Synthesis of 1-aryl-2-alkenyldiazene 1-oxides

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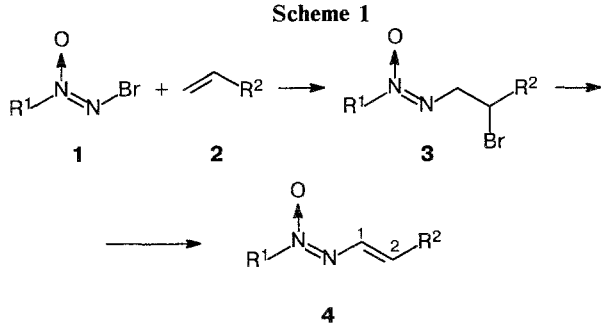
1-Aryl-2-alkenyldiazene 1-oxides were prepared by the reactions of 1-aryl-2-bromodiazene 1-oxides with olefins followed by dehydrobromination of the intermediate 1-aryl-2-(β-bromoalkyl)diazene 1-oxides by triethylamine.

Key words: diazene oxides, alkenes, azoxyolefines.

In recent years 2-alkenyldiazene 1-oxides have attracted considerable attention as biologically active materials.[1] However, no regiospecific methods for the synthesis of this class of compounds have been reported. In fact, alkyl-*ONN*-azoxyolefins are prepared by oxidation of the corresponding azoolefins by peracids;[2] however, this reaction frequently yields isomeric *N*-oxides and oxiranes. In the present paper we have shown that aryl-*ONN*-azoxyolefins (Scheme 1) **4** can be conveniently synthesized by addition of 1-aryl-2-bromodiazene 1-oxides (BDO) to olefins[3] followed by abstraction of HBr from the intermediate β-bromo-substituted diazene oxides **3**.

Scheme 1



1: R^1 = Ph (**a**); 2,4,6-$Cl_3C_6H_2$ (**b**); 2,4,6-$Br_3C_6H_2$ (**c**); 4-$NO_2C_6H_4$ (**d**); Me–(5-membered ring) (**e**)

2: $R^2 = {}^{3}CH_2{}^{4}CH_2{}^{5}CH_2{}^{6}CH_3$ (**a**); Ph (**b**)

3, 4: R^1 = Ph, R^2 = Bu (**a**); R^1 = 2,4,6-$Cl_3C_6H_2$, R^2 = Bu (**b**); R^1 = 2,4,6-$Br_3C_6H_2$, R^2 = Bu (**c**); $R^1 = R^2$ = Ph (**d**); R^1 = 2,4,6-$Cl_3C_6H_2$, R^2 = Ph (**e**); R^1 = 2,4,6-$Br_3C_6H_2$, R^2 = Ph (**f**); R^1 = 4-$NO_2C_6H_4$, R^2 = Ph (**g**); R^1 = Me–(5-membered ring), R^2 = Ph (**h**)

The reaction can be carried out by two methods. One of these (method *A*) is a two-step procedure. Initially, the reaction of BDO with olefin[3] is carried out, the excess of the olefin is distilled off, and compound **3** is treated with triethylamine without purification.

The other method (*B*) is a one-step procedure. BDO is added to olefin in the presence of triethylamine. This method has two peculiarities. First, in the presence of Et_3N, the rate of the reaction of BDO with olefins dramatically increases. It is likely that Et_3N initiates the reaction (as hydroperoxides do[3]) owing to single-electron transfer. This effect is especially pronounced for the reaction of compound **1c** with hexene: in the presence of 20 % triethylamine this reaction is completed over a period of 1 h, whereas without the initiator it does not occur at all. The second peculiarity of this method is that an excess of Et_3N rapidly converts diazene oxide **3** into olefin **4**, thus preventing it from decomposing. This makes it possible to obtain product **4d** ($R^1 = R^2$ = Ph), which could not be prepared by method *A*, since the intermediate diazene oxide **3** is unstable.

