FMN are ineffective. It is noteworthy that FADMO undergoes the oxidation, although Enz(4a-FlHOOH) has no substituent at the 5(N)-position. Charge-transfer complexation between Enz-(4a-FlHOOH) and NAD(P)$^+$ retards the elimination of hydrogen peroxide to lead to the oxidation.[2,3a]

We used $FlEt^+ClO_4^-$ as a catalyst because of its efficiency and stability. The representative results of the $FlEt^+ClO_4^-$-catalyzed oxidation of amines and sulfur compounds are summarized in Table I. Nitrones[11] and sulfoxides, which are versatile synthetic intermediates, can be prepared in a highly efficient manner. Sulfoxides are also oxidized, although the rate of the oxidation is much slower than that of sulfides.

The present catalytic reaction can be rationalized by assuming Scheme I. 4a-FlEtOOH reacts with substrate (S) to give oxidized substrate (SO) and 4a-FlEtOH (the second-order rate constant: k_5').[4a,5,7] 4a-FlEtOH undergoes ionization (k_1, k_2) to give $FlEt^+$ which reacts with hydrogen peroxide to afford 4a-FlEtOOH (k_3, k_4), where k_1, k_2, k_3, and k_4 are pseudo-first-order rate constants.

In order to gain insight into the mechanism, the $FlEt^+$-ClO_4^--catalyzed monooxygenation of methyl phenylsulfide (**3**) with hydrogen peroxide has been investigated in detail by using a solution of H_2O_2 (15 mM), $FlEt^+ClO_4^-$ (0.25 mM), and **3** (0.1-2.0 M) in methanol at 30 °C. The observed initial rate (v, $k_5' \times [S] \times [4a\text{-FlEtOOH}]$) of the formation of methyl phenylsulfoxide (**4**) has been determined by GLC analysis of **4**. The maximum rate of the reaction (V_{max}) and the substrate concentration that produced half-maximal rate (K_m) were obtained to be 83 ± 6 mM/h and 4.0 ± 0.3 M, respectively, from Woolf double reciprocal plot. Under the same conditions, 4a-FlEtOOH reacts with **3** to give **4** and 4a-FlEtOH. The second-order rate constant k_5' in MeOH (30 °C) was determined to be 0.18 M^{-1} s^{-1} by monitoring the disappearance of 4a-FlEtOOH at 370 nm. The first-order rate constant of the decomposition of 4a-FlEtOOH (k_6) in MeOH (30 °C) to give 10a-spirohydantoin **5**[12] has been determined to be 1.6×10^{-5} s^{-1} by monitoring the disappearance of the UV absorption of 4a-FlEtOOH at 370 nm. Since k_6 is negligible, V_{max}, K_m, and the concentration of $FlEt^+$ cation ([$FlEt^+$]) can be represented by the following equations: $V_{max} = 0.25\ mM \times k_1k_3/(k_1 + k_2 + k_3) = 83 \pm 6$ mM/h, $K_m = (k_1k_3 + k_1k_4 + k_2k_4)/(k_1 + k_2 + k_3)/k_5' = 4.0 \pm 0.3$ M, $[FlEt^+] = 0.25\ mM \times (k_1k_4 + k_1k_5'[MeSPh])/(k_1k_3 + (k_1 + k_2)k_4 + (k_1 + k_2 + k_3)k_5'[MeSPh])$. Concentration of $FlEt^+$ was determined by the UV spectra of the reaction mixture (545 nm).[13] The pseudo-first-order rate constant for the reaction of $FlEt^+ClO_4^-$ with aqueous 30% H_2O_2 in MeOH (15 mM solution) to give 4a-FlEtOOH was determined by stopped-flow spectrophotometer to be 5.7 s^{-1}. These results lead to solve the above equations, giving $k_1 = 0.11$ s^{-1}, $k_2 = 0.46$ s^{-1}, $k_3 = 2.5$ s^{-1}, and $k_4 = 3.2$ s^{-1}. Therefore, the rate-determining step is the formation of $FlEt^+$ from 4a-FlEtOH.

