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HETEROCYCLIZATION OF CAPROLACTAM HYDRAZIDINE BY THE ACTION OF 2,3-DIOXO-PYRROLO[2,1-*a*]ISOQUINOLINES

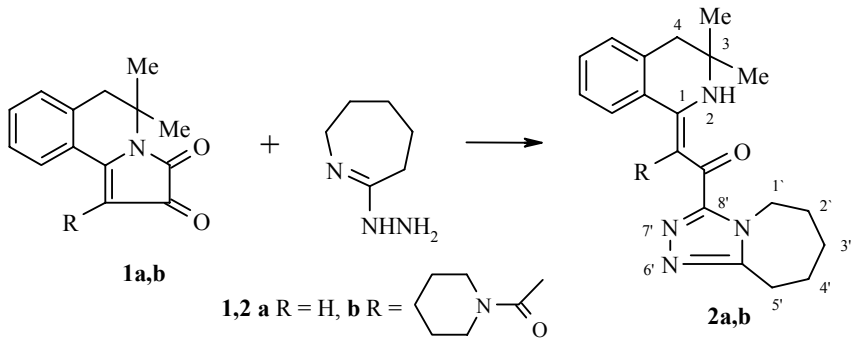
O. V. Surikova, A. G. Mikhailovskii, and M. I. Vakhrin

Keywords: 2-hydrazino-3,4,5,6-tetrahydro-2H-azepine, 2,3-dioxopyrrolo[2,1-*a*]isoquinolines, 3,3-dimethyl-1-(1,2,4-triazolo[4,5-*a*]azepan-8-ylcarbonylmethylideno)-1,2,3,4-tetrahydroisoquinolines, opening of the dioxopyrroline ring.

In previous work [1, 2], we showed that the reaction of 2,3-dioxopyrrolo[2,1-*a*]isoquinolines with several dinucleophiles might proceed with opening of the lactam bond and concurrent heterocyclization. The reactions of these compounds with cyclic hydrazidines have not yet been reported. In a continuation of a study of the chemical properties of these compounds, we found that dioxopyrrolines **1a**,**1b** readily undergo opening of the pyrroline ring upon moderate heating in benzene to give enamino ketones **2a**,**b**.

This method was used to synthesize various compounds with potential biological activity. In the case R = H, the compounds obtained are enamino ketones, which are capable of further transformations.

The ^{1}H NMR spectra were taken on a Bruker-300 spectrometer at 300 MHz in $CDCl_3$ with HMDS as the internal standard. The IR spectra were taken on a Specord M-80 spectrometer for vaseline mulls. The electron impact mass spectra were taken on an MAT-311 at 70 eV.



3,3-Dimethyl-1-(1,2,4-triazolo[4,5-*a*]azepan-8-ylcarbonylmethylideno)-1,2,3,4-tetrahydroisoquinoline (2a). 2-Hydrazino-3,4,5,6-tetrahydro-2H-azepine (caprolactam hydrazidine) (1.91 g, 15 mmol) [3] was added to a solution of compound **1a** (2.27 g, 10 mmol) in benzene (20 ml). The red mixture immediately turned colorless upon heating to 60-70°C. A yellow precipitate formed upon the addition of hexane (50 ml),

Perm State Pharmaceutical Academy, 614990 Perm, Russia; e-mail: perm@pfa.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 298-299, February, 2008. Original article submitted December 24, 2007.

which was filtered off, dried, and recrystallized from hexane to give compound **2a** (2.71 g, 80%). IR spectrum, ν, cm^{-1}: 1630 (C=O), 3150 (NH). ^1H NMR spectrum, δ, ppm: 1.24 (6H, s, $2CH_3$); 1.28-1.81 (6H, m, H-2', H-3', H-4'); 2.39-2.53 (2H, m, H-5'); 2.86 (2H, s, H-4); 3.09-3.23 (2H, m, H-1'); 6.72 (1H, s, =CHCO); 7.14-7.30 (4H, m, Ar); 12.45 (1H, s, NH). Mass spectrum, *m/z* (I_{rel}, %): 336.4 $[M]^+$ (33), 321 $[M^+–CH_3]$) (10), 200 $[M^+–$(1,2,4-triazolo[4,5-*a*]azepane)] (63). Found, %: C 71.3; H 7.1; N 16.8. $C_{20}H_{24}N_4O$. Calculated, %: C 71.4; H 7.2; N 16.7.

N,N-Pentamethylenamide of 2-(3,3-dimethyl)-1,2,3,4-tetrahydroisoquinolin-1-ylidene)-3-oxo-3-(1,2,4-triazolo[4,5-*a*]azepan-8-yl)propanoic Acid (2b) was obtained analogously from compound **1b** (3.38 g, 10 mmol) in 85% yield (3.80 g), mp 93-94°C. IR spectrum, ν, cm^{-1}: 1635, 1670 (C=O); 3120 (NH). ^1H NMR spectrum, δ, ppm: 1.25 (6H, s, $2CH_3$); 1.36-1.93 (6H, m, $3CH_2$–C azepane and 6H, m, $3CH_2$–C piperidine); 2.40-2.55 (2H, m, H-5'); 3.15-3.80 (2H, m, CH_2–N azepane and 4H, m, $2CH_2N$ piperidine); 2.83 (2H, s, H-4); 7.01-7.62 (4H, m, Ar); 12.20 (1H, s, NH). Mass spectrum, *m/z* (I_{rel}, %): 447.6 $[M]^+$ (13), 335 $[M^+–C(O)N(CH_2)_5]$ (33). Found, %: C 69.7; H 7.3; N 15.7. $C_{26}H_{33}N_5O_2$. Calculated, %: C 69.8; H 7.4; N 15.6.

REFERENCES

1. N. N. Polygalova, A. G. Mikhailovskii, and M. I. Vakhrin, in: V. G. Kartsev (editor), *Nitrogen-Containing Heterocycles*, vol. 1, ICSPF, Moscow (2006), p. 402.
2. O. V. Surikova, A. G. Mikhailovskii, N. N. Polygalova, P. G. Neifeld, and M. I. Vakhrin, *Zh. Org. Khim.*, **43**, 1416 (2007).
3. M. V. Rubtsov and A. G. Baichikov, *Synthetic Pharmaceutical Chemical Preparations* [in Russian], Meditsina, Moscow (1971), p. 178.