ALCOHOLYSIS OF *N*-ACETOXY-*N*-ALKOXYCARBAMATES. SYNTHESIS OF *NH-N,N*-DIALKOXYAMINES FROM *N*, *N*-DIALKOXYCARBAMATES

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The alcoholysis of N-acetoxy-N-alkoxycarbamates by methanol or ethanol at 20 – 40 °C yields N,N-dialkoxycarbamates and acetic acid. At the lower temperature the competitive formation of N,N'-bis(alkoxycarbonyl)-N,N'-bis(alkoxy)hydrazines can occur. The alkaline hydrolysis of *N*,*N*-dialkoxycarbamates yields *N*H-*N*,*N*-dialkoxyamines.

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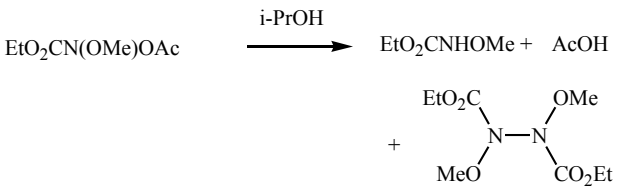
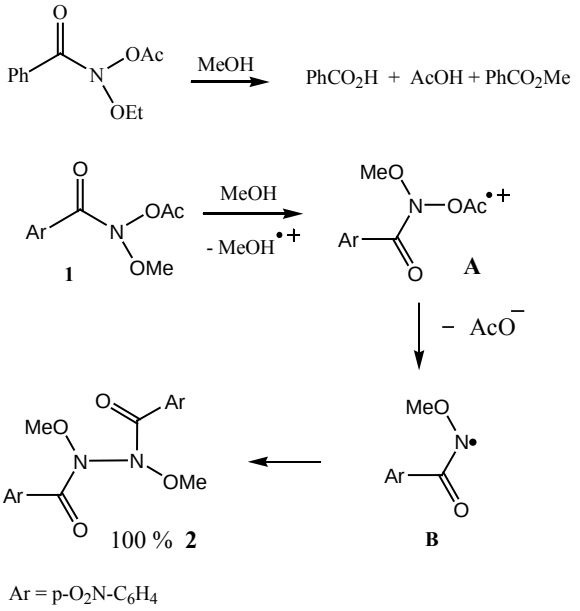
INTRODUCTION

The nature of the products of the alcoholysis of *N*-acyloxy-*N*-alkoxyureas, *N*-acyloxy-*N*-alkoxycarbamates, *N*-acyloxy-*N*-alkoxybenzamides depends of the electronegativity of third substituent at nitrogen atom in the O-N-O geminal system. *N*-Acyloxy-*N*-alkoxyureas[1-3] and *N*-acyloxy-*N*-alkoxy-*N*-*tert*-alkylamines[1] yield respectively the *N*,*N*-dialkoxyureas and *N*,*N*-dialkoxy-*N*-*tert*-alkylamines by the alcoholysis. *N*-Acyloxy-*N*-alkoxycarbamates convert into *N*,*N*-dialkoxycarbamates only by the alcoholysis by primary alcohols.[1] The alcoholysis of *N*-acyloxy-*N*-alkoxycarbamates by *tert*-butanol does not take place, probably, due to sterical hindrances to S_N2 nucleophilic substitution at the nitrogen.[1] Isopropanolysis of ethyl *N*-acetoxy-*N*-methoxycarbamate results in the formation of reduction products such as *N*,*N'*-bis(ethoxycarbonyl)-*N*,*N*-bis(methoxy)hydrazine and ethyl *N*-ethoxycarbamate[1] (Scheme 1).



Scheme 1

The nature of products of *N*-acyloxy-*N*-alkoxobenzamides alcoholysis is strongly depended by of the nature of p-substituent in the phenyl group. Thus, methanolysis of *N*-acetoxy-*N*-ethoxybenzamide yields the mixture of methyl benzoate, benzoic and acetic acid,[1] however, as we have found, the methanolysis[4] of *N*-acetoxy-*N*-methoxy-4-nitrobenzamide (**1**) yields only *N*,*N'*-bis(methoxy)-*N*,*N'*-bis(4-nitrobenzoyl)hydrazine (**2**). Probably, last reaction occurs by a SET mechanism with consecutive formation the anion-radical **A**, then radical **B** (Scheme 2).



Scheme 2.

N-acyloxy-N-alkoxybenzamides,[5-9] N-acyloxy-N-alkoxycarbamates[1,10,11] and N-acyloxy-N-alkoxyureas [1,2,10,11] are called "anomeric amides" due to nO(Alk)→σ*N-OC(O)R anomeric effect domination. In RC(=O)O−N−O(Alk) group the amide nitrogen is sp^3 hybridized and has pyramidal configuration, (Alk)O−N

bond is shortened and N−OC(=O)R bond is elongated and destabilized.[2,4,5,7,10,11] Due to this N−OC(=O)R bond destabilization, the S_N2 nucleophilic substitution at amide nitrogen atom or homolysis of this bond become possible.[1,5,7]

However, in the case of *N*-acyloxy-*N*-alkoxycarbamates, the influence of their structure on the nature of products of alcoholysis remains unknown. We cannot predict under which conditions the alcoholysis of *N*-acyloxy-*N*-alkoxycarbamates by primary alcohols will selectively yield *N,N*-dialkoxycarbamates, which are regarded as the potential sources of *NH-N,N*-dialkoxyamines

EXPERIMENTAL

General

^{1}HNMR spectra were recorded on a "Varian VXP-300" spectrometer (300 MHz), "Mercury-400" (400 MHz) and "Bruker Avance DRX 500" (500 MHz). Me_4Si was used as an internal standard. Chemical shifts were measured in σ-scale (ppm) and coupling constants in Hz. ^{13}CNMR spectra were recorded on a "Varian VXP-300" spectrometer (75 MHz). IR spectra were recorded on "UR-20" spectrometer, in KBr or in the thin layer. Mass spectra were recorded on a "VG-70EQ 770" mass spectrometer in FAB mode (FAB) and on "Kratos MS 890" mass spectrometer, electron impact mode (EI) and chemical ionization mode (CI), gas-reagent was isobutane. MeOH and EtOH were dried by refuxing and distillation over metallic calcium.

