Aliphatic Azoxy Compounds. V. Functionalization of (Z)-Phenylmethyldiazene 1-Oxide[1]

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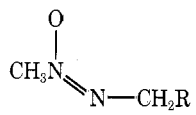
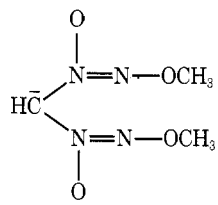
A study of the chemical transformations at the methyl group of azoxy compound (Z)-phenylmethyldiazene 1-oxide (**4a**) has been made. NBS bromination of **4a** gave (Z)-phenylbromomethyldiazene 1-oxide (**5a**), which was used as a substrate for the preparations of compounds **5b–k.** Silver ion assistance gave rapid substitution by oxygen nucleophiles, while strong bases effected a rapid fragmentation of **5a.** Nucleophiles that are weak bases successfully displaced the bromine atom of **5a.** Under neutral conditions, phenylhydroxymethyldiazene 1-oxide (**5b**) decomposed by way of phenyldiazonium ion, a route analogous to the neutral decomposition of methylazoxymethanol (**1b**). Under mildly basic conditions **5b** rapidly decomposed via a pathway initiated by proton abstraction from the CH_2 group of **5b,** yielding phenyldiimide as an intermediate. The sum of the transformations studied indicate that the azoxy group can stabilize a positive charge, an unpaired electron, or a negative charge at the C atom bound to the unoxidized N atom.

Chemical reactions that occur at the carbon atoms adjacent to an azoxy functional group have received little attention until fairly recently. Thus, Matsumoto and co-workers'[2] synthesis of MAM acetate (**1c**) from azoxymethane (**1a**) was not only valuable for its synthetic result, but also



1a, R = H
b, R = OH
c, R = $OCOCH_3$



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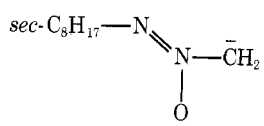

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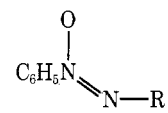
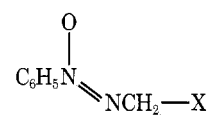
useful as a gauge of the relative reactivities at the proximal[3] and distal[3] α-carbon atoms of an azoxyalkane. The formal structural similarity between nitroalkanes and the proximal terminus of azoxyalkanes has been responsible for the long-held supposition that the two molecules should show similarity in C–H acidity. This similarity was borne out in experiment by Woodward and Wintner,[4] who examined the alkylation and H–D exchange of anion **2,** and by Moss and Love,[5] who examined the alkylation of anion **3.** However, given two equivalent[5b] α-alkyl groups, it is the *distal* rather than proximal α-H which displays the higher (kinetic) acidity. Thus, in azoxymethane (**1a**), the distal α-H's underwent base-catalyzed H–D exchange more rapidly.[6]

We were interested in examining the chemistry at the distal α-carbon atom of azoxyalkanes. It is this position on azoxyalkanes which suffers biological oxidation,[7] a transformation which turns the molecules into alkylating agents (the proximal alkyl group is transferred[6,8]) and hence (presumably) into potent carcinogens toward experimental animals.[7] Apart from Matsumoto's[2] work, little[9] has been reported concerning the chemistry at this carbon atom. We report herein on the functionalization of phenylmethyldiazene 1-oxide (**4a**)[1b] at the distal methyl group, and on some of the transformations of **5b,** a phenyl analogue of the carcinogenic MAM (**1b**).

Functionalization Reactions. Following Matsumoto's



4a, R = CH_3
b, R = CD_3

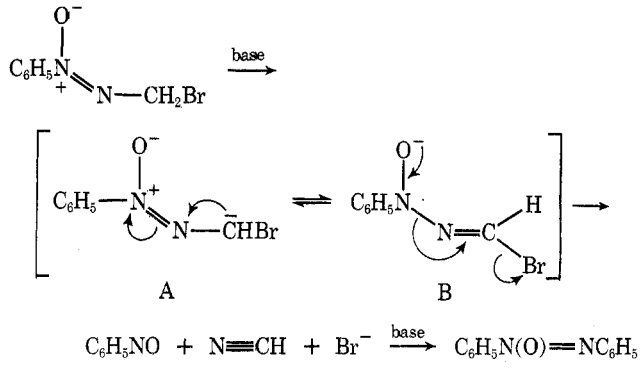


5a, X = Br
b, X = OH
c, X = $OCOCH_3$
d, X = OCH_3
e, X = OC_2H_5
f, X = O-*i*-C_3H_7
g, X = $OCH_2CH{=}CH_2$
h, X = $^{+}N(CH_3)_2CH_2CH_2OH$, Br^{-}
i, X = $-SC(NH_2)_2^{+}$, Br^{-}
j, X = SCN
k, X = Cl

