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New access to azido-substituted alkylnitramines

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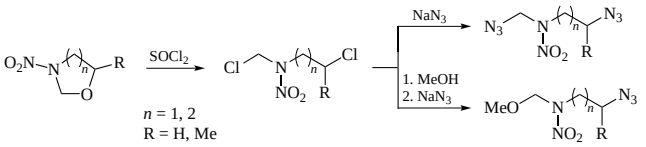
A new versatile access to azido-substituted *N*-alkylnitramines is based on ring opening in *N*-nitrooxazolidines and *N*-nitroperhydro-1,3-oxazines with thionyl chloride followed by treatment with sodium azide. Representative *N*,*N*-bis(azidoalkyl)- and *N*-azidoalkyl-*N*-methoxymethyl-containing nitramines were synthesized and characterized.

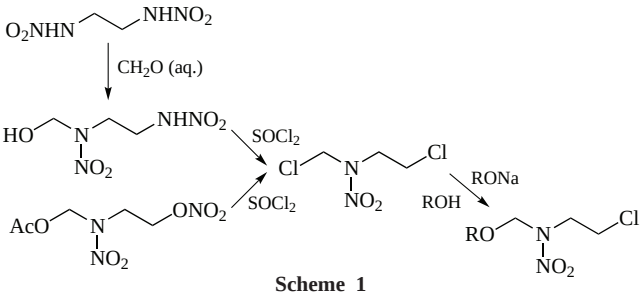


Keywords: *N*-nitrooxazolidine, *N*-nitroperhydro-1,3-oxazine, nitramine, azides, thionyl chloride, chlorination, α,ω-dichloro-2-nitro-2-azaalkanes, azidation, phase transfer catalyst.

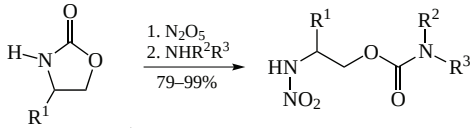
Compounds containing nitramino and azido functional groups belong to energetic compounds, and methods for their synthesis are extensively studied.[1,2] This article suggests a new versatile access to azido-substituted *N*-alkylnitramines. Two documented approaches for synthesizing 1,4-dichloro-2-nitro-2-azabutane comprise reaction of thionyl chloride with monomethylol derivative of ethylenedinitramine[3] or 1-acetoxy-2-nitro-4-nitroxy-2-azabutane.[4] Further chemoselective nucleophilic replacement of one chlorine atom by alkoxy group (possible in activated $ClCH_2N$ fragment) was performed by treatment with the corresponding sodium alcoholate (Scheme 1). However, these multistage methods were not sufficiently selective, and the complicated isolation of target compounds did not provide good yields. In addition, only one available representative of α,ω-dichloro-2-nitro-2-azaalkanes was processed using this method.

Previously,[5] we developed a general method for synthesizing a wide range of functionalized *N*-nitrooxazolidines and *N*-nitroperhydro-1,3-oxazines. Further studies of their properties made it possible to employ them as intermediates in the synthesis of new chemotypes of functionally substituted *N*-nitramines. An example of obtaining substituted *N*-alkylnitramines by opening O,N-heterocycles was documented.[6] In that study,[6] cyclic urethanes of 1,3-oxazolidin-2-one series under the action of nitrogen pentoxide underwent ring opening to give products in high yields. In that reacion, an electrophilic attack of nitronium cation at the nitrogen atom occurred followed by ring opening and the formation of a primary nitramine group (Scheme 2).

In this work that is the part of a systematic study, we present a convenient synthesis of 1,4-dichloro-2-nitro-2-azabutanes and