Metanolysis of *N*-acetoxy-*N*-methoxy-4-nitrobenzamide (1)

A solution of (**1**)[4] (0.06137 mmol, 0.0156 g) in MeOH (3 ml) was kept at 20 °C for 72 h, then methanol was evaporated *in vacuo* (5 Torr) yielding 0.0120 g (100%) of *N,N'*-bis(methoxy)-*N,N'*-bis(4-nitrobenzoyl)hydrazine (**2**) as yellowish white crystals, m.p. 86 – 88 °C (with decomp.). ^{1}HNMR (400 MHz, $CDCl_3$): 3.948 (s, 6H, NOMe), 8.206 (d, 4H, $H_{C6H4}^{2,6}$, ^3J = 9.2 Hz), 8.305 (d, 4H, $H_{C6H4}^{3,5}$, ^3J = 9.2 Hz). ^{1}H NMR (400 MHz, $(CD_3)_2SO$): 3.948 (s, 6H, NOMe), 8.206 (d, 4H, $H_{C6H4}^{2,6}$, ^3J = 9.2 Hz), 8.329 (d, 4H, $H_{C6H4}^{3,5}$, ^3J = 9.2 Hz). MS (FAB, *m/z*, $I_{отн}$, (%)): 391 $[M+H]^+$ (10), 307(88), 289(45), 155(90), 137(96), 79 (100). MS (FAB, Na^+, *m/z*, $I_{отн}$, (%)): 413 $[M+Na]^+$ (10), 329 (100).

Methyl *N*-ethoxycarbamate (3)

A solution of ethoxyamine (29.06 mmol, 1.78 g) in MeCN (7 ml) was added to the solution of MeO_2CCl (37.77 mmol, 3.57 g) in MeCN (15 ml) at 10 °C, then K_2CO_3 (43.59 mmol, 6.0 g) and 18-crown-6 (0.10 g) were added. The reaction mixture was stirred and heated to 20 °C for 3 h, then it was stored at 20 °C for another 24 h. After that the precipitate was filtered off, washed with CH_2Cl_2, and the combined filtrate was evaporated *in vacuo*. The residue was distillated *in vacuo* yielding 2.49 g (72 %) methyl *N*-ethoxycarbamate, colourless liquid, b.p. 74-79 °C (5 Torr), n_D^{21} 1.4247 (cf. 1.4246[12]) identified by comparison its ^{1}HNMR spectra with that of an authentic sample.[12] ^{1}HNMR (300 MHz, $CDCl_3$): 1.18 (t, 3H, $NOCH_2\underline{Me}$, ^3J = 6.9 Hz), 3.69 (s, 3H, CO_2Me), 3.85 (q, 2H, $NO\underline{CH_2}Me$, ^3J = 6.9 Hz), 7.40 (br. s, 1H, NH). IR (ν, cm^{-1}, KBr): 3430 (NH), 1740 (C=O).

Other N-alkoxycarbamates were synthesized in a similar manner.

Methyl *N*-isopropyloxycarbamate (4), yield 78%, colourless liquid, b.p. 87-88 °C (10 Torr), n_D^{27} 1.4237. ^{1}H NMR (300 MHz, $CDCl_3$): 1.15 (d, 6H, $OCH\underline{Me_2}$, ^3J = 6.3 Hz), 3.68 (s, 3H, CO_2Me), 3.98 (sept, 1H, $O\underline{CH}Me_2$, ^3J = 6.3 Hz), 7.33 (br. s, 1H, NH). IR (ν, cm^{-1}, KBr): 3310 (NH), 1745 (C=O). Found (%): N 10.68. Calc. for $C_5H_{11}NO_3$ (%): N 10.52.

Methyl *N-n*-butyloxycarbamate (5), yield 76 %, colourless liquid, b.p. 105-107 °C (5 Torr), n_D^{22} 1.4312. ^{1}H NMR (300 MHz, $CDCl_3$): 0.94 (t, 3H, $OCH_2CH_2CH_2\underline{Me}$, ^3J = 7.2 Hz), 1.40 (sex, 2H, $OCH_2CH_2\underline{CH_2}Me$, ^3J = 7.2 Hz), 1.63 (quint, 2H, $OCH_2\underline{CH_2}CH_2Me$, ^3J = 7.2 Hz), 3.77 (s, 3H, CO_2Me), 3.87 (т, $O\underline{CH_2}CH_2CH_2Me$, ^3J = 7.2 Hz), 7.47 (br. s, 1H, NH). Found (%): N 9.31. Calc. for $C_6H_{13}NO_3$ (%): N 9.52.

Ethyl *N*-isopropyloxycarbamate (6), yield 67 %, colourless liquid, b.p. 68°C (2 Torr), n_D^{20} 1.4255. ^{1}HNMR (300 MHz, $CDCl_3$): 1.22 (d, 6H, $OCH\underline{Me_2}$, ^3J = 6.3 Hz), 1.27 (t, 3H, $CO_2CH_2\underline{Me}$, ^3J = 7.2 Hz), 4.05 (sept, 1H, $O\underline{CH}Me_2$, ^3J = 6.3 Hz), 4.19 (q, 2H, $CO_2\underline{CH_2}Me$, ^3J = 7.2 Hz). Found (%): N 9.43. Calc. for $C_6H_{13}NO_3$ (%): N 9.52.

