tractions, and interligand steric repulsions. If this structure occurs also in solutions of low-polarity solvents, it accounts for the solubility of the complex in such solvents and indicates that LAS might effect membrane transport of transition-metal-ammine complexes.

It is of interest to compare this structure with that of the 1:1 complex of LAS with the cation of (*R*)-(+)-1-amino-1-(4-bromophenyl)ethane.[7] In the 1:1 complex, hydrogen bonds from the $-NH_3^+$ group to O(2), O(6), and O(8) (using the numbering scheme shown in I) were found with N···O distances ranging from 2.80 to 2.90 Å. A similar pattern of hydrogen bonding is observed in the present structure between $N(2)H_3$ and ligand B, except for the bifurcation of the bond from N(2)H(3) (Table III). Ligand B also bonds to $N(1)H_3$, $N(4)H_3$ (long bond), $N(5)H_3$, and $N(6)H_3$. In the 1:1 complex LAS has the usual cyclic conformation, and the pattern of intraligand hydrogen bonding is the same as that of ligand B in the present structure. The O···O hydrogen bond distances reported for the 1:1 complex are all within 0.05 Å of those found here for ligand B.

To our knowledge, this is the first reported X-ray crystal structure of a second-sphere complex involving a *natural* ionophore. It is also the first structure in which *three* carboxylic ionophores are bound to the same cation. As in structures of complexes of carboxylic ionophores with "bare" metal cations, the LAS ligands surround the cation with polar groups directed inward, thus creating a hydrophobic exterior that permits the large, trivalent cation to be dissolved in solvents of low polarity. It is anticipated that other natural, carboxylic ionophores will form similar complexes with inorganic ammines.

Acknowledgment. This work was partially supported by a grant from the National Institutes of Health (GM 37189).

Supplementary Material Available: Tables of bond distances, bond angles, torsion angles, anisotropic thermal parameters, and fractional coordinates and isotopic thermal parameters for hydrogen atoms (23 pages); a table of observed and calculated structure factor amplitudes (47 pages). Ordering information is given on any current masthead page.

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Models for Cytochrome P450 Prosthetic Heme Alkylation. Reaction of Diazoacetophenone with (Tetraphenylporphyrinato)iron(II) Chloride

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The reaction of diazoacetophenone with (tetraphenylporphyrinato)iron(II) yields [*N*-(2-phenyl-2-oxoethyl)tetraphenylporphyrinato]iron(II) chloride. The structure of this product has been established by spectroscopic methods and by X-ray crystallography. The crystal structure shows that the first carbon of the *N*-alkyl group is 2.94 Å from the iron atom and that the oxygen of the *N*-alkyl group points away from the iron. No evidence is seen for the Fe-C-N product expected from insertion of the diazo carbon into the metalloporphyrin iron-nitrogen bond or for intermediates in which the oxygen of the *N*-(2-phenyl-2-oxoethyl) group is coordinated to the iron. These results suggest it is unlikely that carbene-insertion or oxygen-coordinated intermediates will be detected during the N-alkylation of cytochrome P450 by diazo ketones. The results also rationalize the failure to detect iron-chelated enol species during N-alkylation of the prosthetic group of cytochrome P450 by catalytically activated phenylacetylene.

The cytochrome P450 catalyzed reduction of polyhalogenated hydrocarbons gives rise to semistable complexes with Soret bands at 450-490 nm.[1-3] Thus, enzymatic reduction of carbon tetrachloride yields a species with a Soret band at 460 nm believed to be the complex of dichlorocarbene with the ferrous prosthetic heme group ($Fe{=}CCl_2$).[1] The feasibility of this structural assignment is supported by the chemical synthesis and characterization of the (tetraphenylporphyrinato)iron(II)-dichlorocarbene complex.[4,5] The reduction of halothane (2,2,2-trifluoro-1-chloro-1-bromoethane) by cytochrome P450 yields a complex with a Soret band at 470 nm. This was first thought to be the analogous 2,2,2-trifluoroethylcarbene-iron complex, in part because the reaction of cytochrome P450 with 1,1,1-trifluoro-2-diazoethane yields a complex with a very similar Soret maximum (468 nm).[6,7] However, studies of the complex formed in the reaction of halothane with (tetraphenylporphyrinato)iron(II),[8] of the halocarbons produced when the cytochrome P450 complex decomposes,[9] and of the EPR properties of the model and enzymatic complexes[3] have led to the revised proposal that halothane yields a complex in which the 2,2,2-trifluoro-1-chloroethyl anion is coordinated to the prosthetic heme iron atom. Key support for this structural revision is provided by EPR evidence that the halothane complexes are low-spin paramagnetic (ferric) species whereas the putative carbene complexes are low-spin diamagnetic (ferrous) species.[3] The formation of carbene-iron and σ-bonded alkyl-iron complexes in the chemical reactions of ferrous porphyrins with halocarbons thus provides indirect support for the formation of similar types of complexes in the reductive reactions of cytochrome P450 with halocarbons.

