crease in the elongation by a low level of deformation, are obtained, as shown by curves 4 and 5 in Fig. 3. This repeated mechanical behavior, combined with the structural characterization, confirms that the removal of dislocations by annealing and their introduction by slight deformation are the cause of the changes in the mechanical properties. The deformation induced relatively small decreases in yield stress and UTS, and a large increase in the elongation greatly improves the applicability of the material. A further test of the beneficial effect of deformation as a final processing step is to deform the initial ARB sample 15% by cold rolling. The reason is that this sample has been processed by rolling to a large strain per pass and some adiabatic heating may have taken place (i.e., the material may be in a recovered state) (20). Such conditions are also typical of industrial processing. In accordance with the present hypothesis, it is assumed that a light deformation of an ARB sample in the as-delivered state may induce a small decrease in strength followed by an increase in ductility. Curves 1 and 6 in Fig. 5 confirm this assumption.

The present investigation has focused on aluminum. The strategy described above may also apply to metals such as nickel and interstitial free steels that develop deformation microstructure similar to that of aluminum (14, 21). Therefore, this strategy opens up a research area of both fundamental and applied importance.

References and Notes

Diels-Alder in Aqueous Molecular Hosts: Unusual Regioselectivity and Efficient Catalysis
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Self-assembled, hollow molecular structures are appealing as synthetic hosts for mediating chemical reactions. However, product binding has inhibited catalytic turnover in such systems, and selectivity has rarely approached the levels observed in more structurally elaborate natural enzymes. We found that an aqueous organopalladium cage induces highly unusual regioselectivity in the Diels-Alder coupling of anthracene and phthalimide guests, promoting reaction at a terminal rather than central anthracene ring. Moreover, a similar bowl-shaped host attains efficient catalytic turnover in coupling the same substrates (although with the conventional regiochemistry), most likely because the product geometry inhibits the aromatic stacking interactions that attract the planar reagents to the host.

Effective synthetic homogeneous catalysts have generally been structurally simple small molecules, which act by binding to substrates at or near the reaction site. In contrast, enzymes are much larger and more complex and derive much of their selectivity by bonding substrates through multiple interactions in elaborate pockets, thereby forcing the substrates into orientations that favor specific reaction paths (1, 2). In the past decade, chemists have made substantial progress in building molecular hosts that emulate these enzymatic pockets (3, 4). Self-assembly of carefully constructed organic and/or metallic building blocks in solution produces hollow host structures that can bind small molecule guests (5, 6). Among the many potential advantages of this strategy is the creation of hydrophobic reaction environments in aqueous solution, widening the scope of accessible reactivity in ecologically friendly media. However, these synthetic hosts have rarely conferred the orientational precision necessary to guide reactions along otherwise unfavorable pathways. Moreover, catalytic turnover has been inhibited because the hosts bind products as effectively as reactants, if not more so. In earlier reports by Rebek (7, 8), Sanders (9), and our
The Diels-Alder and related cycloadditions are significantly accelerated in synthetic pockets, but the product inhibition prevents the reactions from showing turnover and the stereochemical courses are not well controlled by the pockets. For catalytic reactions by self-assembled hosts, there have appeared only a few examples, including the Diels-Alder (11), epoxidation (12), and the aza-Cope rearrangement (13). Controlling reaction pathways by encapsulation has been discussed in the excited-state chemistry of aromatic guests (14) and also realized by a regioselective cycloaddition (8).

We investigated the host-mediated Diels-Alder coupling of anthracenes and phthalimides. The Diels-Alder reaction of anthracenes in the absence of hosts is extremely well studied and generally yields an adduct bridging the center ring (9,10-position) of the anthracene framework (15–17) as a consequence of the high localization of π-electron density at that site (18, 19). We find that an appropriately designed cage structure can alter this well-established selectivity to favor adduct formation at a terminal ring (1,4-position). This unusual regioselectivity likely stems from topochemical control induced by the proximity of the 1,4-position of the anthracene to the dienophile in the cage. The 1,4-selective Diels-Alder of anthracenes has been previously reported only for a benzyne addition (20) and for the addition with 9,10-diarylanthracenes (21). We further find that the same reaction, through conventional regioselectivity, can be catalyzed with efficient turnover by a related, bowl-shaped host. As in enzymatic reactions (2, 22), the product geometry, bent at the 9,10-position, precludes the aromatic stacking interactions that underlie the host’s affinity for the reagents.

The coordination hosts we used here are octahedral cage 1 and square-pyramidal bowl 2 (Fig. 1) (23–25). Both of them assemble from cis end-capped Pd(II) ions and triazine-cored tridentate ligands in a surprisingly efficient manner (100°C, <5 min, quantitative yields). In aqueous solution, these structures provide an efficient hydrophobic pocket capable of binding a variety of neutral organic compounds. Cage 1 features a three-dimensionally enclosed cavity, which binds substrates in precisely fixed positions. Geometry-fixed encapsulation (26), iso-
When 9-hydroxymethylanthracene (3a) and N-phenylphthalimide (4c) were suspended in an aqueous solution of cage 2 (5.0 mM) at room temperature, the inclusion complexes were formed selectively within 5 min (Fig. 2A). A 1H nuclear magnetic resonance (NMR) analysis confirmed the encapsulation, with the resonances of 3a and 4a shifted far upfield because of interaction with the cage (Fig. S1A) (30). No signals indicating 1 ⊃ (3a), or 1 ⊃ (4a), (n ≤ 2) were observed in the NMR spectrum. On heating the solution at 80°C for 5 hours, the signals derived from 3a and 4a disappeared and were replaced by resonances consistent with a Diels-Alder adduct, distributed between 6.8 and –2.1 parts per million (ppm) (Fig. S1B). Sixteen signals in the 9.7- to 8.4-ppm range were observed for cage 1, indicating the desymmetrization of the cage from $T_d$ to $C_3$ symmetry (25). This symmetry agreed with the restricted motion of a noncentrosymmetric product along the $C_3$ axis, which is perpendicular to one of the triazine ligands (30). After insoluble solids were removed by filtration, the product was extracted into CDCl$_3$ and fully assigned as the syn isomer of 1,4-Diels-Alder adduct 5 (Fig. S4). No other regio- or stereoisomers (1,9-adduct or anti-1,4-adduct) were detected. The yield of 5 was estimated to be >98% (based on 1) from the $^1$H NMR spectra (30). In contrast, in the absence of 1, the reaction gave only the conventional 9,10-Diels-Alder adduct in 44% yield based on 3a.