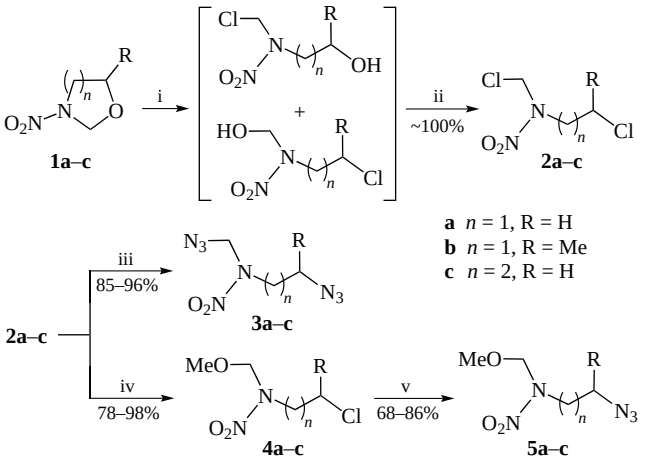


Scheme 1



Scheme 2

1,5-dichloro-2-nitro-2-azapentane by the reaction of *N*-nitrooxazolidines or *N*-nitroperhydro-1,3-oxazine with thionyl chloride. Herein, the nitramine functional group is already present in the initial cycle, so we considered the oxygen atom of the cycle as the center of further functionalization. At the first stage, we thoroughly studied the dichlorination of compounds **1a**–**c** with ring opening in the presence of thionyl chloride (Scheme 3). It should be noted that for the reaction to occur more efficiently, water (× 1–0.9 of the amount equimolar to the initial reactant) was added preliminarily to the excess of thionyl chloride. Upon this operation, a sufficient amount of acids



Scheme 3 *Reagents and conditions*: i, $SOCl_2/H_2O/DMF/BF_3{\cdot}Et_2O$, room temperature, 12 h; ii, $SOCl_2/H_2O/DMF/BF_3{\cdot}Et_2O$, reflux, 25 h; iii, $NaN_3/CaCl_2/DMF$, 95–100 °C, 33 h (for **3a**), 90–95 °C, 15 h (for **3b**,**c**); iv, MeOH, reflux, 3 h (for **4a**,**c**), 20 h (for **4b**); v, $NaN_3/Bu_4NBr/H_2O$, reflux, 12 h (for **3a**,**c**), 35 h (for **3b**).

(hydrogen chloride, chlorosulfinic acid) generated in the reaction mixture were responsible for the initial step of the reaction, namely, protonation of the oxygen atom followed by ring opening. Alternatively, in the medium of pure thionyl chloride, the reaction time required for full transformation was elongated to *ca*. 50 h thus causing decrease in the yield of the product and formation of impurities.

At this stage, both isomeric ω-chloro-α-hydroxy- and α-chloro-ω-hydroxy-2-nitro-2-azaalkanes were initially formed. They were further chlorinated at the hydroxy groups, as was shown by ^{1}H NMR monitoring of the reaction course with compound **1a** as an example. Then, with an increase in the reaction time, the products of ring opening were exhaustively chlorinated with thionyl chloride to give the target α,ω-dichloro-2-nitro-2-azaalkanes **2a**–**c** in nearly quantitative yields (see Scheme 3, steps i, ii). Compounds of type **2a**–**c** seem to be challenging synthons for the preparation of a bunch of promising polyfunctionalized *N*-alkylnitramines. Further functionalization at their chlorine atoms by treatment with NaN_3 in DMF afforded the corresponding α,ω-diazido derivatives **3a**–**c** in high yields (step iii).

It should be noted that the chlorine atoms at position 1 of compounds **2a**–**c** exhibited very high reactivity in the nucleophilic displacement by an azido group, and this reaction was completed within 1 h (^{1}H NMR monitoring). In contrast, the rate of replacement of remote chlorine atoms varied markedly depending on the substrate, most likely due to their lower activity and the steric factor, which is of major importance in this case. Considering the discrimination in chemical behavior of the two chlorine atoms in compounds **2a**–**c**, we thought of possibility for their bisfunctionalization. It is known[7,8] that chlorine atoms α-positioned in respect to nitramino group react with alcohols to form an ether group with elimination of hydrogen chloride. In this way, chloro ethers **4a**–**c** were selectively obtained by methanolysis of compounds **2a**–**c** (see Scheme 3, step iv). In these reactions, the reactivity of α-positioned chlorine atoms was observed in the sequence **2a** ≈ **2c** ≫ **2b**, which may be explained by the difference between activating effects of *N*-2-chloroethylnitramino, *N*-3-chloropropylnitramino and *N*-2-chloropropylnitramino groups. The presence of less reactive chlorine atoms at positions 4 or 5 makes it possible to further functionalize compounds **4a**–**c** by azidation. Since these chlorine atoms are much more hydrolytically stable than at position 1, their substitution in aqueous medium in the presence of a phase transfer catalyst (Bu_4NBr) became possible, which simplified the process significantly. In this way, *N*-azidoalkyl-*N*-(methoxymethyl)nitramines **5a**–**c** were synthesized in high yields (see Scheme 3, step v). In these reactions, the chlorine atoms in compounds **4a**–**c** were also replaced with an azido group at different rates (**4a** ≈ **4c** > **4b**) presumably due to steric factors.

