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SHORT COMMUNICATIONS

Dedicated to Academician of the Russian Academy of Sciences N.S.Zefirov on occasion of his70th anniversary

Cycloaddition of Ethylenediamine to Acetylene γ-Hydroxyaldehydes

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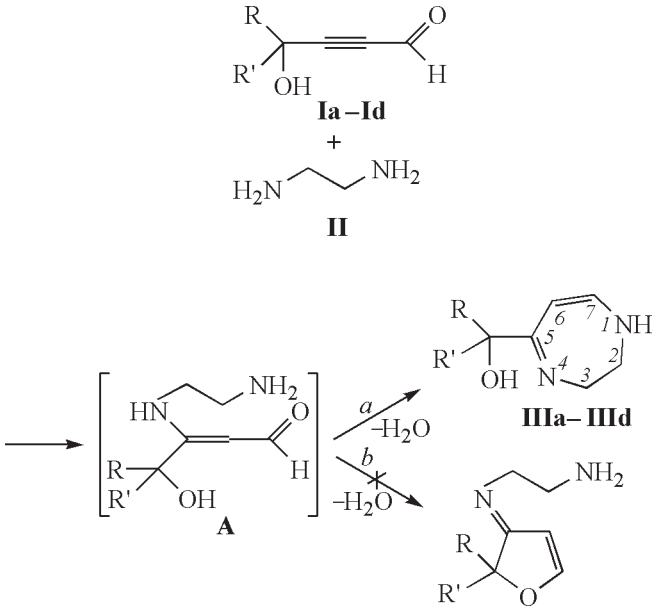
Acetylene γ-hydroxyaldehydes in reactions with amines behave as ambident electrophiles, and therewith the hydroxy group can favor heterocyclization of the intermediate aminoenals into furan derivatives. Thus whereas the primary amines add to the aldehyde group affording azomethines [1], the dialkylamines and aziridines add to the triple bond furnishing respectively 4-dialkylamino-2-methoxydihydrofurans (in methanol) [2] or 4-aziridino-5,5-dialkyl-2-hydroxydihydrofurans (in ethyl ether) [3]. We demonstrated that the reaction of 4-hydroxy-4-methyl-2-pentyn-1-al with a N,O-binucleophile, 2-amino-2-methylpropan-1-ol, instead of the expected azomethine or its cyclodehydration product, the corresponding 1,3-oxazolidine, gave rise to an azomethine



R = R' = Me (**a**); R = Me, R' = Et (**b**), Pr (**c**); CRR' = *cyclo*-$(CH_2)_5$ (**d**).

of a polyfunctional 1,3-dioxolane, a dimer of the initial hydroxyaldehyde [4]. The dimerisation process readily proceeded also in the presence of catalytic amounts of the aminoalcohol (5 mol%) or other amines.

We found that acetylene γ-hydroxyaldehydes **Ia–Id** reacted with N,N-binucleophile, 1,2-ethylenediamine (**II**), in polar solvent (DMSO, methanol) at room temperature by the cycloaddition type to furnish in high yields previously unknown 5-hydroxyalkyl-2,3-dihydro-1*H*-1,4-diazepines **IIIa–IIId**. The 1,4-benzodiazepines are known to possess a wide range of biological activity [5]. The formation of diazepines **IIIa–IIId** apparently occurs by ethylenediamine addition to the triple bond of the hydroxypropynals with subsequent heterocyclization of the intermediate aminoenals **A**.

Compounds **IIIa–IIId** were isolated as oily fluids in 94–98% yields. According to ^1H and ^{13}C NMR spectra and elemental analyses they are individual substances, but the attempt to subject them to column chromatography on SiO_2 or preparative chromatography on Al_2O_3 leads to decomposition of the compounds. It should be noted that the majority of the known 1,4-diazepines either belong to the benzodiazepine series [5–7] or are stabilized by the presence of a polyfluoroalkyl substituent in the position *5* [8, 9].

The structure of compounds **IIIa–IIId** was proved by means of IR, NMR (HMBC, NOESY, HSAQ) spectroscopy, and by mass spectrometry; their composition was confirmed by elemental analysis. According to the NOESY spectrum in the push-pull fragment of diazepine **IIIa** a cross-peak is observed between the methyl group and proton of the CH= group in the position *6* (the "pull" part of the olefin fragment). In the alternative structure of iminodihydrofuran the Overhauser effect

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cannot arise between the protons of the methyl group and the olefin proton of the corresponding "pull" moiety because the proton of the CH= group in the position *3* is too far from the methyl group in the position *5* (a cross-peak with the proton in the position *2* corresponding to the "push" part of the olefin fragment would be more probable, but it is not observed). Diazepines **IIIa–IIId** are probably stabilized by an intramolecular hydrogen bond OH···N=.

