N,N-Dimethoxy-N-tert-alkylamines: new synthesis methods and the crystal structure of the precursor

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Under the methanolysis of N-methoxy-N-(1-pyridinium)amines salts 1a–c, nucleophilic substitution occurs at the nitrogen atom to form N,N-dimethoxyamines 2a,b; the crystal structure of precursor 1c has been studied.

Nucleophilic substitution at the nitrogen atom is known for different N-chloro-N-alkoxy- and N-acloxy-N-alkoxy geminal systems. N,N-Dialkoxyamines are formed under the alcoholyis of N-chloro-N-alkoxy-N-tert-alkylamines and N-acloxy-N-alkoxy-N-tert-alkylamines. The corresponding N,N-dialkoxyamines were obtained by the alcoholyis of N-chloro-N-alkoxyureas, N-chloro-N-alkoxybenzamides, N-chloro-N-alkoxycarbamates, N-acloxy-N-alkoxyureas and N-acloxy-N-alkoxycarbamates. Nucleophilic substitution at the nitrogen atom takes place in the reactions of N-acloxy-N-alkoxybenzamides with amines and NaN₃,9,10 under their alkaline hydrolysis;11 in reactions of N-acloxy-N-alkoxyamines with K and Na carboxylates.12 However, nucleophilic substitution at the central nitrogen atom in the RO-N⁺ geometrical system was unknown. Prepared from N-chloro-N-alkoxyamines, N,N-dimethoxy-N-(pyridinium)amine salts 1 are stable in the methanol solution at room temperature and nucleophilic substitution at the central N atom in this geometrical system was not studied.13

We found previously that salts 1a–c under methanolysis in the presence of AcONa at 100 °C (in a sealed glass tube) are converted into corresponding N,N-dimethoxyamines2 2a (74% yield from 1a) and 2b (67% and 70% yields from 1b and 1c, respectively) (Scheme 1).

Scheme 1 Reagents and conditions: ~100 equiv. of MeOH, ~10 equiv. of AcONa, 100 °C, 2.5 h.

Pyridine was liberated in the form of acetate. Thus, the first example of nucleophilic substitution at the nitrogen atom for this kind of geminal systems was developed. The N-pyridinium substituent in salts 1a–c can be considered as a protective group that substantially stabilises these geminal systems in comparison with N-chloro-N-alkoxyamines. Based on this new method of synthesis, the first optically active compounds with asymmetric nitrogen in open chains have been obtained.2 Obviously, the above method might be extended to the synthesis of cyclic N,N-dialkoxyamines14,15 and trialkoxyamines (orthonitriles).16

The configurational stability of salts 1a (ΔGθ = 14.3–15.3 kcal mol⁻¹ at 2–27 °C)13 is noticeably lower than that of dialkoxyamines (ΔGθ = 21.9–24.6 kcal mol⁻¹ at 20 °C).2 To understand the nature of this decrease, an XRD study of salt 1c was performed (crystals were grown from MeOH).8

Compound 1c crystallises as a racemate (space group PT). The N(2) atom is characterised by pronounced pyramidality with the deviation of N(2) from the plane of O(1), C(7) and N(1) atoms equal to 0.53(2) Å; the sum of bond angles at the N(2) atom is 322.8°. The latter value is noticeably higher than those of (MeO)₂NN(OMe)₂ (311.6°),16[(MeO)₂NN(MeO)(OMe)₂] (315.7°) and 2-metoxy-3,3-dicarbamoyl-1,2-oxazolidine (317.5°).15 Although it was reasonable to propose that the configuration stability of 1c is the consequence of conjugation between the electron lone pair (LP) with the pyridine π system, the pseudorotation angle LP-N(2)-N(1)-C(1) (φ) is equal to 27.3°. On the other hand, the observed conformation can be stabilised by stereo-electronic interaction between the LP and the σ⁺ orbitals of the N(1)-C(5) bond. However, the lengths of the N(1)-C(5) and N(1)-C(1) bonds are almost equal. Finally, cation conformation can be influenced by crystal packing effects. Nevertheless, the

