reagents are being examined for use in the catalytic cyclopropanation of alkenes and alkynes. In addition, further mechanistic investigation is under way.

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Catalytic Conversion of Simple Haloporphyrins into Alkyl-, Aryl-, Pyridyl-, and Vinyl-Substituted Porphyrins

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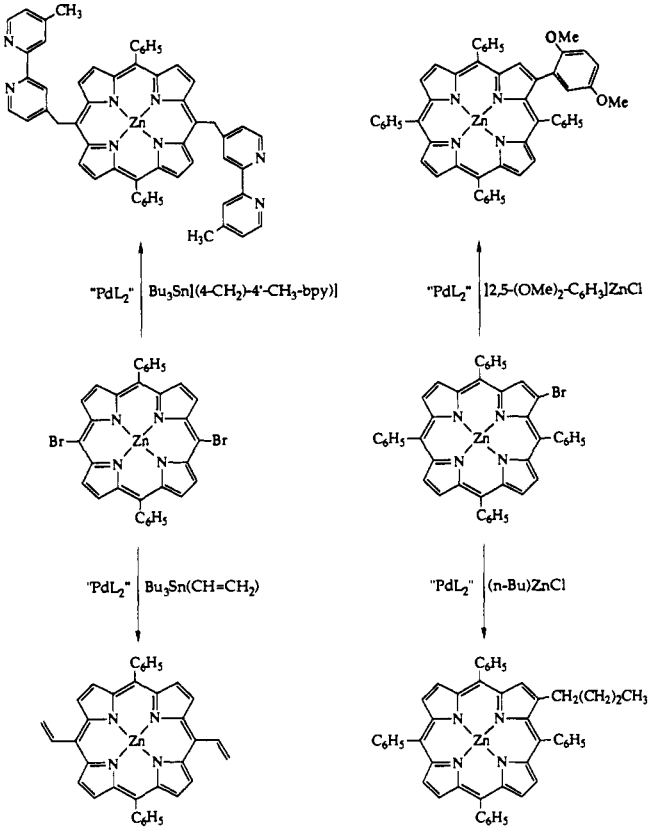
Appending unusual organic moieties to the porphyrin periphery has often involved elaborate synthetic strategies and difficult separations of reactants from product(s).[1] For example, typical routes to porphyrins that possess one or more differing *meso* or β substituents have employed condensation of the appropriate aldehyde(s) with various monopyrroles,[2] substituted dipyrrylmethanes,[3] or prefabricated 1,19-dideoxybiladienes.[4] In addition to the considerable chromatography that is generally required, other limitations inherent in these approaches include (1) the sensitivity of the cyclization step in a porphyrin synthesis to the steric and electronic features of substituents at the methine and pyrrolic positions and (2) the potential incompatibility of one or more of the components in the syntheses to conditions common to all previous porphyrin preparations, namely, protic or Lewis acid catalysis[5] or high temperature.[6] We report herein a powerful new approach to both mixed meso-substituted porphyrins and unsymmetrical porphyrins; this methodology greatly simplifies the fabrication of such molecules and *dramatically* amplifies[7,8] the types of porphyrins which can now be synthesized.

Metal-mediated cross-coupling methodology, developed largely by Kumada,[9] Negishi,[10] Heck,[11] and Stille,[12] has become an important tool in modern organic chemistry to facilitate formation of carbon–carbon bonds between aryl or alkenyl halide substrates and a variety of alkyl, aryl, and vinyl organometallic reagents. We have recently discovered in our laboratory that this methodology is directly applicable to a wide variety of porphyrin synthetic schemes, provided the reducing power of the organometallic species used in the reaction is insufficient to participate in an outer sphere electron transfer reaction with the porphyrin.

Scheme I



In a typical reaction, (5,15-dibromo-10,20-diphenylporphinato)zinc (**1**)[13] or (2-bromotetraphenylporphinato)zinc (**2**)[14] and an excess of the desired organometallic reagent (RZnX or Bu_3SnR) were brought together in dry THF under nitrogen at 60 °C for 12–48 h in the presence of a catalytic amount of $Pd(PPh_3)_4$. Over the course of several hours, the initially nonfluorescent reaction mixture became increasingly more fluorescent, signaling the gradual transformation of the halogenated porphyrin complex to the alkyl-, vinyl-, aryl-, or pyridyl-substituted zinc porphyrin. For the organometallic reagents depicted in Scheme I, quantitative conversion of reactants to products took place within 48 h.[15]

It is interesting to note that the oxidative addition–transmetalation–reductive elimination reaction sequence occurs much more rapidly at the porphyrin pyrrolic carbon than the analogous re-

(1) *Porphyrins and Metalloporphyrins*; Smith, K. D., Ed.; Elsevier: New York, 1975.

