calculation using molar response factors of BPA and succinimide. Typical set of retention times (160 °C, 10 psi): succinimide, 1.27 min; BPA, 1.46 min.

(B) A measured amount of photolysate was evaporated as above. The residue was dissolved in $CDCl_3$ for FT-NMR analysis with a Bruker WH400 spectrometer.

For a control experiment, a $CDCl_3$ solution containing succinimide (ca. 2 mg), NBS (ca. 2 mg), and bromine (2.5×10^{-2} M) was placed in two NMR tubes inside a dark hood. After 5 min, one tube was emptied into a 5-mL flask wrapped in aluminum foil and was evaporated. The glass part of the Rotavapor was covered with black paper. The residue was taken up with $CDCl_3$ (0.8 mL) and transferred back to the NMR tube. Two tubes were analyzed by NMR to give an identical ratio of $I_{2.96}/I_{2.76}$ (the intensities at 2.96 and 2.76 ppm). In order to obtain accurate peak height, caution was exercised in choosing NMR parameters so that the second pulse always began only after the protons in question relaxed totally from the excited state resulting from the first pulse: protons on 5-mm ^{13}C probe, ~25° pulse, SF = 400.134 395 6 MHz, SI = 32K, SW = 4000.000 Hz, AO = 4.096. The BPI percentage was calculated according to $(I_{3.63} + I_{2.81})/(I_{2.76} + I_{3.63} + I_{2.81})$, where $I_{3.63}$ and $I_{2.81}$ stand for the intensity of the triplet of BPA at 3.63 and 2.81 ppm (J = 6.62 Hz), respectively, and $I_{2.76}$ is the intensity of the singlet of succinimide at 2.76 ppm. The percentage conversion of NBS was calculated according to $I_{2.96}/(I_{2.96} + I_{3.63} + I_{2.81} + I_{2.76})$ where $I_{2.96}$ stands for the intensity of the singlet of NBS at 2.96 ppm.

(C) The BPI yields in Table IV were determined with a Bruker SY100 (100 MHz) as follows. The measured amount of photolysate was added with a measured volume of *p*-bromotoluene (0.1 M in CH_2Cl_2), and the resultant mixture was evaporated. The residue was taken up in $CDCl_3$ (0.7 mL), and the NMR spectrum was recorded. The integration of the triplet at 3.65 ppm for BPA was compared with that of the singlet of *p*-bromotoluene at 2.31 ppm (standard) to calculate the concentration of BPA. From the percent conversion of NBS and the BPI concentration, the yield of succinimide was calculated. Control experiments showed that before and after the evaporation ca. 2% of the *p*-bromotoluene was lost with respect to succinimide.

For each experiment, two tubes of solutions were photolyzed, and mean values and errors were obtained. For each reaction, two to three readings were obtained, and standard deviations were calculated. Each series of experiments was repeated, and maximum deviations from mean values are given in the tables.

Other Product Analyses. The yields of $CHBrCl_2$, cyclohexyl bromide ($C_6H_{11}Br$), and *trans*-1,2-dibromocyclohexane ($C_6H_{10}Br_2$) were determined with GC. $CHBr_3$ was chosen as an internal standard. The molar response factor of cyclohexyl bromide to $CHBr_3$ was obtained by analyzing standard mixtures in various ratios. It was assumed that the molar response factor of $C_6H_{10}Br_2$ was the same as that of $C_6H_{11}Br$. The photolysate was washed with 10% $NaHSO_3$ and then was dried with $MgSO_4$, followed by the addition of $CHBr_3$ (1–3 μL). The filtrate was used for the determination of *r* values. Typical sets of the retention times (min) were as follows: $CHBrCl_2$ 1.84, $CHBr_3$ 4.84, cyclohexyl bromide 9.40 at 55 °C and 8 psi; $CHBr_3$ 1.25, cyclohexyl bromide 1.55, succinimide 1.84, $C_6H_{10}Br_2$ 2.84 under temperature programming of 120–200 °C, 10 °C/min at 8 psi. The yield of succinimide was determined with GC. Benzophenone as the internal standard was added prior to injection to the sample prepared by method B. The molar response factor of succinimide was obtained by analyzing graded standard mixtures. The typical set of the retention times were for succinimide 1.27 min and for benzophenone 5.87 min at conditions of 160 °C and 10 psi. The collection of data and the evaluation of errors were the same as described above. When the yields of $C_6H_{10}Br_2$ were >3 mM, two small minor peaks closely attached to the major peaks were noticed. GC–MS analysis of these peaks showed that the major peak showed a mass spectral pattern identical with that of *trans*-1,2-dibromocyclohexane and the minor peaks were probably isomers of the dibromide.

