δ 165.8, 154.3, 141.9, 138.8, 132.0, 131.2, 126.2, 118.2, 103.9, 33.5, 11.8 (no assignments made); IR (KBr) 3421, 3358, 1682, 1644, 1606, 1499, 1235, 1293, 1022 cm^{-1}; MS (EI) m/z 246 (M^+). Anal. Calcd for $C_{11}H_{10}N_4O_3 \cdot HBr \cdot H_2O$: C, 38.28; H, 3.80; N, 16.23. Found: C, 38.04; H, 3.44; N, 16.07.

Xanthine Oxidase Mediated Oxidation of Imidazo[4,5-*g*]quinazolinetriones 1b and 1d. The imidazo[4,5-*g*]-quinazolinetrione (0.13 mmol) was either dispersed or dissolved in 5 mL of 0.05 M pH 7.4 phosphate buffer (μ = 0.1, KCl) containing 22 μM EDTA. Addition of 6.3 units of Sigma grade IV xanthine oxidase was followed by stirring for 3 h at room temperature. During this time the reaction mixture became dark amber concomitant with crystallization of the product as its potassium salt. The completed reaction mixture was diluted to 100 mL with distilled water, resulting in a homogeneous amber solution. This solution was placed on a 25-mL Dowex 1-X2 50–100-mesh ion-exchange resin column that was then washed with 500 mL of distilled water to remove salts and the enzyme. The product was removed by elution with 0.1 N HCl; evaporation of eluants to ~5 mL resulted in crystallization of the product in an analytically pure form. In what follows are spectral and analytical data for the respective oxidation products **2a** and **2b**.

2,3-Dimethylimidazo[4,5-*g*]quinazoline-4,6,8,9-(3*H*,5*H*,7*H*)-tetrone (2a): dec pt >350 °C; ^{1}H NMR (trifluoroacetic acid-d_1 with two drops of D_2O) δ 4.25 (3 H, s, *N*-(3)-methyl), 2.94 (3 H, s, 2-methyl); IR (KBr) 3541, 3488, 1726, 1700, 1516, 1405 cm^{-1}. Anal. Calcd for $C_{11}H_8N_4O_4$: C, 50.77; H, 3.10; N, 21.53. Found: C, 50.62; H, 2.98; N, 21.49.

pK_a for N(5)-H acid dissociation is 5.82 ± 0.04. UV/vis [λ_{max}, nm (ϵ)]: (**2a**) 245 (1.35 × 10^4), 312 (1.12 × 10^4); (**2a**$^-$) 232 (1.8 × 10^4), 262 (1.0 × 10^4), 325 (1.06 × 10^4), 450 (1000).

2-(Methoxymethyl)-3-methylimidazo[4,5-*g*]quinazoline-4,6,8,9(3*H*,5*H*,7*H*)-tetrone (2b): dec pt >300 °C; R_f 0.36; ^{1}H NMR (Me_2SO-d_6) δ 4.64 (2 H, s, methylene), 3.92 (3 H, s, *N*-(3)-methyl), 3.32 (3 H, s, methoxy); IR (KBr) 3566, 3465, 3008, 2777, 1730, 1699, 1686, 1634, 1584, 1531, 1521, 1499, 1413 cm^{-1}; MS (EI) m/z 290 (M^+), 260 ($M^+ - CH_2O$). Anal. Calcd for $C_{12}H_{10}N_4O_5 \cdot 1H_2O$: C, 47.45; H, 3.81; N, 18.43. Found: C, 47.65; H, 3.53; N, 18.08.

Acknowledgment. The research was supported by a Faculty Grant-in-Aid from Arizona State University, a Cottrell Research Grant from the Research Corp., a grant from the donors of the Petroleum Research Foundation, administered by the American Chemical Society, and an award from the National Cancer Institute, Grant DHHS (PHS #1 R01 CA 36876-01). The Bruker AM-400 was purchased and supported by an instrumentation grant from the National Science Foundation (CHE-8409644).

