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REDUCTIVE DEACETYLATION OF 3,3,3-TRIFLUORO-1-(2-THENOYL)ACETONE

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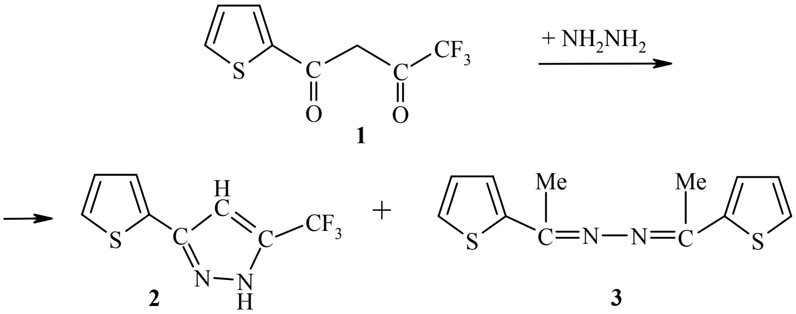
The reaction of 3,3,3-trifluoro-1-(2-thenoyl)acetone with sulfur–hydrazine hydrate–alkali and hydrazine hydrate–alkali systems is effected by reductive fission of the trifluoroacetyl group and leads to the formation of nitrogen-containing derivatives of 2-acetylthiophene. Sodium polysulfide assists the reductive fission of 3,3,3-trifluoro-1-(2-thenoyl)acetone.

Keywords: hydrazine, polysulfide anions, 3,3,3-trifluoro-1-(2-thenoyl)acetone, deacetylation.

The reaction of β-diketones with hydrazine is a classic method of obtaining pyrazoles [1]. However the reaction of 3,3,3-trifluoro-1-(2-thenoyl)acetone (**1**) with hydrazine leads to the formation of a product of nonaromatic nature, 5-hydroxy-2-(2-thenoyl)-5-trifluoromethylpyrazoline, which only on extended storage or on heating is converted into the corresponding pyrazole, existing in two tautomeric forms [2].

Continuing investigations on the activation of reactions of hydrazine with carbonyl compounds by polysulfide anions (the sulfur–hydrazine hydrate–alkali system) [3], we investigated the interaction of compound **1** with the system sulfur–aqueous hydrazine–KOH, as a result of which a mixture of two products is formed, 3-(2-thienyl)-5-trifluoromethylpyrazole (**2**) and 2-acetylthiophene azine (**3**).



Compounds **2** and **3** are formed in approximately equimolar quantities and the yield of each of them was ~20% (according to ^{1}H NMR data). In the ^{1}H NMR spectrum of compound **2** only one singlet signal at 6.65 ppm (cf. [2]) corresponds to the CH proton of the pyrazole ring, which indicates the formation of only one isomer. This may be caused by the presence of alkali in the reaction system, which assists formation of enolate anion **4**, where the carbonyl group linked with the trifluoromethyl substituent is subject to enolization [2, 4]. Such a structure for the enolate determines the further reaction with hydrazine, and also the structure of the obtained pyrazole.

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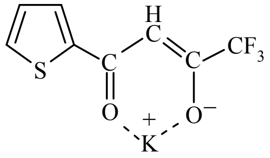

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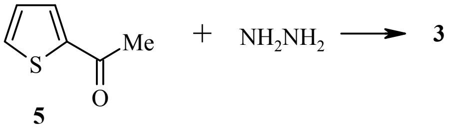
Azine **3** is the product of reductive deacetylation of compound **1** with the formation of 2-acetylthiophene **5** and its subsequent reaction with hydrazine. 2-Acetylthiophene **5** is converted into azine **3** in the system sulfur–hydrazine hydrate–KOH, in 85% yield.



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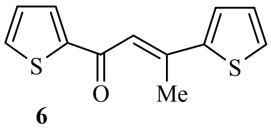

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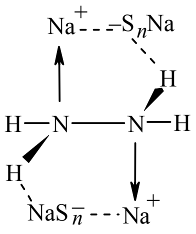
The azine obtained according to the last reaction contains ~10% contamination, which was assigned structure **6** on the basis of ^{1}H NMR spectral data and corresponds to the product of crotonate condensation of ketone **5**.

