Letters to the Editor

Reaction of DL-2-aminopropiohydroxamic acid with acetone: selective synthesis of 3-hydroxy-2,2,5-trimethylimidazolidin-4-one

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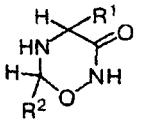
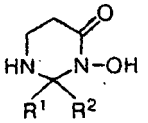
Competitive *N*- or *O*-alkylation of hydroxamic acids (HA) mainly results in the formation of *O*-alkyl hydroxamates.[1] For example, the cyclic products of reaction of α-amino HA with aldehydes have the structure of *O*-alkylated derivatives **1**.[2] However, the interaction of 3-aminopropio-HA with aliphatic aldehydes and ketones affords *N*-alkyl hydroxamates **2**.[3]



1: R^1 = H, Alk; R^2 = Alk, Ar

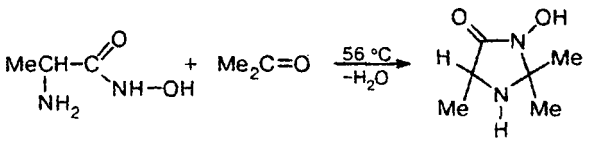


2: $R^1 = R^2$ = H, Alk

We have shown that the reaction of racemic 2-aminopropiohydroxamic acid (**3**) with ketone, unlike the reaction with aldehydes,[2] gives cyclic HA **4** in a high yield (Scheme 1). The structure of product **4** was established by X-ray diffraction analysis (Fig. 1) and confirmed by the spectral data and positive hydroxamic test reaction with $FeCl_3$.

3-Hydroxy-2,2,5-trimethylimidazolidin-4-one (4) was obtained by refluxing of compound **3** (300 mg, 2.88 mmol) (synthesized by the previously described procedure[4]) in anhydrous acetone (30 mL) followed by evaporation of the solution to dryness and sublimation of the residue at 115—120 °C

Scheme 1



3 **4**

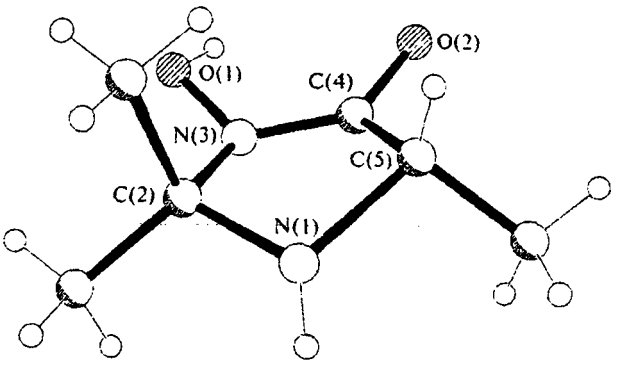


Fig. 1. Molecular structure of compound **4** (using (*S*)-enantiomer as an example).

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(35 Torr). Compound **4** (347 mg, 83.5%) was obtained as a white downy powder with m.p. 157—158 °C. Found (%): C, 49.63; H, 8.83; N, 19.39. $C_6H_{12}N_2O_2$. Calculated (%): C, 49.98; H, 8.39; N, 19.43. IR (Vaseline oil), ν/cm^{-1}: 3236 (NH); 2700—2500 (OH); 1720, 1704 (C=O). ^1H NMR (200 MHz, CD_3OD), δ: 1.35 (d, 3 H, C(5)Me, ^3J = 7.0 Hz); 1.37, 1.47 (both s, 6 H, 2 C(2)Me); 3.54 (q, 1 H, H(5), ^3J = 7.0 Hz). ^{13}C NMR (50 MHz, CD_3OD), δ: 17.5 (MeC(5)); 24.0, 26.8 (2 MeC(2)); 52.7 (C(5)); 77.7 (C(2)); 173.6 (C=O).

The sample for X-ray analysis was obtained by the crystallization of powder **4** from acetone. Crystals **4** are monoclinic, m.p. 159—160 °C, M = 144.173, a = 17.178(3) Å, b = 9.410(2) Å, c = 10.270(2) Å, β = 107.32(3)°, V = 1584.8(5) Å^3, d_{calc} = 1.209 g cm^{-3}, space group $P2_1/c$, Z = 8. (Detailed X-ray analysis data will be published elsewhere.)

It is assumed that *N*-alkylation is the predominant direction of the reaction of α-amino HA with ketones because it corresponds to the preferential *NH*-deprotonation of HA.[1] At the same time, the selective formation of HA **4** (see Scheme 1) can be due to the position of tautomeric equilibrium of imidazolidinone **4**, the *O*-alkylated derivative of type **1**, and the corresponding Schiff's base.[3]

References

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Nitrile cleavage of heterocycle in the electrochemical reduction of 1-chloro-4-(isopropylthio)phthalazine

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We have recently found[1] the previously unknown electron transfer-induced disclosure of the pyridazine cycle in 1-Cl-4-X-phthalazines (X = Cl, OAr, and OAlk) with elimination of the Cl^- and X^- anions, resulting in the formation of phthalonitrile. It was of interest to reveal the possibility of a similar reaction for other phthalazine derivatives containing two nucleophilic groups in positions 1 and 4. Therefore, we studied the electrochemical reduction (ECR) of 1-chloro-4-(isopropylthio)phthalazine (**1**) and 1,4-di(isopropylthio)phthalazine (**2**) in the DMF—Bu_4NI system (0.1 mol L^{-1} Bu_4NI) by voltammetry and electrolysis, which was carried out directly in the cavity of an ESR spectrometer.

The character of the voltammograms and the direction of reduction of phthalazine **1** are completely similar to the ECR of 1,4-dichlorophthalazine. The transfer of two electrons of the first irreversible wave ($E_{1/2}^1$ = −1.04 V relative to Hg/I^-, n = 2) results in the nitrile cleavage of the pyridazine cycle with elimination of chloride and isopropyl thiolate ions and formation of phthalonitrile. The reduction of the latter at potentials of the subsequent two waves is accompanied by the generation of phthalonitrile ($E_{1/2}^2$ = −1.15 V, n = 1) and benzonitrile ($E_{1/2}^3$ = −2.15 V, n = 2, 4) radical anions, respectively (Scheme 1). The one-electron level of the second reversible reduction wave, whose potential coincides with that of the reduction wave of

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