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Dedicated to the Full Member of the Russian Academy of Sciences V.A.Tartakovsky on occasion of his 75th birthday

N'-Tetrazolylmethoxyl Derivatives of *N*-Methyldiazene *N*-Oxides

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Abstract—A preparation method was developed for previously unknown tetrazole derivatives containing in the *1*, *2*, and/or *5* positions of the tetrazole ring *N*-methyldiazene-*N*-oxide-*N*'-oxymethyl groups.

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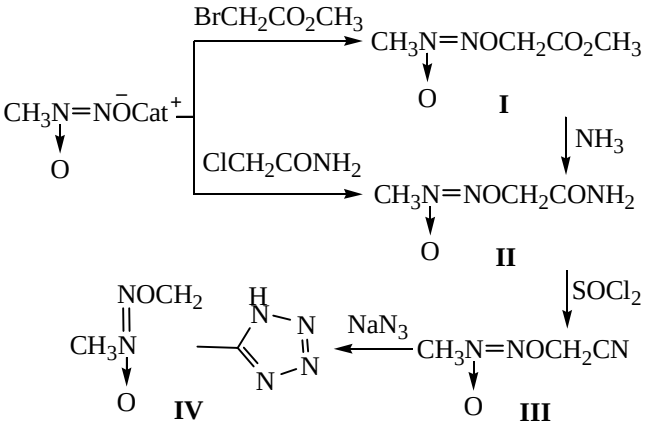
The power of common energy-intensive compounds depends first of all on their elemental composition, the oxygen content, the enthalpy of formation, and density. The oxygen mostly is present in the compounds in the form of nitro groups (attached to carbon, nitrogen, or oxygen atoms), and the desired enthalpy of formation is provided by the structural fragments with N–N bonds. In keeping with above previously unknown *N*'-tetrazolyl methoxyl derivatives of *N*-methyldiazene *N*-oxides also held a certain interest as potential energy-intensive compounds. Their enthalpy of formation is governed mainly by the enthalpy of formation of the tetrazole ring (ΔH_f of tetrazole is 3390 kJ kg^{-1} [1]), and oxygen is supplied by *N*-methyldiazene-*N*-oxid-*N*'-yloxyl group. The latter has the same elemental composition as a secondary nitramine group N_2O_2. Although one oxygen atom in the *N*-alkyl-*N*'-alkoxydiazene N-oxides is bonded to carbon (unlike the oxygen atoms in the secondary nitramines) the enthalpy of formation of *N*'-oxydiazene *N*-oxides is even somewhat larger than the enthalpy of formation of the secondary nitramines [2].

In this report the preparation method of tetrazole derivatives containing *N*-methyldiazene-*N*-oxid-*N*'-yloxymethyl groups in the positions *1*, *2* and/or *5* of the tetrazole ring is described for the first time.

The reactions sequence used for preparation of *N*-methyl-*N*'-(tetrazol-5-ylmethoxy)diazene *N*-oxide (**IV**) with a heterocycle unsubstituted at the nitrogen atoms is shown on Scheme 1.

The preparation procedure for tetrazole **IV** is based on a reaction of 1,3-dipolar cycloaddition of hydrazoic acid to an *N*-methyldiazene-*N*-oxid-*N*'-ylacetonitrile (**III**). To this end the sodium salt of methylnitrosohydroxylamine in DMF was treated at heating with methyl bromoacetate to obtain methyl *N*-methyldiazene-*N*-oxid-*N*'-yloxyacetate (**I**) in 60% yield. The latter cleanly reacted with aqueous ammonia at room temperature to give the corresponding amide **II** in 78% yield. The same amide in an alternative procedure was obtained in 37% yield in one stage by alkylating a sodium salt of methylnitrosohydroxylamine with chloroacetamide. Although in the latter case amide **II** was obtained in one stage the two-stage method is preferable for the overall yield of amide was here by ~10% higher than in the one-stage process. Amide **II** was treated at heating with excess thionyl chloride, and the arising **III** was brought into the reaction of 1,3-dipolar addition with sodium azide in DMF in the presence of ammonium

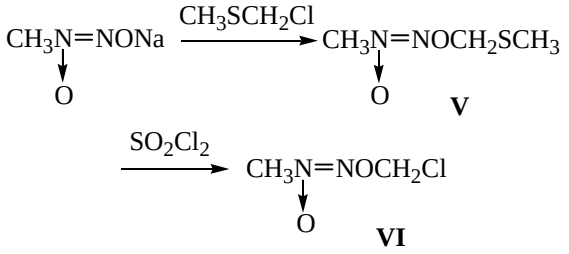
Scheme 1.



