***N*,*N*-Dimethyl-2-methyl-1-propenylamine**: (THF-d_8) δ 1.58 (s, 3 H, CH_3), 1.67 (s, 3 H, CH_3), 2.37 (s, 6 H, $N(CH_3)_2$), 5.31 (m, 1 H, CH=).

(*E*)-*N*,*N*-Dimethyl-3-methyl-1-butenylamine: (THF-d_8) δ 0.96 (d, J = 6.7 Hz, 6 H, $CH(CH_3)_2$), 2.18–2.37 (m, 1 H, CH), 2.48 (s, 6 H, $N(CH_3)_2$), 4.15 (d of d, J = 13.9, 7.2 Hz, 1 H, CH=), 5.91 (d of d, J = 13.9, 0.8 Hz, 1 H, CH=).

Estimation of the Maximum Optical Rotation of (*E*)-*N*,*N*-Diethyl-3,7-dimethyl-1,6-octadienylamine (3) and Determination of the Absolute Configuration. The enamine **3** (8.3 g, 40 mmol; purity 82.6%; $[\alpha]^{21}_D$ −73.1 (*c* 5.27, *n*-hexane)), prepared by the present isomerization from **1**, was acidified to pH 4 by addition of 30% aqueous acetic acid below 40 °C (under ice-cooling), and the resulting solution was stirred for further 15 min. The organic layer was extracted with several portions of *n*-hexane, and the combined extracts were washed with aqueous sodium carbonate, dried over magnesium sulfate, and distilled under reduced pressure to give 5.0 g (80%) of (+)-citronellal (bp 94–96 °C (8 mm); purity 97.3%; $[\alpha]^{21}_D$ +16.4° (neat)), which was transformed into *l*-menthol without further purification. Thus, to a solution of the citronellal (5.0 g) in benzene (20 mL) was added gradually 7.32 g of $ZnBr_2$ at 5–10 °C, and the resulting suspension was stirred for 15 min. After filtration of $ZnBr_2$, the reaction mixture was washed with water and then aqueous sodium carbonate and dried over sodium sulfate. Distillation of the product, after removal of the solvent, gave 3.5 of isopulegol (bp 50–60 °C (2 mm)),[51] which was hydrogenated to *l*-menthol in ethanol with Raney nickel catalysts (100 °C, 100 kg/cm^2 H_2, 2 h). After usual workup the resulting *l*-menthol was isolated with preparative gas chromatography for the measurement of optical rotation. During this isolation, any procedure involving crystallization was avoided. The sample of *l*-menthol in our hand was found to be 99.1% pure containing 0.9% of isomenthol by GLC analysis and showed optical rotation of $[\alpha]^{21}_D$ −47.1° (*c* 2.70, EtOH) after correction for the small amount of isomenthol. The optical purity of the *l*-menthol was determined to be 94.2% ee based on the optical rotation of pure *l*-menthol.[52] Thus, the maximum optical rotation of (−)-(*E*)-*N*,*N*-diethyl-3,7-dimethyl-1,6-octadienylamine (**3**) was estimated to be $[\alpha]^{21}_D$ −77.6° (*n*-hexane), and the absolute configuration of (−)-**3** was determined to be *R*.

Registry No. 1, 40137-00-6; **2**, 40267-53-6; (±)-**3**, 67362-90-7; (*R*)-**3**, 67392-56-7; (*S*)-**3**, 67392-54-5; (*R*)-BINAP, 76189-55-4; (*S*)-BINAP, 76189-56-5; (±)-BINAP, 76144-87-1; (−)-DIOP, 32305-98-9; (−)-Cy-DIOP, 82239-68-7; (−)-*i*-PrDIOP, 82239-67-6; (−)-EtDIOP, 82239-66-5; (−)-BPPM, 61478-28-2; (*S*)-(*R*)-BPPFA, 55650-59-4; diphos, 1663-45-2; DIPP, 91159-11-4; BDPF, 12150-46-8; [Rh(diphos)(COD)]ClO_4, 32799-70-5; [Rh((−)-BINAP)(NBD)]ClO_4, 76155-69-6; [Rh((−)-Cy-DIOP)(NBD)]ClO_4, 82268-72-2; [Rh((−)-*i*-PrDIOP)(NBD)]ClO_4, 82268-70-0; [Rh((−)-EtDIOP)(NBD)]ClO_4, 82283-92-9; [Rh(PPh_3)$_2$-(COD)]ClO_4, 32799-30-7; [Rh(diphos)$_2$]ClO_4, 30513-14-5; [Rh(DIP-P)(COD)]ClO_4, 91159-08-9; [Rh(BDPF)(COD)]ClO_4, 91159-10-3; [Rh((*S*)-(*R*)-BPPFA)(COD)]ClO_4, 69228-79-1; [Rh(BPPM)(COD)]-ClO_4, 67322-49-0; [Rh(COD)Cl]$_2$, 12092-47-6; [Rh((±)-BINAP)-(COD)]ClO_4, 82864-73-1; [Rh((+)-BINAP)(COD)]ClO_4, 82822-45-5; [Rh((−)-BINAP)(COD)]ClO_4, 82889-98-3; [Rh((−)-DIOP)(COD)]-ClO_4, 70832-57-4; cyclohexylgeranylamine, 70548-83-3; (*E*)-*N*,*N*-diethyl-7-hydroxy-3,7-dimethyl-2-octenylamine, 68759-12-6; (*Z*)-*N*,*N*-diethyl-7-hydroxy-3,7-dimethyl-2-octenylamine, 57745-79-6; *N*,*N*-dimethylallylamine, 2155-94-4; cyclohexylmethylgeranylamine, 87560-13-2; myrcene, 123-35-3; methylcyclohexylamine, 100-60-7; (*E*)-*N*,*N*-diphenyl-3,7-dimethyl-2,6-octadienylamine, 87560-06-3; geranyl chloride, 5389-87-7; lithium diphenylamide, 5856-89-3; phenylgeranylamine, 65559-74-2; lithium anilide, 20732-26-7; *N*,*N*-dimethyl-3-methyl-2-butenylamine, 2588-79-6; 3-methyl-2-buten-1-ol, 556-82-1; 1-chloro-3-methyl-2-butene, 503-60-6; dimethylamine, 124-40-3; (*E*)-*N*,*N*-dimethyl-2-methyl-2-butenylamine, 91159-12-5; methyl (*E*)-2-methyl-2-butenoate, 6622-76-0; (*E*)-1-chloro-2-methyl-2-butene, 23009-73-6; (*E*)-*N*,*N*-dimethyl-3-phenyl-2-butenylamine, 82822-01-3; ethyl (*E*)-3-phenyl-2-butenoate, 1504-72-9; (*E*)-*N*,*N*-dimethyl-2-butenylamine, 51752-08-0; (*E*)-1-chloro-2-butene, 4894-61-5; *N*,*N*-dimethyl-1-methyl-2-propenylamine, 52113-79-8; *N*,*N*-dimethyl-2-methyl-2-propenylamine, 6000-82-4; 3-chloro-1-methyl-1-propene, 563-47-3; 3-chloro-1-butene, 563-52-0; (±)-3-diethylaminocyclohexene, 91159-13-6; 3-hydroxycyclohexene, 822-67-3; diethylamine, 109-89-7; (±)-*trans*-diethylpiperitylamine, 91159-14-7; (±)-*trans*-piperityl acetate, 91159-15-8; cyclohexylmethylgeranylamine (*E*)-enamine, 91159-16-9; *N*-(3,7-dimethyl-6-octenylidene)cyclohexylamine, 70548-84-4; (*E*)-*N*,*N*-diethyl-7-hydroxy-3,7-dimethyl-1-octenylamine, 85793-96-0; (+)-7-hydroxy-3,7-dimethyloctanol, 34212-48-1; (−)-(*E*)-*N*,*N*-dimethyl-3-phenyl-1-butenylamine, 82822-02-4; 3-phenylbutanoic acid, 4593-90-2; (*E*)-*N*,*N*-dimethyl-1-propenylamine, 13222-51-0; (*E*)-*N*,*N*-dimethyl-1-butenylamine, 22644-52-6; *N*,*N*-dimethyl-2-methyl-1-propenylamine, 6906-32-7; (*E*)-*N*,*N*-dimethyl-3-methyl-1-butenylamine, 91159-17-0.

