coupled activities of transketolase and DAHP synthase, the catalytic cornerstone of multistep immobilized enzyme synthesis of DAHP, increase carbon flow into aromatic amino acid biosynthesis, leading to increased synthesis of DAH and DAHP by microbial whole cells. Equally important, this synthesis is accomplished without the need for cofactor, cosubstrates, enzyme purification, enzyme immobilization, and adenosine triphosphate regeneration demanded by multistep enzymatic synthesis.

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Hemicarcerands Permit Entrance to and Egress from Their Inside Phases with High Structural Recognition and Activation Free Energies[1]

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Received October 10, 1989

Previous papers reported that permanent guests were imprisoned during cavitand shell closures to form carceplexes,[2] which are closed-surface, hollow hosts that selectively incarcerate medium components (guests). This paper reports our first hemicarcerand (1), a carcerand[2] with a shell hole large enough to permit entrance and egress of molecule-sized guests (G), but which allows ordinary separations and characterizations of hosts and complexes.

Triol 2[3] was isolated as byproduct (23%) in the synthesis of 3.[2a] Shell closures of 2 were conducted identically with those for 3[2a] (CH₂ClBr–K₂CO₃–solvent). Hemicarceplexes 1·G were purified by chromatography on silica gel–CHCl₃/hexane and crystallized from CHCl₃–CH₃CN. Shell closures in (CH₃)₂SO gave 1·(CH₃)₂SO (51%), in (CH₃)₂NCOCH₃ gave 1·(CH₃)₂NCOCH₃ (42%), and in (CH₃)₂NCHO gave 1·(CH₃)₂NCHO (20%). A stereoview of the crystal structure[4] of 1·(CH₃)₂NCHO·2CH₃CN·2CHCl₃ is shown in 4. Note that (CH₃)₂NCHO is incarcerated. Each solvating CH₃CN is packed between each set of four CH₂CH₂C₆H₅ groups with N directed inward. Each (CH₂CH₂C₆H₅)₄–CH₃CN packet is capped with CHCl₃. The northern hemisphere in 4 is rotated about 20° with respect to the southern. The complex has a pseudo C_2 axis passing through the N and O atoms of (CH₃)₂NCHO, whose C=O group points toward the portal.

(1) We warmly thank the National Science Foundation for supporting Grant NSF CHE 8802800.

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(3) New compounds gave elemental analyses within 0.40% of theory, the expected ¹H NMR, and FAB MS, M + 1 ions.

(4) Crystallization of 1·(CH₃)₂NCHO from CHCl₃–CH₃CN gave 1·(CH₃)₂NCHO·2CH₃CN·2CHCl₃: orthorhombic, *Pbna* (standard setting *Pbcn*), a = 20.455 (5) Å, b = 20.773 (5) Å, c = 30.307 (8) Å, V = 12878 Å³, Z = 4 (molecule has pseudo C_2 symmetry, the guest is disordered about a 2-fold axis, and the chloroform is disordered about an inversion center), R = 0.168. Details will be published elsewhere.

Chart I

$\underline{1}$·G, R = CH₂CH₂C₆H₅

$\underline{2}$, X = H; $\underline{3}$, X = OH
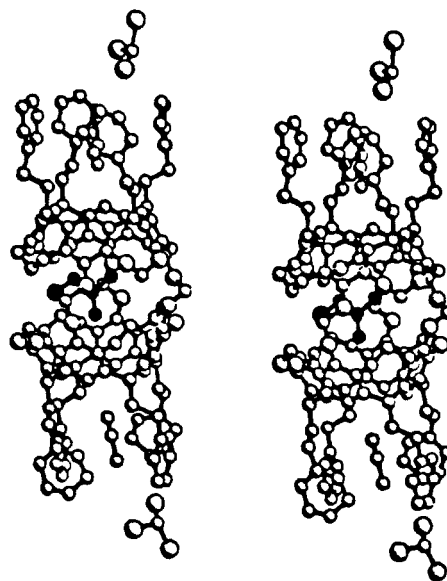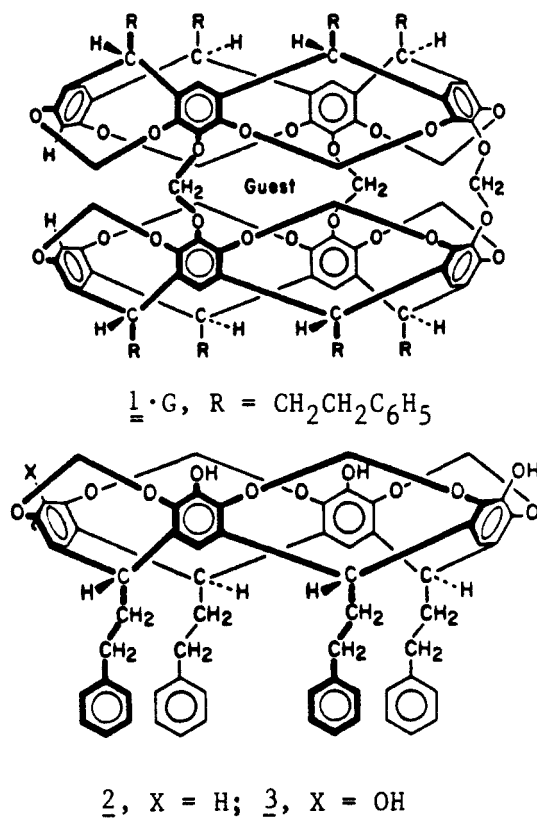
$\underline{4}$ (guest atoms of (CH₃)₂NCHO darkened)

