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1-Alkoxyamino-4-dimethylaminopyridinium salts: synthesis and structure†

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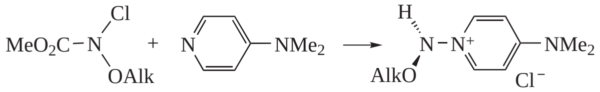
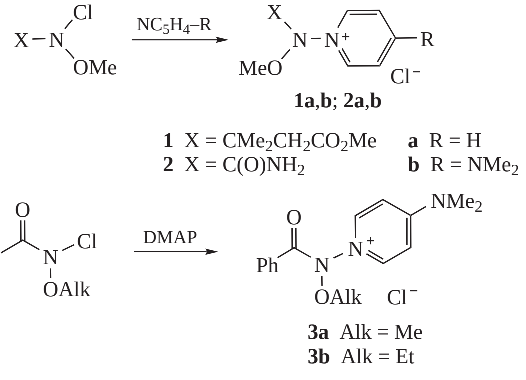
***N*-Alkoxy-*N*-chlorocarbamates react with 4-dimethylaminopyridine yielding 1-alkoxyamino-4-dimethylaminopyridinium chlorides, new type of O–N–N$^+$ geminal systems. The XRD studies of two representative 1-alkoxyaminopyridinium chlorides revealed the high pyramidal configuration of the central nitrogen atom in O–N–N$^+$ geminal system.**



N-Alkoxyhydrazines are unstable due to $n_{N'} \rightarrow \sigma^*_{N-O(Alk)}$ orbital interaction (anomeric effect).[2–17] These compounds relate to O–N–N geminal systems, scarcely studied type of O–N–X geminal systems (X = Cl, O, N).[1–20] Their instability results in elimination of *N*-alkoxy group yielding appropriate diazenes[2,3] or HERON rearrangement with the ester formation.[4–10,12,17] Anyway, salts of *N*-alkoxy-*N*-(pyridin-1-ium-1-yl)-*N*-*tert*-alkylamines of type **1**, *N*-alkoxy-*N*-(pyridin-1-ium-1-yl)ureas of type **2**[3,18,19] and *N*-alkoxy-*N*-(4-dimethylaminopyridin-1-ium-1-yl)benzamides **3**[19] were synthesized by the reaction of the appropriate *N*-alkoxy-*N*-chloroamino derivatives with pyridine or 4-dimethylaminopyridine (DMAP) (Scheme 1).



Scheme 1

The stability of compounds **1**,[2,20] **2**,[3,18,19] **3**[19] may be attributed to diminished $n_{N'} \rightarrow \sigma^*_{N-O(Alk)}$ anomeric effect. The lone pair (Lp) of the central nitrogen atom of their O–N–N$^+$ geminal system is located in the pyridine ring plane,[18–20] thus its LpN conjugation with aromatic π-system becomes impossible too.

In this study, we found that *N*-alkoxy-*N*-chlorocarbamates **4a–d** reacted with DMAP in MeCN or Et_2O yielding unknown 1-alkoxyamino-4-dimethylaminopyridinium chlorides **5a–d**‡ (Scheme 2).

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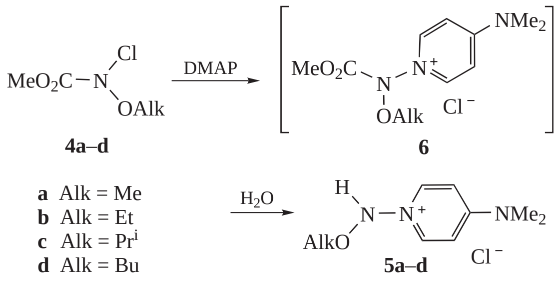
† Geminal systems. Part 64; for previous communication, see ref. 1.