Alkylation of the α and γ Meso Positions of Tetraphenylporphyrin upon Reduction of Allyl and Propargyl Bromide by Iron(II) Tetraphenylporphyrin: A New Route to Porphodimethene Complexes

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Abstract: Reduction of allyl bromide by sodium ascorbate or sodium dithionite, under anaerobic conditions, is catalyzed by (5,10,15,20-tetraphenylporphinato)iron(II). 1,5-Hexadiene has been found to be the only organic product. During this reaction, the iron porphyrin complex is slowly transformed into a mixture of stereoisomers of the (5,15-diallyl-5,10,15,20-tetraphenylporphinato)iron(II) complex. These new complexes, which were found to be very sensitive to dioxygen, have been demetalated into the corresponding stable diallylporphodimethenes whose structure has been established by elemental analysis and spectroscopic techniques. In the case of propargyl bromide, a similar alkylation of the meso positions of the iron porphyrin occurs, by either an allenyl or a propargyl group, leading to stereoisomers of the (diallenyl-, (dipropargyl-, and (allenylpropargylporphodimethene)iron(II) complexes. The mechanism of these reductions is discussed and compared to the general mechanism of reduction of alkyl halides by iron(II) porphyrins in the presence of a reducing agent in excess.

Cytochrome P-450 is able to catalyze the reduction by NADPH of several substrates including nitroarenes and halogenated compounds.[1,2] We have recently described a biphasic heme model system using an iron porphyrin and a phase-transfer agent in

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catalytic amounts and sodium ascorbate as a reducing agent, which is able to mimic most microsomal cytochrome P-450 dependent reductions of substrates.[3] This system was found to be able to perform the reduction of 4-nitrobenzyl chloride[4] and 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane, respectively, into 4-nitrotoluene and 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethane as well as the reductive dehalogenation of hexachloro- and pentachloroethane into tetrachloroethylene and trichloroethylene.[3]

Free radicals derived from the one-electron reduction of a carbon–halogen bond of these halogenated compounds by cytochrome P-450 or model iron(II) porphyrins seem to be the first intermediates of all these enzymatic[2,5] or model reactions.[6] However, depending upon the nature of the starting halogenated compound, these radicals have many possible evolutions. With benzyl halides[4,2d] or halothane $CF_3CHClBr$,[2b] σ-alkyl–ferric complexes are formed. In the case of halothane, the model reaction lead to a stable (porphyrin)Fe^{III}–$CHClCF_3$ complex, which has been isolated.[7] With polyhalogenomethanes such as CCl_4, ferrous–carbene complexes are formed.[2a,8] It is noteworthy that porphyrin–iron(II)–carbene complexes have been isolated from reaction between iron(II) porphyrins and polyhalogenomethanes[8] and fully characterized in the case of the reduction of CCl_4.[9]

This paper describes a study of the reduction of allyl bromide by the aforementioned biphasic heme model system,[3] which shows that 1,5-hexadiene is formed as the only organic product.[10] It also shows that the iron porphyrin catalyst is slowly transformed during this reaction into an iron(II) porphodimethene complex upon alkylation of the α and γ meso positions of the porphyrin by an allyl group.[11] Such an alkylation of the α and γ meso positions of iron porphyrins, in very mild conditions (room temperature, pH 7.4), has been also observed upon reduction of propargyl bromide. It is a new way of evolution of a situation where a free radical is produced upon reduction of a carbon–halogen bond in the presence of an iron(III) porphyrin and a reducing agent in excess. Moreover, the corresponding products are the first examples of isolated porphodimethene compounds derived from tetraphenylporphyrins.[11,12]

Experimental Section

Materials. Allyl bromide, 1,5-hexadiene, and propargyl bromide were purchased from Aldrich, cyclohexane and sodium dithionite from Prolabo, sodium ascorbate from Sigma, and the phase-transfer agent (trioctylmethylammonium chloride = TOMA) from Fluka. The iron porphyrin complex Fe(TPP)(Cl)[13] was prepared as previously reported.[14]

Physical Measurements. Visible spectra were obtained in toluene solution on an Aminco DW2 spectrophotometer. Infrared spectra were recorded as KBr pellets on a Perkin-Elmer 599 spectrophotometer. ^1H NMR spectra were run on a Varian EM 390 spectrometer operating at 90 MHz or on a Cameca 250 spectrometer operating at 250 MHz. ^{13}C NMR spectra were recorded on a Bruker WH 90 spectrometer (sweep width 6000 Hz, 80 000–20 000 45° pulses, 8K point memory blocks, acquisition time 2 s). Mass spectra were performed on a Riber R1010 mass spectrometer coupled with a PDP 8 computer. For combined gas chromatography-mass spectrometry, the mass spectrometer and the computer were coupled with a Girdel chromatograph. The temperature of the 3% SE 52 glass column increased from 80 to 250 °C at a rate of 5 °C per min. The carrier gas was helium at a pressure of 1 bar. GLC was performed on an Intersmat IG 120 FL, equipped with an hydrogen ionization detector, and a 5% OV 210 glass column was used. The injector temperature was 160 °C and the column temperature 60 °C. The carrier gas was N_2 at a pressure of 1 bar. Elemental analysis were done by the Service de Microanalyse du CNRS at Gif sur Yvette.

