Organic Chemistry

Synthesis and some transformations of *N*-allyl-*N'*-methoxy- and *N*-allyl-*N'*-tosyloxydiazene *N*-oxides

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The first representatives of *N*-2-alkenyl-*N'*-alkoxydiazene *N*-oxides and *N*-2-alkenyl-*N'*-sulphonyloxydiazene *N*-oxides have been synthesized. Some reactions of the double bond in these compounds have been studied. The possibility of isomerization of *N*-2-alkenyl-*N'*-alkoxydiazene *N*-oxides to *N*-alk-1-enyl derivatives has been discovered.

Key words: *N*-allyl-*N'*-methoxydiazene *N*-oxide, *N*-allyl-*N'*-tosyloxydiazene *N*-oxide, alkylation, tosylation, bromination, isomerization, 1,3-dipolar cycloaddition.

Although ethers of *N*-alkyl-*N'*-hydroxydiazene *N*-oxides (AHDO) have been known since the middle of last century,* this class of compounds has been studied insufficiently. In the series of AHDO ethers with *N*-alkenyl radicals, only a few representatives with the α,β-arrangement of the double bond are known,[2] while unsaturated AHDO sulfonates have not been reported. We obtained *N*-allyl-*N'*-methoxydiazene *N*-oxide (**1**) and *N*-allyl-*N'*-tosyloxydiazene *N*-oxide (**2**), *i.e.*, the first representatives of AHDO ethers and sulfonates with a β,γ-double bond with respect to the nitrogen atom and studied some of their transformations.

The main method for the synthesis of alkyl ethers of AHDO and the only way to obtain AHDO sulfonates is the reaction of AHDO salts with alkylating reagents and sulfonic acid halides, respectively.[1] In view of this, we elaborated a convenient method for the synthesis of salts of *N*-allyl-*N'*-hydroxydiazene *N*-oxide (**3**) by nitrosation of *N*-allylhydroxylamine (in the form of hydrochloride or oxalate) followed by treatment of the resulting compound with bases. In this way, the sodium salt **3a** is formed readily in 85% yield.

$$CH_2{=}CHCH_2NHOH \cdot HX \xrightarrow{NaNO_2} CH_2{=}CHCH_2N(O){=}NOH \xrightarrow{NaOH} CH_2{=}CHCH_2N_2O_2^-Na^+$$

3 **3a**

HX = HCl, $C_2H_2O_4$

A convenient method to obtain the salts of copper (**3b**), silver (**3c**), and tetrabutylammonium (**3d**) involves cation exchange in salts **3**.

$$\mathbf{3a} + CuSO_4 \longrightarrow \underset{\mathbf{3b}}{(CH_2{=}CHCH_2N_2O_2)_2Cu} + Na_2SO_4$$

$$\mathbf{3a} + AgNO_3 \longrightarrow \underset{\mathbf{3c}}{CH_2{=}CHCH_2N_2O_2^-Ag^+} + NaNO_3$$

$$\mathbf{3a} + Bu_4NI \longrightarrow \underset{\mathbf{3d}}{CH_2{=}CHCH_2N_2O_2^-Bu_4N^+} + AgI$$

* See Ref. 1 and the references therein.

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The salts **3a—d** obtained this way are solid (**3a—c**) or oil-like (**3d**), quite stable compounds; unlike the others, the silver salt is poorly soluble in water.

In order to synthesize compound **1**, we studied the methylation of salts **3** with MeI or $(MeO)_2SO_2$. AHDO anions manifest ambident properties, and their alkylation generally gives mixtures of *N*-alkyl-*N'*-alkoxydiazene *N*-oxides and *N*-alkyl-*N*-nitroso-*O*-alkylhydroxylamines.[1] Many of the latter compounds are very reactive and therefore cannot be isolated. However, their formation decreases the yields of *N*-alkyl-*N'*-alkoxydiazene *N*-oxides. Evidently, formation of a mixture of compound **1** with *N*-allyl-*N*-nitroso-*O*-methylhydroxylamine was observed in our case, too. The conclusion on the structure of compound **1** was made on the basis of ^1H NMR and IR spectra, elemental analyses, and a negative reaction for the *N*-nitroso group with a diphenylamine—H_2SO_4 mixture.

