Reaction of vinyloxyalkylamines with mercaptoacetic acid

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N-[2(3)-Hydroxyalkyl]-4-thiazolidinones have been synthesized by the reaction of 2(3)-vinyloxyalkylamines with mercaptoacetic acid in 24—69 % yield. The structure of the compounds obtained was supported by IR and ^{1}H NMR spectroscopic data.

Key words: 2(3)-vinyloxyalkylamines, mercaptoacetic acid, *N*-[2(3)-hydroxyalkyl]-4-thiazolidinones.

It is well known that, depending on their structure,[1,2] nature of acylating agent, reaction conditions, and even the techniques used for product isolation,[3,4] acylation of vinyl ethers of aminoalcohols gives either their linear *N*-acyl derivatives[1,4—7] or *N*-acyl-2-methyl-1,3-oxazacycloalkanes.[2—4,8]

In this reaction acid derivatives — anhydrides,[5] acyl halides,[1,2,8] esters,[3,4,6] and amides[7] — were used as acylating agents. Carboxylic acids themselves were not used for acylation of vinyloxyalkylamines. This may be attributed to the widespread views of instability of vinyl esters in acid media,[9,10] and, specifically, of the well-known ability of *N*-(2-vinyloxyethyl)amides to undergo cyclization into oxazolidines under the action of protic acids.[11—13]

In this work we studied acylation of 2- and 3-vinyloxyalkylamines (**1a—c**) with mercaptoacetic acid. The reaction was carried out by mixing the reagents in benzene followed by boiling and azeotropic distillation of water.

Based on the literature date we expected that acylation of compounds **1a—c** followed by cyclization of amides (**3a—c**) would result in 1,3-oxazacycloalkanes (**4a—c**).

Actually, by the reaction we obtained products whose IR and ^{1}H NMR spectra did not contain absorption bands and the signals of protons of the vinyl group, and their elemental analysis data were consistent with the theoretical values for the expected 1,3-oxazacycloalkanes **4a—c**. However, there was no adsorption band of stretching vibrations of the S—H group in the region of 2550—2600 cm^{-1} in the IR spectra of these compounds, and they contained the broad strong absorption band of the hydroxy group at 3380—3400 cm^{-1}. The presence of the hydroxy group and the absence of the SH group in the product obtained from 2-vinyloxyethylamine **1a** are also confirmed by its mass spectrum which contains the peak of ion $[M-18]^+$ whose intensity is 25 times higher than that of the ion peak $[M-34]^+$.

In the ^{1}H NMR spectra of the compounds obtained the signals of protons of the CH group manifest themselves as quartets at 4.77—4.96 ppm. This value is 0.3—0.6 ppm lower than those observed for 3-acyl-2-methyloxazolidines.[3,4,11] The observed value of chemical shift more closely corresponds to the *S,N*-acetal moiety, SCHN, than to the *O,N*-acetal moiety. All these data suggest that the products of acylation of vinyloxyalkylamines **1a—c** have the structure of thiazolidinones (**5a—c**), not 1,3-oxaazacycloalkanes **4a—c** (Scheme 1).

Two routes for the formation of thiazolidinone **5a—c** seem to be possible. The first route is the acid-catalyzed isomerization of amines **1a—c** to 1,3-oxaazacycloalkanes (**6a—c**) or the tautomeric azomethine alcohols (**7a—c**), which react with thioacetic acid in a well-known manner,[14] to form thiazolidinones **5a—c**. The second route consists in the acylation of **1a—c** to **3a—c** followed by cyclization of **3a—c** to **4a—c** and intramolecular transacetalization of **4a—c** in thermodynamically more stable thiazolidinones **5a—c**.

We have attempted to synthesize of thiazolidinones **5a** using the first route. For this purpose we performed the reaction of mercaptoacetic acid with product **6a** formed by condensation of monoethylamine with acetaldehyde (without isolation of the pure **6a**). In this case compound **5a** was obtained in a yield not greater than 3 %. Such a low yield of **5a** is most likely to be explained by the well known fact[15] that the condensation product **6a** itself is not very stable and formed in a very low yield.

Additionally, one more fact testifies against the first route, namely, the salt of amine and mercaptoacetic acid we isolated, which is formed at the first step of the reaction, has the structure **2a** (assigned according to the 1H NMR spectra), not **8a**.

An indirect confirmation of the occurrence of the reaction in accordance with the second route is the formation of *N*-acetyl-2-vinyloxyethylamine (**9**) and 3-acetyl-2-methyloxazolidine (**10**) in 36 and 5 % yields,