General method for the synthesis of *N*-chloro-*N*-alkoxycarbamates

A solution of *t*-BuOCl (15 mmol) in CH_2Cl_2 (3 ml) was added to the solution of the alkyl *N*-alkoxycarbamate (5 mmol) in CH_2Cl_2 (6 ml) at -20 °C, the reaction solution was kept at 5 °C for 2 h, then it was evaporated *in vacuo* (10 Torr), the residue was kept at 3 Torr for 5 min. The yields were quantitative.

Methyl *N*-chloro-*N*-ethoxycarbamate (7), yellowish oil. ^{1}HNMR (300 MHz, $CDCl_3$): 1.31 (t, 3H, $NOCH_2\underline{Me}$, ^3J = 6.9 Hz), 3.92 (s, 3H, CO_2Me), 4.07 (q, 2H, $NO\underline{CH_2}Me$, ^3J = 6.9 Hz). IR (ν, cm^{-1}, thin layer): 1795 (C=O). Found(%): Cl 22.85. Calc. for $C_4H_8ClNO_3$ (%): Cl 23.09.

Methyl *N*-chloro-*N*-isopropyloxycarbamate (8), yellow oil. ^{1}HNMR (300 MHz, $CDCl_3$): 1.28 (d, 6H, $NOCH\underline{Me_2}$, ^3J = 6.3 Hz), 3.91 (s, 3H, CO_2Me), 4.31 (sept, 1H, $NOC\underline{H}Me_2$, ^3J = 6.3 Hz). IR (ν, cm^{-1}, thin layer): 1780 (C=O). Found (%): Cl 21.04. Calc. for $C_5H_{10}ClNO_3$ (%): Cl 21.15

Methyl *N*-chloro-*N-n*-butyloxycarbamate (9), yellowish oil, n_D^{25} 1.4383. ^{1}H NMR (300 MHz, $CDCl_3$): 0.95 (t, $OCH_2CH_2CH_2\underline{Me}$, ^3J = 7.3 Hz), 1.45 (sex, 2H, $OCH_2CH_2\underline{CH_2}Me$, ^3J = 7.3 Hz), 1.57 (quint, 2H, $OCH_2\underline{CH_2}CH_2Me$, ^3J = 7.3 Hz), 3.90 (s, 3H, CO_2Me), 3.97 (t, 2H, $O\underline{CH_2}CH_2CH_2Me$, ^3J =7.3 Hz). Found (%): Cl 19.16. Calc. for $C_6H_{12}ClNO_3$ (%): Cl 19.52.

Ethyl *N*-chloro-*N*-isopropyloxycarbamate (10), yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): 1.28 (d, 6H, $NOCH\underline{Me_2}$, ^3J = 6.3 Hz), 1.36 (t, 3H, $CO_2CH_2\underline{Me}$, ^3J = 7.0

Hz), 4.31 (sept, 1H, NOCHMe$_2$, ^3J = 6.3 Hz), 4.33 (q, 2H, CO$_2$CH$_2$Me, ^3J = 7.0 Hz). Found (%): Cl 19.46. Calc. $C_6H_{12}ClNO_3$ (%): Cl 19.52.

General method for the synthesis of N-acetoxy-N-alkoxycarbamates

A mixture of the solution of *N*-chloro-*N*-alkoxycarbamate (8 mmol) in MeCN (20 ml) and AcONa (26 mmol) was stirred at 20 °C for 55 h, then CH_2Cl_2 (10 ml) was added, the precipitate was filtered off, washed with CH_2Cl_2, the combined filtrate was evaporated *in vacuo* (20 Torr). The residue was extracted by CH_2Cl_2 (20 ml), the extract was evaporated *in vacuo*, the residue was kept at 3 Torr and 20 °C for 30 min to yield the product.

Methyl *N*-acetoxy-*N*-ethoxycarbamates (11), yield 87 %, colourless liquid, n_D^{19} 1.4269. ^{1}HNMR (300 MHz, $CDCl_3$): 1.30 (t, 3H, NOCH$_2$Me, ^3J = 7.2 Hz), 2.19 (s, 3H, NOC(O)Me), 3.88 (s, 3H, CO$_2$Me), 4.13 (q, 2H, NOCH$_2$Me, ^3J = 7.2 Hz). IR (ν, cm^{-1}, thin layer): 1805 (C=O), 1780 (C=O). Found (%): C 40.41, H 6.31, N 7.78. Calc. for $C_6H_{11}NO_5$ (%): C 40.68, H 6.26, N 7.91.

Methyl *N*-acetoxy-*N*-isopropyloxycarbamate (12), yield 96 %, yellowish liquid. ^{1}HNMR (300 MHz, $CDCl_3$): 1.28 (d, 6H, OCHMe$_2$, ^3J = 6.3 Hz), 2.17 (s, 3H, NOC(O)Me), 3.87 (s, 3H, CO$_2$Me), 4.32 (sept, 1H, OCHMe$_2$, ^3J = 6.3 Hz). IR (ν, cm^{-1}, thin layer): 1805 (C=O), 1780 (C=O). MS (CI, *m/z*, I_{rel}, (%)): 192 $[M+H]^+$ (0.6), 191 M^+ (1.5), 148 (4.0), 132 (3.1), 59 (23.9), 45 (20.4), 43 (100). Found (%): C 43.81, H 6.82, N 7.18. Calc for $C_7H_{13}NO_5$ (%): C 43.98, H 6.85, N 7.33.

Methyl *N*-acetoxy-*N*-*n*-butyloxycarbamate (13), yield 81 %, yellowish liquid. ^{1}HNMR (300 MHz, $CDCl_3$): 0.95 (t, 3H, NO(CH$_2$)$_3$Me, ^3J = 7.5 Hz), 1.41 (sex, 2H, NOCH$_2$CH$_2$CH$_2$Me, ^3J = 7.5 Hz), 1.66 (quint, 2H, NOCH$_2$CH$_2$CH$_2$Me, ^3J = 7.5 Hz), 2.19 (s, 3H, NOC(O)Me), 3.88 (s, 3H, CO$_2$Me), 4.08 t (2H, NOCH$_2$CH$_2$CH$_2$Me, ^3J = 7.5 Hz). IR (ν, cm^{-1}, thin layer): 1805 (C=O), 1780 (C=O). Found (%): C 46.68, H 7.34, N 6.79. Calc. for $C_8H_{15}NO_5$ (%): C 46.83, H 7.38, N 6.83.

