The nitrolysis of *N*,*N*-dialkylcarboxamides in liquid carbon dioxide

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A method for the synthesis of *N*,*N*-dialkylnitramines by the ninrolysis of *N*,*N*-dialkylcarboxamides with a mixture of N_2O_5 and 100% HNO_3 in liquid carbon dioxide was developed.

Key words: nitration, *N*,*N*-dialkylacetamides, *N*,*N*-dialkylformamides, nitramines, carbon dioxide, green chemistry.

Nitro compounds are widely used as components of energetic materials.[1—4] In general, nitro compounds synthesized by nitration of aromatic compounds, alcohols, and amine derivatives with various nitrating agents, *i.e.*, nitric acid,[5,6] mixtures of sulfuric and nitric acids,[7—9] acetyl nitrates,[9—13] nitronium salts,[14—17] acetone cyanohydrin nitrate,[18] and *etc*. However, industrial implementation of these methods involves several problems,[1—4,19,20] for example, elimination of heat evolved in the exothermic nitration reaction and undesirable side reactions, utilization of large volumes of acidic wastes, and explosive hazard of the process.

Some difficulties could be overcome by employing of N_2O_5 (see Ref. 21a) and liquid carbon dioxide for the nitration. Dinitrogen pentoxide is a versatile nitrating agent effective in *C*-, *N*-, and *O*-nitration[21b—23] including destructive nitration.[24,25] Due to high reactivity, N_2O_5 could be used for nitration in lower amounts as compared with the mixtures containing nitric acid. Nitric acid that formed in the reaction could be then converted into N_2O_5 or used as an independent nitrating agent. Nitration with N_2O_5 usually performed in toxic chlorinated organic solvents.[21b,23—25] Combined use of N_2O_5 and liquid carbon dioxide for nitration serves to the reduction of environmental and technological risks.

Carbon dioxide is nonflammable, thermally stable substance characterized by high heat capacity (C_p = = 6.35 J g^{-1} K^{-1} at 25 °C and 64 bar[26] (for dichloromethane C_p = 1.70 J g^{-1} K^{-1} at 20 °C)[27]) and, therefore, CO_2 is capable of effective removal of heat from the reaction zone significantly reducing the explosion and fire hazards of the process. Being non-toxic, cheap, abundantly available, carbon dioxide is an ideal solvent from the viewpoint of green chemistry.[28,29]

Synthesis of organic nitrates by nitration of alcohols with N_2O_5 in CO_2 was documented[30—32] and it was suggested that the developed conditions could be applied for the synthesis of *N*-nitramines. Later, nitration of naphthalene with dinitrogen pentoxide in liquid CO_2 was reported,[33] however, the cited publication is an abstract of the conference where no experimental details were given.

The aim of our work was studying the nitrolysis of *N*,*N*-dialkylamides using a system N_2O_5—CO_2 (liquid) as a promising approach for the synthesis of *N*-nitramines, which is an important class of energetic compounds. The nitrolysis of *N*,*N*-disubstituted carboxamides with a HNO_3—$(CF_3CO)_2O$ mixture[11,12] and nitronium trifluoroborate[15] were documented, although these methods are not widely used due to the high cost of the nitrating agents.

We used a high-pressure laboratory setup consisting of a cylinder *A* with carbon dioxide, a high-pressure manual pump *B*, a dispenser *C*, and an autoclave-nitrator *D* (Fig. 1). Nitrating agent was fed into the autoclave *D* from the dispenser *C* by the flow of liquid CO_2 in which it is good soluble.

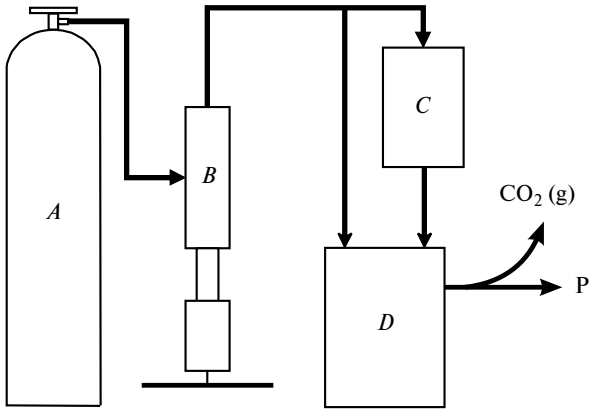

Fig. 1. Scheme of laboratory setup for nitration in liquid carbon dioxide; P denotes products, CO_2 (g) denotes gaseous CO_2.