Separation of the contamination of compound **6** by crystallization was unsuccessful, which is evident since azine **3** has an understated melting point (see Experimental). In the ^{1}H NMR spectrum of compound **6** two closely located singlets of 4.74 and 4.75 ppm (*E*- and *Z*-isomers) correspond to the proton at the double bond, and the singlet at 1.61 ppm corresponds to the CH_3 group. The signals of the thiophene ring protons are disposed in the usual area at 7.07-7.38 ppm.

Both hydrazine and polysulfide anions are effective reducing agents in the system sulfur–hydrazine hydrate–alkali. To assess their effect on the reductive deacetylation of diketone **1** reaction of the latter was carried out with hydrazine hydrate in the presence of alkali (Kischner [5] reaction conditions) and with sodium disulfide, obtained by melting sodium sulfide with sulfur. Only azine **3** (57% yield) was successfully isolated in the reaction of diketone **1** with the system hydrazine hydrate–alkali, which indicates the participation of hydrazine in the reductive deacetylation of the diketone. The reaction of diketone **1** with Na_2S_2 leads to 2-acetylthiophene **5,** the yield of which amounted to 84%. It is evident that sodium disulfide also aids reductive fission of compound **1**. It was not possible to detect in any of the reaction mixtures products of the conversion of the detached trifluoracetyl group (hydrazides of trifluoroacetic acid, trifluoroacetic acid, trifluoroacetaldehyde azine), evidently due to their good solubility in water.

$$\mathbf{1} + Na_2S_2 \xrightarrow{H_2O} \mathbf{5} + [CF_3COSNa] + S + NaOH$$

On interacting diketone **1** with the system sulfur–hydrazine hydrate–alkali a mixture of two compounds is formed, pyrazole **2** and azine **3**. In the reaction of diketone **1** with the system hydrazine hydrate–alkali only azine **3** is formed. Sodium disulfide in its turn decomposes diketone **1** to 2-acetylthiophene **5**. The discovered regularities confirm the hypotheses expressed by us previously on the formation of a complex reactant **A** on activation of sulfur in the system hydrazine hydrate–base [6]. This reactant, depending on the nature of the substrate, may possess both sulfurating and aminating properties. The thiolate anion component of complex **A** is mostly responsible for the reductive fission of the diketone, and the activated hydrazine reacts with diketone **1** with the formation of pyrazole **2**. Pyrazole **2** is not formed in the absence of sulfur.

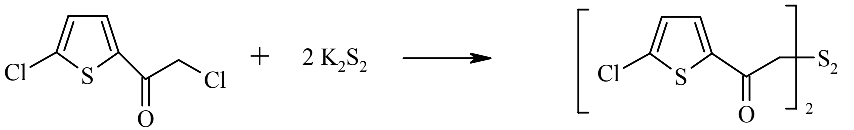


A

Usually β-diketones are subject to fission under the action of strong oxidizing agents, while the action of alkali may cause a retro Klaisen condensation only of β-diketones capable of enolization [7]. The facts of the reductive decomposition of compound **1** noted by us must be taken into consideration, particularly when using it in analytical chemistry [8].

Only the trifluoracetyl group of diketone **1** is subject to reductive fission, the other substituents in the methyl group of 2-acetylthiophene behave differently. In the reaction of 2-chloroacetyl-5-chlorothiophene (**7**) with the system sulfur–hydrazine hydrate–alkali in aqueous solution a product is formed of the usual nucleophilic substitution of the chlorine atoms by dithiolate anions, *viz.* bis(5-chloro-2-thenoyl) disulfide (**8**), in 32% yield.

$$4\,S + 4\,KOH + N_2H_4 \longrightarrow 2\,K_2S_2 + N_2 + 4\,H_2O$$



7 **8**

No nitrogen-containing compounds were detected. Here the complex reagent **A** displays only sulfurating properties.

3,3,3-Trifluoro-1-(2-thenoyl)acetone is therefore subject to reductive fission under the action of the system sulfur–aqueous hydrazine–KOH with the formation of 2-acetylthiophene derivatives, and also reacts with hydrazine with the formation of the corresponding pyrazole. The pyrazole is not formed in the absence of sulfur. Sodium polysulfide assists the reductive fission of 3,3,3-trifluoro-1-(2-thenoyl)acetone into 2-acetylthiophene.