Photochemical Reinvestigation of a 5-Phenyl-2-pyrazoline and Its Product Azocyclopropanes

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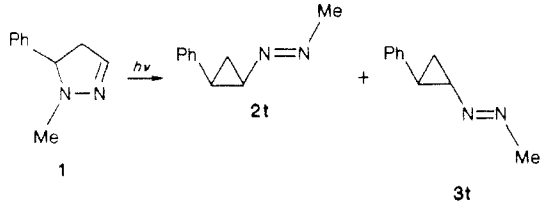
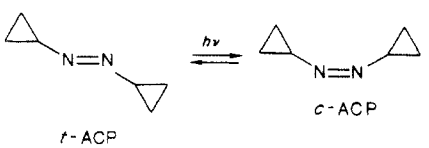
Received June 19, 1986

Irradiation of 1-methyl-5-phenyl-2-pyrazoline (**1**) affords the previously reported azocyclopropanes **2t** and **3t**; however, the major product of this reaction is β-(methylamino)-β-phenylpropionitrile (**4**). Although the azo linkage in **2t** and **3t** has the trans configuration, irradiation of either isomer causes azo trans → cis isomerization, slower interconversion of the ring isomers, reversion to pyrazoline **1**, and cleavage to styrene. Thermolysis of **2t** proceeds twice as fast as that of **3t** to interconvert the ring isomers and ultimately to afford exclusively **1**. The rapid thermolysis rate of **2t** and **3t** relative to a model phenylvinylcyclopropane is interpreted in terms of an unusually high facile formation of the α-azo (hydrazonyl) radical.

In 1968, Rosenkranz and Schmid[1] reported that UV irradiation of 1-methyl-5-phenyl-2-pyrazoline (**1**) produced isomers **2t** and **3t**. These product azoalkanes, which were



the first azocyclopropanes in the literature, caught our attention because of their unexpected photochemical behavior relative to azocyclopropane (*t*-ACP).[2] Whereas irradiation of *t*-ACP gave exclusive trans–cis isomerization of the azo group (*t*-ACP ⇄ *c*-ACP), Rosenkranz and Schmid said nothing about the configuration of the N=N linkage in **2t** and **3t**; in fact, they originally depicted the MeN=N group as semilinear. Irradiation of **2t** and **3t** was said to interconvert these ring isomers without causing reversion to **1**.[1] We found this result unusual because cis–trans ring isomerization most likely involves a 1,3-biradical[3,4] that should sometimes reclose to a pyrazoline. In fact, **2t** and **3t** are interconverted by thermolysis but they also lead to **1**.[1]



Other aspects of the system **1**–**3** appeared worthy of further exploration. For example, the total yield of **2t** and **3t** from **1** was only 35%, leading us to wonder whether any other photoproducts were formed. The use of benzene as solvent seemed unusual because it would absorb the UV light intended for **1**. Moreover, the broad band UV irradiation employed in the original work would not only mask any wavelength effects but could also cause secondary reactions of the UV-absorbing primary photoproducts. Finally, we were interested in the thermolysis rates of **2t** and **3t** because they should exhibit the large rate enhancement previously seen with *t*-ACP.[2]

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(2) Engel, P. S.; Gerth, D. B. *J. Am. Chem. Soc.* **1968**, *103*, 7689.
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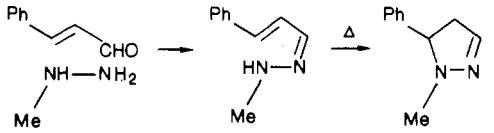
Table I. Quantumm Yields at 254 nm in C_6D_6[a]

reactant	1	2t	2c	3t	3c	4	5	6
1	0.039[b]	0.016	0.0034	0.0037		0.017	0.0049	
2t	0.0062	0.089[b]	0.064	0.0097	0.0037			0.0048

[a] Determined from the initial slope of NMR peak areas vs. time. [b] Disappearance of reactant.

Results

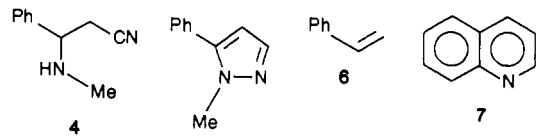
Compound 1 was prepared by condensation of cinnamaldehyde and methylhydrazine followed by ring closure of the intermediate hydrazone.[5] Although the crude product



1

was purified only with difficulty, we were ultimately able to obtain 98% pure 1 by fractional distillation and column chromatography. The pyrazoline was found to be stable toward heating at 150 °C for 12 h in the absence of air.

