Simple synthesis of benzo[*f*]pyrrolizidine and benzo[*g*]indolizidine with the use of products of the reductive allylation of indole and quinoline

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Benzo[*f*]pyrrolizidine and benzo[*g*]indolizidine were synthesized by hydroboration—oxidation—intramolecular cyclization of the corresponding products of the reductive α-allylation of indole (**2**) and quinoline (**6**) with allylboranes.

Key words: allylboranes, reductive mono- and *trans*-α,α′-diallylation, indole, quinoline, hydroboration—oxidation.

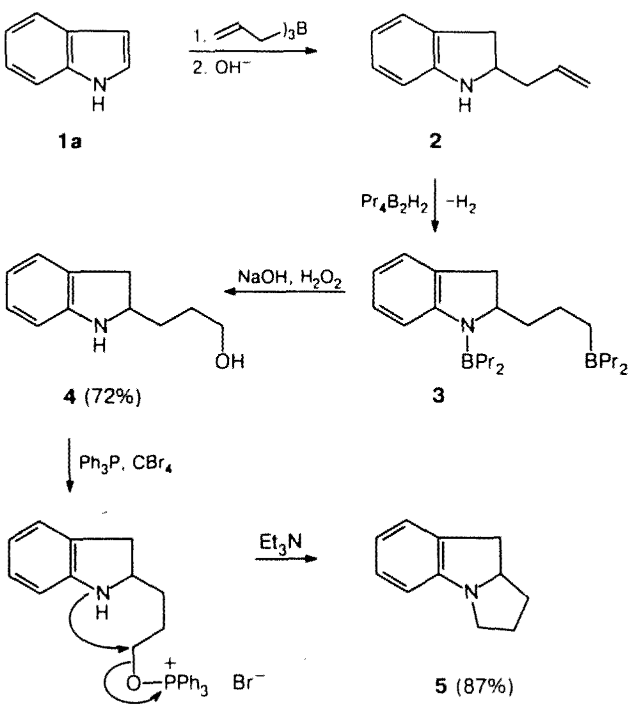
Owing to their broad spectrum of physiological activities, pyrrolizidine[1,2] and indolizidine[3,4] alkaloids continue to attract the attention of chemists involved in synthesis.

Recently, mono- and *trans*-α,α′-diallylation of aromatic nitrogen-containing heterocycles with allylboranes[5,6] was discovered in our laboratory. The α-allylated heterocycles obtained by these regio- and stereoselective reactions contain one NH group and one or several double bonds and, therefore, they are excellent starting compounds for obtaining nitrogen-containing bi- and polycyclic compounds with a tertiary nitrogen atom. For example, allylboration of 3,4-dihydroisoquinolines is a key stage in the synthesis of the benzopyrrocoline system (hexahydropyrrolo[2,1-*a*]isoquinolines).[7] This method is based on hydroboration and oxidation of 1-allyl-1,2,3,4-tetrahydroisoquinolines followed by closure of the pyrrolizidine ring through intramolecular *N*-alkylation.

As part of our continuing studies along this line, we synthesized benzo[*f*]pyrrolizidine and benzo[*g*]indolizidine from the products of the reductive α-monoallylation of indole and quinoline.

Hydroboration of 2-allyl-2,3-dihydroindole (**2**)[8] with tetrapropyldiborane $(Pr_2BH)_2$ (1 mol) yielded *N,C*-bis(dipropylboryl)-substituted compound **3**. The standard treatment of **3** with alkaline hydrogen peroxide afforded 2-(3-hydroxypropyl)-2,3-dihydroindole (**4**) in a yield of 72%. The subsequent direct cyclization of aminoalcohol **4** with Ph_3P/CBr_4[4] produced benzo[*f*]pyrrolizidine **5** (87%).

Quinoline added allyldipropylborane at 20 °C to form 2-allyl-1-dipropylboryl-2-hydroquinoline (**6**).[9] Deboration was not carried out, and adduct **6** was subjected to hydroboration (without isolation of intermediate products **7** and **8**) with $(Pr_2BH)_2$ (0.5 mol), catalytic hydrogenation over $Pd/SrCO_3$, and oxidation with alkaline hydrogen peroxide. The 2-(3-hydroxypropyl)-1,2,3,4-tetrahydroquinoline (**9**) that formed was separated by column chromatography on SiO_2.