Relative Rates of Bromination. A solution containing the reactants was purged with nitrogen and was irradiated with a PEK 212 150-W high-pressure mercury lamp filtering through Corning filter CS-052 (7380) and $NaNO_2$–sodium hydrogen phthalate solution (1-cm thickness) to give >400-nm light; alternatively, the light source was filtered with a GVW filter to give >380-nm light. Two solutions containing NBS + Br_2 and Br_2 + K_2CO_3 were irradiated under the same conditions for the same duration, and the yields of brominated products were determined as described above. The solution of Br_2 + K_2CO_3 was heterogeneous and was magnetically stirred.

Bromination of Toluene with NBS and Br_2. Solutions containing CH_2Cl_2 (1 mL), toluene (0.09 M), NBS (0.11 M), and bromine (2×10^{-4}–2×10^{-2} M) were photolyzed through a GWV filter as above until 90 ∓ 5% of the NBS was consumed. The photolysates were worked up in the usual manner for GC analysis, which showed only benzyl bromide as the product but no BPA.

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Deuterium Isotope Effects on the Oxygen Atom Transfer Reactions of α-Azo Hydroperoxides

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Cyclic α-azo hydroperoxide **1** (*cis*-3-bromo-4,5-dihydro-5-hydroperoxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole) and acyclic α-azo hydroperoxide **2** [(4-methoxyphenyl)(phenylazo)methyl hydroperoxide] were converted to the ROOD analogues **1-*d*** and **2-*d***. The reactions of **1** and **1-*d*** in $CDCl_3$ at 34 °C with amines, diphenyl sulfide, and 2,3-dimethyl-2-butene yielded the corresponding amine oxides, sulfoxides, and epoxides in better than 90% yields. The reactions were found to be of the first order in both hydroperoxide and substrate (second order overall). Deuterium isotope effects (k_H/k_D) of 1.3 ± 0.1 were found for the oxidation of the three types of substrate. The reactions of **2** and **2-*d*** with benzyl methyl sulfide and 2,3-dimethyl-2-butene, carried out in C_6D_6 at 34 °C, produced the corresonding sulfoxide and epoxide in 90%+ yields. As expected, the reactions were of the second order overall (first order in hydroperoxide) in the aprotic medium. Values of k_H/k_D of 1.3 ± 0.1 were found for these oxidations. The mechanistic implications of these results are discussed.

The chemistry of organic hydroperoxides is often considered to deal largely with free-radical formation and the related metal ion catalyzed decompositions. An additional property of hydroperoxides is their ability to transfer ox-

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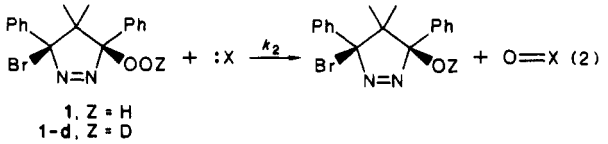
ygen atoms under electrophilic conditions (reaction 1).[2]

