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A new three-component one pot reaction of trinitromethane, epoxides and alkenes via dinitronitronates: synthesis of highly functionalized 3,3-dinitroisoxazolidines

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Abstract

A novel approach to acyclic alkyldinitronitronates using nucleophilic opening of epoxides with the trinitromethyl anion is presented. The scope and limitations of this synthetic procedure are presented. A series of highly functionalized 3,3-dinitroisoxazolidines were synthesized as mixtures of diastereomers.

Keywords: Trinitromethane; Epoxides; Nitronates; [3+2]-Cycloaddition; Isoxazolidines

1. Introduction

Dinitronitronates are a well-known type of 1,3-dipoles, which produce 3,3-dinitroisoxazolidines via [3+2]-cycloaddition with alkenes.[1] The intermediate formation of dinitronitronates was postulated in the reactions of tetranitromethane and halogenotrinitromethanes [$XC(NO_2)_3$, X=NO_2, Br, I] with alkenes.[2] Exclusively alkenes containing electron-donor groups were able to take part in these reactions affording 3,3-dinitroisoxazolidines.

Recently, we have developed a three-component tandem reaction of $XC(NO_2)_3$ with unsaturated compounds, in which one alkene was trapped selectively by $XC(NO_2)_3$ to generate an alkyldinitronitronate and another unsaturated compound participated as a dipolarophile in a [3+2]-cycloaddition.[3] This method allowed the introduction of both electron-rich and electron-deficient alkenes as well as alkynes in the reaction with $XC(NO_2)_3$ and to produce *gem*-dinitro substituted heterocycles like isoxazolidines,[3a–d] isoxazolines,[3e] piperidones[3f] and aziridines,[3g] bearing various functional groups in the cycle and in the side chain.

Therefore, the trinitromethyl anion attacks the electrophilic *C*-centre of the substrate as an *O*-nucleophile to generate the alkyldinitronitronate. Thus, the extensive search for the substrates, which are suitable for a nucleophilic attack with trinitromethyl anion, will afford a new pathway to alkyldinitronitronates and, as a consequence, to novel highly functionalized heterocycles. We supposed that epoxides were convenient substrates for alkyldinitronitronates' generation of that type. Up to now, there are no data about reactions of epoxides with polynitromethanes in the literature. At the same time, it is well-known that the trinitromethyl anion shows ambident behaviour: it can act as an *O*- or a *C*-nucleophile depending on the substrate type.[1a,c,4] Therefore, it may be assumed that two pathways are possible for the reaction of epoxides and trinitromethyl anion (Scheme 1): *path A* is O-alkylation of oxonium cation **I** giving nitronate **II** and nitronate **II** can be trapped by the alkene via [3+2]-cycloaddition to produce 3,3-dinitroisoxazolidine **III** (three-component reaction); *path B* is C-alkylation of oxonium cation **I** leading to 3,3,3-trinitropropanole **IV** (two-component reaction).

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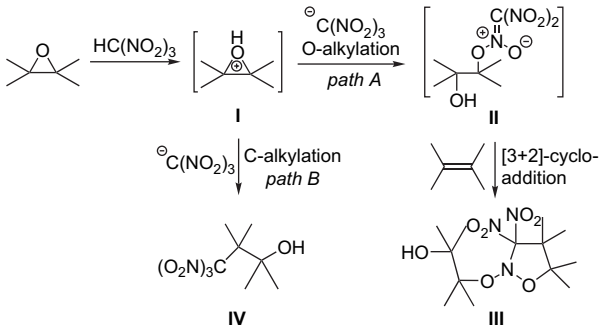


Scheme 1.

According to the literature data[1] and our own results,[3] the trinitromethyl anion generally behaves like *O*-nucleophile because its *C*-centre is strongly hindered by bulky NO_2 groups. C-Alkylation is realized only in few cases.[1c,2a,4] It was shown that the increase in the degree of delocalization of positive charge in the carbocation led to an increase in the yield of the C-alkylation product.[4] Thus, the trinitromethyl anion will most likely behave as an *O*-nucleophile in the reactions with epoxides to produce nitronates **II** (Scheme 1), which will afford highly functionalized isoxazolidines **III** through [3+2]-cycloaddition with diverse dipolarophiles.

