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Dipropargyl ethers possessing nitramine units

Pavel S. Gribov,[a] Tat'yana S. Kon'kova,[b] Kyrill Yu. Suponitsky[a] and Aleksei B. Sheremetev*[a]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: sab@ioc.ac.ru*
[b] *N. N. Semenov Federal Research Center for Chemical Physics, Russian Academy of Sciences, 119991 Moscow, Russian Federation*

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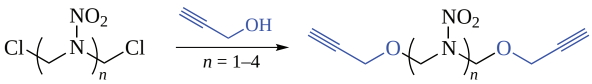
The syntheses and characterization of novel propargyl ethers of *N*-(hydroxymethyl)nitramines that contain from one to four nitramine units are reported. All nitramine-functionalized ethers were well characterized by IR and multinuclear NMR spectroscopy as well as CHN analysis, and the X-ray crystal structures of two of them are described. For ethers bearing two or three nitramine units, the standard molar enthalpies of formation at 298.15 K were determined from the experimental standard molar energies of combustion in oxygen measured by static bomb combustion calorimetry.



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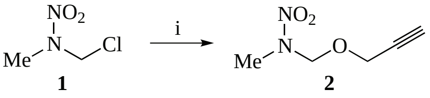
Propargyl ethers are useful synthons for the construction of polyfunctional compounds and diverse heterocycles,[1] whereas dipropargyl ethers are valuable comonomers[2–6] and curing agents[7,8] (for example, through azide−alkyne cycloaddition with the formation of a 1,2,3-triazole ring) for polymer chemistry. Despite the fact that the chemistry of structurally diverse propargyl ethers has achieved significant success, up to date only three their nitramine derivatives have been reported,[9–11] and all have not been fully characterized. Because of our interest in polyfunctional nitramines as building blocks for constructing energetic compounds,[12–17] we have set out to develop a facile and versatile method for accessing dipropargyl ethers of *N*-(hydroxymethyl)nitramines.

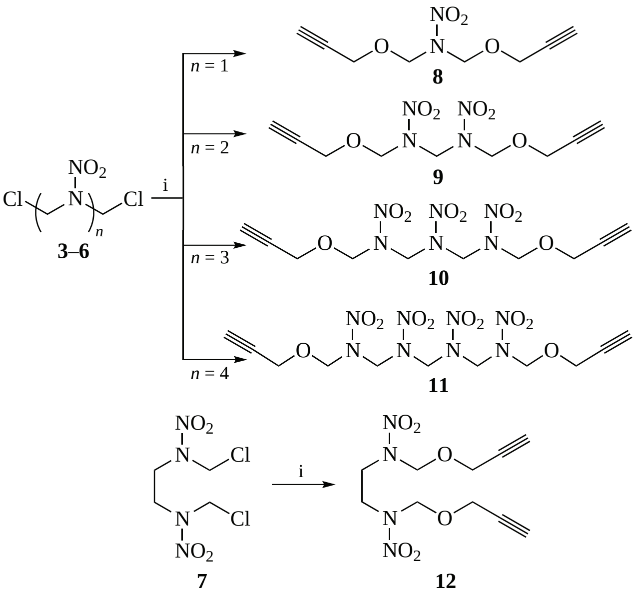
Saturated dialkyl ethers bearing nitramine group have found application in diverse areas ranging from agrochemistry to materials science. The classically employed methods for combining nitramine and ether units in a molecule fall into three main types: (i) alkylation of primary nitramine salts with α-halo ethers, which often results in mixtures of isomers;[9,18–20] (ii) acid-catalyzed substitution of acetoxy group in *N*-(acetoxymethyl)-nitramines with alcohols;[10,21–23] (iii) reactions of *N*-(chloromethyl)nitramines with alcohols.[17,24–26] We believe that the latter pathway should be more versatile, and we therefore have investigated the chlorine displacement in *N*,*N'*-bis(chloromethyl)-nitramines with propargyl alcohol. To the best of our knowledge, there is only one report[11] of a synthesis of propargylic ether from (chloromethyl)nitramine, namely, 1,6-dichloro-2,5-dinitro-2,5-diazahexane, but no synthetic details for this intermediate are given and investigation of scope and limitations of the reaction has not been reported. Herein, we disclose a convenient and scalable (multigram) approach to several dipropargyl ethers bearing up to four nitramino subunits, starting with the readily accessible *N*-(chloromethyl)nitramines.[14]

Initially, we investigated ether bond formation in the reaction of *N*-chloromethyl-*N*-methylnitramine **1** with propargyl alcohol under our previously reported conditions (1,2-dichloroethane, reflux, 12 h).[17] In this event, product **2** was isolated in 42% yield (Scheme 1). In attempts to improve the yield of ether **2**, various promoters such as Na_2CO_3, KF, $SnCl_4$, $ZnCl_2$ and $BF_3 \cdot Et_2O$ were added to the reaction mixture, however these additives did not lead to positive changes. Using a range of anhydrous solvents, including EtOAc, Et_2O, THF, toluene, CH_2Cl_2, and MeCN, afforded no discernible changes to this reaction results, while DMSO was incompatible with this chemistry. To our delight, *N*-(chloromethyl)-*N*-methylnitramine **1** and propargyl alcohol couple at 60 °C in a good yield (73%) for 0.5 h without any promoter or solvent if a considerable excess (10 equiv.) of propargyl alcohol is used and the released HCl is blown out with dry nitrogen. Here, propargyl alcohol serves both as a solvent and a reactant. After the reaction is completed, the excess of propargyl alcohol is removed by vacuum distillation; thus, this alcohol may be recycled and re-used.



