- 10. G. V. Shustov, A. V. Zoloti, and R. G. Kostyanovsky, Tetrahedron, 38, 2319 (1982).
- 11. R. E. White and P. Covacic, J. Am. Chem. Soc., 97, 1180 (1975).
- 12. D. Graus, T. Clark, and P. V. R. Schleyer, Tetrahedron Lett., 21, 3681 (1980).
- 13. V. F. Rudchenko, V. I. Shevchenko, S. M. Ignatov, and R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 2411 (1983).
- 14. A. V. Fokin and Yu. M. Kosyrev, Usp. Khim., 35, 1897 (1966).
- Houben-Weyl, Methoden der Organische Chemie, Georg Tieme Verlag, Stuttgart, Vol. X/1 (1971), p. 1184.
- 16. A. Rougny and M. Daudon, Bull. Soc. Chim. France, 833 (1976).
- 17. R. M. Khomutov, Zh. Obshch. Khim., 31,1992 (1961).
- 18. G. Zinner and W. Kölling, Arch. Pharm., 293/65, 82 (1960).
- 19. B. Loew and J. T. Massengale, J. Org. Chem., 22, 1186 (1957).

GEMINAL SYSTEMS. COMMUNICATION 29*. REACTIONS OF N-CHLORO-N-METHOXY-N',N'-DIMETHYLUREA WITH N-NUCLEOPHILES

V. F. Rudchenko, V. I. Shevchenko, and R. G. Kostyanovskii UDC 542.91:547.495.3

We have previously obtained N-chloro-N-alkoxy-N',N'-dimethylureas [1, 2], which, similarly to N-chloro-N-alkoxy-N-tert-alkylamines [3, 4] and N-chloro-N,N-dialkoxyamines [5], undergo by the action of alcohols, nucleophilic substitution to form N,N-dialkoxyureas [1, 2].

In the present work, we studied the reactions of N-chloro-N-methoxy-N',N'-dimethylurea (I) with N-nucleophiles to verify the possibility of synthesizing NH-alkoxyhydrazines as starting materials for the preparation of amido-esters of orthonitrous acid.

$$\begin{array}{ccc} XN(CI)OMe \xrightarrow{HNR_2} XN(NR_2)OR \xrightarrow{OH^-} HN(NR_2)OR \xrightarrow{CI^+} \\ CIN(NR_2)OR \xrightarrow{OR^-} (RO)_2NNR_2 \end{array}$$
(1)

$$X = Me_{2}NCO.$$

This scheme has recently been applied in the successful synthesis of trialkoxyamines [5]. However, it was shown that in the reaction of (I) with secondary amines, as in the case of N-chloro-N-alkoxy-N-tert-alkylamines [6], the initially formed N-alkoxyhydrazines enter into further reactions under the reaction conditions. Thus, as a result of the reaction of (I) with an excess of Me₂NH, only products (II) and (III) could be isolated:

$$\begin{array}{c} XN(CI)OMe \frac{Me_{i}NH}{-HCI} \left[XN(OMe)NMe_{2} \xrightarrow{H^{+}}{-MeOH} XN = \overset{+}{N}Me_{2} \xrightarrow{H^{+}}{-H^{+}} \\ (I) \\ \rightarrow X\overline{N} - \overset{+}{N} = CH_{2} \xrightarrow{Me_{2}NH} XNHNCH_{2}NMe_{2} \right] \xrightarrow{Me_{i}NH} (Me_{2}N)_{2}CH_{2} + (Me_{2}N)_{2}CO \\ \stackrel{+}{Me} \xrightarrow{He} Me \end{array}$$

$$\begin{array}{c} (II) \\ (III) \\ (III) \\ (IIII) \end{array}$$

According to the data in [6], N-alkoxyhydrazine gives a diazenium salt, from which, as a result of a characteristic deprotonation, a dipole is generated, which adds Me_2NH to form an asymmetric aminal. The latter disproportionates to (II) under the action of Me_2NH . The formation of (III) can be attributed to the carbamoylation of Me_2NH by the action of (I) or one of the intermediate products.