$$\underset{\textbf{3a—c}}{CH_2{=}CHCH_2N(O)NO^-M^+} + CH_3X \longrightarrow CH_2{=}CH{-}CH_2N(O){=}NOMe \quad (\textbf{1})$$

M = Na, Ag, Bu_4N; X = I, SO_4Me

Unlike compound **1**, the second reaction product gave a positive reaction for the *N*-nitroso group, but its structure has not determined because of its reactivity and possible carcinogenic properties.

The possibility to obtain compound **1** by methylation of salts **3** and its yield depend considerably on the counter-ion and the methylating agent.

The highest yields of compound **1** were observed in the reaction of silver salt **3c** with MeI (Table 1).

We managed to isolate 3—5% of a side product, presumably an *N*-nitrosohydroxylamine derivative; the maximum quantity of this compound was obtained in the reaction of Na-salt **3a** with dimethyl sulfate (~15—20%).

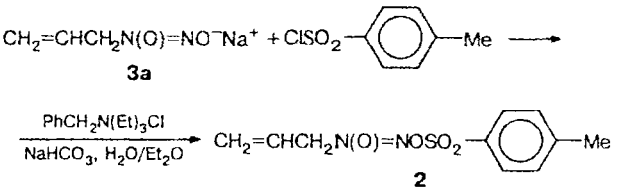
Compound **1** is formed in satisfactory yields in the methylation of sodium salt **3a** with MeI in the presence of phase-transfer catalysts. On the other hand, the copper derivative **3b** (which is though a chelate rather than an ionic compound[4]) does not react with methyl iodide.

Table 1. Yields of *N*-allyl-*N'*-methoxydiazene *N*-oxide (**1**) on treatment of salts $CH_2{=}CHCH_2N_2O_2M$ with methylating agents MeX

M	X	Solvent	Reaction temperature /°C	Reaction time /days	Yield (%)
Ag	I	Ether	20	5	71
Na[a]	I	MeCN	20	7	55
Na[b]	I	CH_3I	20	5	60
Bu_4N	I	MeCN	20	2	35
Na	OSO_2OMe	Acetone—H_2O, 3 : 1	55	2 h	40
Cu	I	MeCN	20	12	—

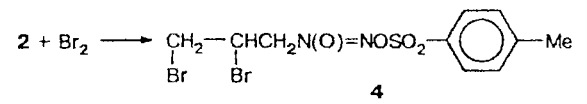
[a] In the presence of 10 mol.% Bu_4NI (with respect to compound **3**).
[b] In the presence of 15-crown-5.

The sodium salt **3a** reacts rather smoothly with TsCl to give compound **2**, a representative of a rather rare type of organic compounds that contain seven directly bound N, S, and O heteroatoms, in ~70% yield.

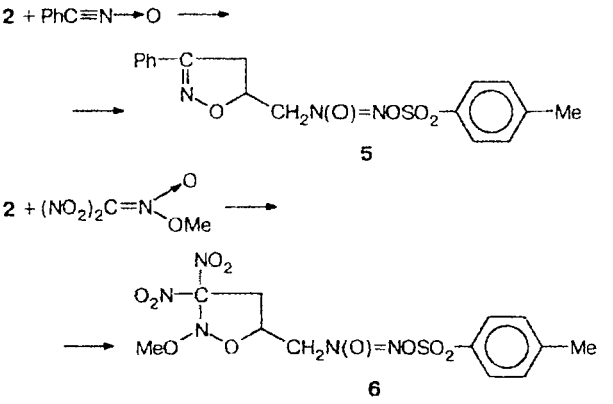


Compounds **1** and **2** are quite stable.