Scheme 1 *Reagents and conditions*: i, $HOCH_2C{\equiv}CH$, different solvents, 20–100 °C.

Reactivity of *N*,*N'*-bis(chloromethyl)nitramines **3**–**7** depends on which nitraminomethylene bridge links the terminal chloromethyl units. Thus, in refluxing 1,2-dichloroethane and a moderate excess (3 equiv.) of propargyl alcohol, short nitramine **3** (*n* = 1) was consumed within 8 h, and the target diether **8** was isolated in 16% yield by flash column chromatography. Under similar conditions, attempts to use a longer dinitramine **4** (*n* = 2) resulted in recovery of the starting material. Based on our success in constructing simple ether **2** using propargyl alcohol as a solvent and a reactant, we employed a similar approach to the synthesis of diethers **8**–**11** (Scheme 2). Reaction of nitramine **3** (*n* = 1) with excess (10 equiv.) of propargyl alcohol at 20 °C



Scheme 2 *Reagents and conditions*: i, $HOCH_2C\equiv CH$, ~60 °C.

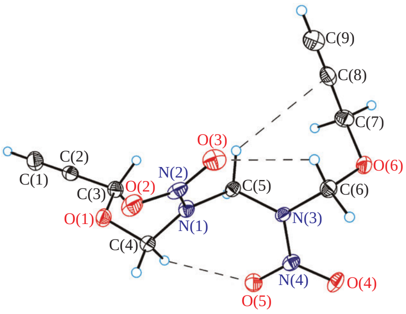


Figure 1 General view of the molecule of **9**. Thermal ellipsoids are given at 50% probability level. Intermolecular noncovalent contacts obtained as a result of topological analysis of the calculated electron density are shown by dashed lines. The energies of C(6)–H(6A)···O(3) and C(4)–H(4A)···O(5) contacts are the same and equal to –2.3 kcal mol^{-1}. Energy of C(5)–H(5A)···C(8) contact is –1.2 kcal mol^{-1}.

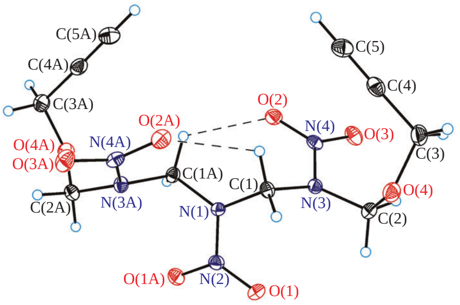


Figure 2 General view of the molecule of **10**. Thermal ellipsoids are given at 50% probability level. Intermolecular noncovalent contacts as obtained from topological analysis of calculated electron density are shown by dashed lines. The energies of C(1)–H(1A)···O(2A) and C(1A)–H(1AA)···O(2) contacts are also equal to –2.3 kcal mol^{-1}.

for 8 h led to very low conversion to the product **8**. However, this reaction at 60 °C is completed in 0.5 h and diether **8** was isolated in 58% yield.

Since nitramine **4**–**7** and products **9**–**12** formed from them are solids, a greater excess of propargyl alcohol (20 equiv.) is required to provide a good reaction medium. Dry nitrogen was slowly bubbled through the reaction mixture to supplanting the released HCl. The desired product **9** was obtained in 59% yield by employing such excess of propargyl alcohol at 60 °C for 1 h. At 80 °C, the product yield is reduced to 42%. For a typical experiment, after the reaction was completed, the excess of propargyl alcohol was removed by vacuum distillation (this alcohol was recycled and reused), and the product was isolated by silica gel chromatography. An extended reaction time of 1.5 h was required for the formation of tri- and tetra-nitramine ethers **10** and **11** at 60 °C; these products were isolated in 80 and 81% yields, respectively. When tri-nitramine precursor **5** was treated with propargyl alcohol at 100 °C, complete conversion was observed after 0.5 h, and diether **10** was isolated in 84% yield. In contrast, the reaction of tetra-nitramine precursor **6** with propargyl alcohol at 100 °C provided a lower yield (60%) of diether **11** as a result of concomitant decomposition.

