REACTIONS OF N-CHLORO-N-ALKOXY-TERT-ALKYLAMINES WITH ISOBUTYLENE AND METHANOL

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The addition of N-chloro-N-methoxy-tert-alkylamines to an olefin, which is assumed to proceed with the participation of alkoxynitrenium ions, was carried out for the first time. The methanolysis of N-chloro-N-alkoxy-tert-alkylamines in the presence of Et_3N gives dialkoxyamines, and depending on the type of the N-alkyl substituent is accompanied by side reactions.

N-Chloro-N-alkoxyamines (CAA) [1] are characterized by chemical properties which are also the chief characteristics of N-chloroalkylamines [2]. Thus, they enter into nucleophilic Cl substitution reactions [1, 3-5], redox reactions [1, 3, 4, 6] and 1,2-rearrangements [6, 7]. A specific reaction for CAA is the formation of C-nitroso compounds, for example, during hydrolysis [3].

In the present work, we continued the investigation of the alkoxyaminating properties of CAA. It was shown for the first time that they add to isobutylene in SO_2. In the absence of the electrophilic catalyst – SO_2 – this addition does not proceed under normal conditions.

$$\underset{\text{(Ia)}}{RN(Cl)OMe} \xrightarrow[SO_2]{CH_2=CMe_2} \underset{\text{(IIa)}}{RN(OMe)CH_2C(Me)_2Cl} + \underset{\text{(IIIa)}}{RN(O)=N(O)R}$$

$$\underset{\text{(Ib)}}{RN(Cl)OMe} \xrightarrow[SO_2]{CH_2=CMe_2} \underset{\text{(IIb)}}{RN(OMe)CH_2C(Me)_2Cl} + MeO_2CCH=CMe_2$$

$$R = MeO_2CCMe_2\ (a);\ MeO_2CCH_2CMe_2\ (b).$$

It had been previously assumed [1, 3, 7] that the reactions of CAA occur with the participation of resonance-stabilized nitrenium ions, formed during the heterolysis of the N–Cl bond, which is facilitated due to the electron assistance of the neighboring O atom (the $n_\pi(O)-\sigma N-Cl^*$ reaction).

$$RN\begin{matrix}\diagup Cl \\ \diagdown OR'\end{matrix} \xrightleftharpoons{-Cl^-} \overset{+}{R}NOR' \longleftrightarrow RN=\overset{+}{O}R'$$

According to calculation by the MNDO method [8], the CAA should in fact dissociate at the N–Cl bond more easily than chloroamines, while nitrenium ions are stabilized due to the unshared electron pair of the neighboring O atom. Calculation in [8] also predicted the preferential existence of the singlet ground electronic state of alkoxynitrenium ions and the maximum localization of the positive charge in the hydroxynitrenium ion on the H atom of the hydroxylic group [9]. The two latter suppositions were confirmed experimentally [10] by the discovery of the stereospecific cycloaddition of the methoxynitrenium ion to olefins and its ambivalent character with respect to nucleophiles. It was shown [10] that the alkoxynitrenium ions have not only aminating, but also alkylating properties due to their O-dealkylation by the action of rigid nucleophiles.

Accordingly, it can be assumed that the initial stage in the reaction CAA (I) with isobutylene is an electrophilically induced heterolysis of the N–Cl bond with the formation of

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nitrenium ions, which subsequently undergo a [2 + 2][π + n]-cycloaddition to olefin. The adducts thus formed – the N-alkyl-N-methoxyaziridinium chlorides – undergo a nucleophilic ring opening to form the end products (II). In the case of CAA (Ia), the competing dealkylation of the methoxynitrenium ion by the action of the Cl^- nucleophile present in the medium, leads to the dimer of the nitroso compound (IIIa). For CAA (Ib), the fragmentation of the nitrenium ion at the C–N bond with the formation of a tertiary carbocation, which is more stable than that obtained from (Ia), occurs preferentially; elimination of H^+ from this nitrenium ion gives β,β-dimethyl acrylate. A similar fragmentation was previously observed in the reaction of CAA with Ag^+ salts [3].