lead,[2] we brominated **4a** using the Wohl–Ziegler reaction. Thus, refluxing **4a** in CCl_4 with *N*-bromosuccinimide and benzoyl peroxide gave crystalline, red-orange **5a,** in 70% yield, after silica gel chromatography. Bromination with molecular bromine also gave **5a,** but in poor yields. This free-radical transformation, together with those reported by Matsumoto[2] and Woodward and Wintner,[9] give indication that the azoxy function is capable of stabilizing an unpaired electron on the distal α-carbon atom (presumably via π-electron delocalization). Bromo compound **5a** was the substrate used for subsequent transformations.

Optimal substitution of **5a** by oxygen nucleophiles required silver ion assistance. Thus silver acetate–acetic acid treatment[2] of **5a** at room temperature rapidly converted it to crystalline **5c** in 80% yield. By contrast, the same transformation using sodium acetate required reflux temperature and longer reaction time. The conversion of **5a** to alcohol **5b** was smoothly effected using conditions similar to the Koenigs–Knorr reaction for converting glycosyl halides to free sugars or acetals: acetone–water, 25°, Ag_2CO_3. Alcohol **5b** was a stable, crystalline, off-white solid obtained consistently in 65–85% yields. Acetylation of **5b** gave **5c.** With the addition of calcium sulfate as a water scavenger, the Koenigs–Knorr conditions were applied to the syntheses of ethers **5d–g.** Other silver salts were tried in addition to silver carbonate. For example, silver nitrate assisted coupling of **5a** and allyl alcohol gave, in addition to **5g,** a product tentatively characterized as the nitrate ester of **5b** [**5,** X = ONO_2; ir 1650 and 1270 cm^{-1}; NMR δ 6.0 (s, ~2 H, NCH_2O)]. The methyl ether **5d** was also conveniently prepared using silver perchlorate in methanol, but with other

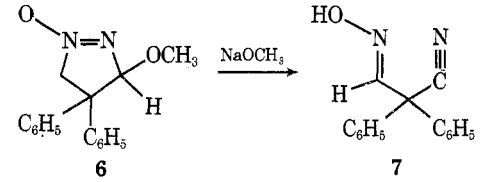
Scheme I



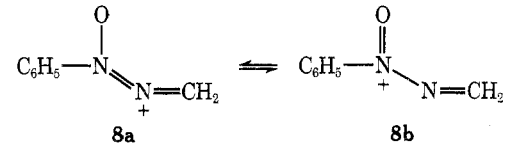
$$C_6H_5NO + N{\equiv}CH + Br^- \xrightarrow{base} C_6H_5N(O){=}NC_6H_5$$

alcohols, for example, allyl alcohol, this silver salt gave, again, a by-product in small amounts which was, in this instance, a shock-sensitive solid.

The attempted conversion of **5a** to ether **5d** using sodium methoxide in methanol led to the rapid fragmentation reaction shown in Scheme I. The products, nitrosobenzene, cyanide ion, and bromide ion, were all identified, as was azoxybenzene (produced from nitrosobenzene in a secondary reaction[10,11]). Other strong bases such as sodium hydroxide and the sodium salts of diethyl malonate and nitromethane also effected the fragmentation, as did weaker bases such as cyanide ion and amines (mixture of fragmentation and substitution). The initial reaction must be a proton abstraction by the base to give the anion A (Scheme I), which, presumably, can equilibrate with tautomeric form B. From tautomer B, Grob-type fragmentation yields the products shown. Some chemical support for the existence of tautomer B will be provided in a subsequent section. Jones and Northington[12] reported a similar fragmentation of cyclic azoxy compound **6**, using sodium methoxide in methanol, to give **7**. The initial step was the removal of the proton from the distal α-C atom.



