INTERACTION OF N-HALOMETHYL-N-NITRAMIDES WITH NUCLEOPHILIC REAGENTS

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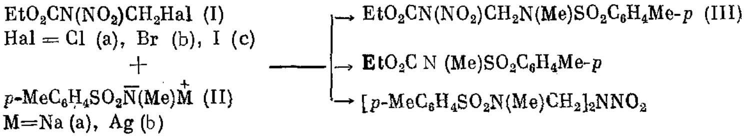
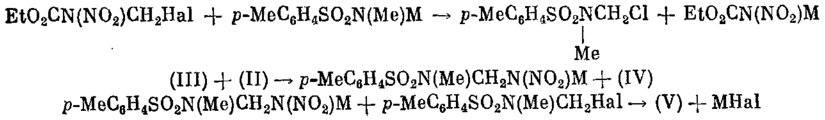
The reaction of N-chloromethyl-N-nitramines with nucleophilic reagents is fairly widely used in the synthesis of various functional derivatives of nitramines [1-4]. The interaction of recently synthesized N-halomethyl-N-nitramides [5] with a series of nucleophilic reagents has been studied by us with the aim of clarifying the possibility of an analogous synthesis of derivatives of N-nitramides and the main principles of the reaction. The reaction of N-halomethyl-N-nitrourethanes (I) with salts of N-methyltoluene-p-sulfonamide (II) has been studied most completely. It was established that three main products were formed, viz., N-carbethoxy-N'-toluene-p-sulfonamide-N'-methyl-N-nitromethylenediamine (III), N-carbethoxy-N-methyltoluene-p-sulfonamide (IV), and 1,5-ditoluene-p-sulfonyl-1,5-dimethyl-3-nitro-1,3,5-triazapentane (V). The formation of (III) and (IV) is evidently explained by nucleophilic attack by the anion (II) at the methylene or carbethoxyl groups, respectively. Various schemes may be proposed for the formation of (V), particularly the following in which primary attack of the methylene group is also proposed, as for the formation of (III), but the role of the leaving group is taken not by Cl$^-$ but by the nitromethane anion. The ratio of products depends on the character of the halogen in (I) and the metal in (II) (Table 1). The preferential formation of the product of nitramidomethylation (III) was observed when using the Ag$^+$ salt (IIb) due to the high affinity of Ag$^+$ for halogen and the electrophilic cooperation of their substituents. It should be mentioned that of the halogen derivatives (I), the bromo derivative (Ib) gave the best results, which is explained by the mobility of Br in comparison with Cl in (Ia) and the seemingly lower stability of the iodo derivative (Ic) in comparison with (Ib). Compound (Ia) is also a completely acceptable nitramidomethylating agent, which was demonstrated by its reactions with Ag$^+$ salts of nitric and nitrous acids, N-nitrotoluene-p-sulfonamide, and N-nitroethylurethane (Table 2).



$$\begin{array}{l} EtO_2CN(NO_2)CH_2Hal\ (I) \\ Hal = Cl\ (a),\ Br\ (b),\ I\ (c) \\ \qquad\qquad + \\ p\text{-}MeC_6H_4SO_2\overline{N}(Me)\overset{+}{M}\ (II) \\ M{=}Na\ (a),\ Ag\ (b) \end{array} \longrightarrow \left[\begin{array}{l} \to EtO_2CN(NO_2)CH_2N(Me)SO_2C_6H_4Me\text{-}p\ (III) \\ \to EtO_2CN(Me)SO_2C_6H_4Me\text{-}p \\ \to [p\text{-}MeC_6H_4SO_2N(Me)CH_2]_2NNO_2 \end{array}\right.$$



$$EtO_2CN(NO_2)CH_2Hal + p\text{-}MeC_6H_4SO_2N(Me)M \to p\text{-}MeC_6H_4SO_2\underset{\substack{|\\ Me}}{N}CH_2Cl + EtO_2CN(NO_2)M$$

$$(III) + (II) \to p\text{-}MeC_6H_4SO_2N(Me)CH_2N(NO_2)M + (IV)$$

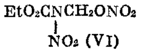
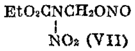
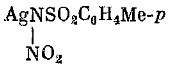
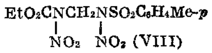
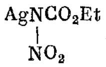
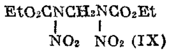
$$p\text{-}MeC_6H_4SO_2N(Me)CH_2N(NO_2)M + p\text{-}MeC_6H_4SO_2N(Me)CH_2Hal \to (V) + MHal$$

