Reduction of the furoxan ring to the furazan ring in some carbonyl-substituted furoxans

A. S. Kulikov, N. N. Makhova, T. I. Godovikova, S. P. Golova, and L. I. Khmel'nitskii*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation. Fax: +7 (095) 135 5328

It was shown that the furoxan ring is efficiently reduced to the furazan ring in carbonyl-substituted furoxans with other functional groups by the action of the $SnCl_2$—HCl—AcOH system.

Key words: furazans, furoxans, reduction.

Previously we have studied some transformations of carbonyl-containing derivatives of furazans and furoxans involving a carbonyl-containing group (bromination,[1] nitrosation[2]) or a substituent at the C atom adjacent to the heterocycle (diazotization of the amino group[3]). In the present work the reduction of the furoxan ring to the furazan ring in carbonyl-substituted furoxans containing other functional groups was studied. The problem was set this way because furoxan derivatives are often more accessible than the corresponding furazan derivatives, and hence their reduction may be of interest from the synthetic viewpoint.

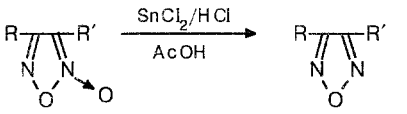
The reduction of the furoxan ring in aroylfuroxans to the furazan ring by treatment with the system $SnCl_2$—HCl—AcOH at 40—55 °C for 1—5 h has been described in the literature.[4,5] Only a few examples of transformations of carbonyl-substituted furoxans into furazans using toxic trialkylphosphites as reducing agents have been reported.[6,7]

We found that tin(II) chloride dissolved in a mixture of hydrochloric and acetic acids can be used instead of trialkylphosphites for reducing carbonyl-substituted furoxans (**1a—f**), but under somewhat different conditions than in the case of aroylfuroxans. The reaction conditions (reagent ratio, temperature, and reaction time) were selected using 4-acetyl-3-methylfuroxan (**1a**) as an example. The optimum ratio of the reducing agent and compound **1a** was found to be ~2 : 1, and the highest yield (74 %) of 4-acetyl-3-methylfurazan (**2a**) was reached in 48 h at ~20 °C. Both increasing the amount of the reducing agent and increasing the temperature result in a noticeable decrease in the yield of product **2a** and in its contamination with admixtures, which is probably related to an increased tendency of the furoxan ring to undergo deeper reduction by the action of $SnCl_2$, *e.g.*, to a glyoxime moiety.

We used similar conditions for reducing 3,4-diacetylfuroxan (**1b**) as well as 3-acetyl-, 3-ethoxycarbonyl-, 3-bromoacetyl-, and 3-azidocarbonyl-4-aminofuroxans (**1c—f**).

The following products of the reduction of compounds **1b—d** were obtained in preparative yields: 3,4-diacetylfurazan (**2b**), 4-amino-3-acetylfurazan (**2c**), and 4-amino-3-ethoxycarbonylfurazan (**2d**) (Scheme 1). A greater excess of the reductant (mole ratio ~4 : 1) was required for the reduction of carbonyl-substituted furoxans containing an amino group as the second substituent. Evidently, this resulted from the ability of $SnCl_2$ to form a complex with the amino group.[8]

Scheme 1



1a—d **2a—d** (40—74 %)

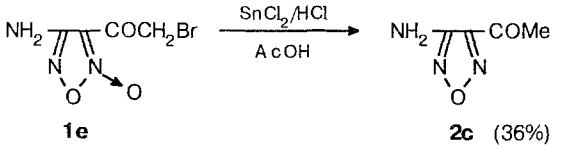
1a, 2a: R = COMe, R' = Me
1b, 2b: R = R' = COMe
1c, 2c: R = NH_2, R' = COMe
1d, 2d: R = NH_2, R' = COOEt

In the case of 4-amino-3-bromoacetylfuroxan (**1e**) one could expect not only reduction of the furoxan ring but also debromination of the bromoacetyl group. In fact, the reaction of **1e** with the $SnCl_2$—HCl—AcOH system under the conditions studied results in furazan **2c** in an only slightly lower yield than in the case of furoxan **1c** (Scheme 2). The reaction with azidocarbonylfuroxan **1f** initially results in reduction of the azidocarbonyl group to an amide group, which takes three to four minutes. The 4-amino-3-furoxancarboxa-

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 4, pp. 679—680, April, 1994.

