OPENING OF THE AZEPINE RING IN 2,3,4,5-TETRAHYDRO-1H-AZEPINO[3,4-b]INDOLE ON ALKYLATION WITH AN ALCOHOL IN THE PRESENCE OF RANEY NICKEL

R. G. Glushkov, V. A. Volskova, N. P. Kostyuchenko, Yu. N. Sheinker, and O. Yu. Magidson

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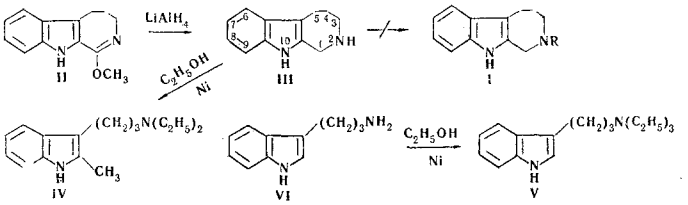
Developing our investigations on the chemistry of the azepino[3,4-b]indoles [1], we have studied the possibility of obtaining 2-alkyl-2,3,4,5-tetrahydro-1H-azepino[3,4-b]indoles (I) from 1-methoxy-4,5-dihydro-3H-azepino[3,4-b] indole (II). The reduction of II with $LiAlH_4$ in absolute ether formed 2,3,4,5-tetrahydro-1H-azepino[3,4-b]indole (III), yield 71%, mp 182–186° C (from ethyl acetate). Found, %: C 77.72; H 7.53; N 15.09. Calculated for $C_{12}H_{14}N_2$, %: C 77.41; H 7.52; N 15.05; hydrochloride of III, mp 280–282° C. However, attempts to alkylate III with CH_3I, $(CH_3)_2SO_4$, and with CH_2O in the presence of HCOOH in order to obtain I (R = CH_3) or its quaternary salts were unsuccessful. When an attempt was made to synthesize I (R = C_2H_5) from II by the method of alkylating amines with alcohols and, in particular, ethanol, in the presence of Raney nickel [2], a substance IV with bp 165–167° C (2 mm) was isolated. Found, %: C 79.11; H 9.59; N 11.62. Calculated for $C_{16}H_{24}N_2$, C 78.68; H 9.83; N 11.47. The IR spectrum, λ_{max} 284 nm (shoulder at 289 nm), was similar to that of III.



The assumption that IV was the 2,10-diethyl derivative of III was excluded, since the IR spectrum of IV, like that of II, had an absorption band at 3170 cm^{-1} which is characteristic for an indole NH band and lacked the band at 3310 cm^{-1} apparently corresponding to the NH group of an azepine ring. It is possible that the alkylation of III with ethanol in the presence of Raney nickel does first form I (R = C_2H_5), which is the cyclic analog of 2-(α-dimethylaminomethyl)indole [3], with properties similar to those of gramine. Consequently, we assume that in this case reduction of the $C_{(1)}-N_{(2)}$ bond of the azepine ring, accompanied by its opening and alkylation, takes place and that IV is 3-(γ-diethylaminopropyl)-2-methylindole.

The structure of IV was confirmed by PMR spectroscopy. As model compounds we used III and 3-(γ-diethylaminopropyl)indole (V) [bp 160–165° C (2 mm). Found, %: C 78.77; H 9.16; N 11.90. Calculated for $C_{15}H_{22}N_2$, %: C 78.26; H 9.56; N 12.17] obtained in a similar manner to IV from 3-(γ-aminopropyl)indole (VI) [1,4] by alkylation with 96% ethanol in the presence of Raney nickel.

PMR spectrum of IV: singlet signal at 2.29 ppm with an intensity of three proton units (p. u.)—methyl group in position 2 of an indole ring; triplet at 0.98 ppm (6 p. u.); quartet in the 2.47 ppm region (4 p. u.) due to an $N(C_2H_5)_2$ group; multiplet at 1.81 ppm (2 p. u.) corresponding to the protons of a CH_2 unit in the β-position of the side chain of IV; multiplet at 2.48 ppm corresponding to the signals of the protons of CH_2 groups [in the α- and γ-positions of the side chain of IV; the position and structure of these signals are similar to those of the corresponding CH_2 groups of the model compound V]. The aromatic protons give signals in the 6.8–7.4 ppm region, and the NH group of the indole ring a broad signal at 7.86 ppm. Furthermore, the PMR spectrum of IV lacks a singlet in the 3.9–4.0 ppm region corresponding to the protons of the CH_2 in position 1 group of III.

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Ordzhonikidze All-Union Scientific-Research of
Chemistry and Pharmacy, Moscow