(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]

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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.

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A Catalytic Antibody Model for PLP-Dependent Decarboxylases

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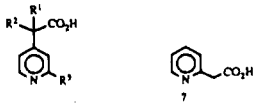
The decarboxylases represent a family of enzymes capable of generating enormous catalytic power. A coenzyme or prosthetic residue often serves as an electron sink to aid in affording rate accelerations of 10^{10}–10^{12} over background.[1] Furthermore, immersion of the substrate carboxyl group in an 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%.

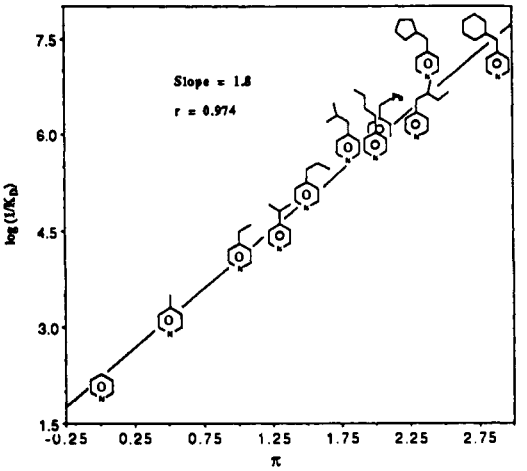
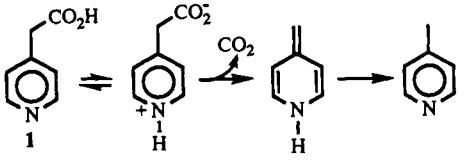
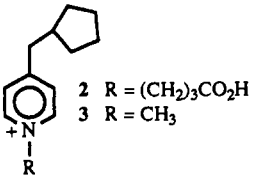


Figure 1. Hansch plot used to measure the hydrophobicity of the active site.



(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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examined, the monoclonal antibody CPD32A11 showed the highest initial velocity using **1** as a substrate, could be saturated with **1**, and was inhibited by **3** (K_i = 10 nM). The kinetic constants are shown in Table I. The k_{cat}/k_{uncat} of 10^5 might be representative of contributions to catalysis by enzymatic decarboxylases solely as a result of the microenvironment of the active site. The reduced k_{cat} for **7** suggests that an apolar surrounding is more localized in the desired area.

A measure of the hydrophobicity of the active site was garnered using a Hansch correlation analysis (Figure 1). The coefficient of 1.8 suggests that the region occupied by a 4-substituent can partition organic solutes more effectively than the solvent octanol.[8] While direct evidence is sparse, a recent crystal structure of a histidine decarboxylase–substrate analog complex situates the carboxyl group in a crevasse lined with apolar residues.[9] Clearly, such a medium could support destabilization as a component of the catalytic mechanism.[10] The association of antibody and hapten-like molecules is facilitated by classical hydrophobic effects.[11] On the other hand, it requires energy, reflected in the high K_m, to introduce a charged group into a hydrophobic pocket. The antibody operates by binding the pyridinium moiety through noncovalent interactions to position the carboxylate and therein promote the loss of carbon dioxide. Although PLP enzymes engage a covalent imine linkage, the noncovalent contributions to the stability of the enzyme–cofactor complex are 20–40 times greater.[12] However, the tight binding of PLP results from the summation of several substituent interactions not available in **1**.

A 2-methyl group in **6** did not yield a more specific (k_{cat}/K_m) substrate, as might be expected from the anchor principle.[13] It was anticipated that the binding energy could be utilized to improve substrate turnover. There has been speculation that hydrophobic binding of this group in PLP provides fine-tuning of catalysis for individual enzymes.[14] In enzymes, the optimization of cofactor binding and reactivity arises through evolution. However, in this model, favorable interactions adopted by the methyl group could alter the proper ionic contact necessary for reaction since it was not programmed in the hapten design of **2**, although occurrence of an antibody which utilizes **6** as its most efficient substrate is also possible.[15] Interestingly, the presence of an α-methyl group in substrate **4** lowers K_m as anticipated, but also reduces k_{cat}. The substituent could cause a decrease in rotational entropy of the carboxyl about the C_α–C_4 bond which prevents the optimum stereoelectronic orientation for decarboxylation.[16] A second methyl, as in **5**, shows a further reduction in K_m but not k_{cat} and indicates that the lowered k_{cat} of **4** is not a result of the chiral center. This nascent catalyst cannot foster the demanding spatial relationships which must exist between the amino acid and cofactor functionalities united in the pyridylacetic acid structure.

The simple model described provides a foundation for more complex designs. Most importantly, this investigation again demonstrates that catalytic antibodies can be useful tools for exploring the nature of biological catalysis.

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Asymmetric Substitution: Highly Enantioselective Substitutions Induced at the Carbanion of a Racemic Organolithium Substrate by (−)-Sparteine

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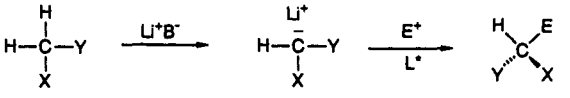
An inviting concept in asymmetric synthesis is the creation of an asymmetric carbon at an initially racemic nucleophilic carbanion under the influence of an external enantioenriched ligand upon electrophilic substitution.[1] In the sequence shown below for replacement of a prochiral proton via an organolithium intermediate, the second step is such an asymmetric substitution.

Asymmetric Substitution



racemic

Li^+B^- = organolithium base
L* = enantioenriched ligand
E^+ = electrophile

To the best of our knowledge, this kind of reaction has been observed with organolithium substrates only for a few electrophile dependent reactions of lithium enolates or with stereocontrol achieved by selective crystallization of an enantioenriched ligand–allyllithium reagent.[2,3] We now report experiments which

(1) Focus on the creation of the asymmetric center at the nucleophilic carbon is in contrast to most previous work using external enantioenriched ligands in which the new asymmetric center is created in the electrophile. For reviews and discussion, see: (a) Cox, P. J.; Simpkins, N. S. *Tetrahedron: Asymmetry* **1991**, *2*, 1. (b) Tomioka, K. *Synthesis* **1990**, 541. (c) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49.

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