Procedure for the Anaerobic Reduction of Allyl Bromide by the Biphasic Heme Model System. Fe(TPP)(Cl)(10^{-2} mmol), allyl bromide (10^{-1} mmol), and an unreactive internal standard (cyclohexane, 10^{-2} mmol), for yields determination, were dissolved in 4 mL of previously deaerated toluene. A previously deaerated 1 M aqueous phosphate buffer (4 mL, pH 7.4) containing 1 mmol of sodium ascorbate and 2×10^{-2} mmol of trioctylmethylammonium chloride were added in the organic phase. Dioxygen was entirely removed from the biphasic system by bubbling argon for at least 10 min. The reaction was started by vigorously stirring the system. The organic phase was analyzed by GLC and mass spectrometry. We observed only one peak which coemerged with an authentic sample of 1,5-hexadiene. Its mass spectrum was identical with that of 1,5-hexadiene. The evolution of the iron porphyrin catalyst was studied during the reaction by visible spectroscopy. One observed the slow increase of an absorption band at 471 nm, in addition to the bands of the complex Fe^{II}(TPP), indicating the slow formation of the new complex **1a**.

(5,15-Diallyl-5,10,15,20-tetraphenylporphinato)iron(II) (1a). Fe(TPP)(Cl) (0.4 mmol) and allyl bromide (2 mmol) were dissolved in 50 mL of deaerated toluene. Sodium dithionite (10 mmol) and one drop of trioctylmethylammonium chloride were dissolved in 30 mL of deaerated 1 M aqueous phosphate buffer pH 7.4. Argon was bubbled through the biphasic system for 10 min and the reaction mixture was stirred, at 20 °C, for 8 h until the visible spectrum of the organic phase exhibits only one absorption band at 471 nm (ϵ = 80 000 M^{-1} cm^{-1}), characteristic of pure complex **1a** in solution. This complex is highly sensitive to dioxygen, and we could not isolate it as a pure solid.

5,15-Diallyl-5,10,15,20-tetraphenylporphodimethene (2a). The organic phase containing complex **1a** was treated with 3 mL of CF_3COOH for demetalation and washed 3 times with 20 mL of water. 1 mL of Et_3N was added. The crude product was purified by column chromatography (silica gel, CH_2Cl_2–CH_3COCH_3, 95–5 as eluant). After solvent evaporation, crystallization was achieved by dissolving the product in a min-

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(10) Formation of 1,5-hexadiene upon reduction of allyl halides by stoichiometric amounts of an iron(II) porphyrin has been previously reported.[6a]

(11) Porphodimethenes (5,15-dihydroporphyrins) are derived from porphyrins by saturation of the α and γ meso carbon atoms. Scheer, H. In "The Porphyrins"; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. III, pp 1–44. They have been suggested as intermediates in porphyrin synthesis. Dolphin, D. *J. Heterocycl. Chem.* **1970**, *7*, 273. They have been proposed as the primary products of the chemical and photochemical hydrogenation of metalloporphyrins. Seely, G. R.; Talmadge, K. *Photochem. Photobiol.* **1964**, *3*, 195. Sidorov, A. N. *Biofizika* **1965**, *10*, 226. 5,15-Alkylporphodimethenes have been, so far, only prepared by reductive alkylation of metallooctaethylporphyrins.[12]

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(13) Abbreviations: TPP = *meso*-tetraphenylporphinato dianion ligand, OEP = octaethylporphinato dianion ligand, TOMA = trioctylmethylammonium chloride.

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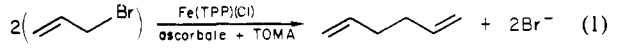
imum amount of CH_2Cl_2 and adding an excess of CH_3OH. Compound **2a** was obtained as orange-red crystals (85% yield based on starting Fe(TPP)(Cl)). Its spectroscopic characteristics are in agreement with a porphodimethene structure. Anal. Calcd ($C_{50}H_{40}N_4, H_2O$): C, 84.03; H, 5.88; N, 7.84. Found: C 84.06; H, 5.74; N, 7.73. ^1H NMR δ (pyrrole) 6.12 (d, J = 4 Hz, 2 H), 6.34 (d, J = 4 Hz, 2 H), 6.37 (d, J = 4 Hz, 2 H), 6.38 (d, J = 4 Hz, 2 H); ^{13}C NMR (aromatic carbons) 117.2, 117.7, 126.4, 127.2, 127.6, 127.8, 128.4, 129, 130.8, 130.9, 137.2, 140.1, 140.3, 140.5, 144.3, 146.6, 162.2, 162.6. For other ^1H and ^{13}C NMR signals, see Table II.

Anaerobic Reduction of Propargyl Bromide by the Biphasic System: Formation of a Mixture of Three Iron(II)Porphodimethenes. The anaerobic reduction of propargyl bromide (2 mmol) by the biphasic system was performed under the conditions used for the reduction of allyl bromide (Fe(TPP)(Cl), 0.4 mmol in toluene; $Na_2S_2O_4$, 10 mmol in a phosphate buffer pH 7.4). This reaction leads within 8 h to the complete formation of complex **1b**, absorbing at 471 nm (ϵ = 80 000 M^{-1} cm^{-1}) and very sensitive to dioxygen. After treatment of complex **1b** by 3 mL of CF_3COOH for demetalation, purification by column chromatography, and recrystallization from CH_2Cl_2–MeOH, compound **2b** was obtained (80% yield). In fact, its spectroscopic characteristics clearly indicate that **2b** is a mixture of three porphodimethenes, because either a propargyl or an allenyl group was found to be attached at the α and γ meso positions (see Results). Anal. Calcd ($C_{50}H_{36}N_4, H_2O$): C, 84.51; H, 5.35; N, 7.89. Found: C, 84.96; H, 5.35; N, 7.53. ^1H NMR δ (pyrrole) (for **2b′**) 6.11 (d, J = 4 Hz, 4 H), 6.35 (d, J = 4 Hz, 4 H), (for **2b″**) 6.02 (d, J = 4 Hz, 4 H), 6.15 (d, J = 4 Hz, 4 H), (for **2b‴**) 6.35 (d, J = 4 Hz, 2 H), 6.41 (d, J = 4 Hz, 2 H), 6.48 (m, 4 H); ^{13}C NMR (aromatic carbons) 116.9, 117.8, 127.1, 127.4, 127.7, 128.4, 130.8, 136.9, 137.5, 140.2, 140.5, 140.7, 141.0, 143.7, 144.1, 146.6, 160.5, 160.8, 161.2. For other ^1H and ^{13}C NMR signals, see Table II.

