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REARRANGEMENT OF 2-(2-ARYL-2-OXOETHYL)-1,2-DIHYDROPYRIDO-[2,3-*b*]PYRAZIN-3(4H)-ONES

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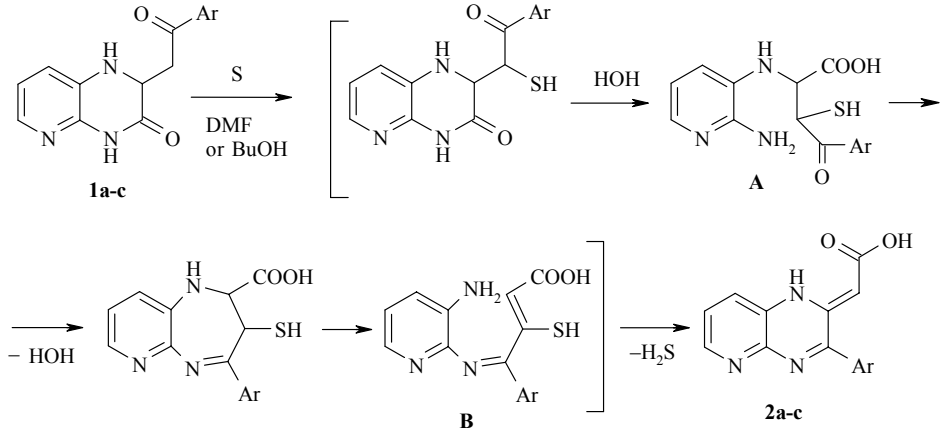
In previous work [1], we established that 3-(*n*-R-phenacyl)quinoxalin-2-ones undergo thermal rearrangement to give 3-aryl-2-methylidenecarboxyquinoxalines upon heating in acetic acid. However, the yields of the acids were low and 2-(2-aryl-2-oxoethyl)-1,2-dihydropyrido[2,3-*b*]pyrazin-3(4H)-ones (**1**) remain unchanged under these conditions [2].

In the present work, we have shown that heating pyrido[2,3-*b*]pyrazin-3-ones **1a-c** in DMF (or in 1-butanol) in the presence of molecular sulfur leads to acids **2a-c**, which were isolated in satisfactory and high yields. The rearrangement could not be carried out in the absence of sulfur. Our experimental data showed that the yield of pyridopyrazines **2** is greater when the phenacyl fragment has an electron-withdrawing substituent. Only pyrazine **1c** undergoes rearrangement upon heating above the melting point though the yield of product **2c** does not exceed 20% under these conditions.



1, 2 a Ar = Ph, **b** Ar = C_6H_4OMe-4, **c** Ar = C_6H_4Cl-4

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The first reaction step is presumably thiolation of the methylene group of the phenacyl moiety, which occurs through an enolic form [3, 4]. Opening of the amide bond by the action of traces of moisture leads to intermediate **A**, which undergoes cyclization to give a 1,5-benzodiazepine derivative. A subsequent transformation of the seven-membered ring involves formation of intermediate **B**, which cyclizes to give 2-(3-arylpyrido[2,3-*b*]pyrazin-2-ylidene)acetic acids **2**.

The configuration of **2a-c** was established by ^{1}H NMR spectroscopy using NOE. Saturation of the signal of the vinylidene proton at 6.80 ppm in **2b** leads to a response on the *ortho* protons of the aryl group, indicating *Z*-configuration of the rearrangement product.

The ^{1}H NMR spectra were taken on a Varian Mercury VX-200 spectrometer at 200 MHz in DMSO-d_6 using TMS as the internal standard.

Pyrazinones **1b**,**c** were obtained by the reaction of the corresponding β-aroylacrylic acids with 2,3-diaminopyridine by a procedure described in our previous work [2].