TABLE 1. Yields of Products from the Reaction of N-Halomethyl-N-nitroethylurethanes (I) with Na$^+$ (IIa) and Ag$^+$ (IIb) Salts of N-Methyltoluene-p-sulfonamide

Reactants		Yield of products, %		
(I)	(II)	$TsN(Me)CH_2N(NO_2)\cdot CO_2Et$ (III)	$TsN(Me)CO_2Et$ (IV)	$(Ts\underset{\substack{|\\ Me}}{N}{-}CH_2)_2NNO_2$ (V)
(Ia)	(IIa)	11	49	23
(Ia)	(IIb)	37	24	17
(Ib)	(IIa)	19	39	20
(Ib)	(IIb)	62	–	–
(Ic)	(IIa)	–	31	58
(Ic)	(IIb)	49	–	–

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 12, pp. 2738-2741, December, 1982. Original article submitted February 1, 1982.

TABLE 2. Alkylation Products of N-Chloromethylurethane (Ia)

Alkylatable compound	Reaction product	Yield, %	Characteristics	PMR spectrum in CCl_4 (δ, ppm)	IR spectrum (ν, cm^{-1})	Empirical formula	$\frac{\text{Found}}{\text{Calculated}}$, %		
							C	H	N
$AgNO_3$	 $EtO_2C\underset{NO_2}{N}CH_2ONO_2$ (VI)	68	bp 93–95 (1 mm) n_D^{21} 1,4609	1,35 t, 4,37 q (Et), 6,23 s (CH_2)	1800 (C=O) 1668 (ONO_2) 1605, 1276 (NNO_2)	$C_4H_7N_3O_7$	$\frac{23,35}{22,99}$	$\frac{3,42}{3,35}$	$\frac{20,08}{20,12}$
$AgNO_2$	 $EtO_2C\underset{NO_2}{N}CH_2ONO$ (VII)	64	n_D^{20} 1,4611	1,33 t, 4,33 q (Et), 6,23 s (CH_2)	1797 (C=O) 1675 (ON=O) 1612, 1290 (NNO_2)	$C_4H_7N_3O_6$	$\frac{25,17}{24,85}$	$\frac{3,83}{3,62}$	–
 $Ag\underset{NO_2}{N}SO_2C_6H_4Me\text{-}p$	 $EtO_2C\underset{NO_2}{N}CH_2\underset{NO_2}{N}SO_2C_6H_4Me\text{-}p$ (VIII)	41	mp 50–51° (C_6H_6–(hexane)	1,25 t, 4,28 q (Et), 2,34 s, 7,52 q (p-Me-C_6H_4), 6,27 s (CH_2)	1780 (C=O) 1620, 1600, 1290, 1260 (NNO_2) 1390, 1180 (S=O)	$C_{11}H_{14}N_4O_8S$	$\frac{36,42}{36,43}$	$\frac{3,82}{3,87}$	$\frac{15,50}{15,46}$
 $Ag\underset{NO_2}{N}CO_2Et$	 $EtO_2C\underset{NO_2}{N}CH_2\underset{NO_2}{N}CO_2Et$ (IX)	36	n_D^{20} 1,4756	1,32 t, 4,32 q (Et), 6,11 s (CH_2)	1800 (C=O) 1613, 1268 (NNO_2)	$C_7H_{12}N_4O_8$	$\frac{29,79}{30,00}$	$\frac{4,32}{4,30}$	–

As is evident from the data obtained and those presented in [5], the yields of the nitramidomethylation reaction were reduced according to the extent of the transition from nucleophiles in which the charge is centered on the group VII atoms (Br^-, I^-) to nucleophiles with the charge localized on the group VI atom (NO_2^-, NO_3^-) and then to nuclophiles with delocalized charges on the group VI and V atoms (anions of N-nitramides). The low yields of nitramidomethylation products in the case of nitramide salts are seemingly explained not only by the possibility of acylation of amides but also by the formation of unstable derivatives at the second center of the ambident anion, viz., the O atom of the nitro group. Evidently it is possible to explain by the latter circumstance the unsuccessful attempts at nitramidomethylation by Na^+, Et_3NH^+, or Ag^+ salts of methylnitramide in reactions with (Ia) since alkylnitramines are more inclined to undergo electrophilic attack at the oxygen of the NO_2 group than are N-nitramides.