Metalation of Compounds 2. The insertion of iron into the free bases **2** (0.2 mmol) was done with $FeCl_2$ (0.3 mmol) in 50 mL of deaerated THF[15] or with $Fe(CO)_5$ (3 mmol) and I_2 (0.4 mmol) in 50 mL of toluene as solvent.[12d] After 3 h of refluxing under an argon atmosphere, the solution was filtered and then stirred with an aqueous solution of sodium dithionite in excess. Complexes **1** were quantitatively obtained as shown by their characteristic absorption band at 471 nm in the visible spectrum of the organic phase.

Results

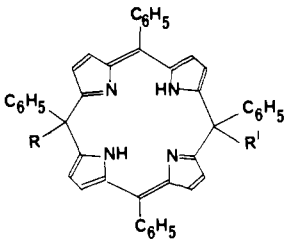
Anaerobic reduction of allyl bromide (25 mM) by a biphasic system using sodium ascrobate (250 mM) as a reducing agent in water (phosphate buffer pH 7.4) and an iron porphyrin $Fe^{III}(TPP)(Cl)$[13] (2.5 mM) in catalytic amounts in toluene, in the presence of trioctylmethylammonium chloride (TOMA) as a phase-transfer agent, at 20 °C, leads to only one product, which was found to be 1,5-hexadiene (eq 1). The yield, based on the



(1)

substrate, is ca. 70% after a 10-h reaction, the initial rate being 25 mmol of 1,5-hexadiene formed per mol of Fe(TPP)(Cl) and per min. No reduction takes place if either TOMA or Fe(TPP)(Cl) is omitted, showing that both phase-transfer and electron-transfer catalysis are absolutely required.

Under the aforementioned conditions and during the reduction of allyl bromide, one observes, by visible spectroscopy of the organic phase, the slow transformation of the $Fe^{II}(TPP)$ catalyst into a complex **1a**. This is shown by the slow increase of a band at 471 nm and the decrease of the bands at 418 and 540 nm characteristic of the complex $Fe^{II}(TPP)$. When the substrate is completely consumed, the yield of complex **1a**, based on the iron porphyrin, is only ca. 60%. In order to obtain this complex in better yields, the reduction of allyl bromide (2 mmol) was performed with higher amounts of Fe(TPP)(Cl) (0.4 mmol) and with sodium dithionite (10 mmol) instead of sodium ascorbate, as a reducing agent. Under these conditions, the formation of complex **1a** is complete after an 8-h reaction, as shown by the very characteristic visible spectrum of the organic phase which exhibits only one absorption band at 471 nm. Under identical conditions, the reduction of propargyl bromide leads, after a 3-h reaction, to complex **1b**, whose visible spectrum exhibiting an absorption band at 471 nm is identical with that of complex **1a**.



2a R = R′ = $CH_2CH{=}CH_2$

2b { **2b′** R = R′ = $CH_2C{\equiv}CH$; **2b″** R = R′ = $CH{=}C{=}CH_2$; **2b‴** R = $CH_2C{\equiv}CH$, R′ = $CH{=}C{=}CH_2$

Figure 1. Formula of the isolated 5,15-dialkylporphodimethenes (**2**).

Table I. UV–Visible, Infrared and Mass Spectrum Characteristics of Compound **2**

compd	UV–vis $\lambda(\epsilon)^a$	IR ν, cm^{-1} [b]	MS data, m/e
2a	424 (70 000)	1580 (s)	614, 100% ($-2C_3H_5$)
		840, 925, 1230 (w)	655, 22% ($-C_3H_5$)
		1640 (w)	696, 4% (M^+)
		3060 (w)	
2b	426 (72 000)	1575 (s)	614, 100% ($-2C_3H_3$)
		840, 925, 1230 (w)	653, 12% ($-C_3H_3$)
		1950 (w)	692, 50% (M^+)
		3280, 2280 (w)	

[a] In C_6H_6 at 27 °C, λ in nm (ϵ in M^{-1} cm^{-1}). [b] Spectra of samples recorded as KBr pellets, ν in cm^{-1}.

These two complexes are highly sensitive to dioxygen, and we failed to isolate them as pure solids. However, after demetalation by CF_3COOH, purification by column chromatography, and crystallization from CH_2Cl_2–MeOH, stable compounds **2** (λ_{max}(**2a**), 424; λ_{max}(**2b**), 426 nm) were obtained as orange-red crystals in good yields (80%). Metalation of compounds **2a** and **2b** with $FeCl_2$ in THF[15] or with $Fe(CO)_5/I_2$ in toluene[12d] and reduction, under inert atmosphere by sodium dithionite in excess, lead respectively to complexes **1a** and **1b**. This indicates that complexes **1** are iron(II) complexes of compounds **2** (eq 2). Thus

(2)

the structure of these very unstable complexes **1** can be deduced from those of compounds **2**, which have been identified as 5,15-diallylporphodimethenes (Figure 1) by their elemental analysis and their spectroscopic characteristics (Tables I and II) as described in the following section.