‡ *4-Dimethylamino-1-ethoxyaminopyridinium chloride* **5b**. The solution of DMAP (0.198 g, 1.623 mmol) in MeCN (10 ml) was added to the solution of methyl *N*-chloro-*N*-ethoxycarbamate **4b**[22] (0.248 g, 1.612 mmol) in MeCN (5 ml) at –17 °C. The mixture was kept at –11 °C for 1 h, then at 12 °C for 42 h, after that the solvent was evaporated on 2/3 *in vacuo*, the formed precipitate was filtered, dried *in vacuo* (2 Torr) to yield 0.158 g (45%) of product **5b**, colorless crystals, mp 168–172 °C (decomp.) (MeCN). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.13 (t, 3H, NOCH$_2$*Me*, ^3J 7.0 Hz), 3.25 (s, 6H, NMe$_2$), 3.83 (q, 2H, NOC*H*$_2$Me, ^3J 7.0 Hz), 7.04 (d, 2H, C^{3}H, C^{5}H, ^3J 7.8 Hz), 8.46 (d, 2H, C^{2}H, C^{6}H, ^3J 7.8 Hz), 10.90 (s, 1H, NHO). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 13.43 (NOCH$_2$*Me*), 40.61 (NMe$_2$), 68.64 (NO*C*H$_2$Me), 107.16 (C^3, C^5), 142.19 (C^2, C^6), 156.68 (C^4). MS (FAB), *m/z* (%): 401 [$2M^+ \cdot Cl^-$] (2), 399 [$2M^+ \cdot Cl^-$] (7), 182 [M$^+$] (100), 137 (13), 123 (17). Found (%): N, 19.16; Cl, 16.21. Calc. for $C_9H_{16}ClN_3O$ (%): N, 19.30; Cl, 16.29. The MeCN-filtrate was evaporated *in vacuo*, the residue was dissolved in CH_2Cl_2 (5 ml), and Et_2O (5 ml) was added. After keeping at –16 °C the formed precipitate was filtered, dried *in vacuo*, additionally yielding 0.095 g (27%) of compound **5b**.

In the same manner, 1-isopropyloxyamino-4-dimethylaminopyridinium chloride **5c** was obtained from methyl *N*-chloro-*N*-isopropyloxycarbamate **4c**[22] in Et_2O solution, yield 81%, colorless crystals, mp 175–177 °C (MeCN–Et_2O, decomp.).

4-Dimethylamino-1-methoxyaminopyridinium chloride **5a**. The solution of DMAP (0.207 g, 1.694 mmol) in MeCN (13 ml) was added to the solution of methyl *N*-chloro-*N*-methoxycarbamate **4a**[23] (0.236 g, 1.694 mmol) in MeCN (6 ml) at –15 °C. The mixture was heated to 20 °C within 17 h, then kept at 5 °C for 5 h, after that the solvent was evaporated *in vacuo*, the residue was extracted with benzene (8 ml) at 5 °C for 20 h, then benzene extract was discarded, the solid residue was dried at 20 °C

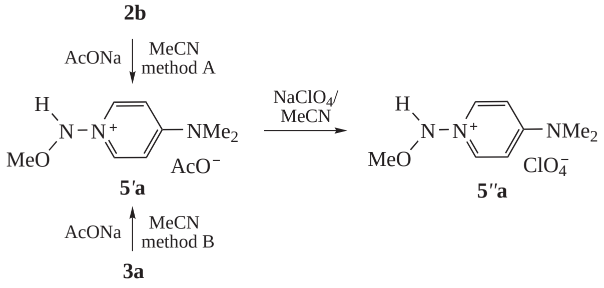


Scheme 2

The structures of products **5** have been characterized by ^{1}H, ^{13}C NMR and MS spectra, the structures of compounds **5a**,**b** have been studied by XRD.

As the mechanism of compounds **5** formation remains unclear, one may assume that unstable intermediates **6** form at the first stage of this reaction as products of the nucleophilic substitution at the nitrogen atom. Their further hydrolysis gives the final aminopyridinium salts **5a–d** (see Scheme 2).

We also found that salts of type **5** can be obtained from carbamoyl (**2b**) and benzoyl (**3a**) derivatives on treatment with AcONa (Scheme 3). Anion exchange in acetate **5′a** with $NaClO_4$ in MeCN affords perchlorate **5″a**.