Heating hemicarceplexes in solvents too large to become guests gave 1[5,6] by expelling guests: 1·(CH₃)₂SO[5] required 214 °C for

(5) Analyses for *all* elements present when summed came to 99.78–100.08%, individual analyses being within 0.40% of theory except for xenon in 1·Xe (0.83% below 6.05% theory by thermal gravimetric analysis, summed analysis, 99.14%). Nitrogen analysis of 1 indicated that no nitrogen was present in the solid after drying at 70 °C for 12 h at 10⁻⁵ Torr.

(6) When a 5 mM solution of 1 in CDCl₃ was saturated at 25 °C with N₂ (5.6 × 10⁻³ M), ¹H NMR integrations of inward-turned intrahemisphere OCH₂O protons of the 1·N₂ produced (δ, d, 3.97, 4.12 vs 1, δ, d, 3.93, 4.09) gave a 1:1 ratio of species, which provides a K_a estimate of 180 M⁻¹ for 1 + N₂ ⇌ 1·N₂. In a similar experiment with O₂ (11.5 mM), a 1:2 ratio of 1·O₂ to 1 was obtained, the inward OCH₂O protons of 1·O₂ disappearing into the base line. The Ar₂CHR signals of 1 (δ, t, 4.80 and t, 4.90) were broadened and moved to δ, 5.24 and 5.38 in 1·O₂, and their integrals were used in the K_a estimate of 44 M⁻¹ for 1 + O₂ ⇌ 1·O₂.

48 h in 1,2,4-Cl$_3$C$_6$H$_3$; 1·(CH$_3$)$_2$NCOCH$_3$,[5] 165 °C for 24 h in 1,3,5-(CH$_3$)$_3$C$_6$H$_3$; 1·(CH$_3$)$_2$NCHO,[5] 165 °C for 12 h. In the 360-MHz ^{1}H NMR spectra, proton signals of incarcerated guests are far upfield of guests simply dissolved in CDCl$_3$: 1·(CH$_3$)$_2$SO, δ −1.02; 1·(CH$_3$)$_2$NCOCH$_3$, δ −2.30, −1.33, 1.05; 1·(CH$_3$)$_2$NCHO, δ −1.04, −0.21, and 4.14. Proton signals of the northern and southern hemispheres of the host are identical at 25 °C for 1, for 1·(CH$_3$)$_2$SO, and for 1·(CH$_3$)$_2$NCHO, but different for 1·(CH$_3$)$_2$NCOCH$_3$. Thus end-to-end guest rotation relative to the host's north–south axis is inhibited only in 1·(CH$_3$)$_2$NCOCH$_3$.

Treating free 1 in appropriate solvents gave new hemicarceplexes, e.g.: 1·CH$_3$CN^3 (δ −2.42); 1·CS$_2$,[3] 1·pyridine[5] (heat required); 1·CH$_2$Br$_2$.[3] When treated with a 0.14 M solution of xenon in CDCl$_3$ at 25 °C, 1·Xe[5] formed, whose 1·^{129}Xe NMR signal was at −101 ppm (dissolved xenon, 0 ppm).[7] On silica gel −15% hexane/85% CHCl$_3$ (v/v), most complexes (and free 1) had different R_f (TLC) values. These one-to-one complexes (^{1}H NMR proton counting and elemental analyses) were stable to laboratory manipulations at room temperature, but released their guests when subjected to FAB MS to give strong M + 1 signals for 1.[7,8]

These results demonstrate that hemicarcerands can be designed and prepared whose portals show high structural recognition in guest entry, departure, and residence. We envision potential uses for hemicarceplexes: drug delivery systems; organ imaging; protection of bone from deposition of heavy metal salts useful in radiation therapy; light switches; information storage. We are examining these possibilities in many carceplexes.

