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SHORT COMMUNICATIONS

Reactions of Secondary Amines with Dichlorocarbene Generated in Aqueous–Alkaline Medium in the Presence of *N*-Methylmorpholine *N*-Oxide

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Abstract—Dichlorocarbene generated from chloroform in aqueous–alkaline medium in the presence of *N*-methylmorpholine *N*-oxide is converted to phosgene which reacts *in situ* with secondary amines to afford tetrasubstituted ureas.

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We have recently proposed a novel medium for the alkylation of secondary amines, a 50% aqueous solution of *N*-methylmorpholine *N*-oxide (NMMO) [1–3]. In order to explore the scope of application of this system, we have studied formylation of secondary amines **1**–**4** by reaction with dichlorocarbene generated in the presence of NMMO. It has long been known [4–6] that insertion of dichlorocarbene into the NH bond of secondary amines under conditions of phase-transfer catalysis (PTC) leads to the formation of the corresponding *N*,*N*-dialkylformamides as the major products.

Unlike PTC conditions [6], dichlorocarbene generated in aqueous NMMO from chloroform in the presence of sodium hydroxide reacts with NMMO to give phosgene. Reaction of the latter with secondary amines **1**–**4** afforded *N*,*N*,*N*′,*N*′-tetraalkylureas **5**–**8** in 25–55% yield. The structure of **5**–**8** was confirmed by IR and ^{1}H and ^{13}C NMR spectra and elemental analyses.

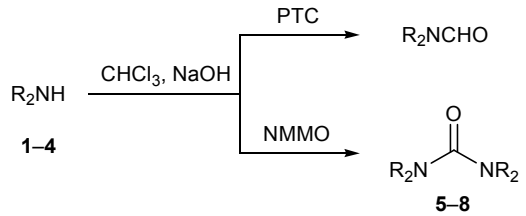
A probable reaction mechanism involves addition of dichlorocarbene to the *N*-oxide oxygen atom to give zwitterionic intermediate which is converted to phosgene while NMMO is reduced to morpholine [7].

Di(morpholin-4-yl)methanone (5). *a*. A solution of 20.0 g (0.4 mol) of sodium hydroxide in 30 mL of water was added dropwise to a mixture of 8.7 g (0.1 mol) of morpholine, 50 mL of chloroform, and 50 mL of 50% aqueous NMMO, heated to 50°C. The mixture was stirred for 1 h at 50°C, cooled, and treated with chloroform, and the extract was evaporated. Yield 3.5 g (35%), mp 143–145°C (from EtOAc); published data [8]: mp 142.2°C. IR spectrum: ν 1643 cm^{-1} (C=O). ^{1}H NMR spectrum, δ, ppm: 3.14–3.19 m (8H, CH_2), 3.55–3.69 m (8H, CH_2). ^{13}C NMR spectrum, δ_C, ppm: 46.60, 65.66, 162.38.

b. Following an analogous procedure, from 8.7 g (0.1 mol) of morpholine, 50 mL of chloroform, and 50 mL of 70% aqueous NMMO we obtained 5.5 g (55%) of **5** with mp 144–145°C.

Compounds **6**–**8** were synthesized in a similar way.

Di(piperidin-1-yl)methanone (6) was synthesized from 8.5 g (0.1 mol) of piperidine. Yield 2.2 g (22%),



1, **5**, R_2N = morpholin-4-yl; **2**, **6**, R_2N = piperidin-1-yl; **3**, **7**, R = Me; **4**, **8**, R = Et; NMMO stands for *N*-methylmorpholine *N*-oxide.

bp 130°C (1 mm), n_D^{20} = 1.5000; published data: bp 120–122°C (0.02 mm) [9], n_D^{28} = 1.5055 [10]. IR spectrum: ν 1650 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 1.48–1.63 m (12H, CH_2), 3.03–3.14 m [8H, $N(CH_2)_2$]. ^{13}C NMR spectrum, δ_C, ppm: 24.2, 25.1, 47.1, 163.2.

