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SHORT COMMUNICATIONS

Ketone *O*-(Tetrahydro-1,3-oxazin-3-ylmethyl)- and *O*-(Oxazolidin-3-ylmethyl)oximes

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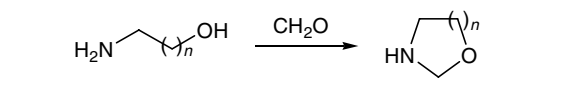
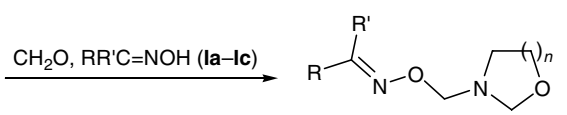
Five- and six-membered cyclic N,O-acetals exhibit versatile biological activity; they are used in various fields of technics and as intermediate products in fine organic synthesis [1]. We recently reported that ketone oximes are capable of undergoing Mannich aminomethylation with formaldehyde and 4,5-dihydropyrazoles [2].

With a view to obtain potential biologically active compounds having both linear and cyclic N,O-acetal fragments, we examined aminomethylation of ketone oximes **Ia**–**Ic** with oxazolidine (**IIa**) and tetrahydro-1,3-oxazine (**IIb**).

It is known that free oxazolidine (**IIa**) and tetrahydro-1,3-oxazine (**IIb**) are very unstable compounds and that they undergo trimerization to *N*,*N*′,*N*″-tris(hydroxyalkyl)triazines [3]. Therefore, the reaction was performed in a one-pot mode. Initially, amino alcohol **IIIa** and **IIIb** was reacted with paraformaldehyde, and an additional portion of paraformaldehyde and ketone oxime **Ia**–**Ic** were then added to the mixture. The amounts of the reactants were stoichiometric.



IIIa, **IIIb** **IIa**, **IIb**



IVa–**IVf**

I, R = R′ = Me (**a**), RR′ = $(CH_2)_5$ (**b**), R = Me, R′ = Ph (**c**); **II**, **III**, *n* = 1 (**a**), 2 (**b**); **IV**, R = R′ = Me (**a**, **b**), RR′ = $(CH_2)_5$ (**c**, **d**), R = Me, R′ = Ph (**e**, **f**); *n* = 1 (**a**, **c**, **e**), 2 (**b**, **d**, **f**).

Both steps were carried out by heating in benzene with simultaneous removal of water as azeotrope. The yields of aminomethylation products **IVa**–**IVf** were 44–58%.

Compounds **IVa**–**IVf** showed in the IR spectra absorption bands in the region 1640–1665 cm^{-1} due to stretching vibrations of the oxime C=N bond, while neither amino nor hydroxy group absorption was observed at 3200–3500 cm^{-1}. The ^1H NMR spectra of **IVa**–**IVf** contained singlets at δ 4.25–4.52 and 4.33–4.98 ppm from protons of the NCH_2OC and NCH_2ON fragments, respectively. In addition, signals from the other protons in the acetal ring and oxime moiety were present. According to the ^1H NMR data, oximes **IVe** and **IVf** were isolated as a single isomer. Taking into account the chemical shift of the methyl protons (δ 2.23 ppm) in the acetophenone fragment and published NMR data for various acetophenone oxime derivatives [4], we can conclude that compounds **IVe** and **IVf** are *E* isomers.

Ketone *O*-(tetrahydro-1,3-oxazin-3-ylmethyl)- and *O*-(oxazolidin-3-ylmethyl)oximes IVa–IVf (*general procedure*). A mixture of 0.1 mol of amino alcohol **IIIa** or **IIIb**, 0.1 mol of paraformaldehyde, and 100 ml of benzene was heated under reflux in a flask equipped with a Dean–Stark trap until water no longer separated. The mixture was cooled, 0.1 mol of oxime **Ia**–**Ic** and 0.1 mol of paraformaldehyde was added, and the mixture was heated again under reflux until water no longer separated. Compounds **IVa**–**IVf** were isolated by vacuum distillation.

Acetone *O*-(oxazolidin-3-ylmethyl)oxime (IVa). Yield 48%, bp 73–76°C (6 mm), d_4^{20} = 1.0507, n_D^{20} = 1.4759. ^1H NMR spectrum, δ, ppm: 1.85 s (6H, Me),

3.19 t (2H, NC**H**$_2$CH$_2$O, ^3J = 6.8 Hz), 3.7 t (2H, NCH$_2$C**H**$_2$O, ^3J = 6.8 Hz), 4.5 s (2H, OCH$_2$N), 4.89 s (2H, NCH$_2$ON). Found, %: C 53.02; H 9.03; N 17.59. $C_7H_{14}N_2O_2$. Calculated, %: C 53.15; H 8.92; N 17.71.

