8,10-Dimethyl-7,13-dioxa-10-azaspiro[5.7]tridecane — the first representative of perhydro-1,3-dioxa-6-azocines

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The first representative of perhydro-1,3-dioxa-6-azocines, 8,10-dimethyl-7,13-dioxa-10-azaspiro[5.7]tridecane, was synthesized by the reaction of 4-methyl-1-oxa-4-azaspiro[4.5]decane with propylene oxide. The structure of the compound has been confirmed by IR and ^1H and ^{13}C NMR spectroscopy and mass spectrometry.

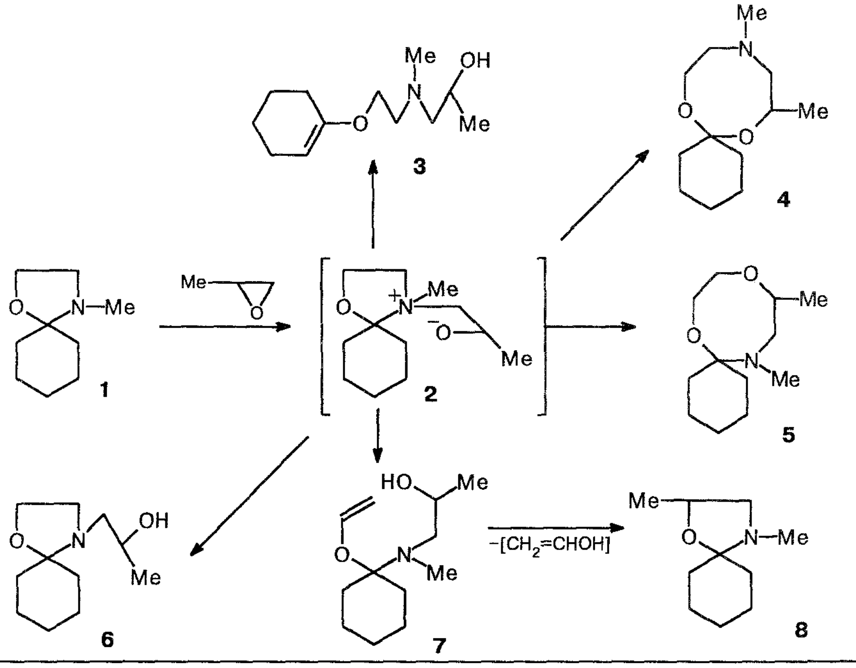
Key words: 8,10-dimethyl-7,13-dioxa-10-azaspiro[5.7]tridecane, perhydro-1,3-dioxa-6-azocines; 4-methyl-1-oxa-4-azaspiro[4.5]decane, propylene oxide, reaction.

It is well known that the reaction of 4-methyl-1-oxa-4-azaspiro[4.5]decane (**1**) with propylene oxide (Scheme 1) gives *N*-(2-hydroxypropyl)-*N*-methyl-2-(1-cyclohexenyloxy)ethylamine (**3**).[1]

We have found that 8,10-dimethyl-7,13-dioxa-10-azaspiro[5.7]tridecane (**4**) also is one of the products of this reaction; it is likely formed as a result of nucleophilic substitution at the spiro atom in intermediate **2** (see Scheme 1).

The structure of the compound obtained corresponds to 1,3-dioxa-6-azocine, rather than 1,6-dioxa-3-azocine (**5**), whose formation could be expected as a result of substitution at the C(4) atom of the oxazolidine cycle in intermediate **2**. Structure **4** is supported by the value of total integral intensity of the signals assigned to OCH_2 groups (δ 3.74), corresponding to two protons, not to four as would be the case with structure **5** (the multiplet at 4.16 ppm is assigned to the OCH group proton, because only this signal is simplified when spin-spin interaction is suppressed by irradiation of the doublet of MeC protons at 1.08 ppm). Additionally, in the ^{13}C NMR spectrum of compound **4** the chemical shift (CS) of the spirane carbon atom (δ 95) corresponds to the CS of the OCO moiety in 1,3-dioxanes (δ 92—96),[2]

Scheme 1



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whereas a lower CS value (by 5—10 ppm) would be expected for the OCN moiety of compound **5**,[3] for example, in oxazolidines (δ 88).[4]

