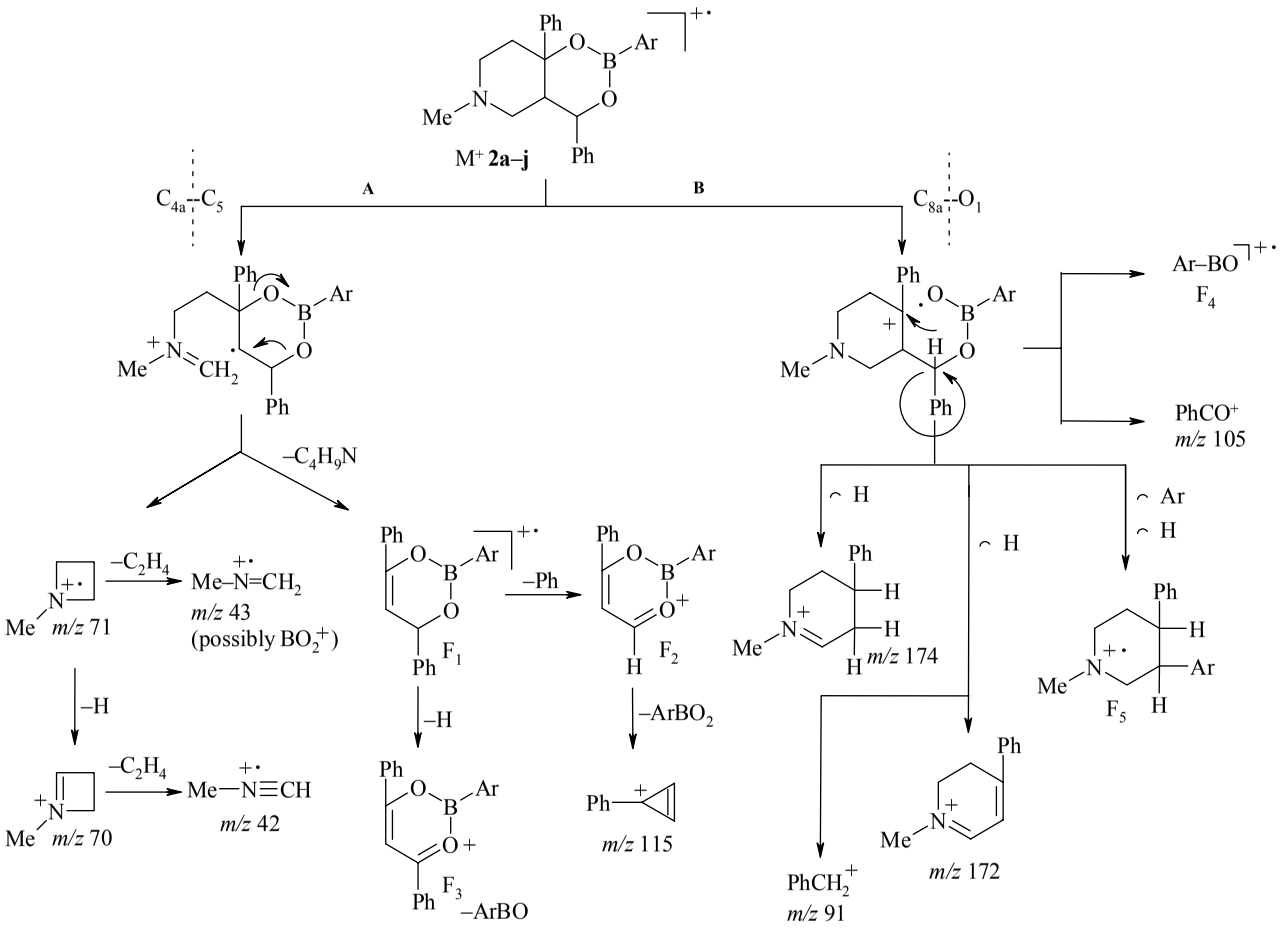

M+ 2a–j
A
B
C4a–C5
C8a–O1
–C4H9N
–C2H4
Me–N=CH2
m/z 43
(possibly BO2+)
m/z 71
–H
m/z 70
Me–N≡CH
m/z 42
–Ph
F1
F2
–ArBO2
m/z 115
F3
–ArBO
Ar–BO+·
F4
PhCO+
m/z 105
m/z 174
F5
PhCH2+
m/z 91
m/z 172

