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SHORT COMMUNICATIONS

Reaction with Hydrazine of 2-Alkoxyimino-3-oxobutanoic Acid Esters

V. V. Zakharychev, M. D. Golubtsova, and L. V. Kovalenko

Mendeleev Russian Chemicotechnological University, Moscow, 125047 Russia

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Reactions of 2-alkoxyimino-3-oxobutanoic acids esters with various N-nucleophiles afford cyclic and acyclic compounds; some among them possess antimicrobial and fungicidal activity [1–3] and are extensively applied to preparation of chefalosporin antibiotics. However the reactivity of 2-alkoxyimino-3-oxobutanoates in these reactions is poorly known.

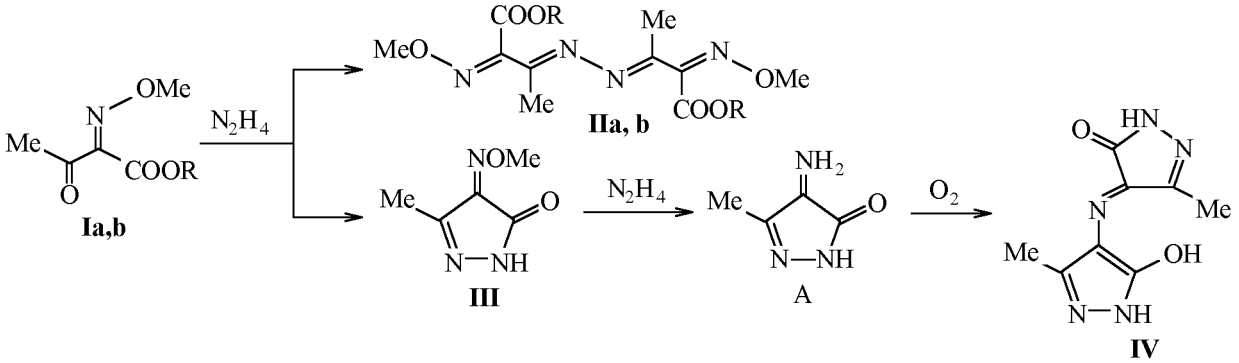
The reaction between monosubstituted hydrazines and acetoacetic acid derivatives commonly results in 1-substituted-3-methylpyrazolin-5-ones. However we formerly demonstrated that sometimes 2-alkoxyimino-3-oxobutanoates form quite stable acyclic hydrazones [4, 5].

Methyl (**Ia**) and ethyl (**Ib**) 2-methoxyimino-3-oxobutanoates with unsubstituted hydrazine afford different products depending on reaction conditions (see the scheme). At excess ketoesters predominantly arise the corresponding acyclic azines (compounds **IIa, b** respectively); that is unusual for β-dicarbonyl compounds. At nearly equimolar reagents ratio the expected 3-methyl-4-methoxyiminopyrazolin-5-one (**III**) forms in a high yield. This compound can be isolated in reaction of esters with excess hydrazine in the cold (around 0°C). On raising the temperature to ambient pyrazolone **III** vigorously reacts with excess hydrazine transforming into 4-(5-hydroxy-3-methyl-1*H*-pyrazol-4-ylimino)-5-methyl-2,4-dihydropyrazolone (**IV**) apparently via unstable 4-amino-3-methylpyrazolin-5-one (A). A similar reduction has been observed with 4-isonitrosopyrazoles [6, 7], and now it is clear that in this reaction can undergo reduction not only the nitrogen atom of the nitroso group as has been formerly presumed but also the C^4 atom of the pyrazolone ring.

Thus the 2-methoxyimino3-oxobutanoates are capable of selective reactions at each carbonyl group (including that one which is in oxime form), and the reactivity of the groups decreases in the series $C^3 > C^1 > C^2$. (*Z*)-Methyl 3-oxo-2-methoxyiminobutanoate (**Ia**) and (*Z*)-ethyl 3-oxo-2-methoxyiminobutanoate (**Ib**) were obtained by nitrosation of the corresponding acetoacetates followed by alkylation of the formed isonitroso derivatives [1].