(2) (a) Kim, J. B.; Adler, A. D.; Longo, F. R. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: London, 1978; Vol. I. (b) For a recent example of a porphyrin synthesized via this approach, see: O'Neil, M. P.; Niemczyk, M. P.; Svec, W. A.; Gosztola, D.; Gaines, G. L.; Wasielewski, M. R. *Science (Washington, D.C.)* **1992**, *257*, 63–65.

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(4) (a) Johnson, A. W. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: London, 1978; Vol. I. (b) For a recent example of a porphyrin synthesized via this approach, see: Joran, A. D.; Leland, B. A.; Geller, G. G.; Hopfield, J. J.; Dervan, P. B. *J. Am. Chem. Soc.* **1984**, *106*, 6090–6092.

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(8) (a) DiMagno, S. G.; Lin, V.S.-Y.; Therien, M. J., manuscript in preparation. (b) Lin, V.S.-Y.; DiMagno, S. G.; Therien, M. J. Manuscript in preparation.

(9) (a) Tamao, K.; Sumitani, K.; Kiso, Y.; Zembayashi, M.; Fijioka, A.; Kodama, S.-I.; Nakajima, I.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1958–1969. (b) Kumada, M. *Pure Appl. Chem.* **1980**, *52*, 669–678.

(10) Negishi, E.-I.; Luo, F. T.; Frisbee, R.; Matsushita, H. *Heterocycles* **1982**, *18*, 117–122.

(11) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146–151.

(12) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508–524.

(13) Prepared in high yield (88%) from 5,15-diphenylporphyrin under conditions analogous to those employed by Longo for the halogenation of porphine. Nudy, L. R.; Hutchinson, H. G.; Schieber, C.; Longo, F. R. *Tetrahedron* **1984**, *40*, 2359–2363. The selective bromination of porphyrins at free meso positions can be carried out with a *wide variety* of substituents present.

(14) (a) Samuels, E.; Shuttleworth, R.; Stevens, T. S. *J. Chem. Soc. C* **1968**, 145–147. (b) Callot, H. J. *Bull. Soc. Chim. Fr.* **1974**, 1492. 2-Bromoporphyrin and 2-nitroporphyrin have been utilized previously for several direct substitution reactions. Direct substitution reactions involving porphyrin substrates are neither general nor efficient; see: (c) Callot, H. J. *Tetrahedron Lett.* **1973**, *50*, 4987–4990. (d) Crossley, M. J.; Harding, M. M.; Sternhall, S. *J. Am. Chem. Soc.* **1986**, *108*, 3608–3613.

(15) More recent work in our lab[7] has shown that Pd^0(dppf) [dppf = 1,1'-bis(diphenylphosphino)ferrocene] is a much more reactive catalyst for cross-coupling chemistry on porphyrin templates; reactions similar to those described in the text have been observed to go to completion within 1 h at room temperature with the Pd^0(dppf) catalyst. See: Hayashi, T.; Konishi, M.; Kumada, M. *Tetrahedron Lett.* **1979**, *21*, 1871–1874.

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action sequence at the porphyrin methine carbon.[7] For the transformations depicted in Scheme I, typical reaction times required for complete conversion of reactants to products were ~12 h (60 °C) for a $Pd(PPh_3)_4$-catalyzed coupling utilizing a (2-bromotetraphenylporphinato)zinc substrate while couplings employing (5,15-dibromo-10,20-diphenylporphinato)zinc templates required longer reaction times (~48 h). These results are in accord with what has been observed for Pd-catalyzed cross-coupling reactions involving simple aromatic halide substrates: the observed rate of product formation depends critically on the electronic features of the aromatic substrate, with more electron rich aromatics being more slowly converted to products.[16] Numerous experimental[17] and theoretical studies[18] concur that porphyrin methine carbons are more electron rich than pyrrolic ones.

