suming that the asymmetry parameter is 0. By use of the known viscosity of CO_2, the oxygen quadrupole coupling constant of CO_2 is estimated to be about 3.4 MHz. While we could not find a literature value for CO_2 to which this can be compared, the value compares reasonably well to the 4.4 MHz reported for the ^{17}O quadrupole coupling constant of CO.[17]

In conclusion, we believe that these results demonstrate the potential of supercritical fluid solvents for the acquisition of high-resolution NMR spectra of quadrupolar nuclei. We are examining other nuclei and nonvolatile compounds and will report those results in future publications.

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N-Alkylporphyrin Formation during the Reactions of Cytochrome P-450 Model Systems†

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We have recently found that the electronegatively substituted hemin [5,10,15,20-tetrakis(2,6-dichlorophenyl)porphinato]iron(III) chloride (**1**) is an effective catalyst for the rapid oxidation of organic compounds with the oxidant iodosopentafluorobenzene (**2**).[1] Unlike all other hemin catalysts so far described, compound **1** is especially robust. We have, for instance, measured 10000 turnovers, at room temperature, for the epoxidation of norbornene! During our studies we noticed that the reaction solution was at first green. However, at the end of the reaction, the hemin was either destroyed (no or very resistant substrate), returned to its original spectrum (reactive substrate), or changed to a new species having a different spectrum. The latter observation occurred mostly with terminal olefins.

Recently, isolations of *N*-alkylporphyrins from the livers of animals treated with cytochrome P-450 inhibitors such as terminal olefins and acetylenes, monoalkylhydrazines, 4-alkyl-3,5-bis-(ethoxycarbonyl)-2,6-dimethyl-1,4-dihydropyridines, and 1-aminobenzotriazoles have been reported.[2] The *N*-alkyl hemes, derived from such suicide inhibitors, have been shown to result in hepatic porphyrias accompanied by the formation of the so-called "green pigment".

Since the hemin **1** can catalyze numerous turnovers, it might be used to explore the less frequent P-450 chemistry wherein suicide labeling of liver microsomes occurs approximately 1 in 200 turnovers. In this paper we report a reaction that closely mimics the self-catalyzed inactivation of P-450 enzymes.

In a typical experiment the oxidant **2** (1 g) was added in five portions, every 15 min, to a mixture of the hemin **1** (50 mg) and 4,4-dimethyl-1-pentene (**3**, 3 g) in dichloromethane (50 mL) and the mixture stirred at room temperature for 15 min.[3] The solution

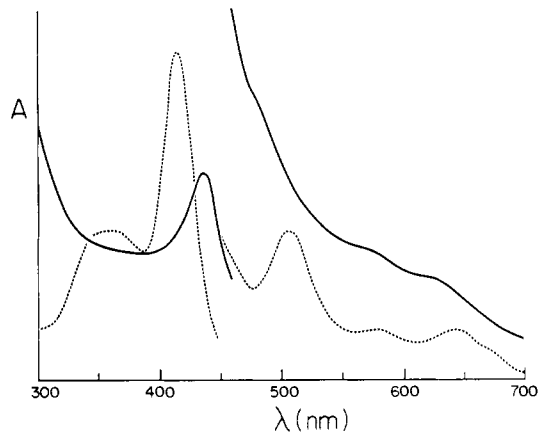

Figure 1. Visible absorption spectra, in CH_2Cl_2, of the reaction mixtures of hemin **1** and 4,4-dimethyl-1-pentene (**3**) before (---) and after (—) the addition of iodosopentafluorobenzene (**2**).

changed from brown to green-brown and the reaction was monitored by the disappearance of the Soret band of **1** (417 nm) coupled with the development of a new band at 435 nm (Figure 1). The remaining oxidant was destroyed with 10% aqueous sodium metabisulfite (10 mL), and the green product was demetalated in a mixture of concentrated HCl (1 mL) and acetic acid (20 mL). After chromatography the *N*-alkylporphyrin **4**[4] was isolated in 53% yield.