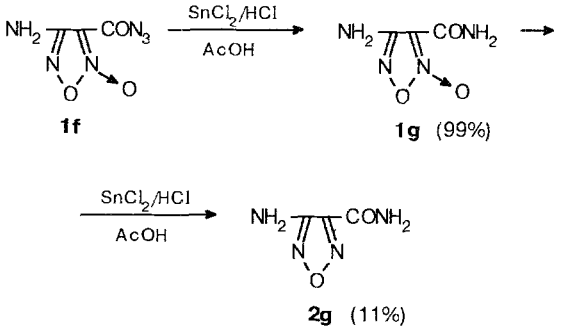
mide (**1g**) formed can be isolated in a practically quantitative yield. Keeping the reaction mixture for a longer time or reducing the previously isolated compound **1g** affords a product of the reduction of the furoxan ring, 4-amino-3-furazancarboxamide **2g**, in a low yield (Scheme 3).

Scheme 2



1e **2c** (36%)

Scheme 3



1f **1g** (99%)

2g (11%)

Experimental

^1H and ^{13}C NMR spectra (δ) were obtained in acetone-d_6 on a Bruker AM-300 instrument at operating frequencies of 300 and 75.5 MHz, respectively. The chemical shifts were measured against $SiMe_4$ as the internal standard. The reactions were monitored by ^1H NMR spectral data. The reducing solution was prepared by dissolving $SnCl_2 \cdot 2H_2O$ (22.6 g) in a mixture of acetic anhydride (20 mL), acetic acid (100 mL), and hydrochloric acid (20 mL); 10 mL of the solution thus obtained contained 7 mmol of the reductant.

3-Acetyl-4-methylfurazan (2a). The solution of the reductant (30 mL) was added dropwise with stirring at a temperature no higher than 20—22 °C to a solution of furoxan **1a** (1.42 g, 10 mmol) in AcOH (4 mL). The reaction mixture was kept for 48 h with intermittent stirring, diluted with an equal amount of water, and extracted with $CHCl_3$ (4×40 mL). The extracts were washed with dilute HCl (1 : 1; 20 mL) and water (3×20 mL) until the solution no longer evolved CO_2 on treatment with a Na_2CO_3 solution. The extracts were dried with $MgSO_4$, and the solvent was distilled off under reduced pressure to give 0.93 g (74 %) of furazan **2a** as a colorless liquid. ^1H NMR: 2.6 (s, $COCH_3$), 2.7 (s, CH_3) (coincides with the spectrum of compound **2a** obtained by the procedure in Ref. 9). The reaction requires 4 h at 30—35 °C; the yield of product **2a** is 32 %. When a twofold amount of the reductant is used, the reaction takes 18 h at 20 °C, and the yield of **2a** is 47 %.

3,4-Diacetylfurazan (2b). In a similar way, 1.11 g of furazan **2b**, b.p. 56—58 °C at 7—8 Torr, was obtained from furoxan **1b** (1.70 g, 10 mmol). ^1H NMR: 2.71 (s, CH_3) (*cf.* Ref. 7: 2.71). ^{13}C NMR: 30.00 (CH_3), 153.03 (C_{cycle}), 190.19 (CO).