TABLE 2. ^{1}H NMR Spectra of Compounds **2a-j** and **3a-d**

Compound	Chemical shifts, δ, ppm (*J*, Hz)					
	H-4 (1H, br. s)	H-4a (1H, t)	CH_2–N–CH_2 (m)	$C_{(8)}H_2$ (1H, m), (1H, m)	CH_3 (3H, s)	H arom.
2g	5.12	2.53 (*J* = 11.0)	2.45 (1H); 2.72 (1H); 3.02 (1H); 3.11 (1H)	1.91, 2.10	2.39 (NCH_3) 3.89 (OCH_3)	6.86-6.92 (8H, br. s); 7.09 (1H, br. s); 7.10 (2H, dd, J_1 = 5.8, J_2 = 2.2); 7.42 (1H, t, *J* = 2.2); 7.62 (1H, br. s); 7.71 (1H, d, *J* = 5.8)
2h	5.15	2.47 (*J* = 11.1)	2.38 (1H); 2.65 (1H); 2.98 (1H); 3.08 (1H)	1.97, 2.11	2.36 (NCH_3)	6.87-7.06 (10H, br. s); 7.71 (2H, d, *J* = 7.8); 8.12 (2H, d, *J* = 7.3)
2i	5.08	2.55 (*J* = 11.0)	2.44 (1H); 2.66 (1H); 3.01 (1H); 3.10 (1H)	1.92, 2.08	2.39 (NCH_3)	6.83-6.90 (9H, br. s); 7.09 (1H, br. s); 7.28 (1H, dd, J_1 = 3.6, J_2 = 4.3); 7.69 (1H, d, *J* = 4.3); 7.84 (1H, d, *J* = 3.6)
2j	5.12	2.48 (*J* = 11.3)	2.40 (1H); 2.65 (1H); 2.95 (1H); 3.08 (1H)	1.97, 2.19	2.37 (NCH_3)	6.85-7.05 (10H, br. s); 7.47 (1H, t, *J* = 7.4); 7.68 (1H, d, *J* = 6.2); 7.74 (1H, d, *J* = 7.9)
3a	5.17	2.64 (*J* = 10.8)	2.53 (1H); 2.74 (1H); 3.03 (2H); 3.72*	2.06, 2.22		6.90-7.50 (18H, m); 8.05 (2H, d, *J* = 6.3)
3b	5.24	2.74 (*J* = 11.0)	2.70 (1H); 2.83 (1H); 2.90 (1H); 3.14 (1H); 3.70*	2.15, 2.29	2.64 ($C_{Ar}CH_3$)	7.04-7.60 (17H, m); 8.19 (2H, d, *J* = 6.3)
3c	5.15	2.62 (*J* = 10.8)	2.60 (1H); 2.75 (1H); 3.00 (2H); 3.57*	2.00, 2.14	2.68 ($C_{Ar}CH_3$)	6.94-7.50 (17H, m); 8.10 (2H, m)
3d	5.10	2.54 (*J* = 11.0)	2.70 (1H); 2.83 (1H); 2.95 (1H); 3.22 (1H); 3.59*	1.95, 2.15		6.80-7.93 (18H, m)

* $PhC\underline{H}_2$ (2H, s).

