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Dedicated to Professor V.A.Ostrovskii on occasion of his sixtieth birthday

Oxidative Nitration of Mononitroalkanes in a System Sodium Nitrite-Polyhaloalkane

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Abstract—In reaction of nitroethane lithium salt with sodium nitrite in DMSO, DMF or HMPA involving polyhaloalkanes 1,1-dinitroethane formed in a high yield. The highest yield was obtained with bromo- and iododerivatives. The reaction fits to a kinetic equation of overall second order: the first with respect to the nitroethane anion, and the first in polyhaloalkane. The rate constants of the process are linearly dependent on the electron affinities of the perhaloalkanes molecules.

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The procedures for mononitroalkanes nitration into *gem*-dinitroalkanes known now belong as a rule to ion-radical processes since they include a stage of a single-electron transfer (SET) [1, 2]. Nitroalkanes in alkaline media give nitrocarbanions that are sufficiently active electron-donors with respect to acceptors of diverse character: molecular oxygen [3], aromatic nitro compounds [4–6], polynitro- and halonitroalkanes [2, 7]. As a result of the single-electron oxidation with these acceptors the nitrocarbanions form highly reactive nitroalkyl radicals. These radicals either undergo recombination with other radicals present in the system (oxidation products of other ions) (path *a*), or react with nucleophilic agents to form anion-radicals [8] (path *b*). The latter in the presence of single-electron oxidants can convert into α-substituted nitroalkanes that in event of terminal nitro compounds provide anions (Scheme 1). A chain reaction mechanism occurs frequently in the case *b*.

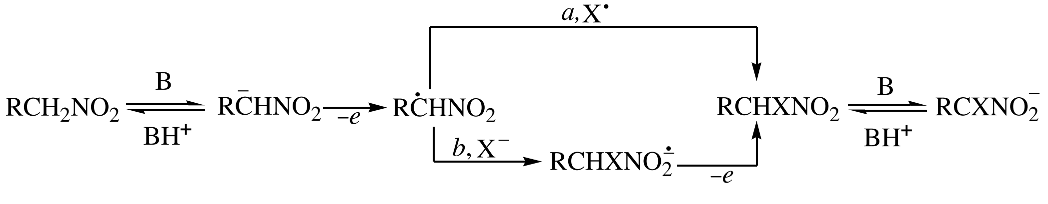
The existing methods of 1,1-dinitroalkanes preparation from mononitroalkanes possess significant disadvantages, like the formation of hazardous side products (trinitromethane salts) in nitration with tetranitromethane in the presence of bases [9], the application of expensive silver salt in the oxidative nitration with silver nitrate [10], and a multistage process in the ter Meer reaction of 1-nitro-1-chloroalkanes with sodium nitrite [11].

Therefore the development of new efficient synthetic procedures for *gem*-dinitroalkanes is desirable, in particular, by means of oxidative nitration of mononitroalkanes applying more available oxidants. It is presumable that geminal dinitro compounds can form in oxidation of nitrocarbanions in the presece of excess nitrite ion.

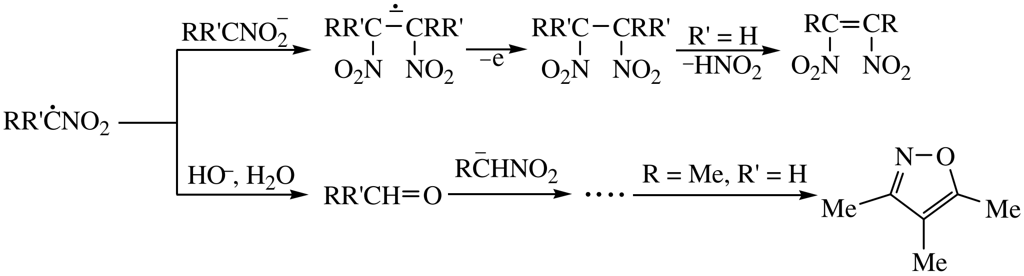
A persulfate dianion is a well-known reagent capable of oxidating nitrocarbanions into nitroalkyl radicals in a water environment [12, 13]. Just at the use of this oxidant an intermediate formation of nitroalkyl radicals was proved [14, 15]. It is curious in this connection why in [12] was stated that no formation of gem-dinitroalkanes occurred in oxidation of nitroalkanes salts with ammonium persulfate in the presence of sodium nitrite.