*For Communication 28 see [1].

Institute of Chemical Physics, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 3, pp. 606-610, March, 1986. Original article submitted October 1, 1984.

In the reaction of (I) with MeONHMe, similarly to [6], the intermediate aminal obtained by an analogous scheme does not disproportionate but, by splitting off MeOH, gives diazene (IV):

$$(I) \xrightarrow[-HCI, -MeOH}^{MeONHMe/ELO} \left[X\overline{N} - \widetilde{N} = CH_2 \xrightarrow[]{MeONHMe} XNHNCH_2N(Me)OMe \right] \xrightarrow[-MeOH]{-MeOH} (3)$$

$$(IV) \xrightarrow[(IV)]{}$$

The products of the first stage of the reaction (nucleophilic substitution of the Cl atom at N) could be obtained in the reaction of (I) with Me₃N or C_5H_5N (similarly to [6]):

$$(I) \frac{R_{s}N}{Et_{s}O} \frac{XN - \mathring{N}R_{3}Cl^{-}}{H_{s}O} \frac{AgClO_{4}}{H_{s}O} \frac{XN - \mathring{N}R_{3}ClO_{4}^{-}}{\mathring{N}R_{3}ClO_{4}^{-}}$$

$$OMe \qquad OMe \qquad (Va), (Va) \qquad (Vb), (Vb)$$

$$R_{3}N = Me_{3}N (Va, b); C_{5}H_{5}N (VIa, b). \qquad (4)$$

The hygroscopic N-alkoxyhydrazinium chlorides (Va) and (VIa) were transformed into stable perchlorates (Vb) and (VIb), which crystallize well from H_2O .

The tertiary amine Et_3N , which is more bulky than Me_3N because of steric hindrances to a nucleophilic attack, acts in the reaction with (I), as in [6] as a one-electron reducing agent. Products (III), (VII), and (VIII) are thus formed, possibly as the result of the transformations of the intermediate N-methoxycarbamidyl radical:

(I)
$$\xrightarrow{\text{Et}_{g}N/C_{g}H_{g}} [X - \dot{N}OMe] \rightarrow XNHOMe + (III) + XNHNHX$$

$$(5)$$

$$(VII) (VIII)$$

During the decomposition of the latter with the elimination of methoxynitrene (cf. [7]), secondary radicals Me_2NCO and Me_2N are formed, and their recombination leads to (III). The formation of (VIII) from N-ethoxy-N',N'-dimethylurea by oxidation with Ag_2O is discussed in [8].

Thus, the introduction of a carbamoyl substituent at the central N atom does not lead to the stabilization of N-alkoxyhydrazines, which in the presence of a terminal donor N' atom decompose as a result of the dissociation of the N-O bond due to a $n_{N'} - \sigma_{N-O}^*$ orbital interaction [9]. Elimination of this interaction by blocking the unshared electron pair of the donor N atom leads to a stabilization of the alkoxyhydrazinium salts (Va, b) and (VIa, b). Similar stable hydrazinium salts t-AlkN(OMe)NC₅H₅X⁻ were obtained in [6]. N-Alkoxyhydrazine, in which the n- σ^* interaction is sterically prohibited because of inclusion of the donor H

atom at the head of a bicyclic system [10], and also t-AlkN(OMe)N \langle [6] and oxadiaziridines

[11], in which the donor ability of the N atom is weakened because of its inclusion in a three-membered ring, are also stable. Another path for the stabilization of N-alkoxyhydrazines is the introduction of electron-acceptor substituents to the donor N atom: $MeO_2CN(OMe)NHCO_2Me$ [12], $ArN(OH)NAr_2$ [13], $CF_3N(OCF_3)N(CF_3)_2$ [14], RN(OR')N(OR')R, where R = AlkCO [15, 16], ArCO [17], RO_2C [8], ArNHCO [18], $PhSO_2$ [19], C_3 [20].