DOI: 10.1070/MC2006v016n02ABEH002222

1 Crystallographic data for 1c at 120 K of crystals of C₉H₇Cl₂O₄ are triclinic, space group P T, a = 5.9922(7), b = 8.2161(6), c = 15.162(2) Å, α = 90.334(5), β = 92.939(5), γ = 91.281(5), V = 745.3(2) Å³, Z = 2, M = 324.72, dcal = 1.447 g cm⁻³, μ(MoKα) = 2.90 cm⁻¹, F(000) = 340. Intensities of 7719 reflections were measured with a Smart 1000 CCD diffractometer at 120K [μ(MoKα) = 0.71072 Å, ω-scans with a 0.3° step in θ and 8 s per frame exposure, 2θ ≤ 56°], and 3569 independent reflections (Rint = 0.0290) were used in the further refinement. The structure was solved by a direct method and refined by the full-matrix least-squares technique against F² in the anisotropic-isotropic approximation. The positions of hydrogen atoms were calculated and refined in an isotropic approximation in a riding model. The analysis of the Fourier electron density synthesis revealed that ClO₄ anions are disordered by two positions with relative oxygen atom occupancies of 7:3. The refinement converged to wR₁ = 0.1106 and GoF = 0.997 for all independent reflections [R₁ = 0.0459 was calculated against F for 2748 observed reflections with I > 2σ(I)]. All calculations were performed using SHELXTL PLUS 5.0.

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (and from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 299193. For details, see ‘Notice to Authors’, Mendeley Commun., Issue 1, 2006.
Figure 1 General view of the cation of 1c. The selected bond lengths (Å): N(1)–C(5) 1.345(2), N(1)–C(1) 1.348(2), N(1)–N(2) 1.466(2), N(2)–O(1) 1.412(16), N(2)–C(7) 1.500(2), O(1)–C(6) 1.440(2), C(7)–C(8) 1.524(2), C(7)–C(9) 1.526(2), C(7)–C(10) 1.540(2), C(10)–O(2) 1.199(2), C(10)–O(3) 1.331(2); bond angles (°): N(2)–O(1)–C(6) 107.86(12), C(5)–N(1)–C(7) 110.9(1), O(1)–N(2)–N(1) 106.6(1), O(1)–N(2)–C(7) 105.3(1), N(1)–N(2)–C(7) 114.7(1), O(1)–N(2)–N(1) 106.6(1), O(1)–N(2)–C(7) 105.3(1), N(1)–N(2)–C(7) 114.7(1).

B3PW91/6-31G* calculation has revealed that the above conformation is also preserved in the isolated cation (φ is 33.8°). In addition, note that the potential energy scan along the φ coordinate for the cation has revealed that the difference in energy between the minimum and a conformer with f = 90° is 11.49 kcal mol⁻¹.

In order to estimate the inversion barrier, we have carried out the additional optimization of the transition state (TS) with the planar N(2) atom. The additional verifications of transition state localization have been obtained within the frequency calculation: one imaginary frequency (1461 cm⁻¹) corresponding to the out-of-plane bending of the N(2) atom was found. The energy difference between the minimum and transition state with the ZPE correction according to B3PW91/6-31G* optimization is 6.81 kcal mol–¹, which is about two times lower than the energy difference between the minimum and transition state with the Planewave program package17 at the B3PW91/6-31G* level of theory.

Surprisingly, the analysis of TS geometry has revealed that, in spite of a lower barrier of inversion, the mutual disposition of the Lp of the N(2) atom and the pyridine π system found in the isolated cation retains in the transition state (φ is 33.8°). Such a conformation in the TS is a fortiori unexpected assuming the Lp is totally from 1.451 Å [1.466(2) Å in crystal] in an energy minimum coordination for the cation has revealed that the difference in energy between the minimum and a conformer with f = 90° is 11.49 kcal mol⁻¹.

This work was supported by the Russian Academy of Sciences and the Russian Foundation for Basic Research (grant nos. 03-03-04010 and 06-03-32840).

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