The double bond in the resulting β,γ-unsaturated derivatives of AHDO behaves in the usual way. This opens up prospects to synthesize a number of compounds with the *N'*-hydroxydiazene *N*-oxide fragment, which are difficult or as yet impossible to obtain by other methods, from these derivatives. For example, compound **2** readily adds bromine, giving the first representative of *N*-β,γ-dibromoalkyl-*N'*-hydroxydiazene *N*-oxide sulfonates (**4**).



The double bond can be easily made to participate in 1,3-dipolar cycloaddition reactions, which makes it possible to obtain diverse heterocyclic compounds containing the *N'*-hydroxydiazene *N*-oxide fragment in the side chain. As an example of this kind of reactions one could present the reaction of compound **2** with benzonitrile oxide and a trinitromethane nitronate.



Taking into consideration that the *N'*-hydroxydiazene *N*-oxide fragment favors α-deprotonation,[2] one could hope that *N*-2-alkenyl-*N'*-hydroxydiazene *N*-oxides would undergo isomerization to *N*-1-alkenyl derivatives in the presence of strong bases. In fact, prolonged

keeping of compound **1** in MeOH in the presence of MeONa results in its transformation to *N*-1-propenyl-*N'*-methoxydiazene *N*-oxide (**7**) in high yield.

$$CH_2{=}CHCH_2N(O){=}NOMe \xrightarrow[MeOH]{MeONa} CH_3{-}CH{=}CHN(O){=}NOMe$$

7

Thus, the first representatives of *N*-2-alkenyl-*N'*-alkoxydiazene *N*-oxides and *N*-2-alkenyl-*N'*-sulfonyloxydiazene *N*-oxides have been synthesized. Some of their reactions on the double bond have been studied, and the possibility of isomerization of *N*-2-alkenyl-*N'*-alkoxydiazene *N*-oxides into *N*-1-alkenyl derivatives has been established. This type of isomerization opens a new way for the synthesis of α,β-unsaturated *N*-alkenyl-*N'*-alkoxydiazene *N*-oxides.

Experimental

^{1}H NMR spectra were recorded on a Tesla BS-467 instrument with a working frequency of 60 MHz in acetone-d_6 using HMDS as the reference. IR spectra were obtained on a Specord IR spectrophotometer in KBr pellets (crystalline compounds) or in thin films (liquid compounds). Isolation of pure compounds was performed by TLC using Silpearl silica gel with a luminophore. Salts of *N*-allylhydroxylamine were obtained according to the known procedure.[3]

Salts of *N*-allyl-*N'*-hydroxydiazene *N*-oxide (3a—d). *A.* $NaNO_2$ (2.1 g, 0.03 mol) in a minimum amount of water was added at 0 °C to a solution of *N*-allylhydroxylamine hydrochloride (3.34 g, 0.03 mol) in 10 mL of water, the reaction mixture was stirred for 5 min, and compound **3** was extracted with ether. The extract was dried with Na_2SO_4 and treated with methanolic NaOH to give 2.29 g (85%) of product **3a**, m.p. 228—232 °C (from EtOH). IR, ν/cm^{-1}: 760, 930, 1100, 1180, 1370.

B. Aqueous solutions of compound **3a** (1 g, 0.008 mol) and $CuSO_4$ (0.7 g, 0.0044 mol) were mixed, the reaction mixture was stirred for 45 min, and copper salt **3b** was extracted with ether. Yield 87%, m.p. 82—86 °C (Ref. 4: m.p. 73 °C)*. IR, ν/cm^{-1}: 770, 930, 990, 1100, 1170, 1215, 1250, 1400.

C. Aqueous solutions of sodium salt **3a** (1.4 g, 0.01 mol) and $AgNO_3$ (1.9 g, 0.01 mol) were mixed. The precipitate was filtered off and washed with ether to give 2.05 g (87%) of silver salt **3c** as a brown powder. IR, ν/cm^{-1}: 760, 905, 1100, 1190, 1360, 1410.