Scheme 3

The structures of compounds **5′a**, **5″a** were established by ^{1}H NMR and MS spectra. Probably, decarbamoylation (or debenzoylation) in salts **2b**, **3a** results from AcO^- nucleophilic addition on the C=O moiety with subsequent elimination of AcOC(O)X species.

XRD studies of monocrystals of **5a** and **5b** (Figure 1)[§] revealed that in these compounds nitrogen atoms N(2) had the same high pyramidal configuration. The sums of bond angles centered on N(2) ($\Sigma\beta$) are 312°. In the carbamoyl precursor of **5a**, namely, compound **2b**, the nitrogen pyramidality degree is substantially

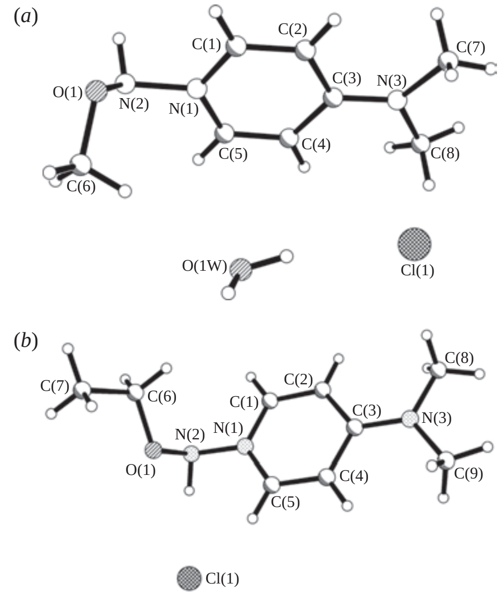


Figure 1 Molecular structures of chlorides (*a*) **5a** (monohydrate) and (*b*) **5b**.

(3 Torr), then extracted with CH_2Cl_2 (11 ml) at 6 °C for 19 h, then the undissolved solid was filtered and dried at 3 Torr, yielding 0.146 g (39%) of pure compound **5a**·H_2O, colorless crystals, mp 83–85 °C (monohydrate) (CH_2Cl_2–benzene). ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.26 (s, 6H, NMe_2), 3.58 (s, 3H, NOMe), 7.05 (d, 2H, C^{3}H, C^{5}H, ^3J 7.5 Hz), 8.46 (d, 2H, C^{2}H, C^{6}H, ^3J 7.5 Hz), 11.08 (s, 1H, NHO). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 40.77 (NMe_2), 60.76 (NOMe), 107.39 (C^3, C^5), 142.49 (C^2, C^6), 156.96 (C^4). MS (FAB), *m/z* (%): 373 [2M$^+$·Cl$^-$] (3), 371 [2M$^+$·Cl$^-$] (9), 168 [M$^+$] (100), 137 (24), 121 (8). Found (%): N, 18.76; Cl, 15.65. Calc. for $C_8H_{14}ClN_3O\cdot H_2O$ (%): N, 18.95; Cl, 15.99. Et_2O (17 ml) was added to the CH_2Cl_2 filtrate, the mixture was kept at –16 °C for 3 h, the formed precipitate was filtered and dried at 3 Torr, additionally yielding 0.099 g (26%) of compound **5a**·H_2O.

In the analogous manner, 1-butyloxyamino-4-dimethylaminopyridinium chloride (monohydrate) **5d**·H_2O was obtained from methyl *N*-butyloxy-*N*-chlorocarbamate **4d**[24] in MeCN solution, yield 46%, hygroscopic colorless crystals, mp 49–51 °C (monohydrate).

For characteristics of compounds **5c** and **5d**·H_2O, see Online Supplementary Materials.