$$ROOH + :X \xrightarrow{k_2} ROH + O{=}X \quad (1)$$

However, the noncatalyzed (metal ion free) oxygen atom transfer reactions for many hydroperoxides are slow when compared to free-radical pathways. We have recently shown[3] that α-azo hydroperoxides ($R_1R_2C(OOH)N{=}NR_3$)[4] are highly reactive in oxygen atom transfer reactions (ionic oxidations) with alkenes, amines, and sulfides to produce the corresponding epoxides, amine oxides, and sulfoxides in good yield. Two general types of α-azo hydroperoxides have been studied:[3] acylic and cyclic. The only known cyclic compound,[5] *cis*-3-bromo-4,5-dihydro-5-hydroperoxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole (**1**), has been found[6] to be extremely reactive, similar in reactivity to that of flavin 4a-hydroperoxides,[7] in electrophilic oxygen atom transfer chemistry. Acylic α-azo hydroperoxides, approximately 2 orders of magnitude less reactive[8] than **1**, are at least 10^3-fold more reactive than alkyl hydroperoxides. For these ionic oxidations, selectivity appears to be essentiallyl invariant (at the values found for peracid oxidations) and thus independent of reactivity and α-azo hydroperoxide structure.[3] Mechanistically, the ionic oxidations of α-azo hydroperoxides have been rationalized[6,8] to occur via a concerted reaction in which the transition state involves partial intramolecular transfer or hydrogen bonding of the peroxy proton to a nitrogen atom during the nucleophilic attack of substrate on that terminal oxygen atom. We present here an isotope effect study on the deuteriation of the hydroperoxide proton of the oxygen atom transfer reactions of both acyclic and cyclic α-azo hydroperoxides with amines, sulfides, and alkenes in aprotic media.

Results

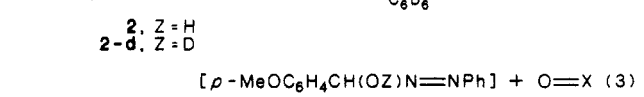
Cyclic α-azo hydroperoxide **1** (*cis*-3-bromo-4,5-dihydro-5-hydroperoxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole) and acyclic α-azo hydroperoxide **2** [(4-methoxyphenyl)(phenylazo)methyl hydroperoxide], prepared according to published procedures,[5,8a] were converted to the ROOD analogues (**1-*d*** and **2-*d***, respectively) by exchange of the hydroperoxy protons with D_2O. The reactions of cyclic α-azo hydroperoxides **1** and **1-*d*** with *N*-methylmorpholine, *N*,*N*-dimethylbenzylamine, diphenyl sulfide, and 2,3-dimethyl-2-butene were carried out in $CDCl_3$ at 34 °C (reaction 2). The products (amine oxides, sulfoxides, and



1, Z = H
1-*d*, Z = D

epoxides) were formed in better than 90% yield in all cases. As expected, the reactions were of the first order in both hydroperoxide and substrate. In all cases, the OOD compound **1-*d*** was found to render oxygen atom transfer reactions slower than those of the normal hydroperoxide. Deuterium isotope effects (k_H/k_D values) of roughly 1.3 ± 0.1 were found for the oxidation of the three types of substrate. The results are summarized in Table I.

The reactions of acyclic α-azo hydroperoxides **2** and **2-*d*** with benzyl methyl sulfide and 2,3-dimethyl-2-butene were carried out in benzene-d_6 at 34 °C to yield the corresponding sulfoxide and epoxide in high yield (reaction 3).



As previously noted, the reactions followed second-order behavior overall (first order in hydroperoxide). Similar to those obtained for the cyclic compound, deuterium isotope effects (k_H/k_D values) of ~1.3 ± 0.1 were found for the ionic oxidations with the acyclic compounds. The results are listed in Table II.

Table I. Second-Order Rate Constants[a] for the Reaction of 1 and 1-*d* in $CDCl_3$ at 34 °C

hydroperoxide	substrate[b]	k_2, M^{-1} s^{-1}	k_H/k_D
1	*N*-methylmorpholine	$(5.2 \pm 0.2) \times 10^{-2}$	
1-*d*	*N*-methylmorpholine	$(3.5 \pm 0.2) \times 10^{-2}$	1.48 ± 0.14
1	$BzNMe_2$	$(1.56 \pm 0.05) \times 10^{-1}$	
1-*d*	$BzNMe_2$	$(1.22 \pm 0.05) \times 10^{-1}$	1.28 ± 0.09
1	Ph_2S	$(9.8 \pm 0.1) \times 10^{-3}$	
1-*d*	Ph_2S	$(7.7 \pm 0.1) \times 10^{-3}$	1.34 ± 0.03
1	$Me_2C{=}CMe_2$	$(3.96 \pm 0.15) \times 10^{-3}$	
1-*d*	$Me_2C{=}CMe_2$	$(3.0 \pm 0.3) \times 10^{-3}$	1.32 ± 0.19

[a] Average of two or more experiments. [b] Product yields ≥90% all cases.

