ISSN 1070-4280, Russian Journal of Organic Chemistry, 2006, Vol. 42, No. 9, pp. 1360–1363. © Pleiades Publishing, Inc., 2006.
Original Russian Text © A.S. Ermakov, E.Yu. Petrov, D.B. Vinogradov, 2006, published in Zhurnal Organicheskoi Khimii, 2006, Vol. 42, No. 9, pp. 1377–1379.

Nucleophilic Reactions in the *N*-Nitrooxazolidine Series

A. S. Ermakov, E. Yu. Petrov, and D. B. Vinogradov

Zelinskii Institute of Organic Chemistry, Russian Academy of Sciences, Leninskii pr. 47, Moscow, 117913 Russia
e-mail: secretary@ioc.as.ru

Received November 9, 2004

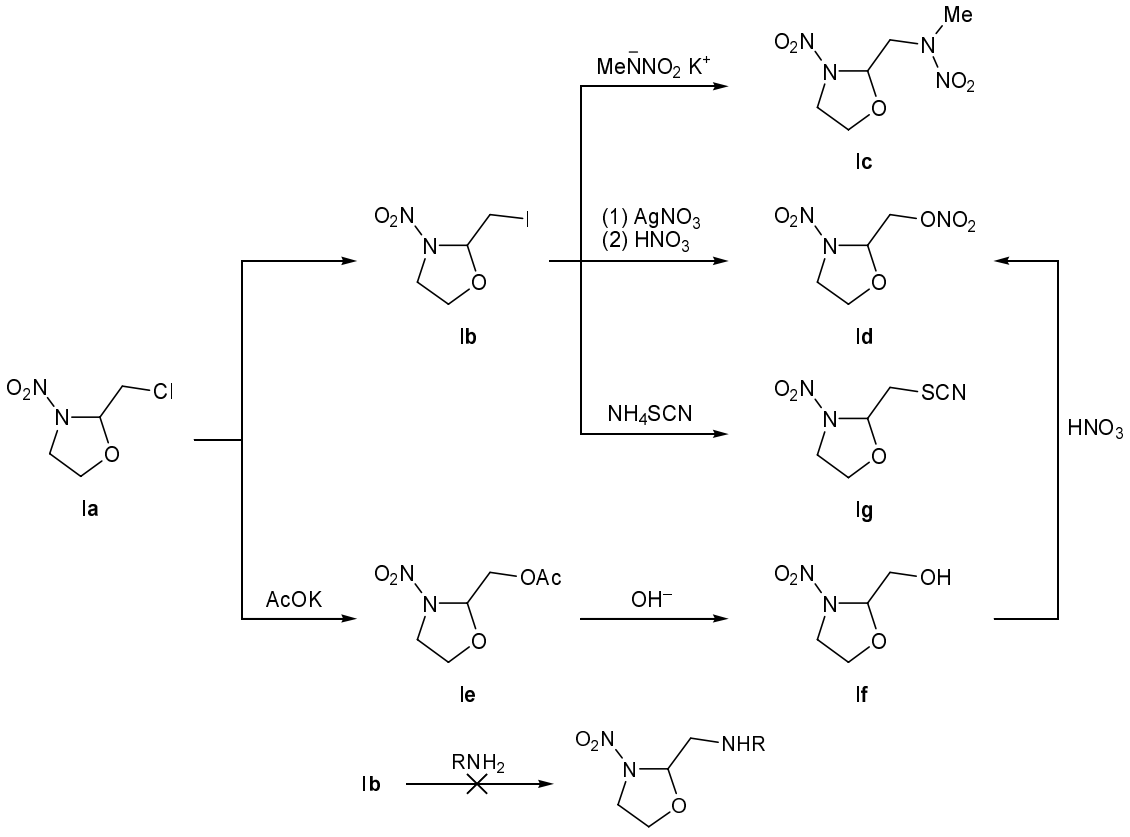
Abstract—A number of new 2- and 5-substituted *N*-nitrooxazolidines were synthesized by nucleophilic replacement in 2- and 5-halomethyl-*N*-nitrooxazolidines.

