also be envisioned since maleimides with activating substituents in the 3- or 4-position have been reported to undergo Diels-Alder reactions with cyclopentadiene.[16]

This route provides an efficient method of synthesizing pure 3-pyrrolines which were previously unattainable.

Experimental Section

General Methods. Melting points (uncorrected) were taken in open capillaries on a Hoover-Thomas Unimelt apparatus. NMR Spectra were determined for deuteriochloroform solutions containing ca. 1% tetramethylsilane as internal standard on Varian T60A and FT80 spectrometers. IR spectra were determined for KBr pellets with a Nicolet FT-IR infrared interferometer. Elemental analyses were performed by Atlantic Microlabs, Inc., Atlanta, GA.

***N*-Methyl-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide.** A stirred solution of *N*-methylmaleimide (4.44 g; 40 mmol) and furan (27.2 g; 400 mmol) in benzene (125 mL) was heated at reflux for 15 h. The reaction mixture was concentrated to dryness in vacuo and the pale yellow solid residue was crystallized from diethyl ether to give the adduct[13] (6.9 g; 96%) as white needles (a mixture of endo and exo isomers in a ratio of ca. 3:2): mp 138–141 °C; ^{1}H NMR δ 2.83 (s), 3.13 (s), 3.53 (m), 5.22 (s), 6.43 (s), 6.50 (s); IR 3013, 1690, 1439, 1381, 1293, 1134, 1018, 971 cm^{-1}. Anal. Calcd for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.45; H, 5.11; N, 7.80.

***N*-Phenyl-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide** was obtained in 71% yield as white plates (diethyl ether): mp 167–169 °C dec (lit.[17] mp 165.5 °C); ^{1}H NMR δ 3.00 (s, 2 H), 5.36 (m, 2 H), 6.53 (m, 2 H), 7.36 (m, 2 H); IR 3062, 3020, 1710, 1499, 1386, 1287, 1196, 1083, 1013, 872 cm^{-1}.

4-Methyl-4-aza-10-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene. A solution of *N*-methyl-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboximide (6.5 g; 35 mmol) in dichloromethane (50 mL) was added dropwise to a stirred suspension of lithium aluminum hydride (3.99 g; 100 mmol) in anhydrous ether (100 mL). The mixture was stirred at 25 °C for 1 h and then carefully quenched with water. The salts were filtered and washed with chloroform (100 mL). The filtrate and chloroform washings were dried (sodium sulfate) and concentrated in vacuo. The yellow oily residue was distilled in vacuo to give the product (4.7 g; 89%) as a clear oil: bp 33–35 °C (0.05 torr); ^{1}H NMR δ 2.23 (s), 2.36 (s), 3.06 (m), 4.7 (s), 4.9 (m), 6.33 (s), 6.46 (s); IR 2950, 2781, 1456, 1252, 1146, 1013, 900 cm^{-1}. Anal. Calcd for $C_9H_{13}O_3 \cdot 0.75H_2O$: C, 65.63; H, 8.87; N, 8.50. Found: C, 65.71; H, 8.87; N, 8.48.

***N*-Phenyl-4-aza-10-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene** was prepared in 88% yield as a crude yellow powder: mp 119–121 °C; ^{1}H NMR δ 2.53 (m), 3.00 (m), 4.76 (m), 6.36 (s), 6.93 (m), 7.16 (m); IR 2964, 1597, 1506, 1365, 1210, 1153, 991, 907 cm^{-1}.

1-Methyl-3-pyrroline. A solution of 4-methyl-4-aza-10-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene (4.53 g; 30 mmol) in silicon oil [50 mL; bp >140 °C (0.002 torr)] was placed in a 100-mL round-bottom flask equipped with a short-path distillation apparatus and a gas bubbler. The receiver was cooled to −78 °C. The solution was heated to 250–300 °C for 2 h under an argon purge. The crude distillate (3.7 g), a 1:1 mixture of furan and 1-methyl-3-pyrroline, was fractionally distilled to give 1-methyl-3-pyrroline (1.5 g; 60%): bp 75–77 °C; mp of HCl salt 185–187 °C; ^{1}H NMR δ 2.5 (s, 3 H), 3.47 (s, 4 H), 5.77 (s, 2 H). Anal. Calcd for $C_5H_9N \cdot HCl \cdot 0.5H_2O$: C, 46.70; H, 8.62; N, 10.89; Cl, 27.57. Found: C, 46.61; H, 8.65; N, 10.84; Cl, 27.68.

