strongly that Asp-tRNA$_{CUA}$ accurately delivers aspartic acid to amber mutant 20 of T4L.

Suppression experiments were then carried out with the caged aspartyl β-nitrobenzyl ester. When the pT4LD20am-programmed in vitro protein synthesis reaction was supplemented with 7.5 μg of NB-Asp-tRNA$_{CUA}$, a T4L of the correct molecular weight was produced (lane 5, Figure 3). The NB-Asp-suppressed pT4LD20am produced about 37 ± 4% of full-length T4L compared to wild-type control, and the caged protein was catalytically inactive. However, the 2-nitrobenzyl group can be easily removed by photolysis: irradiation of the crude in vitro reaction supernatants (lane 5, Figure 3) at $\lambda > 315$ nm (Oriel Hg–Xe arc lamp, 1000 W) restored lytic activity to the NB-Asp-suppressed T4L. The irradiated material yielded 32 ± 3% of the activity of the wild-type enzyme, agreeing very closely with suppression levels based on scintillation counting of gel bands. These results show that NB-Asp-tRNA$_{CUA}$ efficiently suppresses pT4LD20am to produce mutant T4L with latent activity that can be released by rapid photolysis. Moreover, virtually all of the caged protein is converted to the active form. We are currently extending this methodology to other amino acids such as serine, tyrosine, lysine, and cysteine located at both internal and external sites in a number of proteins.

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Second-Sphere Coordination of Transition-Metal Complexes by Calix[4]arenes

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Second-sphere coordination has been defined by Stoddart as the "non-covalent bonding of chemical entities to the first coordination sphere of a transition metal complex."[1b] The importance of such systems for biological receptors[2–4] and for supramolecular assemblies[5] has been noted.[1] The use of crown ethers as second-sphere ligands via hydrogen bonding is well documented.[6,7] Numerous studies of cyclodextrins coordinated to transition-metal complexes have also appeared.[1,7,8–14] However, even though calixarenes are one of the most readily accessible three-dimensional macrocycles[15] and are under intense investigation by numerous groups,[16–18] no examples of second-sphere coordination have appeared. We report herein that the hydrophobic cavity of [calix[4]arene sulfonate]$^{5-}$ can be employed for such second-sphere coordination. In addition, the title compounds also exhibit a new type of intercalation behavior with regard to the bilayer assembly of the calixarenes.[19–21]

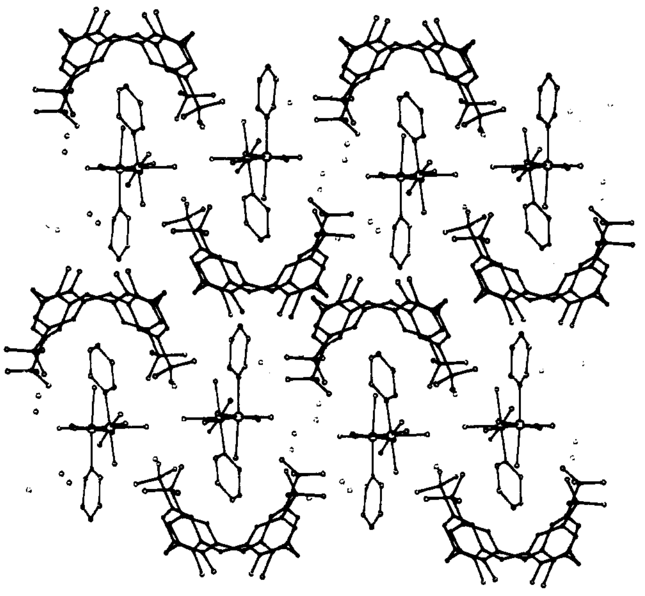

Figure 1. Structure of $[(H_2O)_5Ni(NC_5H_5)]_2(Na)$[calix[4]arene sulfonate]$\cdot 3.5H_2O$ illustrating the bilayer arrangement of the calixarenes, the intercalation into the bilayer, and the second-sphere coordination of the transition-metal complex. The two independent Ni–N distances are 2.08 (1) Å, and the Ni–O(water) lengths range from 2.05 (1) to 2.18 (1) Å.