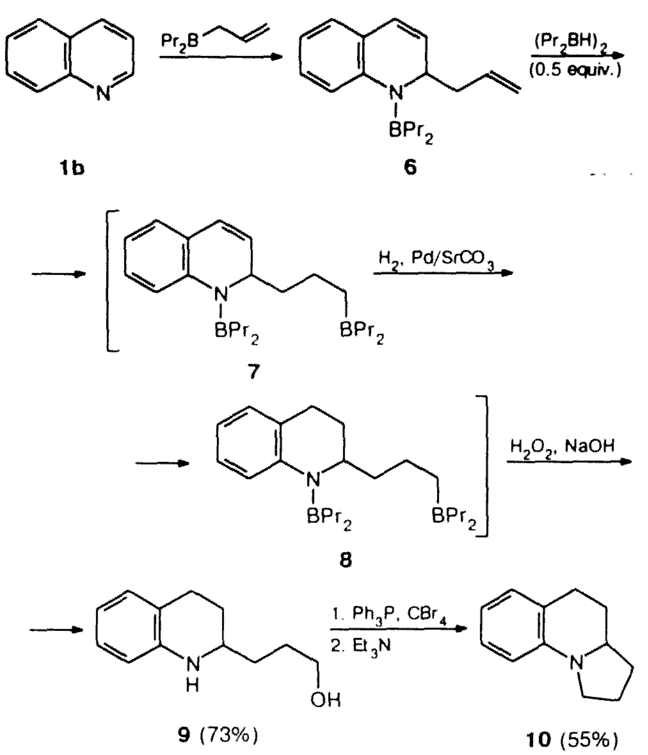
Subsequent cyclization of aminoalcohol and distillation *in vacuo* gave the desired benzo[*g*]indolizidine (**10**) in a yield of 55%. The structures of the products were confirmed by the data of elemental analysis and physicochemical studies.

Experimental

All experiments with organoboron compounds were carried out under an atmosphere of dry argon. The NMR spectra were

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 11, pp. 2807—2809, November, 1996.

1066-5285/96/4511-2665 $15.00



recorded on a Bruker AC-200P spectrometer. Compounds **2** and **6** were synthesized according to the procedures reported previously.[8,9]

2-(3-Hydroxypropyl)-2,3-dihydroindole (4). A tetrahydrofuran solution (22 mL, 2.87 mol) of Pr_2BH (63 mmol) was added dropwise to a solution of olefin **2** (5 g, 31.4 mmol) in THF (10 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h. Then the temperature was raised to 20 °C, and the excess Pr_2BH was decomposed with MeOH (3 mL). The solvent was removed *in vacuo* with the use of a water jet pump. The residue was dissolved in ether (25 mL). The ether solution was treated with a NaOH (2.5 g) solution in H_2O (20 mL) and a 30% H_2O_2 solution (16 mL) at 0 °C. The reaction mixture was refluxed for 1 h using a reflux condenser and kept for 12 h. The organic layer was separated, and the aqueous layer was extracted with ether. The organic extracts were dried over K_2CO_3. The ether was removed, and the residue was distilled *in vacuo*. Aminoalcohol **4** was obtained in a yield of 3.98 g (71.5%) as a thick oil, b.p. 142—145 °C (1.5 Torr). Found (%): C, 74.99; H, 8.91. $C_{11}H_{15}NO$. Calculated (%): C, 74.54; H, 8.53. ^1H NMR ($CDCl_3$, δ, J/Hz): 1.72 (m, 4 H, $H_2C(2')$ and $H_2C(1')$); 2.96 (the AB portion of the ABX spectrum, 2H, $H_2C(3)$), δ_A = 2.75, δ_B = 3.18, J_{AB} = 15.5, J_{AX} = J_{BX} = 8.6); 3.70 (t, 2 H, H_2CO, J = 5.6); 3.91 (m, 1 H, HCN); 6.68 (d, 1 H, HC(7), J = 7.7); 6.78 (t, 1 H, HC(5), J = 7.4); 7.09 (t, 1 H, HC(6), J = 7.7); 7.15 (d, 1 H, HC(4), J = 7.2). ^{13}C NMR ($CDCl_3$, δ): 29.44 (C-2'); 32.99 (C-1'); 36.00 (C-3); 59.72 (C-2); 62.55 (C-3'); 109.48 (C-7); 118.8 (C-5); 124.7 (C-4); 127.2 (C-6); 129.0 (C-7a); 150.7 (C-3a).