The oxidation of a 3-((arylthio)ethyl)-4-methylsydnone by cytochrome P450 was recently shown to result in the formation of pyruvic acid and *N*-vinyl heme.[10] *N*-Vinyl heme formation is readily rationalized by enzymatic oxidation of the sydnone to a diazoalkane, insertion of the diazoalkane into one of the iron-nitrogen bonds of the heme group, and intramolecular β-elimination of the thioaryl moiety. This process occurs without the

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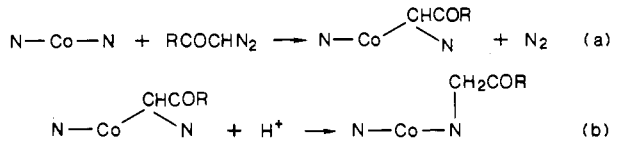
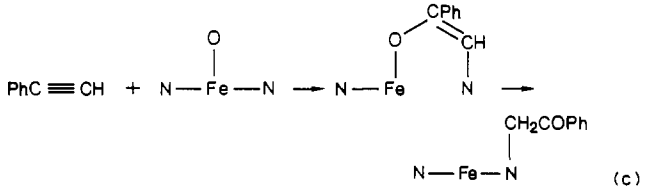
formation of spectroscopically detectable intermediates when the sydnone is incubated with purified, reconstituted cytochrome P450b.[11] This contrasts with the only report in the literature of the reaction of a diazoalkane with cytochrome P450, that of 1,1,1-trifluoro-2-diazoethane with liver microsomes, which yields a complex with a Soret band at 468 nm.[7] As already noted, this was first thought to be a carbene complex but is now thought to be a σ-bonded alkyl-iron complex.[3] Nevertheless, the reactions of cytochrome P450 with diazoalkanes have essentially not been investigated and therefore remain particularly obscure.

Diazo compounds react with cobalt porphyrins to give products with the carbon of the diazo functionality inserted into one of the cobalt–nitrogen bonds (reaction a).[12-16] The carbon-bridged

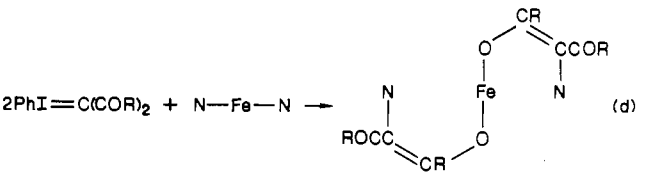


species can then be converted to the *N*-alkylporphyrin by reaction with acids under conditions that favor reduction of the cobalt (reaction b).[12,13,16] Cobalt–carbene complexes, which conceivably are precursors of the Co–CH(COR)–N bridged species, have not been detected in the reactions of diazo compounds with cobalt porphyrins, although carbene complex formation has been clearly demonstrated in the reaction of carbon tetrachloride with iron tetraphenylporphyrin.[4,5] However, to our knowledge, the reactions of iron porphyrins with diazoalkanes have not been described except for the very early, and at this point relatively uninformative, study by Clezy and Morell of the reaction of diazomethane with hemin chloride.[17]

The oxidation of terminal acetylenes by cytochrome P450 results in N-alkylation of the prosthetic heme group.[18-20] The *N*-(2-oxoalkyl) heme adducts thus obtained reflect addition of a porphyrin nitrogen to the terminal carbon and the catalytically activated oxygen to the internal carbon of the acetylenic bond:



Analysis of the probable reaction trajectories suggests that N-alkylation should produce a species in which the oxygen added to the triple bond is still coordinated to the iron because a proton is required to disrupt the iron–oxygen bond. Alkylation of the prosthetic group of cytochrome P450 by acetylenes can thus be viewed formally as insertion of an O—C=C group into one of the Fe—N bonds. Exactly the same adduct can, in principle, be formed in reactions of cytochrome P450 with diazo ketones (equations a and b). Metalloporphyrins with an O—C=C bridge between the metal and one of the pyrrole nitrogens have recently been prepared by Mansuy et al. by reaction of iron tetraarylporphyrins with a dicarbonyl-substituted carbon equivalent of iodosylbenzene:[21,22]



In order to clarify the mechanisms of the reactions of cytochrome P450 with diazoalkanes and acetylenes, particularly the nature of the adducts present before denaturation of the proteins, we have undertaken parallel investigations of the reactions of diazoalkanes with cytochrome P450 and iron tetraphenylporphyrin. We report here the structure of the product formed in the reaction of diazoacetophenone with iron tetraphenylporphyrin and discuss the implications of the results for the structures of heme adducts formed with cytochrome P450.

Methods and Materials

Analytical and Spectroscopic Methods. Routine electron impact (70 eV) mass spectra were obtained on a Kratos MS 25 instrument. The mass spectra of *N*-alkylporphyrins and metalloporphyrins were obtained by the LSIMS technique[43] on a Kratos MS 50 instrument using sulfolane as the matrix. Electronic absorption spectra were recorded on a Hewlett-Packard 8450A diode array spectrophotometer. Infrared spectra were obtained on a Nicolet FT/IR 5 DX spectrophotometer in $CHCl_3$. Routine ^1H NMR spectra were obtained in deuteriated chloroform on a Varian FT-80 instrument. Chemical shift values were determined relative to the proton signal of chloroform at 7.26 ppm. Porphyrin ^1H NMR spectra were recorded on a General Electric GN 500 spectrometer equipped with a Nicolet 1280 data system. Solutions of 50–100 μg of the porphyrins in 0.3 mL of deuteriated chloroform were employed. ^{13}C NMR spectra were obtained in 10-mm tubes on the GN 500 spectrometer operating at a probe frequency of 125.77 Hz. Chemical shifts are given in parts per million relative to the internal tetramethylsilane peak at 77.5 ppm. The magnetic susceptibility was determined by the method of Evans[23] on the GN 500 instrument. EPR spectra were obtained at −196 °C on a Varian Model E-104 instrument cus'om-interfaced with an IBM XT computer. Cyclic voltammetry was carried out in CH_2Cl_2 with 0.1 M tetrabutylammonium perchlorate as the supporting electrolyte on a Bioanalytical Systems voltammograph. The working electrode was a platinum disk, the counter electrode a platinum wire, and the reference electrode saturated calomel.

