Reaction of N-chlorotriazoles with Chloride Ion in Benzene. A sample of 0.072 g (0.32 mmole) TEBAC was added with stirring to a solution of 0.5 g (3.4 mmoles) 1-chloro-3-nitro-1,2,4-triazole in 5 ml benzene at 20°C. N-Phenyltriazole was not detected by thin-layer chromatography after 24 h.

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NEW REGIOSPECIFIC METHODS FOR THE SYNTHESIS OF N'-CYANODIAZENE N-OXIDES

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New regiospecific methods have been developed for the synthesis of aliphatic, aromatic, and heterocyclic N'-cyanodiazene N-oxides based on the reactions of nitroso compounds with a system containing the sodium salt of cyanamide and tert-butyl hypochlorite and with a system containing cyanamide and dibromoisocyanurate.

Some compounds with the N'-cyanodiazene N-oxide groups have bactericidal [1-4], fungicidal [4-8], and anti-inflammatory properties [9], which lends importance to the search for their preparative synthesis. The methods described for the synthesis of N'-cyanodiazene N-oxides entail the oxidation of the cyanodiazenes by 85% H_2O_2 [5,6,10], the degradation of N'-carbamaoyldiazene N-oxides by the action of $SOCl_2$ [11], the reaction of nitroso compounds with cyanazide [6] and with a system containing cyanamide and phenyl iododiacetate [3,9,12].

In the present work, we propose new approaches for the preparation of N'-cyanodiazene N-oxides based on the reactions of nitroso compounds with cyanamide and its salts in the presence of oxidizing agents.

The former method is based on the capacity of the sodium salt of N-chlorocyanamide, formed in the reaction of the sodium salt of cyanamide with tert-butyl hypochlorite, to lose NaCl under mild conditions with the formation of cyanonitrene [13,14]. We are the first to report that the product of the reaction of the sodium salt of cyanamide with t-BuOCl reacts

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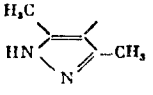
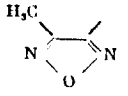
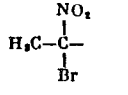
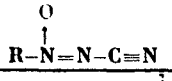
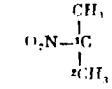
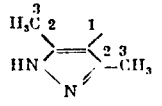
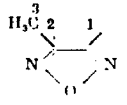
TABLE 1. Yields and Properties of N′-Cyanodiazene N-Oxides

Compound	R	Yield, % A	Yield, % B	Mp,°C (solvent), Bp,°C (p, mm Hg)	IR spectrum ν, cm^{-1}	PMR spectrum, δ, ppm	Found/Calculated, % C	H	N	Br
(I)	C_6H_5-	29	95	66,5–66 (heptane–ether)	–	–	–	–	–	–
(II)	$O_2N(H_3C)_2C-$	54	80	111–113(2)	1495(N=N), 1575(NO_2), 2205(CN)	2,22 s(6H, CH_3)	30,64 / 30,38	3,77 / 3,80	34,81 / 35,44	–
(III)		40	27	156–157 (water)	3160,3240(NH, CH_3), 2220(CN), 1480(N=N)	2,52 s(6H, CH_3)	43,64 / 43,61	4,24 / 4,07	42,42 / 42,75	–
(IV)		56	81	95–96(2)	1495(N=N), 2215(C≡N), 1585 (ring)	2,68s (3H, CH_3)	31,71 / 31,37	2,06 / 1,96	45,93 / 45,75	
(V)	$Br(H_3C)_2C-$	–	32 *	60–65(2)	1500(N=N), 2210(CN), 2800–3000(CH_3)	2,41 s (6H, CH_3)	25,53 / 25,00	3,27 / 3,13	–	41,67 / 41,67
(VI)		–	83 **	130(2)	1510, 1520(N=N), 1600(NO_2), 2210(CN)	2,90 s(3H, CH_3)	16,35 / 16,14	1,61 / 1,31	25,16 / 25,11	36,03 / 35,87

*Yield relative to acetone oxime.
**Yield relative to ethanenitrolic acid.

TABLE 2. ^{13}C and ^{14}N NMR Spectral Parameters of N′-Cyanodiazene N-Oxides



Compound	R	^{13}C NMR δ, ppm				^{14}N NMR (δ, ppm; $\Delta\nu_{1/2}$, Hz								Note
		C≡N	C¹	C²	C³	C≡N		=N→O		=N—		NO_2		
						δ	$\Delta\nu_{1/2}$	δ	$\Delta\nu_{1/2}$	δ	$\Delta\nu_{1/2}$	δ	$\Delta\nu_{1/2}$	
(II)		109.92	116.05	24,80	–	−118,5	370	−16,8	33	−98	370	−3,0	23	
(III)		111,79	128,20	145,03	13.77	−139	>700	−27.5	142	–	–	–	–	$^2J_{C^3-CH_3}$=6,8 Hz $^3J_{C^1-CH_3}$=2,6 Hz
(IV)		109.90	159,71	149,44	9,79	−115,5	330	−44,3	21	−94,8	~440	–	–	$^2J_{C^3-CH_3}$=8,3 Hz
(V)		110,93	87,20	32,61	–	−122	390	−2,4	53	−102	330	–	–	$^2J_{C^1-CH_3}$=4,7 Hz
(VI)		109,54	111,19	30,47	–	−115	~400	−23,9	80	−85	~400	−13,6	60	

with nitroso compounds to give the desired N′-cyanodiazene N-oxides. This reaction proceeds readily in methanol at from −10 to −15°C. The yields of products (I)-(IV) are 29-56% (Table 1).