Besides the nature of the halogen in (I), the nucleophilic reagent, and the nature of the counter ion in it, there is still one factor showing to a lesser extent an influence on the yields of nitramidomethylation product. This is the relative activity of the acidic residue in the N-halomethyl-N-nitramide toward nucleophilic attack, a reduction of which must be conducive to an increase in the yield of nitramidomethylation products. Confirmation of this may be served by the reaction of Ag^+ salts of N-nitrotoluene-p-sulfonamide (X) with N-chloromethyl-N-nitromethanesulfonamide (XI) in which the yield of nitramidomethylation product was ~1.5 times greater than for the analogous reaction of (X) with (Ia).

$$\underset{\text{(XI)}}{MeSO_2N(NO_2)CH_2Cl} + \underset{\text{(X)}}{AgN(NO_2)SO_2C_6H_4Me\text{-}p} \rightarrow$$

$$MeSO_2N(NO_2)CH_2N(NO_2)SO_2C_6H_4Me\text{-}p \text{ (XII) } 56\%$$

EXPERIMENTAL

General Procedure for Reactions of N-Halomethyl-N-nitroethylurethanes (I) with Na^+ and Ag^+ Salts of N-Methyltoluene-p-sulfonamide (II). Compound (II) (36 mmole) was added to a solution of (I) (33 mmole) in abs. MeCN (10 ml) and stirred for 7 h at ~25°C. The precipitate was filtered off and the solution evaporated. Products were identified in the mixture by PMR spectra compared with spectra of known specimens. The filtered-off precipitate was placed in water (20 ml), acidified with H_2SO_4, extracted with $CHCl_3$ (5 × 15 ml), and the extracts dried over Na_2SO_4. After evaporation of the solvent the organic residue was analyzed by PMR spectrum. The obtained results are presented in Table 1.

N-Carbethoxy-N'-toluene-p-sulfonyl-N'-methyl-N-nitromethylenediamine (III). A saturated solution of $EtO_2CN(NO_2)Ag$ (0.9 g, 37 mmole) was added to a solution of $p\text{-}MeC_6H_4SO_2N(Me)CH_2Cl$ (0.9 g, 37 mmole) in abs. MeCN and stirred for 2 h. The solid was filtered off and the solvent evaporated. Absolute Et_2O (15 ml) was added to the oily residue and the mixture placed in a Dewar vessel with dry ice for 2 h. The solid which separated was filtered off and washed with Et_2O. Compound (III) (0.9 g, 71%) of mp 76.5-77.5°C (C_6H_6–hexane) was obtained. PMR spectrum ($CDCl_3$, δ, ppm): 1.30 t ($MeCH_2$), 2.34 (MeC_6H_4), 2.82 s (MeN), 4.27 q (CH_2Me), 5.32 s (CH_2), 7.40 q (H-arom.). IR spectrum (ν, cm^{-1}): 1780 (C=O), 1608, 1270 (NNO_2), 1348, 1170 (S=O). Found: C 43.65; H 5.13; S 9.62%. $C_{12}H_{17}N_3O_6S$. Calculated: C 43.55; H 5.14; S 9.68%.

N-Carbethoxy-N-methyltoluene-p-sulfonamide (IV). $p\text{-}MeC_6H_4SO_2N(Me)Na$ (2.07 g, 10 mmole) was added in portions to a solution of EtOCOCl (1.09 g, 10 mmole) in abs. MeCN (20 ml) and stirred for 4 h at 30-40°C. The precipitate was filtered off, the solvent evaporated, and the residue distilled. Compound (IV) (2.0 g, 78% of bp 133°C) (0.7 mm) and n_D^{21} 1.4563 was obtained. PMR spectrum (acetone-d_6, δ, ppm): 1.10 t ($MeCH_2$), 2.34 s (MeC_6H_4), 3.33 s (MeN), 4.03 q (CH_2Me), 7.55 q (H-arom.). IR spectrum (ν, cm^{-1}): 1750 (C=O), 1610 (C=C), 1300, 1175 (S=O). Found: C 51.11; H 5.93%. $C_{11}H_{15}NO_4S$. Calculated: C 51.40; H 5.84%.

1,5-Ditoluene-p-sulfonyl-1,5-dimethyl-3-nitro-1,3,5-triazapentane (V) (isolated from the reaction mixture). Mp 188-189.5°C (from EtOH). Spectrum (d_6-DMSO, δ, ppm): 2.34 s (MeC_6H_4), 2.82 s (MeN), 5.18 s (CH_2), 7.56 q (H-arom.). IR spectrum (KBr, ν, cm^{-1}): 1610 (C=C), 1558, 1292 (NNO_2), 1344, 1160 (S=O). Found: C 47.25; H 5.28%. $C_{18}H_{24}N_4O_6S_2$. Calculated: C 47.38; H 5.27%.