Method *B* is less time-consuming; however, the products obtained by this procedure are sometimes contaminated with resins. In these cases, version *A* is preferred (Table 1). In general, the method suggested makes

Table 1. Synthesis of azoxyolefins **4** (see Scheme 1)

Compound	Method of synthesis	Reaction conditions	Yield (%) (*E*/*Z*)	M.p./°C
4a*	*A*	40 °C, 8 h	55 (50/50)	Oil
4b	*A*	24 °C, 6 days	78 (60/40)	Oil
4c	*B*		50 (44/56)	Oil
4d	*B*		32 (90/10)	90—92
4e	*A*	40 °C, 1 h	92 (95/5)	102—104
4f	*A*	40 °C, 1 h**	95 (85/15)	128—130
4g	*A*	24 °C, 48 h	65 (100/0)	144—145 (dec.)
4h	*A*	24 °C, 24 h	70 (100/0)	116—117

* The synthesis of aryl-*ONN*-azoxyolefin **4a** was described in our previous paper.[3] ** Without a solvent.

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Table 2. Data of NMR spectroscopy for azoxyolefins **4**

Compound	^{1}H NMR, δ (J_{vic}/Hz)	^{13}C NMR, δ	^{14}N NMR, δ ($\Delta\nu_{1/2}$/Hz)
4b	0.93 (t, *E*, *Z*, HC(6)); 1.30—1.50 (m, *E*, *Z*, HC(5)); 1.45—1.55 (m, *E*, *Z*, HC(4)); 2.33 (dt, *E*, HC(3)); 2.49 (dt, *Z*, HC(3)); 6.07 (dt, *Z*, HC(2)); 6.65 (dt, *E*, HC(2)); 7.42 (s, *E*, *Z*, H_m); 7.71 (dt, *Z*, HC(1), J = 8.0); 7.87 (dt, *E*, HC(1), J = 13.7)	13.83 (*E*, *Z*, C(6)); 22.18, 22.34 (*E*, *Z*, C(5)); 27.18, 30.72, 30.98, 31.21 (*E*, *Z*, C(3), C(4)); 128.74, 128.82 (*E*, *Z*, C_m, R^1); 129.84 (*E*, *Z*, C_o,R^1); 132.96 (*Z*, C(1)); 135.61 (*E*, *Z*, C_p, R^1); 135.61 (*E*, C(1)); 140.29 (*Z*, C(2)); 142.92 (*E*, C(2))	−74 (220)
4c	0.89 (t, *Z*, HC(6)); 0.93 (t, *E*, HC(6)); 1.30—1.54 (m, *E*, *Z*, HC(5), HC(4)); 2.33 (dt, *E*, HC(3)); 2.49 (dt, *Z*, HC(3)); 6.08 (dt, *Z*, HC(2)); 6.65 (dt, *E*, HC(2)); 7.69 (dt, *Z*, HC(1), J = 8.1); 7.767 (s, *E*, H_m); 7.773 (s, *Z*, H_m); 7.84 (dt, *E*, HC(1), J = 13.7)	13.64 (*E*, *Z*, C(6)); 22.16, 22.30 (*E*, *Z*, C(5)); 27.14, 30.64, 30.92, 31.21 (*E*, *Z*, C(3), C(4)); 117.75 (*E*, *Z*, C_o, R^1); 123.36, 123.45 (*E*, *Z*, C_p, R^1); 130.62 (*Z*, C(1)); 132.82 (*E*, C(1)); 134.91, 135.01 (*E*, *Z*, C_m, R^1); 140.40 (*Z*, C(2)); 142.99 (*E*, C(2)); 146.24, 146.49 (br, *E*, *Z*, CN, R^1)	−69 (290)
4d	7.37 (d, *E*, HC(2)); 7.27—7.37 (m, *E*, H_m and H_p, R^1); 7.35—7.45 (m, *E*, H_m and H_p, R^2); 7.60 (d, *E*, H_o, R^2); 7.92 (d, *Z*, HC(2)); 8.0 (d, *Z*, HC(1), J = 10.0); 8.28 (d, *E*, H_o, R^1); 8.69 (d, *E*, HC(1), J = 13.5)	122.17 (*E*, C_o, R^1); 127.86 (*E*, C_o, R^2); 128.74 or 128.94 (*E*, C_m, R^1 or R^2); 129.94 (*E*, C_p, R^1); 131.46 (*E*, C_p, R^2); 132.20 (*E*, C(1)); 135.80 (*E*, C—CH, R^2); 136.08 (*E*, C(2)); 146.71 (br, *E*, CN, R^1)	−64 (170)
4e	7.35 (d, *E*, HC(2)); 7.35—7.40 (m, *E*, H_m and H_p, R^2); 7.40 (s, *E*, H_m, R^1); 7.56 (dd, *E*, H_o, R^2); 8.57 (d, *E*, HC(1), J = 14)	128.13 (*E*, C_o, R^2); 128.76 (*E*, C_m, R^1); 128.98 (*E*, C_m, R^2); 129.91 (*E*, C_o, R^1); 130.09 (*E*, C_p, R^2); 131.01 (*E*, C(1)); 134.65 (*E*, C—CH, R^2); 135.73 (*E*, C_p, R^1); 138.36 (*E*, C(2)); 142.93 (br, *E*, CN, R^1)	−73 (270)
4f	6.70 (d, *Z*, HC(2)); 7.35 (d, *E*, HC(2)); 7.34—7.39 (m, *E*, *Z*, H_m and H_p, R^2); 7.56 (d, *E*, *Z*, H_o, R^2); 7.77 (s, *E*, H_m, R^1); 7.78 (s, *Z*, H_m, R^1); 7.84 (d, *Z*, HC(1), J = 11.1); 8.56 (d, *E*, HC(1), J = 14.0)	117.89 (*E*, C_o, R^1); 123.85 (*E*, C_p, R^1); 128.14 (*E*, C_o, R^2); 128.98 (*E*, C_m, R^2); 130.09 (*E*, C_p, R^2); 131.36 (*E*, C(1)); 134.64 (*E*, C—CH, R^2); 134.97 (*E*, C_m, R^1); 138.43 (*E*, C(2)); 146.28 (br, *E*, CN, R^1)	−67 (140)
4g	7.40—7.43 (m, *E*, H_m and H_p, R^2); 7.45 (d, *E*, HC(2)); 7.63 (d, *E*, H_o, R^2); 8.35 (d, *E*, H_o, R^1); 8.45 (d, *E*, H_m, R^1); 8.63 (d, *E*, HC(1), J = 13.9)	123.25 and 124.32 (*E*, C_o and C_m, R^1); 128.20, 129.09 (*E*, C_o and C_m, R^2); 130.20 (*E*, C_p, R^2); 132.03 (*E*, C(1)); 135.08 (*E*, C—CH, R^2); 138.55 (*E*, C(2)); 149.23 and 150.1 (br, *E*, CN and C_p, R^1)	−71 (100); −13 (300), NO_2
4h	2.69 (s, *E*, CH_3); 7.40—7.43 (m, *E*, H_m and H_p, R^2); 7.49 (d, *E*, HC(2)); 7.61 (dd, *E*, H_o, R^2); 8.59 (d, *E*, HC(1), J = 14.5)	10.0 (CH_3, R^1); 128.54 (*E*, C_o, R^2); 129.20, 130.82 (*E*, C_m and C_p, R^2); 131.13 (*E*, C(1)); 134.54 (*E*, C—CH, R^2); 140.45 (*E*, C(2)); 147.20 (*E*, C—CH_3, R^1); 158.14 (br, *E*, CN, R^1)	−84 (130)