Metalation of **4** with $FeCl_2$ in refluxing THF[5] followed by workup in dichloromethane using 1% aqueous HCl and then H_2O gave the aquoiron(III) complex **5**.[6] Addition of the oxidant **2** to **5**, in dichloromethane, gave virtually the same optical spectrum (λ_{max} 435, 570, and 620 nm) as that of the initial green-brown reaction mixture. The analogous spectrum was obtained when a solution of **5**, in dichloromethane, which had been previously treated with 1% aqueous HCl[7] or saturated aqueous $NaHCO_3$[8]

† Presented in part at the 36th Southeastern Regional Meeting of the American Chemical Society, Raleigh, NC, Oct 24–26, 1984.

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(2) Ortiz de Montellano, P. R.; Correia, M. A. *Ann. Rev. Pharmacol. Toxicol.* **1983**, *23*, 481 and references therein.

(3) The principal product from the reaction is the epoxide. Thus during a catalytic experiment a solution of the hemin **1** (10^{-4} mmol) in 20 μL of dichloromethane was added to **2** (2 mg, 6.5×10^{-3} mmol) and **3** (0.2 mmol) in 80 μL of dichloromethane. The suspension was shaken until the oxidant dissolved. This required about 3 min. Analysis of the reaction mixture on GLC with Carbowax-20M showed that the yield of epoxide was close to 100% based upon **2**. A diluted sample of the reaction mixture had a Soret absorption at 435 nm. The same results were obtained when the reaction was run under argon in the absence of air.

(4) 21-(4,4-Dimethyl-2-hydroxypentyl)-5,10,15,20-tetrakis(2,6-dichlorophenyl)porphine (**4**): mp 285–286 °C (CH_2Cl_2–hexane). Anal. Calcd for $C_{51}H_{36}N_4OCl_8(CH_2Cl_2)_{0.45}$: C, 59.27; H, 3.57; N, 5.37. Found: C, 59.54; H, 3.66; N, 5.07. Calcd *m/e* for $^{12}C_{51}{}^1H_{36}{}^{14}N_4{}^{16}O^{35}Cl_8$: 1000.0397. Found: 1000.0355. UV λ_{max} (CH_2Cl_2, log ε) 428 (5.41), 521 (4.57), 555 (4.36), 608 (4.16), 665 (v weak) nm. This optical spectrum is comparable to that of the *N*-alkylporphyrin derived from protoporphyrin after the liver microsomal metabolism of allylisopropylacetamide: Ortiz de Montellano, P. R.; Mico, B. A.; Yost, G. S. *Biochem. Biophys. Res. Commun.* **1978**, *83*, 132–137. IR ν_{max} (KBr pellet) 3300 (NH), 3580 (OH) cm^{-1}. ^1H NMR (CD_2Cl_2) δ −4.48 (d of d, J_{AB} = 14.5, J_{AX} = 2.2 Hz, NCH_AH_B), −4.21 (d of d, J_{AB} = 14.5, J_{BX} = 11.1 Hz, NCH_AH_B), −2.28 (d of d, J_{AB} = 14.2, J_{AX} = 4.2 Hz, $CH_AH_BC(CH_3)_3$), −2.18 (br s, NH), −0.92 (d of d, J_{AB} = 14.2, J_{BX} = 6.1 Hz, $CH_AH_BC(CH_3)_3$), −0.68 (s, $C(CH_3)_3$), −0.54 (d, *J* = 5.6 Hz, OH), 0.64–0.72 (m, CHOH), 7.63–7.98 (m, phenyl H × 12), 8.32–8.43 (m, pyrrole H × 8).

(5) Anderson, O. P.; Kopelov, A. B.; Lavallee, D. K. *Inorg. Chem.* **1980**, *19*, 2101.

(6) [21-(4,4-Dimethyl-2-oxidopentyl)-5,10,15,20-tetrakis(2,6-dichlorophenyl)porphinato]aquoiron(III) chloride **5**: Anal. Calcd for $C_{51}H_{36}N_4O_2Cl_9Fe$: C, 55.10; H, 3.26; N, 5.04. Found: C, 55.23; H, 3.52; N, 4.84. UV λ_{max} (CH_2Cl_2, log ε) 425 (sh), 444 (4.70), 455 (sh), 556 (3.93), 599 (3.88), 640 (sh), 670 (sh). IR ν_{max} (KBr pellet) 1750, 3420 (H_2O) cm^{-1}. An example of the five-membered chelate ring formation of the N-substituent in an iron (*N*-alkylporphyrin) complex was shown by: Mansuy, D.; Battioni, J.-P.; Akhrem, I.; Dupré, D.; Fischer, J.; Weiss, R.; Morgenstern-Badarau, I. *J. Am. Chem. Soc.* **1984**, *106*, 6112.