Table II. Second-Order Rate Constants[a] for the Reaction of 2 and 2-*d* in C_6D_6 at 34 °C

hydroperoxides	substrate[b]	k_2, M^{-1} s^{-1}	k_H/k_D
2	BzSMe	$(8.1 \pm 0.5) \times 10^{-3}$	
2-*d*	BzSMe	$(6.3 \pm 0.3) \times 10^{-3}$	1.29 ± 0.14
2	$Me_2C{=}CMe_2$	$(1.36 \pm 0.05) \times 10^{-5}$	
2-*d*	$Me_2C{=}CMe_2$	$(1.07 \pm 0.05) \times 10^{-5}$	1.27 ± 0.10

[a] Average of two or more experiments. [b] Product yields ≥90% all cases.

Discussion

The work of Rebek[9] has shown that α-substituted hydroperoxides (α-hydroperoxy ethers, amines, ketones, esters, nitriles) are effective epoxidation agents. The reactivity of these systems was thought to be due (in part)

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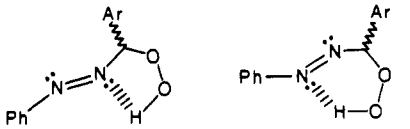
(2) (a) For a recent discussion, see: Plesnicar, B. In *The Chemistry of Functional Groups, Peroxides*; Patai, S., Ed.; Wiley: New York, 1983; Chapter 17. (b) Lewis, S. N. In *Oxidation*; Augustine, R. L., Ed.; Marcel Dekker: New York, 1969; Vol. I, Chapter 5, pp 213–258. (c) Hiatt, R. In *Organic Peroxides*; Swern, D., Ed.; Wiley-Interscience: New York, 1971; Vol. II, pp 83–86. (d) March, J. *Advanced Organic Chemistry*, 3rd ed.; McGraw-Hill: New York, 1985; pp 735–737.
(3) For a review of the ionic reactions of α-azo hydroperoxides, see: Baumstark, A. L. *Bioorg. Chem.* **1986**, *14*, 326.
(4) A detailed discussion of the free-radial chemistry of α-azo hydroperoxides is beyond the scope of this paper. For leading references, see: (a) Dixon, D. W.; Barbush, M. *J. Org. Chem.* **1985**, *50*, 3194. (b) Osei-Twum, E. Y.; McCallion, D.; Nazran, A. S.; Panicucci, R.; Risbood, P. A.; Warkentin, J. *J. Org. Chem.* **1984**, *49*, 336. (c) Tezuka, T.; Ichikawa, K.; Marusawa, H.; Nasita, N. *Chem. Lett.* **1983**, 1013. (d) Tezuka, T.; Narita, N.; Ando, W.; Oae, S. *J. Am. Chem. Soc.* **1981**, *103*, 3045.
(5) Landis, M. E.; Lindsey, R. L.; Watson, W. H. Zabel, V. *J. Org. Chem.* **1980**, *45*, 525.
(6) (a) Baumstark, A. L.; Chrisope, D. R.; Landis, M. R. *J. Org. Chem.* **1981**, *46*, 1964. (b) Baumstark, A. L.; Chrisope, D. R. *Tetrahedron Lett.* **1981**, 4591. (c) Baumstark, A. L.; Pilcher, R. S. *J. Org. Chem.* **1982**, *47*, 1141.
(7) (a) Bruice, T. C.; Noar, J. B.; Ball, S.; Venkataran, U. V. *J. Am. Chem. Soc.* **1983**, *105*, 2452 and references therein. (b) Ball, S.; Bruice, T. C. *Ibid.* **1980**, *102*, 6498.
(8) (a) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1983**, *48*, 65. (b) Baumstark, A. L.; Vasquez, P. C. *Tetrahedron Lett.* **1983**, 123. (c) Baumstark, A. L.; Vasquez, P. C.; Balakrishnan, P. *Tetrahedron Lett.* **1985**, 205. (d) Baumstark, A. L.; Vasquez, P. C. *J. Org. Chem.* **1985**, *50*, 3657.
(9) Rebek, Jr., J.; McCready, R. *J. Am. Chem. Soc.* **1980**, *102*, 5602.