On the basis of the above data, we studied the reaction of (I) with Na salts of p-toluenesulfonamides, which proceeded smoothly to form the relatively stable N-methoxy-N-dimethylcarbamoyl-N'-tosyl-N-methyl- (IX) and N-methoxy-N-dimethylcarbamoyl-N'-tosyl-N'-phenylhydrazines (X):

> (I) $\frac{Ts\overline{N}RNa^{+}}{MeCN} XN - NTs$ OMe R (IX), (X) (6)

R = Me (IX), Ph (X).

It was proposed to carry out further synthesis from these compounds according to scheme (1). However, compounds (IX) and (X) could not be decarbamoylated by alkaline hydrolysis under the conditions of [2].

EXPERIMENTAL

The PMR spectra were measured on a JNM-C-60-NL spectrometer with reference to HMDS. The chemical shifts are given in ppm; J in Hz.

N-Chloro-N-methoxy-N', N'-dimethylurea (I) was obtained according to [1].

Reaction of (I) with Me₂NH. A 1.29 g (8.5 mmoles) portion of (I) was gradually added, with stirring, at -78° C to 10 ml of Me₂NH. The mixture was held for 1 h at 0°C, the excess of Me₂NH was removed at 20°C, and the residue was fractionated to yield 0.23 g (26.4%) of bisdimethylaminomethane (II) (bp 84°C) and 0.09 (9.1%) of tetramethylurea (III) (bp 178°C).

 $\frac{1-(N-Methoxy-N-methylaminomethyl)-2-(N,N-dimethylcarbamoyl)diazene (IV). A solution of 1.29 g (8.5 mmoles) of (I) in 20 ml of absolute Et₂O was added, with stirring, at -78°C to a solution of 1.56 g (25.5 mmoles) of MeONHMe in 20 ml of absolute Et₂O. The mixture was held for 12 h at 0°C, the precipitate was separated, and from the filtrate the solvent was removed in vacuo. The residue was crystallized from cold Et₂O to yield 0.56 g (37.6%) of (IV), which decomposes at 20°C. PMR spectrum (CCl₄): 2.80, 2.84 (Me₂N), 2.98 (MeN), 3.40 (MeO), 4.23 (CH₂). Found: C 40.99; H 7.69; N 31.72%. C₆H₁₄N₄O₂, Calculated: C 41.37; H 8.10; N 32.16%.$

<u>1-Methoxy-1-dimethylcarbamoyl-2,2,2-trimethylhydrazinium Chloride (Va) and Perchlorate</u> (Vb). A solution of 1.29 g (8.5 mmoles) of (I) in 10 ml of absolute Et₂O was added, with stirring, at -78°C to a solution of 0.50 g (8.5 mmoles) of Me₃N in 10 ml of absolute Et₂O. The precipitate was separated and crystallized from a MeCN-Et₂O mixture to yield 1.2 g (66.7%) of the hygroscopic chloride (Va). PMR spectrum (CDCl₃): 3.09, 3.36 (Me₂N), 3.86 (Me₃N), 4.03 (MeO). Found: C 39.70; H 8.97; N 20.00%. $C_7H_{18}N_3O_2Cl$. Calculated: C 39.72; H 8.57; N 19.85%. A solution of 0.079 g (0.38 mmole) of (Va) in 1 ml of H₂O was added to a solution of 0.078 g (0.38 mmole) of AgClO₄ in 2 ml of H₂O. The precipitate was separated, and from the filtrate the solvent was removed in vacuo (1 mm). The residue was crystallized from H₂O to yield 0.075 g (72.12%) of (Vb), mp 83°C (dec). Found: C 30.48; H 7.11; N 15.44%. $C_7H_{18}N_3$ - O_6Cl . Calculated: C 30.50; H 6.58; N 15.24%.