The 5,15-diallylporphodimethene structure of compound **2a** is strongly suggested by the following UV–vis and IR data, which are very similar to those of the 5,15-dialkylporphodimethene compounds reported so far in the OEP series:[12] (i) a characteristic visible spectrum with a single peak around 424 nm as in $((OEP)Me_2)H_2$,[12b,c,19] (ii) four bands at 1680, 840, 925, and 1230 cm^{-1} in the IR spectrum, which have been found as characteristic of a porphodimethene structure in the OEP series.[12a] The IR spectrum also exhibits two bands at 1640 and 3060 cm^{-1} suggesting the presence of the allyl group. This structure is also supported by the elemental analysis of compound **2a** that corresponds to $((TPP)(C_3H_5)_2)H_2$ and by its mass spectrum (70 eV, 220 °C), which exhibits a molecular peak at m/e 696 (M^+ corresponding to $((TPP)(C_3H_5)_2)H_2$) and fragments at m/e 655 and 614 (characteristic of the $(TPP)H_2$ moiety), in agreement with the successive loss of two allyl (m = 41) groups.

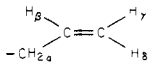
The ^1H NMR characteristics of compound **2a** are very different from those of tetraphenylporphyrin (Table II). The comparison of the ^1H NMR spectra of compound **2a** and of its analogue

(15) Anderson, O. P.; Kobelove, A. B.; Lavallee, D. K. *Inorg. Chem.* **1980**, *19*, 2101–2107.

Table II. Selected ^1H and ^{13}C NMR Data for Porphodimethenes $((TPP)RR')H_2$, **2**

	^1H NMR[a,b]			^{13}C NMR[a,c]	
	NH	phenyl	R, R'[d]	C_{meso}^{sp3}	R, R'
2a	13.48 s, 13.46 s (2H)	7.56 m (4 H), 7.41 m (4 H), 7.47 m (6 H), 7.17 m (6 H)	3.16 d (6.5), 3.22 d (6.5) (4 H_α), 5.66 m, 5.69 m (2 H_β), 4.98, 4.85 (2 H_γ),[e] 5.05, 4.93 (2 H_δ)[e]	51.6, 52.2	43.8, 134.6, 127.5, 45.4, 134.0
2b'	13.10 m (2 H)	7.56 m, 7.48 m, 7.39 m, 7.13 m (20 H)	1.40 t (2) 1.27 t (2) (2 H), 3.24 d (2) (4 H)	51.3	30.8, 72.8, 80.7
2b''	13.10 m (2 H)	7.56 m, 7.48 m, 7.39 m, 7.13 m (20 H)	5.98 t (7) (2 H), 4.36 d (7) (4 H)	51.1 51.5	207.6[f]
2b'''	13.46 m (2 H)	7.56 m, 7.48 m, 7.39 m, 7.13 m (20 H)	1.91 m (1 H), 3.17 d, (2), 3.12 d (2) (2 H), 5.98 t (7) (1 H), 4.58 d (7), 4.56 d (7) (2 H)	53.5	30.4, 72.3, 81.1, 208.5[f]

[a] For other ^1H and ^{13}C NMR data, see Experimental Section. [b] Assignments were made by using spin-decoupling techniques and by comparison with corresponding porphodimethenes prepared from a partially deuterated porphyrin complex.[16] In $DCCl_3$ at 20 °C, δ (ppm from Me_4Si), multiplicity, J (Hz) (number of ^1H). [c] Assignments were made by using off-resonance techniques. In $DCCl_3$ at 20 °C, δ (ppm from Me_4Si). [d] Labels as in



[e] Each signal is a doublet of doublets J_{gem} = 1.5, J_{cis} = 10, J_{trans} = 17.5. [f] It was not possible to assign the other signals of the allenic moiety since they are superimposed on those of $DCCl_3$.

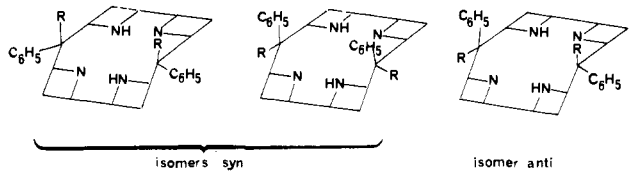


Figure 2. Stereoisomers of folded porphodimethenes $((TPP)R_2)H_2$ after ref 12.

prepared as described in the Experimental Section from a tetrakis(pentadeuteriophenyl)porphyrin partially deuterated on the pyrrole rings,[16] and the results of spin decoupling experiments allowed us to assign the different signals of compound **2a** and to establish that two allyl groups are linked on two symmetrical meso positions of the porphyrin ring.

The following ^1H NMR data are in good agreement with the proposed porphodimethene structure: (i) the presence and the number of the $CH_2CH{=}CH_2$ groups in the molecule are indicated by the chemical shifts, the coupling constants, and the integration of the protons between 3 and 6 ppm; (ii) two types of phenyl groups (between 7 and 7.5 ppm) are observed in the ^1H NMR spectrum, those on a saturated meso carbon and those on an unsaturated meso carbon; (iii) the low-field shifted signal around 13.5 ppm, which disappears upon addition of D_2O, was assigned to the N–H protons; its chemical shift is characteristic of the absence of the ring current usually found in $(TPP)H_2$ because of the loss of aromaticity in porphodimethenes.[17,18] Moreover, the ^{13}C NMR spectrum of compound **2a** (Table II) indicates the presence of two types of sp^3 carbon atoms, as shown by off-resonance experiments, a quaternary one (ca. 52 ppm) which can only be assigned to alkylated meso carbon atoms and a secondary one (ca. 45 ppm) which is assigned to the allylic carbons.

In the ^1H and ^{13}C NMR spectra of compound **2a**, several signals appeared as two identical set of peaks with nearly the same integration (Table II). For instance, the allylic protons appear as two doublets (δ 3.22 and 3.16, J = 6.5 Hz) and the allylic carbons as two peaks (δ 43.8 and 45.4). It has been clearly shown by Buchler et al. that the porphodimethene macrocycle is folded like a roof along the line joining the two saturated meso carbons,[12a,c] implying that two syn and one anti stereoisomers[20a] (Figure 2) can exist.

Our NMR data on compound **2a** only show that it contains two allyl groups in different environments. This could either correspond to the anti isomer of **2a** with an equatorial and an axial allyl group or to a 1:1 mixture of the syn diaxial and the syn diequatorial isomers.[20b] One cannot completely exclude a mixture of the anti isomer with the syn isomers provided that these syn isomers be in a 1:1 ratio. Further sophisticated experiments are needed to conclude between these different possibilities.

The above results show that reduction of allyl bromide by iron(II) tetraphenylporphyrin, in the presence of a reducing agent in excess, leads to a mixture of stereoisomers of the (5,15-diallyl-5,10,15,20-tetraphenylporphinato)iron(II) complex (**1a**).

