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REACTION OF β-KETOSULFIDES WITH UNSATURATED NITRILES AS A METHOD OF SYNTHESIS OF PYRANS

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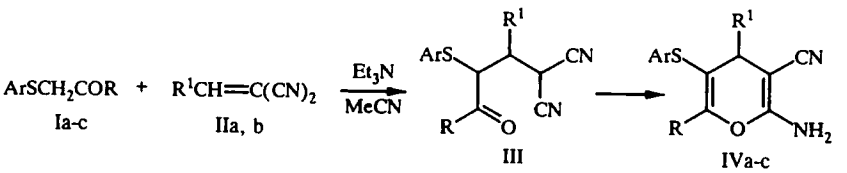
β-Ketosulfides are widely used in organic chemistry [1, 2], particularly in synthesis of heterocycles (indoles, for example) [3]. The reactivity of these compounds is to a significant degree correlated with the capacity of the sulfur atom to stabilize the negative charge on the neighboring carbon atom and as a consequence, the high CH acidity of the α proton. At the same time, such an important reaction for CH acids as Michael addition has been studied very little for β-ketosulfides (in contrast to β-ketosulfoxides and β-ketosulfones) [2, 4]. To the best of our knowledge, there are no data on the study of this reaction of β-ketosulfides in synthesis of heterocycles.

We found that β-ketosulfides Ia-c react in very soft conditions (MeCN, 20°C, Et_3N) with unsaturated dinitriles IIa, b, forming 5-arylthio-2-amino-4H-pyran-3-carbonitriles IVa-c with satisfactory yields:



Ia, IIIa, IVa Ar = 4-tolyl; Ib, c, IVb, c 4-$O_2NC_6H_4$; Ia, b, IIIa, IVa, b R = Ph; Ic, IVc Me; IIa, IIIa, IVa, b R^1 = 3-pyridyl; IIb, IVc Ph

The reaction takes place through the product of Michael addition III and when Ar = 4-tolyl, R = Ph, and R^1 = 3-pyridyl, corresponding adduct IIIa can be isolated (in the form of a mixture of diastereomers, 7:1). Compound IIIa is converted into pyran IVa on heating in MeCN (60-70°C) in the presence of Et_3N. The duration of the reaction is from 30 min (in preparation of IIIa and IVb) to 1.5 h in preparation of IVa from IIIa and 15 h from IVb.

The PMR spectra were made in $(CD_3)_2CO$ (IIIIa, IVa, c) and $(CD_3)_2SO$ (IVb); the IR spectra were recorded in KBr pellets.

5-Oxo-3-(3-pyridyl)-4-(4-tolylthio)-5-phenyl-2-cyanopentanonitrile (IIIa). Yield of 46%. Mp = 209-211°C (decomp.). Found, %: C 72.07; H 4.90; N 10.82; S 7.96. $C_{24}H_{19}N_3OS$. Calculated, %: C 72.52; H 4.82; N 10.57; S 8.07. PMR spectrum (spectrum of predominant isomer): 2.32 (3H, s, Me); 3.97 (1H, d.d, J = 11.0, 4.4 Hz, 3-H); 4.98 (d, J = 4.4 Hz, 2-H); 5.60 (1H, d, J = 11 Hz, 4-H); 6.89 (2H, d, H_{Ar}); 7.12 (2H, d, H_{Ar}); 7.60 (3H, m, $2H_{Ar}$ and 5-H_{Py}); 7.72 (1H, distorted t, H_{Ar}); 8.25 (3H, m, $2H_{Ar}$ and 4-H_{Py}); 8.72 (1H, br. d, 6-H_{Py}); 8.91 ppm (1H, br. s, 2-H_{Py}).

2-Amino-4-(3-pyridyl)-5-(4-tolylthio)-6-phenyl-4H-pyran-3-carbonitrile (IVa). Yield of 42%. Mp = 234-236°C (decomp.). Found, %: C 72.60; H 5.00; N 10.44; S 7.82. $C_{24}H_{19}N_3OS$. Calculated, %: C 72.52; H 4.82; N 10.57; S 8.07. PMR spectrum: 2.30 (3H, s, Me); 4.10 (1H, s, 4-H); 6.3 (1H, br. s, NH_2); 7.16 (4H, s, H_{Ar}); 7.34 (1H, dist. T, 5-H_{Py}); 7.43 (3H, m, H_{Ar}); 7.62 (3H, m, $2H_{Ar}$ and 4-H_{Py}); 8.37 (1H, br. s, 2-H_{Py}); 8.48 ppm (1H, br. d, 6-H_{Py}). IR spectrum: 3360, 3305 (ν_{NH2}), 2200 (ν_{CN}), 1670 (δ_{NH2}).

2-Amino-5-(4-nitrophenylthio)-4-(3-pyridyl)-6-phenyl-4H-pyran-3-carbonitrile (IVb). Yield of 40%. Mp = 260-263°C (decomp.). Found, %: C 64.65; H 3.95; N 12.80; S 7.33. $C_{23}H_{16}N_4O_3S$. Calculated, %: C 64.48; H 3.76; N 13.08;

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S 7.48. PMR spectrum: 4.18 (1H, s, 4-H); 7.1 (1H, br. s, NH_2); 7.16 (4H, s, H_{Ar}); 7.34 (1H, dist. t, 5-H_{Py}); 7.4 (6H, m); 7.60 (3H, m, two H_{Ar} and 4H_{Py}); 8.13 (2H, d, H_{Ar}); 8.38 (1H, br. s, 2H_{Py}); 8.45 ppm (1H, br. d, 6-H_{Py}). IR spectrum: 3355, 3305 (ν_{NH2}), 2200 (ν_{CN}), 1670 (δ_{NH2}), 1510, 1345 (ν_{NO2}).

2-Amino-6-methyl-5-(4-nitrophenylthio)-4-phenyl-4H-pyran-3-carbonitrile (IVc). Yield of 53%, mp = 207-209°C. Found, %: C 62.07; H 4.10; N 11.67; S 8.90. $C_{19}H_{15}N_3O_3S$. Calculated, %: C 62.45; H 4.14; N 11.50; S 8.77. PMR spectrum: 2.21 (3H, s, Me); 4.06 (1H, s, 4-H); 6.2 (1H, br. s, NH_2); 7.2-7.35 (5H, m, H_{Ar}); 7.42 (2H, d, H_{Ar}); 8.15 ppm (2H, d, H_{Ar}). IR spectrum: 3450, 3345 (ν_{NH2}), 2205 (ν_{CN}), 1675 (δ_{NH2}), 1510, 1345 (ν_{NO2}).

REFERENCES

1. B. Trost, *Acc. Chem. Res.*, **11**, 453 (1978).
2. B. Trost, *Chem. Rev.*, **78**, 363 (1978).
3. P. Gassman, T. van Bergen, D. Gilbert, and B. Cue, *J. Am. Chem. Soc.*, **96**, 5495 (1974).
4. L. I. Belen'kii (ed.), *Preparation and Properties of Organic Sulfur Compounds* [in Russian], Khimiya, Moscow (1998).