Ethyl *N*-acetoxy-*N*-isopropyloxycarbamate (14), yield 98 %, yellowish liquid, n_D^{22} 1.4211. ^{1}HNMR (300 MHz, $CDCl_3$): 1.28 (d, 6H, OCHMe$_2$, ^3J = 6.3 Hz), 1.33 (t, 3H, CO$_2$CH$_2$Me, ^3J = 7.2 Hz), 2.17 (s, 3H, NOC(O)Me), 4.30 (q, 2H, CO$_2$CH$_2$Me, ^3J = 7.2 Hz), 4.33 (sept, 1H, NOCHMe$_2$, ^3J = 6.3 Hz). MS (CI, *m/z*, I_{rel}, (%)): 206 $[M+H]^+$ (2.0), 204 (0.6), 132 (100). Found (%): C 46.61, H 7.35, N 6.59. Calc. for $C_8H_{15}NO_5$ (%): C 46.82, H 7.37, N 6.83.

Methyl *N*-ethoxy-*N*-methoxycarbamate (15). Methyl *N*-acetoxy-*N*-ethoxycarbamate **11** (2.442 mmol, 0.432 g) was dissolved in MeOH (5 ml) at -12°C, the solution was heated to 0°C for 3 h, then it was kept at 24 °C for 44 h. Then it was evaporated *in vacuo* (2 Torr) yielding 0.248 g (68%) methyl *N*-ethoxy-*N*-methoxycarbamate (**15**), which was contaminated with some *N,N'*-bis(ethoxy)-*N,N'*-bis(methoxycarbonyl)hydrazine[12] (**16)** according to ^{1}HNMR. After distillation *in vacuo* 0.080 g (22 %) pure (**15**) was obtained as colourless liquid. ^{1}HNMR (300 MHz, $CDCl_3$): 1.33 (t, 3H, NOCH$_2$Me, ^3J = 7.0 Hz), 3.84 (s, 3H, NOMe), 3.90 (s, 3H, CO$_2$Me), 4.11 (q, 2H, NOCH$_2$Me, ^3J = 7.0 Hz). Found (%): C 40.55, H 7.35. Calc. for $C_5H_{11}NO_4$ (%): C 40.27, H 7.43.

Ethanolysis of methyl *N*-acetoxy-*N*-ethoxycarbamate (11) at 4°C. Methyl *N*-acetoxy-*N*-ethoxycarbamate (**11**) (6.960 mmol, 1.232 g) was dissolved in EtOH (12 ml) at 4°C, this solution was kept at 4 - 5°C for 94 h, then it was evaporated *in vacuo,* yielding 1.1986 g of a yellowish liquid. According to ^{1}HNMR this residue is a mixture of unreacted (**11**) and *N,N'*-bis(ethoxy)-*N,N'*-bis(methoxycarbonyl)hydrazine[12] (**16)** in molar ratio 97:3. ^{1}H NMR of hydrazine (**16**) (300 MHz, $CDCl_3$): 1.31 (t, 6H, NOCH$_2$Me, ^3J = 7.2 Hz), 3.91 (3, 6H, CO$_2$Me), 4.05 (q, 4H, NOCH$_2$Me, ^3J = 7.2 Hz). On keeping of the solution of (**11**) in EtOH at 4 – 5 °C for 163 h, the ratio of compounds (**11**) and (**16**) became 63:37.

Ethanolysis of methyl *N*-acetoxy-*N*-ethoxycarbamate (11) at 18 °C. Methyl *N*-acetoxy-*N*-ethoxycarbamate (**11**) (6.766 mmol, 1.199 g) was dissolved in EtOH (12 ml) at 18°C, this solution was kept at 17 – 18 °C for 219 h, then it was evaporated *in vacuo* (8 Torr), the residue was kept at 2 Torr and 20 °C yielding 0.563 g (51 %) methyl *N,N*-diethoxycarbamate (**17**), colourless liquid, b.p. 46-47 °C(2 Torr), n_D^{25} 1.4139. ^{1}HNMR (300 MHz, $CDCl_3$): 1.30 (t, 6H, NOCH$_2$Me ^3J = 7.2 Hz), 3.87 (s, 3H, CO$_2$Me), 4.07 (q, 4H, NOCH$_2$Me, ^3J = 7.2 Hz). ^{13}CNMR (75 MHz, $CDCl_3$): 13.40 (NOCH$_2$Me), 54.25 (NOCH$_2$Me); 69.86 (CO$_2$Me), 159.84 (C=O). MS (EI, *m/z*, I_{rel}.(%)): 164 $[M+H]^+$ (0.4), 163 M^+ (2.0), 118 (1.7), 105 (3.1), 104 (2.7), 59 (59.8), 43 (100). Found (%): C 44.08, H 8.14, N 8.51. Calc. for $C_6H_{13}NO_4$ (%): C 44.17, H, 8.03, N 8.58.