Therefore we carried out a thorough investigation of oxidation under the said conditions of nitroethane, 1-nitrobutane, and 2-nitropropane alkali metal salts. We established spectrophotometrically that from the nitroethane and 1-nitrobutane *gem*-dinitroalkanes formed in 15 and 18% yield respectively. Yet the main products of

Scheme 1.



Scheme 2.



this reaction were carbonyl compounds and transformation products of trimer and dimer character respectively: 3,4,5-trimethylisoxazole from 1-nitroethane and 4-nitro-4-octene from 1-nitrobutane, the product of nitrous acid elimination from the intermediately formed 4,5-dinitrooctane.

The oxidation of 2-nitropropane anion with ammonium persulfate in the presence of a double excess of $NaNO_2$ gave rise to 2,3-dimethyl-2,3-dinitrobutane (35%) and acetone (30%) like in the process of oxidative dimerization of nitroalkanes salts without sodium nitrate [12].

The low yield of *gem*-dinitro compounds from the primary mononitroalkanes is understandable taking into account that under the given conditions the reaction mixture besides the nitrite ion contains also other nucleophilic agents: the initial nitrocarbanion, hydroxy ion, and water that successfully compete with the nitrite ion for the nitroalkyl radicals (Scheme 2). Therewith the reaction with the two latter nucleophiles results in the formation of carbonyl compounds and consequently of trialkylisoxazoles [13]. This suggestion is well consistent with numerous data on carbonyl compounds formation as final or side products in nitrocarbanions oxidation in water environment [3, 12, 13]. Therefore the application of hydroxy-containing solvents is hardly feasible.

Suitable media with a minimum number of nucleophiles competing for the nitroalkyl radical and therefore with minimum opportunities for the side reactions are aprotic bipolar solvents. Since in these solvents lacks the specific solvation of mononitrocarbanions prone to hydrogen bonds formation with the hydroxy-containing solvents [16] lacks and thanks to this circumstance the energy expenditure decreases for desolvation in the course of single-electron oxidation it is conceivable that milder organic electron-acceptors might be applied. Tetrachloro-methane may be used like such reagent as is shown by an example of 2-nitropropane lithium salt oxidation in DMSO [17]. The oxidative action of the tetrachloro-methane consists in an electron capture from the 2-nitro-propane anion to form 2-nitropropyl radical. Inasmuch as the tetrachloromethane is widely available its application as oxidant merits attention.

In oxidation of nitroethane lithium salt with tetrachloromethane in the presence of a double excess of sodium nitrite in DMSO we obtained 1,1-dinitroethane in 35% yield. The discovered reaction of oxidative nitration is sensitive to the solvent character: It proceeds only in aprotic bipolar solvents DMSO, DMF, and HMPA (Table 1) confirming the above suggestion of a considerable influence of specific solvation on the reaction under study.

The result of the reaction depends besides to a significant extent on the solubility of the nitroalkane salt in the applied solvent. For instance, at the use of dioxane and acetonitrile where the nitroethane lithium salt is nearly insoluble only traces of *gem*-dinitroethane were found.

The insufficiently high yield of the nitromethane in DMSO (35%) was presumably due to the low efficiency

Table 1. Effect of solvent on the yield of 1,1-dinitroethane in oxidative nitration of nitroethane lithium salt in a system sodium nitrite–tetrachloromethane, $CH_3CHNO_2Li : CCl_4 : NaNO_2$ = 1:2:3

Solvent	Yield, %	Time, h[a]
DMSO	35	0.3
DMSO–H_2O, 7:1	35	1
DMSO–H_2O, 6:1	27	2
DMSO–H_2O, 2:1	21	3.5
HMPA	22	0.5
DMF	21	2
Dioxane–H_2O, 7:1	Trace	3
Acetonitrile	Trace	3
Ethanol	0	10

[a] Optimum reaction time is presented determined by spectrophotometric monitoring of 1,1-dinitroethane accumulation.