The kinetics of the catalytic oxidation of amines is complex, because an equilibrium between $FlEt^+$ and the adduct of substrates, 4a-FlEtS (Scheme I, k_7, k_8), has to be considered. It is known that secondary amines add to $FlEt^+$ to give the 4a-amino adducts.[4a] The pseudo-first-order rate constant of the formation of 4a-FlEt-NBu_2 from $FlEt^+$ and **1** has been determined to be $>10^3$ s^{-1}. The reaction of 4a-FlEtOH with **1** in MeOH gave 4a-FlEt-NBu_2 quantitatively. The pseudo-first-order rate constants of the formation of 4a-FlEt-NBu_2 (355 nm, ϵ 7100) from 4a-FlEtOH and **1** in MeOH were determined to be constant (1.5×10^{-4} s^{-1}) upon changing the concentration of **1** (0.007-0.10 M) by monitoring the UV absorption of 4a-FlEtOH (355 nm, ϵ 8600). Apparently, 4a-FlEtOH undergoes ionization to give $FlEt^+$, which reacts with **1** to afford 4a-FlEt-NBu_2. Under the same conditions, $FlEt^+$ also reacts with H_2O_2 to give 4a-FlEtOOH because of higher nucleophilicity of OOH^- in comparison with secondary amines.[14] The v value of the oxidation of **1** (0.2 M, 0.20 mM/h) is smaller than that of **3** (0.2 M, 3.9 mM/h); however, the k_5' value of the oxidation of **1** (0.36 M^{-1} s^{-1}) is larger than that of **3** (0.18 M^{-1} s^{-1}). The k_1 value of **1** (ca. 10^{-4} s^{-1}) is smaller than that of **3** (0.11 s^{-1}), and the k_3 value of **1** is larger than that of **3**.[15] The v value of the oxidation of **3** (0.3M) in the presence of **1** (0.04 M) by using 4a-FlEtOH as the catalyst (0.015 M) was determined to be 1.4 mM/h, which is smaller than the v value (2.5 mM/h) obtained under the same conditions by using 4a-FlEt-NBu_2 as the catalyst, indicating that the k_1 value is smaller than the k_8 value. Therefore, the rate-determining step of the oxidation of secondary amines seems to be the formation of $FlEt^+$ ion (k_1).

The present catalytic oxidation is highly useful, because potential flavin hydroperoxide, which has ca. 10^4 times oxidizing potential in comparison with hydrogen peroxide,[4a] can be generated catalytically.[16]

Acknowledgment. We thank Dr. M. Sawada (The Institute of Scientific and Industrial Research, Osaka University) for use of a stopped-flow spectrophotometer and for helpful discussions.

Supplementary Material Available: A listing of observed initial rates of formation of **4** (Table S1) (1 page). Ordering information is given on any current masthead page.

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(13) [$FlEt^+$]:[4a-FlEtOH]:[4a-FlEtOOH] was determined to be 15:73:12 ([MeSPh] = 0.2 M).

(14) N_+ value of OOH^- (8) is larger than those of R_2NH (5-6) and OH^- (4.8), see: Ritchie, C. D. in *Solute-Solvent Interactions*; Coetzee, J. F., Ritchie, C. D., Eds.; Marcel Dekker: New York, 1976; Vol. 2, pp 229-270.

(15) k_3 value of **1** (under basic conditions) is larger than that of **3** (under acid conditions) because of higher concentration of OOH^- in the presence of amine substrate.

(16) Application of our process, see: Shinkai, S.; Yamaguchi, T.; Manabe, O.; Toda, F. *J. Chem. Soc., Chem. Commun.* **1988**, 1399-1401.

Formation of a Cyclopropyl Eicosanoid via an Allene Oxide in the Coral *Plexaura homomalla*: Implications for the Biosynthesis of 5,6-*trans*-Prostaglandin A_2

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Received March 13, 1989

The Caribbean soft coral *Plexaura homomalla* produces large quantities of prostaglandin (PG) A_2 (**1**) as the methyl ester acetate (ca. 2-3% of its dry weight) by a pathway which is distinct from the mammalian cyclooxygenase/endoperoxide route.[1] This alternative pathway may involve an 8-lipoxygenase and formation of an allene oxide intermediate, although there is as yet no firm evidence linking either to biosynthesis of the prostaglandins.[2] Allene oxide **2** was recently isolated from incubation of 8(*R*)-hydroperoxyeicosatetraenoic acid (**3**) with an acetone powder preparation of *P. homomalla*.[3] It is the facility with which allene oxides can form cyclopentenones[4] which makes this pathway seem attractive for the biosynthesis of PGA_2.

[†] Department of Chemistry.

