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SATURATED NITROGEN-CONTAINING HETEROCYCLES. 20.* CATALYTIC REDUCTION OF N-HYDROXYETHYLPYRIDINIUM AND -QUINOLINIUM SALTS

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Previously unknown N-(2-hydroxyethyl)perhydroquinolines and N-(2-hydroxyethyl)piperidines were synthesized by catalytic reduction of N-(2-hydroxyethyl)tetrahydroquinolinium and N-(2-hydroxyethyl)tetrahydropyridinium tetrafluoroborates. A scheme for the formation of the hydrogenation products is presented.

Keywords: N-(2-hydroxyethyl)perhydroquinolines, N-(2-hydroxyethyl)piperidine, N-(2-hydroxyethyl)-pyridinium, N-(2-hydroxyethyl)quinolinium, tetrafluoroborates, reduction.

A method that has been studied fairly well for the synthesis of saturated nitrogen-containing heterocycles is the catalytic reductive amination of δ-diketones [2]. However, with noncyclic and semicyclic δ-diketones and ethanolamine the reaction stops at the amination stage with subsequent intramolecular O-cyclization of the intermediate and the formation of perhydrooxazolo[3,2-*a*]pyridines and octahydrooxazolo[3,2-*j*]quinolines [3].

We found that it was possible to synthesize N-(2-hydroxyethyl)-substituted piperidines and perhydroquinolines by catalytic reduction of N-(2-hydroxyethyl)pyridinium salts [4]. In the present work we present new data on the reaction.

High yields of the initial salts, i.e., N-(2-hydroxyethyl)-2,4,6-triphenylpyridinium (**4**), N-(2-hydroxyethyl)-2,4-diphenyl-5,6,7,8-tetrahydroquinolinium (**5**), and N-(2-hydroxyethyl)-2-phenyl-4-*p*-methoxyphenyl-5,6,7,8-tetrahydroquinolinium (**6**) tetrafluoroborates, were obtained by recyclization of the corresponding pyrylium and tetrahydroquinolinium salts by the action of ethanolamine.

The hydrogenation of the pyridinium **4** and quinolinium **5**, **6** salts was conducted in an autoclave in 96% ethanol at 120°C at an initial hydrogen pressure of 10 MPa in the presence of Raney nickel catalyst. Under these conditions selective reduction of the pyridinium cycle occurs, and N-(2-hydroxyethyl)piperidine (**7**) and -perhydroquinolines **8**, **9** are formed with yields of 60-80%.

The products **7**-**9** were obtained in the form of the free bases and were colorless oils, isolated by column chromatography on aluminum oxide.

* For Communication 19, see [1].

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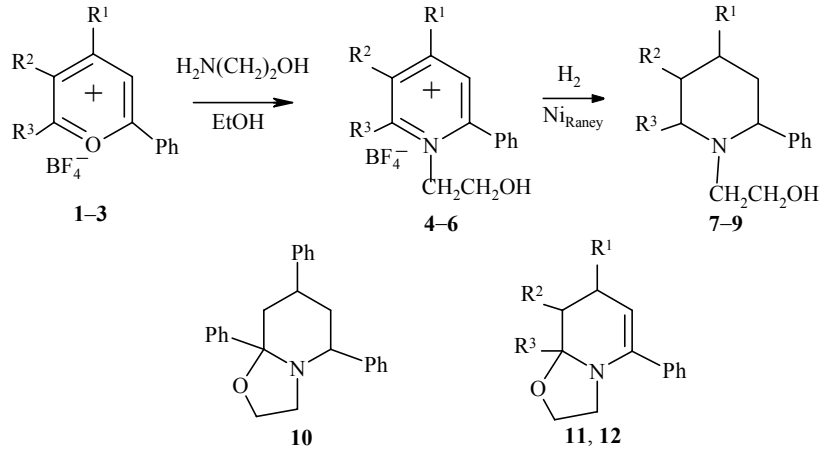
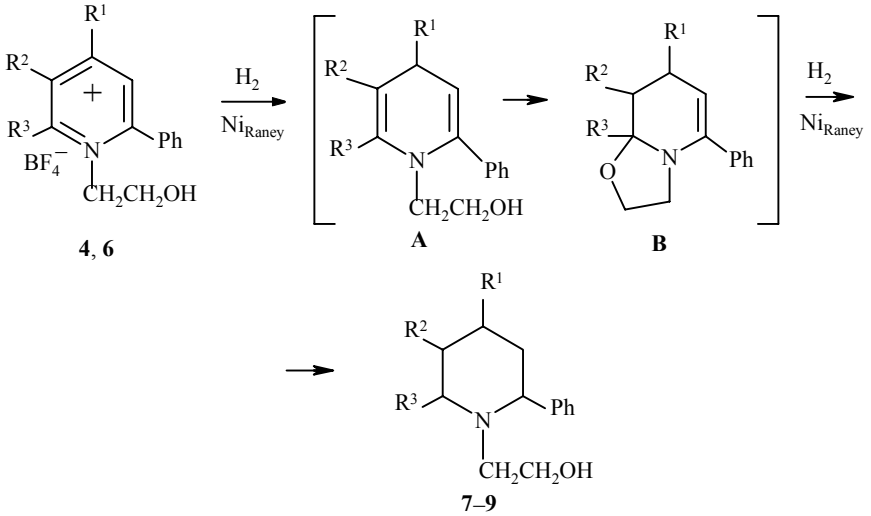