$$[HNCN^{\ominus}]Na^{\oplus} \xrightarrow{t\text{-}BuOCl} [ClNCN^{\ominus}]Na^{\oplus} \xrightarrow[CH_3OH]{RNO} R-\overset{O}{\overset{\uparrow}{N}}=N-C\equiv N$$

(I)—(IV)

The second approach to the synthesis of cyanoazoxy compounds is based on our previous method [15,16] for the formation of the diazene N-oxide group entailing the oxidation of nitroso compounds with amines and dibromoisocyanurate (DBI). The use of cyanamide as the amine component permits the synthesis of the corresponding N′-cyanodiazene N-oxides (I)-(VI) in high yields (Table 1).

$$R-NO + H_2NCN + DBI \xrightarrow[-20^{\circ}]{CH_2Cl_2} R-\overset{O}{\overset{\uparrow}{N}}=N-C\equiv N$$

(I) — (VI)

The reaction has a broad region of application. Aliphatic, aromatic, and heterocyclic nitroso compounds containing other functional substituents easily enter into it. This is a promising method for synthesizing new N-(haloalkyl)-N′-cyanodiazene N-oxides (V), (VI) from the available oximinoalkanes without separation of the intermediate α-halonitrosoalkanes

$$\begin{matrix} R^1 \\ \diagdown \\ C=NOH \\ \diagup \\ R^2 \end{matrix} \xrightarrow{Br_2} \left[\begin{matrix} R^1 \\ \diagdown \\ Br-C-NO \\ \diagup \\ R^2 \end{matrix} \right] \xrightarrow{DBI\ /H_2NCN} \begin{matrix} R^1 & O \\ | & \uparrow \\ Br-C-N=N-C\equiv N \\ | \\ R^2 \end{matrix}$$

(V), (VI)

$R^1 = R^2 = CH_3$ (V); $R^1 = CH_3$, $R^2 = NO_2$ (VI).

The reaction of nitroso compounds with cyanamide and DBI probably proceeds through the formation of unstable N,N-dihalocyanamide, which then reacts with the nitroso compound according to the scheme proposed by Zawalski [17] and Nelson [18]. The important role of DBI in this reaction is indicated by the sharp drop in the yield of (II) when weaker brominating agents are used: the yield is 80% using DBI, 10% using N-bromosuccinimide, and 0% using bromine.

The proposed methods for the synthesis of N′-cyanodiazene N-oxides are regiospecific. Products (I)-(VI) are pure regioisomers as indicated by thin-layer chromatography and PMR spectroscopy. The structure of (I) was confirmed by showing that this compound is identical to N-phenyl-N′-cyanodiazene N-oxide obtained according to Fruttero et al. [12] as indicated by lack of depression of the melting point of a mixed sample and identical R_f values. The structures of the (II)-(VI), which had not been previously reported, were established by elemental analysis, IR, PMR (Table 1), and ^{13}C and ^{14}N NMR spectroscopy (Table 2).

The assignment of the signals in the ^{13}C and ^{14}N NMR spectra of (II)-(VI) was carried out by analyzing the chemical shifts and spin-spin coupling constants and taking account of literature analogies [19,20]. The complete averaging of the ^{13}C NMR signals for heterocyclic C^2 and methyl C^3 in (III) is apparently a result of the high rate of proton migration between the heterocyclic nitrogen atoms. The downfield signals at −3.0 and −13.6 ppm, which have the least width ($\Delta\nu_{\frac{1}{2}}$ = 23-60 Hz) in the ^{14}N NMR spectra of (II) and (V) were assigned to the nitro group. The electronic environment of the central nitrogen atom of this group has the greatest symmetry [21].

The ^{13}C NMR signal for C^1 in all the compounds studied is much broader due to spin-spin coupling through one bond with the oxidized nitrogen atoms of the nitro and diazene N-oxide groups, which give rather narrow lines in the ^{14}N NMR spectrum [22]. The selective suppression of the ^{14}N NMR signal of the diazene N-oxide group under $^{13}C-\{^1H,^{14}N\}$ triple resonance conditions reduce this broadening. These data along with the observation of narrow ^{13}C NMR signals of the nitrile group in (II)-(VI) unequivocally shows the position of the oxygen atom in the diazene N-oxide group and permits us to assign N′-cyanodiazene N-oxide structure to all the compounds synthesized.