2-[2-(*p*-Methoxyphenyl)-2-oxoethyl]-1,2-dihydropyrido[2,3-*b*]pyrazin-3(4H)-one (1b). Yield 55%; mp 210-211°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.48 (1H, d, *J* = 6.8, $H_A(CH_2)$); 3.75 (1H, dd, *J* = 17.8, $H_B(CH_2)$); 3.83 (3H, s, OCH_3); 4.39 (1H, t, *J* = 4.7, CH); 6.17 (1H, s, NH); 6.78 (1H, m, H-7); 6.97 (2H, d, *J* = 8.5, *m*-Ar); 7.03 (1H, d, *J* = 7.5, H-8); 7.54 (1H, d, *J* = 7.5, H-6); 7.96 (2H, d, *J* = 8.5, *o*-Ar); 10.75 (1H, s, NH). Found, %: N 14.43. $C_{16}H_{15}N_3O_2$. Calculated, %: N, 14.13.

2-[2-(*p*-Chlorophenyl)-2-oxoethyl]-1,2-dihydropyrido[2,3-*b*]pyrazin-3(4H)-one (1c). Yield 62%; mp 239-240°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.39 (1H, d, *J* = 6.6, $H_A(CH_2)$); 3.55 (1H, dd, *J* = 17.8, $H_B(CH_2)$); 4.42 (1H, t, *J* = 4.8, CH); 6.17 (1H, s, NH); 6.76 (1H, m, H-7); 6.96 (1H, d, *J* = 7.6, H-8); 7.54 (1H, d, *J* = 7.6, H-6); 7.58 (2H, d, *J* = 8.5, *m*-Ar); 7.99 (2H, d, *J* = 8.5, *o*-Ar); 10.74 (1H, s, NH). Found, %: N 14.00. $C_{15}H_{12}ClN_3O_2$. Calculated, %: N 13.93.

Synthesis of Pyrido[2,3-*b*]pyrazines 2a,c (General Method). A solution of pyrido-2-pyrazinone **1** (1 mmol) and sulfur (0.064 g, 2 mmol) in DMF (10 ml) was heated at reflux for 6 h and cooled. The precipitate formed was filtered off, washed with hot ethanol, and dried in the air.

(2*Z*)-2-(3-Phenylpyrido[2,3-*b*]pyrazin-2(1H)-ylidene)acetic Acid (2a). Yield 72%; mp 257-258°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.85 (1H, s, =CH); 7.15 (1H, m, H-7); 7.56 (2H, m, *m*-C_6H_5, *p*-C_6H_5); 7.99 (3H, d, *J* = 7.6, *o*-C_6H_5 + H-8); 8.08 (1H, d, *J* = 6.4, H-6); 12.45 (2H, s, NH, OH). Found, %: N 15.48. $C_{15}H_{11}N_3O_2$. Calculated, %: N 15.84.

(2*Z*)-2-(3-*p*-Methoxyphenylpyrido[2,3-*b*]pyrazin-2(1H)-ylidene)acetic Acid (2b). Yield 45%; mp 269-270°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.82 (3H, s, OCH_3); 6.80 (1H, s, =CH); 7.05 (2H, d, *J* = 8.6, *m*-Ar); 7.13 (1H, m, H-7); 7.91 (1H, d, *J* = 7.2, H-8); 7.97 (2H, d, *J* = 8.4, *o*-Ar); 8.04 (1H, d, *J* = 5.9, H-6); 11.87 (1H, s, NH); 13.30 (1H, s, OH). Found, %: N 14.00. $C_{16}H_{13}N_3O_2$. Calculated, %: N 14.23.

(2*Z*)-2-(3-*p*-Chlorophenylpyrido[2,3-*b*]pyrazin-2(1H)-ylidene)acetic Acid (2c). Yield 89%; mp 307-308°C (ethanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.83 (1H, s, =CH); 7.58 (2H, d, *J* = 8.9, *m*-Ar); 7.16 (1H, m, H-7); 8.01 (3H, d, *J* = 8.9, H-8+*o*-Ar); 8.09 (1H, d, *J* = 5.8, H-6); 12.44 (1H, s, NH); 13.37 (1H, s, OH). Found, %: N 13.85. $C_{15}H_{10}ClN_3O_2$. Calculated, %: N 14.02.

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