it possible to prepare azoxyolefins with various substituents; R^1 may be aromatic or heterocyclic, and R^2 is aliphatic or aromatic. The starting azoxybromides **1a—c** were prepared by the reaction of the corresponding nitroso compounds, R^1—N=O with NBr_3 generated *in situ* from NH_4Br and *N*-bromosuccinimide. This method is inconvenient for the preparation of azoxybromide **1d** (R^1 = *p*-$NO_2C_6H_4$) due to the poor solubility of compound **1d** in pentane, which is used for extraction in the last step of the synthesis. We found that if NBr_3 is generated with the help of dibromoisocyanuric acid, extraction with methylene chloride makes it possible to obtain virtually pure azoxybromide **1d**.

NMR spectroscopy plays a special role in establishing the structure and configuration of compounds **4** (Table 2). As a rule, all of the C atoms and the protons in the diazene oxides studied can be identified by this method. The presence of the N(O)=N fragment is confirmed by the typical narrow signal between −65 and −85 ppm corresponding to the N atom bound to the *N*-oxide O atom (see the ^{14}N NMR data in Table 2). Due to spin-spin interaction with the N nucleus exhibiting a narrow signal in the ^{14}N NMR spectrum, the signal for the *ipso*-C atom of the aromatic ring (see the ^{13}C NMR spectrum) is broadened, which confirms the position of the O atom in the azoxy fragment. The presence of the C=C bond is evidenced by the typical chemical shifts of the ^{13}C and ^{1}H signals of the corresponding atoms. In the case where the signals of the protons at the C=C double bond overlap with the multi-

plet of the protons of the aromatic ring, the identification and determination of chemical shifts were carried out using two-dimensional $^{13}C—^{1}H$ NMR spectroscopy. When R^2 = Bu, compounds **4** are formed as mixtures of *Z*- and *E*-isomers with respect to the C=C bond in a ratio of ~1 : 1. When R^2 = Ph, *Z*-isomer is formed in very small quantities or is not formed at all (**4g,h**) (see Table 1). The assignment of the isomers was based on a comparison of vicinal spin coupling constants of the protons at the C=C bond in the *E*/*Z* pair. In the case of *E*-isomers, the spin coupling constants are greater (13.5—14 Hz) than those for *Z*-isomers (8—11 Hz).[4]

