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SHORT COMMUNICATIONS

Perhydro[1,3,2]dioxaborinino[5,4-*c*]pyridine— A New Heterocyclic System

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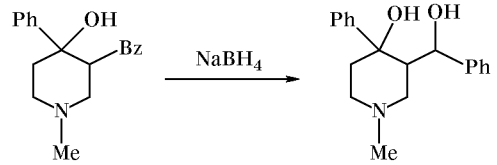
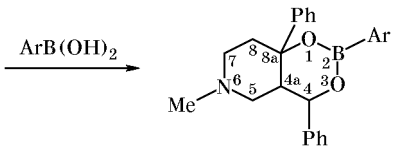
With the goal of synthesizing first representatives of a new heterocyclic system, perhydro[1,3,2]dioxaborinino[5,4-*c*]pyridines **III**, we effected condensation of 1,3-diol **II** with tolylboronic acids. Initial diol **II** was prepared by reduction of 3-benzoyl-4-hydroxy-1-methyl-4-phenylpiperidine (**I**) [1] with sodium tetrahydridoborate. The condensation of diol **II** with tolylboronic acids was carried out by heating the reactants in boiling toluene (reaction time 3–5 h) with simultaneous removal of the liberated water as azeotropic mixture with toluene. When the reaction was complete (according to the TLC data), the solvent was distilled off, and products **IIIa**–**IIIc** were isolated by column chromatography as yellowish crystalline substances in 76–95% yield.



I **II**



IIIa–IIIc

III, Ar = 4-MeC_6H_4 (**a**), 3-MeC_6H_4 (**b**), 2-MeC_6H_4 (**c**).

According to the X-ray diffraction data for hydroxy ketone **I** [2] and ^{1}H NMR data for diol **II**, the 4-phenyl and 3-benzoyl substituents occupy equatorial positions; therefore, the two heterorings in **III** should be fused *cis* at the 4-*ax*/3-*eq* positions of the piperidine ring. This assumption is confirmed by the ^{1}H NMR spectra of bicyclic compounds **IIIa**–**IIIc**, where the 4-H signal appears as a broadened singlet with a $J_{1/2}$ value of 15.6 to 16.2 Hz and the 4a-H signal is a triplet with J 11.6 and 11.3 Hz. These values of the coupling constants indicate that the dioxaborinane ring has a *sofa* conformation [3] and that the piperidine fragment is likely to adopt a distorted *chair* conformation due to 1–3 steric interactions involving the phenyl group at the bridgehead carbon atom (C^{8a}).

Synthesis of various derivatives of heterocyclic system **III** can attract interest from the viewpoint of search for potential mesomorphogenic [3] and biologically active substances, e.g., those capable of selectively accumulating in tumor cells and hence being useful for boron neutron-capture therapy [4].

4-Hydroxy-3-(α-hydroxybenzyl)-1-methyl-4-phenylpiperidine (II). Yield 90%. mp 195–197°C (compound **II** was previously synthesized [1] in 30% yield by hydrogenation over PtO_2 and was characterized as the corresponding hydrochloride). ^{1}H NMR spectrum, δ, ppm: 1.62 m (3H, 5-H, OH), 2.05 t.t (1H, 5-H, J = 11.5, 4.0 Hz), 2.30 s (3H, Me), 2.39 d.d (1H, 2-H, J = 12.6, 3.5 Hz), 2.44 t.t (1H, 3-H_{ax}, J = 11.4, 2.6 Hz), 2.63–2.76 m (3H, 2-H, 6-H), 3.09 br.s (1H, OCH), 4.72 d (1H, OH, J = 4.7 Hz), 7.00–7.40 m (10H, H_{arom}). Mass spectrum, m/z (I_{rel}, %): 297 (18) M^+, 190 (10) [M – PhCHOH]$^+$ (F_1), 172 (100) [F_1 – H_2O]$^+$, 105 (35) [PhCO]$^+$, 77 (54) [Ph]$^+$.