5-(2-Hydroxy-2-methylethyl)-2,3-dihydro-1*H*-1,4-diazepine (IIIa). A solution of 0.1 g (0.892 mmol) of aldehyde **Ia** and 0.053 g (0.892 mmol) of 1,2-ethylenediamine in 1.5 ml of methanol was left standing for 24 h at room temperature. On removing the solvent in a vacuum we obtained 0.15 g (97%) of viscous oily substance. IR spectrum, cm^{-1}: 1540, 1560, 1620, 3280. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.23 s [6H, (C$\underline{H}_3$)$_2$C], 3.24 br.s (2H, C$\underline{H}_2$NH), 3.72 br.s (2H, C$\underline{H}_2$N=), 4.40 br.s (2H, NH, OH), 4.67 d (1H, =CH, ^3J 8.8 Hz), 6.65 d (1H, =CH). ^{13}C NMR spectrum, (DMSO-d_6), δ, ppm: 29.47 [(C$\underline{H}_3$)$_2$C], 48.51 (C^2), 53.16 (C^3), 71.34 (COH), 86.11 (C^6), 145.17 (C^7), 174.08 (C^5). Mass spectrum, *m/z* (I_{rel}, %) [*M*]$^+$ 154 (2.39). Found, %: C 62.10; H 9.08; N 17.98. $C_8H_{14}N_2O$. Calculated, %: C 62.31; H 9.15; N 18.17.

Compounds **IIIb–IIId** were prepared in a similar way.

5-(2-Hydroxy-2-methylpropyl)-2,3-dihydro-1*H*-1,4-diazepine (IIIb). Yield 98%, viscous oily substance. IR spectrum, cm^{-1}: 1530, 1610, 3250. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.78 t (3H, C$\underline{H}_3$CH$_2$), 1.32 s [3H, (C$\underline{H}_3$)COH], 1.67 q (2H, CH$_3$C$\underline{H}_2$), 4.30 br.s (2H, OH, NH), 3.47 br.s (2H, C$\underline{H}_2$NH), 3.95 br.s (2H, C$\underline{H}_2$N=), 4.72 d (1H, =CH, ^3J 9.24 Hz), 6.55 d (1H, =CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 7.90 (C$\underline{H}_3$CH$_2$), 27.89 [(C$\underline{H}_3$)COH], 33.81 (C$\underline{H}_3$CH$_2$), 49.04 (C^2), 53.61 (C^3), 74.03 (COH), 88.43 (C^6), 143.45 (C^7), 174.55 (C^5). Mass spectrum, *m/z* (I_{rel}, %) [*M*]$^+$ 168 (1.81). Found, %: C 64.10; H 9.57; N 16.38. $C_9H_{16}N_2O$. Calculated, %: C 64.25; H 9.59; N 16.65.

5-(2-Hydroxy-2-methylbutyl)-2,3-dihydro-1*H*-1,4-diazepine (IIIc). Yield 94%, viscous oily substance. IR spectrum, cm^{-1}: 1530, 1560, 1620, 3250. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 t (3H, C$\underline{H}_3$CH$_2$CH$_2$), 1.32 s [3H, (C$\underline{H}_3$)COH], 1.43 m (2H, CH$_3$C$\underline{H}_2$CH$_2$), 1.63 t (2H, CH$_3$CH$_2$C$\underline{H}_2$), 4.35 br.s (2H, OH, NH), 3.39 br.s (2H, C$\underline{H}_2$NH), 3.92 br.s (2H, C$\underline{H}_2$N=), 4.73 d (1H, =CH, ^3J 9.28 Hz), 6.54 d (1H, =CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.57 (C$\underline{H}_3$CH$_2$CH$_2$), 16.87 (CH$_3$C$\underline{H}_2$CH$_2$), 28.19 [(C$\underline{H}_3$)COH], 43.64 (CH$_3$CH$_2$C$\underline{H}_2$), 48.98 (C^2), 53.47 (C^3), 73.91 (COH), 88.38 (C^6), 143.63 (C^7), 174.89 (C^5). Mass spectrum, *m/z* (I_{rel}, %) [*M*]$^+$ 182 (4.23). Found, %: C 65.08; H 9.71; N 15.28. $C_{10}H_{18}N_2O$. Calculated, %: C 65.90; H 9.95; N 15.37.

5-(1-Hydroxycyclohexyl)-2,3-dihydro-1*H*-1,4-diazepine (IIId). Yield 94%. IR spectrum, cm^{-1}: 1520 sh, 1540, 1600, 3250. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.23 t (2H, γ-CH$_2$), 1.45–1.65 m (8H, α,β-CH$_2$), 4.30 br.s (2H, OH, NH), 3.39 br.s (2H, C$\underline{H}_2$NH), 3.95 br.s (2H, C$\underline{H}_2$N=), 4.55 d (1H, =CH, ^3J 9.28 Hz), 6.85 d (1H, =CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.95 (γ-C), 25.50 (β-C), 36.43 (α-C), 49.91 (C^2), 52.30 (C^3), 73.47 (COH), 87.32 (C^6), 145.95 (C^7), 175.23 (C^5). Mass spectrum, *m/z* (I_{rel}, %) [*M*]$^+$ 194 (2.52). Found, %: C 68.58; H 9.71; N 15.08. $C_{11}H_{18}N_2O$. Calculated, %: C 68.01; H 9.34; N 14.41.

IR spectra were recorded on a spectrometer Specord 75IR from microfilm. ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker DPX-400, internal reference HMDS. Mass spectra were measured on GC-MS instrument LKB-2091 with direct admission of the sample into the ion source, ionizing electrons energy 57 eV.

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