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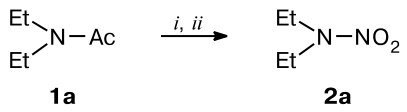
First of all, we studied reactions of *N*,*N*-diethylacetamide **1a** with N_2O_5 and the HNO_3—N_2O_5 mixtures of different composition in liquid carbon dioxide (Scheme 1, Table 1). The reactions were performed under comparable conditions (20 °C, 100 bar, 4 h). Nitramine **2a** was formed in all cases.

Scheme 1



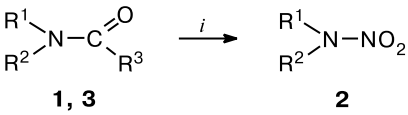
1a **2a**

Reagents and conditions: *i*. N_2O_5 (1—3 equiv.), CO_2 (100 bar), 20 °C, 4 h; *ii*. N_2O_5 (1.5 equiv.), 100% HNO_3 (0.5—3 equiv.), CO_2 (100 bar), 20 °C, 4 h.

The highest yield of compound **2a** (84%) was achieved with a N_2O_5 (1.5 equiv.)—100% HNO_3 (2.0 equiv.) mixture (see Table 1, entry *6*). Nitration without HNO_3 is less effective even in the presence of significant excess of N_2O_5 (see entries *1—3*). Probably, addition of HNO_3 increases the nitronium cation concentration in the system, which in the absence of HNO_3 is insufficient for the effective nitration due to low dissociation constant of $N_2O_5 \rightleftharpoons NO_2^+ + NO_3^-$ in nonpolar CO_2.[34]

The developed conditions were applied for the synthesis of linear and cyclic nitramines **2b—e** from the corresponding *N*,*N*-dialkylacetamides **1b—e** (Scheme 2, Table 2).

Scheme 2



1, 3 **2**

1, 3: $R^1 = R^2$ = Et (**a**), Me (**b**), Bu^n (**c**);
R^1—R^2 = —$CH_2CH_2OCH_2CH_2$— (**d**), —$(CH_2)_5$— (**e**);
R^3 = Me (**1**), H (**3**)

Reagents and conditions: *i*. N_2O_5 (1.5 equiv.), 100% HNO_3 (2 equiv.), CO_2 (100 bar), 20 °C, 4 h.

Table 1. The nitrolysis of *N*,*N*-diethylacetamide in liquid CO_2

Entry	*N*/equiv.		Yield of compound **2a** (%)
	N_2O_5	HNO_3	
1	1.0	—	13
2	2.0	—	60
3	3.0	—	62
4	1.5	0.5	42
5	1.5	1.0	66
6	1.5	2.0	84
7	1.5	3.0	81

Table 2. The nitrolysis of *N*,*N*-dialkylacetamides and *N*,*N*-dialkylformamides in liquid CO_2

2	R^1	R^2	Yield of compound **2** (%)		
			R^3 = H	R^3 = Me	Published data*
a	Et	Et	75	84	45 (75)
b	Me	Me	80	57	67 (63)
c	Bu^n	Bu^n	59	56	75 (65)
d	$(CH_2)_2O(CH_2)_2$		62	59	80 (78)
e	$(CH_2)_5$		70	62	76 (63)

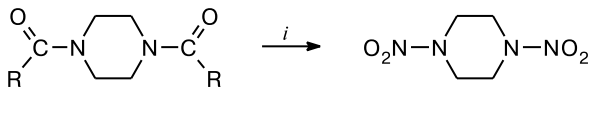
* Yields of compounds **2** in the reactions of dialkylamine nitrates with a HNO_3—AcO_2 mixture in the presence of $ZnCl_2$ in liquid (supercritical) carbon dioxide.[35]

The yields of compounds **2b—e** are comparable with that achieved by catalytic ($ZnCl_2$) nitration of dialkylamine nitrates with HNO_3/AcO_2 mixture in liquid carbon dioxide,[35] however, in our case no formation of side products, *N*,*N*-dialkylnitrosoamines, was observed.