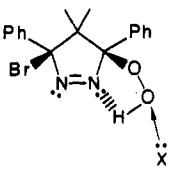
to an internal hydrogen bond between the hydroperoxy proton and the α-substituent.[10] The oxygen atom transfer reactions of flavin 4a-hydroperoxides, an extremely reactive group of compounds, have been reported by Bruice.[7,11] No evidence of electrophilic oxygen atom transfer to 2,3-dimethyl-2-butene from flavin 4a-hydroperoxide model compounds was found. This data and that with other hydroperoxides[7] placed the contribution of the internal hydrogen bond to the driving force for epoxidation in doubt. The relative reactivity of flavin 4a-hydroperoxides was attributed to the increased pK_a of the flavin 4a-hydroperoxide product (stability of the anion). For example, an excellent (linear) correlation of log k for S-oxidation vs. pK_a of ROH was found for a series of ROOH and interpreted[7] to indicate that intramolecular proton transfer did not provide a driving force for this type of oxygen atom transfer reaction in protic media. However, the use of *tert*-butyl alcohol as a solvent that could provide hydrogen-bonding bridges in the transition state could possibly obscure an intramolecular hydrogen-bonding component. It was observed[11] that S-oxidation by flavin 4a-hydroperoxides in aprotic medium did not show a change in reaction order in hydroperoxide (from that of the first order to that of the second) as previously had been found[12] for this type of oxidation with *tert*-butyl hydroperoxide and hydrogen peroxide. This lack of order change is usually interpreted[10] to be indicative of intramolecular hydrogen bonding in the reaction mechanism.

Analogous deuterium isotope effect studies for ionic oxidations with alkyl hydroperoxides are not well-documented. However, the deuterium isotope effects (k_H/k_D = 1.3 ± 0.1), observed for electrophilic oxygen atom transfer from both cyclic and acyclic α-azo hydroperoxides, are of sufficient magnitude to be regarded as primary. The data support a mechanism in which, as previously postulated, intramolecular hydrogen bonding (proton transfer) of the hydroperoxy proton to the azo function is important in the transition state. Thus, there is a strong mechanistic similarity between α-azo hydroperoxide ionic oxidations and those of peracids. Fortunately, several isotope-effect studies[13] on the electrophilic oxygen atom transfer chemistry of peracids have been reported. Hanzlik[13a] reported a peracid isotope effect (k_H/k_D) of 1.17 for the epoxidation of *p*-phenylstyrene with *m*-chloroperoxybenzoic acid at 0 °C in aprotic medium. An earlier study by Curci[13b] showed that the reaction of peroxybenzoic acid with diazodiphenylmethane exhibited a peracid isotope effect of 1.33 ± 0.04 in aprotic medium. These data were used to support[13b] a mechanism in which intramolecular proton transfer in the cyclic transition was important. The primary peracid isotope effect found by Hanzlik[13a] was interpreted to indicate that the peroxy proton remained hydrogen bonded (in the transition state) but was regarded as being too small to show complete transfer. Nevertheless, the magnitudes of the primary peracid isotope effects observed in aprotic media are very similar to those reported here for the α-azo hydroperoxide oxidations and strongly support the requirement of the intramolecular hydrogen bond in these electrophilic oxygen atom transfer reactions.