It is seen that the competing paths of transformation in the reactions of CAA with isobutylene depend on the type of the N-substituent in the CAA. In order to obtain additional proofs for the participation of the alkoxy nitrenium ions in the reactions of CAA, we made a detailed study of the influence of the nature of N- and O-substituents on the direction of the alcoholysis of CAA. This reaction was chosen because of its unequivocal occurrence in the case of N-chloro-N-methoxy-tert-alkylamines with the formation of the corresponding dialkoxyamines [1]. The starting CAA (V) were obtained according to the previously developed scheme [1].

$$MeO_2CC(Me)_2Br \xrightarrow{R'ONH_2} RNHOR' \xrightarrow{t\text{-}BuOCl} RN(Cl)OR'$$
$$MeO_2CCH{=}CMe_2 \xrightarrow{R'ONH_2}$$

(IVa–d) (Va–d)

R = MeO_2CCMe_2, R' = $PhCH_2$ (a); R = MeO_2CCMe_2, R' = i-Pr (b); R = $MeO_2CCH_2CMe_2$, R' = $PhCH_2$ (c); R = $MeO_2CCH_2CMe_2$, R' = i-Pr (d).

It was shown that the methanolysis of (Va, b) in the presence of Et_3N leads exclusively to the dialkoxyamines (VIa, b), while CAA (Vc, d) under similar conditions give several by-products with dialkoxyamines (VIc, d).

$$(V\,a, b) \xrightarrow{MeOH/Et_3N} \underset{(VIa, b)}{RN(OMe)OR'}$$

$$(V\,c) \xrightarrow{MeOH/Et_3N} \underset{(VIc)}{RN(OMe)OR'} + MeO_2CCH_2C(Me)_2N{=}O +$$
$$+ PhCH_2Cl + PhCH_2OMe$$
$$(V\,d) \xrightarrow{MeOH/Et_3N} \underset{(VId)}{RN(OMe)OR'} + MeO_2CCH{=}CMe_2$$

The observed difference in the properties of CAA (V) can possibly be explained in the following way. In the case of CAA (Va, b) the heterolysis of the N–Cl bond is hindered because of the destabilization of the nitrenium ion formed by an electron-acceptor MeO_2C group at the α-C atom. Therefore the alcoholysis of CAA (Va, b) occurs rather by the S_N2 mechanism and is not accompanied by fragmentation. In the reaction of CAA (Vc) with MeOH the formation of a nitroso compound, $PhCH_2Cl$ and $PhCH_2OMe$ may serve as evidence for an intermediate formation of an alkoxynitrenium ion, since the above compounds are the products of its O-dealkylation. In the case of (Vd), the O-dealkylation of the nitrenium ion is sterically hindered, and therefore its fragmentation at the C–N bond is observed, as in the reaction of (Ib) with isobutylene.

EXPERIMENTAL

The PMR spectra were measured on "Bruker WP-80-SY" and "Tesla BS-567A" spectrometers with reference to HMDS as internal standard. The chemical shifts are given in δ, ppm; J, Hz. The mass spectra were recorded on a "Hitachi M-80-A" mass spectrometer in a chemical ionization regime (carrier gas isobutane). Peaks with a relative intensity of more than 10% are reported.

N-Chloro-N-alkoxyamines (CAA) (Ia, b) were obtained according to [1] and were used without purification.

Reaction of CAA (Ia) with Isobutylene in SO_2. A solution of 0.92 g (5.1 mmoles) of (Ia) in a mixture of 2.0 g (35.7 mmoles) of isobutylene and 5.2 g (81.3 mmoles) of SO_2 was held in a sealed ampul for 24 h at 7°C and for 2 h at 20°C. The excess of the gaseous reagents was removed and the residue was treated with a mixture of 10 ml of a 10% aqueous solution of $NaHCO_3$ and 15 ml of ether. The organic phase was separated and the aqueous phase was extracted with ether. The combined extract was dried over $MgSO_4$, evaporated under vacuum and the residue was chromatographed on a column (SiO_2, eluent CCl_4–ether, 3:1). Yield 0.32 g (26%) of the methyl ester of α-[N-methoxy-N-(2-chloro-2-methylpropyl)amino]isobutyric acid (IIa), bp 76°C (2 mm). PMR spectrum (100 MHz, $CDCl_3$): 1.31 (Me_2C), 1.56 (Me_2C), 2.97 (CH_2), 3.59, 3.65 (MeO and MeO_2C). Mass spectrum, m/z (I, %): 240 $[M + H]^+$ (33), 239(13), 238 $[M + H]^+$ (100), 237 $[M]^+$ (3), 202(40), 180(13), 178(41), 172(18), 171(20), 170(17), 160(58), 42(21), 41(25), 39(14), 27(12). Found, %: C 50.52; H 8.87; N 6.37. $C_{10}H_{20}ClNO_3$. Calculated, %: C 50.52; H 8.48; N 5.89. In addition, 0.03 g (5%) of a dimer of methyl α-nitrosoisobutyrate (IIIa) was obtained, which was identified by comparison with the PMR and mass spectra of an authentic sample [3].