D. Compound **3c** (1.1 g, 0.005 mol) was added to a solution of Bu_4NI (1.76 g, 0.005 mol) in 10 mL of MeCN, and the reaction mixture was stirred for 3 h. The precipitate was separated, and the solvent was evaporated to give tetrabutylammonium salt **3d** as an oil in quantitative yield.

***N*-Allyl-*N'*-methoxydiazene *N*-oxide (1).** *A.* A suspension of compound **3c** (2.05 g, 0.01 mol), MeI (2.5 mL, 0.04 mol), and 10 mL of dry ether was stirred at ~20 °C for 5 days, the precipitate was separated, the filtrate was concentrated, and compound **1** (0.81 g, 71%) was isolated from the residue by TLC, b.p. 65 °C (6 Torr). Found (%): C, 41.33; H, 6.91. $C_4H_8N_2O_2$. Calculated (%): C, 41.37; H, 6.89. IR, ν/cm^{-1}: 1620 (C=C), 1490, 1290 (N_2O_2), 1050 (C—O). ^{1}H NMR, δ: 3.85 (s, 3 H, CH_3O); 4.60 (d, 2 H, CH_2N, J = 6 Hz); 5.15—6.00 (m, 3 H, CH_2=CH).

B. A suspension consisting of compound **3b** (0.5 g, 0.004 mol), MeI (3 mL, 0.048 mol), and 15-crown-5 (0.09 g) was stirred 5 days, and compound **1** was isolated by TLC in 60% yield.

C. $(MeO)_2SO_2$ (2 mL, 0.02 mol) was added at 55 °C to a mixture of 12.5 mL acetone, 4 mL H_2O, and 1 g (0.008 mol) of compound **3a**, and the mixture was stirred for 1.5 h at 55 °C, adding $NaHCO_3$ periodically to keep the medium neutral. After cooling to 20 °C, the precipitate was separated, and acetone was evaporated. The reaction product was extracted with chloroform from the residue, the extract was dried with $MgSO_4$. TLC gave compound **1**, yield 40%.

***N*-Allyl-*N'*-tosyloxydiazene *N*-oxide (2).** Compound **3a** (2.81 g, 0.022 mol), Et_3NCH_2PhCl (0.3 g, 0.0013 mol), and 39 mL of ether were added to 39 mL of 10% aqueous $NaHCO_3$, and 3.84 g (0.02 mol) of TsCl was added with stirring. The reaction mixture was stirred at ~20 °C for 2 days, the organic layer was separated, and the aqueous layer was additionally washed with ether. The ethereal extracts were dried with $MgSO_4$, and the solvent was distilled off to give 4.47 g of a crystalline compound. TLC of the residue gave 3.65 g (68%) of compound **2**, m.p. 74—76.5 °C (from hexane). Found (%): C, 47.19; H, 4.68; N, 11.27; S, 12.23. $C_{10}H_{12}N_2O_4S$. Calculated (%): C, 46.87; H, 4.68; N, 10.93; S 12.50. IR, ν/cm^{-1}: 1590 (C=C), 1510, 1290 (N_2O_2), 1180, 1380 (SO_3), 1080 (C—O). ^{1}H NMR, δ: 2.42 (s, 3 H, CH_3); 4.78 (d, 2 H, CH_2N, J = 5.5 Hz); 5.10—6.10 (m, 3 H, CH_2=CH); 7.30—7.90 (m, 4 H, arom.).

***N*-β,γ-Dibromopropyl-*N'*-tosyloxydiazene *N*-oxide (4).** Bromine (0.13 mL, 0.0025 mol) was added at 20 °C with stirring to a suspension of compound **2** (0.6 g, 0.0023 mol) in 10 mL CCl_4, and the reaction mixture was stirred for 2 h. During this time, the precipitate of compound **2** dissolved, and product **4** precipitated partially. It was filtered off (0.54 g, m.p. 81—84 °C), and the mother liquor was concentrated; recrystallization of the residue from CCl_4 gave an additional quantity (0.14 g) of product **4**, overall yield 70%, m.p. 83.5—87 °C (from CCl_4). Found (%): C, 29.54; H, 3.16; S, 7.51. $C_{10}H_{12}Br_2N_2O_4S$. Calculated (%): C, 28.84; H, 2.88; S, 7.69. ^{1}H NMR, δ: 2.38 (s, 3 H, CH_3); 3.90 (m, 2 H, CH_2Br); 4.20 (d, 1 H, CHBr, J = 6.5 Hz); 4.70 (m, 2 H, CH_2N); 7.30—7.90 (m, 4 H, arom.).

