5(3)-HYDROXYISOXAZOLIDIN-3(5)-ONES AND 5-HYDROXY-PYRAZOLIDIN-3-ONES AND THEIR RING-CHAIN TAUTOMERISM

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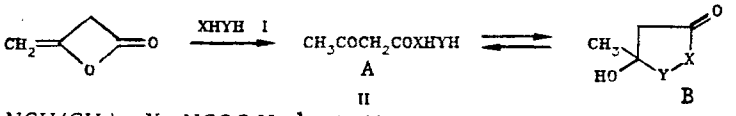
We have found that the unknown β-ketohydrazides (IIa, b) are readily formed by the interaction of diketene with the equivalent amount of the corresponding hydrazide (Ia, b) even only at room temperature.



I, II a $X=NCH(CH_3)_2$, $Y=NCOC_6H_5$; b $X=NCH(CH_3)_2$, $Y=NCOCH_2C_6H_5$; c $X=NC_6H_5$, $Y=O$; d $X=NCH_2C_6H_5$, $Y=O$; e $X=O$, $Y=NCOC_6H_5$

A characteristic feature of the compounds (IIa, b), and of their oxygen analogs (IIc-e), is the tendency for the ring–chain tautomerism A ⇄ B. The last were previously considered to be linear or cyclic isomers, and the phenomenon of the A ⇄ B tautomerism was not observed for them [1, 2].

Compounds (IIa, b, e) occur completely in the linear form A in DMSO, and the A ⇄ B tautomerism takes place in $CDCl_3$ or in other nonpolar media. In contrast, the 5-hydroxyisoxazolidinones (IIc, d) occur in the equilibrium with the linear form A in DMSO, and are presented as the cyclic form B in $CDCl_3$.

1-Benzoyl-2-isopropyl-5-hydroxy-5-methylpyrazolidin-3-one (IIa). mp 86-88°C. PMR spectrum (in $CDCl_3$: form A (~90%) 1.09 (6H, d, J= 7.5 Hz, Me_2), 2.08 (3H, s, CH_3), 3.43 (2H, s, CH_2), 4.75 (1H, m, J = 7 Hz, CH), 7.25-7.82 (5H, m, H_{arom}), and 9.26 ppm (1H, s, NH); form B (~10%) 1.17 (6H, d, Mc_2), 1.78 (3H, s, CH_3), 2.72 (2H, s, CH_2), 4.75 (1H, m, J = 7 Hz, CH), 5.07 (1H, br.s, OH), and 7.25-7.82 ppm (5H, m, H_{arom}).

1-Phenacetyl-2-isopropyl-5-hydroxy-5-methylpyrazolidin-3-one (IIb). mp 95-96°C. PMR spectrum (in $CDCl_3$): form A (~ 95%) 0.85 (6H, d, J = 7 Hz, Me_2), 1.79 (3H, s, CH_3), 3.12 (2H, s, NCH_2), 3.38 (2H, s, CH_2), 4.58 (1H, m, J = 7 Hz, CH), 7.10 (5H, s, H_{arom}), and 8.65 ppm (1H, s, NH); form B (~5%) 1.00 (6H, d, J = 7 Hz, Me_2), 1.55 (3H, s, CH_3), 2.10 (2H, s, 4-CH_2), 3.45 (2H, s, CH_2), 4.58 (1H, m, J = 7 Hz, CH), 4.72 (1H, s, OH), and 7.10 ppm (5H, s, H_{arom}).

2-Phenyl-5-hydroxy-5-methylisoxazolidin-3-one (IIc). mp 126°C [1]. PMR spectrum (in DMSO-D_6): form A (~20%) 2.20 (3H, s, CH_3), 3.75 (2H, s, CH_2), 7.25-7.85 (5H, m, H_{arom}), and 10.73 ppm (1H, br.s, OH); form B (~80%) 1.58 (3H, s, CH_3), 2.66 and 3.24 (2H, AB-system, J_{AB} = 16 Hz, CH_2), 7.12 (1H, s, OH), and 7.25-7.85 ppm (5H, m, H_{arom}). ^{13}C NMR spectrum (in DMSO-D_6): form A 28.9 (CH_3), 50.8 (CH_2), 167.2 (N–C=O), and 203.6 (C=O); form B 24.4 (CH_3), 45.8 (CH_2), 103.9 ($C_{(5)}$), 167.0 (C=O), and 116.4-137.7 ppm (8 signals, C_{arom}).