X-ray Data Collection, Solution, and Refinement. Dark green orthorhombic plates of $C_{54}H_{39}Cl_5FeN_4O$, M_r = 993.04, crystallize from CH_2Cl_2–pentane in the space group $P2_12_12_1$ with cell dimensions (at 130 K) of a = 10.132 (3) Å, b = 17.383 (6) Å, and c = 25.679 (8) Å. For Z = 4, D_{calcd} = 1.46 g cm^{-3}. Data were collected at 130 K by using Mo Kα radiation (λ = 0.71069 Å) on a Syntex $P2_1$ diffractometer to a 2θ maximum of 48°. A total of 4029 reflections were collected, of which 3908 were unique. Of these, 2963 with $I > 3\sigma(I)$ were retained for solution and refinement of the structure. No decay in the intensities of two standard reflections was observed during the course of data collection. The structure was solved by a combination of Patterson and Fourier methods and was refined to a final R value of 0.074. An absorption correction was applied. Final refinement was carried out with anisotropic thermal parameters for Fe and Cl atoms. Hydrogen atoms bonded to carbon were included at calculated positions by using a riding model, with C–H at 0.96 Å and $U_H = 1.2U_C$. The largest feature on the final difference map was 1.2 e Å^{-3} in height in the vicinity of a dichloromethane molecule, and the largest shift in the final cycle of refinement was 0.036 for U of C(11). The crytstal structure includes two molecules of dichloromethane. Tables of anisotropic thermal parameters and hydrogen atom coordinates and complete tables of bond distances and angles are available as supplementary material.

Synthesis of Diazoacetophenone.[24] A solution of 3 mL (0.03 mol) of freshly distilled benzoyl chloride in 30 mL of anhydrous diethyl ether was added dropwise at 0 °C to 75 mL of a stirred solution of diazomethane (approximately 0.07 mol) in diethyl ether. The mixture was stirred an additional 1 h after the addition was complete before the ether was

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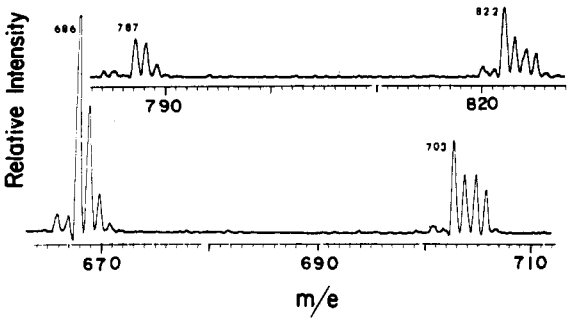

Figure 1. High-mass region of the mass spectrum of complex **1** obtained by LSIMS with sulfolane as the matrix.

removed under a stream of nitrogen. Crystallization of the residue from hexane yielded diazoacetophenone in 30–40% yields: mp 46–48 °C (lit.[24] mp 47.5–48.0 °C); FT IR 2100 (s, –CH=N=N stretch), 1600, 1630 (s), 1430, 1380 cm^{-1}; ^1H NMR 7.82–7.26 (m, 5 H, aromatic protons), 5.89 ppm (s, 1 H, $-CHN_2$).

Synthesis of [1-^{13}C]Diazoacetophenone. The ^{13}C-labeled material was synthesized as described for the unlabeled compound by starting with 0.005 mol of benzoyl chloride and the [^{13}C]diazomethane obtained from 1 g of [^{13}C]Diazald (MSD Isotopes) by the Aldrich method.[25] The labeled compound thus obtained (0.2 g) contained 92% ^{13}C: ^{13}C NMR 72.168, 71.305 ppm (J approximately 204 Hz); ^1H NMR 7.8–7.4 (m, 5 H, aromatic protons), 5.91 ppm (d, 1 H, J = 197.9 Hz, diazomethine H).

Reaction of Iron Tetraphenylporphyrin with Diazo Carbonyl Compounds. The reactions were carried out in Schlenk tubes with solvents that were dried over molecular sieves and degassed immediately before use by repeatedly pumping to 0.1 Torr and purging with argon according to the general procedure of Bruice *et al.*[26] Iron powder (500 mg) placed in a Schlenk tube with a stirring bar was activated by washing twice with glacial acetic acid, twice with methanol, and finally with the reaction solvent (9:1 CH_2Cl_2–MeOH). A degassed solution of an equimolar mixture of (TPP)$Fe^{III}Cl$[43] (50 mg, 0.07 mmol) and the diazo compound in 9:1 CH_2Cl_2–MeOH was then transferred via a cannula to the Schlenk tube, and the resulting mixture was stirred for 30–60 min. Stable products were isolated in good yield by filtration, solvent removal under vacuum, and recrystallization from CH_2Cl_2–pentane.