6 **7**



8a **8b**

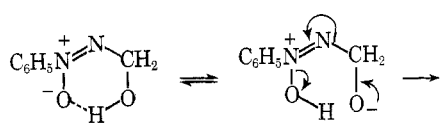
Nucleophiles which were weak bases did yield substitution products. As mentioned above, amines gave a mixture of fragmentation (major) and substitution (minor). However, the products of such substitution, e.g., **5** (X = NH-*i*-C_3H_7), being basic and carrying the seeds of their own destruction, were not stable. Interestingly, the tertiary amine *N,N*-dimethylethanolamine gave a substitution product, **5h**, in 64% yield. That **5a** had reacted with the ethanolamine with attack by nitrogen rather than attack by oxygen was indicated by the ir spectrum (KBr) of **5h**, which has a strong absorption at 3300 cm^{-1} for OH stretch, as does the ir spectrum of choline iodide. In addition, the ir spectra of both compounds had a band at 1470 cm^{-1} ($-CH_2-N^+{\equiv}$ bend) and lacked a 2700-cm^{-1} band for $-NH^+-$stretch. Thiourea reacted smoothly to give **5i** in 89% yield. The sulfur nucleophile thiocyanate ion also reacted readily with **5a**, but the product **5j**, an oil and a single spot in TLC, was unstable and could not be purified for elemental analysis by either distillation or preparative VPC. However, the ir spectrum (2160 cm^{-1}, $-SC{\equiv}N$ stretch) and the NMR spectrum (see Table I) are consistent with structure **5j**. Further, the C–S linkage in **5j** was further supported by the partial acid-catalyzed isomerization[13] of thiocyanate **5j** to a mixture of **5j** and the corresponding isothiocyanate, **5** (X = NCS, ir 2070 cm^{-1}). Lastly, lithium chloride in DMF or acetone gave **5k** in a classic SN2-type displacement reaction.

From the above, it is apparent that, toward substitution reactions, bromide **5a** reacts rapidly with nucleophiles, as would be expected for a primary halide. Thus reactions leading to products **5h–k** are complete in 0.5–1 h at room temperature. However, **5a** is extraordinarily reactive, for a primary halide, toward silver ion assisted substitutions. Thus, **5a** is consumed in minutes at room temperature upon dissolution in solvents containing dissolved silver ion. In an analysis of substitution processes at carbon atoms bound to the azo function, McBride and Malament[14] concluded that the azo group stabilizes adjacent carbonium ions by n-electron delocalization. At present, there is no experimental data which permits a decision between n stabilization (**8a**) or π stabilization (**8b**) or stabilization by both processes (**8a** $\rightleftarrows$ **8b**) of the azoxy cation, **8**, that must result upon reaction of **5a** with Ag^+. In any event, the data indicate that the azoxy group stabilizes an electron-deficient distal α-carbon atom.

Decomposition Reactions of 5b. The decomposition of MAM (**1b**) in the presence of RNA or DNA, in vitro or in vivo, results in the methylation of RNA or DNA as determined by an increase in the amount of 7-methylguanine.[7,15] Diazomethane has often been postulated as the reactive methylating intermediate.[16] Recent evidence obtained from the decomposition of **1b** in neutral[8] or mildly acidic[6] media has shown that diazomethane is not an intermediate in these particular decompositions. Thus, reaction of **1c** in D_2O solution produced (in addition to H_2O, CH_2O, and N_2) CH_3OD, not the CDH_2OD which would have been formed if CH_2N_2 had reacted with solvent.[8] As a result of these experiments[6,8] it appears that methyldiazonium ion is the likely methylating agent produced by **1b**, and by analogy, phenyldiazonium ion should be produced by **5b**. Accordingly, we tested the decomposition of **5b** under neutral and mildly basic conditions. The results follow.

A solution of **5b** in Me_2SO-d_6 and D_2O was maintained at 92° and monitored by NMR spectroscopy. The reaction was observed to have a half-life of 20 h and the products were those that would be predicted by analogy with **1b**, namely, water, formaldehyde, nitrogen, and phenol. Scheme II outlines a possible reaction pathway. Solvent may be involved in the O to O proton transfer of the intramolecularly bonded proton of **5b**, but the formation of diphenyl ether when the decomposition was conducted in molten phenol renders as unlikely a completely intramolecular mechanism for the formation of phenol in Scheme II. The difference in stability between **5b** and **1b** ($t_{1/2}$ = 18.6 h at 37°) must reflect the stabilizing influence of the benzene ring, probably lowering the ground-state energy of **5b** relative to **1b**.

Scheme II



5b

$$C_6H_5\overset{+}{N}{\equiv}N + H_2CO \xrightarrow{D_2O} C_6H_5OD + N_2 + HOD$$
$$+$$
$$OH^-$$

Table I. Spectral Features and Elemental Analyses of Azoxyalkanes 5[a]

