Synthesis and properties of *N'*-(phosphorylalkyl)diazene *N*-oxides

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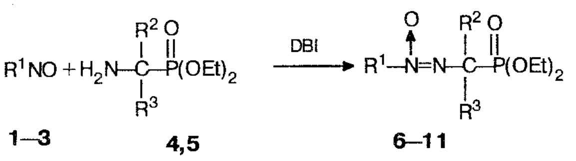
A method has been developed for the synthesis of *N'*-(phosphorylalkyl)diazene *N*-oxides based on the reaction of nitroso compounds with dialkyl (α-aminoalkyl)phosphonates in the presence of dibromoisocyanurate. Some chemical properties of the synthesized compounds have been studied.

Key words: *N'*-(phosphorylalkyl)diazene *N*-oxides; nitroso compounds; dialkyl (α-aminoalkyl)phosphonates; dibromoisocyanurate.

Previously[1—3] we reported the preparation of phosphorus-containing azoxy compounds, in which the P atom is directly linked to the N atom of the diazene oxide group. In the present work, we investigated the synthesis of previously unknown *N'*-(phosphorylalkyl)diazene *N*-oxides, in which the diazene oxide group and the P atom are separated by one C atom.

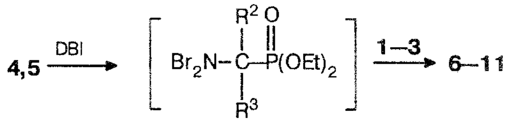
For this purpose we chose the reaction, which has not been studied previously, of nitroso compounds with dialkyl (α-aminoalkyl)phosphonates in the presence of dibromoisocyanurate (DBI) as an oxidizing reagent, which is highly efficient in the formation of the diazene oxide group.[1—8] It was found that aliphatic (**1** and **2**) and aromatic (**3**) nitroso compounds react with aminoalkylphosphonates (**4** and **5**), which contain alkyl and aryl substituents at the carbon atom, in the presence of DBI in chlorinated organic solvents (CH_2Cl_2 and $CHCl_3$) at room temperature to give the corresponding *N'*-(phosphorylalkyl)diazene oxides (**6—11**) in yields of 30—83 % (Table 1).



$$R^1NO + H_2N-\underset{R^3}{\overset{R^2}{C}}-\overset{O}{\overset{\|}{P}}(OEt)_2 \xrightarrow{DBI} R^1-\overset{O}{\overset{\uparrow}{N}}=N-\underset{R^3}{\overset{R^2}{C}}-\overset{O}{\overset{\|}{P}}(OEt)_2$$

1—3 **4,5** **6—11**

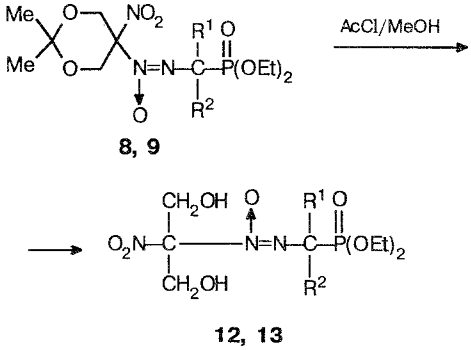
As in the case of the previously studied[1—3] reactions of nitroso compounds with alkylamines in the presence of DBI, the process apparently involves the bromination of amines **4** and **5** and the reaction of the *N*,*N*-dibromoamine derivatives (**A**) generated *in situ* with a nitroso compound according to the scheme of the Kovacic reaction[9] to form the final products (**6—11**).



$$4,5 \xrightarrow{DBI} \left[Br_2N-\underset{R^3}{\overset{R^2}{C}}-\overset{O}{\overset{\|}{P}}(OEt)_2 \right] \xrightarrow{1-3} 6-11$$

A

Diazene oxides (**8** and **9**), which contain a dioxane fragment at the *N*-oxide group, are convenient starting compounds for preparing the previously unavailable compounds of this series with hydroxyl, acetoxyl, and nitrate substituents and halogen atoms. In acidic media, the dioxane cycle in **8** and **9** readily opens to give dihydroxyl derivatives (**12** and **13**) (see Table 1).