Results

Formation and Absorption Spectrum of the Diazoacetophenone–Iron Tetraphenylporphyrin Adduct. The reaction of diazoacetophenone with (TPP)$Fe^{III}Cl$ under anaerobic, reducing (iron powder) conditions yields an emerald green complex (**1**) that crystallizes from CH_2Cl_2–pentane. The Soret band at 455 nm in the electronic absorption spectrum of this green complex, which also has maxima (intensity relative to Soret band) at 563 (0.098), 617 (0.121), and 656 nm (0.094), is similar to those of other *N*-alkyl iron(II) tetraphenylporphyrin complexes, which have Soret maxima at 450–454 nm.[27-29] The Soret maximum, in contrast, is somewhat lower than the Soret band at 462 nm reported by Mansuy and co-workers for the *trans*-bis(*N*-alkyl) derivative of (TPP)Fe in which each of the *N*-alkyl groups provides one oxygen ligand to the iron.[21,30] It is also quite different from the Soret bands of carbene complexes of (TPP)Fe (408–417 nm)[5,25-27] or complexes in which a vinylidene carbon is inserted into one of the iron–nitrogen bonds of the porphyrin (428 nm).[31]

Mass Spectrum. The LSIMS spectrum of **1** shows the molecular ion at m/z 787 expected for an adduct of the acetophenone moiety and (TPP)Fe. Peaks are also found at m/z 822 (M^+ + Cl), 703 ((TPP)Fe^+ + Cl), and 668 ((TPP)Fe^+) (Figure 1). The (TPP)Fe and (TPP)FeCl peaks are consistent with loss of the *N*-alkyl group from *N*-alkylated (TPP)FeCl. The presence of strong peaks due to complexation with Cl^- indicates that the N-alkylated metalloporphyrin is positively charged rather than neutral and has a free coordination site on the iron.

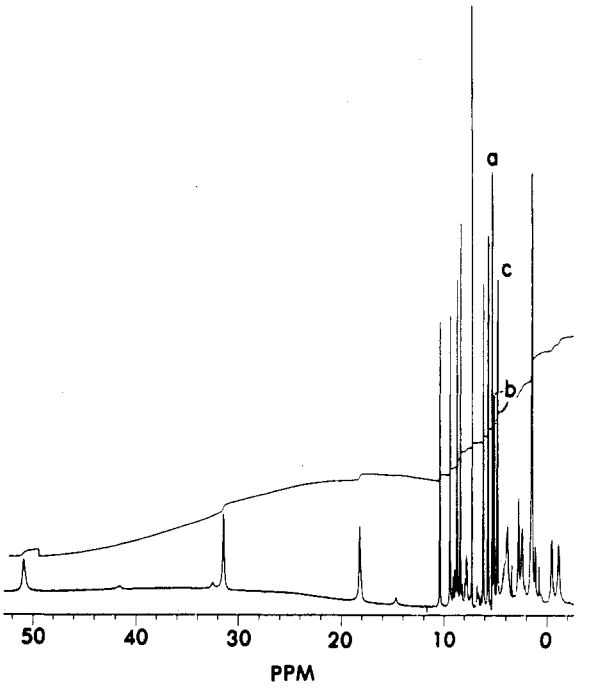

Figure 2. ^1H NMR spectrum (500 MHz) of complex **1** in $CDCl_3$. The para (a), meta (b), and ortho (c) phenyl protons of the *N*-alkyl moiety are indicated.

Table I. Chemical Shifts, Peak Integrals, and Assignments for the Protons in **1**

assignt	chem shift, ppm	integration	assignt	chem shift, ppm	integration
pyrrole	51.01	2	para Ph	8.73	2
	31.41	2		5.70	2
	–0.40	2	*N*-alkyl group		
	–1.1	2	para Ph	5.31	1
ortho Ph	18.18	2	meta Ph	5.11	2
	3.91	2	ortho Ph	4.81	2
	2.87	2	N–CH_2–[a]		
	2.40	2			
meta Ph	10.40	2			
	9.40	2			
	8.91	2			
	6.16	2			

[a] These protons are expected to be far downfield and very broad and were not detected.[32]

^1H NMR Spectrum. The 500-MHz ^1H NMR spectrum of adduct **1** exhibits the pattern of phenyl and pyrrole ring protons expected for the (*N*-alkylTPP)$Fe^{II}Cl$ structure (Figure 2, Table I).[32,33] The peak assignments in Table I have been made by correlating the chemical shifts with the values reported by Balch et al. for the corresponding protons in (*N*-MeTPP)$Fe^{II}Cl$.[32] The signals of the phenyl moiety of the *N*-alkyl group have been assigned on the assumption that the chemical shift value will decrease as the distance of the proton from the porphyrin ring current and the paramagnetic metal increases. The close analogy between the NMR spectrum of the *N*-methyl ferrous porphyrin and the spectrum of adduct **1** strongly supports the identification of **1** as a ferrous *N*-alkylporphyrin.

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Table II. Chemical Shifts and Peak Integrals for **2** and **3**

assignt	chem shift, ppm (multiplicity, no. of protons) free base (**2**)	Zn complex (**3**)
pyrroles and phenyls	8.89 (s, 2)	8.99–8.77 (m, 6)
	8.64 (s, 2)	8.52 (s, 2)
	8.59–8.07 (m, 10)	8.39–8.05 (m, 8)
	7.97–7.60 (m, 14)	7.89–7.66 (m, 12)
N-alkyl group		
$N-CH_2-$	−3.10 (s, 2)	−3.19 (s, 2)
para Ph	6.73 (t, 1)	6.91 (t, 1)
meta Ph	6.36 (dd, 2)	5.63 (dd, 2)
ortho Ph	5.05 (d, 2)	5.30 (d, 2)

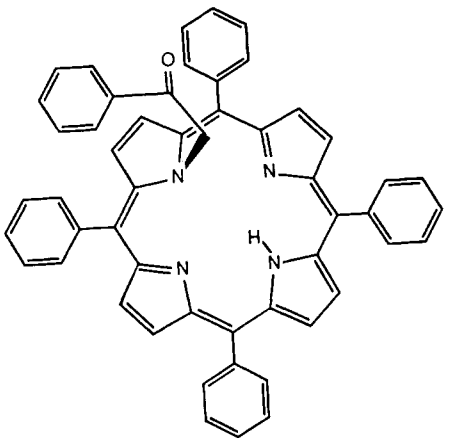


Figure 3. Structure of **2**, the free-base porphyrin obtained by demetalation of **1**. Structure **3** is the zinc complex of this porphyrin.

