Preliminary studies on trimethylamine reactions with the halogenated *closo*-carboranes 5,6-Cl_2-2,4-$C_2B_5H_5$ and 2-Cl-1,6-$C_2B_4H_5$ definitely implicate pyramidal nido adducts, although the subsequent removal of halide ion appears more complicated than in the case of the 5-chloro-2,4-dicarbaheptaborane adduct.

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References and Notes

(1) T. Onak, "Boron Hydride Chemistry", E. L. Muetterties, Ed., Academic Press, New York, 1975, Chapter 10, pp 349–382.
(2) T. Onak, *Spec. Period. Rep. Organomet. Chem.*, **1–6**, Chapter 4 (1972–1977); J. Leach, *ibid.*, 7 (1978).
(3) L. Lew, G. Haran, R. Dobbie, M. Black, and T. Onak, *J. Organomet. Chem.*, 111, 123–130 (1976).
(4) R. J. Thompson and J. C. Davis, *Inorg. Chem.*, **4**, 1464–1467 (1965); H. D. Johnson, V. T. Brice, G. L. Brubaker, and S. G. Shore, *J. Am. Chem. Soc.*, **94**, 6711–6714 (1972).
(5) R. Warren, D. Paquin, T. Onak, G. Dunks, and J. R. Spielman, *Inorg. Chem.*, **9**, 2285–2287 (1970).
(6) R. N. Grimes, *J. Am. Chem. Soc.*, **88**, 1895–1899 (1966).
(7) J. F. Ditter, E. B. Klusmann, R. E. Williams, and T. Onak, *Inorg. Chem.*, **15**, 1063–1065 (1976).
(8) T. Onak, A. P. Fung, G. Siwapinyoyos, and J. B. Leach, *Inorg. Chem.*, **18**, 2878–2882 (1979).
(9) B. Lockman and T. Onak, *J. Am. Chem. Soc.*, **94**, 7923–7924 (1972).
(10) T. Onak, B. Lockman, and G. Haran, *J. Chem. Soc., Dalton Trans.*, 2115–2118 (1973).
(11) R. E. Williams, *Inorg. Chem.* **10**, 210–214 (1971); K. Wade, *Chem. Commun.*, 792–793 (1971); K. Wade, *Inorg. Nucl. Chem. Lett.*, **8**, 823–827 (1972); R. W. Rudolph and W. R. Pretzer, *Inorg. Chem.*, 11, 1974–1978 (1972).

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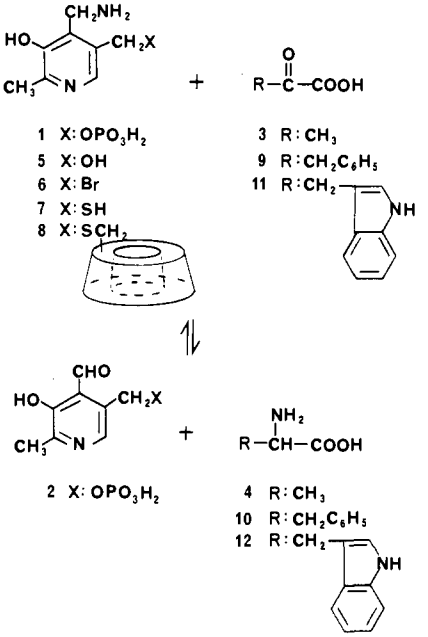
Selective Transamination and Optical Induction by a β-Cyclodextrin–Pyridoxamine Artificial Enzyme

Sir:

Pyridoxamine phosphate (**1**) and pyridoxal phosphate (**2**) are the characteristic coenzymes of amino acid metabolism.[1] Along with appropriate enzymes they perform a variety of carbon–carbon bond formations and cleavages, rearrangements, etc., on the paths to and from amino acids. However, the prototypical reaction involving these coenzymes is transamination. Pyridoxamine phosphate reacts with an α-keto acid such as pyruvic acid (**3**) to form a Schiff base which tautomerizes and cleaves to pyridoxal phosphate (**2**) and an amino acid, in this case alanine (**4**). In the complete cycle the sequence is then reversed, using a different amino acid such as phenylalanine (**10**) to convert the pyridoxal coenzyme back into **1**, while the amino acid **10** is converted into keto acid **9**.