After irradiation of 1 in degassed hexane or benzene at 254 nm, HPLC analysis of the crude photolysate revealed a shockingly complex mixture of about 21 products. Both solvents gave essentially the same results, though the benzene solution remained clearer during irradiation, probably because it dissolves the products better than hexane does. Fortunately, most of the HPLC peaks turned out to be minor and preparative HPLC allowed isolation of four compounds (4–7) in addition to the two (2t, 3t) originally reported by Rosenkranz and Schmid. The



structure of 4 was proven by comparison with an authentic sample prepared by conjugate addition of methylamine to cinnamonitrile. The NMR spectrum of 5 was found to be identical with the one published for this compound.[6] Styrene (6) and quinoline (7) were identified on the basis of their NMR spectra and comparison of HPLC retention times with those of authentic material.

Initial quantum yields for disappearance of 1 and formation of the major products were determined by NMR. As seen in Table I, the reaction is inefficient, but the product balance is high, supporting our hypothesis that most of the HPLC peaks are due to strongly UV absorbing but minor products. Although compounds 6 and 7 were formed in very low yields, it is surprising that Rosenkranz and Schmid missed 4, the major photoproduct. The ratio of 2t to 3t (4.5) is higher than the value of 3.3 reported by Rosenkranz and Schmid. Extended irradiation of 1 formed 2c, a secondary photoproduct of 2t (see below).

Because substantial quantities of 2t could be isolated by preparative HPLC, the photochemistry of this compound was investigated separately. Irradiation of 2t in C_6D_6 at 254 nm led to a rapid buildup of an NMR singlet at 3.12 ppm and a slower increase in the peaks due to 1, 3t, and 6. The 3.12 ppm singlet disappeared on extended irradiation, a behavior consistent with its assignment as the methyl group of cis-azoalkane 2c. Although we were

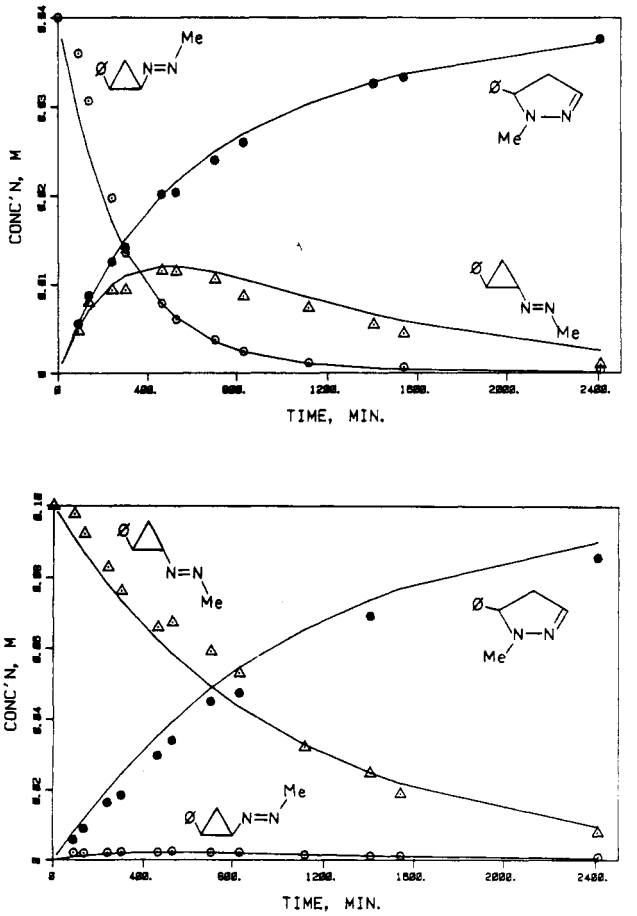


Figure 1. Top: Thermolysis of 2t in C_6D_6 at 141 °C monitored by ^1H NMR. Bottom: Thermolysis of 3t under the same conditions. The decrease in starting material concentration, rise and fall of the ring isomer, and ultimate formation of pyrazoline 1 are shown.