TABLE 3. Mass Spectra of Compounds **2b-j** and **3b**

Com-pound	*m/z* (I_{max}, %)*
2b	397 [M] (29), 326 (10), 325 (12), 265 (7), 234 (5), 174 (29), 172 (34), 159 (20), 117 (29), 115 (33), 105 (37), 91 (38), 77 (32), 71 (29), 70 (49), 57 (69)
2c	397 [M] (33), 326 (27), 325 (32), 265 (22), 174 (33), 172 (43), 159 (19), 117 (20), 115 (25), 105 (50), 104 (27), 91 (40), 77 (45), 71 (37), 70 (55), 57 (79)
2d	397 [M] (30), 326 (12), 325 (13), 265 (11), 174 (30), 172 (35), 159 (21), 117 (15), 115 (20), 105 (37), 103 (20), 91 (37), 77 (32), 71 (30), 70 (50), 57 (64)
2e	425 [M] (59), 354 (11), 174 (27), 172 (45), 159 (30), 147 (15), 146 (20), 131 (25), 117 (23), 115 (37), 105 (78), 103 (32), 91 (49), 77 (47), 71 (29), 70 (54), 57 (88)
2f	451 [M] (20), 380 (5), 379 (7), 174 (13), 172 (24), 159 (7), 129 (10), 117 (10), 115 (27), 105 (4), 103 (17), 91 (27), 77 (30), 71 (21), 70 (27), 57 (56)
2g	413 [M] (45), 342 (8), 341 (13), 281 (13), 174 (26), 172 (47), 159 (16), 134 (26), 115 (21), 105 (47), 103 (37), 91 (39), 77 (48), 71 (34), 70 (47), 57 (48)
2h	408 [M] (35), 336 (10), 174 (37), 172 (37), 159 (15), 130 (7), 129 (11), 117 (12), 115 (28), 105 (40), 103 (26), 91 (35), 77 (50), 71 (44), 70 (70), 57 (98)
2i	389 [M] (34), 318 (7), 317 (8), 174 (8), 172 (15), 159 (6), 115 (14), 111 (6), 110 (7), 105 (19), 103 (11), 91 (12), 77 (30), 71 (20), 70 (32), 57 (73)
2j	435*[2] [M] (20), 364*[2](10), 363*[2](13), 302 (7), 174 (67), 172 (74), 159 (30), 117 (16), 115 (40), 105 (60), 103 (37), 91 (33), 77 (55), 71 (39), 70 (61), 57 (90)
3b	473 [M] (22), 326 (2), 325 (5), 250 (21), 248 (17), 159 (3), 146 (6), 120 (9), 117 (12), 115 (7), 105 (19), 103 (6), 91 (100), 79 (13), 77 (20), 65 (14)

* The 15 strongest ion peaks in the range from M^+ to *m/z* 57 are given. Ion peaks with *m/z* 42-44 are the strongest in the mass spectra of **2b-j** and **3b**.
*[2] The *m/z* values are given for ions containing the ^{11}B and ^{35}Cl isotopes.

Products **2a,c-j, 3a,b** did not display activity relative to *E. coli 1157* (a hospital strain of wound infections) and *Staphilococcus albus.*

EXPERIMENTAL

The EI mass spectra were obtained on a Finnigan MAT Incos 50 mass spectrometer with direct sample inlet into the ion source at 70 eV ionization energy. The ^1H NMR spectra were taken on a Bruker WM-400 spectrometer at 400 MHz in $CDCl_3$ with TMS as the internal standard. L-60 (40/100) silica gel was used for column chromatography. The reaction course and purity of the isolated products were monitored by thin-layer chromatography on Silufol UV-254 plates with ethyl acetate as the eluent and development by iodine vapor. Piperidols **1a** and **1b** were obtained in three steps: 1) condensation of acetophenone with formaldehyde and methylamine or benzylamine, leading to the corresponding Mannich salts [3]; 2) cyclization of these salts to give 3-benzyl-4-phenylpiperidols [3]; 3) reduction of these piperidols to 1,3-diols [2, 3].

2-Aryl-6-methyl- (2a-j) and 2-aryl-6-benzyl-4,8a-diphenylperhydro[1,3,2]dioxaborinino[5,4-*c*]pyridines 3a-d (General Method). A solution of arylboronic acid (2.72 mmol) and 4-hydroxy-3-(α-hydroxybenzyl)-1-methyl- (**1a**) (or 1-benzyl-4-phenylpiperidine (**1b**) (2.69 mmol) in toluene (50 ml) was heated at reflux with a Dean–Stark trap for 3-5 h. The mixture was cooled and placed on a silica gel column. Elution with toluene gave by-products, while elution with acetone gave the desired product. After evaporation of the solvent, the product was crystallized from toluene. Products **2** and **3** were obtained as white or yellowish crystals.