(7) Chemical and spectroscopic properties of the species generated by this treatment suggest it is the chloride **6** (Scheme I): UV λ_{max} (CH_2Cl_2) 425, 442, 510, 580 nm; MS, *m/e* 1054 (M^+ − Cl).

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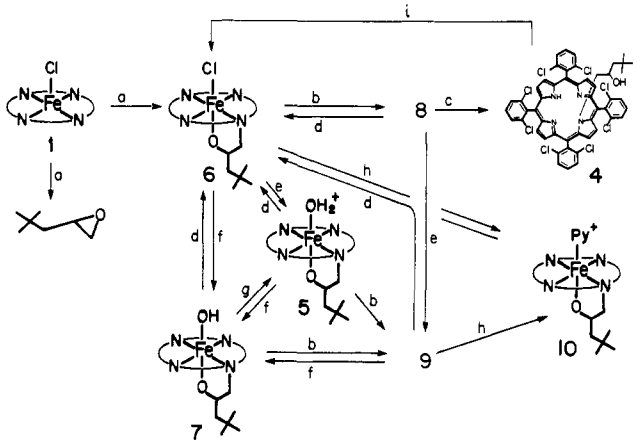
Scheme I. Interconversions of the *N*-Alkylporphyrin and Its Iron Complexes[a]



[a] (a) 4,4-Dimethyl-1-pentene, C_6F_5IO/CH_2Cl_2; (b) C_6F_5IO/CH_2Cl_2; (c) concentrated HCl/AcOH; (d) 1% aqueous HCl/CH_2Cl_2; (e) H_2O/CH_2Cl_2; (f) aqueous $NaHCO_3/CH_2Cl_2$; (g) $AcOH/CH_2Cl_2$; (h) pyridine/CH_2Cl_2; (i) $FeCl_2$/THF.

was treated with **2**. All of the species shown in Scheme I were interconvertible, though gradual decomposition of **8** and **9** was observed spectroscopically. These observations suggest that **8** and **9** may be the [chloro(pentafluorophenyl)iodoxo]iron(III) and the [hydroxo(pentafluorophenyl)iodoxo]iron(III) complexes.[9] The ferric oxidation state in **8** and **9** is supported by their rhombic ESR spectra (g = 8.57, 5.35, 2.05, CH_2Cl_2, -196 °C), which change to those of typical low-spin ferric complexes (g = 2.38, 2.14, 1.94) on the addition of pyridine.[10]

In most respects hemins and iodosobenzene mimic the hydroxylations and epoxidations catalyzed by the cytochromes P-450.[11] The additional parallels reported here, where an in vitro system mimics the suicide inhibitors characteristic of microsomal P-450, add further support to the validity of using the chemical to model the enzymic systems.

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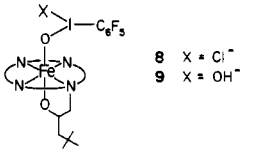
Registry No. **1**, 91042-27-2; **2**, 827-15-6; **3**, 762-62-9; **4**, 96326-84-0; **5**, 96326-85-1; **6**, 96326-86-2; **7**, 96326-87-3; **8**, 96326-88-4; **9**, 96326-89-5; **10**, 96326-90-8; cytochrome P-450, 9035-51-2.

(8) We tentatively assigned the hydroxide structure **7** for the species generated by this treatment (Scheme I): UV λ_{max} (CH_2Cl_2) 361, 444, 570, 585, 640 nm.

