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Nitration of glycoluril derivatives in liquid carbon dioxide

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Dinitroglycolurils and 1,4,6-trinitrohexahydroimidazo[4,5-d]imidazol-2(1H)-one were prepared in 56–89% yield by N-nitration of the corresponding glycoluril precursors with dinitrogen pentoxide in liquid carbon dioxide.

Dinitroglycoluril **1a** is a high-energy (velocity of detonation, ~7580 m s⁻¹, d = 1.99 g cm⁻³), termally (deflagration temperature, 225–250 °C) and hydrolytically stable explosive that is used in a low-sensitive molding compositions with trinitrotoluene, as a substitute for the Research Department explosive (RDX, 1,3,5-trinitro-1,3,5-triazacyclohexane).¹ Commonly, it is prepared by N-nitration of glycoluril **2a** with nitric acid, acetyl nitrate or mixed acids at 20–65 °C under neat conditions.² This procedure requires the use of a significant concentration of the reactants, which complicates efficient temperature control and enhances the fire and explosion risks.

Recently, we have developed an alternative procedure for the synthesis of *N*-nitroamides and *N*-nitroureas by nitration of the corresponding *N*-alkylamides or *N*-alkylureas with dinitrogen pentoxide in liquid carbon dioxide (liq-CO₂) medium.³ Due to a considerably higher heat capacity of liq-CO₂ as compared to conventional solvents (Cp 6.35 J g⁻¹ K⁻¹ at 25 °C and a pressure of 64 bar,⁴ *cf*. for dichloromethane Cp 1.70 J g⁻¹ K⁻¹ at 20 °C⁵), this neoteric solvent efficiently consumes exothermic reaction heat and suppresses undesirable side reactions and makes a work-up operation significantly simpler (decompression of CO₂).

Herein, we report the use of liq-CO₂ as reaction medium for nitration of glycoluril derivatives. First, to find optimal conditions, we studied the nitration of **2a** as a model. Treatment of suspended in liq-CO₂ **2a** with a solution of N₂O₅ (2.2–4.0 equiv.) in the same solvent at 5–20 °C and 80 bar afforded desirable 1,4-dinitroglycoluril **1a** (Scheme 1, Table 1, entries 1–5). The

Table 1 Synthesis of dinitroglycolurils in liquid CO2.ª

Entry	Product	Nitrating agent (equiv.)	t/h	Yield (%)
1	1a	$N_2O_5(2.2)$	0.5	46
2	1a	$N_2O_5(2.2)$	1.0	49
3	1a	N ₂ O ₅ (2.2)	2.0	52
4	1a	$N_2O_5(4.0)$	1.0	64
5	1a	N ₂ O ₅ (4.0)	2.0	82
6^b	1a	N ₂ O ₅ (2.2) + 100% HNO ₃ (2.2)	2.0	50
7^c	1a	$N_2O_5(2.2) + Ac_2O(2.2)$	2.0	_
8^d	1a	$HNO_3(4.4) + Ac_2O(4.4)$	2.0	_
9 ^e	1a	HNO ₃ (4.4) + TFAA (2.2)	2.0	89
10^{f}	1a	$NH_4NO_3(4.4) + TFAA(4.4)$	2.0	70
11	1b	$N_2O_5(4.0)$	2.0	76
12	1c	$N_2O_5(4.0)$	2.0	83
13	4	$N_2O_5(4.0)$	2.0	73

^{*a*} Unless otherwise specified, the reactions were carried out with **2** or **3** (2.5 mmol), N₂O₅ (5.5–10.0 mmol) at 80 bar and 5–20 °C. ^{*b*}N₂O₅ and 100% HNO₃ (5.5 mmol each). ^{*c*}N₂O₅ and Ac₂O (5.5 mmol each), 100 bar, 45 °C. ^{*d*} HNO₃ (11.0 mmol), Ac₂O (5.5 mmol), 100 bar, 45 °C. ^{*e*} HNO₃ (11.0 mmol). ^{*j*}NH₄NO₃ and TFAA (11.0 mmol each).



best yield of **1a** (82%) was attained on using 4.0 equiv. of N_2O_5 within 2 h (entry 5). Nitric acid additive ($N_2O_5/100\%$ HNO₃, 1:1) did not affect the reaction (entry 6 *vs.* entry 3). Mixtures of N_2O_5 (or 100% HNO₃) with acetic anhydride when acetyl nitrate is generated⁶ appeared inactive under these or even more rigorous conditions corresponding to a supercritical CO₂ state (entries 7 and 8). However, under the action of 100% HNO₃–TFAA or NH₄NO₃–TFAA mixtures (TFAA is trifluoroacetic anhydride) when nitronium trifluoroacetate would likely form as the nitrating agent⁷ **2a** was converted to **1a** in up to 89% yield (entries 9 and 10). Based on these results, we chose less environmentally harmful (producing just recoverable nitric acid as acidic by-product) nitrogen(V) oxide as nitrating agent in further experiments.

The *C*- or *N*-alkylglycolurils **2b,c** and **3** gave the corresponding dinitro compounds **1b,c** and **4** in 73–83% yield under proposed conditions (4.0 equiv. of N₂O₅, liq-CO₂, 2 h) (Scheme 1, Table 1, entries 11–13).[†] Notably, compound **4** contained both nitro groups at the same urea fragment.