We suggest here a new approach to dinitroisoxazolidines via sequential nucleophilic cleavage of the epoxide ring by the trinitromethyl anion followed by [3+2] cycloaddition of the generated dinitronitronate to an alkene.

2. Results and discussion

We investigated the reaction of cyclohexene oxide (**1a**) with $XC(NO_2)_3$ in the presence of vinyl acetate (**2a**) as dipolarophile as a model experiment (Table 1). Trinitromethane (X=H) and potassium trinitromethanide (X=K) were employed as sources of the trinitromethyl anion in polar and nonpolar solvents. Usually, nucleophilic cleavage of epoxides is carried out with excess of nucleophile and of catalyst (Lewis or Brønsted acids).[5] Moreover, trinitromethyl anion is known to be a nucleophile. Therefore, we used double excess of $XC(NO_2)_3$ and of dipolarophile **2a** in comparison with epoxide **1a**.

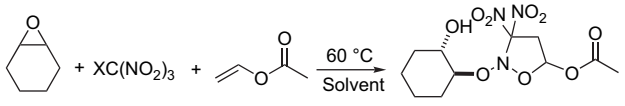
We found that the reaction of epoxide **1a** with $HC(NO_2)_3$ and alkene **2a** led to isoxazolidine **3a** in good yield (65% after column chromatography) in 1,4-dioxane at 60 °C (Table 1, entry 1). Isoxazolidine **3a** was obtained in comparable yield in the case of hexane as a solvent (Table 1, entry 2). However, the attempt to use potassium trinitromethanide as a source of the trinitromethyl anion was less successful: isoxazolidine **3a** was obtained in 11% yield only (Table 1, entry 4).

According to the ^1H and ^{13}C NMR spectroscopic data, isoxazolidine **3a** was produced as a mixture of four diastereomers in 35:29:24:12 ratio. The signals of H- and C-atoms had similar or coinciding chemical shifts for the isomers that were the evidences of high regioselectivity of the [3+2]-cycloaddition of nitronate to alkene **2a**. Mono- and *gem*-disubstituted alkenes are known to add nitronates to yield mainly 5-substituted isoxazolidines.[1,3] Isoxazolidine **3a** was formed as a mixture of four diastereomers due to the presence of four asymmetric centres in its molecule: three carbon atoms of the heterocyclic and cyclohexane rings and one N atom of the isoxazolidine ring. According to the literature and our recent data, N-atom is asymmetric due to a high value of N-inversion barrier in five-membered cycle (60–120 kJ/mol).[3a,c,d,6] Moreover, under Furst–Plattner rule the cleavage of the ring of cyclohexene oxide (**1a**) always affords the product with trans-orientation of CHOH and CHNu centres.[6] Thus, isoxazolidine **3a** was formed as a mixture of four diastereomers with fixed relative orientation of stereocentres in cyclohexane fragment.

Running the model reaction in water did not lead to isoxazolidine **3a** (Table 1, entry 5). Instead, trinitropropanol **4** was obtained as a major product after hydrolysis of the adduct of $HC(NO_2)_3$ to vinyl acetate. The same product **4** was synthesized in 45% yield (after column chromatography) by a direct treatment of vinyl acetate with $HC(NO_2)_3$ in water (Scheme 2).

Hence, the best result was obtained in the case of treating the mixture of epoxide and alkene with $HC(NO_2)_3$ in 1,4-dioxane at rt followed by keeping the reaction mixture at 60 °C for 5 h (Table 1, entry 1). To probe the scope of this reaction, a number of epoxides **1** and alkenes **2** were investigated under the same conditions.

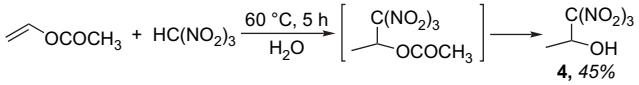
Table 1
Model three-component reaction of cyclohexene oxide with trinitromethane and vinyl acetate



1a **2a** **3a**

Entry	$XC(NO_2)_3$	Solvent	Reaction time (h)	Yield[a] of **3a** (%)
1	$HC(NO_2)_3$	1,4-Dioxane	5	65
2	$HC(NO_2)_3$	Hexane	4	50
3	$HC(NO_2)_3$	CH_3CN	4	32
4	$KC(NO_2)_3$	(1) CH_3CN, (2) H^+, H_2O	4	11
5	$HC(NO_2)_3$	H_2O	4	—[b]

[a] Yield of isolated product (after column chromatography).
[b] The major product of the reaction in water is 1,1,1-trinitropropan-2-ole (**4**) (Scheme 2).