Similar to *N*,*N*-dialkylacetamides **1**, under developed conditions, *N*,*N*-dialkylformamides **3** undergo nitration to give the corresponding nitramines **2a—e** in the yields from moderate to high. The nitrolysis of *N*,*N*-dimethylformamide **3b** proceeds most effectively giving *N*,*N*-dimethylnitramine **2b** in the yield up to 80%.

The suggested method could be used for the synthesis of compounds bearing several nitramine groups. Thus, 1,4-dinitropiperazine (**2f**) was synthesized from 1,4-diacetylpiperazine (**1f**) and 1,4-diformylpiperazine (**3f**) in 95 and 76% yields, respectively (Scheme 3). It is of note that nitrolysis of 1,4-diformylpiperazine with HNO_3 in $(CF_3CO)_2O$ resulted in the target product in 45% yield only.[11]

Scheme 3



1f, 3f **2f**

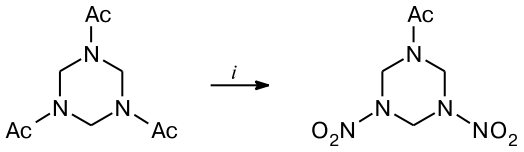
R = Me (**1f**), H (**3f**)

Reagents, conditions, and yields: *i*. N_2O_5 (3 equiv.), 100% HNO_3 (4 equiv.), CO_2 (100 bar), 20 °C, 4 h; yields of **1f** and **3f** are 95 and 76%, respectively.

Nitration of 1,3,5-triacetylhexahydro-1,3,5-triazine (**5**) with a N_2O_5—100% HNO_3 mixture in liquid CO_2 (Scheme 4) resulted in dinitro derivative **6**.

In summary, it was found that *N*,*N*-dialkylnitramines can be synthesized from *N*,*N*-dialkylcarboxamides by the action of a mixture of N_2O_5 and 100% nitric acid in liquid carbon dioxide. The absence of organic solvents and car-

Scheme 4



5 **6** (57%)

Reagents and conditions: *i*. N_2O_5 (3 equiv.), 100% HNO_3 (4 equiv.), CO_2 (100 bar), 0—20 °C, 4 h.

cinogenic side products, *N*-nitrosoamines, are the advantages of the suggested procedure.

Experimental

^{1}H NMR spectra were recorded on a Bruker AM-300 instrument (300 MHz) in $CDCl_3$ or DMSO-d_6 relative to Me_4Si as internal standard. Dichloromethane, *N,N*-dimethylacetamide, *N,N*-dimethylformamide were distilled prior to use. *N,N*-Dialkylacetamides **1a,c—f** and *N,N*-dialkylformamides **3a,c—e** were synthesized by the known methods.[36] 1,4-Diformylpiperazine,[11] 1,3,5-triacetylhexahydro-1,3,5-triazine,[37] and N_2O_5 (see Ref. 38) were prepared according to the previously described procedures.

The nitrolysis of *N,N*-diethylacetamide (1a) with N_2O_5 in liquid CO_2. A steel autoclave (V = 35 mL) containing *N,N*-diethylacetamide (**1a**) (1.15 g, 10 mmol) was filled with CO_2 (60 bar) and cooled to 0 °C. Then N_2O_5 was added with stirring (see Table 1, entries *1—3*), the reaction mixture was heated up to 20 °C, and the pressure of CO_2 was increased up to 80 bar. The reaction mixture was stirred for 4 h, CO_2 was removed, and the residue was poured into ice water (50 mL). The product was extracted with CH_2Cl_2 (4×10 mL), combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (2×20 mL), water (25 mL), and dried with Na_2SO_4. Removal of the solvent *in vacuo* afforded nitramine **2a** (the yield is given in Table 1). Physicochemical parameters and spectral characteristics of **2a** are consistent with that previously published[35].

The nitrolysis of *N,N*-diethylacetamide (1a) with a mixture of N_2O_5 and 100% HNO_3 in liquid CO_2. A steel autoclave (V = 35 mL) containing *N,N*-diethylacetamide (**1a**) (1.15 g, 10 mmol) was filled with CO_2 (60 bar) and then cooled to 0 °C. A mixture of N_2O_5 and 100% HNO_3 was added with stirring (see Table 1, entries *4—6*). The reaction was carried out and the product was isolated as described above. Removal of the solvent *in vacuo* afforded nitramine **2a** (the yield is given in Table 1).