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(7) A k_{in} second-order rate constant for filling 1 (5 mM) with Xe (0.14 M) in CDCl$_3$ at 25 °C was estimated to be 0.055 min^{-1} M^{-1} (followed by ^{1}H NMR changes). A k_{out} first-order rate constant estimate in CD$_2$Cl$_2$ at 25 °C for 1·Xe + CD$_2$Cl$_2$ → 1·CD$_2$Cl$_2$ + Xe (followed by ^{1}H NMR changes) gave 2.5 × 10^{-4} min^{-1}. If we assume that k_{out} in CD$_2$Cl$_2$ ~ k_{out} in CDCl$_3$, K_e for 1 + Xe ⇌ 1·Xe is estimated to be ≈200 M^{-1}.

(8) The closest precedents to our hemicarcerands are the elegant *cryptophanes* of A. Collet (summarized in *Tetrahedron* **1987**, *43*, 5725–5759), who joined two cyclotriveratrylene-like modules with three ethylene bridges to give hollow molecules with three equivalent portals.

On the Mechanism of Action of Vitamin K. A New Nonenzymic Model
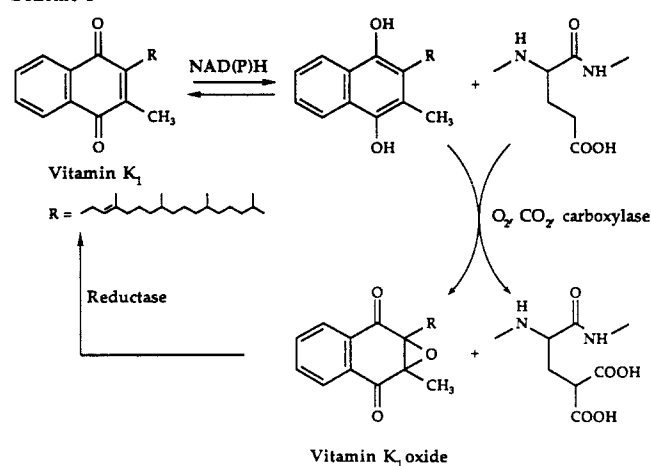
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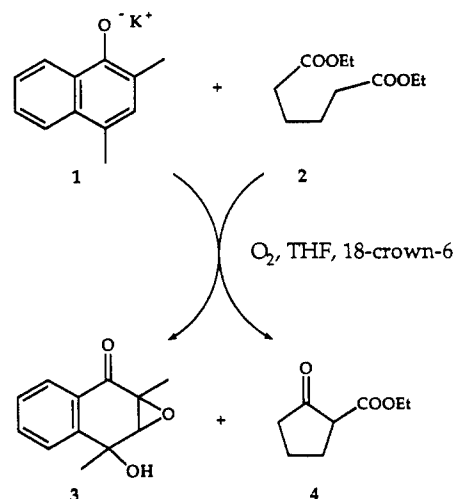
Received October 23, 1989

Vitamin K is essential for blood clotting.[1] It may also play a role in bone calcification[2] and have other broad functions in biological systems.[3] At the enzyme level, vitamin K is an obligatory cofactor promoting the posttranslational carboxylation[4] of selected glutamic acid residues in many of the proteins of the blood clotting cascade, including factor II (prothrombin), factor VII, factor IX, factor X, protein C, protein M, protein S, and protein Z, as well as the bone protein osteocalcin.[5]

The carboxylative conversion of glutamate to γ-carboxyglutamate requires the hydroquinone form of vitamin K (or vitamin K and NAD(P)H), oxygen, carbon dioxide, and a membrane-bound carboxylase[1] only recently isolated in pure form.[6] In the course of the carboxylation (Scheme I), vitamin K is

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Scheme I

Scheme II

converted to vitamin K oxide.[7] A second, reductase-catalyzed pathway returns vitamin K oxide to vitamin K for a new catalytic cycle.[8,9]

In coming to grips with the mechanism of action of vitamin K, it is important to establish whether the formation of vitamin K oxide is an integral part of the step that effects the carboxylation.[10] Through the recent efforts of Suttie and his collaborators,[11] it has been shown that the degree of carboxylation closely parallels the extent of formation of vitamin K oxide under diverse circumstances.[6]

Since the discovery of the vitamin K dependent carboxylation, a variety of mechanistic proposals have been advanced ranging from free-radical[12,13] to base-promoted pathways.[14–17] Missing

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