The elemental analysis of compound **2b** as well as its mass spectrum (70 eV, 220 °C), which exhibits a molecular peak at m/e 692 and fragments at m/e 653 and 614 (corresponding to $(TPP)H_2$), indicate a $((TPP)(C_3H_3)_2)H_2$ structure. The reasons for which a porphodimethene structure is proposed for **2b** are identical with those indicated for **2a**: (i) a characteristic UV–vis spectrum with a single band at 426 nm;[12b,c] (ii) four bands (1675, 840, 925, and 1230 cm^{-1}) in its IR spectrum characteristic of the porphodimethene ring,[12a] (iii) the low-shifted ^1H NMR resonances of the N–H protons around 13 ppm, (iv) the presence of quaternary sp^3 carbons as shown by the ^{13}C NMR spectrum.

Concerning the nature of the C_3H_3 groups linked to the α and γ meso positions the presence of an allenyl group is indicated by a 1950-cm^{-1} band in the IR spectrum and by the low-field shifted signals in the ^{13}C NMR spectrum at 207.6 and 208.5 ppm. The presence of a propargyl group is indicated by the 3280- and 2280-cm^{-1} bands in the IR spectrum and by the peaks at 30.8 and 30.4 ppm in the ^{13}C NMR spectrum, which correspond to saturated secondary carbons as shown by off-resonance experiments. Thus, the spectroscopic characteristics of compound **2b** (Tables I and II) can be only interpreted if one considers that this compound is a mixture of three 5,15-dialkylporphodimethene isomers, with either a propargyl or an allenyl group bound to two meso carbon atoms of the porphyrin ring (Figure 1). The proton signals

(16) Prepared by condensation of pentadeuteriobenzaldehyde and pyrrole in CH_3CH_2COOD by the usual technique.[14a] The obtained porphyin was found by ^1H NMR and mass spectrometry to be completely deuterated on the phenyl rings and only partially deuterated on the pyrrole rings; its dianion corresponds to the formula *meso*-tetrakis(pentadeuteriophenyl)porphyrin $[C_{44}H_3D_{25}N_4]^{2-}$.

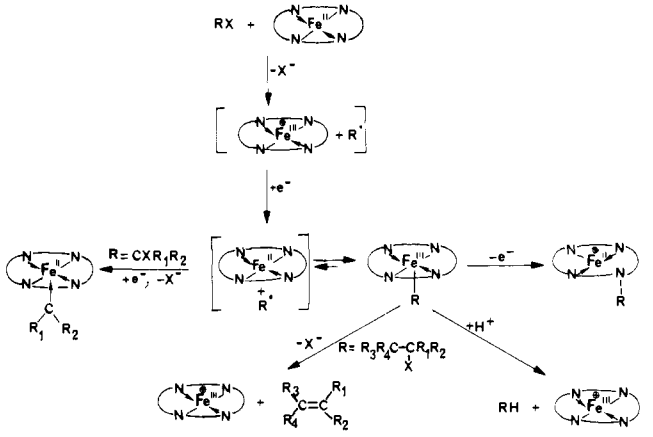
(17) Scheer, H.; Katz, J. J. In "Porphyrins and Metalloporphyrins"; Smith, K. M., Ed.; Elsevier: New York, 1975; pp 448–457.

(18) For comparison, the N–H protons appear at 12.58 ppm in the ^1H NMR spectrum of the porphodimethene $((OEP)Me_2)H_2$ previously described.[12b,c]

(19) The comparison can also be done between compound **1a** and various previously reported metal complexes of porphodimethenes derived from OEP, which generally exhibit, in their visible spectra, a single strong band between 460 and 480 nm.[12]

(20) (a) In the case of porphodimethene compounds containing two different alkyl groups, $((TPP)RR')H_2$, four stereoisomers are possible (two syn and two anti). (b) Very recently, the two syn-axial and syn-equatorial isomers of $((OEP)R_2)H_2$ porphodimethenes have been isolated in the case of R = C_2H_5, i-C_3H_7, t-C_4H_9, upon reductive dialkylation of Zn(OEP) by using sodium anthracenide and the corresponding alkyl iodide and acidic demetalation: Botulinski, A.; Buchler, J. W.; Lay, K. L.; Stoppa, H. *Liebigs Ann. Chem.*, in press.

Scheme I. Different Types of Reactions Observed during Reduction of Alkyl Halides by Ferroporphyrins



integration and the use of spin-decoupling techniques allowed us to establish that compound **2b** is actually a mixture of three porphodimethenes: **2b′** $[(TPP)(CH_2C{\equiv}CH)_2]H_2$ (75%), **2b″** $[(TPP)(CH{=}C{=}CH_2)_2]H_2$ (10%), and **2b‴** $[(TPP)(CH_2C{\equiv}CH)(CH{=}C{=}CH_2)]H_2$ (15%).

As three isomers are possible for **2b′** and **2b″** (two syn and one anti for each of them) and four stereoisomers for **2b‴** (two syn and two anti), **2b** has 10 different possible isomers. Its very complex ^1H NMR spectrum reveals that the acetylenic protons of **2b′** appear as three signals of 2:1:1 relative intensity and that the propargylic CH_2 and allenyl CH_2 protons of **2b‴** appear each as two doublets of 70:30 relative proportions. This suggests that **2b′** is at least a mixture of two different stereoisomers. This also suggests that **2b‴** is a 70:30 mixture of two stereoisomers. In the case of **2b″**, the signals of allenyl CH (or CH_2) protons of the different stereoisomers are not enough separated to estimate their proportions. However, it is noteworthy that because of the complexity of the spectra of **2b** and the possible superimposition of some signals of the different stereoisomers, it is presently difficult to give a definitive conclusion on the nature and proportions of these stereoisomers.