(9) The reversible formation of **8** and **9** from 6 and **5**, coupled with the ESR results, suggests the structures shown. The coordination of iodoso-



8 X = Cl^-
9 X = OH^-

benzene to manganese(IV) porphyrins in the chloro-, acyloxy-, and alkoxy(phenyl)iodoxo forms has been reported. Smegal, J. A.; Hill, C. L. *J. Am. Chem. Soc.* **1983**, *105*, 2920. Smegal, J. A.; Schardt, B. C.; Hill, C. L. *J. Am. Chem. Soc.* **1983**, *105*, 3510. Birchall, T.; Smegal, J. A.; Hill, C. L. *Inorg. Chem.* **1984**, *23*, 1910. The iodosopentafluorobenzene (**2**) is essential for the conversion of **6** and **5** (or **7**) to **8** and **9**. Neither *m*-chloroperbenzoic acid nor *tert*-butyl hydroperoxide gave any **8** or **9**.

(10) The structure assigned to **10** is most likely for the species formed in the presence of excess pyridine (Scheme I). UV λ_{max} (CH_2Cl_2-1 drop of pyridine) 432, 585 (sh), 618 (sh) nm. The *N*-alkyl group prevents coordination on both sides of the metal, a similar reaction, $[Fe^{III}(N\text{-MeOEP})Cl]^+$ + pyridine ⇄ $[Fe^{III}(N\text{-MeOEP})py]^{2+}$ + Cl^- ($K \sim 1.66$ (where OEP = octaethylporphyrin), has been previously reported: Ogoshi, H.; Kitamura, S.; Toi, H.; Aoyama, Y. *Chem. Lett.* **1982**, 495.

(11) Groves, J. T.; Nemo, T. E. *J. Am. Chem. Soc.* **1983**, *105*, 5786 and references therein.

Formation of an Iron(IV)-Oxo "Picket-Fence" Porphyrin Derivative via Reduction of the Ferrous Dioxygen Adduct and Reaction with Carbon Dioxide

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The catalytic cycle of cytochrome P 450 involves the binding of molecular oxygen to the ferrous heme protein and the conversion of this dioxygen adduct to a high-valent iron-oxo heme derivative with two oxidation equivalents above iron(III).[3-5] Synthetic metalloporphyrin-dioxygen complexes have been obtained which model the spectroscopic properties of the oxy states of P 450 and cobalt-substituted P 450_{CAM}.[6-9] The conversion of such complexes into reactive high-valent iron-oxo species has so far not been achieved. However, acylation of a manganese(III)-peroxo system by acid chlorides has been described by Groves et al.[10] and formation of an iron(IV)-oxo-porphyrin radical cation by reaction with acid chlorides and acid anhydrides was reported by Khenkin et al.[11] In this paper, we show that the peroxo-iron(III)-porphyrin derivatives which can be obtained by chemical reduction of ferrous-porphyrin-dioxygen adducts are converted into iron(IV)-oxo-porphyrin derivatives by reaction with carbon dioxide.

Reaction of the known $(THF)_2$-iron(II)-tetrakis(pivaloylphenyl)porphyrin derivative, $[Fe(THF)_2TP(piv)P]$[12] with O_2 at -40 °C in dry degassed THF resulted in the formation of the ferrous dioxygen adduct $[Fe(O_2)(THF)TP(piv)P]$[13] (**1**). The visible spectrum of **1** showed bands at 419 and 538 nm. Treatment of **1**, after purging the solution under vacuum at -40 °C in order to remove noncoordinated dioxygen, with a 1 to 1 equiv THF solution of sodium bis(2-methoxyethoxy)aluminum hydride (Redal) yielded species **2** having a visible spectrum with bands at 438, 563, and 604 nm (Figure 1) and EPR spectral properties ($g \simeq 2$, 4.2, 8) very close to those known for the peroxo-iron(III) porphyrin derivatives.[14-16] These results indicated the formation

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(8) Schappacher, M.; Ricard, L.; Weiss, R.; Montiel-Montoya, R.; Gonser, U.; Bill, E.; Trautwein, A. *Inorg. Chim. Acta* **1983**, *78*, L9-L12.

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(12) $Fe(THF)_2TP(piv)P$ was prepared by zinc-amalgam reduction of [Fe(Br)TP(piv)P] in THF. See also: Collman, J. P.; Gagne, R. R.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, W. T. *J. Am. Chem. Soc.* **1975**, *97*, 1427-1439.

(13) $[Fe(THF)_2TP(piv)P]$ absorbs O_2 in the solid state to form $[Fe(O_2)(THF)_2TP(piv)P]$; see ref 12.

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