To sum up, based on compounds of *N*-nitrooxazolidine and *N*-nitroperhydro-1,3-oxazine series, a convenient general method for the synthesis of a wide range of α,ω-dichloro-2-nitro-2-azaalkanes was suggested. As these compounds were polyfunctional, they were used as synthons to obtain a bunch of functionally substituted *N*-alkylnitramines. As a result, a series of *N*,*N*-bis(azidoalkyl)- and *N*-alkoxymethyl-*N*-(azidoalkyl)-nitramines were synthesized. These alkylnitramine azido derivatives have either satisfactory or high thermal stability and, due to the combination of their physicochemical properties (Table 1), they can be used as energetic compounds for various purposes.

Table 1 The properties of functionalized *N*-alkylnitramines.

Compound	bp/ °C (Torr)	T_{dec}[a]/ °C	ΔH_f (calc.)/ kcal mol^{-1}	Hydrogen content (%)	Ω[b] (%)
2a	62.5 (0.29)[c]	–	n.d.	n.d.	–
2b	52.5 (0.20)	–	n.d.	n.d.	–
2c	84.0 (0.33)	–	n.d.	n.d.	–
3a	–	151	138.5	3.25	–60.2
3b	–	158	131.5	4.03	–79.9
3c	–	163	130.0	4.03	–79.9
4a	75.0 (0.70)	–	n.d.	n.d.	–
4b	72.5 (0.64)	–	n.d.	n.d.	–
4c	89.5 (0.59)	–	n.d.	n.d.	–
5a	–	213	36.5	5.18	–86.8
5b	–	187	29.5	5.86	–105.7
5c	–	202	28.0	5.86	–105.7

[a] Stuart SMP-10 instrument (2 K min^{-1}). [b] Oxygen balance based on CO_2, for compounds $C_aH_bN_cO_d$, Ω (%) = 1600 × (d – 2a – b/2)/MW (MW is molecular weight). [c] 115 °C (7 Torr),[9] 105 °C (3 Torr).[10]

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2021.11.008.

References

1 V. M. Zinov'ev, G. V. Kutsenko and A. S. Ermilov, *Sovremennye i perspektivnye vysokoenergeticheskie komponenty smesevykh i ballisticheskikh tverdykh raketnykh topliv* (*Modern and Prospective High-Energetic Components of Composite and Ballistic Solid Propellants)*, PGTU publishing, Perm, 2010 (in Russian).
2 R. L. Simmons, in *25th International Annual Conference of ICT 'Thermochemistry of NENA Plasticizers'*, Karlsruhe, Germany, 1994, pp. 1–10.
3 V. P. Ivshin, M. S. Komelin and N. P. Belik, *J. Org. Chem. USSR*, 1980, **16**, 1006 (*Zh. Org. Khim*., 1980, **16**, 1166).
4 G. A. Marchenko, L. N. Punegova, T. S. Shitova, N. A. Roman'ko, L. S. Egorova and Yu. M. Kargin, *J. Org. Chem. USSR*, 1986, **22**, 33 (*Zh. Org. Khim*., 1986, **22**, 40).
5 V. A. Tartakovsky, A. S. Ermakov, Yu. A. Strelenko, D. B. Vinogradov and S. A. Serkov, *Russ. Chem. Bull., Int. Ed*., 2001, **50**, 911 (*Izv. Akad. Nauk, Ser. Khim.*, 2001, 872).
6 S. S. Arabadzhi, M. N. Zharkov, I. V. Kuchurov and S. G. Zlotin, *Synthesis*, 2020, **52**, 3485.
7 E. F. Witucki, E. R. Wilson, J. E. Flanagan and M. B. Frankel, *J. Chem. Eng. Data*, 1983, **28**, 285.
8 B. Unterhalt and F. Leiblein, *Arch. Pharm.*, 1978, **311**, 879.

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