Free Base and Zinc Complex. Complex **1** is readily converted to its free base by treatment with acids or even with silica gel. The free base has a Soret band at 432 nm and peaks at 532, 574, 612, and 674 nm (relative intensity 100:5.3:7.2:3.7:3.2) in the absorption spectrum. The pattern of the peaks and their positions are essentially identical with those of other *N*-alkyltetraphenylporphyrins.[34-36] The LSIMS mass spectrum has a molecular ion at m/z 732, consistent with replacement of the iron of **1** by two protons. The NMR spectrum of the *N*-alkyltetraphenylporphyrin thus obtained (Table II) is consistent with structure **2** (Figure 3). The free-base porphyrin is converted to its Zn^{2+} complex (**3**) by treatment with $Zn(OAc)_2$ in methanol. The zinc complex has a Soret maximum at 440 nm and bands at 564, 616, and 658 nm (relative intensity 100:4.9:8.6:5.0), values consistent with those for other (*N*-alkylTPP)Zn^{II} complexes.[36,37] The LSIMS mass spectrum shows a molecular ion cluster centered at m/z 795 with the pattern expected for the natural isotopic abundance of zinc. The NMR spectrum of the zinc complex (Table II) is that expected for the zinc complex of **2**.

Magnetic Susceptibility. Studies of the magnetic susceptibility by the Evans method give a value of 5.6 ± 0.2 μ_B for **1**.[23] The expected values for μ_{eff} calculated from the equation $\mu_{eff} = [4S(S + 1) + L(L + 1)]^{1/2}$ give values of 5.48 μ_B for high-spin Fe(II) and 5.92 μ_B for high-spin Fe(III).[38] The experimental value of 5.6 μ_B is thus most consistent with an Fe(II) porphyrin system. This is consistent with the absence of an EPR signal at −196 °C (not shown).

Electrochemistry. The value of $E_{1/2}$ for oxidation of the ferrous to the ferric complex was found by cyclic voltammetry in CH_2Cl_2 containing 0.1 M tetrabutylammonium perchlorate to be 0.47 V vs SCE. The oxidation and reduction peaks are separated by 0.07 V in the cyclic voltammogram, a value that is close to the theoretical value of 0.06 V for a one-electron redox change. A plot of the square root of the scan rate against the peak current was linear, as required for a reversible redox process. The $E_{1/2}$ value found for the present complex (0.47 V vs SCE) is similar to that reported by Battioni et al. for a *bis*alkylated complex ($E_{1/2}$ = 0.41 V vs SCE).[30]

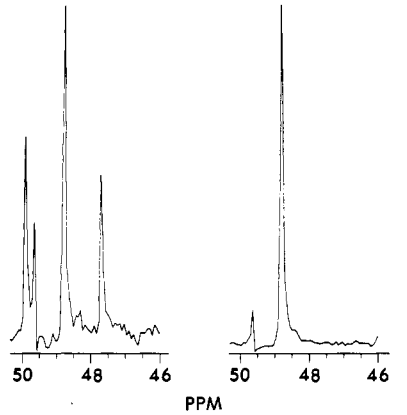
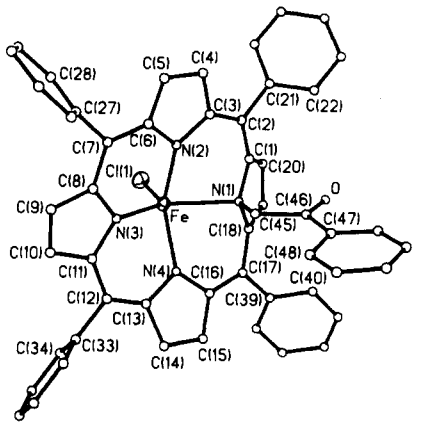


Figure 4. ^{13}C NMR spectra of **2** obtained from the complex formed by reaction of (TPP)$Fe^{III}Cl$ with [1-^{13}C]diazoacetophenone under reducing conditions. The proton-undecoupled spectrum is shown on the left and the proton-decoupled spectrum on the right.



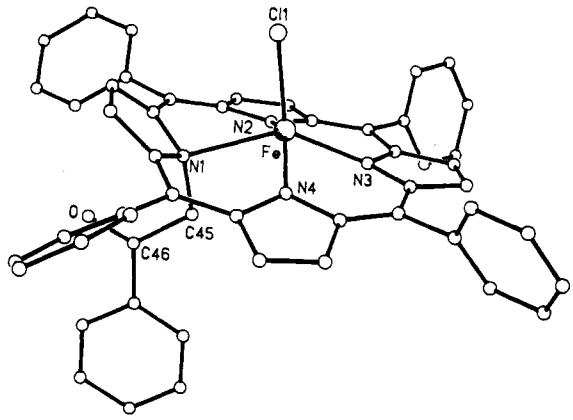


Figure 5. Perspective drawings of **1** based on the X-ray crystal structure. The atomic numbering scheme is shown.