Methyl *N*-isopropyloxy-*N*-metoxycarbamate (18). Methyl *N*-acetoxy-*N*-isopropyloxycarbamate (**12**) (8.68 mmol, 1.66 g) was dissolved in MeOH (21 ml) and kept at -32 °C, for 4 h, the solution was then heated to 20 °C and was kept at 20 °C for 7 days. The solution was then evaporated *in vacuo* (20 Torr). MeOH-condensate was trapped. The residue was distillated *in vacuo* yielding 0.86 g (60.4 %) methyl *N*-isopropyloxy-*N*-metoxycarbamate (**18**), colourless liquid, b.p. 50-53 °C (3 Torr), n_D^{23} 1.4168. IR (ν, cm^{-1}, thin layer): 1770 (C=O). ^{1}HNMR (300 MHz, $CDCl_3$): 1.29 (д, 6H, OCHMe$_2$, ^3J = 6.3 Hz), 3.77 (s, 3H, NOMe), 3.86 (s, 3H, CO$_2$Me), 4.27 (sept, 1H, OCHMe$_2$, ^3J = 6.3 Hz). MS (EI, 70 Ev, *m/z*, $I_{отн}$ (%)): 163 M^+ (3.4), 105 (5.6), 91 (14.0), 60 (21.3), 59 (54.8), 58 (24.3), 46 (16.9), 45 (36.7), 44 (21.3), 43 (100). Found (%): C 44.23, H 8.17, N 8.42. Calc. for $C_6H_{13}NO_4$ (%): C 44.17, H 8.03, N 8.58.

In the MeOH-condensate 0.076 g (9.7 %) of dimethylcarbonate was found by GLC.

Methyl *N*-*n*-butyloxy-*N*-methoxycarbamate (19). Methyl *N*-acetoxy-*N*-*n*-butyloxycarbamate (**13**) (7.718 mmol, 1.584 g) was dissolved in MeOH (11 ml), the solution was kept at 18°C for 148 h, then MeOH was evaporated *in vacuo* (20 Torr) and the MeOH-condensate was collected in a cold trap. The residue was kept at 20 °C and 3 Torr for 1 h yielding 1.122 g (82.3%) of methyl *N*-*n*-butyloxy-*N*-methoxycarbamate (**19),** colourless liquid, ^{1}HNMR (300 MHz, $CDCl_3$): 0.95 (t, 3H, NO(CH$_2$)$_3$Me, ^3J = 7.2 Hz), 1.45 (sex, 2H, NO(CH$_2$)$_2$CH$_2$Me, ^3J = 7.2 Hz), 1.66 (quint, 2H, NOCH$_2$CH$_2$CH$_2$Me, ^3J = 7.2 Hz), 3.90 (s, 6H,

NOMe and CO_2Me), 3.97 (t, 2H, $NOCH_2$, ^3J = 7.2 Hz). IR (ν, cm^{-1}, thin layer): 1780 (C=O). MS (EI, *m/z*, I_{rel} (%)): 177 M^+ (3.8), 150 (76.7), 149 (87.6), 146 (40.9), 118 (14.6), 115 (9.7), 105 (29.1), 91 (57.5), 90 (52.1), 60 (64.9), 59 (100), 58 (22.1), 57 (76.5). Found (%): C 47.29, H 8.39, N 7.64. Calc. for $C_7H_{15}NO_4$ (%): C 47.45, H 8.53, N 7.90.

In the MeOH-condensate 0.0028 g (0.4 %) of dimethylcarbonate was found by GLC.

Ethyl *N*-ethoxy-*N*-isopropyloxycarbamate (20). A solution of ethyl *N*-acetoxy-*N*-isopropyloxycarbamate (**14**) (0.817 mmol, 0.168 g) in EtOH (2 ml) was kept at 20 °C for 66 h, then at 40 °C for 57 h. Then it was evaporated *in vacuo* (13 Torr) and EtOH-condensate was caught in a cold trap. The residue was kept at 20 °C and 2 Torr for 20 min yielding 0.097 g (62.2%) of ethyl *N*-ethoxy-*N*-isopropyloxycarbamate (**20**), colourless liquid, ^{1}HNMR (300 MHz, $CDCl_3$): 1.276 (t, 3H, $NOCH_2\underline{Me}$, ^3J = 7.2 Hz), 1.278 (d, 6H, $NOCH\underline{Me_2}$, ^3J = 6.3 Hz), 1.34 (t, $CO_2CH_2\underline{Me}$, ^3J = 7.2 Hz), 4.04 (q, 2H, $NO\underline{CH_2}Me$, ^3J = 7.2 Hz), 4.26 (sept, 1H, $NO\underline{CH}Me_2$, ^3J = 6.3 Hz), 4.27 (q, 2H, $CO_2\underline{CH_2}Me$, ^3J = 7.2 Hz). MS (FAB, K^+, *m/z*, I_{rel} (%)): 230 $[M+K]^+$ (6), 215 (5), 192 $[M+H]^+$ (100), 176 (10). Found (%): N 7.05. Calc. for $C_8H_{17}NO_4$ (%): N 7.32.

In the EtOH-condensate 0.023 g (23.4 %) of diethylcarbonate was found by GLC.

***NH*-*N*-Methoxy-*N*-*n*-octyloxyamine (22)**. A sodium methylate solution, prepared by dissolving Na (13.82 mmol, 0.318 g) in MeOH (20 ml), was added to the solution of methyl *N*-methoxy-*N*-*n*-octyloxycarbamate (**21**)[1] (6.910 mmol, 1.612 g) in MeOH (20 ml) The reaction mixture was kept at 18-20 °C for 7 h, then a solution of acetic acid (17.275 mmol, 1.04 g) in MeOH (7 ml) was added. The precipitate was filtered off, washed with MeOH, the combined MeOH-filtrate evaporated *in vacuo* (20 Torr). The residue was extracted by hexane (23 ml), the extract was evaporated *in vacuo* (20 Torr). The residue was kept at 20°C and 2 Torr for 30 min yielding 1.148 g (94.8 %) *NH*-*N*-methoxy-*N*-*n*-octyloxyamine (**22**), colourless liquid, ^{1}HNMR (300 MHz, $CDCl_3$): 0.82 (t, 3H, $NO(CH_2)_7\underline{Me}$, ^3J = 6.9 Hz), 1.12-1.35 (m, 10H, $NOCH_2CH_2\underline{(CH_2)_5}Me$), 1.52 (quint, 2H, $NOCH_2\underline{CH_2}$, ^3J = 6.9 Hz), 3.62 (s, 3H, NOMe), 3.80 (t, 2H, $NOCH_2$, ^3J = 6.9 Hz), 7.80 (br. s, 1H, NH). Found (%): N 7.72. Calc. for $C_9H_{21}NO_2$ (%): N 7.99.