Synthesis of [5,15-bis[[2-(4′-methyl-2′-pyridyl)-4-pyridyl]-methyl]-10,20-diphenylporphinato]zinc(II),[19] [5,15-divinyl-10,20-diphenylporphinato]zinc(II),[20] [2-(2,5-dimethoxyphenyl)-5,10,15,20-tetraphenylporphinato]zinc(II),[21] and [2-*n*-butyl-5,10,15,20-tetraphenylporphinato]zinc(II),[22] from the appropriate brominated zinc porphyrin, the Pd^0 catalyst, and $Bu_3Sn[(4\text{-}CH_2)\text{-}4'\text{-}CH_3\text{-}bpy)]$, $Bu_3Sn(CH{=}CH_2)$, $[2,5\text{-}(MeO)_2C_6H_3]ZnCl$, and *n*-BuZnCl, respectively, illustrates the versatility of this new approach. The typical *isolated* yield of each of these new porphyrin compounds was 90%; in general, our reactions were carried out with 100–250 mg of the haloporphyrin starting material in ~50 mL of solvent.

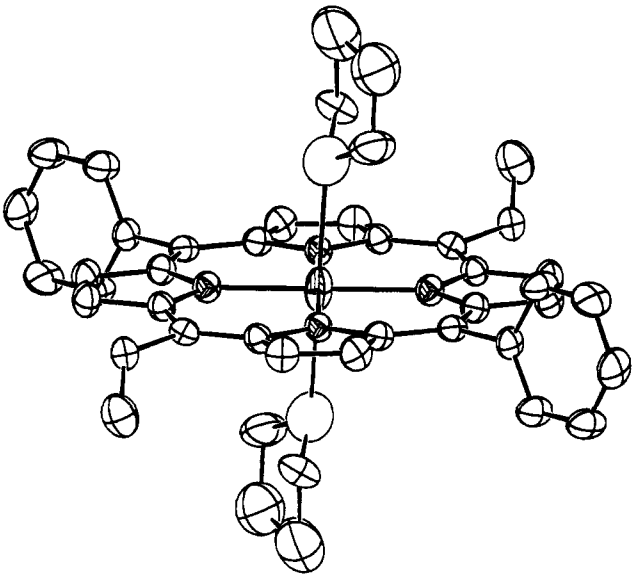

Figure 1. ORTEP view of [5,15-divinyl-10,20-diphenylporphinato]-zinc(II)$(THF)_2$ with thermal ellipsoids at 50% probability.

Although it is apparent from the compounds presented in Scheme I that a variety of organic functionalities can be cross-coupled to porphyrins, the synthesis of [5,15-divinyl-10,20-diphenylporphinato]zinc(II) demonstrates both the power and the scope of this method. The di-*meso*-vinyl-substituted porphyrin is extraordinary in the sense that, prior to this report, no straightforward route to this complex existed.[23] Introduction of *meso*-vinyl groups by a conventional porphyrin synthesis would require the condensation of acrolein with pyrrole or some pyrrole-containing porphyrin precursor; major experimental obstacles preclude such approaches: (1) Lindsey-type porphyrin syntheses[5] are impractical since acrolein polymerizes in the presence of strong acids and undergoes Lewis acid catalyzed ene reactions, and (2) Adler–Longo high-temperature porphyrin syntheses[6] are inappropriate since acrolein undergoes a Diels–Alder reaction with itself.

The results of our single-crystal X-ray crystallographic study[24] of [5,15-dinvyl-10,20-diphenylporphinato]zinc(II) are shown in Figure 1. The long Zn–O bond length [2.536(7) Å] is similar to that reported for the bis THF adduct of [5,10,15,20-tetraphenylporphyrinato]zinc(II),[25] in which the Zn axial ligands are only weakly coordinated [Zn–O = 2.380(2) Å]. The dihedral angle (84.0°) of the phenyl rings of [5,15-divinyl-10,20-diphenylporphinato]zinc(II) with respect to the porphyrin plane resembles that in [5,10,15,20-tetraphenylporphyrinato]zinc(II)