Model studies[1,2] have shown that all of the known enzymatic reactions in which pyridoxal or pyridoxamine phosphate play a role can be duplicated to some extent with the coenzyme alone, without an enzyme. However, the reactions without an enzyme are much slower and are quite unselective among the possible reactions which the coenzymes can catalyze. Since β-cyclodextrin (cycloheptaamylose)[3] can be used in enzyme models which under the best circumstances show rate accelerations of enzymatic magnitude,[4] and since reactions of substrates bound into the cyclodextrin cavity are frequently very selective with respect to substrate and pathway,[5] it was attractive to link the pyridoxal–pyridoxamine coenzymes to β-cyclodextrin. We report here the first example of such a linked molecule (**8**). As expected, the combination in this molecule of an enzyme-like binding site with a coenzyme has led to good substrate specificity in transaminations and to some chiral induction.

Pyridoxamine (**5**) dihydrochloride was converted into the bromomethyl derivative (**6**) dihydrobromide[6,7] with 48% HBr. This with potassium thioacetate and then acetic anhydride afforded the *O,S,N*-triacetyl derivative[7] of **7**, mp 168–169 °C, in 85% yield (Anal. C, H, N, S) which with 48% HBr at 100 °C for 5 h gave a 70% yield of **7** dihydrobromide.[7,8] The air-sensitive thiol was heated at 60 °C for 16 h in H_2O-NH_4HCO_3 with β-cyclodextrin 6-tosylate;[9] isolation on Sephadex CM-25 with NH_4HCO_3 afforded **8**, which was analyzed[10] as a hexahydrate.[7]

To examine the selectivity of this compound in a typical pyridoxamine reaction, **8** was compared with simple pyridoxamine (**5**) and with **5** plus 1 equiv of added β-cyclodextrin in the reductive amination of three α-keto acids, **3**, **9**, and **11**. Reactions of the keto acids were run either singly or competitively, with, e.g., 1 equiv each of pyruvic acid (**3**), phenylpyruvic acid (**9**), and pyridoxamine (**5**) at concentrations of 0.05–5 mM in 4.0 M phosphate buffer,[11] pH 8. After a given time at room temperature, an excess of dinitrofluorobenzene was added in ethanol–water and the mixture was heated[12] at 60 °C for 90 min. Acidification, extraction with ether, and concentration were followed by LC analysis,[13] calibrated with authentic samples of dinitrophenyl derivatives of **4**, **10**, and **12**.

With pyridoxamine (**5**) the three keto acids had similar reactivity, reaction leading to equal yields of each amino acid in 1:1 competitive studies. When β-cyclodextrin was also present the result was similar, although the aromatic substrate **9** was now ~20% less reactive than was pyruvic acid (**3**), presumably because of some binding of **9** by β-cyclodextrin. However, with the artificial enzyme **8** the results were strikingly different. Indolepyruvic acid (**11**) was converted into tryptophan (**12**) by **8** at a rate[14] ~200 times than that for reaction of **11** with **5**, but **3** reacted at essentially the same rate[15] with **8** or with **5**. As expected from this, competitive reaction of **8** with **11** and **3** led almost exclusively to the formation of tryptophan (**12**) under appropriate conditions. At early times (~10 min), the product from 1:1 competition is at least 97% tryptophan, although the ratio then decreases as the system equilibrates. With phenylpyruvic acid (**9**) vs. pyruvic acid (**3**) the product is at least 98% phenylalanine (**10**) before equilibration decreases the ratio.