[‡] Department of Pharmacology.

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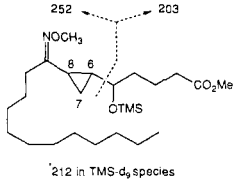
We have examined minor metabolites of arachidonic acid in *P. homomalla* in the hope of discovering intermediates or other species that might shed light on the missing steps in the pathway. These studies have yielded an unusual fatty acid containing a cyclopropyl ring. The compound is assigned as **4** on the basis of the spectral data summarized below.

Incubation of arachidonic acid with an acetone powder of *P. homomalla* var. S (collected offshore Grand Cayman Island, B.W.I.) in pH 8 Tris buffer yielded 8(*R*)-HPETE (**3**), together with several other products: these included α-ketol **5**, cyclopentenone **6**, and γ-ketol **7**.[5] Fractionation of the mixture by successive RP-HPLC and SP-HPLC yielded ~150 μg (ca. equivalent to yield of γ-ketol **7**) of a new fatty acid with an α,β-unsaturated ketone chromophore (λ_{max} = 227 nm in MeOH). Mass spectrometry with derivatization of functional groups gave a molecular weight for the carboxylic acid of 336 and an empirical formula of $C_{20}H_{32}O_4$ and indicated the presence of single carboxyl, keto, and hydroxyl groups.[6] Hydrogenation increased the molecular weight by only 4 mass units, which suggested that enone **4** contained a ring structure and two double bonds. The presence of a cyclopropyl ring was inferred from the complex multiplet in the ^{1}H NMR spectrum in the region of 1 ppm.[7]

The location of the hydroxyl group at C-5 was deduced from the mass spectral fragmentation pattern of derivatives of the hydrogenated species.[6] Spontaneous lactonization of the methyl ester to give **8** occurred over 48 h in $C^2H_2Cl_2$. After cyclization, the ^{1}H NMR spectrum showed loss of the methoxy signal (3.65 ppm) and appearance of the methyl signal for methanol (3.43 ppm); the resonance for H-5 shifted from 3.18 to 3.81 ppm. Detailed ^{1}H NMR studies were conducted on δ-lactone **8** with assignments[7] being made from a COSY spectrum aided by selective decoupling experiments. The configurations of the 10,11 and 14,15 double bonds are assigned as *E* and *Z*, respectively, on the basis of the magnitude of the vicinal coupling constants. The chemical shifts assigned to the cyclopropyl protons were almost superimposable with the reported values of model compound **9**, and comparison of coupling constants indicated that the ring substituents are trans.[8,9] Finally, the circular dichroism spectrum was featureless,[10] suggesting that cyclopropyl enone **4** may be racemic, although we were unable to resolve enantiomers by chiral phase HPLC.

(5) Arachidonic acid (70 mg) was incubated with an acetone powder[2] (5.6 g) of *Plexaura homomalla* in 1.8 L of pH 8 Tris buffer containing 1 M NaCl for 40 min at room temperature.

(6) Deduced from the electron impact mass spectra of derivatives of **4**: methyl ester TMS ether derivative, M^+ = 422; the corresponding TMS-d_9, M^+ = 431; derivatization to the methyloxime increased the molecular weight by 29 amu, and hydrogenation increased the molecular weight by 4 amu. Location of the hydroxyl at C-5 was deduced from the mass spectra of derivatives of hydrogenated **4**: the base peak of the methyl ester methyloxime TMS ether was observed at *m/z* 252. The complimentary ion at *m/z* 203 (M^+ − 252 = 203) was shifted to 212 in the corresponding TMS-d_9 derivative, with the base peak (*m/z* 252) unchanged.



(7) Lactone **8**: ^{1}H NMR (400 MHz, $C^2H_2Cl_2$) H2a (2.415, m [6 lines], H2b (2.523, m), H3a (1.73–1.88, m), H3b (1.88–2.00, m), H4a (1.61–1.74, m), H4b (1.95–2.10, m), H5 (3.814, m [7 lines]), H6 (1.64–1.74, m, $J_{6,7a}$ = 6.1 Hz), H7a (0.91–1.00, m [8 lines], $J_{7a,8}$ = 8.2 Hz, $J_{7a,7b}$ = 3.8 Hz), H7b (1.22–1.31, m), H8 (2.25–2.33, m), H10 (6.248, d-t, $J_{10,11}$ = 15.7 Hz, $J_{10,12ab}$ = 1.5 Hz), H11 (6.937, d-t, $J_{11,12}$ = 6.5 Hz), H12ab (2.24–2.34, m), H13ab (2.20–2.28, m), H14,15 (5.31–5.48, m, $J_{14,15}$ = 10.76 Hz), H16ab (2.035, ~q), H17ab (1.25–1.45, m), H18-19ab (1.20–1.35, m [br]), H20abc (0.886, t). $J_{10,11}$, $J_{11,12}$, and $J_{14,15}$ were measured in benzene-d_6.