5	X	Chemical shift, δ (Me_4Si)[b,c]					Uv λ_{max},[d] nm (log ε)	Anal, %					
		o-C_6H_5	m, p-C_6H_5	CH_2	α	β	γ		Calcd			Found	
									C	H	N	C	H	N
a	Br[e]	8.2	7.5	5.40				265 (4.04)	39.00	3.28		39.30	3.43	
b	OH	8.2	7.5	5.20				246 (4.05)	55.25	5.30	18.41	55.44	5.35	18.45
c	$OCOCH_{3\alpha}$	8.2	7.5	5.60	2.18 (1)			250 (4.12)	55.67	5.19	14.43	55.70	5.32	14.43
d	$OCH_{3\alpha}$	8.2	7.4	5.01	3.50 (1)			246 (4.27)	57.82	6.07	16.86	58.00	6.24	17.14
e	$OCH_{2\alpha}CH_{3\beta}$	8.2	7.4	5.20	3.78 (4)	1.75 (3)			59.99	6.71		59.63	6.94	
f	$OCH_\alpha(CH_3)_{2\beta}$	8.5	7.6	5.36	4.10 (7)	1.36 (2)		248 (4.04)	61.84	7.27	14.43	61.67	7.27	14.20
g	$OCH_{2\alpha}CH_\beta{=}CH_{2\gamma}$	8.1	7.4	5.15	4.25 (m)	5.90 (m)	5.31 (m)		62.49	6.29		62.61	6.55	
h[e,f]	$\overset{+}{N}(CH_3)_{2\alpha}CH_{2\beta}CH_{2\gamma}OH$	8.5	7.8	5.38	3.45 (1)	3.19 (m)	4.18 (m)		43.20	5.89	13.73	43.40	5.92	13.90
i[f,g]	$SC(NH_2)_2^+$	8.1	7.6	5.37				260 (4.28)	32.97	3.80	19.24	33.01	3.73	19.20
j	SCN	8.2	7.3	5.23										
k	Cl	8.5	7.7	5.42				258 (4.04)	49.28	4.14		49.39	4.41	

[a] Satisfactory analytical data (±0.35%) for C, H, N for all compounds were submitted for review. Ed. [b] NMR solvents were CCl_4 for compounds 5a–d,f,j,k; $CDCl_3$ for 5e,g; D_2O (external Me_4Si) for 5h; Me_2SO-d_6 for 5i; all phenyl signals were multiplets; all distal CH_2 signals were singlets. [c] For the designations α, β, and γ see the columns headed by X; multiplicities of symmetrical signals are given in parentheses after the chemical shifts; more complex multiplets are indicated by m. [d] Solvent 95% ethanol. [e] Br: Calcd: 13.00. Found: 12.96. [f] Counterion is Br^-. [g] Br: Calcd: 26.10. Found: 26.00.

Scheme III

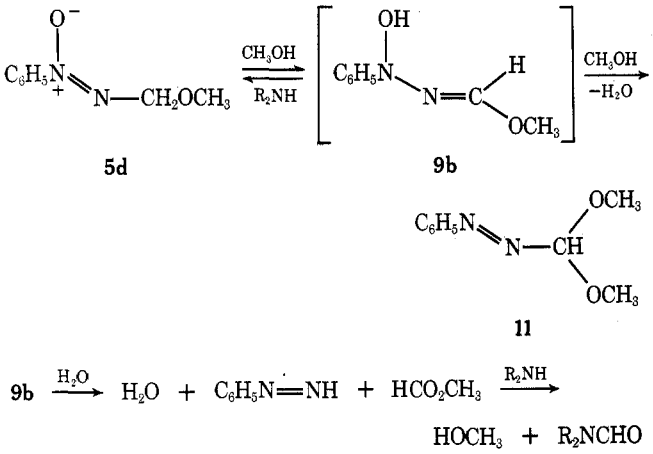
$$R_2N{-}CH{=}O + [C_6H_5N{=}N{-}D] \longrightarrow C_6H_5D + N_2$$

The decomposition of **5b** under basic conditions followed an entirely different course. Treatment of a methanol solution of **5b** with 1 equiv of methanolic sodium hydroxide at room temperature gave, immediately, a red solution followed by the rapid evolution of N_2. VPC analysis of the reaction after 1 h detected benzene (88% of theoretical) but *no* phenol or anisole. Use of the weaker base piperidine slowed the rate of decomposition permitting monitoring of the reaction by NMR spectroscopy. Upon addition of 1 equiv of piperidine to **5b** in CD_3OD the solution turned red and a slow evolution of N_2 started. NMR analysis after 2 min showed a weak CIDNP emission signal at δ 7.3 for benzene formed via phenyl *radical*. The major products (VPC analysis) of this reaction were benzene (29%), biphenyl (10%), and *N*-formylpiperidine (75%). Phenol and anisole were not present. The half-life of **5b** under these conditions was 2–3 h and the *N*-formylpiperidine formed in this reaction showed less than 5% deuterium incorporation in the formyl group. Scheme III can accommodate these results.