4-Dimethylamino-1-methoxyaminopyridinium acetate **5′a**. *Method A.* Sodium acetate (0.260 g, 3.169 mmol) was added to the solution of *N*-(4-dimethylaminopyridin-1-ium-1-yl)-*N*-methoxyurea chloride **2b**[19] (0.092 g, 0.373 mmol) in MeCN (10 ml), the mixture was stirred at 24–25 °C for 14 h, then the solid was filtered off. The MeCN filtrate was evaporated *in vacuo*, the residue was kept at 25 °C (1 Torr), yielding 0.082 g (94%) of product **5′a** as viscous yellowish oil. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 1.83 (s, 3H, AcO), 3.25 (s, 6H, NMe_2), 3.58 (s, 3H, NOMe), 7.04 (d, 2H, C^{3}H, C^{5}H, ^3J 7.8 Hz), 8.46 (d, 2H, C^{2}H, C^{6}H, ^3J 7.8 Hz). MS (FAB), *m/z* (%): 168 [M$^+$] (100), 137 (40), 123 (27). *Method B.* Similarly, compound **5′a** was synthesized in 93% yield by AcONa reaction with *N*-(4-dimethylaminopyridin-1-ium-1-yl)-*N*-methoxybenzamide chloride **3a** (prepared from *N*-chloro-*N*-methoxybenzamide,[19] for characteristics of **3a**, see Online Supplementary Materials) in MeCN and identified by ^{1}H NMR and MS spectra.

4-Dimethylamino-1-methoxyaminopyridinium perchlorate **5″a**. The solution of acetate **5′a** (0.029 g, 0.127 mmol) in MeCN (7 ml) was added to the solution of $NaClO_4$ (0.016 g, 0.127 mmol) in MeCN (3 ml), while the white precipitate forms. The mixture was kept at 5 °C for 20 h, then the solid was filtered off, the MeCN filtrate was evaporated *in vacuo*, the residue was kept at 25 °C (3 Torr), yielding 0.032 g (94%) of perchlorate **5″a**, colorless crystals. ^{1}H NMR (300 MHz, DMSO-d_6) δ: 3.26 (s, 6H, NMe_2), 3.59 (s, 3H, NOMe), 7.03 (d, 2H, C^{3}H, C^{5}H, ^3J 7.8 Hz), 8.39 (d, 2H, C^{2}H, C^{6}H, ^3J 7.8 Hz), 10.55 (s, 1H, NHO).

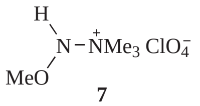
[§] *Crystal data for* **5a**: crystals were grown from CH_2Cl_2–benzene, $C_8H_{14}N_3O\cdot Cl\cdot H_2O$, monoclinic, space group $P2_1/c$, a = 10.0703(4), b = 9.0552(4) and c = 13.1133(6) Å, β = 108.010(4)°, V = 1137.19(9) Å^3, F(000) = 472, d_{calc} = 1.295 g cm^{-3}, Z = 4, μ = 0.318 mm^{-1}, M_r = 221.69.

Crystal data for **5b**: crystals were grown from MeCN, $C_9H_{16}N_3O\cdot Cl$, orthorhombic, space group *Pbca*, a = 12.6834(3), b = 9.8820(2) and c = 18.6806(4) Å, V = 2341.38(9) Å^3, F(000) = 928, d_{calc} = 1.235 g cm^{-3}, Z = 8, μ = 0.302 mm^{-1}, M_r = 217.70.

The measurements were performed using an Xcalibur 3 diffractometer [T = 298 K (**5a**), 100 K (**5b**); graphite-monochromated MoKα radiation, $2\theta/\theta$ scan, $2\theta_{max}$ = 60.0° (**5a** and **5b**)]. The structures were solved by direct method using the SHELXTL PLUS program package.[25] Refinement against F^2 in an anisotropic approximation (the hydrogen atoms isotropic in the riding model) by a full matrix least-squares method for 3221 reflections was carried out to wR_2 = 0.112 [R_1 = 0.039 for 2235 reflections with $F > 4\sigma(F)$, S = 0.966] for **5a**, and for 3371 reflections was carried out to wR_2 = 0.089 [R_1 = 0.032 for 2800 reflections with $F > 4\sigma(F)$, S = 1.063] for **5b**.