<u>N-(1-Pyridinium)-N-methoxy-N',N'-dimethylurea Perchlorate (VIb)</u>. A solution of 0.367 g (4.6 mmoles) of Py in 5 ml of absolute Et₂O was added to a solution of 0.336 g (2.2 mmoles) of (I) in 5 ml of absolute Et₂O. The mixture was held for 12 h at -5° C, the precipitate was separated and crystallized from a MeCN-Et₂O mixture to yield 0.42 g (97.2%) of chloride (VIa). PMR spectrum (CDCl)₃: 3.23, 3.31 (Me₂N), 3.96 (MeO), 8.81-9.98 (C₅H₅N). Compound (VIa) was hygroscopic and was characterized in the form of perchlorate (VIb). A solution of 0.11 g (0.5 mmole) of (VIa) in 1 ml of H₂O was added to a solution of 0.10 g (0.5 mmole) of AgClO₄ in 2 ml of H₂O. The precipitate was separated, the solvent was removed in vacuo, and the residue was crystallized from H₂O to yield 0.11 g (75.2%) of (VIb), mp 163-164°C. PMR spectrum (CD₃OD): 3.10 (Me₂N), 3.86 (MeO), 8.08-9.24 (C₅H₅N). Found: C 36.41; H 4.81; N 13.92%. C₉H₁4N₃O₆Cl. Calculated: C 36.56; H 4.77; N 14.21%.

<u>Reaction of (I) with Et₃N.</u> A solution of 1.67 g (10.9 mmoles) of (I) in 10 ml of absolute C_6H_6 was added at 7°C to a solution of 1.11 g (10.9 mmoles) of Et₃N in 10 ml of absolute C_6H_6 . The precipitate of Et₃N•HCl was rapidly separated, the filtrate was warmed to 20°C, and the precipitate of 1,2-bis(N,N-dimethylcarbamoyl)hydrazine (VIII) was separated. From the filtrate, the solvent was removed in vacuo and the residue was chromatographed on a column (Al₂O₃, eluent CHCl₃- C_6H_6 , 1:6). Yield 0.29 g (22.7%) of (III), 0.09 g (7.2%) of N-methoxy-N',N'dimethylurea (VII) [1] and (VIII), which was combined with previously obtained portion and crystallized from a 1:1 EtOH-MeCO₂Et mixture. Yield, 0.17 g (17.4%) of (VIII), mp 217-218°C (cf [8]). PMR spectrum (CD₃OD): 3.0 (Me₂N). Found: C 41.37; H 8.23; N 32.20%. $C_6H_{14}O_2N_4$. Calculated: C41.37; H 8.10; N 32.16%.

<u>1-Toluenesulfonyl-1-methyl-2-methoxy-2-dimethylcarbamoylhydrazine (IX)</u>. A solution of 2.04 g (14.49 mmoles) of (I) in 20 ml of absolute MeCN was added with stirring, at -20°C, to a suspension of 3.0 g (14.49 mmoles) of TosNNaMe in 30 ml of absolute MeCN. The solvent was removed in vacuo, and the residue was extracted by Et_2O . The extract was evaporated in vacuo, and the residue was extracted by Et_2O . The extract was evaporated in vacuo, and the residue was crystallized from an Et_2O -pentane mixture to yield 0.95 g (21.7%) of (IX), mp 70-72°C, PMR spectrum (CCl₄): 2.40 (p-MeC₆H₄), 2.90 (Me₂N), 2.97 (MeN), 3.46 (MeO), 7.26, 7.69 (C₆H₄, J_{AB} = 2.25). Found: C 48.02; H 6.46; N 13.90%. C₁₂H₁₉N₃O₄. Calculated: C 47.83; H 6.36; N 13.94%.