3-Phenyl-5-(*N'*-tosyloxydiazene-*N*-oxido-*N*-methyl)-2-isoxazoline (5). A solution of Et_3N (0.11 g, 0.001 mol) in 3 mL ether was added at 20 °C with stirring to a solution of chlorobenzaldoxime (0.18 g, 0.001 mol) in 10 mL anhydrous ether; after 5 min, a solution of compound **2** (0.3 g, 0.001 mol) in 5 mL anhydrous ether was added. The reaction mixture was stirred for 2 days, the precipitate was separated, ether was evaporated, and the residue was washed with water to give 0.28 g (63%) of compound **5**, m.p. 142.5—144.5 °C (from acetone). Found (%): C, 54.14; H, 4.78; N, 11.22; S, 8.42. $C_{17}H_{17}N_3O_5S$. Calculated (%): C, 54.40; H, 4.53; N, 11.20; S, 8.53. IR, ν/cm^{-1}: 1510, 1300 (N_2O_2), 1190, 1385 (SO_3), 1600 (arom.). ^{1}H NMR, δ: 2.40 (s, 3 H, CH_3); 3.40 (m, 2 H, CCH_2C); 4.40 (m, 2 H, CH_2N); 5.08 (m, 1 H, CH); 7.33—7.88 (m, 9 H, arom.).

2-Methoxy-3,3-dinitro-5-(*N'*-tosyloxydiazene-*N*-oxido-*N*-methyl)isoxazolidine (6). A small excess of diazomethane in 12 mL of a benzene—toluene mixture (2:1) was added at 0 °C to a solution of trinitromethane (0.37 g, 0.0026 mol) in 5 mL of a benzene—toluene mixture, and then compound **2** (0.32 g,

* This salt has been obtained previously[4] in ~30% yield by treatment of the AllMgHal—NO adduct with copper sulfate.

(0.0012 mol) was added. The reaction mixture was stirred for 3 h at 0 °C and kept for 12 h at ~20 °C. The solvents were evaporated *in vacuo*, and the residue was redissolved in benzene, washed with a $NaHCO_3$ solution and water, dried with $MgSO_4$, and the solvent was evaporated. The remaining oil (0.38 g) was washed with a small amount of hexane and ether to obtain a crystalline precipitate **6**, m.p. 120—121 °C (from an acetone—hexane mixture). Found (%): C, 34.31; H, 3.50; S, 7.45. $C_{12}H_{15}N_5O_{10}S$. Calculated (%): C, 34.20; H, 3.56; S, 7.60. IR, ν/cm^{-1}: 1600, 1320 (NO_2), 1510, 1290 (N_2O_2), 1390, 1200 (SO_3).

***N*-Prop-1-enyl-*N'*-methoxydiazene *N*-oxide (7).** A solution of compound **1** (1.76 g, 0.015 mol) in 5 mL dry MeOH containing a small granule of Na was kept at ~20 °C for 10 days, then CO_2 was passed through it, anhydrous ether was added, the precipitate was separated, and the solvents were evaporated *in vacuo* to give 1.4 g (80%) of compound **7**, b.p. 47 °C (1 Torr), n_D^{22} 1.4892. Found (%): C, 41.87; H, 7.64; N, 23.78. $C_4H_8N_2O_2$. Calculated (%): C, 41.37; H, 6.89; N, 24.13. ^1H NMR (δ: 1.80 (d, 3 H, CH_3C, J = 6 Hz); 3.93 (s, 3 H, CH_3O); 6.38—7.16 (m, 2 H, CH=CH).

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