Mendeleev Commun., 1991, 1(1), 9–10

Is there Ring–Chain Tautomerism in γ-Nitrosoalkanols?

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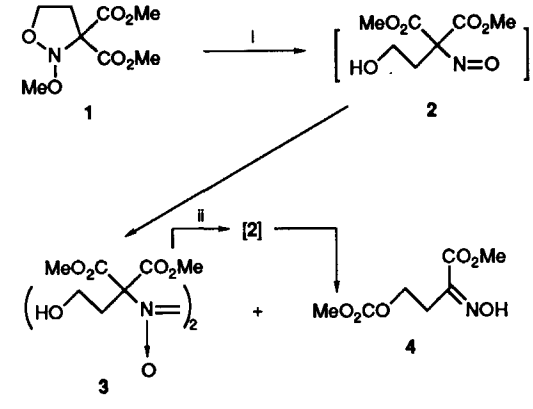
γ-Nitrosoalkanols **2**, **6** and **8**, obtained upon acid hydrolysis of 2-methoxyisoxazolidines **1** and **7** and of dimethoxyamine **5**, respectively, do not display ring–chain tautomerism, *i.e.* formation of the corresponding 2-hydroxyisoxazolidines ('heminitrosals'); nitrosoalkanol **2** smoothly rearranges to oxime **4**, whilst compound **8** in MeOH gives diol **9**, probably *via* aerial oxidation to the corresponding nitrite followed by denitrosation.

Ring–chain tautomerism is well known for monosaccharides[1] in addition to more conventional aliphatic hydroxyaldehydes, such as γ-hydroxybutanal,[2] which exist mainly as cyclic hemiacetals. The same kind of tautomerism might be expected to occur in the series of γ- and δ-nitrosoalkanols owing to the similar reactivity of acetals[3] and their nitrogen analogues,† dialkoxyamines.[5–9] Thus, the latter are smoothly converted into nitrosoalkanes upon acid-catalysed hydrolysis[5] or alcoholysis.[7] In order to examine the possibility of the reverse intramolecular reaction, we synthesized a number of γ-nitrosoalkanols with electron withdrawing substituents, reasoning that such substituents should increase the electrophilicity of the nitroso group and therefore facilitate the formation of the cyclic heminitrosals.

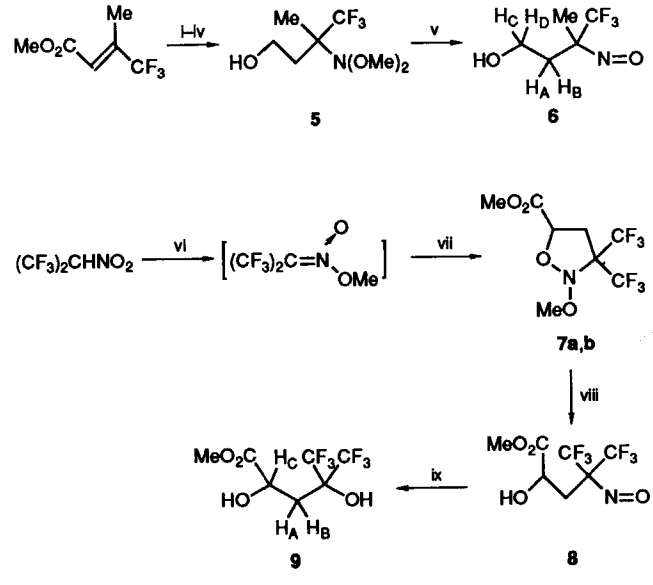
It has been found that 2-methoxyisoxazolidine **1**,[10] in analogy to acyclic dialkoxyamines (*cf.* refs. 5, 7), affords, upon acid hydrolysis, γ-nitrosoalkanol **2**, isolated as a colourless crystalline dimer **3** (Scheme 1).‡ However, the main product of this reaction is formed by the rearrangement of **2** into oxime **4** which proceeds with migration of the methoxycarbonyl substituent to the OH group. On dissolution of pure **3** in MeOH a light blue colour (due to the monomer **2**) appears first and then gradually fades as the quantitative transformation of **2** into **4** takes place.

In order to avoid such rearrangement we further synthetized γ-nitrosoalkanols **6** and **8** (Scheme 2) with CF_3 groups as non-migrating substituents. Dimethoxyamine **5**, the precursor of compound **6**, was obtained as outlined in Scheme 2 by analogy with the corresponding transformation[6,7] of β,β-dimethylacrylate.

γ-Nitrosoalkanols **6** and **8** exist as monomers and hence display an intense light blue colouring. Their ^{1}H NMR spectra in C_6D_6 and in [$^2H_8$]dioxane–D_2O (3:1) contain only signals attributable to the acyclic (chain) forms. Under aldehyde acetalization conditions[3] in dilute MeOH solution in the presence of Dowex (H^+), nitrosoalkanol **8** gives rise to diol **9** (Scheme 2) – probably as a result of oxidation to the corresponding nitrite by atmospheric O_2 (*cf.* ref. 11) and subsequent denitrosation in the presence of MeOH.