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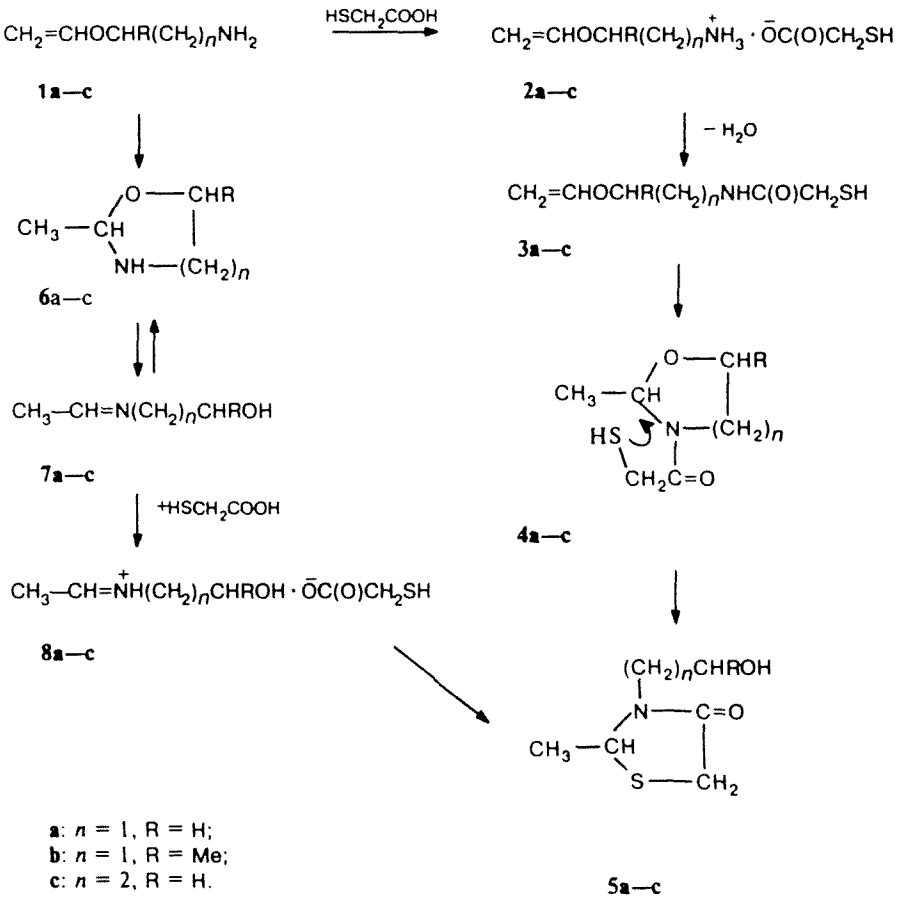
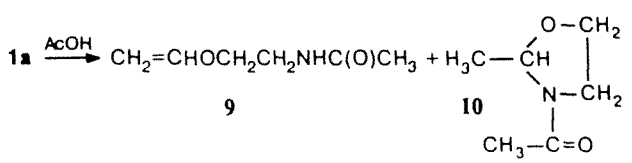
Scheme 1



respectively, which we observed in the acylation of amine **1a** with acetic acid.



Experimental

The ^{1}H NMR spectra were recorded on a Jeol FX 90Q (90 MHz) instrument at 30 °C (internal standard — HMDS). The IR spectra were obtained on a Specord 75 IR spectrophotometer (thin layer). The mass spectrum was recorded on a LKB-2091-051 GC-mass spectrometer.

Monitoring of the purity of the compounds and their identification in the reaction mixture were performed by GLC using an LKhM-80 chromatograph (detector — katharometer, helium as carrier gas, a 3000×3 mm steel column packed with 5 % OV-17 on Inerton Super (0.160—0.200 mm)). The temperature was programmed from 90 to 260 °C at a rate of 4 °C per min.

Synthesis of thiazolidinones (1a—c) (general procedure). To a solution of 0.1 mol of vinyloxyalkylamine **1a—c** in 100 mL of benzene 0.1 mol of mercaptoacetic acid was added, and the mixture was boiled with Dean and Stark distillation head until water separation stopped. The reaction mixture was cooled, and thiazolidinones **5a—c** were isolated by distillation *in vacuo*.

***N*-(2-Hydroxyethyl)-4-thiazolidinone (5a).** Yield 69 %, b.p. 165—167 °C (4 Torr), d_4^{20} 1.2511, n_D^{20} 1.5405. Found (%): C, 44.92; H, 6.73; N, 8.47; S, 19.21. $C_6H_{11}NO_2S$. Calculated (%): C, 44.70; H, 6.88; N, 8.69; S, 19.89. IR, ν/cm^{-1}: 3380 (OH), 2960, 2920, 2870, 1650 (CO), 1440, 1405, 1370, 1350, 1325, 1300, 1255, 1220, 1170, 1045, 1010, 960, 900, 845, 785, 600. ^{1}H NMR ($CDCl_3$), δ: 1.56 (d, ^3J = 6.1 Hz, 3 H, Me), 3.06—3.85 (m, 4 H, OCH_2CH_2N), 3.58 (s, 2 H, SCH_2), 4.08 (br.s, 1 H, OH), 4.92 (q, ^3J = 6.1 Hz, 1 H, SCHN). MS (EI, 70 eV), m/z (I_{rel}(%)): 161 $[M]^{+\cdot}$ (58), 146 $[M-Me]^+$ (99), 143 $[M-H_2O]^+$ (5), 127 $[M-34]^+$ (0.2), 118 $[M-43)^+$ (37), 102 $[M-59]^+$ (69), 74 $[M-87]^+$ (25), 56 $[M-105]^+$ (100).