1-Phenyl-3-pyrroline. Method A. A suspension of 4-phenyl-4-aza-oxatricyclo[5.2.1.0^{2,6}]dec-8-ene (2.13 g; 10 mmol) and silicon oil [50 mL, bp >140 °C (0.002 torr)] was placed in a 100-mL round-bottom flask equipped with a short-path distillation apparatus and a gas bubbler. The condenser was heated to 80 °C and the receiver cooled to −78 °C. The suspension was heated to 250–300 °C for 2 h at 60 torr under a bleed of argon. The distillate, which collected as a yellow solid, was chromatographed (silica gel eluted with dichloromethane) to give a white powder that was crystallized from methanol, yielding 1-phenyl-3-pyrroline as white flakes (1.2 g; 83%), mp 99–101 °C.

Method B. A solution of *cis*-1,4-dichloro-2-butene (2.5 g; 20 mmol), aniline (5.5 g; 60 mmol), and benzene (25 mL) was stirred at reflux for 2 h. The reaction mixture was cooled to 25 °C and washed with water (2 × 50 mL). The organic solution was dried (sodium sulfate) and concentrated under reduced pressure to give a red gum that was crystallized from methanol to yield 1-phenyl-3-pyrroline as white flakes (1.01 g, 35%): mp 99–101 °C (lit.[14] mp 101–102 °C); ^{1}H NMR ($CDCl_3$/Me_4Si) δ 4.03 (s, 4 H), 5.86 (s, 2 H), 6.36–7.40 (complex m, 5 H); IR (KBr) 3041, 2964, 1632, 1597, 1513, 1393, 1189, 998, 745 cm^{-1}.

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Mechanism of Singlet Oxygen Addition to Conjugated Butadienes.[1] Solvent Effects on the Formation of a 1,4-Diradical. The 1,4-Diradical/1,4-Zwitterion Dichotomy

Edward L. Clennan* and Robert P. L'Esperance
Department of Chemistry, The University of Wyoming, Laramie, Wyoming 82071

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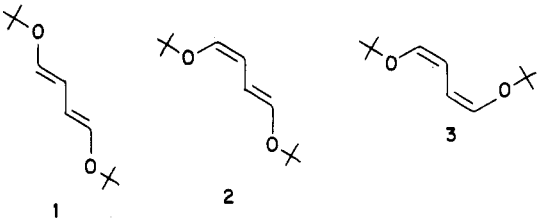
A more detailed examination[1] of solvent effects on the addition of singlet oxygen to isomeric dienes 1–3[2] has



uncovered a very revealing isomerization that implicates diradical intermediates on the energy surface for the formation of dioxetanes. These results corroborate our earlier suggestion[1] of competing concerted and stepwise dioxetane production and most importantly, from a synthetic viewpoint, demonstrate that careful consideration must be given to the proper choice of solvent for singlet oxygen diene reactions.

The photooxidations of dienes 1–3 were accomplished by irradiation of dilute solutions of each diene in the presence of a sensitizer at −78 °C (see the Experimental Section). The low temperatures were required to prevent decomposition of the sensitive dioxetane products (Chart I). The dilute solutions were necessary in order to prevent substrate dye interactions which compromised the configurational integreties of the dienes. Control reactions in both acetone-d_6 and THF-d_8 under the identical conditions utilized for the photooxidations except under an inert atmosphere (acetone-d_6–nitrogen; THF-d_8–argon) verified that less than 5% isomerization of any of the three dienes could occur. Under these carefully controlled conditions integrations of the proton NMR spectra of the reaction mixtures allowed quantitation of the product distributions as a function of solvent.[3] These data, which

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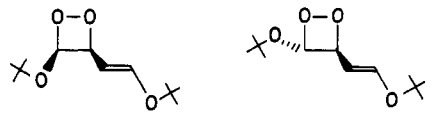
Table I. Product Distribution in the Reactions of 1-3 with Singlet Oxygen as a Function of Solvent

diene	solvent[a]	products, % 4	5	6	7	8
EE	$(CD_3)_2CO$	84	16			
	$(CD_3)_2CO/CD_2Cl_2$ (4)	88	12			
	CD_2Cl_2	91	9			
	$(CD_3)_2CO/CD_3CN$ (1)	88	12			
	THF-d_8	82	18			
EZ	$(CD_3)_2CO$	8	33	40		18
	$(CD_3)_2CO/CD_2Cl_2$ (4)	6	30	39		25
	$(CD_3)_2CO/CD_2Cl_2$ (1)	2	31	42	4	20
	$(CD_3)_2CO/CD_2Cl_2$ (0.25)	5	22	39	6	27
	$(CD_3)_2CO/CD_3CN$ (1)	4	27	44		25
	THF-d_8	33	26	14		27
ZZ	$(CD_3)_2CO$			73	27	
	$(CD_3)_2CO/CD_2Cl_2$ (4)			71	29	
	$(CD_3)_2CO/CD_2Cl_2$ (1)			39	61	
	$(CD_3)_2CO/CD_2Cl_2$ (0.25)			12	88	
	CD_2Cl_2			10	90	
	$(CD_3)_2CO/CD_3CN$			63	37	
	THF-d_8	7	10	38	31	14

[a] The number in the parentheses after the solvent is the volume/volume ratio of the solvents in the mixture.