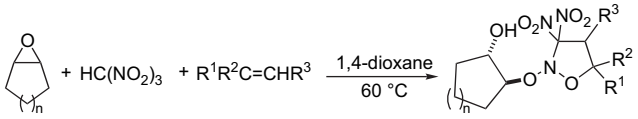


Scheme 2.

We found that reactions of epoxide **1a** with $HC(NO_2)_3$ and alkenes **2a–d** most likely proceeded through the nitronate generation followed by [3+2]-cycloaddition to give 3,3-dinitroisoxazolidines **3a–d** of mixed composition (Table 2, entries 1–4). Isoxazolidines **3a–d** were obtained as mixtures of two or four diastereomers depending on the number of stereocenters.

Reactions of epoxide **1b** with $HC(NO_2)_3$ and alkenes **2a**,**e** proceeded in the same manner to form isoxazolidines **3e**,**f** as

Table 2
Three-component reaction of epoxides **1a**,**b** with trinitromethane and alkenes **2a**–**e**



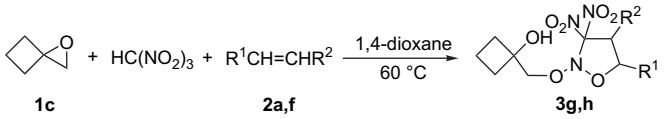
Entry	Epoxide	*n*	Alkene	R^1	R^2	R^3	Reaction time (h)	Isoxazolidine	dr	Yield[a] of **3** (%)
1	**1a**	2	**2a**	OCOMe	H	H	5	**3a**	35:29:24:12	62
2	**1a**	2	**2b**	Ph	Ph	H	4	**3b**	65:35	71
3	**1a**	2	**2c**	$-(CH_2)_3-$		H	4	**3c**	60:40	79
4	**1a**	2	**2d**	OBu	H	H	4	**3d**	40:35:20:5	55
5	**1b**	1	**2a**	OCOMe	H	H	5	**3e**	38:24:20:18	45
6	**1b**	1	**2e**	H	$-(CH_2)_4-$		5	**3f**[b]	55:15:15:15	25

[a] Yield of isolated product (after column chromatography).
[b] Isoxazolidine **3f** was isolated after column chromatography in low yield due to its instability under storage and on SiO_2.

mixtures of four diastereomers (Table 2, entries 5 and 6). Utilization of vinylbutyl ether (**2d**) as dipolarophile in this reaction led to unstable isoxazolidine, which decomposed during its isolation by column chromatography.

Methylenecyclobutane oxide (**1c**) was found to be more reactive in comparison with cyclopentene oxide (**1b**): three-component reactions of **1c** with $HC(NO_2)_3$ and alkenes **2a**,**f** were complete within 3–4 h to produce isoxazolidines **3g**,**h** in higher yields (Table 3). The reactions proceeded with high regio- and diastereoselectivity and isoxazolidines **3g**,**h** were formed as mixtures of two diastereomers. In this case nucleophile attacks unsubstituted and more accessible C-centre of CH_2 group of epoxide **1c** that is in accordance with the literature data[5a] concerning nucleophilic cleavage of alkyl substituted asymmetric epoxides.

Table 3
Three-component reaction of methylenecyclobutane oxide (**1c**) with trinitromethane and alkenes **2a**,**f**



Entry	Alkene	R^1	R^2	Reaction time (h)	Isoxazolidine	dr	Yield of **3** (%)
1	**2a**	OCOMe	H	3	**3g**	75:25	65
2	**2f**	$-(CH_2)_3-$		4	**3h**	55:45	42

The generation of nitronates via the reaction of epoxides with $HC(NO_2)_3$ turns out to be limited by electronic and steric factors as well as to the stability of epoxide towards polymerization under the action of $HC(NO_2)_3$. Thus, for example, cyclooctene oxide and epichlorohydrin were inert in three-component reactions with $HC(NO_2)_3$ while epoxides such as ethylene and propylene oxides were polymerized when treated with $HC(NO_2)_3$. Moreover, we could use only nucleophilic alkenes such as **2a**–**e** as dipolarophiles for the trapping of generated nitronates, because electrophilic alkenes as Michael acceptor react directly with $HC(NO_2)_3$[7] and cannot be introduced in three-component, one pot reactions.

