BRIEF COMMUNICATIONS

N,N-DIALKOXY-N′-ALKYLUREAS

V. F. Rudchenko, S. M. Ignatov, and R. G. Kostyanovskii

UDC 542.91:547.495.3

The chlorination of N-alkoxy-N′-alkylureas (1) by the action of t-*BuOCl proceeds regiospecifically to give stable N-chloro-N-alkoxy-N′-alkylureas (2). The alcoholysis of 2 leads to N,N-dialkoxy-N′-alkylureas (3). The alkaline hydrolysis of 3 is a new, convenient method for the preparation of dialkoxyamines.*

Keywords: *N-alkoxy-N′-alkylureas, N-chloro-N-alkoxy-N′-alkylureas, N,N-dialkoxy-N′-alkylureas, dialkoxyamines.*

Only one N,N-dialkoxy-N′-alkylurea has been described, namely, the simplest representative of this class, N,N-dimethoxy-N′-methylurea. This compound was obtained by the transamination of N,N-dimethoxy-N′,N′-dimethylurea by the action of methylamine [1] and by the reaction of dimethoxyamine with methyl isocyanate [2]. On the other hand, a preparative method has been reported for N,N-dialkoxy-N′,N′-dialkylureas by the alcoholysis of the corresponding N-chloro-N-alkoxyureas [3-6]. In the present work, we show that this method is also suitable for the synthesis of N,N-dialkoxy-N′-alkylureas.

Starting ureas **1** were obtained by the carbamoylation of O-alkylhydroxylamines using isocyanates. The chlorination of **1** proceeds regiospecifically to give stable N-chloro-N-alkoxyureas (**2**), while the second nitrogen atom is not affected even by the action of excess *t*-BuOCl. Alcoholysis of ureas **2** by the action of alcoholic NaOH or alcoholates leads to N,N-dialkoxyureas (**3**). The synthesis of **3** from **1** may be carried out in a single step without the isolation of intermediate N-chloroureas **2**.

$$R'ONH_2 \xrightarrow{RNCO} \underset{(1a-c)}{RNHCONHOR'} \xrightarrow{t\text{-BuOCl}} \underset{(2a-c)}{RNHCON(Cl)OR'} \xrightarrow{R^2OH/B} \underset{(3a-d)}{RNHCON(OR^2)OR'}$$

R=R′=Me (1, 2a);
R=Me, R′=PhCH$_2$ (1, 2b);
R=Et, R′=Me (1, 2c).

B=NaOH or R^{2}ONa;
R=R′=Me, R^2=Me (3a);
R=R′=Me, R^2=Et (3b);
R=Me, R′=PhCH$_2$, R^2=Me (3c);
R=Et, R′=Me, R^2=Me (3d).

In a study of the alkaline hydrolysis of **3a**, we found that ureas **3**, similarly to N,N-dialkoxy-N′,N′-dialkylureas [3, 5-7], are rather available starting reagents for the synthesis of dialkoxyamines, which are new, general reagents in organic synthesis [6-9].

$$3a \xrightarrow{KOH/H_2O} \underset{(4)}{(MeO)_2NH}$$

EXPERIMENTAL

The PMR spectra were taken on Bruker WP-80SY and WM-400 spectrometers.

N-Alkoxy-N′-alkylureas **1** were obtained according to Crescenzi et al. [10] by the reaction of O-alkylhydroxylamines with isocyanates in absolute ether.

N-Methoxy-N′-methylurea (1a) was obtained in 67% yield, mp 63°C [10].

N-Benzyloxy-N′-methylurea (1b) was obtained in 65% yield, mp 90-91°C. Found: C, 59.99; H, 6.67; N, 15.58%. Calculated for $C_9H_{12}N_2O_2$: C, 59.98; H, 6.71; N, 15.64%. PMR spectrum at 80 MHz in $CDCl_3$ (δ, ppm, J, Hz): 2.78 br.s (3H, Me), 4.79 s (2H, CH_2), 5.59 br.s (1H, NHMe), 7.37 m (5H, Ph), 7.56 br.s (1H, NH).

N. N. Semenov Institute of Chemical Physics, Russian Academy of Sciences, 117913 Moscow. Translated from Izvestiya Akademii Nauk, Seriya Khimicheskaya, No. 10, pp. 2441-2443, October, 1992. Original article submitted February 12, 1992.

 1063-5211/92/4110-1920$12.50

N-Methoxy-N′-ethylurea (1c) was obtained in 68% yield, mp 63°C. Found: C, 40.67; H, 8.68; N, 23.70%. Calculated for $C_4H_{10}N_2O_2$: C, 40.66; H, 8.53; N, 23.71%. PMR spectrum in C_6D_6 at 400 MHz (δ, ppm, J, Hz): 0.81 t (3H, $\underline{Me}CH_2$), J = 7.3), 3.08 d.q (2H, $MeC\underline{H}_2$, J_{CHNH} = 6.1), 3.26 s (3H, OMe), 5.37 br.t (1H, $N\underline{H}CH_2$), 9.17 br.s (1H, NHO).

