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STEREOCONTROLLED CATALYTIC SYNTHESIS OF SUBSTITUTED HYDROXYETHYL-PIPERIDINES FROM PYRYLIUM SALTS

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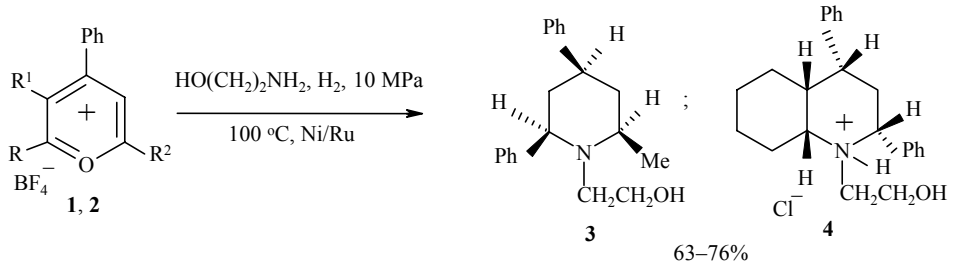
In previous work [1, 2], we demonstrated the feasibility of using catalytic methods for the stereocontrolled synthesis of N-hydroxyethyl derivatives of (cyclano)piperidines by means of the catalytic hydroethanolamination of bicyclic 1,5-diketones or the hydrogenation of pyridinium salts.

The use of this approach in the case of pyrylium salts, which may be obtained from readily available raw materials by a broad variety of synthetic methods, would have great preparative significance.

In the present work, we are the first to show that 2-methyl-4,6-diphenylpyrylium (**1**) and 2,4-diphenyl-5,6,7,8-tetrahydrochromylium tetrafluoroborates (**2**) undergo reductive recyclization under catalytic hydroethanolamination conditions to give the corresponding piperidine bases, namely, N-(2-hydroxyethyl)-2-methyl-4,6-diphenylpiperidine (**3**) and N-(2-hydroxyethyl)-2,4-diphenyldecahydroquinoline, which was isolated and characterized as hydrochloride salt **4**. The yields of **3** and **4** were 63 and 76%, respectively.

This reaction was carried out under 10 MPa hydrogen pressure at 100°C over a Ni/Ru catalyst in absolute ethanol. The salt/ethanolamine mole ratio was 1:2. Excess amine is necessary to bind HBF_4.



1, **2** → **3** (63–76%); **4**

1 R = Ph, R^1 = H, R^2 = Me, **2** R + R^1 = $(–CH_2–)_4$, R^2 = Ph

Distinguishing features of the structure of bases **3** and **4** are found in the equatorial position of all the substituent groups in piperidine **3** and the *cis* configuration of decahydroquinoline hydrochloride **4** with equatorial orientation of the phenyl substituents at $C_{(2)}$ and $C_{(4)}$ atoms.

This reaction is a new example of the direct conversion of pyrylium salts into nonaromatic azaheterocycles and a new approach to the stereocontrolled synthesis of N-hydroxyalkylpiperidines.

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The IR spectra were taken on a Specord M80 spectrophotometer in hexachlorobutadiene, vaseline oil, and KBr. The ^{1}H NMR spectra were taken at 80 MHz and the ^{13}C NMR spectra were taken at 20 MHz in $CDCl_3$ with TMS as the internal standard.

N-(2-Hydroxyethyl)-2-methyl-4,6-diphenylpiperidine (3). Mixture of pyrylium tetrafluoroborate **1** (4.34 g, 13 mmol), ethanolamine (1.6 g, 26 mmol), ethanol (80 ml), and Ni/Ru catalyst (the catalyst/initial salt mass ratio was 1:10) was placed into a 150-ml autoclave. The initial hydrogen pressure was 10 MPa. The reaction was carried out at 100°C. After absorption of 39 mmol of hydrogen, the hydrogenate was filtered to remove the catalyst and the solvent was distilled off. The oil obtained was purified by chromatography on a column (20 × 250 mm) packed with silica gel 40/100 using 3:1 hexane–ether as the eluent. The yield of crystalline colorless base **3** was 2.4 g (63%); mp 119-121°C (ethanol). IR spectrum, ν, cm^{-1}: 3340 (OH); 3080, 3060, 704, 760 (CH arom); 2996, 2884 (CH aliph). ^{13}C NMR spectrum, δ, ppm: 58.28 ($C_{(2)}$); 41.85 ($C_{(3)}$); 43.40 ($C_{(4)}$); 42.16 ($C_{(5)}$); 68.28 ($C_{(6)}$); 22.01 (CH_3); 52.70 (NCH_2); 59.23 (OCH_2). Found, %: C 81.05; H 8.69; N 4.52. $C_{20}H_{25}NO$. Calculated, %: C 81.31; H 8.53; N 4.74.

N-(2-Hydroxyethyl)-2,4-diphenyldecahydroquinoline Hydrochloride (4) was obtained analogously to compound **3** from tetrahydrochromylium tetrafluoroborate **2** (4.86 g, 13 mmol) and ethanolamine (1.6 g, 26 mmol). The oily free base was treated with diethyl ether (50 ml) saturated with HCl (20 mmol) to give 3.7 g (76%) of hydrochloride **4**; mp 240-241°C (ethanol). IR spectrum, ν, cm^{-1}: 3325 (OH); 3082, 3064, 702, 766 (CH arom); 2996, 2884 (CH aliph); 2600 (N^{+}–H). ^{13}C NMR spectrum, δ, ppm: 73.16 ($C_{(2)}$); 33.84 ($C_{(3)}$); 45.88 ($C_{(4)}$); 44.02 ($C_{(4a)}$); 21.81 ($C_{(5)}$); 26.35 ($C_{(6)}$); 20.46 ($C_{(7)}$); 29.14 ($C_{(8)}$); 44.02 ($C_{(8a)}$); 50.84 (NCH_2); 56.73 (OCH_2). Found, %: C 74.59; H 8.00; N 3.93. $C_{23}H_{30}ClNO$. Calculated, %: C 74.27; H 8.13; N 3.77.

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REFERENCES

1. T. G. Nikolaeva, P. V. Reshetov, A. P. Kriven'ko, and V. G. Kharchenko, *Khim. Geterotsikl. Soedin.*, 1370 (1983).
2. A. G. Golikov, P. V. Reshetov, and A. P. Kriven'ko, *Khim. Geterotsikl. Soedin.*, 1339 (2001).