Reaction of CAA (Ib) with Isobutylene in SO_2. Under the conditions of the preceding synthesis, the reaction of 1.14 g of (Ib), 1.2 g of isobutylene and 2.8 g of SO_2 gave 0.98 g (67%) of the methyl ester of β-[N-methoxy-N-(2-chloro-2-methylpropyl)amino]isovaleric acid (IIb), bp 97°C (2 mm). PMR spectrum (100 MHz, $CDCl_3$): 1.17 (Me_2C), 1.56 (Me_2C), 2.44 (CH_2), 2.92 (CH_2N), 3.58, 3.59 (MeO and MeO_2C). Mass spectrum, m/z (I, %): 255 $[M + 2H]^+$ (3), 254 $[M + H]^+$ (33), 253 $[M + 2H]^+$ (11), 252 $[M + H]^+$ (100), 216 (17%), 178(33), 174(76), 73(62), 56(14). Found, %: C 52.90; H 9.07; N 5.89. $C_{11}H_{22}ClNO_3$. Calculated, %: C 52.48; H 8.80; N 5.56. From the ether distillate, 0.08 g (13%) of methyl β,β-dimethylacrylate was obtained, which was identified by comparison with the PMR spectrum of an authentic sample.

Methyl Ester of α-(N-benzyloxyamino)isobutyric Acid (IVa). A mixture of 3.7 g (30 mmoles) of benzyloxyamine, 5.43 g (30 mmoles) of methyl α-bromoisobutyrate, 3.18 g (30 mmoles) of Na_2CO_3 and 20 ml of absolute MeCN was heated in a sealed ampul for 68 h at 117°C, and then was evaporated in vacuo. The residue was diluted with 20 ml of a 10% aqueous Na_2CO_3 solution and the mixture was extracted with ether. The extract was dried over $MgSO_4$, evaporated in vacuo, and the residue was distilled. Yield, 1.3 g (19%) of (IVa), bp 121°C (3 mm). PMR spectrum (100 MHz, $CDCl_3$): 1.24 (Me_2C), 3.66 (MeO_2C), 4.65 (CH_2), 7.26 (Ph). Found, %: C 64.67; H 7.90; N 6.38. $C_{12}H_{17}NO_3$. Calculated, %: C 64.65; H 7.67; N 6.27.

Methyl Ester of α-(N-isopropoxyamino)isobutyric Acid (IVb). A mixture of 9.05 g (50 mmoles) of methyl α-bromoisobutyrate, 5.63 g (75 mmoles) of isopropoxyamine, 5.3 g (50 mmoles) of Na_2CO_3 and 10 ml of absolute MeCN was heated in a sealed ampul for 22 h at 110-115°C and for 77 h at 125°C, and then was evaporated in vacuo. The residue was diluted with 10 ml of H_2O and extracted with ether (3 × 50 ml). The extract was shaken with 20 ml of concentrated HCl, the aqueous phase was separated, neutralized with Na_2CO_3 and extracted with ether. The extract was dried over $MgSO_4$, evaporated in vacuo and the residue was distilled. Yield 3.0 g (34%) of (IVb), bp 52°C (5 mm). PMR spectrum (80 MHz, $CDCl_3$): 1.11 ($\underline{Me}_2CH$, J = 6), 1.26 (Me_2C), 3.72 (MeO_2C), 3.75 (CH), 5.3 (NH). Found, %: C 54.84; H 10.04; N 7.81. $C_8H_{17}NO_3$. Calculated, %: C 54.84; H 9.78; N 7.99.

Methyl Ester of β-(N-benzyloxyamino)isovaleric Acid (IVc). A mixture of 3.9 g (34.2 mmoles) of methyl β,β-dimethylacrylate and 3.6 g (29.3 mmoles) of benzyloxyamine was heated in a sealed ampul for 149 h at 117°C, and then distilled. Yield, 5.1 g (74%) of (IVc), bp 109°C (2 mm). PMR spectrum (80 MHz, $CDCl_3$): 1.15 (Me_2C), 2.50 (CH_2), 3.63 (MeO_2C), 4.70 (CH_2O), 7.30 (Ph). Found, %: C 65.79; H 7.82; N 5.38. $C_{13}H_{19}NO_3$. Calculated, %: C 65.80; H 8.07; N 5.90.