unable to isolate 2c, its full NMR spectrum could be constructed by subtracting the NMR spectrum of 2t from that of 2t irradiated for intermediate times, i.e., before too much 1, 3t, and 6 had built up. The upfield shift of 2c relative to 2t (δ_{CH_3} 3.12 vs. 3.35) was at first surprising but azocyclopropane and 2-(cyclopropylazo)-2-methylpropane show a similar trend.[7] Another singlet at 3.09 ppm that appeared during irradiation of 2t was assigned to 3c (compare 3t at 3.53 ppm). These results make it clear that photoisomerization of the azo linkage is an important reaction not found by these authors. In contrast to the earlier statements of Rosenkranz and Schmid, we further find that irradiation of 2t does give rise to 1, preventing the attainment of a photoequilibrium between 2t and 3t. The styrene (6) we observed on irradiation of 1 appears to be a secondary photoproduct arising from 2t.

Irradiation of 2t was also carried out at 366 nm to check for a wavelength effect. Under these conditions, isomerization of the azo linkage became even more dominant, its efficiency being at least 200 times greater than isomeri-

(5) Auwers, K. V.; Heimke, P. *Justus Liebigs Ann. Chem.* **1927**, *458*, 186.

(6) Aubagnac, J. L.; Elguero, J.; Jacquier, R. *Bull. Soc. Chim. Fr.* **1969**, 3306.

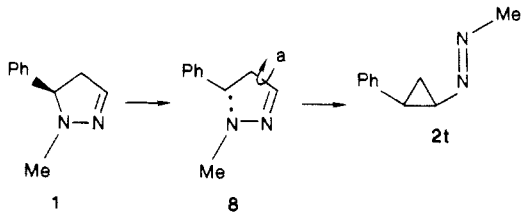
(7) δ of H α to N: *t*-ACP, 3.44, and *c*-ACP, 3.20 in C_6D_6; *trans*-2-(cyclopropylazo)-2-methylpropane, 3.66, and *cis*-2-(cyclopropylazo)-2-methylpropane 3.47 in C_6D_6.

zation of the ring or any other photoreaction. The same trend was seen for **3t**, supporting our assignment of the new methyl singlets at 3.12 and 3.09 ppm as cis azo isomers.

In agreement with Rosenkranz and Schmid, we found that heating **2t** and **3t** to 141 °C caused interconversion of these ring isomers and rearrangement to pyrazoline **1**. The concentration of all three compounds was monitored by NMR, with the results shown in Figure 1. The solid lines represent calculated fits to the experimental points using a scheme described below.

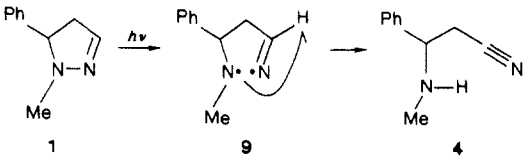
Discussion

While some of the results of Rosenkranz and Schmid turned out to be correct, most of our doubts proved well-founded. The fact that the photorearrangement of **1** proceeds as well in benzene as in hexane suggests that the benzene serves as a singlet sensitizer. Rosenkranz and Schmid carefully proved the correct structure of **2t** and **3t**. Like them, we find **2t** to predominate over **3t**, a surprising observation in view of the crowding in **2t**. A possible explanation can be found in the theories of biradical behavior set forth by Salem and Rowland.[8] The singlet excited pyrazoline should cross to the ground-state biradical surface to give a geometry with the maximum interaction between electrons. The interelectronic distance in such a favored "tight" biradical[9] is smaller if the azo group moves upward out of plane about bond a in structure **8** instead of rotating downward. Thus **2t** is favored

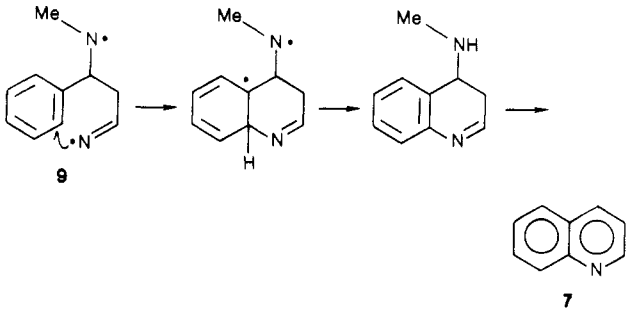


electronically over **3t** despite its greater steric hindrance. Since biradical **8** should often reclose to **1**, the low overall quantum yield is not surprising.

