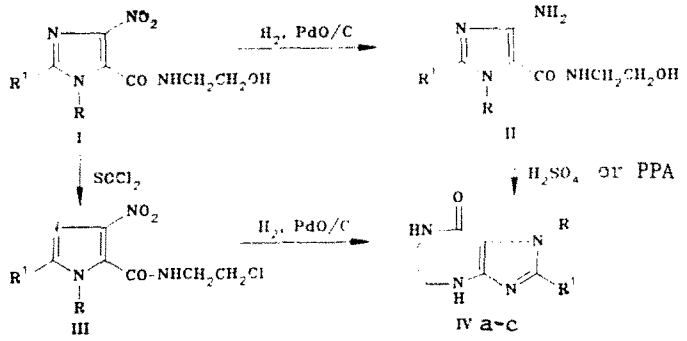
NOVEL SYNTHESIS OF IMIDAZO[4,5-e][1,4]DIAZEPINES

L. A. Reznichenko and P. M. Kochergin

UDC 547.547.892'784.1.07

Imidazo[4,5-e][1,4]diazepine derivatives were synthesized previously by recyclization of the pyrimidine ring of caffeine [1, 2] or by multistep transformations of esters of nitroimidazolecarboxylic acids with N-hydroxysuccinimide [3].

We have developed a novel method for the synthesis of derivatives of imidazo[4,5-e][1,4]diazepine IV by intramolecular cyclodehydration of N-(2-hydroxyethyl)amides of 1-methyl- and 1,2-dialkyl-4-aminoimidazole-5-carboxylic acids in concentrated H_2SO_4 or polyphosphoric acid (PPA). An alternative route for the synthesis of compounds IV is reductive cyclization of nitro chloroethylamides III over PdO/C.



IVa R=CH_3, R^1=H; b R=R^1=CH_3, c R=*i*-C_4H_9, R^1=*i*-C_3H_7

Compounds I were prepared by the reaction of chlorides or esters of 1-methyl- and 1,2-dialkyl-4-nitroimidazole-5-carboxylic acids with monoethanolamine and subsequent catalytic reduction of the NO_2 group over PdO/C.

Chloroethylamides III were synthesized by treating hydroxyethylamides I with thionyl chloride in benzene.

The formation of a diazepine ring condensed with an imidazole ring was confirmed by a shift of the peaks of CH_2-group protons in the PMR spectra (CF_3COOD) of compounds IVa-c to a weaker field (two triplets at 3.9 ppm and 4.8 ppm) in comparison with the starting compounds II and III, in whose PMR spectra the peaks of these groups were observed in the form of an unresolved multiplet (a shoulder on the singlet of the N-CH_3 group) at 3.3-3.6 ppm.

The IR spectra of tetrahydroimidazo[4,5-e][1,4]diazepin-8-ones IVa-c were characterized by the presence of bands of stretching vibrations of NH groups (3370-3400 and 3450 cm^{-1}) and also two bands of a secondary amide $\nu_{C=O}$ (1630-1650 cm^{-1}, split) and δ_{NH} (1550 cm^{-1}).

Compound IVa ($C_7H_{10}N_4O$). Yield 40.0%, mp 154-155°C (aqueous alcohol) and M^+ 166.

Compound IVb ($C_3H_{12}N_4O$). Yield 70.0%, mp 186-188°C (ethyl acetate) and M^+ 180.

Compound IVc ($C_{13}H_{22}N_4O$). Yield 64.0%, mp 106-108°C (aqueous alcohol) and M^+ 250.

The data of elemental analysis for C, H, and N correspond to the calculated data.

LITERATURE CITED

1. A. V. Bogatskii and É. I. Ivanov, *Ukr. Khim. Zh.*, No. 10, 1074 (1980).
2. T. Ohsaki, T. Kuriki, J. Sakakibara, and M. Asano, *Chem. Pharm. Bull.*, **34**, 3573 (1986).
3. R. S. Hosmane, A. Bhan, and M. E. Rauser, *Heterocycles*, **24**, 2743 (1986).

Novokuznetsk Pharmaceutical-Chemical Scientific-Research Institute, Novokuznetsk 654034. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1140-1141, August, 1990. Original article submitted June 26, 1989.

 0009-3122/90/2608-0956$12.50