EXPERIMENTAL

The IR spectra of the synthesized compounds were obtained on a Specord IR 75 spectrometer in KBr disks. The ^{1}H NMR spectra were recorded on a Bruker DPX 400 (400 MHz) instrument for 15-20% solutions of substances in $CDCl_3$, internal standard was HMDS (δ 0.05 ppm). The GLC was carried out on a DKhM 80 MD 2 chromatograph, column 2000 x 3 mm, liquid phase XE-60 (5%), linear programming of temperature 12 deg/min, carrier gas was helium.

Reaction of 3,3,3-Trifluoro-1-(2-thenoyl)acetone (1) with the System Sulfur–Hydrazine Hydrate–Alkali. A mixture of KOH (2 g, 0.036 mol), water (10 ml), and hydrazine hydrate (2 g, 0.05 mol) was heated to 40-50°C and sulfur (1.15 g, 0.036 mol) ground to a powder was added in portions. After dissolution of the sulfur the reaction mixture was heated for 1 h at 80°C, then cooled to 30°C, and diketone **1** (mp 42-43°C) (4 g, 0.018 mol) was added dropwise. The mixture was stirred for 4 h at 80°C, cooled, and the mixture of compounds

2 and **3** was filtered off. IR spectrum, ν, cm^{-1}: 3230, 3050, 3030, 2920, 1600, 1520, 1450, 1400, 1350. ^{1}H NMR spectrum, δ, ppm: compound **2**, 6.65 (1H, s, CH pyrazole); 7.07-7.47 (3H, m, CH thiophene); 11.91 (1H, br. s, NH); compound **3**, 2.42 (3H, s, CH_3); 7.05-7.40 (3H, m, CH thiophene).

2-Acetylthiophene Azine (3). A. From diketone **1**. The diketone (after the method described above) was added to a mixture of KOH (2 g, 0.036 mol) and hydrazine hydrate (15 ml) and processed analogously to the previous experiment. Azine **3** (1.3 g, 57%) was filtered off as yellow needle-like crystals of mp 94-95°C (ethanol) (lit. mp 95-96°C [9]). The ^{1}H NMR spectrum corresponded to that of pure azine **3**.

B. From 2-acetylthiophene **5**. Compound **5** (6.3 g, 0.05 mol) was added dropwise to a solution of sulfur (1.6 g, 0.05 mol) in hydrazine (10 ml) containing KOH (2.8 g, 0.05 mol). After treating the reaction mixture as described above azine **3** (5 g) was filtered off, having mp 84-87°C (ethanol). In the ^{1}H NMR spectrum, together with the signals belonging to the protons of compound **3**, signals were present which presumably belong to compound **6**. ^{1}H NMR spectrum, δ, ppm: 1.61 (3H, s, CH_3); 4.74, 4.75 (1H, s, CH=C); 7.07-7.38 (6H, m, CH thiophene).

2-Acetylthiophene 5. Sodium sulfide nonahydrate (8.64 g, 0.036 mol) was melted with sulfur (1.15 g, 0.036 mol) at 40-60°C. Diketone **1** (4 g, 0.018 mol) was added dropwise to the mixture. The obtained reaction mixture was distilled in vacuum. A substance (1.9 g) was obtained with bp 90°C/10 mm Hg (lit. bp 90-92°C/10 mm Hg [10]). The compound was identified by GLC by comparison with an authentic sample.

Bis(5-chloro-2-thenoyl) Disulfide (8). 2-Chloroacetyl-5-chlorothiophene (**7**) (9.75 g, 0.05 mol) was added dropwise to a solution of sulfur (1.6 g, 0.05 mol) in a mixture of water (15 ml), hydrazine hydrate (2 ml, 0.05 mol), and KOH (2.8 g, 0.05 mol). After processing the reaction mixture light-brown crystals of disulfide **8** (3.2 g, 32%) were filtered off having mp 128-129°C (ethanol). ^{1}H NMR spectrum, δ, ppm: 4.00 (2H, s, CH_2); 6.97, 7.54 (2H, m, CH thiophene). Found, %: C 37.30; H 1.82; Cl 17.92; S 34.00. $C_{12}H_8Cl_2O_2S_4$. Calculated, %: C 37.60; H 2.09; Cl 18.56; S 33.42.

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