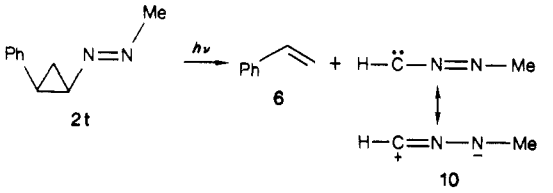
In our hands, irradiation of **1** yielded many products not mentioned by Rosenkranz and Schmid. Cyano amine **4**, the major product, was undoubtedly formed by homolysis of the N–N bond followed by internal hydrogen transfer.



Indeed, this very reaction was discovered in 1971,[10,11] but the pyrazolines had an *N*-phenyl group to facilitate *N–N* homolysis. Photooxidation of pyrazolines to pyrazoles is well-known,[10,12] offering an explanation for the presence of **5** among our products. Unfortunately, the continued formation of **5** in degassed solution is not easily rationalized, though some kind of reduction product certainly could be present in the complex mixture.[13] Products **2c** and **6** are attributed to secondary photoreactions of **2t** because their quantum yield is much higher starting from **2t** than from **1**. In fact, **6** was formed in such low yield from **1** that it could be seen by HPLC but not by NMR until very late in the reaction. Quinoline (**7**) was also a minor product, but its strong UV absorbance allowed easy detection by HPLC. We propose that biradical **9** sometimes undergoes intramolecular attack of the iminyl radical on the benzene ring.[14] One or more hydrogen shifts followed by loss of methylamine gives **7**.



Irradiation of azocyclopropane **2t** revealed its most important photoreaction to be trans–cis isomerization of the azo group, though the quantum yield is much lower than the usual value of 0.5.[15,16] Cleavage of the cyclopropane ring takes place from a quasi-equilibrium mixture of **2t** and **2c** to give the 1,3-biradical responsible for ring isomerization and pyrazoline formation. The presence of styrene among the products was unexpected and in fact represents a new photoreaction of azocyclopropanes. By analogy with



the formation of carbenes and olefins from photolysis of cyclopropanes,[17] we propose that methyl nitrile imine **10**[11,18] is the byproduct from **2t** → **6**. None of the identified products contain this moiety, though it could certainly be present in one of the many minor products. It is intriguing to consider the possibility that nitrile imine formation might be the exclusive photoreaction of 7-methylazodibenzonorcaradiene.[19]

The thermal rearrangement data for **2t** and **3t** were fitted to a simple kinetic scheme involving a single biradical **11**. Thermolysis of either azoalkane is postulated to give **11**, which then partitions itself to **2t**, and **3t** and **1**. Four differential equations involving five rate constants were used with the computer program EPFIT[20] to generate con-

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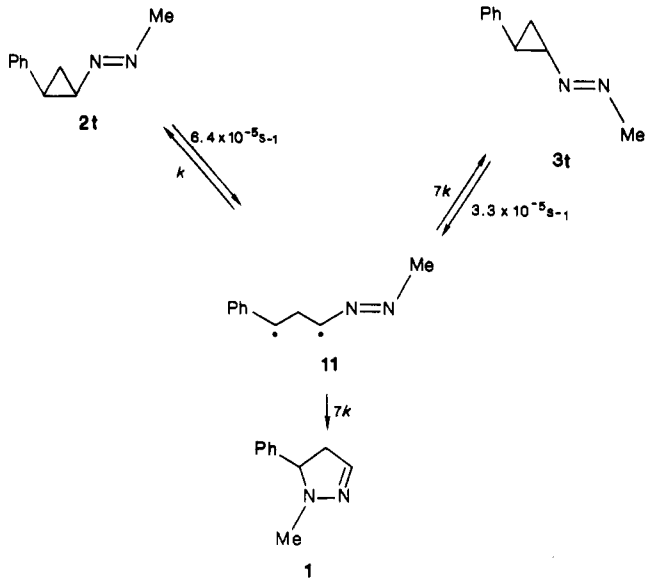
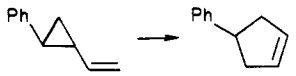