***NH*-*N*-*n*-Butyloxy-*N*-methoxyamine** (**23**). The mixture of a solution of methyl *N*-*n*-butyloxy-*N*-methoxycarbamate (**19**) (2.240 mmol, 0.397 g) in Et_2O (4 ml) and a solution of NaOH (3.360 mmol, 0.134 g) in water (16 ml) was stirred at 20 °C for 1 h, then it was extracted by Et_2O (25 ml). The extract was dried over $MgSO_4$ and after that it was evaporated *in vacuo*. The residue was kept at 5 Torr and 20 °C for 1 h to yield 0.253 g (94.5 %) *NH*-*N*-*n*-butyloxy-*N*-methoxyamine **23**, colourless liquid, ^{1}HNMR (300 MHz, $CDCl_3$): 0.95 (t, 3H, $NO(CH_2)_3\underline{Me}$, ^3J = 7.2 Hz), 1.41 (sextett, 2H, $NOCH_2CH_2\underline{CH_2}Me$, ^3J = 7.2 Hz), 1.63 (quint, 2H, $NOCH_2\underline{CH_2}CH_2Me$, ^3J = 7.2 Hz), 3.78 (s, 3H, NOMe), 3.87 (t, 2H, $NOCH_2$, ^3J = 7.2 Hz), 7.36 (br. s, 1H, NH). MS (EI, *m/z*, I_{rel} (%)): 120 $[M+H]^+$ (1.2), 119 M^+ (6.1), 118 (1.9), 88 (2.1), 72 (14.7), 57 Bu^+ (81.2), 56 (53.4), 46 (21.7), 44 (31.2), 43 (100). Found (%): C 50.25, H 11.17, N 11.72. Calc. for $C_5H_{13}NO_2$ (%): C 50.40, H 11.00, N 11.75.

Hydrolysis of methyl *N*-isopropyloxy-*N*-metoxycarbamate (**18**). A mixture of a solution of methyl *N*-isopropyloxy-*N*-metoxycarbamate (**18**) (6.429 mmol, 1.049 g) in Et_2O (7 ml) and that of NaOH (12.858 mmol, 0.51 g) and 15-crown-5 (0.15 g) in water (26 ml) was stirred at 25 °C for 1 h, and then Et_2O (15 ml), acetic acid (11.66 mmol, 0.7 g) and water (2 ml) were added. The ether extract was separated, the aqueous phase was extracted with another 15 ml of Et_2O. Combined ether extract was dried over $MgSO_4$, and concentrated by removing of 3/4 of the ether (the bath temperature must be lower than 45 °C). The residue was condensed in two cold traps at different regime *in vacuo*:

(1) at 55 Torr and 35 °C to yield 0.176 g (26.0 %) *NH*-*N*-isopropyloxy-*N*-methoxyamine (**24**), colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): 1.21 (d, 6H, $NOCH\underline{Me_2}$, ^3J = 6.3 Hz), 3.,66 (s, 3H, NOMe), 4.15 (септ, 1H, $NO\underline{CH}Me_2$, ^3J = 6.3 Hz), 7.87 (br. s, 1H, NH). Found (%): N 13.03. Calc. for $C_4H_{11}NO_2$ (%): N 13.32.

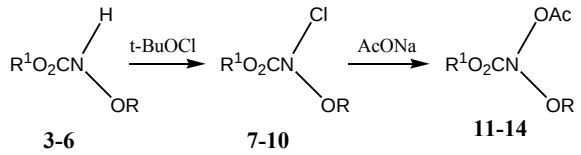
(2) at 3 Torr and 26 °C to yield 0.367 g (54.8 %) *N,N'*-bis(isopropyloxy)-*N,N'*-bis(methoxy)hydrazine (**25**), colourless liquid, ^{1}HNMR (300 MHz, $CDCl_3$): 1.224 (d, 12H, $NOCH\underline{Me_2}$, ^3J = 6.3 Hz), 3.68 (s, 6H, NOMe), 4.17 (sept, 2H, $NO\underline{CH}Me_2$, ^3J = 6.3 Hz). MS (EI, *m/z*, I_{rel} (%)): 209 $[M+H]^+$ (0.4), 208 M^+ (2.0), 207 (0.9), 177 (2.2), 105 (3.4), 104 (14.7), 60 (10.7), 59 (39.8), 58 (55.7), 46 (10.3), 45 (58.7), 44 (78.1), 43 (100). Found (%): N 13.34. Calc. for $C_8H_{20}N_2O_4$ (%): N 13.45.

***NH*-*N,N*-diethoxyamine (26)**. The mixture of a solution of methyl *N,N*-diethoxycarbamate (**17**) (2.542 mmol, 0.415 g) in Et_2O (2 ml) and that of NaOH (7.62 mmol, 0.31 g) and 15-crown-5 (0.06 g) in water (5 ml) was stirred at 20 °C for 2 h, then a solution of acetic acid (7.62 mmol, 0.457 g) in Et_2O (10 ml) was added. The ether layer was separated, the aqueous phase was extracted with Et_2O (6 ml). The combined ether extract was dried over $MgSO_4$. The extract was concentrated by evaporation (the bath temperature must be lower than 50 °C). The residue was recondensed in cold trap *in vacuo* (67 Torr) at 72 °C yielding 0.0141 g (5.2 %) *NH*-*N,N*-diethoxyamine (**26**), colourless liquid, ^{1}H NMR (300 MHz, $CDCl_3$): 1.23 (t, 6H, $NOCH_2\underline{Me}$, ^3J = 7.0 Hz), 3.93 (q, 4H, $NO\underline{CH_2}Me$, ^3J = 7.0 Hz), 7.95 (br. s, 1H, NH).

