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N,O-ACYLOTROPY IN N-METHYLPENTANEHYDROXAMIC ACID

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Summary. N-Methylpentanehydroxamic acid (N-methyl-N-pentanoylhydroxylamine) **1** rearranges into N-methyl-O-pentanoylhydroxylamine **2** through spontaneous N⟶O acyl migration.

In context of our previous investigations of heterocentered acyloxy and amidyl radicals generated from alkanoic acids and their amides in oxidative systems containing peroxydisulfates[1,2] the study of heterocentered radicals produced from pentanehydroxamic acid and corresponding N-methyl derivative was necessary.

Therefore we undertook the synthesis of N-methylpentanehydroxamic acid (N-methyl-N-pentanoylhydroxylamine) **1**. MeNHOH obtained according to the known procedure[3] was acylated by BuCOOMe to prepare **1**. To 7 g (0.1 mole) of MeNHOH•HCl in a mixture of 15 ml of water and 12 ml of EtOH, cooled to 10°C, 20 ml of 10 N NaOH (0.2 mole) were added, then 11.6 g (0.1 mole) of BuCOOMe were added dropwise, the reaction mixture was stirred 3 h at 20°C and then 2 h at 50°C. The mixture was filtered, the filtrate acidified with 7.5 g (0.09 mole) of conc. HCl up to pH 5-6 and then extracted with boiling AcOEt (2x100 ml). The organic layer was washed with 10% aq. $NaHCO_3$ and water, dried over $MgSO_4$ and the solvent was evaporated. Distillation of the residue gave 10.0 g (yield 76%) of product[4], $C_6H_{13}NO_2$, b.p. 77-83°C (0.01 mm), mass spectrum (m/z, rel. intensity): 131(M^+,15), 86(20), 85(90),73(40), 60(20), 58(40), 57(100), 55(40), 43(18), 41(70); IR spectrum (solution in $CHCl_3$): 1620, 1680, 1780, 3200-3500 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 250 MHz): δ 0.90 (t, 3H); 1.29 (m, 2H); 1.45 (m, 2H); 2.15 and 2.38 (m, 2H); 2.70 (d), 3.20(s), and 3.25 (s) (total intensity of the last three signals corresponds to 3H); 7.12 and 7.50 (unresolved multiplets, total intensity 1H) ppm. Irradiating of the signal at 7.12 ppm (ascribed to N<u>H</u> or O<u>H</u>) resulted in the coalescence of the doublet at 2.70 ppm (N-Me) into singlet with the same intensity. This fact (as well as the presence of a weak band at 1780 cm^{-1} in IR spectrum) allowed us to assume the formation of isomeric N-methyl-O-pentanoylhydroxylamine **2** alongwith the desired **1** during the acylation of MeNHOH; the ratio of **1** to **2** being 3:1

(based on the ^1H NMR spectral data):

$$\mathrm{BuCOOMe + MeNHOH \longrightarrow \underset{\mathbf{1}}{BuCON(Me)OH} + \underset{\mathbf{2}}{BuCOONHMe}}$$

The formation of a mixture of N- and O-acyl derivatives could be interpreted in terms of ambident reactivity of MeNHOH (cf.[5]). In order to test the above assumption we have examined the following alternative synthetic scheme that ultimately excludes the direct O-acylation. The reaction of $NH_2OH{\cdot}HCl$ with BuCOOMe in the presence of MeONa and then with $PhCH_2Cl$ produces **3**[6] (75%) as a viscous liquid, n_D^{22} 1.5167. N-Methylation of 3 (NaH-MeJ in a dried xylene) gives **4** (80%), b.p. 105°C(0.01 mm). During debenzylation of **4** with Me_3SiJ[7] or by hydrogenolysis over 10% Pd/C according to[8] a mixture of **1** and **2** in a ratio 3.1:1 (based on the ^1H NMR data) was obtained.

$$\mathrm{BuCOOMe + NH_2OH{\cdot}HCl + PhCH_2Cl \xrightarrow{NaOMe} \underset{\mathbf{3}}{BuCONHOCH_2Ph} \xrightarrow{NaH-MeJ} \underset{\mathbf{4}}{BuCON(Me)OCH_2Ph}}$$

$$\mathbf{4}\ \xrightarrow[\mathrm{or\ H_2,\ Pd/C}]{\mathrm{1.Me_3SiJ,\ 2.H_2O}}\ \mathbf{1} + \mathbf{2}$$

The present data demonstrate unambiquosly that formation of **2** is the result of N→O migration of pentanoyl group in **1**.

$$\mathrm{\underset{\mathbf{1}}{BuCON(Me)OH} \longrightarrow \underset{\mathbf{2}}{BuCOONHMe}}$$

The tendency of **1** to such unusual isomerisation involving N→O acylotropy is probably due to the absence in **2** of non-bonding interactions between N-Me group and H atoms of the acyl moiety.

Such an acylotropy is not characteristic of BuCON(Ph)OH that has been obtained without isomeric BuCOONHPh by acylation of PhNHOH with BuCOCl.

The present results should be taken into consideration in experiments on acylation of N-substituted hydroxylamines.

References and Notes.

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