6-Methyl-4,8a-diphenyl-2-(4-tolyl)perhydro-[1,3,2]dioxaborinino[5,4-*c*]pyridine (IIIa). Yield 95%, yellowish crystals with mp 104–106°C, R_f 0.53 (acetone). ^{1}H NMR spectrum, δ, ppm: 1.92 br.m (1H, 8-H), 2.09 br.m (1H, 8-H), 2.40 s (3H, NMe),

2.43 br.m (1H, 5-H), 2.45 s (3H, CMe), 2.57 br.t (1H, 4a-H, J = 11.6, 11.3 Hz), 2.72 br.m (1H, 5-H), 3.10 br.m (2H, 7-H), 5.07 br.s (1H, 4-H, $J_{1/2}$ = 15.6 Hz), 6.85–7.06 m (10H, H_{arom}), 7.31 br.d and 8.00 br.d (2H each, H_{arom}, *AA′BB′* system, J = 7.5 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 397 (46) M^+, 396 (32), 326 (18), 325 (23), 265 (27), 174 (38), 172 (38) 159 (26), 105 (31), 91 (23), 77 (30), 70 (57), 57 (71), 44 (100), 43 (69), 42 (70). Found, %: C 78.30; H 7.23; N 3.41. $C_{26}H_{28}BNO_2$. Calculated, %: C 78.59; H 7.05; N 3.53.

6-Methyl-4,8a-diphenyl-2-(3-tolyl)perhydro-[1,3,2]dioxaborinino[5,4-*c*]pyridine (IIIb). Yield 90%, mp 52–54°C, R_f 0.46 (acetone). ^{1}H NMR spectrum, δ, ppm: 1.92 br.m (1H, 8-H), 2.14 br.m (1H, 8-H), 2.44 br.s (6H, Me), 2.53 m (1H, 5-H), 2.59 br.t (1H, 4a-H, J = 11.6, 11.2 Hz), 2.80 br.m (1H, 5-H), 3.16 br.m (2H, 7-H), 5.07 br.s (1H, 4-H, $J_{1/2}$ = 16.2 Hz), 6.70–7.42 m (12H, H_{arom}), 7.91 m (2H, 2′-H_{arom} and 6′-H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 397 (55) M^+, 396 (16), 326 (15), 325 (19), 265 (22), 174 (33), 172 (42), 159 (21), 105 (48), 91 (40), 77 (44), 70 (51), 57 (77), 44 (100), 43 (83), 42 (95). Found, %: N 3.32. $C_{26}H_{28}BNO_2$. Calculated, %: N 3.53.

6-Methyl-4,8a-diphenyl-2-(2-tolyl)perhydro-[1,3,2]dioxaborinino[5,4-*c*]pyridine (IIIc). Yield 76%, mp 50–52°C, R_f 0.4 (acetone). ^{1}H NMR spectrum, δ, ppm: 1.92 br.m (1H, 8-H), 2.12 br.m (1H, 8-H), 2.44 s (3H, NMe), 2.50 br.t (1H, 5-H, J = 11.2 Hz), 2.60 br.t (1H, 4a-H, J = 11.6, 11.3 Hz), 2.71 s (3H, CMe), 2.73 br.m (1H, 5-H), 3.16 br.m (2H, 7-H), 5.08 br.s (1H, 4-H, $J_{1/2}$ = 16.2 Hz), 6.85–7.45 m (13H, H_{arom}), 8.12 d (1H, 6′-H_{arom}, J = 7.1 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 397 (32) M^+, 396 (18), 326 (11), 325 (13), 265 (11), 174 (29), 172 (33), 159 (21), 105 (38), 91 (38), 77 (33), 70 (49), 57 (65), 44 (100), 43 (62), 42 (72). Found, %: N 3.47. $C_{26}H_{28}BNO_2$. Calculated, %: N 3.53.

The ^{1}H NMR spectra were recorded on a Bruker WM-400 spectrometer (400 MHz) from solutions in $CDCl_3$ using TMS as internal reference. The mass spectra were obtained on an MKh-1321 instrument. Silufol UV-254 plates were used for TLC analysis; the chromatograms were developed with iodine vapor.

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