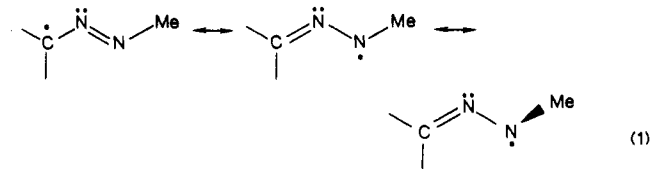
centration vs. time curves for all three compounds. These curves were compared graphically with the experimental data (cf. Figure 1) until a set of rate constants was found that gave the best fit to *both* sets of data, i.e., those arising from each starting material. Thermolysis of **2t** is about twice as fast as that of **3t**, probably because steric interference between cis groups on the cyclopropane ring is relieved on homolysis of **2t**. Although there are too many independent variables for a complete mathematical solution, the ratios of rate constants for biradical partitioning again reveal steric effects at work. Thus closure of **11** to the cis ring isomer **2t** is only one seventh as likely as closure to either **3t** or pyrazoline.

The rate constant for thermolysis of **3t** to give **1** is one-half of the 3.3×10^{-5} s^{-1} deduced for **3t** → **11** because half of **11** reverts to **3t**. This rate constant corresponds to $\Delta G^{\ddagger}$(141 °C) = 33.6 kcal/mol for **3t** → **1**, a value that is considerably below the 40.2 kcal/mol found by Simpson and Ritchie[21] for the analogous conversion of **12** to **13**. We



12 **13**

propose that the 6.6 kcal/mol difference is caused at least partly by the large resonance stabilization of α-azo radicals[22] previously noted in the thermolysis of azocyclopropane.[2] These radicals are not only allylic but they are stabilized by a three-electron bond[24] with the lone electron pair on the adjacent nitrogen. In view of its large effect in α-amino radicals,[25] three-electron bonding is not only expected in α-azo radicals, but it is manifested by much more facile twisting about the N=N bond than in the analogous allyl radicals[23] (eq 1). Another factor that



(1)

contributes to the lability of **3t** is its high heat of formation relative to that of **1**.[26]

(20) We thank Professor David Stanbury for providing this program.
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(22) α-Azo radicals are also called hydrazonyl radicals.[23]
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In summary, we have verified that irradiation of pyrazoline **1** produces azoalkanes **2t** and **3t**, but it also gives many other products including **4**–**7**. The main photoreaction of **2t** is trans–cis isomerization of the azo group, especially under long wavelength (366-nm) irradiation. Contrary to the results of Rosenkranz and Schmid, **2t** reverts photochemically to **1** and is also responsible for the formation of styrene. Although the ultimate thermolysis product of **2t** and **3t** is **1**, these isomers are interconverted via a presumed 1,3-biradical **11**. Finally, the high stabilization energy of α-azo radicals is verified by the facile thermolysis of **2t** relative to its vinyl analogue **12**.

Experimental Section

General. NMR spectra were taken on a JEOL FX90 or an IBM AF300 spectrometer, while UV spectra were obtained on a Cary 17. HPLC analyses were done on a Beckman Model 342 equipped with a Model 165 dual variable wavelength UV detector. All solvents were HPLC or spectrophotometric grade and were used without further purification. Photolyses at 254 nm were carried out with three GE 15-W low-pressure mercury lamps with quartz sample tubes and a Vycor filter. Irradiations at 366 nm were done with a Hanovia 450-W medium-pressure mercury lamp with a 2,7-dimethyl-3,6-diazacyclohepta-1,6-diene perchlorate filter solution and Corning 7-60 UV filters.

1-Methyl-5-phenyl-2-pyrazoline (1). Methylhydrazine (0.47 mol) was added dropwise to a stirred solution of *trans*-cinnamaldehyde (0.45 mol) in 130 mL of methanol over about an hour. The temperature was maintained between 10–15 °C by using an ice bath. The solution was allowed to stir for an additional hour while it warmed to room temperature. The methanol was then distilled off at 1 atm, followed by vacuum distillation to cyclize the hydrazone. The crude product boiled at 60–63 °C (0.02–0.03 mm). Light-absorbing impurities were removed from the pale lime-green oil by gravity column chromatography on silica gel eluting with 10% EtOAc/hexane followed by MPLC: ^{1}H NMR ($CDCl_3$) δ 2.4–3.2 (m, 2 H), 2.75 (s, 3 H), 3.7–4.0 (m, 1 H), 6.77 (s, 1 H), 7.3–7.5 (m, 5 H); UV (hexane) λ_{max} 245 nm (ε 4000).