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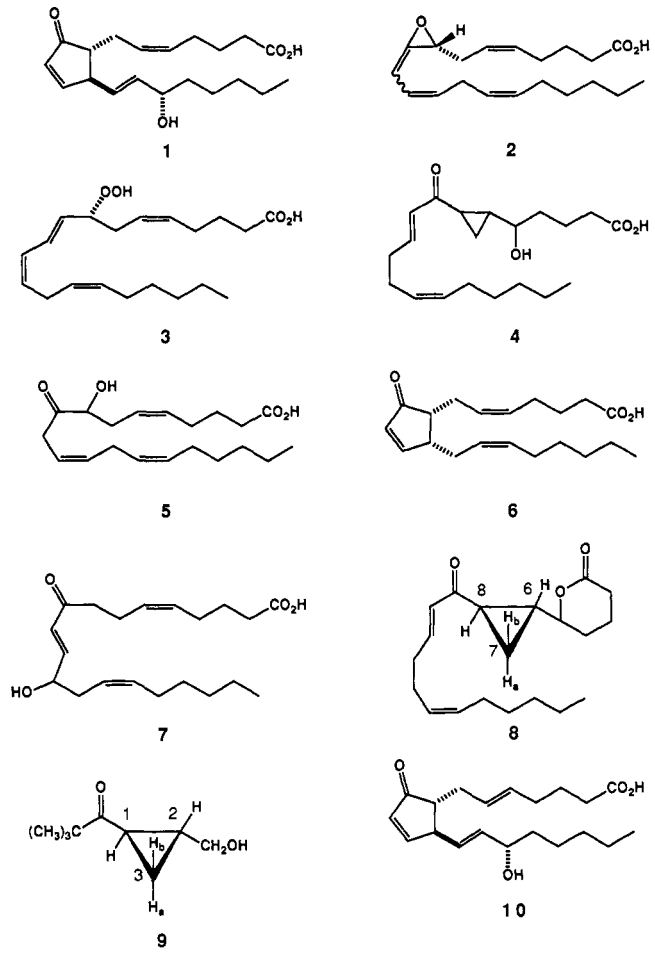
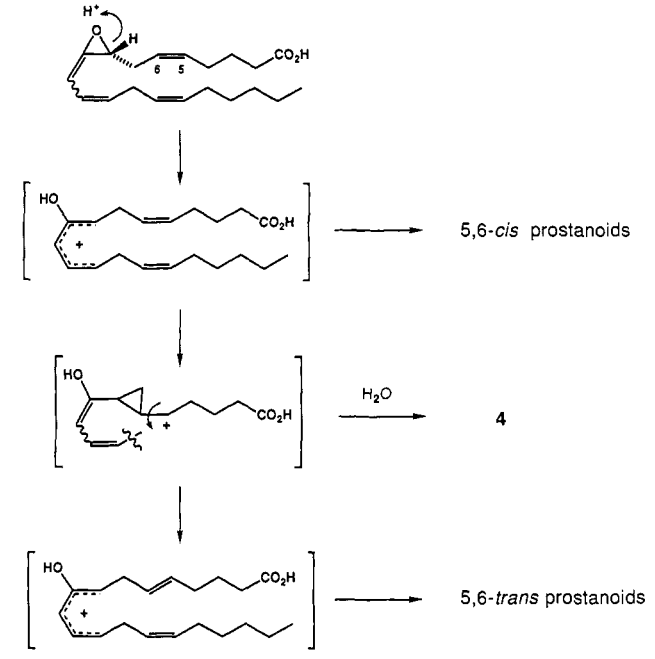
(9) ^{1}H NMR for **9**: (250 MHz, CCl_4) H1 (2.16), H2 (1.60), H3a (0.89, $J_{1,3a}$ = 8.1 Hz [cis], $J_{2,3a}$ = 5.6 Hz [trans], $J_{3a,3b}$ = 4.1 Hz [gem]), H3b (1.16).[8]

(10) The CD spectrum was recorded at a concentration in CH_3CN which yielded an absorbance of ~1.3 au at 227 nm.