Experimental data indicate[8,10] that acyclic α-azo hydroperoxides exist predominantly in the intramolecular hydrogen-bonded structure. This conclusion is supported by the inherent difficulties (see the Experimental Section) encountered in exchange of these protons.[14] The X-ray data[5] on **1** have been reported, but unfortunately the hydrogen atoms were not located. An X-ray structure[15] of an acyclic α-azo hydroperoxide [1-hydroperoxy-1-(*o*-methoxyphenyl)azo-2-phenylcyclohexane] has been reported and shows evidence of a bent O–H···N intramolecular hydrogen bond (NHO angle 148°) in the form of a six-membered ring. In the case of cyclic α-azo hydroperoxide **1**, only a five-membered intramolecular hydrogen bond is possible. For acyclic α-azo hydroperoxides, previous mechanistic representations[3] of the transition state for oxygen atom transfer have assumed a five-membered intramolecular hydrogen bond. However, the six-membered intramolecular hydrogen-bonded transition state is also possible and if correct may explain, in part, the observed reactivity difference between acyclic and cyclic α-azo hydroperoxides.



Diverse data[3] including ρ values, relative selectivities, solvent effects, and hydroperoxide deuterium isotope effects support a mechanism of oxygen atom transfer similar to that of peracids in which intramolecular hydrogen bonding is important in the transition state as shown for **1**. Since the α-carbon of α-azo hydroperoxides is saturated, the striking similarities in behavior to those of peracids[2a] are mechanistically important and seem to support an unsymmetrical transition state for peracid oxidation similar to that postulated by Hanzlik.[13a]



Experimental Section

All solvents were of reagent grade. 2,3-Dimethyl-2-butene and the sulfides were available commercially and were used without further purification. The amines were distilled over potassium hydroxide under anhydrous conditions and were stored over molecular sieves before use. 3-Bromo-4,5-dihydro-5-hydroperoxy-4,4-dimethyl-3,5-diphenyl-3*H*-pyrazole (**1**) was prepared according to the published procedure[5] (Caution! Danger of explosion!) and recrystallized at −30 °C from methylene chloride/petroleum ether containing small amounts (~1%) of *cis*-3-hexene as stabilizer. (4-Methoxyphenyl)(phenylazo)methyl hydroperoxide (**2**) was prepared by the oxidation of the corresponding phenylhydrazone with molecular oxygen (Caution! Extreme danger of explosion! Although **2** has not been noted to be explosive, we have observed detonations[8a] of closely related compounds.) and

(10) For a review and discussion of hydrogen bonding in hydroperoxides, see: Richardson, W. H. In *The Chemistry of Functional Groups, Peroxides*, Patai, S., Ed.; Wiley: New York, 1983; Chapter 5.

(11) Bruice, T. C. In *Biomimetic Chemistry*; Dolphin, D., McKenna, C., Murakani, Y., Tabushi, I., Eds.; Advances in Chemistry 191; American Chemical Society: Washington, DC, 1980; pp 89–118.

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(13) (a) Hanzlik, R. P.; Shearer, G. O. *J. Am. Chem. Soc.* **1975**, *97*, 5230. (b) Curci, R.; Furia, F. D.; Marcuzzi, F. *J. Org. Chem.* **1971**, *36*, 3774.

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(15) (a) Bozzini, S.; Gratton, S.; Risaliti, A.; Stener, A.; Calligaris, M.; Nardin, G. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1377. (b) See: Gougoutas, J. Z. In *The Chemistry of Functional Groups, Peroxides*; Patai, S., Ed.; Wiley: New York, 1983; Chapter 12.

recrystallized at 0 °C from benzene/petroleum ether.[3] The physical and spectral data[5,8] for 1 and 2 showed the compounds to be pure (≥99%).

Deuteriated α-Azo Hydroperoxides 1-*d* and 2-*d*. One gram of α-azo hydroperoxide 1 or 2 was dissolved in 5.0 mL of dry acetonitrile, and 1.0 mL of deuterium oxide was added. The homogeneous solution was capped and allowed to sit at −10 °C overnight. Dry diethyl ether was added, and the aqueous phase separated. The organic layer was dried over anhydrous magnesium sulfate, and the solvents were removed under reduced pressure. The deuteriated compounds were recrystallized from the standard solvents, and *small quantities* were dried under vacuum at 0 °C. (Caution!) Preparation of 2-*d* was carried out in the dark since the compound is light sensitive. Total deuterium incorporation, assessed by ^{1}H NMR spectroscopy, was determined to be ≥90% for both compounds. (Note: Shaking of solutions of the α-azo hydroperoxides with D_2O at room temperature did not result in the rapid incorporation of significant amounts of deuterium.)