The removal (or C to O transfer) of the distal methylene proton from **5b** must be essentially irreversible since there was very little, if any, deuterium incorporated into the formyl group of *N*-formylpiperidine. We attribute this to a rapid dehydration step which converts tautomer **9a** to *N*-formyl-*N'*-phenyldiimide (**10**). Then, an amide interchange reaction transfers the formyl group yielding *N*-formylpiperidine and phenyldiimide. Phenyldiimide is known to undergo rapid decomposition in the presence of oxygen via the phenyl radical to give benzene and biphenyl.[17]

The reaction of methyl ether **5d** with piperidine in methanol gave results which support the reactions of Scheme III. From this reaction benzene (10%) and *N*-formylpiperidine (low yield) were detected, and a new compound, *N*-dimethoxymethyl-*N'*-phenyldiimide (**11**), was isolated (40%). When the decomposition was conducted in CD_3OD and monitored by NMR spectroscopy, a strong CIDNP emission singlet at δ 7.3 was observed for benzene. Hydrogen–deuterium exchange at the methylene group of **5d** was also observed, and NMR analysis of the *N*-formylpiperidine formed after 6-h reaction showed 32% deuterium incorporation in the formyl group. Scheme IV summarizes these results. The structure of azo compound **11**, also prepared from **5d** using triethylamine in methanol, was based on spectral data and elemental analysis. The UV spectrum showed maxima at 215 nm (ε 13 000) and 270 (1900), consistent with an aryl–alkylazo formulation, and the NMR spectrum showed signals for the following protons: *o*-phenyl at δ 7.7; *m*- and *p*-phenyl at δ 7.45; the formyl proton at δ 4.90; and the six methoxyl group protons at δ 3.5. Scheme IV suggests a possible route for the formation of *N*-formylpiperidine and phenyldiimide from **5d**, and while many mechanistic details are not clear (e.g., the mode of reaction of piperdine with **9b**), it does seem clear that the formation of compound **11** signals the trapping of an intermediate wherein the distal methylene group, formerly singly bound

Scheme IV



to N, has become doubly bound to N. We suggest structure **9b** for this intermediate. The methoxyl group of **9b** would prevent a dehydration step such as is proposed in Scheme III, **9a** → **10**, and, accordingly, we see that H–D exchange at the distal methylene group now can compete with the degradation reaction. Thus, the isolation of **11** serves as evidence for the intermediacy of **9b** in the reactions of Scheme IV, and, by implication, as evidence for **9a** and **10** of Scheme III as well as for B in Scheme I.

The observation of H–D exchange under mild conditions with **5d** indicated that proton abstraction from the distal carbon atom was reversible. Indeed, the piperidine-catalyzed exchange of the methyl hydrogens of **4a** was found to occur with ease at 25°C. Treatment of **4a** with 1 equiv of piperidine in CD_3OD–D_2O (5:1 by volume) gave **4b** with an exchange half-life near 0.5 h. The stability of **4** toward decomposition under these conditions was greater than for any other derivative studied. After 3 h, 89% of **4b** remained as evidenced by VPC analysis. Also, it is interesting to note that in the absence of D_2O, the exchange half-life increased by a factor of 4–5. Thus, the azoxy group appears capable of stabilizing negative charge at the distal carbon atom.

Summary. From the study of the foregoing reactions it appears that the azoxy group is capable of stabilizing a positive charge, an unpaired electron, or a negative charge at the distal carbon atom. Such diversity of character in a heteroatom-containing carbon functional group is rare, and is usually reserved for groups containing elements of the second row, e.g., sulfur. The base-induced decomposition studies with **5b** immediately suggest experiments which should be conducted on **1b**. The discovery of a free-radical decomposition pathway for MAM (**1b**) could have implications regarding the understanding of its mechanism of cancer induction. Finally, it is obvious that a number of questions remain unanswered, principally questions about the nature of the cationic and anionic intermediates and their possible synthetic utility. We hope to answer some of these questions with subsequent work.

Experimental Section

General. For instruments used see the Experimental Section of ref 1b. VPC analyses were performed on the following aluminum columns: column A, 4 ft × 0.125 in. 20% silicone oil Dow 710 on 60/80 mesh Chromosorb W (AW + DMCS); B, 4 ft × 0.25 in. 5% silicone oil Dow 710 on 60/80 Chromosorb W (AW + DMCS); C, 6 ft × 0.25 in. 5% silicone oil Dow 710 on 60/80 mesh Chromosorb W (AW + DMCS); D, 6 ft × 0.25 in. 5% silicone rubber UCW 98 on Diatoport S; E, 10 ft × 0.25 in. 20% SE-30 on 60/80 mesh Chromosorb W (AW + DMCS); F, 6 ft × 0.25 in. 5% silicone rubber UCW 98 on Chromosorb W (AW + DMCS); G, 6 ft × 0.125 in. silicone rubber UCW 98 on Diatoport S; H, 19 ft × 0.25 in. 25% SE-30 on Chromosorb W (AW + DMCS). NMR and uv spectral data and elemental analyses of compounds **5** are collected in Table I.