Chart I



Scheme I



Cyclopropyl enone **4** is a solvolysis product of allene oxide **2**. Aliquots (10 μg) of purified **2**[3] were hydrolyzed in (1) 5 mL of a 50 mM pH 8 Tris buffer at room temperature, (2) the same buffer containing 10 mg/mL coral acetone powder, and (3) buffer containing 10 mg/mL of boiled coral acetone powder. Addition of allene oxide **2** to buffer alone gave α-ketol **5**, cyclopentenone **6**, and γ-ketol **7** but not cyclopropyl fatty acid **4**. In contrast,

4 appeared as an additional product when 2 was added to the buffer containing either intact or boiled coral acetone powder.[11] Thus, constituents of the coral mediate formation of cyclopropyl fatty acid 4 from allene oxide 2.

Prostaglandin A_2 isolated from *P. homomalla* contains 3-15% of the unusual 5,6-trans double bond isomer **10**.[12,13] The origin of **10** is an intriguing biochemical problem in that 5,6-*trans*-arachidonic acid has not been found in the coral.[14] However, 5,6-*cis*-arachidonic acid could give rise to 5,6-*trans*-prostaglandin A_2 by isomerization at a later step. Solvolysis of allene oxide **2** involves heterolytic cleavage of the C8-oxygen bond to yield a carbocation (Scheme I), which if correctly constrained can delocalize over the 5,6-double bond and give trans orientation of substituents on the resulting cyclopropyl ring. Hydrolysis of the cyclopropylcarbinyl cation would give **4**. However, if the lifetime of the cation is sufficient, rotation about the 5,6-bond would occur, and a 5,6-trans double bond could arise by reopening of the cyclopropyl ring.[15] In effect, cyclopropyl fatty acid **4** may be solvolytic trapping evidence for the existence of a cyclopropylcarbinyl cation intermediate in the pathway to 5,6-*trans*-prostaglandins in the coral.

Acknowledgment. The cooperation of the Department of Development & Natural Resources of the Cayman Islands in collection of samples of *P. homomalla* is gratefully acknowledged. We thank Christiana D. Ingram for technical assistance. Research was supported by Grants DK-35275 and ES-07028 from the U.S. Public Health Service.

(11) Taking the HPLC peak areas at 205 nm as an approximate quantitation of the allene oxide-derived products, the relative proportions were as follows: (a) in buffer only, γ-ketol **7** ~0.2, cyclopropyl fatty acid **4** not detected (<0.01), α-ketol **5** ~10, and cyclopentenone **6** ~1. (b) In the presence of coral, the relative proportions were ~0.4, ~1, ~10, ~1, respectively. Hydrolysis in the presence of coral gave a mixture of 11*Z* and 11*E* isomers of α-ketol.

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(15) The relatively low barrier for rotation of the cyclopropyl group in 1,1-dimethylcyclopropylcarbinyl cation (13.7 Kcal/mol) is compatible with an isomerization occurring under ambient conditions, see: Kabakoff, D. S.; Namanworth, E. *J. Am. Chem. Soc.* **1970**, *92*, 3234.

Dynamic Quenching of the Metal-to-Ligand Charge-Transfer Excited State of $Cu_4I_4(pyridine)_4$. Exciplex Formation and Self-Quenching

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Received March 6, 1989

Recently, it has been demonstrated that the lowest lying, triplet metal-to-ligand charge-transfer state (MLCT*) of the copper(I) complex $Cu(dmp)_2^+$ (dmp = 2,9-dimethyl-1,10-phenanthroline) is quenched by various Lewis bases in solution.[1,2] The mechanism proposed by McMillin[1a] involves association between the (formally) Cu(II) center of the MLCT* and the two-electron donor to form a shorter lived, nonemissive five-coordinate exciplex. Another Cu(I) complex shown to be luminescent in ambient temperature solution is the tetranuclear cluster $Cu_4I_4py_4$ (I, py = pyridine),

