exhibits two resonances at δ 175.9 and δ 158.9 for the alkyne C≡C carbons. On the other hand, the cyclobutadiene carbons give a single sharp signal at δ 83.8, revealing that the cyclobutadiene ligand is fluxional with facile ring rotation. This signal broadens at −50 °C, but a slow-exchange spectrum is not recorded due to poor solubility for the complex at lower temperatures.

Solid $W(\eta^4\text{-}C_4Ph_4)(PhC{\equiv}CPh)_2(CO)$ is thermally robust to 220 °C, suggesting a stable electronic configuration for the complex. Since terminal CO and η^4-cyclobutadiene ring are normally considered as two- and four-electron donors, respectively, the remaining two alkyne ligands must supply six electrons, presumably from two $\pi(\|)$ and one $\pi(\perp)$ orbitals,[7] to the neutral tungsten atom to satisfy the 18-electron rule. Therefore, the actual structure is best regarded as a resonance hybrid with two canonical forms involving one four-electron-donor ($\pi(\|) + \pi(\perp)$) and one two-electron-donor ($\pi(\|)$) alkyne ligands. The results are reflected on the C≡C bond lengths and ^{13}C NMR shifts, which are found in between those measured for two- and four-electron-donating alkyne complexes.[15]

Recently we prepared a complex, $W(PhC{\equiv}CPh)_3(NCCH_3)$, which underwent facile ligand substitution with bulky phosphines to yield $W(PhC{\equiv}CPh)_3L$, where L = PPh_3 or $CH_2(PPh_2)_2$.[16] On the contrary, diphenylacetylene reacts with $W(PhC{\equiv}CPh)_3(NCCH_3)$, affording $W(\eta^4\text{-}C_4Ph_4)(PhC{\equiv}CPh)_2(NCCH_3)$[17] in 79% yield; the same product is obtained by treating $W(\eta^4\text{-}C_4Ph_4)(PhC{\equiv}CPh)_2(CO)$ with Me_3NO in acetonitrile solution. Moreover, carbonylation of $W(\eta^4\text{-}C_4Ph_4)(PhC{\equiv}CPh)_2(NCCH_3)$ yields $W(\eta^4\text{-}C_4Ph_4)(PhC{\equiv}CPh)_2(CO)$ quantitatively (Scheme I).

King[7] has shown that in a W(alkyne)$_3$ unit of either D_{3h} or C_{3v} symmetry, the three alkyne ligands can donate a total of only 10 electrons to the tungsten atom. A pathway dissociating CO or $NCCH_3$ from $W(PhC{\equiv}CPh)_3(CO)$ or $W(PhC{\equiv}CPh)_3(NCCH_3)$ to generate an unstable, 16-electron species $[W(PhC{\equiv}CPh)_3]$ is plausible. Alternatively, association of a diphenylacetylene would cause severe steric crowding around the tungsten atom, which could be released through alkyne–alkyne coupling to yield the observed products. However, it remains uncertain whether the tetraphenylcyclobutadiene group is derived from the coordinated PhC≡CPh ligands or the added diphenylacetylene is involved. The details are presently under investigation.

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Registry No. $W(PhC{\equiv}CPh)_3(CO)$, 12120-72-8; PhC≡CPh, 501-65-5; $W(\eta^4\text{-}C_4Ph_4)(PhC{\equiv}CPh)_2(CO)$, 138899-90-8; $W(PhC{\equiv}CPh)_3(NCCH_3)$, 138899-91-9; $W(\eta^4\text{-}C_4Ph_4)(PhC{\equiv}CPh)_2(NCCH_3)$, 138899-92-0.

Supplementary Material Available: Tables of crystal data, atomic coordinates, bond lengths, bond angles, and torsional angles (8 pages). Ordering information is given on any current masthead page.

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(17) $W(PhC{\equiv}CPh)_3(NCCH_3)$ (540 mg, 0.71 mmol), diphenylacetylene (130 mg, 0.73 mmol), and 1,2-dichloroethane (10 mL) were refluxed under nitrogen for 15 min. The solvent was removed under vacuum, and the residue was separated by TLC. $W(\eta^4\text{-}C_4Ph_4)(PhC{\equiv}CPh)_2(NCCH_3)$ (520 mg, 0.55 mmol, 79%) forms air-stable, orange-yellow crystals: mp 175–177 °C dec; mass spectrum (FAB), m/z 937 (M^+, ^{184}W), 896 ($M^+ - CH_3CN$), 718 ($M^+ - CH_3CN - C_2Ph_2$), 540 ($M^+ - CH_3CN - 2C_2Ph_2$); IR (KBr) 1591 (ν C≡C) cm^{-1}; ^1H NMR (CD_2Cl_2, 25 °C) δ 7.33–6.78 (m, Ph), 1.90 (s, CH_3CN); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 25 °C) δ 186.5, 174.8 (≡C), 140.8, 139.6, 135.1, 129.9, 129.2, 128.3, 128.2, 127.8, 127.5, 127.4, 126.1, 125.8, 124.8 (Ph, N≡C), 86.2 (C_4Ph_4), 4.4 (CH_3). Anal. Calcd for $C_{58}H_{43}NW$: C, 74.28; H, 4.62; N, 1.49. Found: C, 74.49; H, 4.70; N, 1.47.