Benzo[*f*]pyrrolizidine (5). Triphenylphosphine (2.4 g) was added to a mixture of aminoborane **3** (1.08 g, 6.1 mmol) and CBr_4 (2.52 g) in CH_2Cl_2 (10 mL) cooled to 0 °C. The mixture was stirred for 30 min, and then Et_3N (14 mL) was added. After 20 min, low-boiling compounds were removed *in vacuo*, and the residue was extracted with pentane. The solvent was evaporated, and the raw product was treated with aqueous HCl. The aqueous layer was washed with ether. Free base was isolated from the aqueous layer with the use of a 10% NaOH solution. This base was extracted with ether and dried. The solvent was removed. Distillation of the residue gave product **5** in a yield of 0.7 g (72%), b.p. 85—86 °C (1.5 Torr), n_D^{20} = 1.5812. Found (%): C, 82.94; H, 8.26. $C_{11}H_{13}N$. Calculated (%): C, 82.97; H, 8.23. ^1H NMR ($CDCl_3$, δ, J/Hz): 1.44 (m, 3 H, $H_AC(4)$); 1.95 (m, 1 H, $H_BC(4)$); 3.07 (d, 1 H, $H_AC(3)$, J_{AB} = 16); 3.29 (m, 2 H, $H_BC(3)$ and $H_AC(2)$); 3.55 (m, 1 H, $H_AC(2)$); 4.05 (m, 1 H, HC—N); 6.72 (m, 1 H, HC(9), J = 7.8); 6.88 (t, 1 H, HC(7), J = 7.4); 7.21 (m, 2 H, HC(6) and HC(8)). ^{13}C NMR ($CDCl_3$, δ): 25.86 (C-6); 31.33 (C-4); 33.92 (C-3); 52.28 (C-2); 65.30 (C-5); 111.0 (C-9); 119.3 (C-7); 124.9 and 127.6 (C-6 и C-8); 129.9 (C-9a); 154.7 (C-5a).

2-(3-Hydroxypropyl)-1,2,3,4-tetrahydroquinoline (9). A solution of Pr_2BH (2.87 mol) in THF (7.85 mL) was added slowly dropwise to a solution of **6** (6.02 g, 22.5 mmol) in THF (10 mL) cooled to −10 °C. The mixture was stirred at 0 °C for 1 h, and then the temperature was raised to ~ 20 °C. After 12 h, Pd/SrCO$_3$ (0.1 g) was added to the reaction mixture, and hydrogenation was carried out until the calculated amount of hydrogen (~0.5 L) was absorbed. The catalyst was filtered off. The solvent was removed *in vacuo*. The residue was dissolved in ether (30 mL) and oxidized with alkaline hydrogen peroxide as described for the preparation of **4**. After evaporation of ether from the organic extract, the raw product was chromatographed on a column packed with SiO_2. Aminoalcohol **9** was obtained in a yield of 3.17 g (73%) as a yellowish oil. Found (%): C, 75.33; H, 8.76. $C_{12}H_{17}NO$. Calculated (%): C, 75.35; H, 8.96. ^1H NMR ($CDCl_3$, δ, J/Hz): 1.62 (m, 2 H, $H_2C(1')$); 1.7 (m, 3 H, $H_2C(2')$ and $H_AC(3)$); 2.0 (m, 1 H, $H_BC(3)$); 2.85 (m, 2 H, $H_2C(4)$); 3.32 (m, 1 H, HC(2)); 3.72 (t, 2 H, CH_2O, J = 5.6); 6.57 (d, 1 H, HC(8)); 6.72 (t, 1 H, HC(6)); 7.07 (m, 2 H, HC(5), HC(7)). ^{13}C NMR ($CDCl_3$, δ): 26.3 (C-4); 27.9 (C-3); 28.7 (C-2'); 32.9 (C-1'); 51.4 (C-2); 62.5 (C-3'); 114.3 (C-8); 117.1 (C-6); 121.5 (C-8a); 126.7 and 129.2 (C-5 and C-7); 144.6 (C-8a).