***N*-(2-Hydroxypropyl)-4-thiazolidinone (5b).** Yield 24 %, b.p. 137—140 °C (3 Torr), d_4^{20} 1.1970, n_D^{20} 1.5260. Found (%): C, 47.67; H, 7.57; N, 8.01; S, 18.42. $C_7H_{13}NO_2S$. Calculated (%): C, 47.98; H, 7.48; N, 7.99; S, 18.30. IR, ν/cm^{-1}: 3400 (OH), 2960, 2920, 2870, 1645 (CO), 1440, 1405, 1365, 1330, 1275, 1225, 1180, 1125, 1080, 1045, 1015, 965, 935, 900, 820, 790, 630. ^{1}H NMR ($CDCl_3$), δ: 1.18 (d, 3 H, OCMe), 1.54 (d, ^3J = 6.1 Hz, 3 H, Me), 2.86—3.79

(m, 2 H, CH_2N), 3.59 (s, 2 H, SCH_2), 4.01 (m, 1 H, CHO), 4.36 (br.s, 1 H, OH), 4.96 (q, ^3J = 6.1 Hz, 1 H, SCHN).

***N*-(3-Hydroxypropyl)-4-thiazolidinone (5c).** Yield 27 %, b.p. 175—178 °C (4 Torr), d_4^{20} 1.1914, n_D^{20} 1.5298. Found (%): C, 48.06; H, 7.33; N, 7.68; S, 18.52. $C_7H_{13}NO_2S$. Calculated (%): C, 47.98; H, 7.48; N, 7.99; S, 18.30. IR, ν/cm^{-1}: 3400 (OH), 2955, 2920, 2865, 1640 (CO), 1445, 1405, 1365, 1325, 1300, 1250, 1220, 1190, 1150, 1050, 965, 900, 850, 780, 675, 590. ^1H NMR ($CDCl_3$), δ: 1.54 (d, ^3J = 6.1 Hz, 3 H, Me), 1.74 (m, 2 H, CCH_2C), 3.01—3.88 (m, 4 H, NCH_2, OCH_2), 3.56 (s, 2 H, SCH_2), 4.18 (br.s, 1 H, OH), 4.77 (q, ^3J = 6.1 Hz, 1 H, SCHN).

2-Vinyloxyethylammonium mercaptoacetate (2a). To a solution of 8.7 g (0.1 mol) of amine **1a** in 100 mL of benzene mercaptoacetic acid (9.2 g, 0.1 mol) was added under cooling to 10 °C. The oil formed was separated, twice washed with benzene (2×50 mL), and dried *in vacuo* to yield product **2a** (16.6 g, 93 %) in the form of noncrystallizable oil. Found (%): C, 40.02; H, 7.12; N, 7.33; S, 18.01. $C_6H_{13}NO_3S$. Calculated (%): C, 40.21; H, 7.31; N, 7.82; S, 17.89. IR, ν/cm^{-1}: 2700—3100 (NH_3^+, CH_2, =CH), 2550 (SH), 1615 (CO), 1570 (COO^-), 1470, 1380, 1315, 1255, 1190, 1145, 1075, 970, 915, 885, 815, 755, 695, 580. ^1H NMR ($CDCl_3$), δ: 2.87 (t, 2 H, NCH_2), 3.03 (s, 2 H, CH_2S), 3.73 (t, 2 H, CH_2O), 3.98 (dd, 1 H, OC=CH-*trans*), 4.17 (dd, 1 H, OC=CH-*cis*), 6.48 (dd, 1 H, OCH=C), 7.25 (br.s, 4 H, NH_3^+, SH).

***N*-Acetyl-2-vinyloxyethylamine (9) and 3-acetyl-2-methyloxazolidine (10).** A mixture of amine **1a** (8.7 g, 0.1 mol), acetic acid (6.0 g, 0.1 mol), and 100 mL of benzene was boiled with Dean and Stark distillation head until water separation ceased. The reaction mixture was cooled and distilled *in vacuo* to give amide **9** (4.4 g, 34 %), b.p. 127—128 °C (10 Torr), d_4^{20} 1.0265, n_D^{20} 1.4680 (see Ref. 6). ^1H NMR ($CDCl_3$), δ: 1.98 (s, 3 H, Me), 3.47 (t, 2 H, CH_2N), 3.74 (t, 2 H, CH_2O), 3.98 (dd, 1 H, OC=CH-*trans*), 4.13 (dd, 1 H, OC=CH-*cis*), 6.44 (dd, 1 H, OCH=C), 7.63 (br.s, 1 H, NH). Oxazolidine **10** (0.7 g, 5 %), b.p. 106—108 °C (10 Torr), d_4^{20} 1.0811, n_D^{20} 1.4662 (see Ref. 11). ^1H NMR ($CDCl_3$), δ: 1.40 (d, 3 H, Me), 2.06 (s, 3 H, MeC=O), 3.62 (m, 2 H, CH_2N), 4.00 (m, 2 H, CH_2O), 5.38 (q, 1 H, NCHO).

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