Methyl Ester of β-(N-isopropoxyamino)isovaleric Acid (IVd). A mixture of 5.7 g (50 mmoles) of methyl β,β-dimethylacrylate and 7.5 g (100 mmoles) of isopropoxyamine was heated in a sealed ampul for 65 h at 117°C, and then was distilled. Yield, 5.7 g (60%) of (IVd), bp 65°C (6 mm). PMR spectrum (80 MHz, $CDCl_3$): 1.04 (Me_2C), 1.05 ($\underline{Me}_2CH$, J = 6.6), 2.38 (CH_2), 3.58 (MeO_2C), 3.68 (CH), 5.28 (NH). Found, %: C 54.55; H 10.00; N 7.00. $C_9H_{19}NO_3$. Calculated, %: C 54.53; H 10.12; N 7.40.

N-Chloro-N-alkoxyamines (CAA) (Va-d) were obtained by the method described in [1]. Yield, quantitative, the compounds were used without additional purification. (Va), PMR spectrum (80 MHz, C_6D_6): 1.49, 1.52 (Me_2C), 3.26 (MeO_2C), 4.78, 4.95 (CH_2, J_{AB} = 12), 7.13 (m, Ph). (Vb), PMR spectrum (80 MHz, C_6D_6): 0.99, 1.04 ($\underline{Me}_2CH$, J = 6), 1.55, 1.57 (Me_2C), 3.46

(MeO_2C), 4.25 (CH). (Vc), PMR spectrum (80 MHz, C_6D_6): 1.36 (Me_2C), 2.65 (CH_2), 3.24 (MeO_2C), 4.70, 4.92 (CH_2O, J_{AB} = 11), 7.13 m (Ph). (Vd), PMR spectrum (80 MHz, C_6D_6): 0.99, 1.01 ($\underline{Me}_2CH$, J = 6), 1.41, 1.44 (Me_2C), 1.76 (CH_2), 3.30 (MeO_2C), 4.21 (CH).

Reaction of CAA (Va) with MeOH. A solution of 0.3 g (2.9 mmoles) of Et_3N in 5 ml of abs. MeOH was added at −55°C to 0.37 g (1.4 mmoles) of (Va). The mixture was held for 6 h at −20°C and 1 h at 20°C, and then MeOH was evaporated in vacuo (30 mm) into a cooled trap, while the residue was extracted with ether. The extract was evaporated in vacuo (at the end at 1 mm), collecting the distillate into the trap. In the residue, 0.36 g (99%) of dialkoxyamine (VIa) was obtained, which was pure according to the PMR spectrum. After chromatography on a column (Al_2O_3, neutral according to Brockman, eluent hexane–ether, 2:1), 0.24 g (65%) of (VIa) was obtained, which was identified by comparison with the PMR and mass spectra of an authentic sample [1].

Reaction of CAA (Vb) with MeOH. Under the conditions of the preceding synthesis, the reaction of 0.7 g (3.4 mmoles) of (Vb) and a solution of 0.5 g (4.9 mmoles) of Et_3N in 5 ml of absolute MeOH gave 0.61 g (89%) of (VIb), which was identified by comparison with the PMR spectrum of an authentic sample [1].

Reaction of CAA (Vc) with MeOH. Under the conditions of the synthesis of (VIa), the reaction of 0.31 g (1.2 mmoles) of (Vc) and a solution of 0.29 g (1.2 mmoles) of Et_3N in 5 ml of abs. MeOH gave 0.23 g (75%) of (VIc), which was identified by comparison with the PMR spectrum of an authentic sample [1]. From the ether condensate, 0.04 g (24%) of methyl β-nitrosoisovalerate was extracted, which was identified by comparison with the PMR spectrum of an authentic sample [3]. In the methanol condensate $PhCH_2Cl$ and $PhCH_2OMe$ were detected by means of GLC.

Reaction of CAA (Vd) with MeOH. Under the conditions of the synthesis of (VIa), the reaction of 0.55 g (0.5 mmole) of (Vd) and a solution of 0.4 g (3.9 mmoles) of Et_3N in 5 ml of absolute MeOH gave 0.47 g (86%) of (VId), which was identified by comparison with the PMR spectrum of an authentic sample [1]. In the methanol condensate, 0.04 g (14%) of methyl β,β-dimethylacrylate was detected.

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