Benzo[g]indolizidine (10). Compound **10** was obtained analogously to compound **5** from aminoalcohol **9** (2 g, 10.4 mmol) in a yield of 0.76 g (55%), b.p. 106—108 °C (1.5 Torr), n_D^{20} 1.5916. Found (%): C, 83.14; H, 8.83. $C_{12}H_{15}N$. Calculated (%): C, 83.19; H, 8.73. ^1H NMR ($CDCl_3$, δ, J/Hz): 1.40 (m, 2 H, $H_AC(4)$ and $H_AC(6)$); 1.87 (m, 1 H, $H_AC(3)$); 2.02 (m, 1 H, $H_BC(3)$); 2.1 (m, 2 H, $H_BC(4)$ and $H_BC(6)$), 2.75 (m, 2 H, $H_2C(7)$); 3.14 (m, 1 H, $H_AC(2)$); 3.27 (m, 1 H, $H_BC(2)$); 3.36 (m, 1 H, HC(5)); 6.35 (d, 1 H, HC(11), J = 8); 6.50 (t, 1H, HC(9), J = 7.3); 6.94 (d, 1 H, HC(8), J = 7.3); 7.02 (t, 1 H, HC(10), J = 8). ^{13}C NMR ($CDCl_3$, δ): 23.61 (C-3); 27.27 (C-6); 28.06 (C-7); 33.05 (C-4); 46.74 (C-2); 57.84 (C-5); 109.71 (C-11); 114.6 (C-9); 121.0 (C-11a); 127.0 (C-10); 128.2 (C-8); 144.6 (C-7a).

This work was financially supported by the Russian Foundation for Basic Research (Project No. 96-03-32555).

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Received June 7, 1996

The reaction of sulfamic acid derivatives with epoxides.
4. Hydrolysis of 3-chloro-2-hydroxypropylsulfamates

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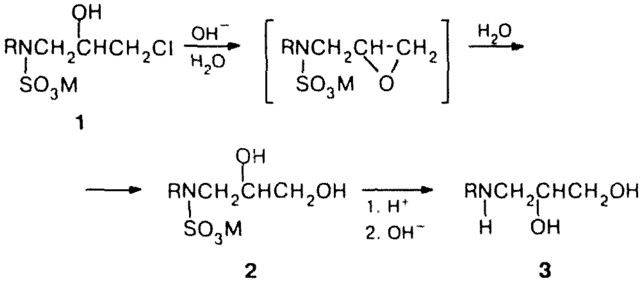
Under basic hydrolysis conditions 3-chloro-2-hydroxypropylsulfamates transform into 2,3-dihydroxypropylsulfamates. Acidic hydrolysis of the latter leads to 3-alkylaminopropane-1,2-diols.

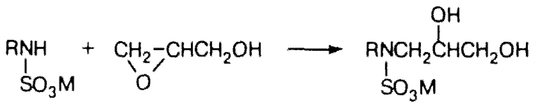
Key words: 3-chloro-2-hydroxypropylsulfamates, 3-alkylaminopropane-1,2-diols, 2,3-dihydroxypropylsulfamates.

It has been shown previously[1] that the interaction of 3-chloro-2-hydroxypropylsulfamates with amines leads to 3-alkylamino-2-hydroxypropylsulfamates. A similar approach was used in the synthesis of 3-alkylaminopropane-1,2-dioles.



M = K, Na; R = H (**a**), Me (**b**), Et (**c**), Bu (**d**)

2,3-Dihydroxypropylsulfamates (**2**) were obtained as a result of basic hydrolysis of 3-chloro-2-hydroxypropylsulfamates (**1**) (2—5 h at 100 °C), evidently, through intermediate epoxides. To exclude the condensation of the resulting compounds **2** with epoxides, a 50—60-fold molar excess of water was used. The yields of products **2** were 90—95 %. Earlier[2] compounds **2** were prepared by the condensation of sulfaminic acid derivatives with glycidols.



M = K, Na; R = H, Alk

Subsequent acidic hydrolysis of sulfamates **2** (20—30% H_2SO_4 at 100—110 °C) gave 3-alkylaminopropane-1,2-diols (**3**) in 92—95 % yields. The hydrolysis could also be carried out by the action of 30—37 % HCl or HNO_3.

Under acidic hydrolysis conditions without preliminary isolation of compounds **2**, overall yields of products **3** were 90—95 %.

The structures of compounds **2** and **3** were confirmed by their NMR spectra, as well as by the correla-

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* For Communication 3 see Ref. 1.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 11, pp. 2809—2810, November, 1996.