^{13}C NMR Spectrum. The methine proton of synthetic [1-^{13}C]diazoacetophenone (92 atom %) is found at 5.91 ppm in the ^1H NMR spectrum as a doublet with a coupling constant of 198 Hz. The labeled carbon appears in the ^{13}C NMR spectrum at 71.74 ppm as a doublet with a coupling constant of approximately 204 Hz (the coupling constant determined from the proton NMR spectrum is more accurate). ^{13}C labeled **1**, produced by the

(34) Callot, A. W.; Fischer, J.; Weiss, R. *J. Am. Chem. Soc.* **1982**, *104*, 1272–1276.
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Table III. Atomic Coordinates ($\times 10^4$) and Isotropic Thermal Parameters ($Å^2 \times 10^3$) for **1**

	x	y	z	U[a]
Fe	2134 (2)	7502 (1)	2205 (1)	16 (1)*
Cl(1)	174 (3)	7073 (2)	1886 (1)	27 (1)*
N(1)	1688 (8)	7428 (5)	3110 (3)	12 (2)
N(2)	3197 (9)	6487 (5)	2358 (3)	18 (2)
N(3)	3635 (9)	7776 (5)	1684 (3)	17 (2)
N(4)	2022 (10)	8693 (5)	2373 (3)	19 (2)
O	2187 (9)	7371 (5)	4140 (3)	37 (2)
C(1)	1240 (12)	6656 (7)	3232 (4)	20 (3)
C(2)	1975 (12)	5993 (6)	3124 (4)	19 (3)
C(3)	2936 (12)	5930 (6)	2740 (4)	16 (3)
C(4)	3789 (12)	5273 (7)	2651 (5)	27 (3)
C(5)	4490 (12)	5413 (7)	2218 (5)	25 (3)
C(6)	4145 (12)	6167 (7)	2044 (4)	18 (3)
C(7)	4673 (13)	6503 (7)	1595 (5)	24 (3)
C(8)	4442 (12)	7274 (7)	1431 (4)	21 (3)
C(9)	5034 (12)	7633 (7)	988 (5)	29 (3)
C(10)	4596 (14)	8355 (8)	969 (5)	34 (3)
C(11)	3736 (13)	8463 (7)	1415 (4)	22 (3)
C(12)	3170 (11)	9154 (7)	1580 (4)	19 (3)
C(13)	2463 (11)	9256 (7)	2027 (4)	19 (3)
C(14)	2136 (12)	9996 (7)	2246 (4)	24 (3)
C(15)	1517 (12)	9888 (7)	2706 (5)	26 (3)
C(16)	1397 (12)	9083 (6)	2775 (4)	18 (3)
C(17)	669 (11)	8727 (6)	3183 (4)	15 (3)
C(18)	658 (11)	7925 (6)	3249 (4)	15 (3)
C(19)	−381 (12)	7478 (8)	3434 (4)	26 (3)
C(20)	−24 (13)	6724 (7)	3412 (4)	22 (3)
C(21)	1690 (12)	5319 (7)	3455 (4)	22 (3)
C(22)	1694 (12)	5417 (7)	3998 (4)	24 (3)
C(23)	1490 (14)	4798 (8)	4322 (5)	36 (3)
C(24)	1184 (14)	4088 (8)	4121 (5)	38 (4)
C(25)	1166 (14)	3987 (8)	3586 (5)	36 (4)
C(26)	1396 (13)	4603 (7)	3264 (5)	25 (3)
C(27)	5592 (12)	6046 (7)	1263 (4)	21 (3)
C(28)	5146 (14)	5469 (7)	958 (5)	30 (3)
C(29)	5964 (14)	5046 (8)	625 (5)	40 (4)
C(30)	7273 (14)	5191 (8)	634 (5)	32 (3)
C(31)	7812 (15)	5757 (7)	956 (4)	28 (3)
C(32)	6971 (15)	6180 (8)	1271 (5)	37 (4)
C(33)	3295 (12)	9850 (7)	1229 (4)	20 (3)
C(34)	2186 (13)	10154 (7)	1004 (4)	22 (3)
C(35)	2336 (13)	10805 (7)	686 (5)	26 (3)
C(36)	3494 (13)	11139 (8)	605 (5)	30 (3)
C(37)	4624 (14)	10835 (8)	824 (5)	29 (3)
C(38)	4539 (12)	10181 (7)	1141 (4)	20 (3)
C(39)	−112 (12)	9201 (7)	3537 (4)	18 (3)
C(40)	−14 (12)	9063 (7)	4074 (4)	21 (3)
C(41)	−1369 (14)	10149 (8)	4277 (5)	36 (4)
C(42)	−644 (12)	9550 (7)	4422 (5)	25 (3)
C(43)	−1519 (14)	10284 (8)	3735 (5)	31 (3)
C(44)	−890 (12)	9813 (7)	3387 (5)	21 (3)
C(45)	2995 (12)	7646 (7)	3294 (4)	24 (3)
C(46)	3089 (11)	7639 (7)	3890 (4)	20 (3)
C(47)	4295 (12)	7942 (7)	4145 (4)	21 (3)
C(48)	5326 (11)	8288 (7)	3882 (4)	18 (3)
C(49)	6405 (14)	8538 (7)	4143 (5)	29 (3)
C(50)	6502 (14)	8452 (7)	4674 (5)	28 (3)
C(51)	5458 (12)	8128 (7)	4942 (5)	27 (3)
C(52)	4371 (13)	7884 (7)	4679 (4)	24 (3)
Cl(2)	6378 (4)	6856 (2)	3045 (2)	42 (1)*
C6(3)	6922 (5)	8376 (2)	2631 (2)	64 (2)*
C(53)	6968 (15)	7384 (8)	2499 (5)	43 (4)
Cl(4)	88 (8)	7068 (3)	387 (2)	110 (3)*
Cl(5)	1787 (6)	8375 (3)	187 (2)	81 (2)*
C(54)	1468 (18)	7584 (11)	621 (7)	68 (5)