DOI: 10.1134/S1070428006090181

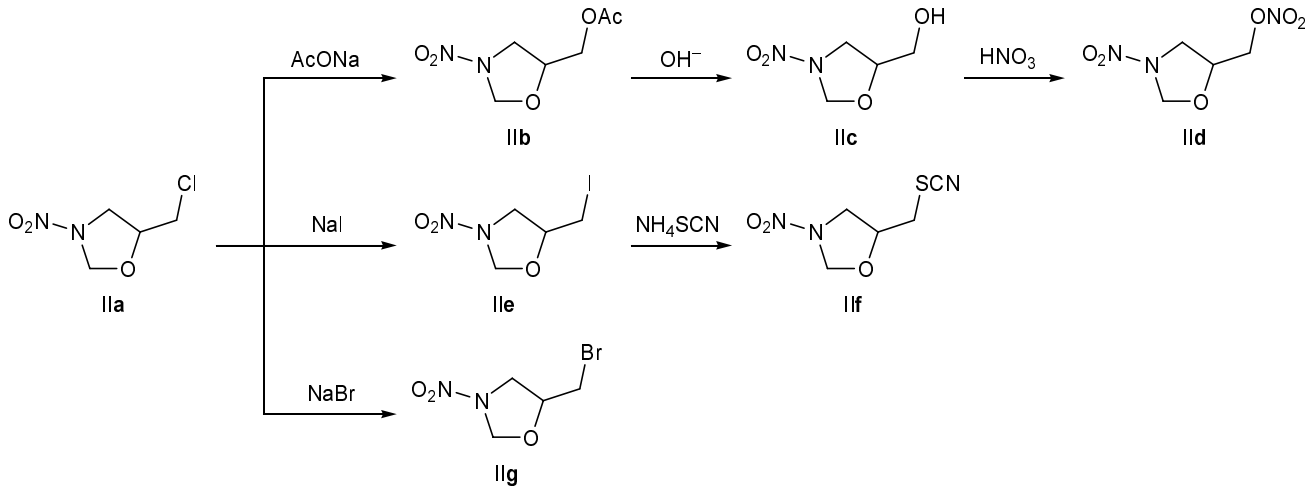
The present work continues our systematic studies in the field of synthesis and chemical properties of differently substituted *N*-nitrooxazolidines [1–3]. Using 5-chloromethyl- and 5-iodomethyl-*N*-nitrooxazolidines as starting compounds we previously synthesized new 5-substituted *N*-nitrooxazolidines having such substituents as nitrooxy, *N*-nitro(alkyl)amino, and some other groups. It seemed to be reasonable to extend the developed approaches to 2-substituted *N*-nitrooxazolidines.

2-Iodomethyl-*N*-nitrooxazolidine (**Ib**) prepared previously [3] from 2-chloromethyl-*N*-nitrooxazolidine (**Ia**) reacted with *N*-nitromethanamine potassium salt to give ~30% of *N*-methyl-*N*-nitro-1-(3-nitro-1,3-oxazolidin-2-yl)methanamine (**Ic**) (Scheme 1). However, an attempt to obtain homologs of **Ic** via replacement of the halogen atom in **Ib** by alkylamino group and subsequent nitration was unsuccessful: the initial compound decomposed even in the first step. Accord-

Scheme 1.



Scheme 2.



ing to the scheme developed in [2], we synthesized 3-nitrooxazolidin-2-ylmethyl nitrate (**Id**) by nucleophilic substitution of the iodine atom in **Ib** by the action of silver nitrate. The ^{1}H NMR data showed that the reaction gave a mixture of the corresponding nitrooxy and nitrosooxy derivatives [δ, ppm: 3.76 m (1H, $NCH_2C\mathbf{H}_2O$), 4.18 m (1H, $NCH_2C\mathbf{H}_2O$, 2H, $NC\mathbf{H}_2CH_2O$), 4.42 d (2H, CH_2ONO), 5.67 t (1H, NCH)]; this mixture was then treated with HNO_3 to give compound **Id** in an overall yield of ~60%. A considerable drawback of this procedure is the use of expensive $AgNO_3$. Therefore, we tried to obtain nitrooxy compound **Id** in another way, by direct nitration of iodomethyl derivative **Ib**. In this case, the target product was isolated in 78% yield, but it was quite difficult to purify it from concomitant decomposition products. One more possible synthetic route to nitrooxy compound **Id** included preparation of acetoxy derivative **Ie**, its hydrolysis to alcohol **If**, and nitration of the 2-hydroxymethyloxazolidine **If** (Scheme 1). In such a way, we succeeded in isolating compound **Id** in ~80% yield.