[†] The ¹H, ¹³C and ¹⁴N NMR spectra were recorded in DMSO- d_6 with Bruker AM 300 at 300, 75 and 22 MHz, respectively. Starting compounds **2a**, ⁸ **2b**, ⁹ **2c**, ¹⁰ **3**, ¹¹ **5**¹² and N₂O₅¹³ were prepared by reported methods. Carbon dioxide (99.995%) was supplied by Linde Gas (Russia).

General nitration procedure. A steel autoclave (25 cm^3) was charged with **2**, **3** or **5** (2.5 mmol), filled with liquid CO₂ to a pressure of 60 bar and cooled to 5 °C. Then nitrating agent (5.5–10.0 mmol, see Table 1) dissolved in liquid CO₂ (~3.5 g) was added in ten steps for 15 min. The reaction mixture was gradually warmed to room temperature and stirred for 2 h at 80 bar [for supercritical conditions (Table 1, entry 8), the temperature and the pressure were raised to 45 °C and 100 bar, respectively, after the addition of the nitrating agent]. After 2 h stirring, the ice water (2 ml) was pressurized into the autoclave to destroy the access of nitrating agent. The CO₂ was removed and additional amount of ice water (20 ml) was added to the residue at atmospheric pressure. The precipitate was filtered and dried at 40 °C for 2 h to afford nitration product **1**, **4** or **6**,

The method is applicable to the nitration of hexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one dihydrochloride **5** in which cyclic urea fragment is fused with the imidazolidine unit. In this case, trinitro derivative **6** formed in 56% yield under the action of N₂O₅ (4 equiv.) in liq-CO₂ medium (Scheme 2).



Scheme 2

The proposed approach significant reduces explosion risks due to the dilution of reaction mixture with $liq-CO_2$ resistant towards the action of nitrating agents. Furthermore, it allows one to avoid the use of mixed acids associated with energyconsuming disposal of corresponding acid wastes and environment pollution problems. Despite of the necessity of rather expensive high-pressure equipment, the method may be even

1,4-Dinitroglycoluril **1a**: $T_{\rm ID}$ 192 °C. ¹H NMR, δ : 6.03 (s, 2H, CH), 9.83 (s, 2H, NH). ¹³C NMR, δ : 149.0, 63.8. ¹⁴N NMR, δ : –39.5.

3a,6a-Dimethyl-1,4-dinitrotetrahydroimidazo[4,5-d]imidazole-2,5(1H,3H)dione **1b**: $T_{\rm ID}$ 194 °C. ¹H NMR, δ : 1.82 (s, 6H, Me), 9.94 (s, 2H, NH). ¹³C NMR, δ : 146.5, 76.9, 17.8. ¹⁴N NMR, δ : -46.6.

3*a*,6*a*-Butano-1,4-dinitrotetrahydroimidazo[4,5-d]imidazole-2,5-dione **1c**: $T_{\rm ID}$ 199 °C. ¹H NMR, δ: 1.29 (m, 2 H, CH₂), 1.63 (m, 2 H, CH₂), 2.08 (m, 2 H, CH₂), 2.59 (d, 2 H, CH₂, *J* 14.0 Hz), 9.97 (s, 2 H, NH). ¹³C NMR, δ: 147.2, 75.9, 28.6, 18.1. ¹⁴N NMR, δ: -48.2.

1,3-Dimethyl-4,6-dinitrotetrahydroimidazo[*4,5-d]imidazole-2,5(1H,3H)-dione* **4**: $T_{\rm ID}$ 206 °C. ¹H NMR, δ : 2.86 (s, 6H, Me), 6.16 (s, 2H, CH). ¹³C NMR, δ : 157.8, 142.0, 69.7, 30.3. ¹⁴N NMR, δ : -48.4.

1,4,6-Trinitrohexahydroimidazo[*4,5*-d]*imidazo*[*-2*(*1*H)*-one* **6**: mp 196 °C (lit., ¹⁵ mp 196–197 °C). ¹H NMR, δ : 5.57, 6.22 (AB quartet, 2H, CH, *J* 10.8 Hz, *J* 185.7 Hz), 6.09, 7.37 (AB quartet, 2H, CH₂, *J* 7.1 Hz, *J* 374.7 Hz), 9.89 (s, 1H, NH). ¹³C NMR, δ : 205.3, 75.2, 67.3, 64.6. ¹⁴N NMR, δ : –48.3, –36.5, –34.5.

economically beneficial: the nitration agent N_2O_5 can be generated from available N_2O_4 ,¹⁶ and the CO₂ solvent is easily separable from the products and can be reused.

In summary, we have developed a new environment-friendly and explosion-safe synthesis of dinitroglycoluril and its analogues by N-nitration of corresponding glycoluril derivatives with N_2O_5 in liquid carbon dioxide medium.

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respectively. Isolated yields are given in Table 1. The NMR spectra of known compounds 1a,² $1b^{14}$ and 6^{15} correspond to reported data. Melting points of compounds 1a–c and 4 were not observed. Temperatures T_{ID} at which originally colorless solids started to become dark (initiation of a decomposition) are given below.