***N*,*N*,*N′*,*N′*-Tetramethylurea (7)** was synthesized from 50 mL of 40% aqueous dimethylamine. Yield 2.3 g (40%), bp 75–77°C (15 mm), n_D^{20} = 1.4500; published data: bp 63.5–64°C (12 mm) [11], n_D^{20} = 1.4495 [12]. IR spectrum: ν 1670 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 2.74 s (12H, CH_3). ^{13}C NMR spectrum, δ_C, ppm: 38.9, 95.46.

***N*,*N*,*N′*,*N′*-Tetraethylurea (8)** was synthesized from 50 mL of 25% aqueous diethylamine. Yield 2.1 g (25%), bp 70°C (1 mm), n_D^{20} = 1.4450; published data: bp 90–91°C (9 mm) [13], n_D^{25} = 1.4448 [14]. IR spectrum: ν 1675 cm^{-1} (C=O). ^1H NMR spectrum, δ, ppm: 1.07 m (12H, CH_3, J = 7.1 Hz), 3.09 q (8H, CH_2, J = 7.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 12.71, 41.54, 163.17.

The IR spectra were recorded on a Thermo Nicolet Nexus spectrometer from samples dispersed in mineral oil. The ^1H and ^{13}C NMR spectra were measured at 300 K on a Varian Mercury-300VX spectrometer at 300 and 75 MHz, respectively, using DMSO-d_6–CCl_4 (1 : 3) as solvent and tetramethylsilane as internal standard. The elemental analyses were obtained on a Eurovector EA 3000 analyzer.

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REFERENCES

1. Zakaryan, G.B., Hayotsyan, S.S., Attaryan, H.S., and Hasratyan, G.V., *Russ. J. Gen. Chem*., 2015, vol. 85, p. 1773.
2. Zakaryan, G.B., Hayotsyan, S.S., Attaryan, H.S., and Hasratyan, G.V., *Russ. J. Gen. Chem*., 2016, vol. 86, p. 1195.
3. Zakaryan, G.B., Hayotsyan, S.S., Ayvazyan, A.G., Tamazyan, R.A., Panosyan, H.G., Danagulyan, G.G., and Attaryan, H.S., *Chem. Heterocycl. Compd*., 2016, vol. 52, no. 4, p. 253.
4. Graefe, J., Frölich, I., and Mühlstädt, M., *Z. Chem.*, 1974, vol. 14, p. 434.
5. Makosza, M. and Kacprowicz, A., *Rocz. Chem*., 1975, vol. 49, p. 1627.
6. Gol'dberg, Yu.Sh. and Shimanovskaya, M.V., *Zh. Org. Khim*., 1982, vol. 18, p. 2036.
7. Shastri, L.A., Shastri, S.L., Bathula, Ch.D., Basanagouda, M., and Kulkazni, M.V., *Synth. Commun*., 2011, vol. 41, p. 476.
8. Mizuno, T., Nakai, T., and Mihara, N., *Synthesis*, 2010, no. 24, p. 4251.
9. Kantlehner, W., Maier, T., Loffler, W., and Kapassakalidis, J.J., *Justus Liebigs Ann. Chem*., 1982, p. 507.
10. Fenton, D.M., US Patent no. 3277061, 1966.
11. Paul, R.C., Johar, S.P., Banalt, J.S., and Narula, S.P., *J. Phys. Chem*., 1976, vol. 80, no. 4, p. 351.
12. Lawson, J.K. and Croom, J.A.T., *J. Org. Chem*., 1963, vol. 28, p. 232.
13. Kirkwood, M.W. and Wright, G.F., *Can. J. Chem*., 1957, vol. 35, p. 527.
14. Rosenfarb, J., Huffman, H.L.J., and Caruso, J.A., *J. Chem. Eng. Data*, 1976, vol. 21, no. 2, p. 150.