RESULTS AND DISCUSSION

The major objective of this work was to study the alcoholysis of *N*-acetoxy-*N*-alkoxycarbamates and to explore of the possibility of synthesis of *NH*-*N,N*-dialkoxyamines from methyl *NH*-*N,N*-dialkoxycarbamates. The last-named compounds may become useful synthones in organic synthesis but as of now only one method of their preparation is known.[13,14]

We have synthesized *N*-alkoxycarbamates (**3-6)** which were chlorinated to *N*-chloro-*N*-alkoxycarbamates (**7-10)** by *tert*-butyl hypochlorite in CH_2Cl_2 solution (Scheme 3). *N*-Chloro-*N*-alkoxycarbamates react with anhydrous AcONa in MeCN selectively yielding *N*-acetoxy-*N*-alkoxycarbamates (**11-14**).

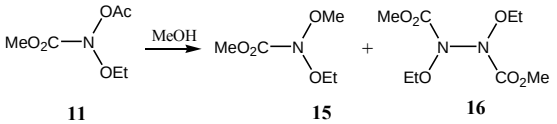


R^1 = Me, R = Et (**3, 7, 11**), i-Pr **(4, 8, 12**), n-Bu (**5, 9, 13**)

R^1 = Et, R = i-Pr **(6, 10, 14**)

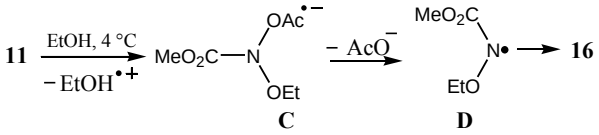
Scheme 3.

We found that methyl *N*-acetoxy-*N*-ethoxycarbamate, (**11**) is converted mainly to methyl *N*-ethoxy-*N*-methoxycarbamate **(15)** by the methanolysis at 24 °C. A by-product of this methanolysis is *N,N'*-bis(ethoxy)-*N,N'*-bis(methoxycarbonyl)hydrazine[12] (Scheme 4).



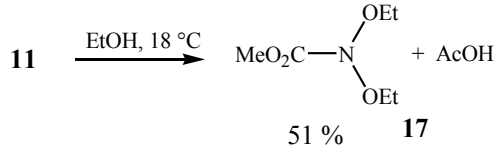
Scheme 4.

A study of ethanolysis of (**11**) showed that at 4 – 5 °C the nucleophilic substitution at nitrogen does not occur. On keeping of a solution of (**11**) in ethanol at 4 – 5 °C for 94 h, a mixture of unreacted (**11**) (main component, 97 mol. %) and *N,N'*-bis(ethoxy)-*N,N'*-bis(methoxycarbonyl)hydrazine (**16**) (3 mol. %) was obtained. On keeping the solution for 163 h, the ratio of unreacted (**11**) and the hydrazine (**16**) is 63:37 mol.%. The presence of methyl *N,N*-diethoxycarbamate (**17**) in reaction mixture was not detected. It may be supposed that at this temperature an S_N2 nucleophilic substitution at nitrogen atom of (**11**) is impossible. But (**11**) is slowly reduced by ethanol to the anion-radical **C** by a SET mechanism (Scheme 5). Then the anion-radical **C** loses an acetate ion and forms radical **D** which couples to yield *N,N'*-bis(ethoxy)hydrazine (**16**).



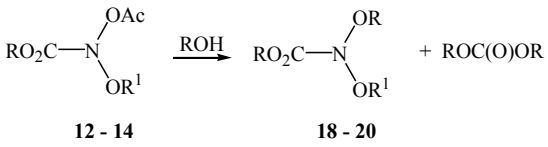
Scheme 5

But if ethanolysis of (**11**) is carried out at 17-18 °C, the S_N2 nucleophilic substitution at nitrogen occurs yielding methyl *N,N*-diethoxycarbamate **17** (Scheme 6).



Scheme 6.

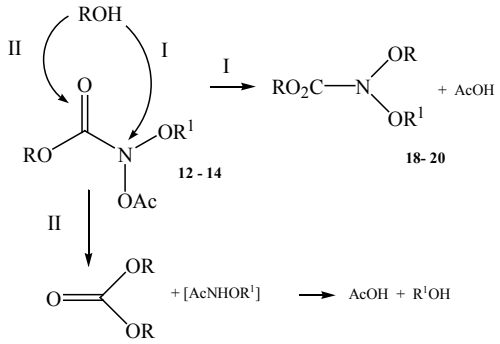
Methanolysis of N-acetoxy-N-alkoxycarbamate (**12,13**) at 20-23°C and of (**14**) at 40 °C yields alkyl *N,N*-dialkoxycarbamates (**18-20)** and AcOH as main products (Scheme 7, Table 1). Dialkylcarbonates are by-products of these cases of alcoholysis.



Scheme 7.

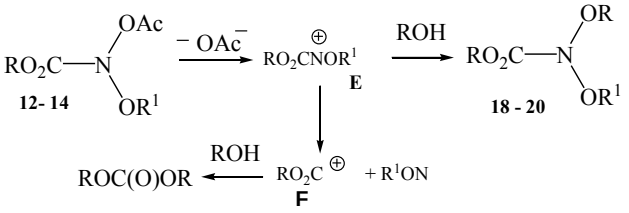
In the case of sterically hindered ethyl *N*-acetoxy-*N*-isopropoxycarbamate (**14)** the ethanolysis occurs more slowly than the methanolysies of *N*-acetoxy-*N*-alkoxycarbamates (**12**, **13)**.