Acetone *O*-(tetrahydro-1,3-oxazin-3-ylmethyl)oxime (IVb). Yield 56%, bp 83–86°C (2 mm), d_4^{20} = 1.0208, n_D^{20} = 1.4648. ^{1}H NMR spectrum, δ, ppm: 1.67 m (2H, NCH$_2$C**H**$_2$CH$_2$O), 1.85 s (6H, Me), 3.07 t (2H, NC**H**$_2$CH$_2$CH$_2$O, ^3J = 5.6 Hz), 3.78 t (2H, NCH$_2$-CH$_2$C**H**$_2$O, ^3J = 5.3 Hz), 4.45 s (2H, OCH$_2$N), 4.81 s (2H, NCH$_2$ON). Found, %: 55.98; H 9.27; N 16.08. $C_8H_{16}N_2O_2$. Calculated, %: C 55.79; H 9.36; N 16.27.

Cyclohexanone *O*-(oxazolidin-3-ylmethyl)oxime (IVc). Yield 52%, bp 106–109°C (3 mm), mp 35–36°C. ^{1}H NMR spectrum, δ, ppm: 1.58–2.50 m [10H, (CH$_2$)$_5$], 3.20 t (2H, NC**H**$_2$CH$_2$O, ^3J = 6.78 Hz), 3.70 t (2H, NCH$_2$C**H**$_2$O, ^3J = 6.78 Hz), 4.51 s (2H, OCH$_2$N), 4.74 s (2H, NCH$_2$ON). Found, %: 59.99; H 9.27; N 14.08. $C_{10}H_{18}N_2O_2$. Calculated, %: C 60.58; H 9.15; N 14.13.

Cyclohexanone *O*-(tetrahydro-1,3-oxazin-3-ylmethyl)oxime (IVd). Yield 54%, bp 128–131°C (1 mm), d_4^{20} = 1.0844, n_D^{20} = 1.5080. ^{1}H NMR spectrum, δ, ppm: 1.65–2.41 m [10H, (CH$_2$)$_5$], 2.89 m (2H, NCH$_2$C**H**$_2$CH$_2$O), 3.45 t (2H, NC**H**$_2$CH$_2$CH$_2$O, ^3J = 6.8 Hz), 3.82 t (2H, NCH$_2$CH$_2$C**H**$_2$O, ^3J = 5.3 Hz), 4.25 s (2H, OCH$_2$N), 4.33 s (2H, NCH$_2$ON). Found, %: C 62.19; H 9.56; N 13.31. $C_{11}H_{20}N_2O_2$. Calculated, %: C 62.23; H 9.50; N 13.20.

Acetophenone *O*-(oxazolidin-3-ylmethyl)oxime (IVe). Yield 44%, bp 155–158°C (3 mm), d_4^{20} = 1.1431, n_D^{20} = 1.5635. ^{1}H NMR spectrum, δ, ppm: 2.23 s (3H, Me), 3.27 t (2H, NC**H**$_2$CH$_2$O, ^3J = 6.8 Hz), 3.71 t (2H, NCH$_2$C**H**$_2$O, ^3J = 6.8 Hz), 4.59 s (2H, OCH$_2$N), 4.97 s (2H, NCH$_2$ON), 7.33–7.63 m (5H, C$_6$H$_5$). Found, %: C 65.38; H 7.45; N 12.78. $C_{12}H_{16}N_2O_2$. Calculated, %: C 65.43; H 7.32; N 12.72.

Acetophenone *O*-(tetrahydro-1,3-oxazin-3-ylmethyl)oxime (IVf). Yield 46%, bp 165–167°C (4 mm), d_4^{20} = 1.0911, n_D^{20} = 1.5490. ^{1}H NMR spectrum, δ, ppm: 1.70 m (2H, NCH$_2$C**H**$_2$CH$_2$O), 2.23 s (3H, Me), 3.12 t (2H, NC**H**$_2$CH$_2$CH$_2$O, ^3J = 5.6 Hz), 3.77 (2H, NCH$_2$CH$_2$C**H**$_2$O, ^3J = 5.3 Hz), 4.52 s (2H, OCH$_2$N), 4.98 s (2H, NCH$_2$ON), 7.31–7.65 m (5H, C$_6$H$_5$). Found, %: C 66.54; H 7.79; N 11.82. $C_{13}H_{18}N_2O_2$. Calculated, %: C 66.64; H 7.74; N 11.96.

The ^{1}H NMR spectra were recorded at 26°C on a Bruker DPX-400 spectrometer (400 MHz) using $CDCl_3$ as solvent and hexamethyldisiloxane as internal reference. Commercial amino alcohols and ketone oximes were distilled just before use; they contained no less than 98.5% of the main substance (according to the GLC data); commercial paraformaldehyde had a purity of 95%.

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