The preferential reaction of **8** with substrates **9** and **11** is expected from models, which show that the aromatic rings of **9** or **11** can bind into the cyclodextrin cavity during transam-

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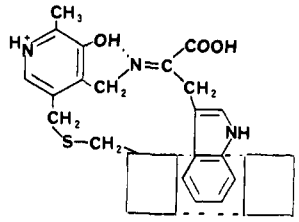

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ination. This is illustrated in structure **13**, an intermediate in the reaction of **8** with **11** to form **12**. The binding should accelerate both the forward and the reverse reactions involving the aromatic substrates; so the product selectivity is lost with time because of rapid equilibration of keto acid with amino acid.

Because β-cyclodextrin is chiral, one might expect that the product amino acids could be optically active. Chiral induction has been seen with cyclodextrin reactions in the past,[16] but our dinitrophenyltryptophan has only 12% enantiomeric excess of the L isomer.[17] However, the dinitrophenylphenylalanine has a 52 ± 5% excess of the L enantiomer,[17] so this reaction shows significant optical induction.

Compound **8** shows selectivity and rate acceleration and is thus a good first generation artificial transaminase. Further improvements should result from better definition of geometry and the addition of other catalytic groups to facilitate the proton transfers involved in the overall reaction.[18]

References and Notes

(1) For reviews, see Bruice, T. C.; Benkovic, S. "Bioorganic Mechanisms"; W. A. Benjamin: New York, 1966; Vol. 2, Chapter 8. Walsh, C. "Enzymatic Reaction Mechanisms"; W. H. Freeman: San Francisco, Calif., 1979; Chapter 24. Note that in enzymatic transaminations the lysine Schiff base of pyridoxal phosphate is the catalytically important structure, rather than the free aldehyde.
(2) Cf. Metzler, D. E.; Ikawa, M.; Snell, E. E. *J. Am. Chem. Soc.* **1954**, *76*, 648-652, and earlier papers.
(3) For a recent review, see Bender, M. L.; Komiyama, M. "Cyclodextrin Chemistry", Springer-Verlag: New York, 1977.
(4) Czarniecki, M. F.; Breslow, R. *J. Am. Chem. Soc.* **1978**, *100*, 7771-7772.
(5) Breslow, R.; Campbell, P. *Bioorg. Chem.* **1971**, *1*, 140-156. Tabushi, I.; Fujita, K.; Kawakubo, H. *J. Am. Chem. Soc.* **1977**, *99*, 6456-6457.
(6) Sakuragi, T.; Kummerow, F. A. *Arch. Biochem. Biophys.* **1957**, *71*, 303-310.
(7) ^{1}H NMR spectrum in accord with the assigned structure.
(8) This compound is reported by Kreisky (Kreisky, S. *Monatsh. Chem.* **1958**, *89*, 685-691), but we could not repeat the reported preparation.
(9) Chao, Y. Ph.D. Thesis, Columbia University, 1972.
(10) Calcd (found): C, 42.61 (42.36); H, 6.58 (6.69); N, 1.98 (1.70); S, 2.27 (1.81).
(11) This high concentration was used since these reactions show buffer catalysis.[1]
(12) The reaction is apparently quenched immediately, since the analyzed yield of DNP-amino acids was a function only of the reaction time before quenching. Qualitatively similar results, e.g., the rapid formation of tryptophan relative to alanine, were also obtained by direct thin layer chromatograph of the original reaction mixture and detection of the amino acids with ninhydrin.
(13) On Partisil PXS 10 with 40% v/v CH_3CN-H_2O containing 2.5 mL of HOAc and 0.4 g of NaOAc/L.
(14) That is, the area of the amino acid peak in the LC of the product from reaction with **8** after 10 min corresponded to a conversion (1-5%, depending on pH and concentration) which was achieved only after 30 h with simple pyridoxamine (**5**).
(15) As judged from the areas of LC peaks after 1 h, when ~0.2-0.5% of alanine was formed with either **8** or **5**.
(16) Reference 3, Chapter VII.
(17) By isolation and comparison of the rotation of the pure compound with the rotation of an authentic sample. The rotation is opposite to that of our cyclodextrin catalyst.
(18) Support of this work by the National Institutes of Health is gratefully acknowledged.
(19) NIH Postdoctoral Fellow.
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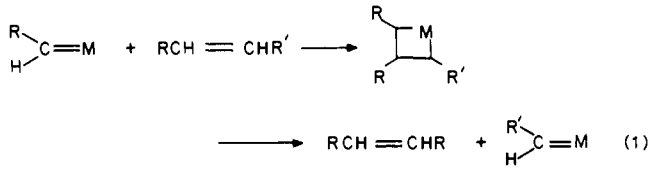
Initiation of Acetylene Polymerization by Metal Carbenes