3. Conclusion

In conclusion, we have presented a novel approach to alkyldinitronitronates via the first reaction of nucleophilic cleavage of epoxides with $HC(NO_2)_3$. The utility of this simple and useful method was demonstrated in the synthesis of a series of highly functionalized 3,3-dinitroisoxazolidines. Such dinitroisoxazolines can be convenient synthetic intermediates, as, for example, masked 1,3-dicarbonyl compounds, and as precursors for nitroisoxazolines and isoxazoles, which reveal a wide range of biological activity.[8]

4. Experimental

4.1. General

NMR spectra (400 MHz) were recorded on a 'Bruker Avance-400' spectrometer at rt; the chemical shifts δ were measured in parts per million with respect to the solvent (^{1}H: $CDCl_3$, δ=7.26 ppm; ^{13}C: $CDCl_3$, δ=77.1 ppm). MS were recorded on the MALDI-TOF mass-spectrometer 'Bruker Ultraflex' in positive mode and dithranol was used as a matrix. Melting point (mp): Electrothermal 9100 capillary melting point apparatus. Column chromatography was performed on silica gel 60 (230–400 mesh, Merck). Trinitromethane and potassium trinitromethanide were synthesized by known procedures.[9,10] Cyclohexene oxide (**1a**), cyclopentene oxide (**1b**), cyclooctene oxide, epichlorohydrin, ethylene oxide, propylene oxide, vinyl acetate (**2a**), 1,1-diphenylethylene (**2b**), methylenecyclobutane (**2c**), butyl vinyl ether (**2d**), cyclohexene (**2e**) and cyclopentene (**2f**) were commercially available. Methylenecyclobutane oxide (**1c**) was prepared by published procedures.[11]

4.2. Preparation of isoxazolidines *3a–h*: general procedure

Trinitromethane (0.3 g, 0.19 mL, 2 mmol) was added as one portion to a solution of epoxide (1 mmol) and olefin (2 mmol) in

1,4-dioxane (2.5 mL) at rt under stirring. Reaction mixture was heated to 60 °C and stirred at that temperature for 3–5 h (Tables 2 and 3). The mixture was concentrated under reduced pressure and the residue was purified by column chromatography.

*4.2.1. 2-(2-Hydroxycyclohexyloxy)-3,3-dinitroisoxazolidin-5-yl acetate (**3a**)*

Mixture of diastereomers (**A/B/C/D**=35:29:24:12); yield: 0.21 g (62%); yellow oil; R_f 0.27 (hexane/EtOAc, 4:1).

^{1}H NMR ($CDCl_3$): δ (for mixture of diastereomers)=1.05–2.49 (m, 8H+8H+8H+8H, *c*-Hex), 2.07 (s, 3H, CH_3, for isomer **D**), 2.09 (s, 3H, CH_3, for isomer **B**), 2.15 (s, 3H, CH_3, for isomer **C**), 2.16 (s, 3H, CH_3, for isomer **A**), 3.15–4.20 [m, 5H+5H+5H+5H, CHO, C*H*OH, $CH_2C(NO_2)_2$, OH], 6.55–6.80 (m, 1H+1H+1H+1H, CHO).

^{13}C NMR ($CDCl_3$): δ (for isomer **A**)=20.6 (CH_3), 23.5, 23.7, 28.9, 32.4 (CH_2, *c*-Hex), 39.7 [*C*$H_2C(NO_2)_2$], 71.6 (CHOH), 88.8 (CHO), 94.7 (CHO), 126.3 [$C(NO_2)_2$], 168.9 (CO).

^{13}C NMR ($CDCl_3$): δ (for isomers **B**)=20.6 (CH_3), 23.5, 23.9, 28.7, 32.4 (CH_2, *c*-Hex), 39.7 [*C*$H_2C(NO_2)_2$], 71.8 (CHOH), 89.2 (CHO), 99.0 (CHO), 126.3 [$C(NO_2)_2$], 168.9 (CO).

^{13}C NMR ($CDCl_3$): δ (for isomer **C**)=20.7 (CH_3), 23.4, 23.9, 28.5, 32.1 (CH_2, *c*-Hex), 40.2 [*C*$H_2C(NO_2)_2$], 71.4 (CHOH), 90.4 (CHO), 99.0 (CHO), 126.1 [$C(NO_2)_2$], 169.0 (CO).

