Russian Journal of Organic Chemistry, Vol. 38, No. 1, 2002, p. 136. Translated from Zhurnal Organicheskoi Khimii, Vol. 38, No. 1, 2002, p. 142.

SHORT COMMUNICATIONS

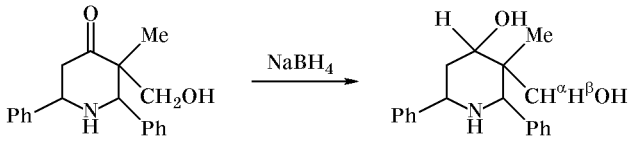
Reduction of 3-Hydroxymethyl-3-methyl-2,6-diphenylpiperidin-4-one

D. G. Kim and G. B. Tulemisova

Institute of Petroleum and Gas, Ministry of Science and Higher Education of Kazakhstan Republic, ul. Azattyk 1, Atyrau, 465002 Kazakhstan

Received April 7, 2001

4-Hydroxypiperidines are starting compounds in the synthesis of various functionally substituted piperidine derivatives which exhibit versatile biologal activity. By the reduction of 3-hydroxymethyl-3-methyl-2,6-diphenylpiperidin-4-one (**I**) [1] with complex metal hydrides (such as lithium tetrahydridoaluminate and sodium tetrahydridoborate) we obtained 4-hydroxy-3-hydroxymethyl-3-methyl-2,6-diphenylpiperidine (**II**) as a single stereoisomer:



I **II**

4-Hydroxy-3-hydroxymethyl-3-methyl-2,6-diphenylpiperidine (II). To a solution of 0.295 g (1 mmol) of 3-hydroxymethyl-3-methyl-2,6-diphenylpiperidin-4-one in ethanol we added 0.038 g (1 mmol) of $NaBH_4$, and the mixture was refluxed until formation of a complex with the initial compound was complete (TLC, Silufol UV-254, acetone–hexane, 1:3). The mixture was diluted with water, and 10% sulfuric acid was added to pH ~1 to decompose the complex. The solution was made strongly alkaline by adding K_2CO_3, and the product was extracted into diethyl ether. The extract was dried over anhydrous sodium sulfate and evaporated to obtain a lemon-yellow crystalline product which was recrystallized from ethanol. Yield 0.202 g (90%). mp 75°C, R_f 0.57. The product is soluble in ethanol and chloroform. IR spectrum, ν, cm^{-1}: 700, 800, 1600, 2960 (C_6H_5); 3300–3500 (OH). ^1H NMR spectrum ($CDCl_3$, 50°C), δ, ppm (*J*, Hz): 4.11 q (1H, 6-H_{ax}, $^3J_{6,5\text{-}ax}$ = 11.44, $^3J_{6,5\text{-}eq}$ = 4.45), 3.52 d (1H, H^{α}, $^2J_{\alpha,\beta}$ = 6.50), 3.91 q (1H, H^{β}, $^2J_{\beta,\alpha}$ = 6.47, $^3J_{\beta,OH}$ = 2.69), 1.85 q (1H, 5-H_{ax}, $^2J_{5\text{-}ax,5\text{-}eq}$ = 11.25, $^3J_{5\text{-}ax,6}$ = 11.25, $^3J_{5\text{-}ax,4}$ = 11.25), 1.87 d.m (1H, 5-H_{eq}, $^2J_{5\text{-}eq,5\text{-}ax}$ = 11.25, $^3J_{5\text{-}eq,4}$ = 3.70, $^3J_{5\text{-}eq,6}$ = 4.40), 2.07 t.d (1H, 4-H_{ax}, $^3J_{4,5\text{-}ax}$ = 11.25, $^3J_{4,5\text{-}eq}$ = 3.70), 3.88 s (1H, 2-H_{ax}), 3.48 s (CH_2O**H**), 3.49 s (4-OH), 1.26 s (NH), 1.04 s (3-CH_3), 7.2–7.6 m (H_{arom}). Found, %: C 76.52; H 7.73. M^+ 297. $C_{19}H_{23}NO_2$. Calculated, %: C 76.73; H 7.79. *M* 297.37. Hydrochloride, mp 203– 205°C (from ethanol). Found, %: Cl 10.30. $C_{19}H_{23}NO_2 \cdot HCl$. Calculated, %: Cl 10.63.

The axial orientation of 4-H was established on the basis of the ^1H NMR data. The 4-H signal appeared as a triplet of doublets due to coupling with two vicinal protons, $^3J_{4,5\text{-}ax}$ (large) and $^3J_{4,5\text{-}eq}$ (small). These data indicate that the hydroxy group on C^4 occupies the equatorial position.

The IR spectrum was recorded on a UR-20 spectrometer in KBr. The ^1H NMR spectra were obtained on a Varian X-400 instrument (400 MHz) using HMDS as internal reference. The mass spectrum was obtained using a Hewlett–Packard HP-5972 mass-selective detector.

REFERENCE

1. Kim, D.G. and Tulemisova, G.B., *Russ. J. Org. Chem.*, 1997, vol. 33, no. 9, pp. 1337–1340.

1070-4280/02/3801-0136 $27.00 © 2002 MAIK "Nauka / Interperiodica"