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(19) [5,15-Bis[[2-(4′-methyl-2′-pyridyl)-4-pyridyl]methyl]-10,20-diphenylporphinato]zinc(II): isolated yield = 81%. Selected characterization data: ^1H NMR (500 MHz, $CDCl_3$) δ 9.37 (d, 4 H, J = 4.7 Hz), 8.87 (d, 4 H, J = 4.7 Hz), 8.52 (s, 2 H), 8.29 (d, 2 H, J = 5.1 Hz), 8.20 (d, 2 H, J = 5.2 Hz), 8.10 (m, 6 H), 7.71 (m, 6 H), 7.01 (d, 2 H, J = 5.0 Hz), 6.88 (d, 2 H, J = 4.2 Hz), 6.46 (s, 4 H), 2.32 (s, 6 H); ^{13}C NMR spectroscopy was performed on a more soluble demetalated sample; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.25(0), 155.83(0), 154.06(0), 149.31(1), 148.89(1), 147.99(0), 141.99(1), 134.35(1), 132.09(1), 132.01(1), 128.50(1), 128.40(1), 127.74(1), 126.56(1), 124.63(1), 124.57(1), 122.06(1), 120.45(1), 119.88(0), 113.81(0), 39.77(2), 21.07(3); vis (CH_2Cl_2) 419 (5.57), 516 (4.27), 550 (3.74), 593 (3.59), 650 (3.31). Anal. Calcd for $C_{56}H_{42}N_8$: C, 81.33; H, 5.12; N, 13.55. Found: C, 81.19; H, 4.97; N, 13.79.

(20) [5,15-Divinyl-10,20-diphenylporphinato]zinc(II): isolated yield = 91%. Selected characterization data: ^1H NMR (500 MHz, $CDCl_3$) δ 9.52 (d, 4 H, J = 4.7 Hz), 9.24 (dd, 2 H, J_1 = 17.3 Hz, J_2 = 9.1 Hz), 8.92 (d, 4 H, J = 4.7 Hz), 8.19 (dd, 4 H, J_1 = 6.8 Hz, J_2 = 2.0 Hz), 7.75 (m, 6 H), 6.48 (dd, 2 H, J_1 = 11.0 Hz, J_2 = 1.9 Hz), 6.05 (dd, 2 H, J_1 = 17.3 Hz, J_2 = 2.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.40(1), 149.90(0), 149.21(0), 142.83(0), 137.97(0), 134.40(1), 132.10(1), 130.39(1), 127.50(1), 126.73(2), 126.57(1), 121.05(0); vis (CH_2Cl_2) 422 (5.58), 554 (4.22), 595 (3.82). An analytical sample was demetalated with HCl. Anal. Calcd for $C_{36}H_{26}N_4$: C, 84.02; H, 5.09; N, 10.89. Found: C, 83.76; H, 4.73; N, 10.57.

(21) [2-(2,5-Dimethoxyphenyl)-5,10,15,20-tetraphenylporphinato]zinc(II): isolated yield = 91%. Selected characterization data: ^1H NMR (500 MHz, $CDCl_3$) δ 8.92 (m, 4 H), 8.85 (s, 1 H), 8.84 (d, 1 H, J = 4.7 Hz), 8.70 (d, 1 H, J = 4.7 Hz), 8.22 (m, 6 H), 7.98 (d, 1 H, J = 7.0 Hz), 7.71 (m, 10 H), 7.24 (m, 2 H), 7.14 (m, 1 H), 6.92 (d, 1 H, J = 3.1 Hz), 6.54 (dd, 1 H, J_1 = 8.9 Hz, J_2 = 3.1 Hz), 6.40 (d, 1 H, J = 8.9 Hz), 3.68 (s, 3 H), 3.42 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.67(0), 151.22(0), 150.46(0), 150.30(0), 150.26(0), 150.11(0), 150.02(0), 148.29(0), 147.71(0), 143.32(0), 142.99(0), 142.88(0), 142.85(0), 140.73(0), 135.65(1), 135.18(1), 134.45(1), 134.38(1), 134.14(1), 132.51(1), 132.00(1), 131.89(1), 131.81(1), 131.31(1), 129.31(0), 127.43(1), 127.36(1), 127.19(1), 126.53(1), 126.49(1), 126.46(1), 124.93(1), 124.70(1), 122.35(0), 121.29(0), 120.89(0), 120.53(0), 118.16(1), 113.01(1), 110.39(1), 55.99(3), 54.88(3); vis ($CHCl_3$) 421 (5.60), 513 (3.45), 550 (4.28), 587 (3.45). An analytical sample was demetalated with HCl. ^1H NMR (500 MHz, $CDCl_3$): δ 8.92 (m, 4 H), 8.79 (s, 1 H), 8.78 (d, 1 H, J = 4.7 Hz), 8.67 (d, 1 H, J = 4.8 Hz), 8.28 (br s, 6 H), 8.02 (br d, 1 H), 7.74 (m, 10 H), 7.24 (br m, 3 H), 7.07 (d, 1 H, J = 3.1 Hz), 6.66 (dd, 1 H, J_1 = 8.8 Hz, J_2 = 3.1 Hz), 6.40 (d, 1 H, J = 8.8 Hz), 3.77 (s, 3 H), 3.37 (s, 3 H), −2.59 (s, 2 H). Anal. Calcd for $C_{52}H_{38}N_4$: C, 83.18; H, 5.10; N, 7.46. Found: C, 83.13; H, 5.06; N, 7.51.