[a] An asterisk denotes an equivalent isotropic U defined as one-third of the trace of the orthogonalized U_{ij} tensor.

reaction of [1-^{13}C]acetophenone with (TPP)Fe^{III}Cl under reducing conditions, shows the labeled carbon in the ^{13}C NMR spectrum as a very broad (line width of 120–150 Hz) signal centered at 562 ppm. The signal is too broad for coupling with vicinal protons to be discerned. Demetalation yields **2**, which shows the labeled carbon as a triplet at 48.756 ppm (J = 142 Hz) in the proton-undecoupled spectrum or a singlet at the same position in the proton-decoupled spectrum (Figure 4).

Table IV. Bond Lengths and Bond Angles for (*N*-Alkyltetraphenylporphyrinato)iron(II) Chlorides

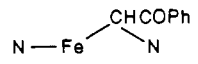
	N-alkyl moiety		
	$Ar_2C{=}CH$[a]	$PhCOCH_2$[b]	Me[c]
	Bond Lengths[d]		
Fe–Cl	2.277 (4)	2.274 (4)	2.244 (1)
Fe–N(1)	2.510 (11)	2.373 (9)	2.329 (2)
Fe–N(2)	2.113 (11)	2.103 (9)	2.116 (2)
Fe–N(3)	2.087 (12)	2.081 (9)	2.082 (2)
Fe–N(4)	2.131 (11)	2.118 (9)	2.118 (2)
Fe–C(45)	2.834 (12)	2.94	
N(1)–C(45)		1.456 (14)	
C(45)–C(46)		1.534 (15)	
C(46)–O		1.210 (14)	
	Bond Angles[e]		
N(1)–Fe–Cl	95.5 (3)	99.7 (3)	103.48 (6)
N(2)–Fe–Cl	102.3 (3)	103.9 (3)	105.36 (7)
N(3)–Fe–Cl	124.2 (3)	118.8 (3)	108.03 (7)
N(4)–Fe–Cl	110.2 (3)	110.3 (3)	114.38 (7)
N(1)–Fe–N(3)	140.3 (4)	118.8 (4)	142.13 (8)
N(2)–Fe–N(4)	143.8 (4)	144.0 (4)	145.60 (9)
N(1)–Fe–N(2)	80.6 (4)	103.9 (4)	82.18 (8)
N(1)–Fe–N(4)	81.0 (4)		82.25 (8)
N(3)–Fe–N(4)	86.9 (4)	87.0 (4)	86.64 (8)
N(2)–Fe–N(3)	87.6 (5)	86.4 (4)	87.12 (8)
N(1)–C(45)–C(46)		112.2 (9)	
C(45)–C(46)–O		119.1 (10)	
O–C(46)–C(47)		121.6 (10)	

[a] From ref 40; atoms renumbered to conform with Figure 5. [b] This work. [c] From ref 39; atoms renumbered to conform with Figure 5. [d] The bond length is given in angstroms and the estimated standard deviation in parentheses. [e] The bond angle is given in degrees and the estimated standard deviation in parentheses.

Crystal Structure. A perspective drawing of adduct **1** is given in Figure 5, and the atomic coordinates and thermal parameters for the structure, based on the numbering scheme in the figure, are given in Table III. Selected structural parameters are also presented in Table IV. Two molecules of dichloromethane are found in the unit cell. The basic ring structure resembles that of (*N*-methyltetraphenylporphyrinato)iron(II) and [*N*-(2,2-bis(*p*-chlorophenyl)vinyl)tetraphenylporphyrinato]iron(II) chlorides, the two ferrous *N*-alkylporphyrins for which crystal structures are currently available (Table IV).[39,40] In all three cases the Fe–N distance to the nitrogen bearing the *N*-alkyl group is substantially longer than the Fe–N distances to the other three pyrrole nitrogens, although the difference is not as pronounced in **1** or in the *N*-methyl adduct as it is in the *N*-(diarylvinyl) compound (Table IV). In all three structures the Fe–N distance to the pyrrole nitrogen opposite to that which is alkylated is shorter than the corresponding distances to the other two pyrrole rings. The alkylated pyrrole ring in **1** is tilted out of the plane defined by the other nitrogens by 36.5°, intermediate between the values for the *N*-methyl (31.6°) and *N*-(diarylvinyl) (37.6°) derivatives. The distance between the iron and the first carbon of the *N*-alkyl group is longer in **1** than it is in the *N*-(diarylvinyl) compound (2.94 vs 2.83 Å), the N(1)–Fe–N(3) angle is smaller than in the other two structures (118.8 vs 140.3 and 142.1 Å), and the N(1)–Fe–N(2) angle is larger (103.9 vs 80.6 and 82.2°).