Three equivalents of the deep blue $Ni(NC_5H_5)_3(NO_3)_2$[22,23] was dissolved in deionized water (with hydrolysis) to which 1 equiv of Na_5[calix[4]arene sulfonate][19] had been added. The resultant pale blue solution yielded pale blue crystals of $[(H_2O)_5Ni(NC_5H_5)]_2(Na)$[calix[4]arene sulfonate]$\cdot 3.5H_2O$ upon slow evaporation in a vacuum desiccator. The structure[24] of the complex is shown in Figure 1.

There are two different $[(H_2O)_5Ni(NC_5H_5)]^{2+}$ cations in the assembly. In one the hydrophobic pyridine ring is complexed by the hydrophobic cavity of the calixarene. The depth of penetration of the aromatic moiety into the cavity may be measured by the distance of the centroid of the pyridine ring from the plane of the calixarene CH_2 carbon atoms. For the nickel complex the value

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(24) $[(H_2O)_5Ni(NC_5H_5)]_2(Na)$[calix[4]arene sulfonate]$\cdot 3.5H_2O$ crystallizes in the triclinic space group $P\bar{1}$ with $a = 12.487$ (4) Å, $b = 14.281$ (2) Å, $c = 15.055$ (5) Å, $\alpha = 85.66$ (2)°, $\beta = 80.07$ (2)°, $\gamma = 80.48$ (2)°, and $D_{calcd} = 1.64$ g cm^{-3} for $Z = 2$. Refinement based on 2441 observed reflections led to a final R value of 0.066.

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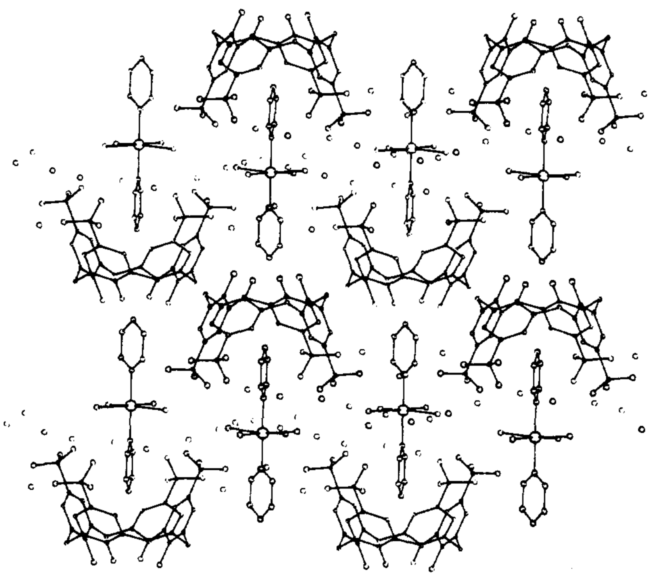

Figure 2. Structure of $[(H_2O)_4Cu(NC_5H_5)_2](H_3O)_3$[calix[4]arene sulfonate]$\cdot 9H_2O$ demonstrating the spanning of the hydrophilic layer by the copper(II) complex with one pyridine intercalated into the calixarene bilayer and the other coordinated in a second-sphere fashion by a calixarene. The Cu-N distances are 1.99 (1) and 2.00 (2) Å, and the Cu-O lengths are 2.10 (2), 2.11 (2), 2.34 (2), and 2.35 (2) Å.

is 4.3 Å, while for $C_5H_5NH^+$ in Na_4(pyridinium)[calix[4]arene sulfonate]$\cdot 8H_2O$ the value is 4.0 Å.[25] Another comparison concerns the angle made by the plane of the aromatic guest with the plane of the CH_2 carbon atoms: 54° for the pyridinium case and a more upright 74° for the nickel complex. The latter value is also reflected in the deviation of the cavity from C_{4v} symmetry for an ideal cone configuration to one of approximately C_{2v} symmetry. The S⋯S(trans) approaches are 8.9 and 11.4 Å, compared to 10.0 and 10.9 Å for the pyridinium complex.[25] The driving force for this is the enhanced van der Waals contacts between guest and host.

Calix[4]arene complexes of this type invariably pack into a structure that is divided into hydrophilic and hydrophobic layers. The hydrophobic layer is organized and held together by favorable van der Waals contacts and by some form of secondary bonding interaction between the sulfonate groups of the "down" calixarenes and the phenolic groups of the "up" ones. In all the previous examples this has resulted in a close-packed bilayer of calix[4]arenes.[19-21] In the title nickel complex, the second independent $[(H_2O)_5Ni(NC_5H_5)]^{2+}$ cation is seen to be intercalated into the calixarene bilayer. As is shown in Figure 1, the penetration of the intercalated transition-metal complex into the bilayer is deeper than that of the one subject to second-sphere coordination.