Chart I



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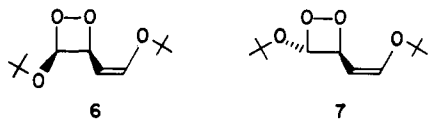

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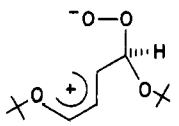
are only accurate to ±5%, are presented in Table I.

Dioxetanes were the major products of these reactions. These products were identified by ^1H and ^{13}C NMR as previously described in detail.[1] In acetone-d_6–methylene chloride solutions the *ZZ* diene **3** but not the *EE* diene **1** exhibits dramatic product variation as a function of solvent composition. The lack of a solvent effect in the reaction of the *EE* diene **1** is even maintained in mixtures containing the much more polar solvent acetonitrile or in the very nonpolar THF-d_8. The very different response of **1** and **3** to changing acetone-d_6–CD_2Cl_2 mixtures previously[1] led us to suggest a concerted addition of singlet oxygen (2s + 2a) to *E* olefinic linkages but a stepwise addition to *Z* olefinic linkages through a freely rotating intermediate. The expanded solvent range examined in this study confirms the very different nature of these two ostensibly similar reactions.

The formation of all four dioxetanes in the addition of singlet oxygen to **3** in THF-d_8 cannot be attributed to rotation in the zwitterionic **8** or diradical intermediate **9**.



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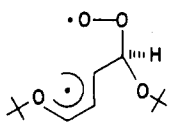

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These intermediates are expected to have high barriers to rotation.[4,5] Instead we suggest that rotation of diradical **9**, decomposition to *EZ* diene **2** and oxygen, and subsequent reaction of **2** is the source of the apparent nonstereospecificity of this reaction. Attempts to observe the *EZ* diene in this reaction mixture before complete conversion to products were unsuccessful. The observation of less than 5% of the isomerized diene is not surprising in view of its greater reactivity in comparison to **3**.[1] The different ratio of **4** to **5** formed in the reaction of the *ZZ* diene **3** and *EZ* diene **2** in THF-d_8 is an artifact of our inability to accurately integrate products formed in minor amounts.[6] The dramatic increase in the yield of dioxetane **4** in the reaction of **2** in THF-d_8 is also symptomatic of diradical decomposition to form the sterically less demanding *EE* diene **1**. Gollnick[7] has recently reported the nonstereospecific formation of an endoperoxide and has also suggested[8] that singlet oxygen induced isomerization through reversible diradical formation is responsible.

Diradicals have received considerable attention with the realization that these intermediates can be invoked to explain product formation in reactions in which concerted pathways are sterically or electronically prohibited. Diradicals that have been examined in detail include trimethylene,[9] trimethylenemethane,[10] and tetramethylene.[11] Theoretical work[12] on the 1,4-diradical tetramethylene has resulted in its description as an extreme on a 1,4-diradical/1,4-zwitterion continuum. The position of a given species on this continuum has been suggested to be a function of the terminal substituents on the tetramethylene chain.[13] The results presented here also suggest that the position on the continuum is a function of the polarity of the medium in which the freely rotating intermediate is formed.[14] The stereospecificities of these reactions and the predominance of the more sterically

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Table II

solvent	diene	irrad time, min	% diene (EE)-1	(EZ)-2	(ZZ)-3
acetone-d_6	1	35	100.0	0.0	0.0
	2	35	2.9	95.4	1.7
	3	35	0.0	4.6	95.4
THF-d_8	1	60	100.0	0.0	0.0
	2	60	0.0	100.0	0.0
	3	60	0.0	4.5	95.5

hindered dioxetane products (the "cis alkoxy" effect[15]) in the more polar media[16] are indicative of 1,4-zwitterion formation. As the medium becomes less polar the character of the intermediate shifts its position on the continuum toward the 1,4-diradical extreme. Diagnostic of this mobility on the continuum is the decreasing predominance of the cis dioxetanes and finally reversion of the intermediate to form the stereochemically scrambled diene.

The rapid loss of oxygen from the diradical intermediate in comparison to the zwitterionic intermediate is most likely related to the ease of intersystem crossing[17] in the former species. Decomposition of a triplet intermediate to form triplet oxygen and singlet ground state diene is 22.5 kcal/mol more exothermic than decomposition of a singlet to form two singlet products.