Synthesis of nitramines 2 and 6 (general procedure). A steel autoclave (V = 35 mL) containing amide **1b—e**, **3a—e** (10 mmol) or cyclic amide **1f**, **3f**, **5** (5 mmol) was filled with CO_2 (60 bar) and cooled to 0 °C. A mixture of N_2O_5 (1.62 g, 15 mmol) and 100% HNO_3 (1.26 g, 20 mmol) was added with stirring. The reaction was carried out and the product was isolated as described above. Removal of the solvent *in vacuo* afforded nitramines **2a—e** (the yields are given in Table 2). Compounds **2f** and **6** were filtered off, successively washed with ethanol (5 mL), diethyl ether (5 mL), and air dried (the yields are given on Schemes 3 and 4).

N,N-Diethylnitramine (**2a**). B.p. 99—100 °C (18 Torr) (*cf.* Ref. 12: b.p. 90—91 °C (14 Torr)); n_D^{20} 1.4522. IR (NaCl), ν/cm^{-1}: 2984, 2936, 1500, 1452, 1376, 1276, 1084. ^{1}H NMR ($CDCl_3$), δ: 1.29 (t, 6 H, Me, J = 6.9 Hz); 3.82 (q, 4 H, NCH_2, J = 6.9 Hz).

N,N-Dimethylnitramine (**2b**). B.p. 57—58 °C (*cf.* Ref. 12: b.p. 55.5—56.5 °C). IR (KBr), ν/cm^{-1}: 3112, 2944, 1500, 1416, 1336, 1280, 1068. ^{1}H NMR ($CDCl_3$), δ: 3.42 (s, 6 H, NMe).

N,N-Di-*n*-butylnitramine (**2c**). B.p. 142—143 °C (18 Torr) (*cf.* Ref. 11: b.p. 123—124 °C (9 Torr)); n_D^{20} 1.4564. IR (NaCl), ν/cm^{-1}: 2960, 2872, 1512, 1464, 1384, 1284, 1112. ^{1}H NMR ($CDCl_3$), δ: 0.94 (t, 6 H, Me, J = 7.0 Hz); 1.33 (m, 4 H, CH_2); 1.64 (m, 4 H, CH_2); 3.70 (t, 4 H, NCH_2, J = 7.3 Hz).

N-Nitromorpholine (**2d**). B.p. 50—51 °C (*cf.* Ref. 13: b.p. 51—52 °C). IR (KBr), ν/cm^{-1}: 2984, 2872, 1512, 1380, 1312, 1256, 1116, 980, 864. ^{1}H NMR ($CDCl_3$), δ: 3.82 (s, 8 H, CH_2).

N-Nitropiperidine (**2e**). B.p. 121—122 °C (18 Torr) (*cf.* Ref. 12: b.p. 116—117 °C (17 Torr)), n_D^{20} 1.4953. IR (NaCl), ν/cm^{-1}: 2944, 2868, 1512, 1444, 1384, 1328, 1276, 1064. ^{1}H NMR ($CDCl_3$), δ: 1.52 (q, 2 H, CH_2, J = 6.0 Hz); 1.68 (m, 4 H, CH_2); 3.82 (t, 4 H, NCH_2, J = 6.0 Hz).

1,4-Dinitropiperazine (**2f**). B.p. 214—215 °C (*cf.* Ref. 11: b.p. 215—216 °C). IR (KBr), ν/cm^{-1}: 2984, 2888, 1556, 1448, 1388, 1244, 1096, 960. ^{1}H NMR (DMSO-d_6), δ: 4.06 (s, 8 H, CH_2).

1-Acetyl-3,5-dinitrohexahydro-1,3,5-triazine (**6**). B.p. 156—157 °C (*cf.* Ref. 39: b.p. 158—159 °C). ^{1}H NMR (DMSO-d_6), δ: 2.17 (s, 3 H, $C(O)CH_3$); 5.64 (s, 4 H, $N(NO_2)CH_2NAc$); 6.14 (s, 2 H, $N(NO_2)CH_2NNO_2$).

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