Very similar behavior has also been found for the $[(H_2O)_4Cu(NC_5H_5)_2]^{2+}$ cation in $[(H_2O)_4Cu(NC_5H_5)_2](H_3O)_3$[calix[4]arene sulfonate]$\cdot 9H_2O$,[26,27] as is shown in Figure 2. In this case there is only one copper-containing cation per calix[4]arene, but one pyridine is embedded in the cavity and the other is intercalated into the bilayer. The cation thus spans the hydrophilic layer.

Acknowledgment. We are grateful to the National Science Foundation for support of this work.

Supplementary Material Available: Details of X-ray crystal studies of **1** and **2** including summary of procedure and data, tables of final fractional coordinates, hydrogen atom coordinates, anisotropic thermal parameters, and bond distances and angles, and calixarene and nickel labeling schemes (18 pages); listing of observed and calculated structure factors for **1** and **2** (39 pages). Ordering information is given on any current masthead page.

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(26) Two equivalents of pyridine was added to 1 equiv of $Cu(NO_3)_2$ in deionized water. This solution was mixed with a second solution of 1 equiv of Na_5[calix[4]arene sulfonate] in deionized water. The resultant pale blue-green crystals of $[(H_2O)_4Cu(NC_5H_5)_2](H_3O)_3$[calix[4]arene sulfonate]$\cdot 9H_2O$ formed upon slow evaporation in a vacuum desiccator.

(27) $[(H_2O)_4Cu(NC_5H_5)_2](H_3O)_3$[calix[4]arene sulfonate]$\cdot 9H_2O$ crystallizes in the triclinic space group $P\bar{1}$ with a = 15.438 (4) Å, b = 15.727 (6) Å, c = 12.121 (9) Å, α = 112.74 (4)°, β = 102.02 (4)°, γ = 85.35 (4)°, and D_{calcd} = 1.57 g cm^{-3} for Z = 2. Refinement based on 3921 observed reflections led to a final R value of 0.125.

The Lithium Perchlorate-Diethyl Ether Rate Acceleration of the Diels-Alder Reaction: Lewis Acid Catalysis by Lithium Ion

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The recent report by Grieco and co-workers[1] concerning the effect of 5 M lithium perchlorate-diethyl ether[2] (LPDE) on the rate of the Diels-Alder reaction was extremely stimulating. Reactions that formerly required high temperatures or high pressures for success could now be performed at room temperature and ambient pressure. We were intrigued by the very interesting suggestion that the source of this effect is due to the very high "internal pressure" of 5 M LPDE solution. As an alternative explanation we now present evidence that the rate acceleration of the Diels-Alder reaction in lithium perchlorate-diethyl ether may be due to Lewis acid catalysis, with lithium ion functioning as the Lewis acid.

If the rate enhancement is due to a "pressure" effect caused by the lithium perchlorate-diethyl ether solution, then the rates of all Diels-Alder reactions should be increased in this medium since all Diels-Alder reactions proceed with a highly negative volume of activation.[3] In contrast to the remarkable examples reported by Grieco, we have discovered that *the rate of the Diels-Alder reaction between 1,3-diphenylisobenzofuran and styrene*[4] *is unaffected by lithium perchlorate-diethyl ether solutions*.[5] A possible explanation for the increased reaction rates for some Diels-Alder reactions and not others is Lewis acid catalysis.

If lithium ion is functioning as a Lewis acid catalyst in some Diels-Alder reactions, then the second-order rate constant should depend on the lithium ion concentration. We have measured the second-order rate constants for the Diels-Alder reaction between acrylonitrile (AN) and 9,10-dimethylanthracene (DMA)[6] in the presence of various concentrations of lithium perchlorate. The reactions were carried out at 28.0 °C in ether under pseudo-first-order conditions using a large excess of dienophile and were monitored by UV spectroscopy at 398 nm by following the disappearance of DMA.[7] The second-order rate constants for the reaction are shown in Table I, and a plot of the data is shown in Figure 1. In 4.5 M LPDE, the rate enhancement is a factor of 9 over the purely thermal reaction.

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