INTRAMOLECULAR ALKYLATION OF ANIONS OF NITRAMINES

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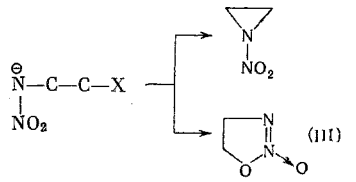
It is known that γ-halo nitro compounds when treated with alkalis form carbanions, which enter into the intramolecular nucleophilic substitution reaction and lead to the formation of either cyclopropane derivatives (C-alkylation) or the N-oxides of isoxazolines (O-alkylation) [1, 2].

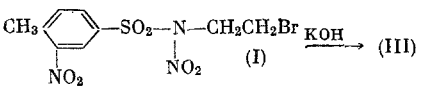
It was interesting to ascertain the behavior of the nitrogen analogs of nitro carbanions under these conditions. It could be expected that the intramolecular alkylation reaction will go in two directions, and lead to the formation of nitroaziridines (N-alkylation) and (or) the 2-oxides of 4,5-dihydro-1,2,3-oxadiazoles (O-alkylation):



(III)

We selected N-(β-bromoethyl)-N-nitro-m-nitro-p-toluenesulfonamide (I), which was obtained by the nitration of N-(β-bromoethyl)-p-toluenesulfonamide (II), as the object to study the reaction for the intramolecular alkylation of the anions of nitramines. It is known that alkylnitrosulfonamides when treated with alkali form alkylnitramine salts [3]. Consequently, the formation of the $\overset{\ominus}{N}(NO_2)-CH_2CH_2Br$ anion could be expected when (I) is treated with alkali.

The reaction of (I) with KOH leads to the formation of 2-hydroxy-4,5-dihydro-1,2,3-oxadiazole (III) in 85% yield, the structure of which was proved by the elemental analysis data, and by the data of mass spectroscopy (M^+, corresponding to the formula $C_2H_4N_2O_2$) and ^{13}C-radiospectroscopy (two similar singlets at 128.5 and 133.5 ppm). In the IR spectrum of (III) the bands at 1250 and 1620 cm^{-1} can be assigned to the $N{=}N\langle^{O}_{OR}$ grouping [4]:



(III)

An absorption maximum at 220 mμ (log ε 3.44) is present in the UV spectrum of (III). A similar picture is observed in the UV spectra of the O-alkyl esters of alkylnitramines, which have a λ_{max} in the region 205-217 mμ, log ε 3.74-3.94 [5].

The reaction of (III) with acids [sulfuric, hydrochloric or acetic acid, N-nitro-m-nitro-p-toluenesulfonamide (IV)] proceeds vigorously, and is apparently accomplished by the scheme:

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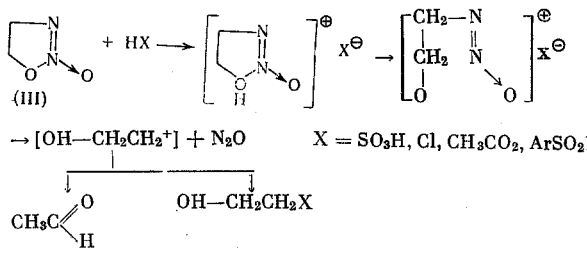
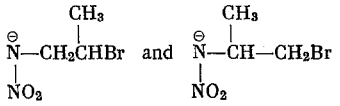
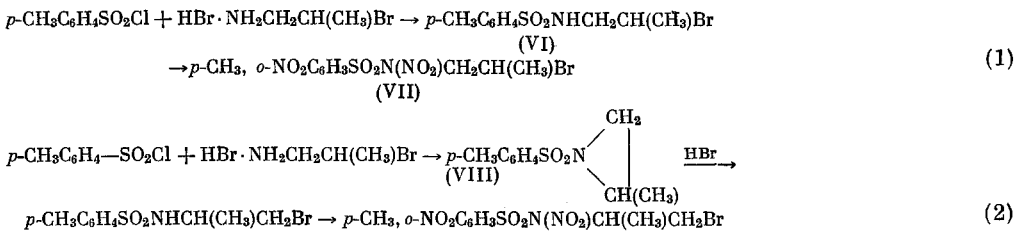


N-(β-Hydroxyethyl)-N-nitro-m-nitro-p-toluenesulfonamide (V) and acetaldehyde were isolated in the reaction with (IV). It is interesting that the reaction of the O-methyl ester of methylnitramine [linear analog of (III)] with (IV) gave N-methyl-N-nitro-m-nitro-p-toluenesulfonamide, which proves the generality of the chemical transformations of the linear and cyclic nitronic esters under the influence of acids.