Using compound **12** as an example, it was shown that hydroxyl-containing *N'*-(phosphorylalkyl)diazene oxides undergo acetylation and nitration typical of alcohols, which proceed with the retention of the diazene oxide and phosphonate groups. As a result, the corresponding nitrodiacetates and nitrodinitrates (**14** and **15**) were obtained in high yields.

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Table 1. Yields, IR and ^1H NMR spectra of *N'*-(phosphorylalkyl)diazene *N*-oxides **6—16**

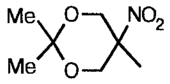
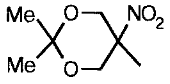
Com-pound	R^1	R^2	R^3	Yield (%)	IR (ν/cm^{-1})				^1H NMR (δ, *J*/Hz)	
					$\overset{\overset{O}{\uparrow}}{N}{=}N$	P=O	P—O—C	NO_2	R^1	R^2, R^3, OEt
6	CMe_2NO_2	Me	Me	34	1520	1250	1030	1580	2.03 (s, 6 H, Me)	1.26 (t, 6 H, $OCH_2\underline{Me}$); 1.46 (d, 6 H, Me, $^3J_{H,P}$ = 16); 4.05 (m, 4 H, $O\underline{CH_2}Me$)
7	CMe_2NO_2	H	Ph	46	1490	1250	1030	1575	2.05 (s, 6 H, Me)	1.21 (t, 6 H, $OCH_2\underline{Me}$); 3.93 (m, 4 H, $O\underline{CH_2}Me$); 5.67 (d, 1 H, CH, $^2J_{H,P}$ = 20); 7.32 (5 H, Ph)
8		Me	Me	83	1500	1250	1040	1580	1.40 (s, 3 H, Me); 1.46 (s, 3 H, Me); 4.60 (s, 4 H, CH_2)	1.32 (t, 6 H, $OCH_2\underline{Me}$); 1.52 (d, 6 H, Me, $^3J_{H,P}$ = 16); 4.12 (m, 4 H, $O\underline{CH_2}Me$)
9		H	Ph	30	1500	1260	1030	1580	1.43(s, 3 H, Me); 1.45 (s, 3 H, Me); 4.68 (m, 4 H, OCH_2)	1.22(t, 6 H, $OCH_2\underline{Me}$); 3.94 (m, 4 H, $O\underline{CH_2}Me$); 5.76(d, 1 H, CH, $^2J_{H,P}$ = 20.0); 7.32 (m, 3 H, *m*-H, *p*-H, Ph); 7.43 (d, 2 H, *o*-H, Ph, *J* = 7.0)
10	Ph	Me	Me	32	1490	1250	1030	—	7.50 (m, 3 H, *m*-H, *p*-H, Ph); 8.13 (d, 2 H, *o*-H, Ph, *J* = 7)	1.35 (t, 6 H, $OCH_2\underline{Me}$); 1.68 (d, 6 H, Me, $^3J_{H,P}$ =10.0); 4.21 (m, 4 H, $O\underline{CH_2}Me$);
11	Ph	H	Ph	58	1480	1260	1020	—	7.50÷7.65 (m, 3 H, *m*-H, *p*-H, Ph); 8.23 (d, 2 H, *o*-H, Ph, *J* = 7.0)	1.21 (d.t, 6 H, $OCH_2\underline{Me}$); 4.00 (m, 4 H, $O\underline{CH_2}Me$); 6.00 (d, 1 H, CH, $^2J_{H,P}$ = 23); 7.35÷7.5 (m, 5 H, Ph)
12	$C(CH_2OH)_2NO_2$	Me	Me	57	1520	1240	1030	1580	4.31 (d.d, 4 H, OCH_2, J_1 = 21, J_2 = 12); 4.70 (br.s, 2 H, OH)	1.34 (t, 6 H, $OCH_2\underline{Me}$); 1.55 (d, 6 H, CH_3, $^3J_{H,P}$ = 16); 4.14 (m, 4 H, $O\underline{CH_2}Me$)
13	$C(CH_2OH)_2NO_2$	H	Ph	50	1500	1250	1030	1580	4.44 (d.d, 4 H, OCH_2, J_1 = 21, J_2 = 12)	1.38 (t, 6 H, $OCH_2\underline{Me}$); 4.02 (m, 4 H, $O\underline{CH_2}Me$); 5.86 (d, 1 H, CH, $^2J_{H,P}$ =23); 7.30÷7.50 (m, 5 H, Ph)
14	$C(CH_2OAs)_2NO_2$	Me	Me	62	1510	1230	1050	1580	2.07 (s, 6 H, Ac); 4.85 (d, 4 H, OCH_2, *J* = 9)	1.34 (t, 6 H, $OCH_2\underline{Me}$); 1.54 (d, 6 H, Me, $^3J_{H,P}$ = 17); 4.14 (m, 4 H, OCH_2)
15	$C(CH_2ONO_2)_2NO_2$	Me	Me	78	1520	1280	1030	1590; 1670(NO_3)	5.48 (d, 4 H, OCH_2, *J* = 4)	1.34 (t, 6 H, $OCH_2\underline{Me}$); 1.55 (d, 6 H, Me,$^3J_{H,P}$ = 16); 4.14 (m, 4 H, $O\underline{CH_2}Me$)
16	CBr_2NO_2	Me	Me	45	1520	1240	1050	1590	—	1.31 (t, 6 H, $OCH_2\underline{Me}$); 1.52 (d, 6 H, Me,$^3J_{H,P}$ = 16); 4.11 (m, 4 H, $O\underline{CH_2}Me$)