The conformation of the *N*-alkyl group in the crystal structure places the carbonyl oxygen as far away as possible from the iron atom. This precludes direct interaction of the oxygen with the iron and clearly establishes that **1** is not an iron-chelated enol structure. The alternative possibility that C(45) is a carbanion covalently bound to N(1) and coordinated to the iron is ruled out by the long distance between the iron and C(45) (2.94 Å):

(39) Anderson, O. P.; Kopelove, A. B.; Lavallee, D. K. *Inorg. Chem.* **1980**, *19*, 2101–2107.
(40) Balch, A. L.; Chan, Y. W.; Olmstead, M. M.; Renner, M. W. *J. Org. Chem.* **1986**, *51*, 4651–4656.



This interpretation is also ruled out by the fact that the bond angles and interatomic distances are those expected for a saturated, tetrahedral carbon at C(45) and a classical sp^2-hybridized carbonyl carbon at C(46). The data thus unambiguously establish that adduct **1** simply bears an *N*-alkyl moiety that does not interact with the iron either as an enol or as a carbanion.

Discussion

The reaction of diazoacetophenone with (TPP)$Fe^{III}Cl$ under reducing conditions yields [*N*-(2-phenyl-2-oxoethyl)tetraphenylporphyrinato]iron(II) chloride (**1**). Formation of this product requires reduction of the iron to the ferrous state, elimination of the equivalent of nitrogen gas from the substrate, and addition of one of the pyrrole nitrogens *plus a proton* to the reactive carbon of the substrate. The reaction of diazo carbonyl compounds with (TPP)Fe^{II} thus yields *N*-alkyl adducts without the formation of stable intermediates with a carbanion or enol bridge to the iron. In contrast, the reactions of diazo carbonyl compounds with (TPP)Co^{III} [43] usually yield structures in which the diazo carbon is inserted into the cobalt–nitrogen bond to give a carbanion-coordinated species (Reaction a). *N*-Alkyl adducts with the enolized *N*-alkyl carbonyl group coordinated have not been detected. The *N*-alkyl adducts are produced from the carbanion-coordinated intermediates by protonation under reducing conditions.[12-16] It is likely that carbanion-bridged species are also formed with the iron porphyrins but that they are too unstable under the strongly reducing reaction conditions to be isolated.

Direct formation of *N*-alkyl product **1** in the reaction of (TPP)$Fe^{II}Cl$ with diazoacetophenone argues that the reactions of diazo carbonyl compounds with cytochrome P450 and other hemoproteins, which are carried out under reducing conditions, are also likely to yield N-alkylated heme derivatives without the detectable accumulation of carbanion- or enol-bridged intermediates. This inference is supported by our finding that enzymatic oxidation of a 3-substituted sydnone with a leaving group at the β position of the substituent results in formation of *N*-vinyl heme without the spectroscopically detectable formation of intermediates.[10,11] Furthermore, the oxidation of 3-(2-phenylethyl)-4-methylsydnone by liver microsomes and by reconstituted cytochrome P450b has recently been shown to yield *N*-(2-phenylethyl)- and *N*-(2-phenylethenyl)protoporphyrin IX without the detectable intervention of reaction intermediates.[11] Further detailed studies of the reactions of diazoalkanes and diazo carbonyl compounds with purified, reconstituted rat liver cytochrome P450b are currently in progress.

The finding that the reaction of diazoacetophenone with iron tetraphenylporphyrin does not yield the iron-coordinated enol structure argues that it is not a particularly stable structure. This finding is consistent with the report by Battioni et al. that the iron-chelated enol structures even of *N*-alkylporphyrins with dicarbonyl-substituted *N*-alkyl groups are not very stable.[22] This readily explains the absence of a spectroscopically detectable intermediate in the reaction of cytochrome P450b with phenylacetylene because N-alkylation of the prosthetic group of cytochrome P450 during the catalytic turnover of phenylacetylene should yield an initial enol-bridged structure that rearranges to the eventually isolated *N*-(2-phenyl-2-oxoethyl) adduct.[41,42] In fact, the reaction of liver microsomes from phenobarbital-induced rats with diazoacetophenone yields, except possibly for regioisomer distribution, exactly the same *N*-alkylporphyrin as does the reaction with phenylacetylene.[41] The identity of the isozyme that reacts with diazoacetophenone in liver microsomes is unclear because preliminary data suggest that diazoacetophenone only gives a reversible complex with reconstituted cytochrome P450b.[42] It will apparently be necessary to construct substrates that yield stabilized enol structures or to target isozymes that stabilize such enol complexes if the enol heme adducts thought to be formed in the reactions of acetylenes with cytochrome P450 are to be detected.

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Registry No. **1**, 115338-86-8; **2**, 115338-84-6; TPP, 917-23-7; $PhCOCHN_2$, 3282-32-4; $PhCO^{13}CHN_2$, 36165-20-5; CH_2N_2, 334-88-3; PhCOCl, 98-88-4; Fe, 7439-89-6; (TPP)$Fe^{III}Cl$, 16456-81-8; cytochrome P450, 9035-51-2.

Supplementary Material Available: Tables of crystal data and data collection parameters, bond lengths and bond angles, anisotropic thermal parameters, and H atom positional parameters and isotropic thermal parameters (5 pages); a table of observed and calculated structure factors (16 pages). Ordering information is given on any current masthead page.

(41) Komives, E. A.; Ortiz de Montellano, P. R. *J. Biol. Chem.* **1987**, *262*, 9793–9802.
(42) Swanson, B. A. Ortiz de Montellano, P. R., unpublished results.
(43) Abbreviations: (TPP)$Fe^{III}Cl$, (tetraphenylporphyrinato)iron(III) chloride; (TPP)$Co^{III}Cl$, (tetraphenylporphyrinato)cobalt(III) chloride; LSIMS, liquid second-ion mass spectrometry.