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Synthesis of 2,2-Dialkyl-5-hydroxyisoxazolidinium and 1,1-Dialkyl-3-hydroxypyrazolidinium Salts

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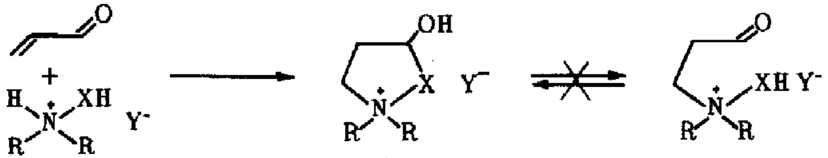
Abstract: Salts of N,N-dialkylhydroxylamines and β-dialkylhydrazides react with acrolein to give 2,2-dialkyl-5-hydroxyisoxazolidinium and 1,1-dialkyl-3-hydroxypyrazolidinium salts.

Alkenals and alkenones classically react with hydrazine (monosubstituted hydrazines) and hydroxylamine forming pyrazolines and isoxazolines respectively. Recently we used β-alkyl (aryl) hydrazides and N-substituted hydroxylamines and by this way 5-hydroxypyrazolidines [1] and 5(3)-hydroxyisoxazolidines [2] were synthesized in good yields. The use of trisubstituted hydrazines and N,N-disubstituted hydroxylamines in such a reaction have not been known yet.

We now report the reaction of salts of N,N-dialkylhydroxylamines (1,2) and dimethylhydrazides (3,4) with acrolein at room temperature in acetonitrile solution gives 5-hydroxyisoxazolidinium and 3-hydroxypyrazolidinium salts (5 - 8) in good yields (80–100 %).



A

B

1 - 4

5 – 8

1,5 R = CH_3, X = O, Y = Cl
2,6 R = $CH_2C_6H_5$, X = O, Y = Cl
3,7 R = CH_3, X = NCHO, Y = CF_3COO
4,8 R = CH_3, X = $NCOC_6H_5$, Y = CF_3COO

Examination of NMR ^1H and ^{13}C spectral data for (5–8)[3] indicates that the compounds exist in cyclic form A in accordance with IR spectra in nujol (absence of characteristic peaks at 1600–1800 cm^{-1}).

The structure of (7) is confirmed by its further aminonitrilic regrouping[4] into β-dimethylaminopropionitrile (yield 12 %)[5].

Treatment of 2-benzyl-5-hydroxyisoxazolidine[6] with benzyl iodide gives 2,2-dibenzyl-5-hydroxyisoxazolidinium iodide (m.p. 130–131 °C, from acetonitrile). ^1H NMR spectrum of it is identical with the spectrum of the salts (6).

Dialkylhydrazides don't react with acrolein but hydroxylamine (2) gives 3-N,N-dibenzylhydroxylaminopropanal[7].

References and Notes

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2. Zelenin, K.N.; Motorina, I.A.; Sviridova, L.A.; Bezhan, I.P.; Ershov, A.Yu.; Golubeva, G.A.; Bundel, Yu.G. ***Khim. Geterocycl. Soedin.*** 1987., 9, 1270–1276.
3. A typical procedure: to a stirred solution of 3 (2.02 g, 10 mmol) in dry CH_3CN (50 ml) acrolein (1 ml, 10 mmol) was added at room temperature. In a week the solution was evaporated in vacuum. The resulting crude mass was recrystallized from CH_3CN to give pure (7) (2.20 g, 85 %).
   New compounds were characterized by spectroscopic data and melting points (from CH_3CN) and by C, H and N elemental analysis. 5 : m.p. 125–126 °C; ^1H NMR (100 MHz, $CDCl_3$ + DMSO–d_6): δ 8.28 (br.s.,1H, OH), 5.96 (m, 1H, H–5), 4.30 (m, 2H, H–3), 3.71 (s, 3H, NCH_3), 3.57 (s, 3H, NCH_3), 3.04 (m, 1H, H–4), 2.78 (m, 1H, H–4); ^{13}C NMR (20.4 MHz, DMSO–d_6): δ 103.1 (C–5), 65.6 (C–3), 57.7, 55.7 ($N(CH_3)_2$), 34.4 (C–4). 6 : m.p. 127–128 °C; ^1H NMR (DMFA–d_7): δ 9.20 (br.s., 1H, OH), 8.00–7.20 (m, 10 H, arom.), 5.82 (d, J=5 Hz, 1H, H–5), 5.36 (m, 3H, H_e–3 and H_A part an AB spin system of two CH_2 benzylic protons), 4.40 (m, 3H, H_a–3 and H_B part of an AB spin system of two CH_2 benzylic protons), 2.06 (m, 1H, H_e–4), 1.18 (m, 1H, H_a–4); ^{13}C NMR (DMSO–d_6): δ 133.2, 132.7, 130.3, 128.7, 128.6, 128.2, 127.7, 127.5 (8 aromatic carbons), 103.2 (C–5), 72.1, 66.6, 61.9(C–3, 2 $CH_2C_6H_5$), 34.4 (C–4). 7 : m.p. 97–98 °C; ^1H NMR ($CDCl_3$ + DMSO–d_6): δ 8.78 (s, 1H, HCO), 6.90 (br.s., 1H, OH), 6.15 (m, 1H, H–3), 4.58 (m, 2H, H–5), 4.00 (s, 3H, NCH_3), 3.84 (s, 3H, NCH_3), 2.84 (m, 1H, H–4), 2.50 (m, 1H, H–4); ^{13}C NMR (DMSO–d_6): δ 159.1 (COO^-, $^2J_{CF}$ =159.1 Hz), 158.5 (HCO), 117.1 (CF_3, $^1J_{CF}$ =298 Hz), 83.3 (C–3), 69.3 (C–5), 56.7 (NCH_3), 53.7 (NCH_3), 30.2 (C–4). 8 : oil, ^1H NMR (DMFA–d_7): δ 8.50 (br.s, 1H, OH), 7.92–7.36 (m, 5H, arom.), 5.86 (m, 1H, H–3), 4.44 (m, 2H, H–5), 3.96 (s, 3H, NCH_3), 3.78 (s, 3H, NCH_3), 2.36 (m, 1H, H–4), 1.92 (m, 1H, H–4).
4. Ioffe, B.V.; Zelenin, K.N. ***Dokl. Akad. Nauk SSSR.*** 1962, 144, 6, 1303–1306.
5. The basification of salt 1 (1 mmol) with 6N potassium hydroxide (5 ml) solution, was followed by extraction with benzene (2 x 10 ml) and evaporation in vacuum resulted in pure aminonitrile.
6. Zelenin, K.N.; Ershov, A. Yu.; Beshan, I.P. ***Khim. Geterocycl. Soedin.*** 1990., 11, 1559–1562.
7. The solution of 1 mmol reagents in 10 ml benzene was boiled for 72 hours, evaporated in vacuum. The product was purified by column chromatography (silica gel, ethyl acetate – hexane = 1:2). ^1H NMR (100 MHz, $CDCl_3$): δ 9.00 (t, 1H), 8.52 (m, 10H), 3.81 (s, 4H), 3.41 (t, 2H), 1.95 (dt., 2H).

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