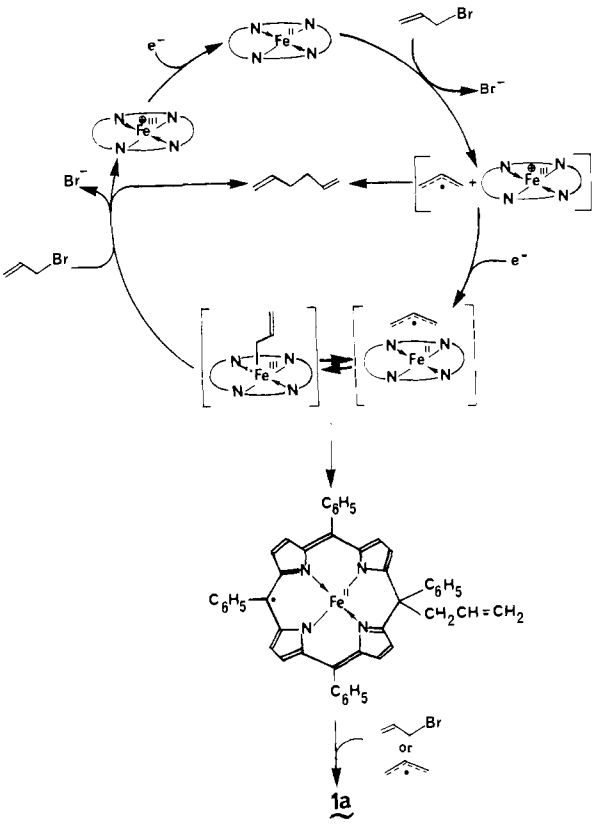
The above results show that reduction of propargyl bromide by Fe^{II}(TPP) in the presence of an excess of reducing agent leads to a mixture of stereoisomers of the (5,15-dipropargyl-5,10,15,20-tetraphenylporphinato)iron(II) (**1b′**), (5,15-diallenyl-5,10,15,20-tetraphenylporphinato)iron(II) (**1b″**), and (5-propargyl-15-allenyl-5,10,15,20-tetraphenylporphinato)iron(II) (**1b‴**) complexes (Figure 1).

Discussion

The various results previously described concerning the reduction of compounds containing at least one reactive carbon–halogen bond either by iron porphyrins[3,4,6-9] or by hemoproteins such as hemoglobin[6b-c] or cytochrome P-450[2,5] can be interpreted as deriving from a common situation where a free radical is generated in close proximity of an iron(III) porphyrin (Scheme I). Upon iron porphyrin reduction, the free radical is then in close proximity of an iron(II) porphyrin. It has been shown by using pulse-radiolysis techniques that methyl, halogenomethyl, and CF_3CHCl radicals react very rapidly with iron(II) porphyrins, and the formation of σ-alkyl ferric complexes has been proposed to occur in these reactions.[21] Evidence has been provided for the formation of such complexes upon reduction of benzyl halides or halothane $CF_3CHClBr$ by iron porphyrins[4,7] and cytochrome P-450.[2b-d] All these results show that the preferred evolution of the Fe^{II} + R· situation is the formation of a σ-alkyl complex Fe^{III}–R. However, since σ-alkyl porphyrin–Fe^{III}–R complexes with R = CH_3 or *n*-Bu were found to slowly decompose in DMF

(21) (a) Brault, D.; Bizet, C.; Morliere, P.; Rougee, M.; Land, E. J.; Santus, R.; Swallow, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 1015–1020. (b) Brault, D.; Neta, P. *Ibid.* **1981**, *103*, 2705–2710. (c) Brault, D.; Neta, P. *J. Phys. Chem.* **1982**, *86*, 3405–3410.

Scheme II. Proposed Mechanism for the Reduction of Allyl Bromide by Fe^{II}(TPP) in the Presence of a Reducing Agent in Excess



at room temperature leading to the corresponding Fe(II)–porphyrin,[22] the Fe^{II} + R· situation could be described in terms of an equilibrium: Fe^{II} + R· ⇌ Fe^{III}–R. Depending upon the nature of R, the σ-alkyl complex can be protonated leading to RH and regenerating the ferric porphyrin as found upon benzyl halides reduction by iron porphyrins[4] or cytochrome P-450[2d] or can undergo the elimination of an halogen substituent in β-position relative to iron as found upon halothane, CCl_3–CCl_3, and C-Cl_3–$CHCl_2$ reduction by iron porphyrins[3] or cytochrome P-450.[2b,c] Another possible evolution of such σ-alkyl complexes is the α-elimination of an halogen substituent to give Fe(II)–carbene complexes.[2a,8,9] Moreover, it has been shown that σ-alkyl Fe^{III}–R complexes with R = methyl, vinyl, or phenyl can be oxidized to the corresponding iron(II) *N*-alkylporphyrin[23] (Scheme I).

The present results on allyl bromide reduction can be easily explained with the same mechanism (Scheme II). The allyl radical formed in a first step can combine with Fe(II) leading to a σ-allyl ferric complex. We could not detect this complex in the used conditions[24] but the σ-allyl–Fe^{III}(OEP) complex has been prepared and found unstable and prone to react with a stoichiometric amount of allyl bromide to give 1,5-hexadiene.[25] Such a reaction would explain our results, the reaction of the σ-allyl complex with allyl bromide in excess leading rapidly to 1,5-hexadiene and regenerating the starting iron(III) porphyrin complex. Thus, the σ-allyl complex would exist in a very low steady-state concentration. Actually, one cannot completely exclude the formation of 1,5-hexadiene by dimerization of the allyl radical. Besides the fast combination of Fe(II) with the allyl radical, which

(22) Lexa, D.; Mispelter, J.; Saveant, J. M. *J. Am. Chem. Soc.* **1981**, *103*, 6806–6812.

(23) (a) Mansuy, D.; Battioni, J. P.; Dupre, D.; Sartori, E.; Chottard, G. *J. Am. Chem. Soc.* **1982**, *104*, 6159–6161. (b) Ortiz de Montellano, P. R.; Kunze, K. L.; Augusto, O. *Ibid.* **1982**, *104*, 3545–3546.

(24) We have prepared the (TPP)Fe^{III}–allyl complex by reaction, at −40 °C, of $CH_2{=}CH{-}CH_2MgBr$ with Fe(TPP)(Cl): λ_{max} (in toluene) 415, 524 nm. Up to −20 °C, it decomposes to give Fe(TPP) with more than 95% yield.

(25) Ogoshi, H.; Sugimoto, H.; Yoshida, Z.; Kobayashi, H.; Sakai, H.; Maeda, Y. *J. Organomet. Chem.* **1982**, *234*, 185–195.

ensures an efficient catalytic cycle, a slower secondary reaction occurs, the reaction of the allyl radical with one of the iron-porphyrin meso positions. In the free radical produced by this process, the meso methine bridge opposite to the methylene bridge has the highest spin density.[26] Reaction of this methine carbon with either allyl bromide or an allyl radical formed in steady-state concentration would lead to the observed iron(II) porphodimethene complex (Scheme II). This mechanism is in agreement with the results obtained with propargyl bromide, the nonsymmetrical radical formed in this case existing as either a propargyl or an allenyl radical. The fact that we never observed such porphodimethene formation upon reduction of halogenated compounds different from allyl or propargyl halides might be explained by the spin delocalization of the allyl and propargyl radicals which places one reactive carbon in good proximity of the meso carbons of the porphyrin ring.