On keeping of an ethanolic solution of (**14**) at 20 °C for 66 h, the molar ratio of unreacted (**14)** and product, *N*-ethoxy-*N*-isopropoxycarbamate (**20**) is 63:37. The complete alcoholysis take place only after keeping it at 40°C for additional 57 h yielding methyl *N*-ethoxy-*N*-isopropoxycarbamate (**20)** as main product (Table 1). The yield of by-product, diethylcarbonate is also quite high. Probably, the two competitive reactions take place simultaneously, the nucleophilic substitution at nitrogen by S_N2 mechanisn (route I) yielding *N,N*-dialkoxycarbamates (**18-20**) and a nucleophilic attack of the alcohol on carbonyl group (route II) yielding dialkylcarbonate (Scheme 8).



Scheme 8

On other hand, the alcoholysis products formation may also arises through generation of *N*-alkoxyntrenium cation, **E** (Scheme 9), which reacts with alcohol yielding *N,N*-dialkoxycarbamates (**18-20)**. The further fragmentation caution **E** to more stable acyl cation **F,** which finally yields the dialkylcarbonate.

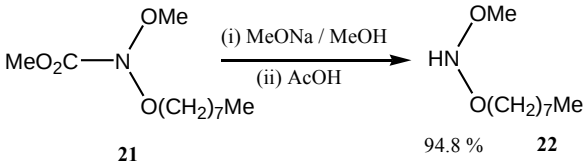


Scheme 9.

Table 1. Yields of products of alcoholysis of N-acetoxy-N-alkoxycarbamate **12-14**

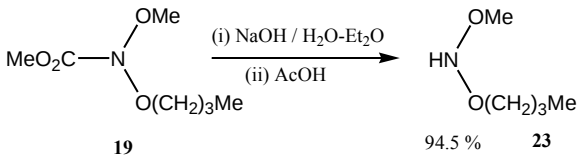
No.	$RO_2CN(OR^1)OAc$		ROH	Temp., °C	Time, h	$RO_2CN(OR^1)OR$		ROC(O)OR
	R	R^1				R	Yield, %	Yield, %
12	Me	i-Pr	MeOH	20	164	Me (18)	60.4	9.7
13	Me	n-Bu	MeOH	21-23	120	Me (19)	82.3	0.4
14	Et	i-Pr	EtOH	(a) 20	66	Et (20)	62.2	23.4
				(b) 40	57			

In methyl *N,N*-dialkoxycarbamates, MeOC(O)-group can be easily eliminated by hydrolysis or alkoholysis in the presence of alkali to yield the particular *NH-N,N*-dialkoxyamines. But in every case the suitable reaction conditions must be carefully selected. Thus, methyl *N*-methoxy-*N*-*n*-octyloxycarbamate **(21)**[1] yields *NH-N*-methoxy-*N*-*n*-octyloxyamine (**22)** by treatment of MeONa solution in methanol then by action of acetic acid (Scheme 10).



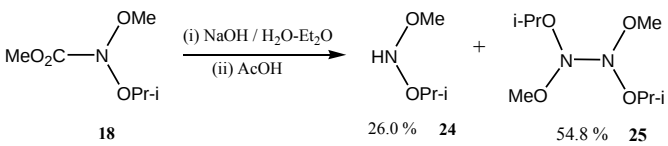
Scheme 10

The hydrolysis of methyl *N*-*n*-butyloxy-*N*-methoxycarbamate **(19)** by 1.5 eqivalent of NaOH in the water solution in the presence of ether (4:1) at 20° C for 1 h selectively yields *NH-N*-*n*-butyloxy-*N*-methoxyamine **23** (Scheme 11).



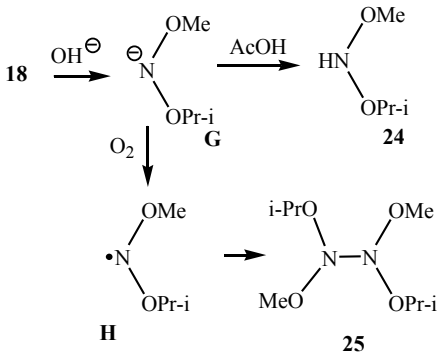
Scheme 11

The alkaline hydrolysis of methyl *N*-isopropyloxy-*N*-metoxycarbamate (**18)** occurs with the formation two main products, unstable *NH-N*-isopropyloxy-*N*-methoxyamine (**24**) and *N,N'*-bis(isopropyloxy)-*N,N'*-bis(methoxy)hydrazine (**25**) (Scheme 12).



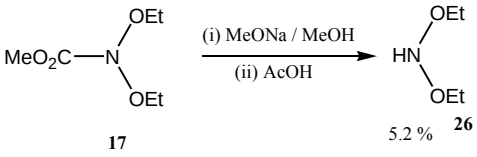
Scheme 12

Probably, in this case (Scheme 13) the initially generated anion **G** may be protonated to unstable (**24**) or may undergo aerial oxidation to a relatively stable dialkoxyaminyl radical **H** which dimerises[15] to (**25**).



Scheme 13

NH-N,N-Diethoxyamine **(26)** was obtained in low yield by alkaline hydrolysis of methyl *N,N*-diethoxycarbamate (**17**) (Scheme 14). Probably the further rapid decomposition of (**17)** occurs in these reaction conditions.



Scheme 14

The structure of *NH-N,N*-dialkoxyamines (**22-24** and **26)** and *N,N,N',N'*-tetraalkoxyhydrazine (**25)** was confirmed by their ^{1}HNMR spectra, the structure of compounds (**23)** and (**25**) were confirmed by mass spectra also. In ^{1}HNMR spectra of (**22-24**) and (**26),** the characteristic signal of NH-proton as the broad singlet in field of 7.36 -7.95 ppm was observed.

Thus it was established that alcoholysis of N-acetoxy-N-alkoxycarbamates by methanol or ethanol at 20 – 40° C yields *N,N*-dialkoxycarbamates and acetic acid. At the lower temperature the competitive formation of *N,N'*-dialkoxycarbonyl-*N,N'*-dialkoxyhydrazines can occur. It was found that alkaline hydrolysis of *N,N*-dialkoxycarbamates yields *NH-N,N*-dialkoxyamines.

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