Taking into account that the latter procedure for the synthesis of 3-nitrooxazolidin-2-ylmethyl nitrate (**Id**) is more practical, it was extended to 5-substituted *N*-nitrooxazolidines. 5-Chloromethyl-3-nitrooxazolidine (**IIa**) [1] was thus converted into acetoxy derivative **IIb** which was hydrolyzed to 5-hydroxymethyl-3-nitrooxazolidine (**IIc**), and nitration of **IIc** gave 3-nitrooxazolidin-5-ylmethyl nitrate (**IId**) (Scheme 2). In addition, by reactions of iodomethyl derivatives **Ib** and **IIe** with ammonium thiocyanate we synthesized thiocyanatomethyl-substituted 3-nitrooxazolidines **Ig** and **IIf**, respectively.

Thus we have developed convenient procedures for the synthesis of a series of functionalized *N*-nitrooxazolidines from 2- and 5-chloromethyl-*N*-nitrooxazolidines.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on Bruker AC-300 (300.13 MHz) and Bruker WM-500 (500.08 MHz) spectrometers using DMSO-d_6 as solvent and hexamethyldisiloxane as internal reference.

***N*-Nitro-*N*-(3-nitrooxazolidin-2-ylmethyl)-methanamine (Ic).** *N*-Nitromethanamine, 0.56 g (7.40 mmol), was added to a solution of 1.29 g (6.74 mmol) of 2-iodomethyl-3-nitrooxazolidine (**Ib**) and 0.79 g (7.42 mmol) of Na_2CO_3 in 15 ml of DMF. The mixture was heated for 8 h at 70–75°C under stirring, poured into 40 ml of water, and extracted with benzene (3×15 ml). The extract was washed with water (7×15 ml) and evaporated under reduced pressure, and the residue was recrystallized from ethanol. Yield 0.43 g (31%), mp 113–115°C. ^{1}H NMR spectrum, δ, ppm: 3.40 s (3H, CH_3N), 3.75 m (1H, CH_2O), 4.20 m (5H, CH_2O, $NC\mathbf{H}_2CH_2O$, $CHC\mathbf{H}_2N$), 5.75 t (1H, NCHO, J = 4.4 Hz). Found, %: C 29.40; H 4.99; N 27.11. $C_5H_{10}N_4O_5$. Calculated, %: C 29.13; H 4.89; N 27.18.

3-Nitrooxazolidin-2-ylmethyl nitrate (Id). *a*. Silver nitrate, 1.40 g (14.0 mmol), was added to a solution of 2.39 g (9.26 mmol) of compound **Ib** in 7 ml of DMF, and the mixture was stirred for 1 h at 75–80°C. The mixture was then filtered from the precipitate of AgI, and the filtrate was poured into 11 ml of water and extracted with benzene (4×8 ml). The extract was

washed with water (7×10 ml) and evaporated under reduced pressure to obtain 1.22 g of a mixture of 2-nitrosooxymethyl and 2-nitrooxymethyl derivatives. This mixture was dissolved in 8 ml of 98% HNO_3 at –30 to –35°C, and the mixture was stirred for 8 min, poured into 50 ml of an ice–water mixture, and extracted with ethyl acetate (3×12 ml). The extract was washed with water and an aqueous solution of sodium carbonate and evaporated under reduced pressure. Yield of **Id** 1.07 g (60%). ^{1}H NMR spectrum, δ, ppm: 3.76 m (1H, CH_2O), 4.18 m (3H, NCH_2, CH_2O), 4.82 d (2H, CH_2ONO_2), 5.76 t (1H, NCHO). Found, %: C 25.03; H 3.74; N 21.23. $C_4H_7N_3O_6$. Calculated, %: C 24.88; H 3.65; N 21.76.

b. 2-Iodomethyl-3-nitrooxazolidine (**Ib**), 0.58 g (2.25 mmol), was added to a mixture of 9 ml of 98% HNO_3 and 1 ml of $CHCl_3$ at –30 to –35°C, and the mixture was stirred for 1 h at that temperature, poured into 50 ml of water containing ice and 8.5 g of NaOH, and extracted with ethyl acetate (3×15 ml). The extract was washed with water and evaporated to isolate 0.35 g (78%) of compound **Id**.

c. A solution of 0.37 g (2.50 mmol) of 3-nitrooxazolidin-2-ylmethanol (**If**) in 1.5 ml of chloroform was added at –25 to –30°C to a mixture of 8 ml of 98% HNO_3 and 2 ml of acetic anhydride. The mixture was stirred for 10 min at –25 to –30°C, poured into 40 ml of an ice–water mixture, and extracted with ethyl acetate (3×20 ml). The extract was washed with water and evaporated under reduced pressure to isolate 0.36 g (76%) of compound **Id**.