π Hydrogen Bonds as a Design Principal in Molecular Recognition

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We wish to report details of guest binding and the X-ray structures of two exceptionally high-efficiency hosts, **1-D** and **1-P**. We conclude that "tilted tee"[5] edge–face arene–arene interactions can be a dominating force in the stabilization of host–guest complexes in organic solvents.

While solvophobic forces dominate molecular recognition in aqueous medium, the situation is less clear in organic solvents. Multiple hydrogen bonding sites[1] and a variety of van der Waals contacts, including π–π and related dipole-induced dipole interactions associated with arene–arene interactions, have been exploited.[2] The remarkable use of physical encapsulation should be noted.[3]

We have reported the powerful molecular recognition behavior of a series of cyclophanes bearing a concave functionality which, having but one concave functionality, are nonetheless remarkably "sticky" toward aromatic hydrogen-bond-donating guests, primarily because of immobilization effects (Figure 1).[4]

Hosts **1-D** and **1-P**[6] are both extraordinarily efficient binders of *p*-nitrophenol ("PNP") in CD_2Cl_2, having K_{assoc} of 35000 M^{-1} for **1-D** and ca. 100 000 M^{-1} [4b] for **1-P**.[8] Competition binding experiments confirm the ca. 3:1 ratio of binding constants favoring **1-P** over **1-D**.[8] X-ray structures of the **1-D** and **1-P** PNP complexes are shown in Figure 2.[9]

The following observations lead us to the opening assertion.

(1) At 21 °C, the proton NMR spectrum of **1-D**:PNP (CD_2Cl_2, 1:2.5) shows the guest protons as broad singlets at δ 6.5 ($\nu_{1/2}$ = 50 Hz) and 7.15 ($\nu_{1/2}$ = 140 Hz). The aromatic protons of free *p*-nitrophenol appear as doublets at δ 6.93 and 8.15 (J = 9.1 Hz). Cooling the sample to −20 °C leads to separate but broad signals for the bound and free phenol. At −80 °C, well-resolved spectra are visible.

(2) At −40 °C, the *bound* PNP protons appear as four separate signals at 6.05, 5.95, 5.5, and 3.78 ppm. This upfield shift of 4.4 ppm is required by the binding model, wherein the two edges of *bound* PNP exist in quite different environments: H2 and H3 straddle the diyne spacer, while H5 and H6 lie over the *p*-xylene.

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(6) Host **1-P** was synthesized as previously reported in ref 4b. Host **1-D** was synthesized by analogous but much improved procedures to be reported.

(7) The association constant was determined by the procedure reported in ref 4b.

(8) The funnel-shaped pouch of **1-D** is probably responsible for its decreased $\Delta\delta$ and K_{assoc} relative to **1-P**.

(9) Data were taken on Syntex P-1 and Siemens P3F diffractometers. Hydrogen positions were determined by the Riding model, with fixed isotropic U in both cases.

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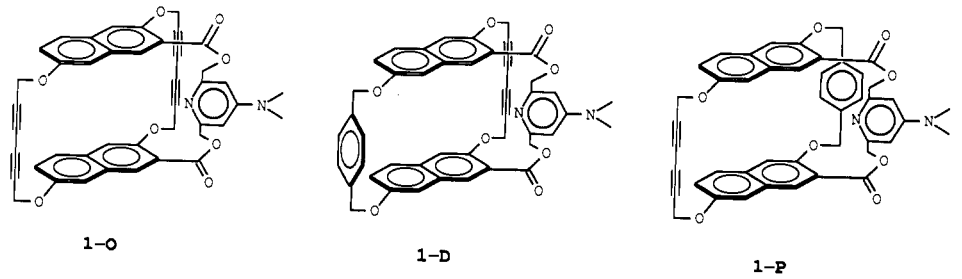

Figure 1.