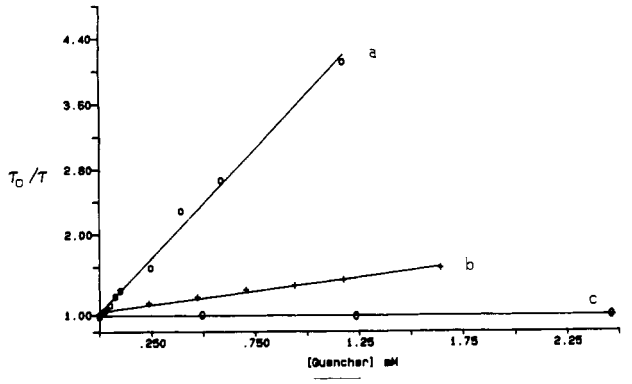

Figure 1. Stern-Volmer plots of the dependence of τ (MLCT) for $Cu_4I_4py_4$ on added quencher concentration in benzene solution (21 ± 1 °C). Quenchers are (a) pyridine, (b) 2,6-dimethylpyridine, and (c) 2,6-di-*tert*-butylpyridine.

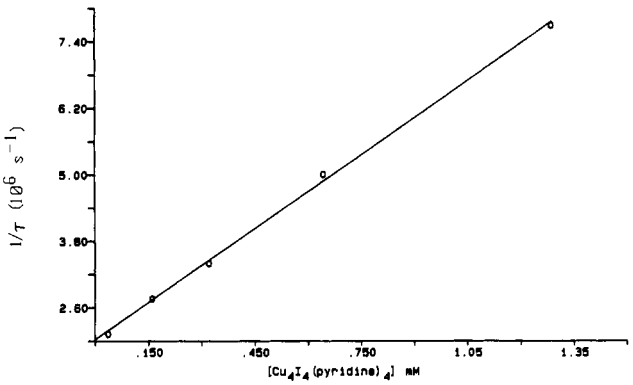

Figure 2. Plot of τ^{-1} (MLCT*) vs $[Cu_4I_4py_4]$ in benzene solution (21 ± 1 °C).

which displays emissions from two remarkably uncoupled states, a MLCT* (λ_{max} = 490 nm, τ = 0.45 μs) and a lower energy metal cluster centered state (MCC*) (λ_{max} = 690 nm, τ = 10.7 μs).[3] Described herein is the demonstration that the MLCT*, *but not the MCC**, of I is subject to analogous dynamic quenching by Lewis bases. Also described is an unusual example of self-quenching of this cluster's MLCT emission which we attribute to bimolecular energy transfer from the higher energy MLCT* of one I to the MCC* of another I. These observations are further manifestations of the remarkably uncoupled nature of these two states.[3]

Addition of pyridine to a $Cu_4I_4py_4$ solution in dry, deaerated benzene led to systematic decreases in the MLCT* emission lifetime,[4,5] but the MCC* lifetime remained invariant within experimental error. Figure 1a depicts the Stern-Volmer plot[6] of τ_0/τ vs [py] (where τ_0 is MLCT* lifetime, 0.45 μs, in the absence of added quencher). The plot is linear with an intercept of 1.0 ± 0.06 and a slope (K_{SV}) of 270 ± 10 M^{-1}. Given that $K_{SV} = k_q\tau_0$, the bimolecular quenching constant k_q equals 5.9 ± 0.5 × 10^9 M^{-1} s^{-1}. Energy transfer from the MLCT* to free pyridine

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(4) (a) Emission lifetimes at 21 ± 1 °C were measured by using an apparatus based on a Quanta-Ray DCR-1A Nd:YAG pulse laser with harmonic generator operating at 355 nm. The emission was monitored at right angles at 510 (MLCT) or 690 (MCC) nm with an RCA 8852 or EMI 9816A PMT through a Spex double monochromator. The PMT signal was processed by a Tektronix 7912AD transient digitizer and a Tektronix 4052 or Zenith ZF-158-24 microcomputer.[4b] (b) Weber, W.; DiBenedetto, J.; Offen, H.; van Eldik, R.; Ford, P. C. *Inorg. Chem.* **1984**, *23*, 2033-2038.

(5) Benzene (Burdick and Jackson high purity grade) was dried over CaH_2 and distilled under N_2 before use. Pyridine (Fisher), 2,6-dimethylpyridine (Aldrich), and 2,4-di-*tert*-butylpyridine (Aldrich) were dried over KOH pellets and distilled under N_2. All solutions and quenchers were deaerated by bubbling with dinitrogen.

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