(26) Fuhrhop, J. H. In "Porphyrins and Metalloporphyrins"; Smith, K. M., Ed.; Elsevier: New York, 1975; pp 594-623.

Conclusion

The aforementioned results indicate a new way of preparation of porphodimethenes in very mild conditions (temperature 20 °C, pH 7.4, mild reducing agent). In that regard it is noteworthy that previously described porphodimethenes have been prepared only in the OEP series and have involved hard conditions (reductive alkylation of metalloporphyrins with sodium anthracenide as reducing agent).[12,20b] A similar irreversible modification of the porphyrin ring could occur during the reductive metabolism of allyl and propargyl halides by cytochrome P-450.

Registry No. 1a, 91128-68-6; **1b'**, 91128-69-7; **1b''**, 91128-70-0; **1b'''**, 91158-26-8; **2a**, 91178-21-1; **2b'**, 91158-27-9; **2b''**, 91158-28-0; **2b'''**, 91158-29-1; allyl bromide, 106-95-6; propargyl bromide, 106-96-7; Fe(TPP)(Cl), 16456-81-8.

Tris(imidazole)-Containing Phosphine:M^{2+} Complexes as Biomimetic Catalysts. Importance of a L:M^{2+}–OH^- in the Catalyzed Bimolecular Hydrolysis of *p*-Nitrophenyl Picolinate

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Contribution from the Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2G2. *Received January 9, 1984*

Abstract: A series of tris(imidazole)-containing phosphines were prepared and their M^{2+} complexes studied as biomimetic catalysts for the hydrolysis of *p*-nitrophenyl picolinate. Triimidazol-2-ylphosphine (**3**) and tris[4(5)-(hydroxyethyl)-imidazol-2-yl]phosphine (**4**) as their Zn^{2+} complexes promote the hydrolysis of pNPP in aqueous solution, their catalytic activities increasing with pH. Because they have relatively low affinities for Zn^{2+}, they are incompletely complexed at concentrations of 5×10^{-4} M which complicates analysis of the kinetic data. Formation of precipitates occurs above pH 7.6. At a given pH, the second-order catalytic rate constants $k_{3:Zn^{2+}}^{cat.}$ and $k_{4:Zn^{2+}}^{cat.}$ are 2–10-fold larger than those for Zn^{2+} or the ligand alone which indicates a cooperative interaction between ligand and Zn^{2+} producing a more active catalyst. Bis(4,5-diisopropyl-imidazol-2-yl)imidazol-2-ylphosphine (**5**) and bis(4,5-diisopropylimidazol-2-yl)[4(5)-(hydroxyethyl)imidazol-2-yl]phosphine (**6**) bind both Zn^{2+} and Co^{2+} more strongly but require media consisting of 80% ethanol–H_2O for their study. As a function of pH, **5**:Zn^{2+} and **6**:Zn^{2+} become increasingly active but precipitation occurs above pH 7.2. However their Co^{2+} complexes are more soluble and can be studied up to pH 8.6. Below pH 7.4 their activities increase with a first-order dependence on $[OH^-]$ and level off thereafter, indicating that a basic form of the complex (L:Co^{2+}–OH^-) with a pK of ~7.6–7.8 is the active species. Since no evidence of a preequilibrium formation of a L:Co^{2+}:pNPP ternary complex is observed, the basic form of the complex is acting as a bimolecular nucleophile toward pNPP.

Introduction

A large number of Zn^{2+}-containing metalloenzymes are known whose physiological role stems from the ability of the active site metal to promote hydrolysis or hydration reactions.[1] Among these are some well-studied hydrolases such as carboxypeptidase A (CPA), Thermolysin, angiotensin-converting enzyme and alkaline phosphatase, and the lyases, the most well-studied member being carbonic anhydrase.[2] Although the detailed mechanisms of action of these enzymes are presently not well understood, the great bulk of evidence points to the ability of the active-site Zn^{2+} to activate H_2O as a nucleophile at some point along the reaction profile. Thus by virtue of ligation to the electropositive M^{2+}, the pK_a of H_2O is said to be reduced from ~15.7 in solution to values approaching 7 in the active site such that at physiological pH, a Zn^{2+}–OH^- is produced that is sufficiently nucleophilic to attack (depending upon the enzyme) the X=O linkage of esters, amides CO_2, and phosphate monoesters.[3] Of course additional roles for the metal are also likely such as a Lewis acid and/or template upon which the reaction can occur. The protein matrix in which the M^{2+} is embedded will also influence the chemistry particularly in terms of substrate specificity and orientation as well as by modifying the activity of the reactants by solvation effects.

A large number of recent studies have shown that small molecules incorporating both a metal-binding site and covalently

(1) For compendia of leading references to Zn^{2+} enzymes see: (a) Galdes, A.; Vallee, B. L. *Met. Ions Biol. Syst.* **1983**, *15*, 1–55. (b) Prince, R. H. *Adv. Inorg. Chem. Radiochem.* **1979**, *22*, 349–440. (c) Galdes, A.; Hill, H. A. O. *Inorg. Biochem.* **1979**, *1*, 317–346. (d) Galdes, A. *Ibid.* **1982**, *3*, 268–313.

(2) For a compendia of references to carbonic anhydrase see: (a) Lindskog, S.; Ibrahim, S. A.; Jonsson, B.-H.; Simonsson, I. in "The Coordination Chemistry of Metalloenzymes"; Bertini, I.; Drago, R. S., Luchinat, C., Eds.; D. Reidel Publishing Co.: Boston, MA, 1983, pp 49–64. (b) Silverman, D. N.; Vincent, S. H. *CRC Crit. Rev. Biochem.* **1983**, *14*, 207–255.

(3) In the case of alkaline phosphates that hydrolyze a wide range of phosphate monoesters, the primary catalytic step is to produce a phosphorylserine intermediate that is subsequently hydrolyzed. This second step requires that H_2O in the active site be activated to the point that it nucleophilically cleaves a normally unreactive phosphate. For discussions of the sequence of events see: Coleman, J. E.; Chlebowski, J. F. *Adv. Inorg. Biochem.* **1979**, *1*, 2–66.

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