1–3 **4–6** **7–9** **10** **11**, **12**

1, 4, 7 $R^1 = R^3 = Ph$, $R^2 = H$; **2, 5, 8**, **11** $R^1 = Ph$, $R^2+R^3 = (–CH_2–)_4$;
3, 6, 9, **12** $R^1 = C_6H_4OMe\text{-}4$, $R^2+R^3 = (–CH_2–)_4$

During the hydrogenation of 2,4,6-triphenylpyridinium tetrafluoroborate **4** 5,7,8a-triphenylperhydrooxazolo[3,2-*a*]pyridine (**10**) was isolated from the hydrogenation product with a yield of 30% in addition to the piperidine base **7**. Such a reaction path is also retained during hydrogenation of the quinolinium salts **5**, **6** with the formation of the O-cyclization products 5,7-diphenyl-4,7,7a,8,9,10,11,11a-octahydrooxazolo[3,2-*j*]quinoline (**11**) and 7-(4-methoxyphenyl)-5-phenyl-4,7,7a,8,9,10,11,11a-octahydrooxazolo[3,2-*j*]quinoline (**12**), which were detected by TLC. The compounds **11**, **12** used as standards for TLC were obtained by an alternative procedure [4] by ethanolamination of propanonylcyclohexanones in the presence of catalytic amounts of hydrochloric acid.

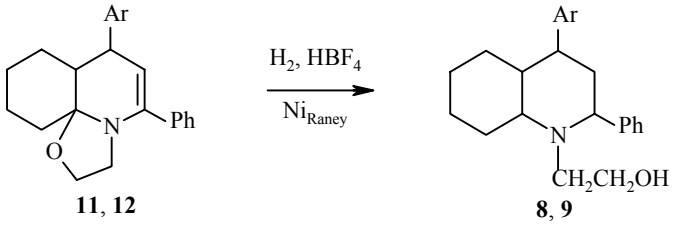


4, **6** **A** **B** **7–9**

4, 7 $R^1 = R^3 = Ph$, $R^2 = H$; **5, 8** $R^1 = Ph$, $R^2+R^3 = (–CH_2–)_4$;
6, 9 $R^1 = C_6H_4OMe\text{-}4$, $R^2+R^3 = (–CH_2–)_4$

The formation of the products **10**, **11**, **12** makes it possible to suppose that the pyridinium ring is reduced through the intermediates **A** containing a 1,4-dihydropyridine fragment followed by intramolecular O-cyclization and the formation of the oxazolohydropyridines **B**, the reduction of which leads to the bases **7-9**.

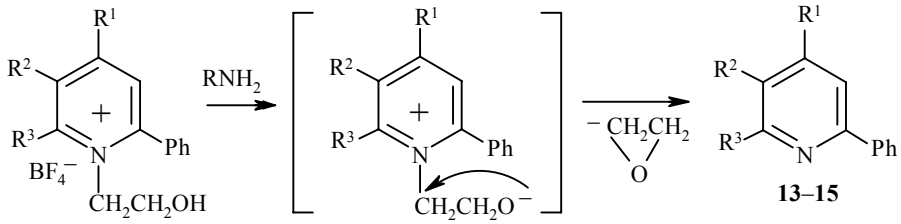
The proposed scheme is supported by the formation of the N-β-hydroxyethylperhydroquinolines **8**, **9** during the hydrogenation of the oxazolohydroquinolines **11**, **12** (120°C, 10 MPa), identical with those obtained during the catalytic reduction of the tetrahydroquinolinium salts **5**, **6**:



11, **12** **8**, **9**

8, **11** Ar = Ph; **9**, **12** Ar = C_6H_4OMe-4

During the hydrogenation of the salts **4-6** in the presence of bases (methylamine, ethanolamine) the hydroxyethyl substituent is eliminated with the formation of 2,4,6-triphenylpyridine (**13**), 2,4-diphenyl-5,6,7,8-tetrahydroquinoline (**14**), and 4-*p*-methoxyphenyl-2-phenyl-5,6,7,8-tetrahydroquinoline (**15**) respectively, which are not reduced under the selected conditions. Such a result can be explained in the light of data in [6] by deprotonation of the hydroxyl group under the action of the amine followed by elimination of ethylene oxide.