Experimental

The ^{1}H, ^{13}C, and ^{14}N NMR spectra (in $CDCl_3$) were recorded on a Bruker AM-300 spectrometer at 300.13, 75.5, and 21.5 MHz, respectively. For the assignment of ^{1}H and ^{13}C signals, $^{1}H—^{1}H$ and $^{1}H—^{13}C$ correlations, ^{13}C NMR spectra recorded with no proton decoupling, and selective transfer of polarization were used. Tetramethylsilane was used as the standard (for ^{1}H and ^{13}C NMR), and nitromethane was used as the external standard (for ^{14}N NMR). IR spectra were recorded on a UR-20 spectrometer (for oils between NaCl glasses or for solids in KBr). Mass spectra were recorded on a Varian MAT CH-6 mass spectrometer. The parameters of the IR and mass spectra of azoxyolefins **4** are listed in Table 3.

Azoxybromides **1a—c** were prepared as described previously.[3]

1-(4-Nitrophenyl)-2-bromodiazene 1-oxide (1d). 4-Nitronitrosobenzene[5] (1 g, 6.58 mmol) was dissolved in a mixture of 25 mL of CH_2Cl_2 and 25 mL of MeCN; *N,N*-dibromoisocyanuric acid (5.7 g, 19.8 mmol) was added, and NH_4Br (0.97 g, 9.9 mmol) was added with intense stirring and cooling to −50 °C. The suspension was stirred for 15 min at −30 °C and evaporated *in vacuo*, and the residue was extracted with CH_2Cl_2 (3×50 mL). Evaporation of the extract under reduced pressure gave 1.3 g of compound **1d** (yield 80 %), m.p. 186—190 °C (dec.). Found (%): C, 29.17; H, 1.69; N, 17.30; Br, 32.35. $C_6H_4N_3BrO_3$. Calculated (%): C, 29.27; H, 1.63; N, 17.07; Br, 32.52. MS, *m/z*: 245 $[M]^+$ (for ^{79}Br). IR, ν/cm^{-1}: 1460 (N(O)N). ^{1}H NMR, δ: 8.38, 8.48 (dd, 4 H, H_o, H_m). ^{13}C NMR, δ: 125.04, 125.82 (C_o, C_m); 133.73 (C_i); 150.27 (C_p). ^{14}N NMR, δ: −14 (NO_2, $\Delta\nu_{1/2}$ = 90 Hz); −41.3 (N(O), $\Delta\nu_{1/2}$ = 30 Hz).

1-Methylfurazyl-2-bromodiazene 1-oxide (1e) was prepared from methylnitrosofurazan[6] by the general procedure,[3] yield 80 % (oil). MS, *m/z*: 206 $[M]^+$ (for ^{79}Br). IR, ν/cm^{-1}: 1500 (N(O)N). ^{1}H NMR, δ: 2.66 (s, 3 H, CH_3). ^{13}C NMR, δ: 9.28 (CH_3); 147.05 (C—CH_3); 156.13 (CN). ^{14}N NMR, δ: −57.5 ($\Delta\nu_{1/2}$ = 20 Hz).

1-Aryl-2-(alkenyl)diazene 1-oxides (4) (general procedure *A*). Azoxy bromide **1** (2.85 mmol) was dissolved in 32 mL of CH_2Cl_2, and an alkene (4.2 mL) was added. The conditions under which the reaction was conducted are given in Table 1. The solvent and excess alkene were evaporated in a vacuum of an oil pump, and the residue was dissolved in 30 mL of CH_2Cl_2. At 0 °C, triethylamine (0.85 mL, 6.1 mmol) was added. After 30 min, 20 mL of water was added, and excess Et_3N was neutralized with 5 % HCl to pH 5—6. The organic phase was separated, washed with water (2×20 mL), and dried with $MgSO_4$. The solvent was evaporated, and the product was purified by column chromatography (silica gel, chloroform—hexane, 1 : 2).