Table 2. Yield of 1,1-dinitroethane in oxidative nitration of nitroethane lithium salt in a system sodium nitrite–polyhaloalkane[a], DMSO, 25°C, CH_3CHNO_2Li:RX:$NaNO_2$ = 1:2:3

Haloalkane	Reaction time, min	Yield, %[b]	$-E_{1/2}$, V [18]
CBr_4	3	86	0.30
$CBrCl_3$	5	73	–
CI_4	30	80	–
C_2Br_6	20	53	0.68
CCl_4	20	35	0.78
C_2Cl_6	20	24	0.62
$C_2Br_2F_4$	45	21	–
CHI_3	60	6	0.49

[a] In the presence of halogen compounds listed further (compound and $-E_{1/2}$, V, value [18]) 1,1-dinitroethane did not form in 24 h under common conditions: CH_2I_2, 1.12; CCl_3F, –; $CHCl_3$, 1.67; CH_2Cl_2, 2.33; $(CFCl_2)_2$, –; $PhCCl_3$, 0.68; C_6Cl_6, 1.44.

[b] Yield measured by spectrophotometry.

of CCl_4, therefore we tested the application in this reaction of other polyhaloalkanes as oxidation agents.

As seen from Table 2, the oxidative nitration of the nitroethane lithium salt with sodium nitrite occurred successfully not only in the presence of tetrachloromethane, but also with other polyhaloalkanes. The highest yield (up to 86%) was attained at the use of bromo- and iododerivatives.

The efficiency of polyhaloalkanes in the reaction in question changed in parallel with the halfwave potential of their polarographic reduction.

The interaction of polyhaloalkanes with electron-donors is known to occur by "dissociative electron capture") [19].

$$RX + e \rightarrow R^{\bullet} + X^{-}$$

The electron affinity of an acceptor molecule EA(RX) depends on the electron affinity of the radical departing as anion $EA(X^{\bullet})$, on the solvation enthalpy of this anion (ΔH_s), and also on the strngth of the broken bond D(R–X) [20].

$$EA(RX) = EA(X^{\bullet}) + \Delta H_s - D(R–X) \quad (1)$$

Energy of bond rupture for C–Br and C–I bonds is considerably less than that for C–Cl (Table 2) resulting in the higher reactivity of the corresponding electron acceptors.

When the molecule contains fragments capable of unpaired electron stabilization, another direction is possible for the acceptor interaction with the electron: a formation of a stable ion-radical. This path is less favorable by energy and as a rule is more difficultly attained [19]. Therefore the presence of stabilizing factors (a fluorine atom [21] and a phenyl ring [22]) reduced the reactivity of the oxidant. Thus the factors favoring the dissociative character of the electron capture by the acceptor increase the efficiency of the latter in the oxidative nitration.

To establish the quantitative relation between the electron-acceptor properties of the oxidant and its efficiency and to refine the suggested scheme of the process we studied the kinetics of the nitroethane lithium salt reaction with sodium nitrite in the presence of a series of active polyhaloalkanes in DMSO. In keeping with the suggested scheme the process involves an electron transfer from the nitrocarbanion to the acceptor (polyhaloalkane) leading to the formation of nitroalkyl radical that can react both with nitrite ion to give the target product and with nitroalkane anion to produce 2,3-dinitrobutane which also is found in the reaction products. We exclude the possibility of the reaction to proceed via successive halogenation of the nitroethane and halogen substitution by the nitrite ion. This pathway requires either appearance of a halogen atom by polyhaloalkane decomposition along a less enegetically favorable route into a halogen radical and carbanion, or a successful competition with the excess nitrite of a halide anion arising in situ in the stage of addition to the nitroalkyl radical.

The radical character of the process is indicated by the influence of the UV irradiation and of oxygen. The irradiation with a strong source (a mercury lamp PRK-4) considerably accelerated the reaction, and the saturation of the solution with oxygen notably reduced the yield of 1,1-dinitroethane. The active nitroalkyl radicals apparently reacted with oxygen to yield peroxy radicals that resulted in side products [6]. Therefore all experiments were carried out using deoxygenated solutions.