Remaining unanswered was the question of whether (III) is formed directly as the result of the intramolecular O-alkylation of the nitramine anion or whether the nitroaziridine is formed first, which then isomerizes to (III) by analogy with the N-acyl derivatives of aziridine [6]. In order to answer this question we studied the intramolecular alkylation of two isomeric anions, which differed in the position of the methyl group with respect to the nitramine group:



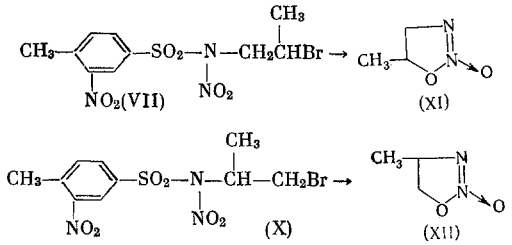
The same as in the previous case, the reaction was run respectively with the N-(β-bromopropyl)- and N-(β-bromoisopropyl)-N-nitro-m-nitro-p-toluenesulfonamides (VII) and (X), which were synthesized by the schemes:



(1)

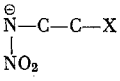
(2)

If the cyclization reaction goes immediately toward the formation of the O-alkylation product, then two different 5-methyl- and "correspondingly" 4-methyl-4,5-dihydro-1,2,3-oxadiazole 2-oxides (XI) and (XII) should be formed when (VII) and (X) are treated with alkali:



If the first reaction act is C-alkylation, then the same methyl-N-nitroaziridine* should be formed from (VII) and (X), which on isomerization can give either (XI) or (XII), or their mixture. Judging by the elemental analysis data and the data of the IR, UV, and NMR spectra, when (VII) and (X) are treated with alkali the 5- and 4-methyl-4,5-dihydro-1,2,3-oxadiazole 2-oxides (XI) and (XII) are respectively obtained.

A characteristic band in the 1610-1620 cm^{-1} region is present in the IR spectra, while the absence of a band in the 1500 cm^{-1} region, which is characteristic for the $N-NO_2$ group in small rings [7], also serves as corroboration for the 5-membered structure of the obtained products.

The presented results show that the transformation of the anions of nitramines of type  in alkaline medium goes strictly by the intramolecular O-alkylation scheme.

*It is probable that the reaction can also stop at the step of the N-nitroaziridine.

EXPERIMENTAL METHOD

The IR spectra were recorded on a UR-10 spectrometer, the UV spectra were recorded on a Unicam SP-800 spectrophotometer, while the NMR spectra were recorded on a Perkin–Elmer R-12 spectrometer.

N-(β-Bromoethyl)-p-toluenesulfonamide (II). With vigorous stirring, to a solution of 40 g of β-bromoethylamine hydrobromide in 300 ml of water at 20°C were added 38 g of p-toluenesulfonyl chloride in 260 ml of ether and 42 g of Na_2CO_3 in 400 ml of water. The mixture was stirred for 5 h, after which the aqueous layer was extracted with ether, dried over Na_2SO_4, and the solvent was distilled off. We obtained 28.85 g (53.5%) of (II), mp 96-98° (benzene–hexane, 4:1).

N-(β-Bromoethyl)-N-nitro-m-nitro-p-toluenesulfonamide (I). To 275 ml of HNO_3 solution (d 1.5) at –5 to 0° was added 15.6 g of (II). The mixture was stirred for 15 min at 0°, 2 h at 20°, and then poured on ice. The crystals were filtered and washed with water. We obtained 18.35 g of (I), mp 67-70°. Infrared spectrum (ν, cm^{-1}): 1585, 1290 (N–NO_2), 1185 (N–SO_2), 1360, 1580 (aromatic NO_2).

NMR spectrum (δ, ppm): 4.6 and 3.75 (triplets of NCH_2 and CH_2 groups), 2.62 (singlet of CH_3), 7.6-8.5 (multiplet of aromatic protons).