It is important to note that the replacement of CH_2- by CH_2CH_2-linkage between nitramino groups, as it occurs during the transition from compound **4** to **7**, significantly increases the reactivity of the initial dichloride **7**. While the reaction of CH_2-precursor **4** with propargyl alcohol at 25 °C after 24 h gave diether **9** in 26% yield, and the main part of **4** remained unchanged, CH_2CH_2-precursor **7** at 25 °C was consumed in 1 h and the target product **12** was isolated in 85% yield. Attempts to synthesize product **12** at 60 °C failed, only decomposition processes were observed.

Our results demonstrate that the relative reactivity of the starting bis-*N*,*N*'-(chloromethyl)nitramines appears to be **7** > **3** > **4** > **5** > **6**.

The above protocol scales well. All dipropargyl ethers of *N*-(hydroxymethyl)nitramines are readily available in decagram scale, which makes it possible to begin their practical use. Propargyl ethers **2** and **8** are slightly yellow oils, and ethers **9**–**12** are colourless solids. Compounds **10** and **12** were found by combustion calorimetry to have enthalpies of formation of +92.0 ± 5.8 and 43.5 ± 3.7 kJ mol^{-1}, respectively (see Online Supplementary Materials). Note that earlier, only calculated enthalpies of formation were published for propargyl ethers bearing any explosophoric groups.[27,28]

All compounds are well characterized by IR, ^{1}H, ^{13}C and ^{14}N NMR spectroscopic data as well as CHN analysis. The structures of dipropargyl ethers that contain bridging groups with two and three nitramine units, compounds **9** and **10**, were unambiguously confirmed by X-ray crystallography[†] (Figures 1 and 2).

Compounds **9** and **10** crystallize in space groups $Pca2_1$ and $P4_32_12$ with densities of 1.515 and 1.541 g cm^{-3} at 298 K, respectively (recalculated from 100 K taking into account the known dependence[29,30]) with four molecules per unit cell for both samples. According to quantum-chemical calculation (for details, see Online Supplementary Materials), experimentally observed molecular conformations of compounds **9** and **10** are quite similar to the local minimum for isolated molecules. For **9**, the mutual orientation of the NNO_2 groups is such that the

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[†] *Crystallographic data for* **9**. $C_9H_{12}N_6O_6$, orthorhombic at 100 K, space group $Pca2_1$, $a = 17.8238(13)$, $b = 10.4861(7)$ and $c = 6.3876(5)$ Å, $V = 1193.86(15)$ Å^3, $Z = 4$, $M = 272.23$, $d_{cryst} = 1.515$ g cm^{-3}, $wR_2 = 0.0705$ calculated on F^2_{hkl} for all 2866 independent reflections with $2\theta < 56.0°$, [GOF = 1.064, $R = 0.0292$ calculated on F_{hkl} for 2528 reflections with $I > 2\sigma(I)$].

Crystallographic data for **10**. $C_{10}H_{14}N_6O_8$, tetragonal at 100 K, space group $P4_32_12$, $a = 6.2958(3)$, $b = 6.2958(3)$ and $c = 37.6668(16)$ Å, $V = 1493.00(16)$ Å^3, $Z = 4$, $M = 346.27$, $d_{cryst} = 1.541$ g cm^{-3}, $wR_2 = 0.0746$ calculated on F^2_{hkl} for all 2030 independent reflections with $2\theta < 58.3°$, [GOF = 1.117, $R = 0.0276$ calculated on F_{hkl} for 1974 reflections with $I > 2\sigma(I)$].

CCDC 2247550 (**9**) and 2247549 (**10**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

interplanar angle is equal to 120.1(2)°. For **10**, the orientation of the side NNO_2 groups relative to the central one is close to that observed for **9** [interplanar angle is equal to 114.9(2)°]; it is stabilized (at least in part) by intramolecular C–H···O contacts (see Figures 1 and 2) as indicated by the results of the topological analysis of the calculated electron density. As a result, the C(6)–N(3)(NO_2)–C5–N(1)(NO_2)–C(4) fragment of **9** and the C(2)–N(3)(NO_2)–C(1)–N(1)(NO_2)–C(1A) fragment of **10** (see Online Supplementary Materials, Figure S1) have similar geometry. Figures 1 and 2 clearly demonstrate that the mutual orientations of the propargyl moieties in structures **9** and **10** differ significantly. For **9**, the C(7)–C(8)≡C(9) moiety is directed 'inside' the molecule, participating in C–H···π intramolecular contact, while the other propargyl moiety is directed 'outside' and not involved in intramolecular noncovalent interactions. In contrast, for **10**, the terminal propargyl moieties are oriented 'inside' the molecule, that is, they are close to each other, and do not participate in intramolecular non-covalent interactions.

In conclusion, an efficient catalyst-free approach providing dipropargyl ethers containing nitramine-modified bridging units in good to excellent yields from readily available *N*-(chloromethyl)nitramines has been developed. This solvent-free reaction in an excess of propargyl alcohol is fast, operationally simple and compatible with substrates bearing some nitramine units. The method is reliable for scale up.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2023.06.008.

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