N-Nitroxymethyl-N-nitroethylurethane (VI). $AgNO_3$ (0.93 g, 54.8 mmole) was added to a solution of (Ia) (0.5 g, 27.4 mmole) in MeCN (10 ml). The mixture was stirred for 1.5 h at ~20°C. The solid was filtered off and the solvent evaporated. The residue was treated with abs. Et_2O (20 ml). The solid was filtered off and Et_2O evaporated. Compound (VI) (0.39 g) was obtained.

N-Hydroxymethyl-N-nitroethylurethane nitrite ester (VII) was obtained in a manner analogous to (VI). Stirring time was 4 h at ~20°C.

N-Carbethoxy-N'-toluene-p-sulfonyl-N,N'-dinitromethylenediamine (VIII). p-$MeC_6H_4SO_2N(NO_2)Ag$ (X) (1.8 g, 81 mmole) was added to a solution of (Ia) (0.98 g, 54 mmole) in MeCN (10 ml), the mixture stirred for 2 h at ~20°C, and then boiled for 4 h. The solid was filtered off and the solvent evaporated. The residue was separated by chromatography on silica gel (C_6H_6). Compound (VIII) (0.8 g) was obtained.

Methylene-bis-N-nitroethylurethane (IX). A solution of $EtO_2CN(NO_2)Ag$ (0.91 g, 38 mmole) in abs. MeCN (40 ml) was added to a solution of (Ia) (0.46 g, 25 mmole) in MeCN (10 ml). The mixture was stirred for 7 h at 20°C and 7 h at 80°C. The solid was filtered off and the solvent evaporated. The residue was separated by chromatography on silica gel ($Et_2O : C_6H_6$-1 : 4).

1-Methanesulfonyl-3-toluene-p-sulfonyl-1,3-dinitro-1,3-diazapropane (XII). Compound (X) (0.49 g, 29 mmole) was added to a solution of (XI) (0.39 g, 20 mmole) in abs. MeCN (40 ml) and the mixture boiled with stirring for 10 h. The solid was filtered off, the solvent evaporated, the oily residue was treated with H_2O (30 ml), the crystalline substance was filtered off, washed with EtOH, and air-dried. Compound (XII) (0.3 g, 56%), mp 148.5-150°C (from EtOH) was obtained. PMR spectrum (d_6-DMSO, δ, ppm): 2.34 s (MeC_6H_4), 3.67 s ($MeSO_2$), 6.45 s (CH_2), 7.65 q (H-arom.). IR spectrum (KBr, ν, cm^{-1}): 1610, 1295 (NNO_2), 1380, 1395, 1200, 1187 (S=O). Found: C 29.39; H 3.31; S 17.2%. $C_9H_{12}N_4O_8S_2$. Calculated: C 29.39; H 3.26; S 17.40%.

CONCLUSIONS

The main features of the reaction of N-halomethyl-N-nitramides with nucleophilic reagents have been established.

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NITROYLIDES

8. INTERACTION OF IODONIUM NITROMETHYLIDES WITH AROMATIC COMPOUNDS

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It was shown previously that nitromethylides of iodine are capable of transfering their nitromethylene fragment to a heteroatom with a free pair of electrons with the formation of new nitromethylides [1, 2]:

$$Ar\overset{+}{I} - \overline{C}(X)NO_2 + R_nE: \rightarrow ArI + R_n\overset{+}{E} - \overline{C}(X)NO_2$$

In the present work the interaction has been investigated of iodonium nitromethylides with a different type of donor, viz., donors of π-electrons (π-donors). Aromatic hydrocarbons possessing additional nucleophilic and also a stable closed system of π-electrons were chosen as π-donors. Dinitromethylides of iodine were selected as models in reactions with liquid derivatives of benzene since it was then possible to operate without solvent, which often interacts with iodine nitromethylides.

Phenyliodonium dinitromethylide (I), unstable in the crystalline state and decomposing in 2-3 min after isolation [3], was decomposed significantly more slowly (~50 min on shaking) in suspension under a layer of benzene at ~20°C with the formation of a homogeneous solution. According to GLC and TLC data, there were only two products in the reaction mixture, viz., iodobenzene and phenyldinitromethane (II):

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