Photolyses at 254 nm of 1. Solutions (0.04 M) of purified **1** (>98% by HPLC) in benzene or hexane were purged with nitrogen and then irradiated at 254 nm. Photolysis progress was followed by HPLC, with products monitored at 280 and 340 nm with the UV detector. The resulting product mixture was separated into groups of four to five components each by MPLC. Individual products were then isolated from a group by preparative HPLC and were analyzed by NMR. After identification of products was made, a 0.1 M solution of **1** in C_6D_6 was degassed and sealed in an NMR tube. The 254-nm photolysis was then monitored by NMR.

Photolysis Products. Cyano amine **4**: ^{1}H NMR ($CDCl_3$) δ 2.11 (s, 1 H), 2.36 (s, 3 H), 2.71 (d, J_{ab} = 6.4 Hz, 2 H), 3.88 (t, J_{ab} = 6.4 Hz, 1 H), 7.36 (s, 5 H), (C_6D_6) δ 0.77 (s, 1 H), 1.82 (d, J_{ab} = 6.6 Hz, 2 H), 1.88 (s, 3 H), 3.19 (4, J_{ab} = 6.6 Hz, 1 H), 7.06 (s, 5 H). Authentic material was prepared by condensing at −78 °C 0.15 mol of methylamine in a tube containing 0.015 mol of cinnamonitrile, sealing the tube, and allowing it to warm to room temperature. After standing overnight, the mixture gave **4** in quantitative yield.

cis-1-Phenyl-2-(methylazo)cyclopropane (**2t**): ^{1}H NMR ($CDCl_3$) δ 1.67 (m, 1 H), 2.02 (m, 1 H), 2.65 (m, 1 H), 3.59 (s, 3 H), 3.66 (m, 1 H), 7.1–7.4 (m, 5 H), (C_6D_6) δ 1.17 (m, 1 H), 1.90 (m, 1 H), 2.19 (m, 1 H), 3.36 (s, 3 H), 3.64 (m, 1 H), 7.0–7.4 (m, 5 H); UV (C_6D_6) λ_{max} 346 nm (ε 54). *trans*-1-Phenyl-2-(methylazo)cyclopropane (**3t**): ^{1}H NMR ($CDCl_3$) δ 1.55 (m, 1 H), 1.94 (m, 1 H), 2.84 (m, 1 H), 3.67 (m, 1 H), 3.73 (s, 3 H), 7.0–7.4 (m, 5 H), (C_6D_6) δ 1.23 (m, 1 H), 1.82 (m, 1 H), 2.84 (m, 1 H), 3.55 (s, 3 H), 3.84 (m, 1 H), 6.7–7.1 (m, 5 H); UV ($CDCl_3$) λ_{max} 341–342 nm. 1-Methyl-5-phenylpyrazole (**5**): ^{1}H NMR ($CDCl_3$) δ 3.90 (s, 3 H), 6.31 (d, J_{ab} = 2 Hz, 1 H), 7.43 (s, 5 H), 7.51 (d, J_{ab} = 2 Hz, 1 H). For quinoline, the structural assignment was made by HPLC coinjection with authentic material and by comparison with lit-

(26) Further work on α-azo radicals is in progress: Engel, P. S.; Chen, Y.; Houk, K. N.; Li, Y., unpublished results.

erature ^1H NMR and ^{13}C NMR data.[27]

Photolysis at 254 nm of 2t. A C_6D_6 (0.5 mL, 0.1 M) solution of **2t** in a quartz NMR tube was sealed under vacuum after three freeze–thaw–degas cycles. The sample was then irradiated at 254 nm in a Vycor sleeve and the reaction progress was monitored by ^1H NMR of the characteristic NCH_3 singlets. A major product with an NMR singlet at δ 3.12 was assigned as the cis azo isomer **2c** on the basis of its photochemical behavior. The NMR spectrum of **2c** was obtained on the IBM 300-MHz spectrometer in the following way. A 0.1 M solution of **2t** in C_6D_6 was irradiated for a short period at 254 nm. A difference NMR spectrum was then generated from the "before" and "after" irradiation spectra. **2c**: ^1H NMR (C_6D_6) δ 1.24 (m, 1 H), 1.82 (m, 1 H), 2.03 (m, 1 H), 2.92 (m, 1 H), 3.12 (s, 3 H).