^{13}C NMR ($CDCl_3$): δ (for isomer **D**)=21.0 (CH_3), 23.4, 24.1, 29.2, 32.6 (CH_2, *c*-Hex), 40.4 [*C*$H_2C(NO_2)_2$], 71.8 (CHOH), 90.0 (CHO), 99.0 (CHO), 126.1 [$C(NO_2)_2$], 169.0 (CO).

Anal. Calcd for $C_{11}H_{17}N_3O_9$: C, 39.41; H, 5.11. Found: C, 39.83; H, 5.46.

*4.2.2. 2-(3,3-Dinitro-5,5-diphenylisoxazolidin-2-yloxy)-cyclohexanol (**3b**)*

Mixture of diastereomers (**A/B**=65:35); yield: 0.30 g (71%); yellow oil; R_f 0.68 ($CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (for mixture of diastereomers)=0.95–2.20 (m, 9H+8H, *c*-Hex, OH), 2.65 (br s, 1H, OH, for isomer **B**), 3.11–3.22 (m, 1H, C*H*OH, for isomer **A**), 3.50–3.62 (m, 1H, C*H*OH, for isomer **B**), 3.80–4.05 (m, 1H+1H, CHO), 3.93 [d, ^2J=15.2 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **A**], 3.99 [d, ^2J=14.9 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **B**], 4.65 [d, ^2J=14.9 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **B**], 4.78 [d, ^2J=15.2 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **A**], 7.10–7.52 (m, 10H+10H, Ph).

^{13}C NMR ($CDCl_3$): δ (for isomer **A**)=23.5, 23.8, 28.6, 32.1 (CH_2, *c*-Hex), 43.9 [*C*$H_2C(NO_2)_2$], 71.4 (CHOH), 88.9 (CHO), 92.7 (C), 124.8, 125.5, 128.3, 128.7, 128.9 (2×CH, Ph), 141.9, 143.8 (C, Ph). A signal of carbon atom of $C(NO_2)_2$ group was not observed.

^{13}C NMR ($CDCl_3$): δ (for isomer **B**)=23.4, 23.8, 28.6, 32.3 (CH_2, *c*-Hex), 44.3 [*C*$H_2C(NO_2)_2$], 72.1 (CHOH), 87.8 (CHO), 92.1 (C), 125.0, 125.7, 128.4, 128.7, 128.8 (2×CH, Ph), 141.1, 143.2 (C, Ph). A signal of carbon atom of $C(NO_2)_2$ group was not observed.

Anal. Calcd for $C_{21}H_{23}N_3O_7$: C, 58.74; H, 5.40; N, 9.79. Found: C, 58.65; H, 5.20; N, 9.53.

*4.2.3. 2-[7,7-Dinitro-5-oxa-6-aza-spiro[3.4]oct-6-yloxy]-cyclohexanol (**3c**)*

Mixture of diastereomers (**A/B**=60:40); yield: 0.25 g (79%); yellow oil; R_f (**A**+**B**) 0.60, 0.52. (hexane/EtOAc, 4:1).

^{1}H NMR ($CDCl_3$): δ (for mixture of diastereomers)=1.05–2.89 (m, 15H+15H, *c*-Hex, *c*-Bu, OH), 3.37 [d, ^2J=15.2 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **B**], 3.39 [d, ^2J=15.2 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **A**], 3.40–3.50 (m, 1H, C*H*OH, for isomer **B**), 3.52–3.65 (m, 1H, C*H*OH, for isomer **A**), 3.87 [d, ^2J=15.2 Hz, 1H+1H, $CH_2C(NO_2)_2$], 3.89–4.02 (m, 1H+1H, CHO).

^{13}C NMR ($CDCl_3$): δ (for isomer **A**)=13.3, 23.4, 23.9, 32.3, 32.4, 34.6, 38.7 (CH_2, *c*-Hex, *c*-Bu), 43.7 [*C*$H_2C(NO_2)_2$], 72.3 (CHOH), 89.2 (CHO), 89.3 (C_{spiro}), 127.9 [$C(NO_2)_2$].