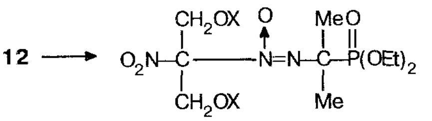
Table 2. ^{13}C NMR spectra of compounds **8—12, 15,** and **16**

Compound	O$\underline{C}$H$_2$Me	OCH$_2\underline{Me}$	N—$\underline{C}$—P	($\underline{Me}$)$_2$CP	$\underline{C}$—N(O)	Other signals
	δ ($J_{C,P}$/Hz)					
8	62.9(7)	16.7(5)	63.1(164)	18.2(1)	106.3	21.7, 25.3 [($\underline{Me}$)C]; 62.5 (O$\underline{C}$H$_2$CNO$_2$); 100.4 [(Me)$_2\underline{C}$]
9	63.3(7); 63.4(7)	16.6(6); 16.7(6)	63.5(150)	—	105.8	21.7, 25.2 [($\underline{Me}$)C]; 62.4 (O$\underline{C}$H$_2$CNO$_2$); 100.4 [(Me)$_2\underline{C}$]; 132.9(8) (*i*-C); 128.5, 128.7, 128.9 (*o*-C, *m*-C, *p*-C, Ph)
10	62.6	17.0	62.5(163)	18.5	148.6	122.5 (*o*-C, Ph); 129.1 (*m*-C, Ph); 132.1 (*p*-C, Ph)
11	63.0(7); 63.2(7)	16.7(6); 16.8(6)	63.4(154)	—	147.9	134.4(*i*-C, Ph); 129.6 (*o*-C, Ph); 128.7 (*m*-C, Ph); 128.3 (*p*-C, Ph); 122.8 (*o*′-C, Ph); 129.3 (*m*′-C, Ph); 132.4 (*p*′-C, Ph)
12	63.6(7)	16.6(5)	62.8(161)	19.1	113.1	60.8 (O$\underline{C}$H$_2$CNO$_2$)
15	63.2(7)	16.8(5)	63.8(165)	17.9	107.0	67.7 (O$\underline{C}$H$_2$CNO$_2$)
16	63.2(6)	16.7(5)	64.4(163)	17.2	98.5	—