Quantum Yields. Light intensities were based on the chemical actinometer 2,3-diazabicyclo[2.2.1]hept-2-ene which evolves nitrogen with unit efficiency. Gas yields were measured using a Töpler pump and gas buret. Each product (except styrene) had an NCH_3 singlet in the NMR which allowed us to follow product concentrations as a function of irradiation time. All quantum yields are based on initial slopes of such concentration vs. time plots.

Thermolysis of 2t and 3t. Solutions of **2t** (0.04 M) and **3t** (0.1 M) in C_6D_6 were degassed and sealed in NMR tubes. The samples were then suspended in an oil bath regulated at 141 °C and were periodically removed for NMR analysis. Concentration vs. thermolysis time plots were then constructed as described above. Theoretical concentration vs. time plots were prepared by modifying the computer program EPFIT[20] to model this system. Both azocyclopropanes were assumed to form a single biradical which then partitions itself among the two azoalkanes and the pyrazoline **1**. Formation of **1** was assumed to be irreversible based on its thermal stability at 141 °C. The curves thus generated from EPFIT were then compared visually with the experimental curves. Changes in the rate constants were made and the new curves again compared to the experimental curves. This process was repeated until a single set of rate constants which gave the "best fit" to the experimental curves was obtained.

Acknowledgment. We thank the National Science Foundation and the Robert A. Welch Foundation for financial support. G.A.B. gratefully acknowledges the ARCS Foundation for a fellowship.

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Total Synthesis of 8(*S*)-, 9(*S*)-, 11(*S*)-, and 12(*S*)-HETE Methyl Esters

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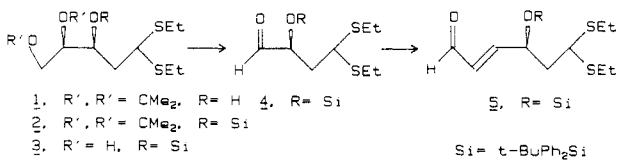
Received June 2, 1986

Starting from D-arabinose, the total syntheses of methyl 8(*S*)-, 9(*S*)-, 11(*S*)-, and 12(*S*)-hydroxyeicosatetraenoates are described.

Enzymic oxidation of arachidonic acid leads to a multitude of biochemically important products that include not only prostaglandins and their transformation products such as thromboxane and prostacycline but also lipoxygenase-derived hydroperoxides (HPETE's) and alcohols (HETE's).[1]

The oxidation of the (*Z*,*Z*)-1,4-diene system characteristic of arachidonic acid (Figure 1) is thought to proceed via radical **B**, itself probably generated by abstraction of an electron from the double bond followed by loss of a proton. This radical **B** may then add oxygen, a superoxide anion, or superoxide to give **C1–3**, which may be further reduced to the HETE's. Six of these intermediates can be produced in theory, and five of them have either been isolated or are postulated to be key intermediates in the biosynthesis of eicosanoids. Thus, the biosynthesis of prostaglandins is thought to proceed via the 11(*S*)-peroxy radical of type **C1**. The related 11-HETE[3] is a key compound in the search for biosynthetically patterned prostaglandin syntheses. 12-HETE, generated from arachidonic acid by 12-lipoxygenase enzyme, is found in human

Scheme I



platelets[4] and skin keratinocytes.[5] It has also been detected in high concentrations in psoriatic lesions[6] and shown to possess both chemotactic and chemokinetic properties. 8-HETE has recently been found to appear, among the various HETE's, as the only biologically active metabolite of arachidonic acid in starfish oocytes.[7] Its 8(*S*) stereochemistry has just been determined.[8] In order to facilitate the study of the biological and biochemical properties of these arachidonic acid metabolites, significant quantities of these HETE's are required. An efficient synthesis of 5-HETE[9] and an enzymatic preparation of

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