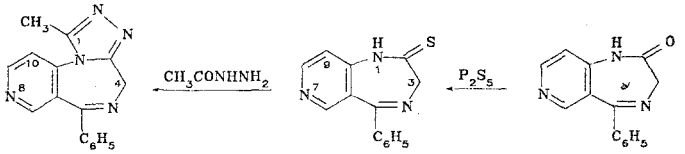
4H-PYRIDO[3,4-f]-1,2,4-TRIAZOLO[4,3-a]-1,4-DIAZEPINE — A NEW HETEROCYCLIC SYSTEM

R. N. Radinov, M. A. Khaimova, and E. M. Simova

UDC 547.89

It is known that 1,4-benzodiazepines and related structures are widely used in medicine as effective tranquilizers (for example, see [1]). A study of the relationship between the structure and activity in 1,4-benzodiazepines led to the synthesis of their structural analogs, the condensed benzene ring of which was replaced by a heterocyclic ring [2].

We have synthesized 1-methyl-6-phenyl-4H-pyrido[3,4-f]-1,2,4-triazolo[4,3-a]-1,4-diazepine (I), which is the 8-aza analog of the known tranquilizer alprazolam [3] and a representative of the heretofore unknown annelated heterocyclic system. Thus the reaction of 5-phenyl-1,3-dihydro-2H-pyrido[3,4-d]-1,4-diazepin-2-one (III) [4] with P_2S_5 leads to 5-phenyl-1,3-dihydro-2H-pyrido[3,4-f]-1,4-diazepine-2-thione (II), the reaction of which with acetylhydrazine gave I.



I II III

Thione II, with mp 194-196°C (ethanol) and empirical formula $C_{14}H_{11}N_3S$ (from the results of elementary analysis), was obtained in 62% yield by refluxing 5 mmole of III and 5 mmole of P_2S_5 in pyridine for 1.5 h, evaporation of the solvent in vacuo, and crystallization of the residue (chloroform–ether). Mass spectrum (m/z): 253 ($M^{+\cdot}$), 252 $[M-H]^+$, 226 $[M-HCN]^{+\cdot}$, 219 $[M-H_2S]^{+\cdot}$, 207, 166, 164, 149, 91 ($C_7H_7^+$), 77 ($C_6H_5^+$), 63 ($C_5H_3^+$), 51 ($C_5H_4^+$). IR spectrum (KBr): 1340, 1380, 1490 (aromatic C=C); 1525 (C=S); 1610, 1620 cm^{-1} (C=N). PMR spectrum ($CDCl_3$): 10.6 (1H, broad s, NH), 8.50 (1H, d, J = 5.5 Hz, 8-H), 8.44 (1H, s, 6-H), 7.30 (5H, m, C_6H_5), 6.92 (1H, d, J = 5.5 Hz, 9-H), and 4.70 ppm (2H, s, CH_2).

Compound I, with mp 206-207°C (from benzene–ether) and empirical formula $C_{16}H_{13}NS$ (from the results of elementary analysis), was obtained in 52% yield by refluxing 2 mmole of II and 6 mmole of acetylhydrazine in dimethylformamide in a stream of nitrogen for 1.5 h, evaporation of the solvent in vacuo, and crystallization of the residue (from chloroform–ether). Mass spectrum (m/z): 275 ($M^{+\cdot}$), 246, 205, 103, 91 ($C_7H_7^+$), 78 ($C_6H_6^{+\cdot}$), 77 ($C_6H_5^+$), 63 ($C_5H_3^+$), 51 ($C_4H_3^+$). IR spectrum (KBr): 1440, 1505, 1605, and 1625 cm^{-1}. PMR spectrum ($CDCl_3$): 8.73 (1H, d, J = 5.5 Hz, 9-H), 8.57 (1H, s, 7-H), 7.30 (6H, m, C_6H_5 and 10-H), 5.42 (1H, d, J = 13.0 Hz, 4-H), 4.03 (1H, d, J = 13.0 Hz, 4-H), and 2.59 ppm (3H, s, 1-CH_3).

LITERATURE CITED

1. A. V. Bogat-skii, S. A. Andronati, and N. Ya. Golovenko, Tranquilizers (1,4-Benzodiazepines and Related Structures) [in Russian], Naukova Dumka, Kiev (1980).
2. R. T. Owan, Drugs of the Future, 6, 342 (1981).
3. J. B. Pento, Drugs of Today, 18, 253 (1982).
4. R. Littel and D. S. Allen, J. Med. Chem., 8, 722 (1965).

K. Okridskii Sofia University, Sofia, Bulgarian People's Republic 1126. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 270-271, February, 1984. Original article submitted September 27, 1983.

0009-3122/84/2002-0229$08.50