Scheme 1 *Reagents and conditions*: i, H_2O–Et_2O/Amberlyst-15, room temp., 48 h, **3** (11%), m.p. 103 °C, **4** (55%), m.p. 50–51 °C; ii, MeOH, room temp., 2 h and 4 °C, 12 h (~ 100% conversion)



Scheme 2 *Reagents and conditions*: i, $MeONH_2$, 100 °C, 65 h (69%), b.p. 89 °C/40 torr; ii, Bu^{t}OCl–Et_2O, – 78 °C (100%); iii, MeOH–γ-collidine, – 78→20 °C (85%), b.p. 60 °C/40 torr; iv, $LiAlH_4$, Et_2O, 35 °C (81%), b.p. 66 °C/2 torr; v, H_2O–C_6H_6/Amberlyst-15, room temp., 12 days (56%), b.p. 60 °C/10 torr; vi, CH_2N_2/Et_2O; vii, CH_2=$CHCO_2Me$, 0 °C, 4 days (39%), b.p. 80 °C/10 torr, ratio of diastereoisomers **7a**:**7b** = 1.8; viii, H_2O–CH_2Cl_2/$SbCl_5$, – 78 °C (93%), m.p. 37 °C; ix, MeOH/Dowex(H^+)/O_2, 20 °C, 7 days (62%)

† These nitrogen analogues have been referred to as 'nitrosoacetals'.[4] In our opinion, the term 'nitrosals' would be more adequate.

‡ All new compounds gave satisfactory analytical and spectral data. *Selected spectral data* for **3**: ^{1}H NMR (400 MHz, [$^2H_6$]Me_2SO, standard $SiMe_4$) δ 2.11 and 3.51[$(CH_2)_2$, ^3J 6.5 Hz], 3.72(OMe), 4.00(OH); CIMS, *m/z* 206(10%) {[1/(2M + 1)]$^+$}, 145(100); IR ν_{max}/cm^{-1} 3250(OH), 1760(CO), 1200(N→O).

4: ^{1}H NMR (C_6D_6) δ 2.93(CH_2, ^3J 6.7 Hz), 3.37(MeOCO$_2$), 3.41 (MeO_2C), 4.26(CH_2O), 10.83(OH); ^{13}C NMR (100.61 MHz, C_6D_6) δ 24.95(CH_2C=N, ^1J 132.5 Hz), 52.32(CH_3OCO_2, ^1J 147.8 Hz), 54.44 (MeO_2C, ^1J 147.7 Hz), 63.98(CH_2O, ^1J 151.2, ^2J 5.6 Hz), 149.10(C=N, ^2J 6.2, ^3J 4.2 Hz), 156.00[CO_3, ^3J 4.0(Me), ^3J 3.9(CH_2)], 163.80[CO_2, ^3J 4.1(Me), ^3J 4.0 Hz (CH_2)]; CIMS *m/z* 206(13.6) [(M + 1)$^+$], 130(100); IR ν/cm^{-1} 3280(OH), 1750, 1726(CO), 1713(C=N).

6: ^{1}H NMR {[$^2H_8$]dioxane–D_2O(3/1)} δ 1.08(Me, $^4J_{HF}$ 0.7 Hz), 2.17(H_A, $^2J_{AB}$ – 14.7, $^3J_{AD}$ 5.9 Hz), 2.46(H_B, $^3J_{BC}$ $^3J_{BD}$ 7.3, $^4J_{BF}$ 0.4 Hz), 3.38(H_C, $^2J_{CD}$ – 11.1 Hz), 3.47(H_D, $^5J_{DF}$ 0.8 Hz).

8: ^{1}H NMR (C_6D_6) δ 0.57(OH), 2.16(CH_2, ^3J 6.7 Hz), 3.03(OMe), 3.83(CH); IR (CCl_4) ν/cm^{-1} 3460(OH), 1740(CO), 1593(NO).

9: ^{1}H NMR (C_6D_6) δ 1.81(H_A, ^2J – 15.3, $^3J_{AC}$ 11.6, $^4J_{ACF_3}$ 2.0 Hz), 2.23(H_B, $^3J_{BC}$ 2.8 Hz), 3.00(OMe), 4.07(H_C), 5.80 (OH); ^{19}F NMR (75.4 MHz, C_6D_6, external standard CF_3CO_2H) δ – 0.81(CF_3, $^4J_{FF}$ 10.0), 2.52(CF_3, $^4J_{FH}$ 2.0 Hz); IR (CCl_4) ν/cm^{-1} 3430(OH), 1740(CO).

Mendeleev Commun., 1991, 1(1), 9–10

Thus, ring–chain tautomerism of the above-mentioned γ-nitrosoalkanols was not observed and the possibility of synthesising cyclic heminitrosals remains an open question.§

Received in USSR, 23rd July 1990
Received in UK, 1st November 1990; Com. 0/03580G

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§ *Cf.* ref. 12, where the irreversible thermal or KF-catalysed transformation of 5-substituted 2-trimethylsilyloxy-3,3-dimethylisoxazolidines into the corresponding *O*-trimethylsilyl derivatives of γ-nitrosoalkanols have been reported.

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