The unusual structure of the 1,4-Diels-Alder adduct was unambiguously determined by x-ray crystallographic analysis of 1 ⊃ 5 (Fig. 3A). A single crystal suitable for x-ray analysis was obtained by the slow evaporation of water from an aqueous solution of 1 ⊃ 5 over 5 days (30). The crystal structure displays the syn stereochemistry of 1,4-adduct 5, which is tightly accommodated in the cavity of 1 via π-π stacking interactions (3.3 Å) between the naphthalene ring of 5 and a triazine ligand of 1.

Because the Diels-Alder reaction has an early transition state (15), the unusual regio- and stereoselectivities can be explained by the fixed orientation of the guests before the reaction. The geometries of 3a and 4a in the 1 ⊃ (3a-4a) complex were modeled by force-field calculation (31). Randomly oriented 3a and 4a guests in several initial structures converged in all cases to a parallel orientation with the C=C bond of 4a in close contact with the 1,4-position of 3a (Fig. 3B). The center-to-center distance between the two reaction centers is only circa (ca.) 3.8 Å, which is comparable to the sum of van der Waals radii. Because of the steric restrictions induced by the cage, the C=C bond of 4a hardly interacts with the 9,10-position of 3a (ca. 4.7 Å). It is also interesting that the cavity of 1 directs exo-selective addition of 4a to the 1,3-diene moiety of 3a, yielding only exo-selective syn adduct 5.

The 1,4-regioselective Diels-Alder reaction also proceeded with varied substrates. Carboxyl-, cyano-, and vinyl-substituted anthracenes coupled with phthalimide 4a to give the corresponding 1,4-adducts in 92, 88, and 80% yields, respectively (Fig. 2B) (30). Unsubstituted anthracene also afforded only the 1,4-adduct in 55% yield. The moderate yield for this substrate is due not to reduced regio- or stereoselectivity but to the less efficient inclusion process before the reaction. The steric bulkiness of the N-substituent on the dienophile is crucial to the 1,4-selectivity. When sterically less demanding N-propylphthalimide (4b) was used, only the 9,10-adduct was formed.

We turned next to investigating Diels-Alder mediation by bowl-shaped host 2 and, strikingly, observed efficient catalytic turnover. Only 10 mole percent (mol %) of 2 sufficed to catalyze the Diels-Alder reaction of 3a and N-phenylphthalimide (4c) (Fig. 4). When 3a (10.0 μmol) and N-phenylphthalimide (4c, 10.0 μmol) were suspended in an aqueous solution of cage 2, leading to 9,10-adduct 6.
ous solution of \(2\) (1.0 µmol in 1.0 ml) at room temperature for 5 hours (Fig. 5, A and B), the Diels-Alder adduct formed quantitatively (>99% based on \(3a\)), as evaluated by NMR analysis of the product (32). NMR analysis also indicated that the reaction took place at the normal 9,10-position of anthracene to give 6 (Fig. 5C). In the absence of bowl 2, the reaction hardly proceeded (only 3% yield) under the same conditions. Surprisingly, even in the presence of 1 mol % of \(2\), adduct \(3a\) was obtained in >99% yield after 1 day as estimated by the NMR spectrum in CDCl\(_3\). Moreover, the metal component, (en)\(\text{Pd(NO}_3\text{)}_2\) (where en is ethylenediamine) alone, did not catalyze the reaction (30). Therefore, the data support promotion of the reaction by the hydrophobic pocket of 2.

Bowl 2 also efficiently catalyzed Diels-Alder coupling of a variety of anthracene and phthalimide derivatives (30). When \(3a\) and \(N\)-propyl- or \(N\)-benzylphthalimide were suspended in an aqueous solution of 2, the corresponding Diels-Alder products were obtained in almost quantitative yields after 5 hours at room temperature. In addition, 9-methyl and 9-vinylanthracene reacted with \(4c\) in the presence of a catalytic amount of 2 (10 mol %).

Product inhibition has been a serious problem in previous examples of cavity-promoted Diels-Alder reactions with synthetic hosts (7–11). Because of the entropic disadvantage arising from the need to bind two reagent molecules, the encapsulated product has generally been a thermodynamic sink. Therefore, the reactions require near-stoichiometric quantities of host. It is noteworthy that, in contrast to previous examples, the present Diels-Alder reaction involves an exclusion step in the catalytic cycle. Before the reaction, anthracene can stack onto the triazine ligand of 2, gaining considerable stabilization via aromatic-aromatic or charge-transfer interactions (Fig. 5D, step a). The reactant-like transition state is similarly stabilized. However, once the reaction is complete, the product framework is bent at the 9,10-position, cutting off the host-guest aromatic stacking interaction (Fig. 5D, step b). Accordingly, the encapsulated product is considerably destabilized and smoothly replaced by incoming reagents (Fig. 5D, step c → a). In this sense, the affinity of the host for reactive substrates and the reductivity for product is markedly similar to enzymatic behavior.