3-Nitrooxazolidin-5-ylmethyl nitrate (IId) was synthesized in a similar way. Yield 88%. ^{1}H NMR spectrum, δ, ppm: 3.78 d.d (1H, NC**H**$_2$CH, J = –13.0, 8.1 Hz), 4.15 d.d (1H, NC**H**$_2$CH, J = –13.0, 8.1 Hz), 4.65 m (1H, CHO), 4.73 d.d (1H, CH_2ONO_2, J = –16.7, 5.7 Hz), 4.82 d.d (1H, CH_2ONO_2, J = –13.0, 2.8 Hz), 5.18 d (1H, NCH_2O, J = –6.5 Hz), 5.38 d (1H, NCH_2O, J = –6.5 Hz). The ^{1}H NMR spectrum of **IId** was similar to that reported in [2].

3-Nitro-2-thiocyanatomethyloxazolidine (Ig). Ammonium thiocyanate, 0.79 g (10.40 mmol), was added to a solution of 1.0 g (5.22 mmol) of 2-iodomethyl-3-nitrooxazolidine (**Ib**) in 8 ml of DMF, and the mixture was stirred for 6 h at 75–80°C, poured into 20 ml of water, and extracted with benzene (5×10 ml). The extract was washed with water (5×10 ml) and evaporated under reduced pressure, and the residue was recrystallized from ethanol. Yield 0.55 g (75%), mp 101–101.5°C. ^{1}H NMR spectrum, δ, ppm: 3.58 d (2H, CH_2SCN), 3.80 m (1H, CH_2O), 4.22 m (3H, CH_2O, NCH_2), 5.75 t (1H, NCH). Found, %: C 31.72; H 3.71; N 22.38. $C_5H_7N_3O_3S$. Calculated, %: C 31.74; H 3.73; N 22.21.

3-Nitro-5-thiocyanatomethyloxazolidine (IIf) was synthesized in a similar way. Yield 75%. ^{1}H NMR spectrum, δ, ppm: 3.36 d.d (1H, CH_2SCN, J = –13.0, 7.4 Hz), 3.47 d.d (1H, CH_2SCN, J = –13.0, 3.7 Hz), 3.73 d.d (1H, NC**H**$_2$CH, J = –13.0, 7.4 Hz), 4.17 d.d (1H, NC**H**$_2$CH, J = –13.0, 7.4 Hz), 4.58 m (1H, CHO), 5.18 d (1H, NCH_2O, J = –5.6 Hz), 5.38 d (1H, NCH_2O, J = –5.6 Hz). Found, %: C 31.66; H 3.69; N 22.32. $C_5H_7N_3O_3S$. Calculated, %: C 31.74; H 3.73; N 22.21.

3-Nitrooxazolidin-2-ylmethyl acetate (Ie). Potassium acetate, 20.58 g (210 mmol), was added to a solution of 7.0 g (42.04 mmol) of 2-chloromethyl-3-nitrooxazolidine (**Ia**) in 45 ml of DMF. The mixture was stirred for 30 h at 95–97°C, poured into 90 ml of water, and extracted with benzene (3×60 ml). The extract was washed with water (5×20 ml) and evaporated under reduced pressure. The residue was purified by fractional distillation, a fraction boiling at 105–106°C (0.5–0.7 mm) being collected. Yield 4.06 g (51%). ^{1}H NMR spectrum, δ, ppm: 2.60 s (3H, CH_3COO), 3.75 m (1H, CH_2O), 4.13 m (3H, CH_2O, NCH_2), 4.30 d.d (2H, CHC**H**$_2$O, J = –11.2, 4.5 Hz), 5.63 t (1H, NCH, J = 3.3 Hz). Found, %: C 37.72; H 5.50; N 14.93. $C_6H_{10}N_2O_5$. Calculated, %: C 37.90; H 5.30; N 14.73.