1-(2,4,6-Tribromophenyl)-2-(1-hexenyl)diazene 1-oxide (4c) (procedure *B*). Azoxy bromide **1c** (1.7 g, 3.88 mmol) was dissolved in 20 mL of CH_2Cl_2, and hexene (1.95 mL, 15.6 mmol) was added. A solution of triethylamine (0.078 g, 0.776 mmol) in 4 mL of CH_2Cl_2 was added dropwise with stirring over a period of 1 h, and then additional Et_3N (2.7 mL, 19.4 mmol) was added in one portion. After 30 min, 20 mL of water was added, and excess Et_3N was neutralized with 5 % HCl to pH 5—6. The organic phase was separated, washed

Table 3. Parameters of the IR and mass spectra and elemental analysis data for azoxyolefins **4**

Compound	IR, ν/cm^{-1}		MS*	Found / Calculated (%)				Molecular formula
	C=C	N(O)N		C	H	N	Cl+Br	
4b	1600	1475	306 $[M]^+$	46.91 46.86	4.20 4.26	9.01 9.11	34.73 34.58	$C_{12}H_{13}N_2OCl_3$
4c	1625	1445	438 $[M]^+$	32.50 32.69	2.89 2.97	6.30 6.35	54.11 54.36	$C_{12}H_{13}N_2OBr_3$
4d	1607	1467	224 $[M]^+$	74.88 75.00	5.29 5.36	12.61 12.50	—	$C_{14}H_{12}N_2O$
4e	1615	1425	326 $[M]^+$	51.52 51.30	2.88 2.75	8.41 8.55	32.39 32.52	$C_{14}H_9N_2OCl_3$
4f	1590	1410	458 $[M]^+$	36.59 36.44	1.81 1.95	6.35 6.07	52.35 52.06	$C_{14}H_9N_2OBr_3$
4g	1590	1480	269 $[M]^+$	62.58 62.45	4.15 4.09	15.78 15.61	—	$C_{14}H_{11}N_3O_3$
4h	1580	1470	230 $[M]^+$	57.51 57.39	4.42 4.35	24.57 24.35	—	$C_{11}H_{10}N_4O_2$

* Mass spectra are given for the ^{35}Cl and ^{79}Br isotopes.

with water (2×20 mL), and dried with $MgSO_4$. The solvent was evaporated, and the product was purified by column chromatography (silica gel, chloroform—hexane, 1 : 2).

1-Phenyl-2-styryldiazene 1-oxide (4d) (procedure *B*). Styrene (2.3 mL, 20 mmol) was added to azoxy bromide **1a** (1 g, 5 mmol) in 0.5 mL of CH_2Cl_2, and at 0 °C, Et_3N (0.7 mL, 5 mmol) was added. The mixture was kept for 1 h at 0 °C, the solvent and excess styrene were evaporated in a vacuum of an oil pump, and the residue was dissolved in 5 mL of CH_2Cl_2 and washed with 10 mL of water. The organic phase was separated, washed with water (2×20 mL), and dried with $MgSO_4$. The solvent was evaporated, and the product was purified by column chromatography (silica gel, chloroform—hexane, 1 : 2).

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References

1. (a) R. J. Parry, Y. Li, and F. Lii, *J. Am. Chem. Soc,* 1992, **114**, 10062; (b) H. Nakano, M. Hara, T. Katsuyama, Y. Uozaki, and K. Gomi, Jpn. Pat. 91/288.675; *Chem. Abstrs.*, 1993, 119: 158353.
2. B. T. Gillis and J. D. Hagarty, *J. Org. Chem*, 1967, **32**, 95.
3. A. M. Churakov, A. Yu. Tyurin, E. L. Goncharova, S. L. Ioffe, Yu. A. Strelenko, and V. A. Tartakovsky, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 917 [*Russ. Chem. Bull.*, 1995, **44**, 890 (Engl. Transl.)].
4. A. Zschunke, *Kernmagnetische Resonanzspektroskopie in der organischen Chemie*, Akademici-Verlag, Berlin, 1971.
5. J. H. Hall and F. W. Donal, *J. Org. Chem,* 1978, **43**, 4608.
6. A. B. Sheremetev, T. S. Novikova, T. M. Mel'nikova, and L. I. Khmel'nitskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 1193 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 1073 (Engl. Transl.)].

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