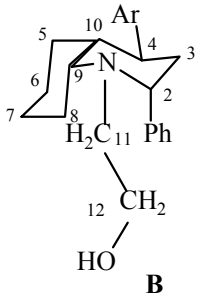
4–6 **13–15**

4, 13 $R^1 = R^3 = Ph$, $R^2 = H$; **5, 14** $R^1 = Ph$, $R^2+R^3 = (–CH_2–)_4$;
6, 15 $R^1 = C_6H_4OMe$-4, $R^2+R^3 = (–CH_2–)_4$; RNH_2 R = Me, $(CH_2)_2OH$

In the IR spectra of the tetrahydroquinolinium salts **5**, **6** there are strong absorption bands in the regions of 3524 cm^{-1} corresponding to the stretching vibrations of the O–H bond and 1060 cm^{-1}, characterizing the BF_4^- anion; the pyridinium ring absorbs at 1560 cm^{-1}. The ^1H NMR spectra of the salts **5**, **6** contain signals for the protons of the hydroxyl group at 2.2 ppm and of the methylene groups $N^+–CH_2$ at 4.75 and CH_2OH at 3.75 ppm.

In the ^{13}C NMR spectra of the perhydroquinolines **8**, **9** the signal of the $C_{(6)}$ atom is in the upfield region (19.50 and 19.57 ppm respectively) on account of γ-*gauche* interaction with the axially oriented $C_{(4)}–C_{(10)}$ bond, indicating *cis*-fusion of the heterocycles and alicycles.

The significant upfield shift of the signals for the $C_{(2)}$, $C_{(4)}$, and $C_{(9)}$ atoms in comparison with those in the spectrum of N-methyl-2,4-diphenylperhydroquinoline [6], caused by interaction with the axially arranged substituents at the $C_{(2)}$ and $C_{(9)}$ positions, indicates that compounds **8**, **9** are fixed in conformation **B**.



B

Thus, the hydrogenation of N-(2-hydroxyethyl)-substituted pyridinium and quinolinium salts is a prospective method for the synthesis of N-(2-hydroxyethyl)piperidines and perhydroquinolines. It makes possible to synthesize compounds inaccessible during the hydroethanolamination of 1,5-diketones.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR were recorded on a Varian FT-80 instrument at 80 and 20 MHz for ^{1}H and ^{13}C respectively (deuterochloroform, internal standard TMS). The IR spectra were recorded on a Specord M-80 instrument (in vaseline oil and in tablets with potassium bromide). Thin-layer chromatography was conducted on Silufol UV-254 plates (1:3:1 ether–hexane–acetone).

N-(2-Hydroxyethyl)-2,4,6-triphenylpyridinium Tetrafluoroborate (4). The compound was obtained by the method described in [6].

N-(2-Hydroxyethyl)-2,4-diphenyl-5,6,7,8-tetrahydroquinolinium Tetrafluoroborate (5). To a solution of 2,4-diphenyl-5,6,7,8-tetrahydrochromylium tetrafluoroborate (**2**) (12 mmol) in ethanol (30 ml) we added dropwise with constant stirring ethanolamine (14 mmol). The mixture was kept at room temperature for 3 h, and diethyl ether (150 ml) was added. The crystals that separated were filtered off and recrystallized from ethanol. The yield was 75%, and the product formed colorless crystals melting at 129-131°C (ethanol). IR spectrum, cm^{-1}: 3524 (O–H); 3028, 3064 (νCH of aromatic ring); 2944, 2876 (CH_2); 1552 (vibrations of pyridinium ring); 1072 (BF_4^-); 764, 700 (δCH of aromatic ring). ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 2.2 (1H, s, OH); 3.75 (2H, t, *J* = 3.9, $C\underline{H}_2OH$); 4.73 (2H, t, *J* = 3.9, $N^+–C\underline{H}_2CH_2OH$); 3.42 (2H, t, *J* = 6.1, $CH_2C=N^+$); 2.80 (2H, t, *J* = 6.3, 5-CH_2); 2.10-1.80 (4H, m, 6-CH_2, 7-CH_2); 7.40-7.53 (10H, m, H_{Ph}). Found, %: C 65.21; H 6.26; N 3.54. $C_{23}H_{24}BF_4NO$. Calculated, %: C 66.19; H 5.75; N 3.35.