The studied reaction is described by a kinetic equation of overall second order: first order in nitroethane anion and first order in polyhaloalkane. The reaction order is zero with respect to nitrite ion thus indicating that this reagent is not involved in the rate-determining stage of the process. Inasmuch as the radical species are very active the limiting stage is evidently the first one, involving the electron transfer from the nitrocarbanion to the polyhaloalkane. Therefore the kinetic data provide the rate constant of this stage only (k). The experimental rate constants (Table 3) are apparent values for they do

Table 3. Parameters of electron affinity and reaction rate between polyhaloalkanes and nitroethane lithium salt (DMSO, 25°C)

Polyhaloalkane	X	$EA(X^-)$ [19, 23], kcal mol^{-1}	ΔH_s [24], kcal mol^{-1}	D(R–X) [23], kcal mol^{-1}	EA(RX), kcal mol^{-1}	$-\log k$	$\Delta G^{\neq}$, kcal mol^{-1}
CBr_4	Br	77.6	38	49.7	65.9	0.36	11.19
$CBrCl_3$	Br	77.6	38	55.8	59.8	0.60	11.57
CI_4	I	70.6	33	44.2	59.4	1.02	12.09
C_2Br_6	Br	77.6	38	–	59.0	1.04	12.12
CCl_4	Cl	83.2	40	73.3	49.9	1.28	12.45
C_2Cl_6	Cl	83.2	40	73.7	51.6	1.32	12.50
$C_2Br_2F_4$	Br	77.6	38	69.6	50.7	1.66	12.96
CHI_3	I	70.6	33	55.0	49.0	1.75	13.09

not take into account the possible reagents association into ion pairs; still they may be used in approximate calculations and correlations with indication of certain limits.

A fair correlation exists between the oxidation rate of nitroethane by polyhaloalkanes and the electron affinity of these acceptors calculated by equation (1); the correlation is described by expression (2). This fact additionally confirms that the electron transfer from the nitrocarbanion to the acceptor is the limiting stage of the process.

$$\Delta G^{\neq} = (0.09 \pm 0.01)\, EA(\mathrm{RX}) - (17 \pm 1); \quad n\ 7,\ r\ 0.95,\ s\ 0.16. \tag{2}$$

Equation (2) is a typical example of fulfillment of the extrathermodynamical relation between the kinetic and thermodynamic parameters of electron transfer process [25]. The slope of this line characterizes the position of the transition state on the reaction coordinate. Its relatively small value (0.09) reveals that the transition state is close to the initial reagents. Inasmuch as the reaction of polyhaloalkanes with nitrocarbanions is exothermal these results are well consistent with the known Hammond rule [26] stating that an early transition state is characteristic of such reactions.

EXPERIMENTAL

^{1}H NMR spectra were registered on a spectrometer Perkin Elmer R-12 (60 MHz) from solutions in acetone-d_6, reference HMDS. IR spectra were recorded on a spectrophotometer Specord 75IR from thin films, UV spectra, on a spectrophotometer Perkin Elmer 402. Molecular weights were measured by reversed ebullioscopic method.

Initial reagents and solvents were purified by standard procedures [27], their characteristics were in agreement with the published data. The purity of compounds was checked by GLC on a chromatograph Tsvet-4 equipped with a katharometer, metal column 3×3000 mm, stationary phase 15% of Carbowax 20M on Chezasorb, oven temperature 60°C, vaporizer temperature 150°C, that of detector 170°C.

Nitroethane oxidation with ammonium persulfate. To a solution of 5 g (0.066 mol) of nitroethane, 4.0 g (0.1 mol) of sodium hydroxide, and 13.8 g (0.2 mol) of sodium nitrite in 200 ml of water was added at 0–10°C 45.6 g (0.2 mol) of a mmonium persulfate. After stirring for 1 h the reaction mixture was diluted to a volume of 250 ml. 10 µl of the solution obtained was injected with a calibrated microsyringe into 6.0 ml of 0.1 N NaOH solution, and the UV spectrum was recorded. The optical density in the absorption maximum at 381 nm (0.29) taking into account the molar extinction [28] corresponded to the 1,1-dinitroethane yield 15%.