4-Amino-3-acetylfurazan (2c). ***a.*** In a similar way, the reaction starting from furoxan **1c** (1.43 g, 10 mmol) and 60 mL (42 mmol) of the reducing solution gave 0.52 g (42 %) of furazan **2c** as colorless crystals, m.p. 96 °C (water) (*cf.* Ref. 10: 96—97 °C). ***b.*** Similarly, the reaction starting from furoxan **1e** (2.22 g) and 120 mL of the reducing solution gave 0.46 g (36 %) of product **2c**, m.p. 96 °C (water).

4-Amino-3-ethoxycarbonylfurazan (2d). Similarly, the reaction starting from furoxan **1d** (1.73 g, 10 mmol) and 60 mL of the reducing solution gave 0.63 g (40 %) of furazan **2d** as colorless crystals, m.p. 101—102 °C (*cf.* Ref. 11: 100—103 °C).

4-Amino-3-aminocarbonylfuroxan (1g). The reducing solution (30 mL) was added dropwise at <20 °C to a solution of furoxan **1f** (1.70 g, 10 mmol) in AcOH (4 mL). When gas evolution was completed, the reaction mixture was diluted with water, and the precipitate was filtered off, washed with cold water, and dried in the air to give 1.42 g (99 %) of furoxan **1g** as colorless crystals, m.p. 203—205 °C (*cf.* Ref. 12: 205 °C). ^1H NMR: 6.47 (s, NH_2), 7.66 s and 8.37 s (NH_2CO). ^{13}C NMR: 104.91 ($C(3)_{cycle}$), 157.54 ($C(4)_{cycle}$), 157.86 (CO).

4-Amino-3-aminocarbonylfurazan (2g) was obtained similarly to compound **2a** from 4-amino-3-azidocarbonylfuroxan **1f** (1.70 g, 10mmol) and 120 mL of the reducing solution (or from furoxan **1g** (1.44 g, 10 mmol) and 90 mL of the reducing solution). Furazan **2g** (0.14 g, 11 %, colorless crystals) was isolated by repeated extraction with chloroform. M.p. 173—175 °C (water) (*cf.* Ref. 11: 174—177 °C).

References

1. A. B. Sheremetev, A. S. Kulikov, and L. I. Khmel'nitskii, *Izv. Akad. Nauk, Ser. Khim.*, 1993, 744 [*Russ. Chem. Bull.*, 1993, **42**, 708 (Engl. Transl.)].
2. A. S. Kulikov, N. N. Makhova, and L. I. Khmel'nitskii, *Izv. Akad. Nauk, Ser. Khim.*, 1994, 485 [*Russ. Chem. Bull.*, 1994, **43**, 445 (Engl. Transl.)].
3. O. A. Rakitin, O. A. Zalesova, A. S. Kulikov, N. N. Makhova, T. I. Godovikova, and L. I. Khmel'nitskii, *Izv. Akad. Nauk, Ser. Khim.*, 1993, 1949 [*Russ. Chem. Bull.*, 1993, **42** (Engl. Transl.)].
4. I. de Paolini, *Gazz. Chim. Ital.*, 1927, **57**, 656.
5. H. Tondys and L. Lange, *Rocz. Chem.*, 1977, **51**, 1531.
6. C. Grundmann, *Chem. Ber.*, 1964, **97**, 575.
7. L. I. Peterson and E. G. Britton, *Tetrahedron Lett.*, 1966, **16**, 1727.
8. I. I. Chernyaev, N. N. Zheligovskaya, and T. N. Leonova, *Zh. Neorg. Khim.*, 1964, **9**, 347 [*J. Inorg. Chem. USSR*,1964, **9** (Engl. Transl.)].
9. G. Ponzio and G. Ruggeri, *Gazz. Chim. Ital.*, 1922, **52**, 289.
10. G. Ponzio and G. Bertini, *Gazz. Chim. Ital.*, 1931, **61**, 51.
11. T. Ichikawa, T. Kato, and T.Kakenishi, *J. Heterocycl. Chem.*, 1965, **2**, 253.
12. G. Tennant and G. M. Wallace, *J. Chem. Soc. Chem. Commun.*, 1982, 267.

Received June 21, 1993