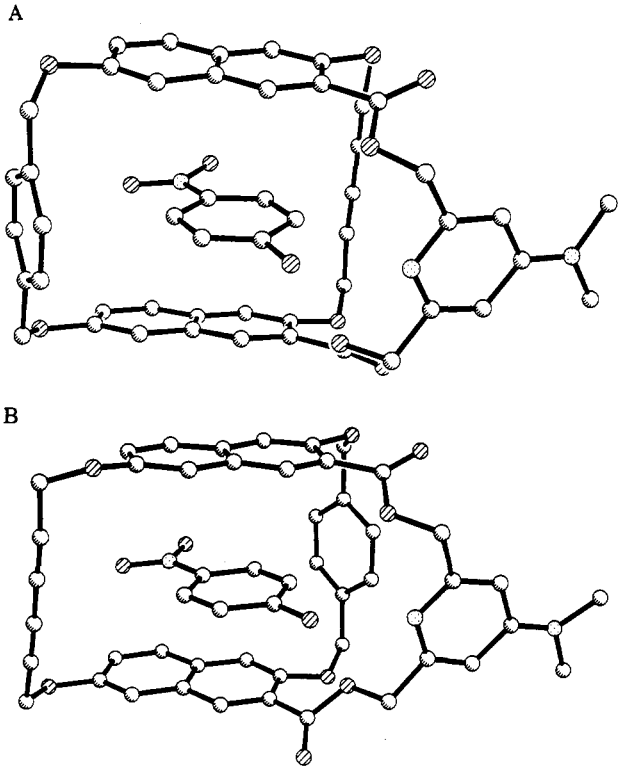

Figure 2. X-ray structure of pyridine–distal *p*-nitrophenol complex **1-D** (A) and structure of pyridine–proximal isomer complex **1-P** (B). Hydrogen atoms are not shown for clarity.

(3) Virtually identical behavior is exhibited by the **1-P** host: at −85 °C the *o*-nitro proton lying over the *p*-xylene spacer appears at δ 3.68, an upfield shift of 4.5 ppm.[4b]

(4) Use of *p*-nitrophenol-*2,6-d*$_2$ shows that it is the aromatic proton ortho to the nitro group of *p*-nitrophenol that is responsible for the high field peaks in the **1-P** complex. A chemical shift change of this magnitude in complexes of **1-D** and **1-P** implies that the *o*-nitro proton is uniquely positioned atop the xylene spacer in both cases.

Observations 1–4 by themselves do not require edge–face stabilization, but the following do.

(5) Single-crystal X-ray structures of these complexes are shown in Figure 1. Examination of them shows the PNP aromatic proton[9] closest to the xylene spacer to be the one ortho to the nitro substituent. It lies 0.1 Å off-center from the mean plane of the xylene in both cases at a distance of 2.72 Å (**1-D**) and 2.56 Å (**1-P**) from the xylene's plane. The corresponding distances from the xylene center to the guests' C3 carbons are 3.51 and 3.44 Å, respectively.

(6) The host naphthalene rings are not parallel: angles of 16° for **1-D** and 4° for **1-P** are found.[8] Nevertheless the guest–xylene angle is 90° within experimental accuracy of the X-ray structure refinement.

Of the series of cyclophane-based hosts possessing concave functionality studied by us, hosts **1-P** and **1-D** enjoy a uniquely high affinity for phenol guests. Both possess a briding *p*-xylene spacer, which is approximately 0.9 Å shorter than a 2,4-hexadiyne unit. This encourages (but does not require) a snugger fit and hence greater degree of immobilization of the phenolic guest. Further, introduction of a *p*-xylene spacer also permits interaction between the edge of the aromatic guest and the face of the spacer. We suggest that the remarkable positioning of the guest in both of the above complexes arises because the detailed geometry of these complexes is dominated by formation of a π hydrogen bond involving the electron-rich *p*-xylene spacer and the acidic *o*-nitro proton of the guest.[10]

Supplementary Material Available: Complete X-ray refinement details and labeled ORTEP drawings of *p*-nitrophenol complexes of **1-P** and **1-D** (24 pages); listings of observed and calculated structure factors (43 pages). Ordering information is given on any current masthead page.

(10) Partial support by the N.S.F and the Department of Navy is acknowledged. We also thank Douglas R. Powell and John M. Desper for the data acquisition and structural refinement of the X-ray structures of **1-P** and **1-D**, respectively.

Mechanism-Based Inactivation of Peptidylglycine α-Hydroxylating Monooxygenase (PHM) by a Substrate Analogue, D-Phenylalanyl-L-Phenylalanyl-D-Vinylglycine: Inhibition of Formation of Peptide C-Terminal Amides

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The biosynthesis of many peptide hormones proceeds by post-translational cleavage of precursor proteins to generate a primary amide functionality at the carboxyl terminus.[1] The amidation results from two-step processing of precursors bearing a C-terminal glycine residue (e.g., **1**, Scheme I).[2] A bifunctional enzyme, peptidylglycine α-amidating monooxygenase (PAM),[2d-f] can catalyze the full transformation or it may be cleaved into two monofunctional proteins. The first, peptidylglycine α-hydroxylating monooxygenase (PHM), catalyzes a stereospecific hydroxylation in a process dependent on oxygen, copper, and ascorbate. The second enzyme, peptidyl-α-hydroxyglycine α-amidating lyase (PAL), then promotes the decomposition of the carbinol amide to a peptide amide and glyoxylate. This final step

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