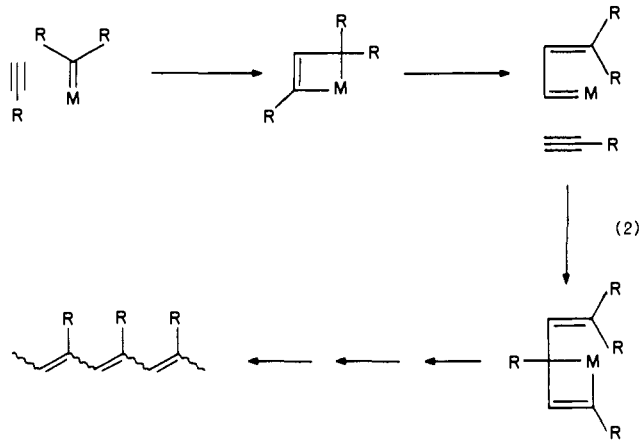
Sir:

A corollary of the hypothesis that metal carbenes combine with olefins as in eq 1 to propagate the metal-catalyzed me-



(1)

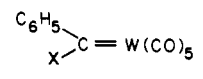
tatheses of olefins[1] is the hypothesis that they similarly combine with acetylenes as in eq 2[2] to propagate the metal-cata-



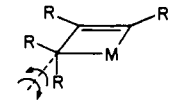
(2)

lyzed polymerizations of acetylenes.[3,4] This suggests that isolable metal carbenes[8] can serve as initiators of acetylene polymerization, and we demonstrate here that they do.

Tables I-III summarize the data. They show that (phenylmethoxycarbene)pentacarbonyltungsten (**1a**)[9] and (diphenylcarbene)pentacarbonyltungsten (**1b**),[10] metal carbenes that previously initiated metatheses of a few olefins,[11] also effect the polymerizations of a variety of acetylenes.



1a : X = OCH_3
b : X = C_6H_5



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The polymerizations are slow, but they do work well. Thus compared with previous preparations, the yield of poly(*tert*-butylacetylene) is 3-12 times the best recorded[12,13] and of poly(2-butyne) 10 times the only one recorded,[16] the purity of polypropyne as indicated by IR and NMR spectra is much greater,[17] and the formation of soluble polymers containing 2-butyne or 4-octyne units is, with possibly one exception,[18] unique. (In fact, polymers of disubstituted acetylenes are very rare,[19] and, except for those of phenyl-1-propyne[6i,7a,b,20] and possibly 2-butyne,[18] none had previously been obtained in soluble form.[16a,21]) The structural purity of each polymer[22] is also high as evidenced by the ^{1}H and ^{13}C NMR spectra (displayed for the homopolymers in the supplementary material) and the IR spectra.[23,24]

A comparable ability to initiate acetylene polymerizations is not displayed by $(C_6H_5)_3PW(CO)_5$;[28] after 7 days at 50 °C with 50 equiv of phenylacetylene it gives no polymer. Mesitylene-$W(CO)_3$ is also said to be a bad initiator.[7b] However, cycloocta-1,5-diene-tungsten tetracarbonyl[29] in a similar experiment (the molar ratio was 100) gives a 30% yield, which could be accounted for if, as noted above for **1a** and **1b** and previously for WCl_6 + $(C_6H_5)_4Sn$[30] and $Re(CO)_5Cl$,[6i] the

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