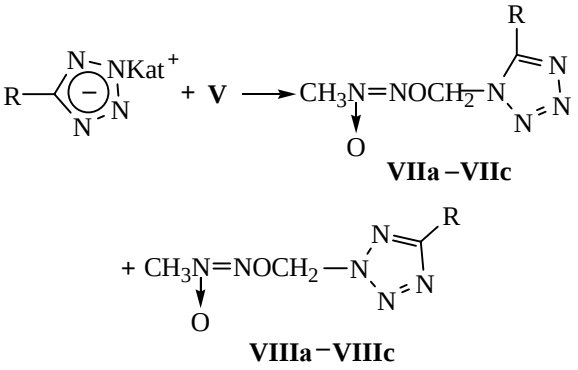
chloride thus obtaining the desired tetrazole **IV**. The latter is a relatively high-melting sufficiently stable compound (decomposition temperature is over 200°C). Its composition and structure were deduced from elemental analysis, IR and ^{1}H NMR spectra.

Tetrazole derivatives containing *N*-methyldiazene-*N*-oxid-*N*'-yloxymethyl groups in the positions *1* or *2* of the tetrazole ring were prepared by alkylation of tetrazole salts with *N*-methyl-*N*'-chloromethoxydiazene *N*-oxide (**VI**). the latter was synthesized in keeping with Scheme 2.

Scheme 2.



Scheme 3.



Cation = Na, Et_3NH; R = H (**a**), CH_3 (**b**), $CH_3N(O)=NOCH_2$ (**c**).

The tetrazoles anions are known to be ambidente [3]. The direction of alkylation of ambidente compounds is mainly governed by the character of the reaction centers, electronic and steric effects of substituents in substrates, the counter ion nature in the charged nucleophile, and the solvents used. The alkylation of tetrazole salts provides in a general case a mixture of alkylation products at N^1 and N^2 atoms of the tetrazole ring; therewith the increased electron-withdrawing property of the substituent in the position *5* of the ring favors the larger yield of N^2-isomers [3].

Evidently a similar trend is observed in alkylation of triethylammonium salts of tetrazole studied by us (see Scheme 3 and the table).

Therewith the products of N-alkylation formed in an overall yield 45–55% and the ratio of products of N^1/N^2-alkylation of tetrazole and methyltetrazole was ~3:1, and in the case of azole **IVc** it equaled 1.6:1; thus the contribution of N^2-alkylated products increased approximately 1.5 times.

This trend was not however observed in the alkylation of sodium salts of the tetrazoles under study. In this case in the first approximation the amounts of the products of N^1- and N^2-alkylation may be regarded as equal.

Thus the results obtained show that the counter ion character in the tetrazole salts affects the ratio of products of N^1- and N^2-alkylation.

It was demonstrated before [4] that 1,5- and 2,5-disubstituted tetrazoles treated with alkylating reagents were capable to yield an equilibrium mixture of 1,5- and 2,5-disubstituted tetrazoles in a ratio 3:1. The same ratio of alkylation products in our case required checking whether under the given conditions the products ratio was caused by a thermodynamically controlled reaction, or in other words, whether the compounds obtained

Yields and ratio of products of N^1- and N^2-alkylation of tetrazoles salts with *N*-methyl-*N*'-chloromethoxydiazene *N*-oxide (**VI**)

R	Cation	Yield, %		**VII/VIII** ratio
		VII	**VIII**	
H	Na	20	20	1:1
	Et_3NH	34	11	3.1:1
CH_3	Na	29	23	1.26:1
	Et_3NH	42	14	3:1
$CH_3N(O)=NOCH_2$	Na	43	38	1.13:1
	Et_3NH	32	20	1.6:1

formed at least partially as a result of isomerization under the effect of the alkylating reagent. It was however cleared that heating azole **VIIIc** under the reaction conditions with the alkylating agent **VI** did not result in the formation of azole **VIIc**.

The composition and structure of azoles **VIIa–VIIc** and **VIIIa–VIIIc** were established from elemental analysis, IR and ^{1}H NMR spectra. The conclusion on the substituents positions at the nitrogen atoms of tetrazole was founded on the formerly found trend that the chemical shift of the protons of methylene groups attached to N^2 atom in the ^{1}H NMR spectra appeared by 0.15–0.45 ppm downfield than those of the corresponding groups at atom N^1 [5, 6].

The synthesized compounds **VIIa–VIIc** and **VIIIa–VIIIc** are low-melting (in the 50–125°C range) crystalline substances sufficiently stable up to ~150°C.