4,5-Dihydro-1,2,3-oxadiazole 2-Oxide (III). To a stirred suspension of 37.65 g of (I) in 380 ml of methanol at 20° was added 13.15 g of KOH powder in small portions. The mixture was stirred for 3.5 h, filtered, and the solvent was distilled off. The residue was extracted with ether, the extract was dried over $MgSO_4$, and the solvent was distilled off. We obtained 7.61 g (84.5%) of (III), bp 40-41° (0.4 mm); n_D^{20} 1.4810; d_4^{20} 1.3311. Found: C 26.96; H 4.54; N 32.60%. $C_2H_5N_2O_2$. Calculated: C 27.27; H 4.58; N 31.81%. NMR spectrum: δ 4.4 ppm (unsymmetrical triplet). Infrared spectrum (ν, cm^{-1}): 1620s, 1340w, 1250m, 1040m, 1010m, 940m, 760s.

Reaction of (III) with N-Nitro-m-nitro-p-toluenesulfonamide (IV) and Hydrochloric Acid. a) To a solution of 0.19 g of (III) in 5 ml of acetone at –70° was added 0.65 g of (IV) in 3 ml of acetone. The acetone was removed, and the residue was washed well with water. We obtained 0.13 g (20%) of (V), mp 117-120° (from $CHCl_3$). Found: N 13.59%. $C_9H_{11}N_3SO_7$. Calculated: N 13.76%. NMR spectrum (δ, ppm): 7.6-8.55 (multiplet of aromatic nucleus), 4.38 (triplet of N-CH_2 group), 3.75 (triplet of HO–CH_2 group), 26.5 (singlet of CH_3).

b) To a solution of 1.53 g of (IV) in 7 ml of absolute ether at 20° was added 0.45 g of (III) in 4 ml of ether (a gas was evolved). The organic layer was washed with water and the wash waters were mixed with a saturated solution of 2,4-dinitrophenylhydrazine in 2 N HCl solution. After 24 h the precipitate was filtered to give 0.16 g (14%) of the acetaldehyde dinitrophenylhydrazone, mp 147.5-150° (from alcohol), which did not depress the mixed melting point with an authentic sample

c) To a stirred emulsion of 0.2 g of (III) in 10 ml of water at a temperature not exceeding 15° was added 1.5 ml of a solution made from 0.5 g of CH_3COOK and 0.5 ml of conc. HCl in 10 ml of water. The mixture was poured into 150 ml of saturated aqueous dimedon solution. The next day the precipitate was filtered to give 0.16 g (23%) of the dimedon derivative of acetaldehyde, mp 137-141° (from methanol), which did not depress the mixed melting point with an authentic sample.

N-(β-Bromopropyl)-p-toluenesulfonamide (VI). To a solution of 3.65 g of β-bromopropylamine hydrobromide in 10 ml of water was added 3.10 g of p-toluenesulfonyl chloride in 30 ml of ether and, with vigorous stirring, a solution of 3.6 g of Na_2CO_3 in 30 ml of water was added rapidly. The mixture was stirred for 5 h at 20°, extracted with ether, and the extract was dried over $MgSO_4$. After removal of the solvent the residue was recrystallized from a 4:1 hexane–benzene mixture. We obtained 2.65 g (55%) of (VI), mp 76-78°. Found: C 41.43; H 4.49; S 11.00; Br 27.38%. $C_{10}H_{14}NSO_2Br$. Calculated: C 41.10; H 4.82; S 10.94, Br 27.38%. Infrared spectrum: 3280 cm^{-1} (NH).

N-(β-Bromopropyl)-N-nitro-m-nitro-p-toluenesulfonamide (VII). To 33 ml of HNO_3 solution (d 1.5) at –2 to 0° was added (VI) in small portions, after which the mixture was stirred at –2 to 0° for 1.25 h and then poured over 70 ml of cracked ice. The crystals were filtered, washed with water, and recrystallized from ethanol. We obtained 1.85 g (71%) of (VII), mp 98-99°. Found: C 31.67; H 3.27; S 8.42; Br 20.99; N 10.85%. $C_{10}H_{12}N_3SO_6Br$. Calculated: C 31.42; H 3.16; S 8.38; Br 20.90; N 10.99%. Infrared spectrum (ν, cm^{-1}): 1183 (–N–SO_2), 1580, 1287 (N–NO_2), 1540, 1360 (aromatic NO_2).