(*Z*)-Phenylbromomethyldiazene 1-Oxide (5a). A mixture of 5 g (36.8 mmol) of **4a**,[1b] 6.53 g (36.8 mmol) of *N*-bromosuccinimide, and 0.896 g (3.68 mmol) of benzoyl peroxide in 150 ml of carbon tetrachloride was refluxed for 24 h. After cooling and filtration, concentration of the filtrate in vacuo gave a red oil. Chromatography on 40 g of silica gel and elution with benzene gave 6.3 g of oil which crystallized upon addition of pentane and cooling: yield of **5a** 6.1 g (78%); mp 31–32°; ir (neat) 1490, 1410, 1340, and 1250 cm^{-1}.

(*Z*)-Phenylhydroxymethyldiazene 1-Oxide (5b). A mixture of 1.68 g (6 mmol) of silver carbonate, 10 ml of acetone, 5 ml of water, and 2.62 g (12 mmol) of **5a** was stirred at 25° for 24 h in the dark. Filtration followed by concentration in vacuo yielded a red oil. This was dissolved in chloroform, washed with three 50-ml portions of water, dried (Na_2SO_4), and reconcentrated in vacuo to give 1.5 g (88%) of yellow, crystalline **5b**, mp 57–59°. Recrystallization from pentane gave an analytical sample: mp 57–58°; ir (CCl_4) 3600 (sharp), 3470 (broad), 1490, 1380, 1340, and 1090 cm^{-1}; the ir spectra of appropriately diluted samples of **5b** in chloroform indicated that the 3470-cm^{-1} band was that of an intramolecularly H-bonded OH group.

(*Z*)-Phenylacetoxymethyldiazene 1-Oxide (5c). A solution of 470 mg (2.19 mmol) of **5a** and 365 mg (2.19 mmol) of silver acetate in 12 ml of glacial acetic acid was stirred at 25° for 1 h in the dark. After filtration (AgBr), concentration of the filtrate in vacuo gave a yellow oil which crystallized upon the addition of ether to give 355 mg (78%) of **5c**, mp 40–42°. Recrystallization from ether–pentane gave an analytical sample: mp 41–44°; ir (CCl_4) 1760, 1490, 1440, and 1215 cm^{-1}.

(*Z*)-Phenylmethoxymethyldiazene 1-Oxide (5d). To a solution of 1.07 g (4.97 mmol) of **5a** in 20 ml of anhydrous methanol was added 1.03 g (4.97 mmol) of anhydrous silver perchlorate dissolved in 10 ml of anhydrous methanol. Immediately, a yellow precipitate formed, but the mixture was stirred for 24 h at 25° in the dark. After filtration of the silver bromide the safest procedure is to mix the reaction solution with chloroform and wash thoroughly with water to remove all perchloric acid. *Failure to do this prior to concentration of the organic solvent has led to an explosion.* Concentration of the chloroform solution in vacuo yielded 680 mg of an orange oil. VPC analysis (column D) showed one major component and no **5a**. Preparative VPC (column D) gave an analytical sample of **5d**: ir (neat) 1490, 1440, and 1340 cm^{-1}.

(*Z*)-Phenylisopropoxymethyldiazene 1-Oxide (5f). To a mixture of 0.077 ml (4 mmol) of 2-propanol, 0.276 g (2 mmol) of silver carbonate, and 0.150 g of dried calcium sulfate in 5 ml of benzene was added 0.215 g (1 mmol) of **5a** dissolved in 3 ml of benzene. After stirring at 25° for 24 h in the dark under a nitrogen atmosphere, the mixture was filtered and the filtrate concentrated in vacuo to give 0.150 g of a red oil. NMR analysis showed that the oil contained ~3% of alcohol **5b** in addition to **5f**. Preparative VPC (column E) using low instrument temperatures gave an analytical sample of **5f**.

(*Z*)-Phenylethoxymethyldiazene 1-Oxide (5e). The procedure outlined above for **5f** was used for the preparation of **5e**, to give 150 mg of crude **5e** from 215 mg of **5a**. Preparative VPC (column F) gave an analytical sample of **5e**: ir ($CHCl_3$) 1490, 1440, and 1340 cm^{-1}.

(*Z*)-Phenyl-(2-propenoxy)methyldiazene 1-Oxide (5g). The procedure outlined above for **5f** was used for the preparation of **5g** to give 0.350 g of crude **5g** from 0.5 g of **5a**. VPC analysis (column C) showed one major component and no **5a**. Preparative VPC (column C) gave pure **5g**: ir (neat) 1650, 1495, 1275 cm^{-1}.