EXPERIMENTAL

The IR spectra of the liquid compounds were taken neat, while the spectra of the solid compound were taken in KBr pellets on a Specord 75IR spectrometer. The ^1H, ^{13}C, and ^{14}N NMR spectra were taken in acetone-d_6 on a Bruker AM 300 spectrometer at 300 MHz (^1H), 75.5 MHz (^{13}C), and 21.7 MHz (^{14}N). The chemical shifts of the ^1H and ^{13}C NMR signals were measured relative to TMS as the internal standard (δ 0.0 ppm), while the chemical shifts of the ^{14}N NMR signals were measured relative to nitromethane as an external standard (δ 0.0 ppm) without correction for diamagnetic susceptibility.

Tert-butyl hypochlorite [23], dibromoisocyanurate [24], 2-nitro-2-nitrosopropane [25], 3,5-dimethyl-4-nitrosopyrazole [26], and ethanenitrolic acid [27] were obtained according to reported methods.

N′-Cyanodiazene N-Oxides (I)-(VI). Reaction of Nitroso Compounds with the NaHNCN–t-BuOCl System (method A). A solution of CH_3ONa obtained by dissolving 10 mmoles sodium in 10 ml absolute methanol was added to a solution of 10 mmoles cyanamide in 6 ml absolute methanol. After maintenance for 1.5 h at 23-28°C, the mixture was added with stirring to a solution of 10 mmoles t-BuOCl in 10 ml absolute methanol at −60°C. A solution of 10 mmoles nitroso compound in 60 ml methanol was added to this mixture, maintained for 2 h at −60°C, 2 h at −15°C, and 1 h at −20°C. When the medium was basic, the mixture was neutralized with sulfuric acid to pH 7. The solvent was removed in vacuum and the residue was extracted with benzene. The benzene solutions of (I), (II), and (IV) were passed through a layer of L40×100 silica gel. The solution of (III) was evaporated immediately after extraction. Products (I) and (III) were separated by crystallization, while (II) and (IV) were separated by vacuum distillation. The yields and properties of the properties of the products are given in Table 1.

Preparation of N′-Cyanodiazene N-Oxides (I)-(III) by the Reaction of Nitroso Compounds with the H_2NCN–DBI System (method B). A solution of 10 mmoles cyanamide in 20 ml dry ether and 15 mmoles DBI were added consecutively with stirring to a solution of 10 mmoles nitroso compound in 60 ml of an organic solvent such as CH_2Cl_2, $CHCl_3$, or CH_3CN at −20°C. The mixture was stirred for 1 h, gradually warming to room temperature, and maintained for an additional 2 h. The precipitate was filtered off and washed with two 20-ml portions of a suitable solvent. The solvent was removed from the mother liquor. Products (I)-(III) were separated analogously to method A. The yields of (I)-(III) are given in Table 1.

2-Bromo-2-(cyanoazoxy)propane (V). A sample of 1.15 g (13.7 mmoles) $NaHCO_3$ and 0.71 ml (13.7 mmoles) Br_2 were added with stirring to a solution of 1.00 g acetone oxime (13.7 mmoles) in 50 ml dry acetonitrile at from −15 to −20°C. After 15 min, a solution of 0.58 g (13.7 mmoles) cyanamide in 10 ml dry ether and 7.86 g (27.4 mmoles) DBI are added consecutively at the same temperature. The mixture was stirred for 1 h with gradual warming to room temperature and maintained for an additional 2 h at 18-23°C. The precipitate was filtered off and the solvent was removed. The residue was extracted with three 40-ml portions of benzene. The benzene solution was passed through a layer of L40×100 silica gel. The solvent was removed and the product was distilled in vacuum to give 0.83 g (32%) (V) as a pale yellow oil. The properties of (V) are given in Table 1.

1-Bromo-1-nitro-1-(cyanoazoxy)ethane (VI). A sample of 2.23 g (28.3 mmoles) pyridine and 4.52 g (28.3 mmoles) Br_2 were added with stirring consecutively with an interval of 15 min to a solution of 3.00 g (28.8 mmoles) ethanenitrolic acid in 150 ml dry CH_2Cl_2 at −20°C. After 30 min, a solution of 1.33 g (31.7 mmoles) cyanamide in 10 ml dry ether and 33.05 (115.2 mmoles) DBI were added to the reaction mixture. Stirring was continued for 1 h at −20°C. The mixture was brought to room temperature over 2 h and maintained for 3 h at 18-23°C. The precipitate was filtered off and the filtrate was evaporated. The residue was extracted with three 70-ml portions of benzene. The benzene solution was passed through a layer of L40×100 silica gel. The solvent was evaporated and the product was distilled in vacuum to give 5.23 g (83%) (VI) as a light yellow oil. The properties of (VI) are given in Table 1.

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