3-Nitrooxazolidin-5-ylmethyl acetate (IIb) was synthesized in a similar way. Yield 56%, bp 130–131°C (0.9–1.1 mm). ^{1}H NMR spectrum, δ, ppm: 2.20 s (3H, CH_3COO), 3.72 d.d (1H, NC**H**$_2$CH, J = –11.2, 7.8 Hz), 4.08 d.d (1H, NC**H**$_2$CH, J = –11.2, 7.8 Hz), 4.20 d.d (2H, CHC**H**$_2$O, J = –11.2, 5.6 Hz), 4.52 m (1H, CHO), 5.21 d (1H, NCH_2O, J = –5.7 Hz), 5.40 d (1H, NCH_2O, J = –5.7 Hz). Found, %: C 38.26; H 5.60; N 14.75. $C_6H_{10}N_2O_5$. Calculated, %: C 37.90; H 5.30; N 14.73.

3-Nitrooxazolidin-2-ylmethanol (If). A solution of 0.25 g (6.25 mmol) of sodium hydroxide in 5 ml of water was added to a solution of 1.0 g (5.26 mmol) of acetoxy derivative **Ie** in 4 ml of methanol, and the mixture was heated for 1 h at ~50°C. The mixture was then neutralized with dilute hydrochloric acid and evaporated under reduced pressure, the residue was extracted with acetone (3×10 ml), and the extract was evaporated under reduced pressure. Yield 0.68 g (88%). ^{1}H NMR spectrum, δ, ppm: 3.81 m (3H, NC**H**$_2$$CH_2O$,

CHC**H**$_2$O), 4.10–4.30 m (4H, NCH$_2$C**H**$_2$O, NC**H**$_2$-CH$_2$O, OH), 5.50 t (1H, NCH). Found, %: C 32.69; H 5.80; N 18.74. $C_4H_8N_2O_4$. Calculated, %: C 32.44; H 5.44; N 18.91.

3-Nitrooxazolidin-5-ylmethanol (IIc) was synthesized in a similar way. Yield 91%. ^{1}H NMR spectrum, δ, ppm: 3.57 d.d (1H, C**H**$_2$OH, J = –11.2, 5.6 Hz), 3.72 d.d (1H, NC**H**$_2$CH, J = –11.2, 7.8 Hz), 3.98 d.d (1H, NC**H**$_2$CH, J = –11.2, 7.8 Hz), 4.32 m (1H, CHO), 4.95 t (1H, OH, J = 5.6 Hz), 5.10 d (1H, NCH$_2$O, J = –5.6 Hz), 5.37 d (1H, NCH$_2$O, J = –5.6 Hz). Found, %: C 32.44; H 6.07; N 18.36. $C_4H_8N_2O_4$. Calculated, %: C 32.44; H 5.44; N 18.91.

5-Bromomethyl-3-nitrooxazolidine (IIg). Sodium bromide, 6.5 g (63.17 mmol), was added to a solution of 2.63 g (15.8 mmol) of 5-chloromethyl-3-nitrooxazolidine (**IIa**) in 40 ml of DMF. The mixture was heated for 37 h at 85–90°C under stirring, poured into 120 ml of water, and extracted with benzene (4× 25 ml). The extract was washed with water (7×30 ml) and evaporated under reduced pressure, and the residue was purified by fractional vacuum distillation, a fraction boiling at 105–107°C (0.9–1.1 mm) being collected. Yield 2.53 g (76%). ^{1}H NMR spectrum, δ, ppm: 3.73 d.d (2H, CH$_2$Br, J = –11.9, 5.2 Hz), 3.87 d.d (1H, NC**H**$_2$CH, J = –11.6, 7.0 Hz), 4.21 d.d (1H, NC**H**$_2$CH, J = –11.9, 6.7 Hz), 4.63 m (1H, CHO), 5.22 d (1H, NCH$_2$O, J = –5.8 Hz), 5.48 d (1H, NCH$_2$O, J = –5.8 Hz). Found, %: N 13.54. $C_4H_7N_2O_3Br$. Calculated, %: N 13.28.

REFERENCES

1. Tartakovskii, V.A., Ermakov, A.S., Strelenko, Yu.A., Vinogradov, D.B., and Serkov, S.A., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2001, p. 872.
2. Tartakovskii, V.A., Ermakov, A.S., and Vinogradov, D.B., *Russ. J. Org. Chem*., 2002, vol. 38, p. 1339.
3. Ermakov, A.S., Petrov, E.Yu., Strelemko, Yu.A., Vinogradov, D.B., and Tartakovskii, V.A., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1196.