Table 3. ^{14}N (δ, $\Delta\nu_{1/2}$/Hz) and ^{31}P (δ) NMR spectra of *N*′-(phosphorylalkyl)diazene *N*-oxides

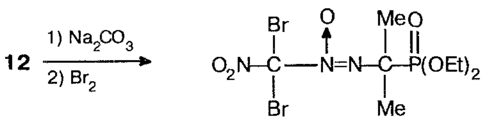
Compound	^{14}N(O)		^{14}NO$_2$		^{31}P
	δ	$\Delta\nu_{1/2}$	δ	$\Delta\nu_{1/2}$	δ
8	−53.7	290	−11.1	280	25.7
9	−54.8	270	−12.3	260	17.8
10	−47.6	320	—	—	*
11	−49.1	240	—	—	19.9
15	−53.3**	220	−17.4	168	25.3
16	−53.3	190	−19.8	80	25.2

* The ^{31}P signal was not found (probably, owing to its broadening); however, the ^{31}P—^{13}C spin coupling constant was observed in the ^{13}C NMR spectrum (see Table 2).
** The signal is overlapped with the signal for the ONO$_2$ group.



14: X = Ac
15: X = NO$_2$

Unlike the reactions with electrophiles, the interaction of **12** with bases is accompanied by cleavage of the bonds between the C atom linked to the nitro group and the C atom of the hydroxymethyl fragment. When this process is carried out in the presence of bromine, which plays the role of a trap for the unstable α-nitroalkyl anions that are formed during the reaction, it is possible to synthesize *N*-(dibromonitromethyl)-*N*′-(1-diethoxyphosphoryl-1-methyl-ethyl)diazene *N*-oxide (**16**) in a yield of 45 %.



16

The diazene *N*-oxides **6—16** obtained are oily substances stable when stored for long periods at room temperature. However, they decompose when heated to 80—100 °C. The structure of the synthesized compounds was established by the IR absorption spectra and by ^{1}H, ^{13}C, ^{14}N, and ^{31}P NMR spectroscopy (Tables 1—3).

In the IR spectra of compounds **6—16**, the absorption bands for the azoxy group (1480—1520 cm^{-1}) and the phosphoryl fragment (1230—1280 and 1020—1080 cm^{-1}) are present (see Table 1). In the ^{13}C NMR spectra of the synthesized diazene *N*-oxides, the coupling constants $^1J_{C,P}$ (150—165 Hz) are observed. As a rule, long-range $J_{C,P}$ coupling constants (2—7 Hz, see Table 2) are also observed. In the ^{13}C NMR spectra for compounds **9** and **11**, which have an asymmetric C atom, the signals for the ethoxyl C atoms occur as a doublet of doublets, which is, apparently, associated with the diastereotropic character of these atoms and with the splitting of the signals for each of them into doublets by the phosphorus atom.

The parameters of the ^{14}N and ^{31}P NMR spectra are close to the corresponding characteristics of compounds in which the diazene oxide and dialkoxyphosphoryl groups are linked directly to each other;[1—3] this fact confirms the presence of the above-mentioned structural fragments in compounds **6—16** (see Table 3).

Thus, *N'*-(phosphorylalkyl)diazene *N*-oxides, new phosphorus—nitrogen—oxygen—carbon systems, have been synthesized for the first time, and some of their conversions have been studied.

Experimental

IR spectra were recorded on a Specord IR-75 spectrometer in thin layer samples. ^1H, ^{13}C, ^{14}N, and ^{31}P NMR spectra were recorded on a Bruker AM-300 instrument with operating frequencies of 300.13 (^1H), 75.5 (^{13}C), 21.7 (^{14}N), and 121.5 MHz (^{31}P) in acetone-d$_6$. The ^{14}N and ^{31}P chemical shifts were measured relative to $MeNO_2$ and H_3PO_4 external standards, respectively.