***N*-[(*Z*)-1-Phenyloxidodiazenylmethyl]-*N*,*N*-dimethylethanolammonium Bromide (5h).** To a solution of 0.215 g (1.0 mmol) of **5a** in 2 ml of acetone was added 0.089 g (1.1 mmol) of *N*,*N*-dimethylethanolmine. The solution turned red, and then, slowly, back to yellow with the formation of a white precipitate. The reaction mixture was stirred for an additional 30 min and then filtered to give 0.270 g of white crystals, mp 172–174°. Recrystallization from ethanol–ether gave 0.193 g (64%) of **5h**: mp 178–179°; ir (KBr) 3300 and 1470 cm^{-1}.

***S*-[(*Z*)-1-Phenyloxidodiazenylmethyl]isothiouronium Bromide (5i).** A solution of 25 mg (0.116 mmol) of **5a** and 8.86 mg (0.116 mmol) of thiourea in 1 ml of ethanol was stirred at room temperature for 1 h. The reaction mixture was poured into 30 ml of anhydrous ether and 30 mg (89%) of **5i** was collected as white crystals by filtration, mp 154–155°. Recrystallization from ethanol–ether gave an analytical sample, mp 154–155°.

(*Z*)-Phenylthiocyanatomethyldiazene 1-Oxide (5j). A solution of 0.905 g (9.3 mmol) of potassium thiocyanate in 25 ml of ace-

tone was added at 0° to a solution of 2.0 g (9.3 mmol) of **5a** in 23 ml of acetone. The mixture was warmed to room temperature, stirred for 24 h, and filtered (KBr). The filtrate was dried (Na_2SO_4) and concentrated in vacuo to give 1.75 g of red oil. Chromatography on 60 g of silica gel gave 1.1 g of red oil which showed one spot on thin layer chromatography (two systems). Attempts at molecular distillation and preparative VPC gave decomposition of **5j**: ir (neat) 2160, 1440, 1390 cm^{-1}.

A solution of 90 mg of **5j**, 0.5 ml of boron trifluoride etherate, and 10 ml of benzene was heated at 60° for 14 hr. After dilution with pentane, two washes with saturated $NaHCO_3$ solution, drying (Na_2SO_4), and concentration in vacuo, a small amount of red oil was obtained: ir (neat) 2170 (sharp), 2070 (broad), 1490, and 1320 cm^{-1} (azoxy group).

(Z)-Phenylchloromethyldiazene 1-Oxide (5k). A solution of 2.95 g (13.7 mmol) of **5a** and 4.24 g (100 mmol) of lithium chloride in 860 mg of acetone was heated at reflux for 3 h. The reaction mixture was further diluted with benzene and washed with water. After drying and evaporation of the organic layer (in vacuo) the crude product (2.49 g, 99% **5k**, 1% **5a** by VPC on column F) was distilled to give an analytical sample: bp 70° (0.25 mm); ir (neat) 1475, 1320, and 1270 cm^{-1}.

Decomposition of 5a under Basic Conditions. To a solution of 15 mg (0.070 mmol) of **5a** in 0.5 ml of methanol containing 3 μl of tetradecane (2.29 mg for VPC internal standard) was added 1 equiv of sodium hydroxide dissolved in 95% methanol. The reaction mixture immediately turned red; no gas was evolved. VPC analysis after 5 min showed 5% unreacted **5a**, plus nitrosobenzene and azoxybenzene (~85% combined). Cyanide ion was detected in an identical reaction using the ferric ferrocyanide "Prussian blue" test. A blank containing nitrosobenzene did not give the Prussian blue precipitate. In reactions of **5a** with other bases (see text) nitrosobenzene and azoxybenzene were detected by VPC analysis of reaction mixtures.

Decomposition of 5b under Neutral Conditions. A solution of 50 mg (0.34 mmol) of alcohol **5b**, 300 μl of Me_2SO-d_6, and 200 μl of D_2O in an NMR tube was maintained at 92° and monitored periodically by NMR analysis. The disappearance of **5b** had a half-life of about 20 h during which time the evolution of gas (N_2) was observed. At the half-life, the ratio of phenol-*O*-*d* to formaldehyde was 50:38. The presence of phenol was confirmed by VPC analysis (column B).