5-Methyl-4,5-dihydro-1,2,3-oxadiazole 2-Oxide (XI). To a stirred suspension of 11.5 g of (VII) at 10-15° was added 3.54 g of pulverized KOH in portions, after which the mixture was stirred for 2 h at 20° and

then evaporated. The residue was diluted with 30 ml of ether, filtered, and the ether solution was washed with water and then dried over $MgSO_4$. After distilling off the solvent the residue was distilled to give 0.92 g (28%) of (XI), bp 85-87° (14 mm); n_D^{20} 1.4685. Found: C 35.16; H 5.84; N 27.59%. $C_3H_6N_2O_2$. Calculated: C 35.29; H 5.92; N 27.44%. Infrared spectrum (ν, cm^{-1}): 960, 1000, 1240, 1620. Ultraviolet spectrum: 233 mμ. NMR spectrum (δ, ppm): 1.35 (doublet, CH_3), 3.3-4.9 (multiplet of ring protons).

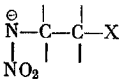
2-Methyltoluenesulfonylaziridine (VIII). To a solution of 4.4 g of β-bromopropylamine hydrobromide in 40 ml of water were added a solution of 3.8 g of p-toluenesulfonyl chloride in 30 ml of ether and a solution of 4 g of NaOH in 40 ml of water. The mixture was stirred vigorously for 2 h at ~20°. The ether layer was separated, and the aqueous layer was extracted with ether. The extracts were washed with water and dried over $MgSO_4$. Then the solvent was distilled off and the residue was recrystallized from a 4:1 hexane–benzene mixture to give 2.82 g (66.5%) of (VIII), mp 64-65°. Found: C 57.11; H 6.36; S 15.40%. $C_{10}H_{14}NSO_2Br$. Calculated: C 56.84; H 6.20; S 15.40%.

N-(β-Bromoisopropyl)-p-toluenesulfonamide (IX). Gaseous HBr was passed through a solution of 7 g of (VIII) in 150 ml of absolute ether at 0-10° until saturated. Then the reaction mass was washed cautiously with $NaHCO_3$ solution, dried over $MgSO_4$, and the solvent was evaporated. Recrystallization of the residue from a 4:1 benzene–hexane mixture gave 6.7 g (69%) of (IX), mp 83-85°. Found: C 41.46; H 4.91; S 11.01; Br 27.43%. $C_{10}H_{14}NSO_2Br$. Calculated: C 41.10; H 4.81; S 10.95; Br 27.38%.

N-(β-Bromoisopropyl)-N-nitro-m-nitro-p-toleuenesulfonamide (X). To 40 ml of HNO_3 solution (d 1.5) at –5 to 0° was added 2.5 g of (IX) in small portions, after which the mixture was stirred for 1 h at –2° and then poured on 60 ml of ice. The obtained white precipitate was filtered, washed with water, and recrystallized from ethanol. We obtained 2.48 g (76%) of (X), mp 86-87.5°. Found: C 31.56; H 3.45; N 10.95; S 8.54; Br 21.28%. $C_{10}H_{12}N_3SO_6Br$. Calculated: C 31.42; H 3.16; N 10.99; S 8.38; Br 20.90%. Infrared spectrum (ν, cm^{-1}): 1180 (SO_2), 1360, 1535 (aromatic NO_2), 1285, 1580 (NO_2).

4-Methyl-4,5-dihydro-1,2,3-oxadiazole 2-Oxide (XII). To a stirred suspension of 6.8 g of (X) in 60 ml of methanol at 15° was added in drops a solution of 2.08 g of KOH in 5 ml of methanol. The mixture was then stirred for 2 h at 20°, filtered, and the solvent was evaporated. To the residue was added 30 ml of ether, and the ether layer was washed with water and then dried over $MgSO_4$. After distilling off the solvent the residue was distilled to give 0.6 g (31%) of (XII), bp 88-89° (14 mm); n_D^{20} – 1.4679. Found: C 35.61; H 5.88; N 27.55%. $C_3H_6N_2O_2$. Calculated: C 35.29; H 5.92; N 27.44%. Infrared spectrum (ν, cm^{-1}): 1020, 1240, 1625. Ultraviolet spectrum: 233 mμ. NMR spectrum (δ, ppm): 1.45 (doublet of CH_3), 3.75-4.8 (multiplet of ring protons).

CONCLUSIONS

The intramolecular alkylation of the anions of nitramines of type  goes by the O-alkylation scheme with the formation of the derivatives of 4,5-dihydro-1,2,3-oxadiazole 2-oxides.

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