 $\frac{1-\text{Toluenesulfony1-1-pheny1-2-methoxy-2-dimethy1carbamoy1hydrazine (X).} \text{ In a similar way,} from \frac{2.83 \text{ g} (7.79 \text{ mmoles}) \text{ of TosNNaPh and 0.92 g} (7.79 \text{ mmoles}) \text{ of (I) in 40 ml of absolute} MeCN, 1.56 g (54.1\%) \text{ of (XII), mp 92-93°C (from ether), was obtained. PMR spectrum (CCl_4):}$

2.48 (p-MeC₆H₄), 2.91 (Me₂N), 3.55 (MeO), 7.23 (Ph), 7.09, 7.52 (C₆H₄, $J_{AB} = 2.25$). Found: C 56.16; H 6.05; N 11.55%. C17H21N3O4. Calculated: C 56.18; H 5.82; N 11.56%.

CONCLUSIONS

In the reaction of N-chloro-N-methoxy-N',N'-dimethylurea with amines, a nucleophilic substitution of the chlorine atom at the N atom takes place to form N-alkoxyhydrazines, which are stable in the reaction with MeaN, pyridine, toluenesulfonamides, and give products of further transformations with Me₂NH and MeONHMe.

LITERATURE CITED

- 1. V. F. Rudchenko, V. I. Shevchenko, and R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 598 (1986).
- 2. V. F. Rudchenko, V. I. Shevchenko, S. M. Ignatov, and R. G.Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 2411 (1983).
- 3. R. G. Kostyanovsky, V. F. Rudchenko, V. G. Shtamburg, I. I. Chervin, and Sh. S. Nasibov, Tetrahedron, 37, 4245 (1981).
- 4. V. F. Rudchenko, V. G. Shtamburg, and R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 1183 (1981).
- 5. V. F. Rudchenko, S. Ignatov, I. I. Chervin, and R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 2414 (1983).
- V. G. Shtamburg, V. F. Rudchenko, Sh. S. Nasibov, I. I. Chervin, A. P. Pleshkova, and 6. R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 2327 (1981).
- V. F. Rudchenko, V. G. Shtamburg, A. P. Pleshkova, Sh. S. Nasibov, I. I. Chervin, and 7. R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 2539 (1981).
- 8. R. J. Crawford and R. Raaph, J. Org. Chem., 28, 2419 (1963).
- 9. G. V. Shustov, N. B. Tavakalyan, and R. G. Kostyanovsky, Tetrahedron, 41, 575 (1985).
- 10. D. L. Trepanier and S. Wang, J. Chem. Soc. Chem. Commun., 642 (1973).
- 11. F. D. Greene and S. S. Hecht, J. Org. Chem., 35, 2482 (1970); J. L. Swigert and K. G. Taylor, J. Am. Chem. Soc., 93, 7337 (1971); K. G. Taylor, S. R. Isaac, and J. L. Swigert, J. Org. Chem., 41, 1146 (1976). O. Dielo and C. Wulff, Ann. Chem., 437, 309 (1924).
- 12.
- 13. S. Goldschmidt and K. Renn, Chem. Ber., 55, 628 (1922); L. Dulog and G. Baum, Chem. Ber., 104, 661 (1971).
- 14. R. N. Haszeldine and A. E. Tipping, J. Chem. Soc., 1236 (1966).
- T. Koenig, J. A. Hoobler, and W. R. Mabey, J. Am. Chem. Soc., 94, 2514 (1972). 15.
- J. H. Cooley, N. W. Mosher, and M. A. Khan, J. Am. Chem. Soc., 90, 1867 (1968). 16.
- A. R. Forrester, V. M. Johansson, and R. H. Thomson, J. Chem. Soc. Perkin Trans. 1, 17. 1112 (1979); R. O. C. Norman, R. Purchase, and C. B. Thomas, J. Chem. Soc. Perkin Trans. 1, 1701 (1972).
- J. H. Cooley and P. T. Jacobs, J. Org. Chem., 40, 552 (1975). 18.
- A. T. Balaban and A. Vasilescu, Tetrahedron Lett., 571 (1972). 19.
- D. H. R. Barton, R. L. Harris, R. H. Hesse, M. M. Pechet, and F. J. Urban, J.Chem. Soc. 20. Perkin Trans. 1, 2344 (1974).