(*Z*)-5-Methyl-2*H*-pyrazole-3,4-dione-3-(*O*-methyloxime) (III). To a solution of 12 mmol of hydrazine hydrate in 1 ml of ethanol was added a solution of

Scheme.



R = Me (**a**), Et (**b**).

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10 mmol of ester **Ia, b** in 1 ml of ethanol. The solution was left for 24 h at room temperature. The separated precipitate was filtered off and washed with ethanol. We obtained 0.95–1.1 g (67–78%) of compound **III** as orange needles or red powder of small crystals, subl. > 140°C, mp 180–184°C (in a sealed capillary). IR spectrum, ν, cm^{-1}: 3300 br, 1740, 1710, 1610. ^1H NMR spectrum, δ, ppm: 2.20 s (3H, Me), 4.35 s (3H, MeON), 8.68 br.s (1H, NH). Found, %: C 42.44; H 4.95; N 29.84. $C_5H_7N_3O_2$. Calculated, %: C 42.55; H 5.00; N 29.77. Under the other conditions (e.g., at boiling) sometimes formed up to 30% of another isomer that was detected in the ^1H NMR spectrum by the signals at 2.30 and 4.30 ppm.

Dimethyl 2,2′-di(methoxyimino)-3,3′-azinodibutanoate (IIa). A mixture of 10 mmol of ester **Ia**, 5 mmol of hydrazine hydrate, and 2 ml of ethanol was left at room temperature for 24 h. The separated precipitate was filtered off and washed with ethanol. We obtained 0.35 g (25%) of pyrazolinone **III**. The filtrate was evaporated, the residue was recrystallized from hexane. We obtained 0.88 g (56%) of compound **IIa** as yellow crystals, mp 120–122°C. IR spectrum, ν, cm^{-1}: 1755, 1615. ^1H NMR spectrum, δ, ppm: 2.05 s (3H, MeC), 3.85 s (3H, MeOCO), 4.05 s (3H, MeON). Found, %: C 45.91; H 5.70; N 17.64. $C_{12}H_{18}N_4O_6$. Calculated, %: C 45.86; H 5.77; N 17.83.

Diethyl 2,2′-di(methoxyimino)-3,3′-azinodibutanoate (IIb) was prepared similarly to compound **IIa**. Yield 0.82 g (48%), orange flakes, mp 114–114.5°C. IR spectrum, ν, cm^{-1}: 1755, 1605. ^1H NMR spectrum, δ, ppm: 1.35 t (3H, $\underline{Me}CH_2$), 2.05 s (3H, MeC), 4.05 s (3H, MeON), 4.30 q (2H, $MeC\underline{H}_2$). Found, %: C 49.20; H 6.47; N 16.49. $C_{14}H_{22}N_4O_6$. Calculated, %: C 49.12; H 6.48; N 16.37.

4-(5-Hydroxy-3-methyl-1*H*-pyrazol-4-ylimino)-5-methyl-2,4-dihydropyrazolone (IV). To 0.141 mol of hydrazine hydrate at stirring and cooling with ice bath was added dropwise 0.047 mol of ester **IIb** in 6 ml of ethanol. After precipitation of pyrazolone **III** the reaction mixture was left standing at room temperature. The mixture self-heated and foaming was observed. In several days from the viscous dark-cherry-colored reaction mixture separated a colorless precipitate that was filtered off. The precipitate turned red on filter. It was washed with ice water, dried in air and recrystallized from ethanol. We obtained 3.5 g (72%) of rubazonic acid **IV** as dark-red needles, mp 295–297°C (publ. mp 295–297°C [6]). Mass spectrum, *m/z* (I_{rel}): 207 M_0 (100%). Found, %: C 45.94; H 4.60; N 33.77. $C_8H_9N_5O_2$. Calculated, %: C 46.37; H 4.38; N 33.80.

^1H NMR spectra were registered on spectrometer Bruker AC-200 (200 MHz) in $CDCl_3$. IR spectra were recorded on IKS-29 spectrophotometer from mulls in mineral oil. Mass spectrum was measured on Kratos MS-30 instrument (ionizing electrons energy 70 eV).

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