^{13}C NMR ($CDCl_3$): δ (for isomer **B**)=13.4, 23.5, 23.9, 29.4, 32.4, 34.4, 38.7 (CH_2, *c*-Hex, *c*-Bu), 43.6 [*C*$H_2C(NO_2)_2$], 72.2 (CHOH), 87.8 (CHO), 89.3 (C_{spiro}), 127.9 [$C(NO_2)_2$].

Anal. Calcd for $C_{12}H_{19}N_3O_7$: C, 47.84; H, 6.36. Found: C, 47.60; H, 6.08.

*4.2.4. 2-(5-Butoxy-3,3-dinitroisoxazolidin-2-yloxy)cyclohexanol (**3d**)*

Mixture of diastereomers (**A/B/C/D**=40:35:20:5); yield: 0.19 g (55%); yellow oil; R_f (**A**+**B**+**C**+**D**) 0.32, 0.43, 0.50, 0.61 (hexane/EtOAc, 4:1).

^{1}H NMR ($CDCl_3$): δ (for mixture of diastereomers)=0.87–2.25 (m, 12H+12H+12H+12H, Bu, *c*-Hex, OH), 1.57, 1.59, 1.66, 1.67 (t, ^3J=7.2 Hz, 3H+3H+3H+3H, CH_3, Bu), 2.75–4.0 [m, 7H+7H+7H+7H, OH, *c*-Hex, Bu, $CH_2C(NO_2)_2$], 5.56–5.58, 5.61–5.63, 5.63–5.66, 5.70–5.71 (m, 1H+1H+1H+1H, CH).

^{13}C NMR ($CDCl_3$): δ (for isomer **A**)=13.5 (CH_3), 18.9, 23.4, 23.7, 28.5, 31.2, 31.9 (CH_2, Bu, *c*-Hex), 39.3 [*C*$H_2C(NO_2)_2$], 69.5 (CH_2O), 72.0 (CHOH), 87.6 (CHO), 108.4 (CH), 126.5 [$C(NO_2)_2$].

^{13}C NMR ($CDCl_3$): δ (for isomer **B**)=13.5 (CH_3), 18.9, 23.4, 23.7, 28.6, 31.4, 31.9 (CH_2, Bu, *c*-Hex), 40.2 [*C*$H_2C(NO_2)_2$], 66.9 (CH_2O), 71.9 (CHOH), 88.1 (CHO), 104.1 (CH), 126.1 [$C(NO_2)_2$].

^{13}C NMR ($CDCl_3$): δ (for isomer **C**)=13.5 (CH_3), 18.8, 23.5, 23.8, 28.7, 31.2, 32.3 (CH_2, Bu, *c*-Hex), 39.4 [*C*$H_2C(NO_2)_2$], 70.7 (CH_2O), 71.4 (CHOH), 89.3 (CHO), 108.2 (CH), 126.8 [$C(NO_2)_2$].

^{13}C NMR ($CDCl_3$): δ (for isomer **D**)=13.5 (CH_3), 19.0, 23.5, 24.2, 29.2, 31.0, 32.2 (CH_2, Bu, *c*-Hex), 39.4 [*C*$H_2C(NO_2)_2$], 69.9 (CH_2O), 71.6 (CHOH), 88.7 (CHO), 103.5 (CH), 126.3 [$C(NO_2)_2$].

Anal. Calcd for $C_{13}H_{23}N_3O_8$: C, 44.70; H, 6.64; N, 12.03. Found: C, 44.77; H, 6.69; N, 11.94.

*4.2.5. 2-(2-Hydroxycyclopentyloxy)-3,3-dinitroisoxazolidin-5-yl acetate (**3e**)*

Mixture of diastereomers (**A/B/C/D**=38:24:20:18); yield: 0.14 g (45%); yellow oil; R_f (**A**+**B**+**C**+**D**) 0.22, 0.41, 0.67, 0.82 (hexane/EtOAc, 1:1).

^{1}H NMR ($CDCl_3$): δ (for mixture of diastereomers)=1.62–2.50 (m, 6H+6H+6H+6H, *c*-Pent), 2.09 (s, 3H, CH_3, for isomer

A), 2.13 (s, 3H, CH_3, for isomer **C**), 2.14 (s, 3H, CH_3, for isomer **B**), 2.15 (s, 3H, CH_3, for isomer **D**), 3.24–4.68 (m, 5H+5H+5H+5H, CHO, C*H*OH, $CH_2C(NO_2)_2$, OH), 6.65 (dd, ^3J=2.8, 7.3 Hz, 1H, CH, for isomer **C**), 6.67–6.74 (m, 1H+1H, CH, for isomers **A** and **B**), 6.98 (dd, ^3J=2.3, 7.6 Hz, 1H, CH, for isomer **D**).