General Method for the Synthesis of N-Chloro-N-alkoxy-N′-alkylureas 2. A solution of *t*-BuOCl (two-fold molar excess) in absolute ether was added to a suspension of urea **1** in absolute ether at −78°C, stirred until the starting urea dissolved, and evaporated in vacuum to give urea **2**.

Product **2a** was obtained in 79% yield, mp 47°C (from ether—pentane). Found: C, 26.28; H, 5.01; N, 20.40%. Calculated for $C_3H_7ClN_2O_2$: C, 26.01; H, 5.09; N, 20.22%. PMR spectrum in $CDCl_3$ at 80 MHz: 2.92 d (3H, Me, J_{CHNH} = 4.9), 3.82 s (3H, OMe), 6.56 br.q (1H, NH).

Product **2b** was obtained in 97% yield as an oil. PMR spectrum in $CDCl_3$ at 80 MHz: 2.82 d (2H, Me, J_{CHNH} = 4.9), 4.98 s (2H, CH_2), 6.10 br.q (1H, NH), 7.38 m (5H, C_6H_5).

General Method for the Synthesis of N,N-Dialkoxy-N′-alkylureas 3. A solution of 1.5 molar equivalents *t*-BuOCl in the corresponding alcohol was added with stirring to a solution of urea **1** in the same alcohol cooling to −78°C. A solution of one molar equivalent NaOH (or sodium alcoholate) in the same alcohol was then added. The mixture was maintained for 1 h at 20°C, saturated with CO_2, and evaporated in vacuum. The residue was extracted with ether. The extract was evaporated in vacuum to give **3**.

Product **3a** was obtained in 75% yield, bp 85°C (1 torr) and identified by comparison with an authentic sample using the PMR spectrum reported in our previous work [1].

Product **3b** was obtained in 31% yield, bp 91°C (1 torr). Found: C, 40.53; H, 8.29; N, 19.36%. Calculated for $C_5H_{12}N_2O_3$: C, 40.53; H, 8.17; N, 18.91%. PMR spectrum in C_6D_6 at 80 MHz: 1.06 t (3H, $\underline{Me}CH_2$, J = 7.1), 2.41 d (3H, Me, J_{CHNH} = 4.8), 3.55 s (3H, OMe), 3.89 br.q (2H, $MeC\underline{H}_2$), 5.67 q (1H, NH).

Product **3c** was obtained in 85% yield as an oil and purified by chromatography on an alumina column (Brockmann neutral) using ether as the eluent. Found: C, 57.12; H, 6.82; N, 13.39%. Calculated for $C_{10}H_{14}N_2O_3$: C, 57.12; H, 6.71; N, 13.33%. PMR spectrum in C_6D_6 at 80 MHz: 2.33 d (3H, Me, J_{CHNH} = 4.9), 3.46 s (3H, OMe), 4.89 s (2H, CH_2), 5.51 br.q (1H, NH), 7.15 m (5H, C_6H_5).

Product **3d** was obtained in 47% yield, bp 80°C (1 torr). Found: C, 40.55; H, 8.03; N, 18.33%. Calculated for $C_5H_{12}N_2O_3$: C, 40.53; H, 8.16; N, 18.91%. PMR spectrum in C_6D_6 at 80 MHz: 0.75 t (3H, $\underline{Me}CH_2$, J = 7.2), 2.97 d.q (2H, $MeC\underline{H}_2$, J_{CHNH} = 5.9), 3.55 s (3H, OMe), 5.72 br.t (1H, NH).

Dimethoxyamine 4. A solution of 0.93 g (6.9 mmoles) **3a** and 0.46 g (8.2 mmoles) KOH in 5 ml water was stirred for 16 h at 20°C and then extracted with ethyl chloride. The extract was dried over $MgSO_4$. Ethyl chloride was left to evaporate spontaneously and the residue was distilled to give 0.19 g (36.5%) **4**, bp 83°C. The product was identified with an authentic sample using the PMR spectrum reported in our previous work [7].

REFERENCES

1. V. F. Rudchenko, V. I. Shchevchenko, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 7, 1556 (1987).
2. V. F. Rudchenko, S. M. Ignatov, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 10, 2384 (1989).
3. V. F. Rudchenko, V. I. Shchevchenko, S. M. Ignatov, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 10, 2411 (1983).
4. V. F. Rudchenko, V. I. Shchevchenko, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 3, 598 (1986).
5. V. F. Rudchenko, I. I. Chervin, V. N. Voznesenskii, V. S. Nosova, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 12, 2788 (1988).
6. A. I. Prokof'ev, V. F. Rudchenko, S. M. Ignatov, I. I. Chervin, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.* No. 8, 1819 (1989).
7. V. F. Rudchenko, S. M. Ignatov, I. I. Chervin, V. S. Nosova, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 5, 1153 (1986).
8. V. F. Rudchenko, S. M. Ignatov, and R. G. Kostyanovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, No. 10, 2384 (1989).
9. V. F. Rudchenko, S. M. Ignatov, and R. G. Kostyanovskii (Kostyanovsky), *J. Chem. Soc., Chem. Commun.*, No. 3, 261 (1990).
10. V. Crescenzi, A. Ciana, V. Giancotti, E. Russo, L. Salvestrini, and L. Ciceri, *Makromol. Chem.*, **141**, 199 (1971).