N-(2-Hydroxyethyl)-4-*p*-methoxyphenyl-2-phenyl-5,6,7,8-tetrahydroquinolinium Tetrafluoroborate (6). This compound was synthesized by analogy with the salt **5** starting from 4-*p*-methoxyphenyl-2-phenyl-5,6,7,8-tetrahydrochromylium tetrafluoroborate (**3**). The yield was 72%, and the product formed colorless crystals melting at 105-106°C (ethanol). IR spectrum, cm^{-1}: 3526 (OH); 2942, 2876 (CH_2); 3024; 3060 (νCH of aromatic ring); 1552 (vibrations of pyridinium ring); 1070 (BF_4^-); 764, 700 (δCH of aromatic ring). ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 2.22 (1H, s, OH); 3.75 (2H, t, *J* = 3.8, $C\underline{H}_2OH$); 4.72 (2H, t, $N^+–C\underline{H}_2CH_2OH$); 3.40 (2H, t, $CH_2–C=N^+$); 2.85 (2H, t, 5-CH_2); 2.04-1.72 (4H, m, 6-CH_2, 7-CH_2); 7.40-7.58 (10H, m, H_{Ph}); 3.84 (3H, s, OCH_3). Found, %: C 64.03; H 5.52; N 3.34. $C_{24}H_{26}BF_4NO_2$. Calculated, %: C 64.43; H 5.82; N 3.13.

N-(2-Hydroxyethyl)-2,4,6-triphenylpiperidine (7) and 5,7,8a-Triphenylperhydrooxazolo-[3,2*a*]pyridine (10). In an autoclave with a capacity of 150 ml we placed ethanol (70 ml), the salt **4** (12 mmol), and Raney nickel catalyst (10% of the mass of the initial salt, initial hydrogen pressure 1-MPa, 120°C). After the absorption of 36 mmol of hydrogen the hydrogenation product was filtered from the catalyst and treated with a 5% solution of sodium hydroxide to pH 8-9, and the obtained base was extracted with 50-ml portions of ether. Compounds **7** and **10** were separated on a column (diameter 20 mm, length 250 mm) filled with aluminum oxide of III activity (3:1 hexane–diethyl ether). The constants and spectral characteristics of compounds **7** and **10** were given in [4].

N-(2-Hydroxyethyl)-2,4-diphenylperhydroquinoline (8). This compound was obtained by analogy with compound **7** from the tetrahydroquinolinium salt **5** [4].

N-(2-Hydroxyethyl)-4-*p*-methoxyphenyl-2-phenylperhydroquinoline (9). This compound was obtained by analogy with compound **7** from the tetrahydroquinolinium salt **6**. The yield was 75%, and the product was a colorless oil; R_f 0.295. ^{13}C NMR spectrum, δ, ppm: $C_{(2)}$ 53.26; $C_{(3)}$ 33.80; $C_{(4)}$ 35.96; $C_{(5)}$ 28.72; $C_{(6)}$ 19.57; $C_{(7)}$ 26.09; $C_{(8)}$ 24.82; $C_{(9)}$ 46.98; $C_{(10)}$ 46.30; $C_{(11)}$ 48.46; $C_{(12)}$ 61.05; O–CH_3 54.89. ^{1}H NMR spectrum, δ, ppm, *J* (Hz): 2.87 (1H, s, OH); 3.42 (2H, t, N–$CH_2C\underline{H}_2OH$); 2.64 (2H, t, N–$C\underline{H}_2CH_2OH$); 3.76 (3H, s, O–CH_3); 6.73-7.36 (9H, m, H_{Ph}). Found, %: C 78.64; H 8.15; N 4.05. $C_{24}H_{31}NO_2$. Calculated, %: C 78.90; H 8.49; N 3.84.

Oxazolohydroquinolines **11** and **12** were obtained by the method described in [5].

N-(2-Hydroxyethyl)-2,4-diphenylperhydroquinoline (8). In an autoclave with a capacity of 150 ml we placed ethanol (70 ml), the oxazolohydroquinoline **11** (15 mmol), 40% HBF_4 (15 mmol, 3.3 ml), and Raney nickel catalyst (10% of the mass of the initial compound, initial hydrogen pressure 10 MPa, 120°C). When 15 mmol of hydrogen had been absorbed the hydrogenation product was filtered from the catalyst and treated with 5% sodium hydroxide solution to pH 8-9. The nitrogen base **8** was obtained with a yield of 82%.

N-(2-Hydroxyethyl)-4-*p*-methoxyphenyl-2-phenylperhydroquinoline **9** was obtained similarly from the oxazolohydroquinoline **12** with a yield of 80%.

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