EXPERIMENTAL

Reactions progress was monitored by TLC on Silufol UV-254 plates. IR spectra were recorded on a spectrophotometer UR-20. ^{1}H NMR spectra were registered on spectrometers Bruker AM-300 and AM-200. Methylnitrosohydroxylamine salts were prepared by published procedure [7].

Methyl 2-(*N*-methyldiazene-*N*-oxid-*N*'-yloxy)-acetate (I). A mixture of 0.5 g (5.1 mmol) of methylnitrosohydroxylamine sodium salt and 0.83 g (5.4 mmol) of methyl bromoacetate in 10 ml of DMF was stirred for 4 h at 50–60°C. The solution was evaporated in a vacuum and from the residue was isolated by preparative TLC (eluent ether) 0.45 g (60%) of compound **I**, mp 70–72°C (ether). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.75 s (3H, CH_3), 3.90 s (3H, CH_3), 4.70 s (2H, CH_2). Found, %: C 32.63; H 5.39; N 18.12. $C_4H_8N_2O_4$. Calculated, %: C 32.40; H 5.44; N 18.90.

2-(*N*-Methyldiazene-*N*-oxid-*N*'-yloxy)acetamide (II). *a*. A mixture of 0.4 g (2.7 mmol) of ester **I** with 10 ml of 25% aqueous ammonia was stirred for 3 h. The reaction mixture was evaporated to dryness, and the residue was recrystallized. Yield 0.28 g (78%), mp 150–151°C (CH_3CN).

b. A mixture of 0.3 g (3.1 mmol) of methylnitrosohydroxylamine sodium salt, 0.3 g (3.2 mmol) of chloracetamide, and 0.05 g of KBr in 10 ml of DMF was stirred for 6 h at 50–60°C. The solution was evaporated in a vacuum and from the residue was isolated by preparative TLC (eluent CH_3CN) 0.15 g (37%) of amide **II**. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 3.80 s (3H, CH_3), 4.55 s (2H, CH_2), 6.6–6.8 br.s (2H, NH_2). Found, %: C 26.55; H 5.25; N 31.16. $C_3H_7N_3O_3$. Calculated, %: C 27.90; H 5.30; N 31.57.

2-(*N*-Methyldiazene-*N*-oxid-*N*'-yloxy)acetonitrile (III). A mixture of 0.3 g (2.2 mmol) of compound **II** in 10 ml of $SOCl_2$ was stirred for 2 h at 70°C, the reaction mixture was evaporated in a vacuum, the residue was dissolved in CH_2Cl_2, and the solution was passed through a thin bed of silica gel. The solvent was evaporated, the residue was recrystallized. Yield 0.17 g (65%), mp 65–68°C (ether–$CHCl_3$). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 4.00 s (3H, CH_3), 5.30 s (2H, CH_2). IR spectrum, ν, cm^{-1}: 1428, 1524 (N_2O_2), 2112, 2172 (CN), 2950, 3000 (CH). Found, %: C 31.36; H 4.54; N 35.37. $C_3H_5N_3O_2$. Calculated, %: C 31.33; H 4.38; N 36.50.

***N*-Methyl-*N*'-(tetrazol-5-ylmethoxy)diazene *N*-oxide (IV).** A mixture of 0.8 g (6.9 mmol) of nitrile **III**, 1.2 g (18.4 mmol) of NaN_3, and 0.5 g (9.4 mmol) of NH_4Cl in 15 ml of DMF was stirred for 12 h at 60–70°C. The solution was evaporated in a vacuum, the residue was dissolved in CH_3CN, the solution was passed through a thin bed of silica gel, evaporated, the residue was washed with a little $CHCl_3$ and recrystallized. Yield 0.65 g (59%), mp 114–116°C (CH_3CN). IR spectrum, ν, cm^{-1}: 1424, 1520 (N_2O_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.95 s (3H, CH_3), 5.70 s (2H, CH_2). Found, %: C 22.93; H 3.72; N 53.16. $C_3H_6N_6O_2$. Calculated, %: C 22.93; H 3.21; N 53.49

***N*-Methyl-*N*'-(methylsulfanylmethyl)diazene *N*-oxide (V).** A mixture of 1 g (0.01 mol) methylnitrosohydroxylamine sodium salt and 1.1 g (0.011 mol) of chloromethyl methyl sulfide in 20 ml of DMF was stirred for 4 h at 50–60°C. The solution was evaporated in a vacuum, the residue was dissolved in $CHCl_3$, the precipitate was filtered off, the mother liquor was evaporated, and from the residue was isolated by preparative TLC (eluent ether) 0.55 g (40%) of oily compound **V**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.22 s (3H, CH_3), 3.90 s (3H, CH_3), 5.28 s (2H, CH_2). Found, %: C 26.67; H 5.87; N 20.21; S 23.25. $C_3H_6N_2O_2S$. Calculated, %: C 26.46; H 5.92; N 20.57; S 23.53.