^{13}C NMR ($CDCl_3$): δ (for isomer **A**)=20.5 (CH_3), 20.7, 28.3, 31.7 (CH_2, *c*-Pent), 39.2 [*C*$H_2C(NO_2)_2$], 75.4 (CHOH), 92.1 (CHO), 99.0 (CH), 126.4 [$C(NO_2)_2$], 169.3 (CO).

^{13}C NMR ($CDCl_3$): δ (for isomer **B**)=20.5 (CH_3), 21.0, 28.3, 31.7 (CH_2, *c*-Pent), 39.4 [*C*$H_2C(NO_2)_2$], 75.3 (CHOH), 90.6 (CHO), 98.9 (CHO), 126.5 [$C(NO_2)_2$], 169.3 (CO).

^{13}C NMR ($CDCl_3$): δ (for isomer **C**)=20.5 (CH_3), 20.8, 27.9, 31.6 (CH_2, *c*-Pent), 39.7 [*C*$H_2C(NO_2)_2$], 75.2 (CHOH), 91.7 (CHO), 95.4 (CHO), 125.1 [$C(NO_2)_2$], 169.0 (CO).

^{13}C NMR ($CDCl_3$): δ (for isomer **D**)=20.5 (CH_3), 20.4, 27.9, 31.7 (CH_2, *c*-Pent), 39.8 [*C*$H_2C(NO_2)_2$], 75.7 (CHOH), 92.8 (CHO), 95.2 (CHO), 125.1 [$C(NO_2)_2$], 169.1 (CO).

ESI-MS: *m*/*z*=339 $(M+H_2O)^+$, 344 $(M+Na)^+$.

Anal. Calcd for $C_{10}H_{15}N_3O_9$: C, 37.39; H, 4.71; N, 13.08. Found: C, 37.49; H, 4.71; N, 12.85.

*4.2.6. 2-[3,3-Dinitrohexahydrobenzo[d]isoxazol-2(3H)-yloxy]cyclopentanol (**3f**)*

Major diastereomer; yield: 0.08 g (25%); yellow oil; R_f 0.54 (hexane/EtOAc, 4:1).

^{1}H NMR ($CDCl_3$): δ=1.25–2.75 (m, 15H, *c*-Pent, *c*-Hex, OH), 4.24–4.31 [m, 1H, $CHC(NO_2)_2$], 4.50–4.54 (m, 1H, C*H*OH), 4.97–5.02 (m, 1H, CHO), 5.08–5.13 (m, 1H, CHO).

^{13}C NMR ($CDCl_3$): δ=21.5, 23.7 (×2), 28.7, 30.6 (×2), 32.7 (CH_2, *c*-Pent, *c*-Hex), 66.5 [*C*$HC(NO_2)_2$], 76.0, 84.0, 91.1 (CHO), 128.3 [$C(NO_2)_2$].

MS MALDI-TOF: *m*/*z*=318 $(M+H)^+$.

*4.2.7. 2-[(1-Hydroxycyclobutyl)methoxy]-3,3-dinitroisoxazolidin-5-yl acetate (**3g**)*

Mixture of diastereomers (**A**/**B**=55:45); yield: 0.13 g (42%); yellow oil; R_f 0.19 ($CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (for mixture of diastereomers)=1.58–1.62, 1.82–1.87, 2.02–2.32 (m, 2H+2H, *c*-Bu), 2.07 (s, 3H, CH_3, for isomer **B**), 2.14 (s, 3H, CH_3, for isomer **A**), 3.29 (dd, ^2J=15.7 Hz, ^3J=1.5 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **A**), 3.66 (AB system, ^2J=12.4 Hz, 1H, CH_2, for isomer **A**), 3.71 (AB system, ^2J=12.3 Hz, 1H, CH_2, for isomer **B**), 3.77 (dd, ^2J=16.2 Hz, ^3J=6.6 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **B**), 3.84 (AB system, ^2J=12.4 Hz, 1H, CH_2, for isomer **A**), 3.85 (AB system, ^2J=12.3 Hz, 1H, CH_2, for isomer **B**), 3.92 (dd, ^2J=16.2 Hz, ^3J=3.6 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **B**), 4.07 (dd, ^2J=15.7 Hz, ^3J=6.6 Hz, 1H, $CH_2C(NO_2)_2$, for isomer **A**) 6.66 (dd, ^3J=1.5, 6.6 Hz, 1H, CH, for isomer **A**), 6.76 (dd, ^3J=3.6, 6.6 Hz, 1H, CH, for isomer **B**). The signals of H-atoms of OH groups were not observed.