The diluted reaction mixture was extracted with ethyl ether (3×100 ml). The ether extracts were washed with water, 5% sodium hydrogen carbonate solution, and dried with magnesium sulfate. The solvent was evaporated, the residue was distilled in a vacuum. We obtained 0.86 g (35%) of 3,4,5-trimethylisoxazole, bp 135–137°C (250 mm Hg) [29], n_D^{20} 1.456 [29]. ^{1}H NMR spectrum, δ, ppm: 2.20 s (3H, 5-CH_3), 2.10 s (3H, 3-CH_3), 1.85 s (3H, 4-CH_3). Found, %: C 64.47; H 7.99; N 12.81. *M* 113 (benzene). C_6H_9NO. Calculated, %: C 64.84; H 8.16; N 12.60. *M* 111.14.

Oxidation of 1-nitrobutane was done similarly. By vacuum distillation we obtained 1.3 g (25%) of 4-nitro-4-octene, bp 67–69°C (2 mm Hg), n_D^{20} 1.4595 {66–68°C (2 mm Hg), n_D^{20} 1.4593 [30]}. Found, %: C 61.34; H 9.47;

N 8.59. *M* 160 (benzene). $C_8H_{15}NO_2$. Calculated, %: C 61.12; H 9.62; N 8.91. *M* 157.21.

The mother liquor remaining after extraction was acidified with hydrochloric acid and then treated with excess 2,4-dinitrophenylhydrazine to obtain butyraldehyde 2,4-dinitrophenylhydrazone in a quantity corresponding to 1.4 g (30%) of butyraldehyde, mp 122°C [31], no melting point depression on mixing with an authentic sample.

Oxidation of 2-nitropropane was done similarly. The reaction mixture was poured on ice, the separated precipitate was filtered off. We obtained 1.8 g (35%) of 2,3-dimethyl-2,3-dinitrobutane, mp 210°C [17], no melting point depression on mixing with an authentic sample.

The filtrate was acidified with 10% HCl and then treated with 2,4-dinitrophenylhydrazine to obtain acetone 2,4-dinitrophenylhydrazone in a quantity corresponding to 1.15 g (30%) of acetone, mp 128°C [32], no melting point depression on mixing with an authentic sample.

Oxidative nitration of nitroethane lithium salt in a system sodium nitrite–polyhaloalkane. Through a solution of 2 g (0.0247 mol) of finely ground nitroethane lithium salt and 5.1 g (0.074 mol) of sodium nitrite in 150 ml of solvent dry nitrogen was passed for 15 min. Under continuous nitrogen flow 0.05 mol of polyhalomethane was quickly added at 25°C. The reaction was monitored spectrophotometrically by taking samples into 0.1 N NaOH. When the optical density at 381 nm (absorption maximum of 1,1-dinitroethane anion) no more increased the reaction mixture was poured into ice water (500 ml), acidified with 10% H_2SO_4 to pH 3, and extracted with ether (3×100 ml). The combined ether extracts were evaporated to 1/4 of the initial volume, then 10% solution of KOH in methanol was added till alkaline reaction. The separated 1,1-dinitroethane potassium salt was recrystallized from 50% ethanol. Yield 1.1 g (27%). UV spectrum (0.1 N NaOH), λ_{max} 381 nm, log μ 4.22 (λ_{max} 381.5 nm, log μ 4.21 [28]). Found, %: C 14.98; H 2.02; N 17.95. $C_2H_3KN_2O_4$. Calculated, %: C 15.19; H 1.91; N 17.71.

Procedure of kinetic experiments. The deoxygenated solutions of nitroethane lithium salt and sodium nitrite of an appropriate concentration were placed into a temperature-controlled at 25±0.1°C reactor equipped with a propeller stirrer and a bubbler for inert gas. On reaching the necessary temperature a weighed quantity of polyhaloalkane was added, the reaction mixture was sampled intermittently by a calibrated microsyringe and poured into a definite volume of 0.1 N NaOH. The reaction progress was monitored by 1,1-dinitroethane anion accumulation. The concentration of nitroethane lithium salt was 0.0825 mol l^{-1}, that of polyhaloalkane, 0.165 mol l^{-1} (stoichiometric ratio), sodium nitrite was taken in excess, 0.5–1.0 mol l^{-1}.

The rate constants were calculated by the known second-order equation [33] as an arithmetic mean of three parallel runs carried out under identical conditions. The errors in constants determination did not exceed 5–7%.

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