CCDC 1407552 and 1407553 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

For more details, see Online Supplementary Materials.



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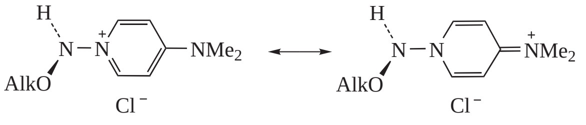
diminished (Σβ is 332.7°).[19] In the latter case the carbamoyl moiety presence favours to the nitrogen inversion and the nitrogen pyramidality diminishing. The other nitrogen atoms in compounds **5a**,**b** have planar configuration: for N(1) and N(3) atoms Σβ = 360°. Note that in 1,1,1-trimethyl-2-methoxyhydrazinium perchlorate **7** the central nitrogen atom of O–N–N$^+$ geminal system has the same degree of pyramidality.[1] However, O(1)–N(2) bonds in compounds **5a**,**b** are longer [1.431(2) Å for N–OMe (**5a**), 1.440(1) Å for N–OEt (**5b**)] than N–OMe bond of salt **7** [1.391(3) Å].[1] On the other hand, N(1)–N(2) bonds [1.428(2) Å (**5a**), 1.426(1) Å (**5b**)] in salts **5a**,**b** are somewhat shorter than N–N$^+$ bond in *N*-methoxyhydrazine **7** [1.483(3) Å].[1] It can be caused by the diminishing action of the $n_{O(1)} \rightarrow \sigma^*_{N(2)-N(1)^+}$ anomeric effect in 1-alkoxyaminopyridiniun chlorides **5a**,**b** as compared with the action of $n_O \rightarrow \sigma^*_{N-N^+}$ anomeric effect in compound **7**.[1] Probably, the positive charge of N(1) atom to a large degree is transfered on N(3) atom and certain contribution of quinonoid structure **5A** takes place (Scheme 4).



5 **5A**

Scheme 4

This assumption is in accord with the some observed shortening of N(3)–C(3) [1.337(2) Å (**5a**), 1.339(1) Å (**5b**)] bonds of compounds **5a**,**b** [*cf.* the N–C$_{arom}$ bond (1.371 Å)].[21] The lengths of N(3)–C(3) bonds are close to that of N=C bond (1.316 Å).[21] Also, the observed altering of pyridine bonds conforms to this assumption: the bonds C(2)–C(3) [1.414(2) Å (**5a**), 1.425(1) Å (**5b**)], C(3)–C(4) [1.416(2) Å (**5a**), 1.421(1) Å (**5b**)] and N(1)–C(1) [1.349(2) Å (**5a**), 1.358(1) Å (**5b**)], N(1)–C(5) [1.354(2) Å (**5a**), 1.359(1) Å (**5b**)] are elongated, whereas the bonds C(1)–C(2) [1.351(2) Å (**5a**) , 1.363(1) Å (**5b**)], C(4)–C(5) [1.355(2) Å (**5a**), 1.358(1) Å (**5b**)] are shortened in comparison with average bond lengths of pyridine (1.379, 1.337 and 1.380 Å, respectively[21]). The similar altering of pyridine bonds and the charge transfer occur in *N*-methoxy-*N*-(4-dimethylaminopyridin-1-ium-1-yl)urea chloride **2b** and *N*-methoxy-*N*-(4-dimethylaminopyridin-1-ium-1-yl)-*N*-*tert*-alkylamine perchlorate.[19]

In conclusion, 1-alkoxyamino-4-dimethylaminopyridinium chlorides **5** were readily synthesized from *N*-alkoxy-*N*-chlorocarbamates and 4-dimethylaminopyridine or from 1-(*N*-acyl-*N*-alkoxyamino)-4-dimethylaminopyridinium chlorides on treatment with AcONa. The XRD studies of salts **5** revealed the high pyramidal configuration of the central nitrogen atom in O–N–N$^+$ geminal system.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.03.030.

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