Kinetic Studies. The following general procedure was employed for all kinetic runs. For 1 and 1-*d*, a small sample of vacuum-dried, pure α-azo hydroperoxide (~0.03 mmol) was weighed in a new 5-mm NMR sample tube. Aliquots of 500 μL of chloroform-d_3 (Aldrich; obtained from a sealed ampule) and 5.0 μL of *cis*-3-hexene (peroxide stabilizer) were added. After the ^{1}H NMR spectrum was recorded, the desired quantity of substrate (alkene, amine, sulfide) was added, via syringe, to the solution at 34 °C and mixed. The ^{1}H NMR signals were recorded and integrated vs. time. The rate data, determined by monitoring the appearance of product and the disappearance of hydroperoxide relative to an internal standard (anisole), were identical. The former set of data was more convenient (accurate), since the product signals were well resolved. Product yields were calculated relative to internal standard (anisole). Product isolation and characterization were performed as previously reported.[3] The kinetic data, obtained for at least 2 half-lives, were analyzed by standard procedures and yielded excellent correlations (correlation coefficients (>0.99 in all cases). For the runs with pure acyclic α-azo hydroperoxides 2 and 2-*d* the above procedure was modified as follows: sample preparation was carried out in the dark; benzene-d_6 (Merck) was used as the solvent (since this type of hydroperoxide is unstable in $CDCl_3$); *tert*-butylbenzene was used as the internal standard; and no *cis*-3-hexene was added. Excellent agreement was obtained with previously published[3] kinetic data for 1 and 2 in all cases except for the results with *N*-methylmorpholine.[6b] The present data supercede the earlier values.

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Decarboxylated Methoxatin Analogues. Synthesis of 7- and 9-Decarboxymethoxatin

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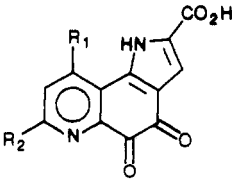
A total synthesis of two monodecarboxylated analogues of methoxatin (1) is described. The synthesis of 9-decarboxymethoxatin (4) was achieved starting with 8-hydroxyquinoline, constructing an appropriately substituted quinolylhydrazone of ethyl pyruvate with a Japp–Klingemann reaction and annulating the remaining pyrrole ring through a Fischer indole synthesis. The synthesis of 7-decarboxymethoxatin (3) first necessitated the construction of an appropriate indole from which the remaining pyridine ring could be annulated via a Doebner reaction.

Methoxatin[1-3] (1) is a novel *o*-quinone cofactor present in certain non-flavin- or nicotinamide-dependent bacterial dehydrogenases (quinoenzymes). Recently 1 was found to serve as a covalently bound coenzyme for bovine serum amine oxidase,[4] suggesting that methoxatin may be a cofactor for other mammalian enzymes, including those of humans, and that it may be a dietary requirement as a vitamin.

In order to evaluate the structural requirements of methoxatin as a reconstitutable cofactor and as an amine and alcohol oxidant,[5-8] we synthesized decarboxylated methoxatin analogues. The synthesis of 7,9-didecarboxymethoxatin (2) has been reported in a previous paper.[8] In this paper we report the total synthesis of 7-decarboxymethoxatin (3) and 9-decarboxymethoxatin (4).[9]



1: R_1 = COOH, R_2 = COOH
2: R_1 = H, R_2 = H
3: R_1 = COOH, R_2 = H
4: R_1 = H, R_2 = COOH

Our strategy for the synthesis of 4 was similar to the strategy employed in the synthesis of 2: i.e., the construction of an appropriately substituted quinolylhydrazone of ethyl pyruvate via a Japp–Klingemann reaction followed by a Fisher indole synthesis to create the third ring.

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