^{13}C NMR ($CDCl_3$): δ (for isomer **A**)=12.8 (CH_2, *c*-Bu), 20.7 (CH_3), 28.1, 28.7 (CH_2, *c*-Bu), 40.2 [*C*$H_2C(NO_2)_2$], 64.5 (CH_2), 87.7 (C, *c*-Bu), 99.0 (CH), 126.5 [$C(NO_2)_2$], 169.0 (CO).

^{13}C NMR ($CDCl_3$): δ (for isomer **B**)=12.7 (CH_2, *c*-Bu), 20.6 (CH_3), 28.5, 28.6 (CH_2, *c*-Bu), 40.1 [*C*$H_2C(NO_2)_2$], 64.3 (CH_2), 88.0 (C, *c*-Bu), 95.1 (CH), 125.5 [$C(NO_2)_2$], 168.8 (CO).

Anal. Calcd for $C_{10}H_{15}N_3O_9$: C, 37.39; H, 4.71; N, 13.08. Found: C, 37.64; H, 4.70; N, 12.96.

*4.2.8. 1-[(3,3-Dinitrohexahydrocyclopenta[d]isoxazol-2-yloxy)methyl]cyclobutanol (**3h**)*

Mixture of diastereomers (**A**/**B**=75:25); yield: 0.20 g (65%); yellow oil; R_f (**A**+**B**) 0.08, 0.19 ($CHCl_3$).

^{1}H NMR ($CDCl_3$): δ (for mixture of diastereomers)=1.25–2.30 (m, 13H+13H, *c*-Bu, *c*-Pent, OH), 3.72 (AB system, ^2J=12.8 Hz, 1H+1H, CH_2), 3.81 (AB system, ^2J=12.8 Hz, 1H+1H, CH_2), 4.29–4.34 [m, 1H+1H, $CHC(NO_2)_2$], 5.44–5.48 (m, 1H+1H, CHO).

^{13}C NMR ($CDCl_3$): δ (for isomer **A**)=12.6, 24.8, 28.2, 28.7, 28.8, 30.4 (CH_2, *c*-Bu, *c*-Pent), 50.7 [*C*$HC(NO_2)_2$], 86.4 (CH_2O), 89.0 (C), 90.0 (CHO), 132.8 [$C(NO_2)_2$].

^{13}C NMR ($CDCl_3$): δ (for isomer **B**)=12.4, 24.8, 27.4, 28.7, 28.8, 30.1 (CH_2, *c*-Bu, *c*-Pent), 50.4 [*C*$HC(NO_2)_2$], 86.1 (CH_2O), 89.0 (C), 90.1 (CHO), 132.9 [$C(NO_2)_2$].

Anal. Calcd for $C_{11}H_{17}N_3O_7$: C, 43.38; H, 5.52; N, 13.71. Found: C, 43.56; H, 5.65; N, 13.86.

*4.2.9. 1,1,1-Trinitropropan-2-ol (**4**)*[12]

Trinitromethane (0.3 g, 0.19 mL, 2 mmol) was added to a stirred solution of vinyl acetate (0.09 g, 0.1 mL, 1 mmol) in H_2O (2.5 mL) at rt. Reaction mixture was heated at 60 °C for 5 h. Then the resulting mixture was extracted with $CHCl_3$ (3×1 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure.

Yield: 0.09 g (45%); yellow liquid.

^{1}H NMR ($CDCl_3$): δ=1.66 (d, ^3J=6.6 Hz, 3H, CH_3), 5.20 (q, ^3J=6.6 Hz, 1H, CH). A signal of H-atom of OH group was not observed.

^{13}C NMR ($CDCl_3$): δ=17.9 (CH_3), 70.0 (CH), 128.7 [$C(NO_2)_3$].

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