SYNTHESIS OF 7,8-DIHYDRO-6H-PYRAZOLO[5',1':3,4][1,2,4]-TRIAZINO[6,5-*d*][1,2]DIAZEPIN-6-ONE, A NEW HETEROCYCLIC SYSTEM

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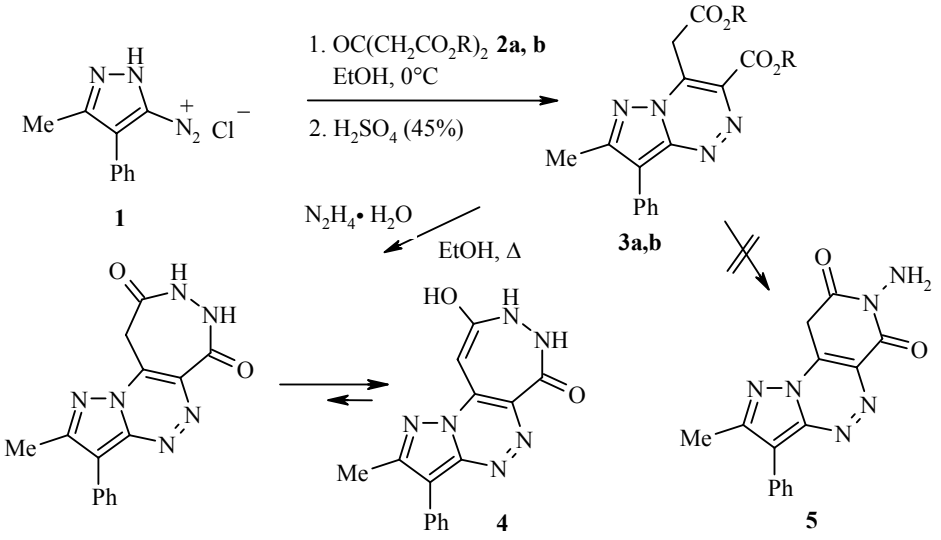
In a continuation of a study of the chemistry of 3(5)-pyrazolediazonium salts [1, 2], we have developed a simple and convenient method for constructing the 1,2-diazepine ring condensed with a pyrazolo-[5,1-*c*]-*as*-triazine fragment.



2, **3 a** R = Me, **b** R = Et

Azo coupling of pyrazolediazonium salt **1** with esters of acetonedicarboxylic acid **2a**,**b** through a stage involving cyclization of the hydrazones gave new pyrazolo[5,1-*c*][1,2,4]triazines **3a**,**b**. The cyclocondensation of triazines **3a**,**b** with hydrazine hydrate proceeded unequivocally to give two regioisomers **4** and **5**. Analysis of the ^{1}H NMR spectrum indicated that this transformation leads exclusively to 9-hydroxy-2-methyl-3-phenyl-

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7,8-dihydro-6H-pyrazolo[5',3':3,4][1,2,4]triazino[6,5-*d*][1,2]diazepin-6-one (**4**), which exists predominantly as the enol tautomer. The spectrum of this product lacks the singlet for the amino group, corresponding to pyrazolotriazine structure **5**. In addition, broad signals are observed for the NH protons of the diazepine fragment at δ 9.60 and 11.40 ppm.

The ^{1}H NMR spectra were taken on a Bruker AC-300 spectrometer at 300 MHz in DMSO-d_6 with TMS as the internal standard. The mass spectra were taken on an LKB-9000 spectrometer at 70 eV ionizing electron energy. The elemental analyses were taken on a Carlo Erba NA 1500 analyzer.

Methyl Ester of 4-(2-Methoxycarbonylmethyl)-7-methyl-8-phenylpyrazolo[5,1-*c*][1,2,4]triazine-3-carboxylic Acid (3a). A solution of 5-amino-3-methyl-4-phenylpyrazole [3] (1.7 g, 1.0 mmol) in water (20 ml) and concentrated hydrochloric acid (3 ml) was treated with $NaNO_2$ (0.7 g, 1.0 mmol) at 0°C. The solution obtained was added in portions to a mixture consisting of ester **2a** (1.9 g, 1.1 mmol), ethanol (20 ml), and saturated aqueous sodium acetate (12 g). The reaction mixture was mixed for 1 h. The precipitate was filtered off and washed with water. Then, 30-40 ml 45% sulfuric acid was added and stirred for 15-30 min. The mixture was poured into water (300 ml). The precipitate formed was filtered off, washed with water until the wash water was neutral to give 2.8 g (83%) compound **3a**; mp 98-100°C (2-propanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.71 (3H, s, CH_3); 3.66 (3H, s, OCH_3); 4.00 (3H, s, OCH_3); 4.75 (2H, s, $C\underline{H}_2CO_2Me$); 7.50-7.92 (5H, m, C_6H_5). Mass spectrum, *m/z* (I_{rel}, %): 340 $[M]^+$ (100). Found, %: C 59.87; H 4.87; N 16.55. $C_{17}H_{16}N_4O_4$. Calculated %: C 59.99; H 4.74; N 16.46.

Ethyl Ester of 4-(2-Ethoxycarbonylmethyl)-7-methyl-8-phenylpyrazolo[5,1-*c*][1,2,4]triazine-3-carboxylic Acid (3b) was obtained in 68% yield (2.5 g); mp 123-125°C (2-propanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.22 (3H, t, *J* = 6.9, $CH_2C\underline{H}_3$); 1.39 (3H, t, *J* = 6.9, $CH_2C\underline{H}_3$); 2.72 (3H, s, CH_3); 4.10-4.40 (4H, m, $2CH_3C\underline{H}_2$); 4.76 (2H, s, $C\underline{H}_2CO_2Et$); 7.44-7.90 (5H, m, C_6H_5). Mass spectrum, *m/z* (I_{rel}, %): 368 $[M]^+$ (100). Found, %: C 61.80; H 5.59; N 15.30. $C_{19}H_{20}N_4O_4$. Calculated, %: 61.95; H 5.47; N 15.21.

9-Hydroxy-2-methyl-3-phenyl-7,8-dihydro-6H-pyrazolo[5',1':3,4][1,2,4]triazino[6,5-*d*]diazepin-6-one (4). A mixture of compounds **3a** or **3b** (1.0 mmol), hydrazine hydrate (1.0 ml, 2.0 mmol), and ethanol (35 ml) was heated at reflux for 30 min. The precipitate formed was filtered off and crystallized to give 1.2 g (40%) compound **4**, mp 210°C (dec.) (acetic acid). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.35 (3H, s, CH_3); 6.23 (1H, s, H-10); 7.26-7.50 (5H, m, C_6H_5); 9.60 (1H, br. s, NH); 11.32-11.58 (1H, br. d, *J* = 17, NH); 14.10 (1H, br. s, OH). Mass spectrum, *m/z* (I_{rel}, %): 308 $[M]^+$ (20), 282 (28), 210 (10), 173 (45), 157 (72), 145 (37), 131 (41), 115 (100), 89 (55), 51 (55), 39 (71). Found, %: C 58.60; H 3.78; N 27.15. $C_{15}H_{12}N_6O_2$. Calculated, %: C 58.44; H 3.92; N 27.20.

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