2-Nitro-2-nitrosopropane,[10] 2,2-dimethyl-5-nitro-5-nitroso-1-3-dioxane,[11] DBI,[12] and dialkyl-(α-aminoalkyl)phosphonates[13,14] were obtained according to the procedures reported previously. Compounds **6—16** were isolated by TLC (Silpearl, ether as the eluent).

***N'*-(Phosphorylalkyl)diazene *N*-oxides (6—11).** A mixture of 10 mmol of a nitroso compound, 10 mmol of aminoalkylphosphonate, and 20 mmol of DBI in 10 mL of CH_2Cl_2 was stirred for 12—24 h at ~20 °C. The excess DBI and cyanuric acid were filtered off and washed with CH_2Cl_2 (2×5 mL) and the filtrate was evaporated *in vacuo* to afford diazene *N*-oxides. The yields and IR and ^1H NMR spectral data are given in Table 1; the ^{13}C NMR spectra are given in Table 2.

***N*-(2-Hydroxy-1-hydroxymethyl-1-nitroethyl)-*N'*-(1-diethoxyphosphoryl-1-methyl-ethyl)diazene *N*-oxide (12), and *N*-(2-hydroxy-1-hydroxymethyl-1-nitroethyl)-*N'*-(α-diethoxyphosphorylbenzyl)diazene *N*-oxide (13).** Acetyl chloride (2.5 mmol) was added with stirring at ~20 °C to a solution of 0.5 mmol of diazene *N*-oxide **8** or **9** in 5 mL of MeOH. The mixture was kept for 12 h at ~20 °C, then the solvent was removed, and products **12** and **13** were isolated.

***N*-(2-Acetoxy-1-acetoxymethyl-1-nitroethyl)-*N'*-(1-diethoxyphosphoryl-1-methyl-ethyl)diazene *N*-oxide (14).** Acetyl chloride (0.06 g, 0.8 mmol) was added dropwise with stirring at −20 °C to a solution of 0.07 g (0.2 mmol) of **12** in 1 mL of absolute ether. The reaction mixture was allowed to warm to ~20 °C, then the solvent was removed *in vacuo* to give 0.05 g (62 %) of diazene *N*-oxide **14**.

***N*-(2-Nitroxy-1-nitroxymethyl-1-nitroethyl)-*N'*-(1-diethoxyphosphoryl-1-methyl-ethyl)diazene *N*-oxide (15).** 0.05 g (0.8 mmol) of HNO_3 (ρ = 1.506 g cm^{-3}) was added at 0 °C to a solution of 0.08 g (0.8 mmol) of acetic anhydride in 1 mL of absolute CH_2Cl_2. The reaction mixture was kept for ~30 min, the temperature was raised gradually to ~20 °C, and then a solution of 0.07 g (0.2 mmol) of **12** in 1 mL of absolute CH_2Cl_2 was added. After ~20 min, the reaction mixture was poured into 3 mL of water. The organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (2×3 mL), the combined extract was dried with $MgSO_4$, and the solvent was evaporated to give product **15**.

***N*-(Dibromonitromethyl)-*N'*-(1-diethoxyphosphoryl-1-methyl-ethyl)diazene *N*-oxide (16).** Na_2CO_3 (0.07 g, 0.6 mmol) was added with stirring at ~20 °C to a solution of 0.09 g (0.2 mmol) of **12** in 5 mL of water; after ~30 min, 0.12 g (0.8 mmol) of Br_2 was added, and the reaction mixture was kept for 10 min at ~20 °C. The organic layer was separated, the aqueous layer was extracted with ether (2×3 mL), and the combined organic extract was dried with $MgSO_4$. The solvent was evaporated to afford product **16**.

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