Decomposition of 5b under Basic Conditions. A solution of 31.8 mg (0.209 mmol) of **5b** and 20.6 μl (0.209 mmol) of piperidine in 350 μl of methanol-d_4 in an NMR tube was maintained at room temperature and monitored at regular intervals by NMR analysis. The evolution of gas (N_2) was observed throughout the reaction which had a half-life of about 2 h. An NMR spectrum taken at t = 19 h indicated 18% of unreacted **5b** and about 70% *N*-formylpiperidine (based on no D incorporation into **5b**). VPC analysis (internal standard, column A) at t = 19 h showed *N*-formylpiperidine (75%), benzene (29%), and biphenyl (10%) as the major products. The initial NMR spectrum of the reaction showed a weak CIDNP emission signal at δ 7.3 for benzene. In an experiment in which **5b** was decomposed with 1 equiv of methanolic sodium hydroxide, VPC analysis (internal standard column A) showed benzene (88%) as the major volatile product. In all of the basic decomposition reactions of **5b**, the reaction mixtures were examined by VPC analysis for products expected from the reactions of phenyldiazonium ion with the nucleophiles H_2O, CH_3OH, and piperidine. None were observed.

Phenyldimethoxymethyldiazene (11). A solution of 196 mg (1.18 mmol) of **5d** and 165 μl (1.18 mmol) of triethylamine in 6 ml of methanol was stirred for 48 h at 25°, and then concentrated in vacuo to a volume of 2 ml. VPC analysis of an aliquot (internal standard, column A) showed the presence of azo compound **11** (50%), starting material **5d** (20%), and benzene. Preparative VPC (column C) gave an analytical sample of **11**: ir (CCl_4) 2830, 1520, 1450, and 1320 cm^{-1}; uv (95% ethanol) λ_{max} 270 nm (ε 1900) and 215 (13 000); NMR (CCl_4) δ 7.70 (m, 2 H, *o*-phenyl H), 7.45 (m, 3 H, *m*-, *p*-phenyl H), 4.91 [s, 1 H, $-CH(OR)_2$], 3.51 (s, 6 H, OCH_3).

Anal. Calcd for $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71. Found: C, 60.18; H, 6.99.

Decomposition of 5d under Basic Conditions. A solution of 23.7 mg (0.143 mmol) of **5d** and 14.1 μl (0.143 mmol) of piperidine in 2 ml of methanol was stirred at 25° for 30 h. VPC analysis (internal standard, column A) showed four major components: starting material **5d** (30%), **11** (40%), benzene (10%), and *N*-formylpiperidine (~20%).

A similar reaction using methanol-d_4 as solvent allowed the reaction to be monitored by NMR spectroscopy. At room temperature the disappearance of **5d** had a half-life approximating 3.5 h (with triethylamine, $t_{1/2} \simeq 6$ h) as estimated by monitoring the signals for the CH_2 and OCH_3 groups of **5d**. In the initial three NMR spectra of the reaction a strong CIDNP emission singlet at δ 7.3 for benzene was observed. At t = 6 h, integration of the signals at δ 7.85 (s, $HCONR_2$) and 2.9 (m, CH_2 groups bound to N of *N*-formylpiperidine) indicated about 32% deuterium incorporated into the formyl group of *N*-formylpiperidine. This observation was consistent with the observations of (1) a more rapid decay of the CH_2 signal of **5d** relative to the OCH_3 signal of **5d** and (2) the stability of *N*-formylpiperidine toward H–D exchange. The NCH_2 groups of piperidine, δ 2.7, were sufficiently separated from the analogous protons of the *N*-formyl derivative to permit an estimation of the extent of deuterium in the latter compound.

Phenyltrideuteriomethyldiazene 1-Oxide (4b). A solution of 36 mg (0.26 mmol) of **4a**, 26.1 μl (0.265 mmol) of piperidine, and 20 μl of methylene chloride (internal standard) in 300 μl of methanol-d_4–deuterium oxide (5:1 by volume) was placed in an NMR tube and maintained at 25°. The $t_{1/2}$ for deuterium exchange was determined by following the disappearance of the methyl group singlet of **4a**, and was found to be 30 min. VPC analysis (internal standard, column A) after 3 h reaction showed 89% of **4** present. The identity of **4** was checked by VPC analysis on column D.

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Registry No.—**4a**, 35150-71-1; **4b**, 57496-78-3; **5a**, 57496-79-4; **5b**, 57496-80-7; **5c**, 57496-81-8; **5d**, 57496-82-9; **5e**, 57496-83-0; **5f**, 57496-84-1; **5g**, 57496-85-2; **5h**, 57496-86-3; **5i**, 57496-87-4; **5j**, 57496-88-5; **5k**, 57496-89-6; **11**, 57496-90-9; *N*-bromosuccinimide, 128-08-5; silver carbonate, 534-16-7; silver acetate, 563-63-3; methanol, 67-56-1; 2-propanol, 67-63-0; *N*,*N*-dimethylethanolamine, 108-01-0; thiourea, 62-56-6; potassium thiocyanate, 333-20-0; lithium chloride, 7447-41-8.

References and Notes

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