Studies to examine these diradical intermediates and their formation in other singlet oxygen reactions is currently under way.

Experimental Section

Preparative gas chromatographic separations were carried out on a Varian Aerograph 90-P utilizing a 0.25 in. by 20 ft column packed with 20% Carbowax 20M on Chromosorb W. Proton NMR spectra and integrations were obtained for dienes 1-3 and their reaction mixtures with a Jeol FX270 at 270 MHz, and the chemical shifts were referenced to Me_4Si. Acetone-d_6 (Aldrich) was distilled from $CaSO_4$ under a N_2 atmosphere and stored over 4A molecular sieves. Methylene chloride-d_2 (Aldrich) was filtered through activity 1 basic alumina prior to use. Acetonitrile-d_3 was obtained from Aldrich and used without further purification.

(EE)-, (EZ)-, and (ZZ)-1,4-Di-*tert*-butoxy-1,3-butadiene (1-3). All three dienes were synthesized by the method of Hiranuma and Miller[2] and purified by preparative gas chromatography. ^1H NMR (acetone-d_6): 1, δ 6.39 (dd, J = 8.1, 2.9 Hz, 2 H), 5.45 (dd, J = 8.1, 2.9 Hz, 2 H), 1.18 (s, 18 H); 2, δ 6.54 (d, J = 12.4 Hz, 1 H), 6.02 (d, J = 6.6 Hz, 1 H), 5.79 (dd, J = 12.4, 11.0 Hz, 1 H), 4.94 (dd, J = 11.0, 6.6 Hz, 1 H), 1.21 (s, 9 H), 1.20 (s, 9 H); 3, δ 6.09 (dd, J = 3.2, 1.5 Hz, 2 H), 5.33 (dd, J = 3.2, 1.5 Hz, 2 H), 1.22 (s, 18 H). ^{13}C NMR (acetone-d_6): 1, δ 141.4, 107.6, 76.4, 28.4; 2, δ 142.4, 137.0, 104.9, 104.6, 76.3, 76.1, 28.1; 3, δ 138.0, 101.9, 76.2, 28.1.

Isomerization Studies. The extent of isomerization was determined in acetone-d_6 and THF-d_8 solutions. A solution that was 0.014-0.03 M in diene and 10^{-5} M in rose bengal was saturated with nitrogen (acetone-d_6) or argon (THF-d_8) for 30-60 min while being protected from room lights. The sample was then irradiated for 35-60 min with continuous bubbling of the inert gas. The extent of isomerization was determined by integration of the NMR spectra (Table II).

Photooxidation Conditions. To a 1-mL volumetric flask were added 2-4 mg (0.01-0.02 mol) of the diene and 10 μL of a 10^{-3} M sensitizer solution, and the resultant mixture was diluted to volume with the NMR solvent. A portion of this solution (0.5-0.7 mL) was pipeted into a 5-mm NMR tube and saturated with oxygen for 25 min at -76 °C while being protected from the room lights. The acetone-d_6 solutions were irradiated through a 0.5% $K_2Cr_2O_7$ filter solution and the THF-d_8 and CD_2Cl_2 through a $NaNO_2$ (75 g in 100 mL of water) filter. Rose bengal was used as a sensitizer in all reactions containing acetone-d_6 and THF-d_8 and TPP in all reactions with pure CD_2Cl_2.

Acknowledgment. We thank the National Science Foundation (Grant CHE-8418603) and the Petroleum Research Foundation, administered by the American Chemical Society, for their generous support of this research.

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Communications

Synthesis and Absolute Configuration of (+)-Averufin

Summary: The absolute configuration of (+)-averufin, a key intermediate in aflatoxin biosynthesis, has been determined to be 1′-*S* by total synthesis from an intermediate whose absolute stereochemistry was established by application of the exciton chirality circular dichroism method.

Sir: Extensive radiochemical experiments with *Aspergillus parasiticus* mutants[1] and the demonstration of a shared polyketide folding pattern[2] have established a sequence of C_{20}-anthraquinone intermediates in the aflatoxin B_1 (**6**) biosynthetic pathway (Scheme I). Notably, hexanoic acid has been found to initiate[3] assembly of the hypothetical intermediate **1** which, on self-condensation and oxidation, affords norsolorinic acid (**2**). Reduction of **2** gives averantin (**3**), whose single asymmetric center[4] has been proposed to prefigure the stereochemical outcome of all subsequent transformations involving the C_6-side chain.[5] Oxidation at C-5′ of **3** and internal ketalization generates averufin (**4**), the key advanced intermediate of the aflatoxin path-

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