(22) [2-*n*-Butyl-5,10,15,20-tetraphenylporphinato]zinc(II):[14d] isolated yield = 92%. Selected characterization data: ^1H NMR (500 MHz, $CDCl_3$) δ 8.96 (d, 1 H, J = 4.6 Hz), 8.94 (s, 2 H), 8.91 (d, 1 H, J = 4.5 Hz), 8.90 (d, 1 H, J = 4.6 Hz), 8.76 (d, 1 H, J = 4.6 Hz), 8.73 (s, 1 H), 8.23 (m, 6 H), 8.11 (d, 2 H, J = 6.8 Hz), 7.71 (m, 12 H), 2.82 (t, 2 H, J = 8.0 Hz), 1.73 (quint, 2 H, J = 8.1 Hz), 1.31 (sextet, 2 H, J = 7.7 Hz), 0.89 (t, 3 H, J = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.11(0), 150.39(0), 150.18(0), 149.81(0), 149.79(0), 149.51(0), 149.51(0), 149.15(0), 148.39(0), 147.95(0), 143.29(0), 143.23(0), 142.92(0), 134.42(1), 134.38(1), 133.12(1), 132.24(1), 132.06(1), 132.03(1), 131.76(1), 131.67(1), 131.59(1), 131.25(1), 127.82(1), 127.40(1), 127.35(1), 126.65(1), 126.50(1), 126.46(1), 121.57(0), 121.01(0), 120.84(0), 119.44(0), 33.39(2), 30.58(2), 23.00(2), 13.91(3); vis ($CHCl_3$) 424 (5.52), 551 (4.22), 590 (3.42). An analytical sample was demetalated with HCl. Anal. Calcd for $C_{48}H_{38}N_4$: C, 85.94; H, 5.71; N, 8.35. Found: C, 85.67; H, 5.63; N, 8.30.

(23) *meso*-Vinyl-substituted porphyrins, though unusual, are not unknown. Previous routes to *singly meso*-vinyl substituted porphyrins typically required the synthesis of a *meso*-formylporphyrin via the Vilsmeier reaction. See: (a) Arnold, D. P.; Johnson, A. W.; Mahendran, M. *J. Chem. Soc., Perkin Trans. I* **1978**, 366–370. (b) Vicente, M. G. H.; Smith, K. M. *J. Org. Chem.* **1991**, *56*, 4407–4418.

(24) Crystal data for [5,15-divinyl-10,20-diphenylporphinato]zinc(II): $ZnC_{44}H_{32}N_4O_2$ crystallizes in the triclinic space group $P\bar{1}$ with a = 8.307(1) Å, b = 10.530(2) Å, c = 12.46(1) Å, α = 62.39(1)°, β = 112.34(1)°, γ = 109.59(1)°, V = 876(1) Å^3, Z = 1, and d_{calc} = 1.353 g/cm^3. Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were included as constant contributions to the structure factors and were not refined. Refinement converged to R_1 = 0.068 and R_2 = 0.091. The structure was determined by Dr. Patrick Carroll at the Chemistry Department's X-ray Facility at the University of Pennsylvania.

(25) Schauer, C. K.; Anderson, O. P.; Eaton, S. S.; Eaton, G. R. *Inorg. Chem.* **1985**, *24*, 4082–4086.

(80.8°). The *meso*-vinyl groups in our structure are held at a dihedral angle of 36.1° with respect to the porphyrin plane; this is not much different than the analogous dihedral angle (32.0°) reported by Ibers[26] for the pyrrolic vinyl group in the protoporphyrin IX structure.

In short, we believe that the ability to catalytically and quantitatively append a wide variety of groups to the porphyrin periphery under mild conditions utilizing readily available haloporphyrin precursors will have tremendous impact in porphyrin chemistry since electronic and steric features as well as chemical reactivity on the porphyrin periphery can be tuned *independently* of the limiting set of experimental conditions that allow for porphyrin ring cyclization. Exploitation of this chemistry in our group has allowed synthesis of novel porphyrin arrays,[8a] monomeric porphyrins with unique electronic properties,[7,8b] unusual cofacial porphyrins,[27] and new porphyrin-based donor–spacer–acceptor systems.[28] Additionally, recent results in our lab indicate that, for at least some organometallic reagents, this methodology can be applied to perhalogented porphyrin templates.[29]

Acknowledgment. M.J.T. thanks the Searle Scholars and Beckman Young Investigator Programs for generous financial support and Timothy M. Swager for helpful discussions.

