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SYNTHESIS OF 2-OXOOXAZOLO[5,4-*b*]PYRIDINES AND THEIR REACTIONS WITH AMINES

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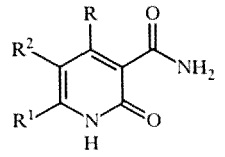
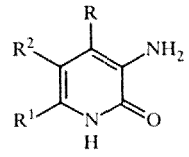
2-Oxooxazolo-[4,5-*b*]pyridines are known to be physiologically active [1, 2]. 2-Oxooxazolo[5,4-*b*]pyridines have been mentioned in just one paper [3].

In studying derivatives of 3-aminocarbonylpyridines (Ia-d) in the Hofmann reaction with the aim of preparing the corresponding 3-amino-2(1H)-pyridones, similar to those we had prepared previously [4, 5], we observed that the reaction occurred analogously to that reported by Graebe [6] for salicylamide.

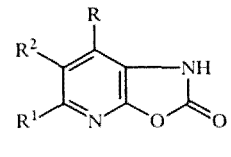
Only compound Id was converted into the corresponding 3-amino derivative IId in the Hofmann reaction with sodium hypochlorite or hypobromite, while compounds Ia-c were transformed into oxooxazalo[5,4-*b*]pyridines (IIIa-c). Chlorinated pyridones Ia-c were not observed in the Hofmann reaction.



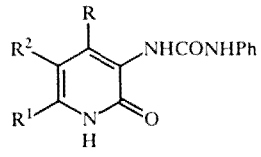
I a-d



II a-d



III a-d



IV a-c

I—IV a R = R^1 = CH_3, R^2 = Br; b R = CH_3, R^1 = Ph, R^2 = Br; c R = CF_3, R^1 = Ph, R^2 = H; d R = H, R^1 = COOH, R^2 = Br

The 2-oxooxazolopyridines IIIa and IIIc reacted with aniline to give N-phenylureidopyridones (IVa, c) while the corresponding 3-aminopyridone (IIa) was obtained with stronger bases (butylamine, diethylamine, piperidine, morpholine).

The Hofmann reaction with a series of pyridones has considerable potential for the synthesis of 2-oxooxazolo[5,4-*b*]pyridines, 3-aminopyridines and 3-N-substituted ureidopyridines. This investigation is continuing.

Compounds Ia-c were obtained by a method described in [7] and compound Id by a method described in [8].

3-Amino-5-bromo-4,6-dimethyl-2(1H)pyridone (IIa, $C_{12}H_9BrN_2O$). T_{dec} >250°C (EtOH). IR spectrum: 1658, 3271, 3375 cm^{-1}. ^1H NMR spectrum (DMSO-D_6): 2.24 (3 H, s, CH_3), 2.31 (3 H, s CH_3), 7.40 (1 H, NH_2), 7.80 (1 H, NH_2), 12.04 ppm (1H, NH).

3-Amino-5-bromo-6-carboxy-2(1H)pyridone (IId, $C_6H_5BrN_2O_3$). T_{dec} 233-234°C. IR spectrum: 1689, 1700, 3072, 3344, 3424 cm^{-1}. ^1H NMR spectrum (DMSO-D_6): 5.68-6.71 (3 H, m, =CH−, NH_2), 11.62 ppm (2 H, NH, OH).

6-Bromo-5,7-dimethyl-2-oxo-(1H)-oxazolo[5,4-*b*]pyridine (IIIa, $C_8H_7BrN_2O_2$). T_{dec} > 240°C. IR spectrum: 1650, 1756, 1776, 3108, 3512 cm^{-1}. ^1H NMR spectrum (DMSO-D_6): 2.28 (3 H, CH_3), 2.48 (3 H, CH_3), 12.00 ppm (1 H, NH).

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6-Bromo-7-methyl-5-phenyl-2-oxo-(1H)-oxazolo[5,4-*b*]pyridine (IIIb, $C_{13}H_9BrN_2O_2$). T_{dec} > 263-265°C (3:1 EtOH-water). IR spectrum: 1625, 1748, 1778, 2794, 2994, 3062 cm^{-1}. ^1H NMR spectrum (DMSO-D_6): 2.42 (3 H, CH_3), 7.47 (5 H, Ph), 12.25 ppm (1 H, NH).

7-Trifluoromethyl-5-phenyl-2-oxo-(1H)-oxazolo[5,4-*b*]pyridine (IIIc, $C_{13}H_7F_3N_2O_2$). M.p. 255-256°C (2:1 EtOH-water). IR spectrum: 1630, 1760, 2937, 3200 cm^{-1}. ^1H NMR spectrum (DMSO-D_6): 7.44 (3 H, Ph), 7.93 (1 H, =CH-), 8.06 (2 H, Ph), 12.64 ppm (1 H, NH).

3-(N-Phenylureido)-4,6-dimethyl-2-(1H)-pyridone (IVa, $C_{14}H_{14}BrN_3O_2$). $T_{dec.}$ 300°C (DMF). IR spectrum: 1578, 1640, 3094, 3120, 3195, 3294 cm^{-1}. ^1H NMR spectrum (DMSO-D_6): 2.13 (3 H, CH_3), 2.31 (3 H, CH_3), 7.27 (5 H, Ph), 7.73 (1 H, NH), 9.02 (1 H, NH), 12.08 ppm (1 H, NH).

3-(N-Phenylureido)-4-trifluoromethyl-6-phenyl-2-(1H)-pyridone (IVb, $C_{19}H_{14}F_3N_3O_2$). M.p. 244-246°C (1:1:1 DMF-EtOH-H_2O). IR spectrum: 1556, 1600, 1638, 2960, 3064, 3268 cm^{-1}. ^1H NMR spectrum (DMSO-D_6): 6.67-7.50 (9 H, 2 Ph, =CH-), 7.86 (2 H, Ph), 8.00 (1 H, NH), 9.11 (1 H, NH), 12.53 ppm (1 H, NH).

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