***N*-Methyl-*N*'-chloromethoxydiazene *N*-oxide (VI)**. A mixture of 0.3 g (2.2 mmol) of oxide **V** in 10 ml of CH_2Cl_2 was cooled to –5–0°C, and 0.3 ml (3.7 mmol) of SO_2Cl_2 was added; the solution obtained was stirred at room temperature for 2 h. The solution was evaporated

in a vacuum, and from the residue was isolated by preparative TLC (eluent ether) 0.25 g (91%) of chloride **VI**. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 4.00 s (3H, CH_3), 6.05 s (2H, CH_2). Found, %: C 19.59; H 4.03; Cl 28.60; N 22.65. $C_2H_5ClN_2O_2$. Calculated, %: C 19.29; H 4.05; Cl 28.50, N 22.50;

Alkylation of tetrazoles salts with *N*-methyl-*N*'-chloromethoxydiazene *N*-oxide. General procedure. A mixture of 0.3 ml (2.9 mmol)of Et_3NH and 2.4 mmol of azole (or an equimolar quantity of azole sodium salt) was boiled for 10 h with 0.35 g (2.8 mmol) of reagent **VI** in 40 ml of CH_3CN. The solvent was evaporated, the residue was subjected to TLC on silica gel; for compounds **VIIa, VIIb** and **VIIIa, VIIIb** eluent ethyl acetate, for compounds **VIIc** and **VIIIc**, a mixture of $CHCl_3$–CH_3OH, 9:1.

***N*-Methyl-*N*'-(tetrazol-1-ylmethoxy)diazene *N*-oxide (VIIa),** mp 51–52°C (ethyl acetate). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 4.00 s (3H, CH_3), 6.58 s (2H, CH_2), 9.40 s (1H, CH). Found, %: C 22.78; H 3.83; N 53.02. $C_3H_6N_6O_2$. Calculated, %: C 22.79; H 3.82; N 53.15.

***N*-Methyl-*N*'-(5-methyltetrazol-1-ylmethoxy)-diazene *N*-oxide (VIIb)**. mp 56–58°C (ether). IR spectrum, ν, cm^{-1}: 1404, 1528 (N_2O_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.65 s (3H, CH_3), 3.85 s (3H, CH_3), 6.25 s (2H, CH_2). Found, %: C 27.99; H 4.65; N 48.10. $C_4H_8N_6O_2$. Calculated, %: C 27.91; H 4.68; N 48.10.

1,5-Bis(*N*-methyldiazene-*N*-oxid-*N*'-yloxymethyl)-tetrazole (VIIc). mp 103–104°C (ethyl acetate–$CHCl_3$). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 3.95 s (3H, CH_3), 4.00 s (3H, CH_3), 5.75 s (2H, CH_2O), 6.60 s (2H, CH_2N). Found, %: C 24.54; H 4.16; N 45.63. $C_5H_{10}N_8O_4$. Calculated, %: C 24.39; H 4.06; N 45.50.

***N*-Methyl-*N*'-(tetrazol-2-ylmethoxy)diazene *N*-oxide (VIIIa).** Yield 11% from triethylammonium salt and 20% from sodium salt of tetrazole, mp 106–107°C (ether). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.90 s (3H, CH_3), 6.50 s (2H, CH_2), 8.59 s (1H, CH). Found, %: C 22.99; H 3.84; N 53.33. $C_3H_6N_6O_2$. Calculated, %: C 22.79; H 3.82; N 53.15.

***N*-Methyl-*N*'-(5-methyltetrazol-2-ylmethoxy)-diazene *N*-oxide (VIIIb).** mp 62–63°C (ether). IR spectrum, ν, cm^{-1}: 1428, 1516 (N_2O_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.65 s (3H, CH_3), 3.85 s (3H, CH_3), 6.45 s (2H, CH_2). Found, %: C 28.00; H 4.64; N 47.95. $C_4H_8N_6O_2$. Calculated, %: C 27.91; H 4.68; N 48.10.

2,5-Bis(*N*-methyldiazene-*N*-oxid-*N*'-yloxymethyl)-tetrazole (VIIIc). mp 122–124°C (ether). ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 3.90 s (3H, CH_3), 3.96 s (3H, CH_3), 5.55 s (2H, CH_2O), 6.65 s (2H, CH_2N). Found, %: C 24.99; H 4.07; N 45.43. $C_5H_{10}N_8O_4$. Calculated, %: C 24.39; H 4.06; N 45.50.

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