2-Benzyl-5-hydroxy-5-methylisoxazolidin-3-one (IId). mp 66-67°C. PMR spectrum (in DMSO-D_6): form A (~30%) 2.15 (3H, s, CH_3), 3.44 (2H, s, CH_2), 4.71 (2H, s, NCH_2), 7.36 (5H, s, H_{arom}), and 10.0 ppm (1H, s, OH); form B (~70%) 1.47 (3H, s, CH_3), 2.53 and 2.96 (2H, AB-system, J_{AB} = 11 Hz, CH_2), 4.69 (2H, s, NCH_2), and 7.13 ppm (1H, s, OH). ^{13}C NMR spectrum (in DMSO-D_6): form A 30.0 (CH_3), 48.4 (NCH_2), 51.1 (CH_2), 167.5 (N–C=O), and 202.4 ppm (C=O); form B, 24.6 (CH_3), 44.0 ($C_{(4)}$), 48.0 (NCH_2), 103.1 ($C_{(5)}$), 168.6 (N–C=O), and 127.5-135.9 ppm (8 signals, C_{arom}).

2-Benzoyl-3-hydroxy-3-methylisoxazolidin-5-one (IIe).* mp 85°C [2]. PMR spectrum (in $CDCl_3$): form A (~90%) 2.23 (3H, s, CH_3), 3.61 (2H, s, CH_2), 7.20-7.87 (5H, s, H_{arom}), and 10.5 ppm (1H, br.s, NH); form B (~10%) 1.97 (3H, s, CH_3), 3.10-3.78 (2H, m, CH_2), and 7.20-7.87 ppm (6H, m, H_{arom} + OH). ^{13}C NMR spectrum (in $CDCl_3$): form A 29.8 (CH_3), 47.0 (CH_2), 127.3-132.5 (4 signals, C_{arom}), 165.1 (NC=O), 166.0 (O–C=O), and 199.4 ppm (C–C=O).

The 5(3)-hydroxyisoxazolidin-3(5)-ones and 5-hydroxypyrazolidin-3-ones present interest as synthons for the isolation of 1,3-bifunctional compounds.

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REACTION OF 6-CYANO-1,2,4-TRIAZOLO[1,5-*a*]PYRIMIDIN-5(8H)-ONE WITH PHOSPHORUS OXYCHLORIDE IN THE PRESENCE OF N,N-DIETHYLANILINE

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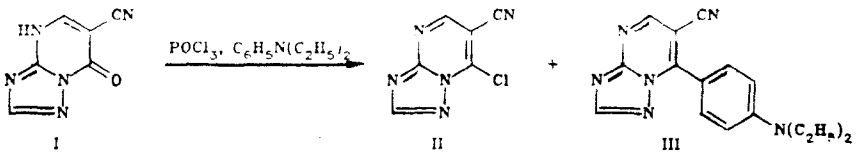
The interaction of the oxy derivatives of nitrogen heterocycles with $POCl_3$ in the presence of N,N-dialkylanilines is often utilized for the conversion of these compounds to the corresponding chlorine derivatives. However, this reaction sometimes proceeds ambiguously. For example, the reaction of some pyrimidinediones with $POCl_3$ in the presence of N,N-dimethylaniline leads to the formation of the mixture of dichloropyrimidines and N-methylanilinopyrimidines [1].

We found that the boiling of 6-cyano-1,2,4-triazolo[1,5-*a*]pyrimidin-5(8H)-one (I) in the mixture of $POCl_3$ and N,N-diethylaniline leads to the unexpected formation of 5-(p-diethylamino)phenyl-6-cyano-1,2,4-triazolo[1,5-*a*]pyrimidine (III) together with the 5-chloro derivative (II):



I II III

The mixture of 1.2 g (7.5 mmoles) of compound (I) [2], 26 ml of $POCl_3$, and 2.4 ml (2.25 g; 15 mmoles) of N,N-diethylaniline is boiled for 2 h. The excess of the $POCl_3$ is distilled off in vacuo, and the residue is poured onto ice. The residue is filtered off and recrystallized prior to the isolation of 0.24 g (18%) of compound (II), which has mp 170°C (from ethyl acetate). PMR spectrum (in CF_3COOD): 8.8 (1H, s, 7-H) and 8.93 ppm (1H, s, 2-H). The aqueous filtrate is extracted with chloroform. The extract is washed with water, dried with $MgSO_4$, and filtered. The chloroform is distilled off, and the residue is chromatographed on a column with silica gel; the fraction with the R_f 0.2 (chloroform) is collected. The yield of compound (III) is 0.44 g (20%); mp 174.5-177°C from ethyl acetate. IR spectrum (KBr): 2222 cm^{-1} (CN). PMR spectrum (CF_3COOD): 0.91 (6H, t, CH_3), 3.54 (4H, q, CH_2), 7.55 (2H, d, arom. prot.), 7.93 (2H, d, arom. prot.), 8.8 (1H, s, 7-H), and 9.1 ppm (1H, s, 2-H). Mass spectrum (m/z) (I_{rel}, %): M^+ 292 (28), $[M - CH_3]^+$ 277 (100), and $[M - CH_3{-}C_2H_4]^+$ 249 (47).

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