In the course of isolation and purification of the products in preparative scale the great losses of compounds **3** and **4** take place. For this reason, to evaluate conversion of **2** to **3**, **4**, and other products we analyzed the untreated reaction mixture using GLC and showed the presence of 15 compounds. Among them we identified 11 compounds listed below (their concentrations (wt. %), determined by an internal standard method[5] are given in parentheses): 2-methylaminoethanol (**9**, 0.145), 1-methylamino-2-propanol (**10**, 0.07), cyclohexanone (**11**, 9.86), 4-methyl-2,2-pentamethylene-1,3-dioxolane (**12**, 0.87), *N*-(2-hydroxyethyl)-*N*-methyl-1-amino-2-propanol (**13**, 7.54), oxazolidine **8** (4.93), oxazolidine **1** (30.81), dioxazocine **4** (6.67), oxazolidine **6** (0.36), 2-cyclohexylidenecyclohexanol (**14**, 1.02), and aminoalcohol **3** (29.11).

Compounds **1**, **3**, **8**, and **11**—**14** were isolated on a preparative scale. Their physical and chemical constants and IR spectra were identical to those of authentic samples.

We have not found the product of C(4)—N bond cleavage of the oxazolidine cycle in intermediate **2**, *N,O*-ketal **7**. This may be connected with its conversion to the more stable oxazolidine **8** under the reaction conditions.

The reaction mixture composition indicates that along with formation of products **3**, **4**, and **8**, the processes occur which are associated with hydrolysis of these compounds and oxazolidine **1** to aminoalcohols and cyclohexanone, as well as the further conversions of the hydrolysis products also proceed. The attempts to exclude the hydrolysis by thorough drying of the starting reagents failed. In all cases we observed the formation of cyclohexanol and products of its autocondensation and its condensation with propylene oxide (**14** and **12**, respectively).

Probably, the water required for the hydrolysis appears as a result of dehydration of aminoalcohols and crotonic condensation of **11**.

Experimental

^{1}H и ^{13}C NMR spectra were recorded on a Jeol FX 90 instrument (90 and 22.49 MHz, respectively) at 30 °C using HMDS as the internal standard. The IR spectrum was obtained on a Specord 75 IR spectrophotometer (thin layer). The mass-spectrum was recorded on a Varian MAT-212 chromato-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, gas carrier — He, steel column 3000×3 mm, 3 % OV-17 on Inerton Super (0.160—0.200 mm)). The temperature was programmed from 50 to 230 °C at a rate of 4 deg per min.

8,10-Dimethyl-7,13-dioxa-10-azaspiro[5.7]tridecane (4). A mixture of oxazolidine **1** (75.5 g, 0.5 mol) and propylene oxide (29 g, 0.5 mol) was heated in an autoclave for 36 h at 190 °C. Distillation *in vacuo* afforded dioxazocine **4** (2.6 g, 2.4 %), b.p. 91—93 °C (4 Torr), d_4^{20} 1.0081, n_D^{20} 1.4792. Found (%): C, 67.88; H, 10.57; N, 6.52. $C_{12}H_{23}NO_2$. Calculated (%): C, 67.57; H, 10.87; N, 6.57. IR, ν/cm^{-1}: 2920, 2840, 2775, 2745, 1435, 1355, 1350, 1325, 1290, 1260, 1230, 1220, 1135, 1095, 1055, 1040, 1025, 980, 945, 920, 905, 850, 825, 805, 770, 715, 620, 600, 585, 520. ^{1}H NMR ($CDCl_3$), δ: 1.08 (d, 3 H, Me); 1.46—1.60 (m, 10 H, $(CH_2)_5$); 2.45 (s, 3 H, NMe); 2.28—3.05 (m, 4 H, $(CH_2)_2N$); 3.74 (m, 2 H, OCH_2); 4.16 (m, 1 H, OCH). ^{13}C NMR ($CDCl_3$), δ: 19.81 (C(3)); 22.28 (C(4)); 22.41 (C(2)); 24.95 (Me); 32.49 (C(5)); 34.05 (C(1)); 45.58 (NMe); 56.23 (C(9)); 60.71 (C(11)); 63.44 (C(8)); 64.16 (C(12)); 99.34 (C(6)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 213 $[M]^+$ (100), 98 $[M-OCH(Me)CH_2N(Me)CH_2CH_2]^+$ (78).

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