TABLE 4. Peak Intensities of the Characteristic Ions in the Mass Spectra of **2b-j** and **3b** (ΣI)*

Com-pound	W_M	F_1	F_2	F_3	F_4	F_5	*m/z* 174	*m/z* 172	*m/z* 115	*m/z* 105	*m/z* 91	*m/z* 77	*m/z* 71	*m/z* 70	$\sum m/z$ 42–44	Σ_N	Σ_B	ΣI, %
2b	2.8	1.0	0.1	1.3	3.0	2.1	1.8	3.6	3.5	3.9	4.0	3.4	3.1	5.0	28.0	17.9	2.4	65.6
2c	6.8	2.1	0.4	2.5	1.5	2.5	2.9	3.3	1.9	3.9	3.1	3.5	2.8	4.3	21.8	15.9	5.0	63.3
2d	4.4	1.2	0.2	1.3	1.2	2.9	2.7	3.4	1.9	3.6	3.6	3.1	2.9	4.8	29.4	17.1	2.7	65.8
2e	5.4	0.7	0.1	0.8	0.9	2.0	2.5	3.4	2.0	4.5	3.6	2.2	1.6	2.0	20.6	11.4	1.6	52.3
2f	4.7	0.6	0.2	0.9	2.0	1.4	0.9	1.7	2.2	2.6	1.9	3.9	2.4	3.4	20.8	10.3	1.7	49.6
2g	3.0	0.2	0.1	0.8	2.2	3.0	1.9	3.0	2.3	3.3	2.9	4.1	3.6	5.8	23.0	17.4	1.6	46.0
2h	3.7	0.6	0.2	0.8	0.6	1.5	2.8	2.8	3.1	4.7	3.1	3.5	2.4	3.1	27.3	11.1	1.6	60.4
2i	6.5	0.8	0.1	0.9	0.8	0.8	0.6	0.9	1.6	2.3	2.0	3.5	2.4	3.8	31.0	9.4	1.8	58.0
2j	4.9	0.6	0.4	0.8	0.2	4.2	4.2	4.8	2.5	3.7	2.1	3.4	2.4	3.8	18.0	17.5	1.8	56.0
3b*[2]	6.8	0.4	2.1	0.9	1.8	4.0	3.9[a]	3.1[b]	1.3	3.5	19.0	3.8	0.9[c]	1.1[d]	6.8	8.8	3.4	53.6

* Σ_N is the sum of the initial nitrogen-containing ions, Σ_B is the sum of the initial boron-containing ions, and ΣI is the total intensity of the molecular and other ions given in the Table.

*[2] The following are given for **3b**: [a] ion *m/z* 250 [(174+76 (C_6H_4)], [b] ion *m/z* 248 [(172+76) (C_6H_4)], [c] ion *m/z* 147 [71+76 (C_6H_4)], and [d] ion *m/z* 146 [(70+76 (C_6H_4)].

REFERENCES

1. K. B. Polyanskii, Le Tuan Anh, A. N. Andresyuk, and A. T. Soldatenkov, *Zh. Org. Khim.*, **39**, 1439 (2003).
2. Le Tuan Anh, K. B. Polyanskii, A. N. Andresyuk, A. T. Soldatenkov, Zh. A. Mamyrbekova, L. P. Kuleshova, and V. N. Khrustalev, *Izv. Akad. Nauk, Ser. Khim.*, 806 (2004).
3. J. T. Plati and W. Wenner, *J. Org. Chem.*, **14**, 543 (1949).
4. V. N. Kondrat'ev (editor), *Bond Dissociation Energies, Ionization Potentials and Electron Affinities* [in Russian], Nauka, Moscow (1974).
5. P. B. Terentiev and A. P. Stankevicius, *Mass Spectrometric Analysis of Biologically Active Nitrogen Compounds* [in Russian], Mokslas, Vilnius (1981).
6. A. T. Lebedev, *Mass Spectrometry in Organic Chemistry* [in Russian], BINOM, Moscow (2003).