Supplementary Material Available: Tables of positional parameters, anisotropic temperature factors, bond distances, and bond angles for the divinylporphinato compound (11 pages); table of observed and calculated structure factors for the divinylporphinato compound (9 pages). Ordering information is given on any current masthead page.

(26) Caughey, W. S.; Ibers, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 6639–6645.
(27) de Rege, P. J. F.; Therien, M. J. To be submitted.
(28) Hyslop, A.; DiMagno, S. G.; Therien, M. J. To be submitted.
(29) DiMagno, S. G.; Therien, M. J. To be submitted.

A Catalytic Antibody Model for PLP-Dependent Decarboxylases

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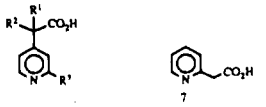
Received December 17, 1992

The decarboxylases represent a family of enzymes capable of generating enormous catalytic power. A coenzyme or prosthetic residue often serves as an electron sink to aid in affording rate accelerations of 10^{10}–10^{12} over background.[1] Furthermore, immersion of the substrate carboxyl group in an apolar site, as found in an antibody,[2] is a driving force which may account for a portion of the large rate enhancements.[3]

O'Leary and co-workers established 4-pyridylacetic acid **1** as a viable chemical model for pyridoxal phosphate (PLP)-utilizing decarboxylases.[4] This compound is known to decompose by way of its zwitterionic form with a rate dependent on the polarity of the medium (eq 1).[5]

Table I. Kinetic Constants for CPD32A11 Substrates[a]



compd no.	R^1	R^2	R^3	k_{cat} (min^{-1}) × 10^2	K_m (mM)	k_{cat}/k_{uncat}
1	H	H	H	2.8	144	1.9×10^5
4	H	CH_3	H	1.3	91	2.3×10^4
5	CH_3	CH_3	H	1.3	41	1.2×10^4
6	H	H	CH_3	0.15	70	2.0×10^5
7				0.077	95	1.4×10^4

[a] Determined at 23 °C in 100 mM MES, 100 mM NaCl, pH 5.5 in the presence or absence of 20 μM antibody. Buffer concentration effects were not observed. Assays were conducted using reversed-phase HPLC (Vydac C_{18}) by following product formation. Experimental errors are ±10%.

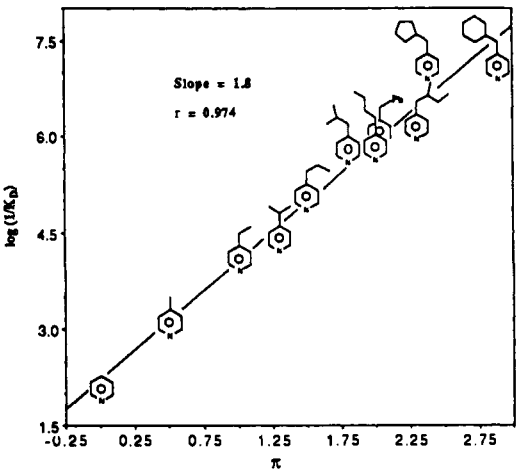
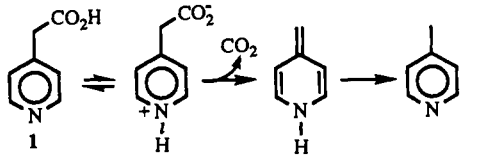
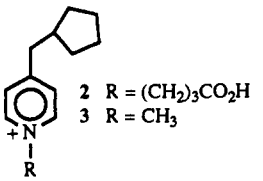


Figure 1. Hansch plot used to measure the hydrophobicity of the active site.



(1)

The evolution of this paradigm would incorporate recognition elements and a hydrophobic cavity within a protein scaffold to create a primitive enzyme. To this end, the hapten **2** was coupled



2 R = $(CH_2)_3CO_2H$
3 R = CH_3

to a carrier protein to finally obtain monoclonal antibodies.[6] It was reasonable to assume that such a structure would elicit combining sites possessing a complementary negative charge and a confined region of low dielectric constant.[7] Of several catalysts

† A. P. Sloan Fellow, 1993–1995.

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