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Enantioselective Guest Binding and Dynamic Resolution of Cationic Ruthenium Complexes by a Chiral Metal−Ligand Assembly

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Enzymes achieve remarkable selectivities in enantiomeric recognition and efficient catalytic activity.[1] We propose that artificial container molecules can fulfill similar functions, mimicking recognition processes or enzyme-catalyzed conversions. Synthetic supramolecular assemblies have demonstrated their ability to encapsulate organic guests based on their size, shape, and functional group complementarity.[2] Also the encapsulation of chiral organic guest molecules into chiral cagelike host structures has been reported to proceed with moderate to good diastereoselectivity.[3] We report here the encapsulation of organometallic complexes, which have been reported to be catalytically active, into a chiral, well-defined cavity. The encapsulations of the chiral ruthenium complexes proceed with diastereoselectivities up to 70%, and the resolved assembly is exploited for a dynamic resolution of one of the organometallic species.

The host−guest chemistry of the tetrahedral $[Ga_4L_6]^{12-}$ structure (L = 1,5-bis(2,3-dihydroxybenzamido)naphthalene) has been investigated by Raymond and co-workers.[4] Self-assembly of achiral components leads to formation of a racemic mixture of homochiral clusters with Δ,Δ,Δ,Δ- or Λ,Λ,Λ,Λ-configuration with respect to each metal center (Figure 1). The capsule is soluble in water and other highly polar solvents but contains a hydrophobic cavity of approximately 300−350 Å^3 which can encapsulate a variety of monocationic species, including $[CpRu(\eta^6\text{-}C_6H_6)]^+$.[5] These observations led to the present investigation of the half-sandwich complexes CpRu(diene)Cl and Cp*Ru(diene)Cl (Cp = C_5H_5, Cp* = η^5-$C_5(CH_3)_5$) which have been reported to mediate a variety of C−C bond-formation reactions.[6] In polar media these complexes undergo halide dissociation to form cationic ruthenium species which are potential guest molecules.

Upon combination and vigorous stirring of an aqueous solution of $[NMe_4{\subset}Ga_4L_6]^{11-}$ (**1a**) and an ethereal layer of CpRu(2,3-dimethylbutadiene)Cl, guest exchange took place, and the host−guest complex [CpRu(2,3-dimethylbutadiene)$(H_2O){\subset}Ga_4L_6]^{11-}$ (**2a**) was isolated from the aqueous layer in almost quantitative yield.[7] The product shows the characteristic upfield shift in the ^{1}H NMR spectrum that is diagnostic for inclusion of one equivalent of ruthenium guest species in the asymmetric cavity. In an analogous fashion the unsymmetrically substituted (and therefore chiral) precursors $[CpRu(isoprene)(H_2O)]^+$ and [CpRu(2-ethylbutadiene)-$(H_2O)]^+$ were encapsulated into the Ga_4L_6 tetrahedral assembly. An interesting stereochemical feature of these encapsulation reactions is the formation of two diastereomeric host−guest complexes, which occur due to the placement of a chiral guest inside a chiral host. The ^{1}H NMR spectrum of [CpRu(2-ethylbutadiene)-$(H_2O){\subset}Ga_4L_6]^{11-}$ (**3**) shows two separate data sets for the two diastereomers, e.g., two peaks for the Cp resonances at 2.08 and 2.00 ppm and two signals for the methyl groups at −0.63 and −0.71 ppm. Further evidence was obtained from the NOESY spectrum, which shows two separate sets of peaks, corresponding to the two

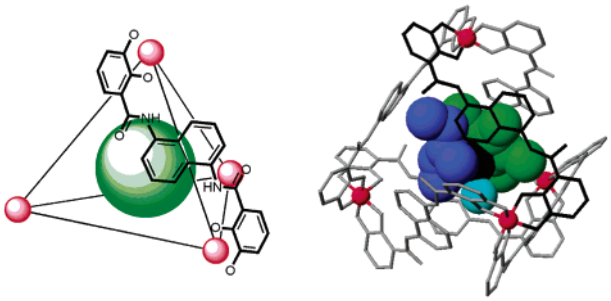

Figure 1. (Left) General schematic of $[Guest{\subset}Ga_4L_6]^{11-}$ assembly; only one of the ligands is drawn, the others are represented as sticks. (Right) Model of [Cp*Ru(2-ethylbutadiene)$(H_2O){\subset}Ga_4L_6]^{11-}$ showing the Λ,Λ,Λ,Λ-(*S*) stereoisomer. (CAChe Workstation Pro, Fujitsu Limited, 5.04, 2002.)

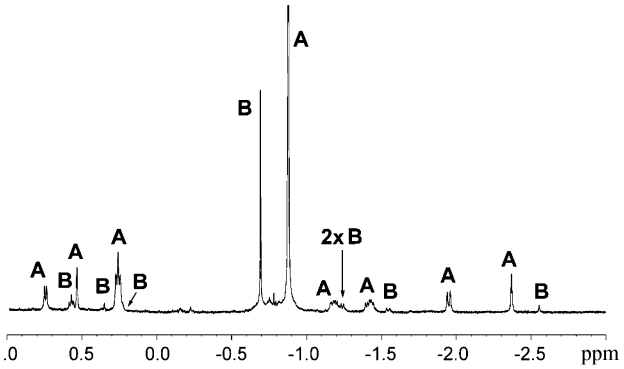

Figure 2. ^{1}H NMR spectrum of [Cp*(Ru(2-ethylbutadiene)$(H_2O){\subset}Ga_4L_6]^{11-}$, illustrating the large diastereomeric excess (A = major diastereomer, B = minor diastereomer).

different species. For both host−guest complexes, **3** and [CpRu(isoprene)$(H_2O){\subset}Ga_4L_6]^{11-}$ (**4**), the two diastereomers were obtained in a 1:1 ratio.

To promote stereoselectivity in the encapsulation reactions, the interaction between the ruthenium guest and the self-assembled host was increased by changing the Cp fragment to the sterically more demanding Cp* moiety. A series of 1- and 2-substituted Cp*Ru-(diene)Cl complexes were synthesized by methods analogous to those described in the literature[8] and encapsulated into the assembly. Formation of the two diastereomeric host−guest complexes of $[Cp^*Ru(isoprene)(H_2O){\subset}Ga_4L_6]^{11-}$ (**5**) was observed by ^{1}H NMR spectroscopy, with one of the diasteromers present in slight excess (4% diastereomeric excess). The encapsulation of Cp*Ru(2-ethylbutadiene)Cl proceeded similarly to yield two diastereomers of [Cp*Ru(2-ethylbutadiene)$(H_2O){\subset}Ga_4L_6]^{11-}$ (**6**). *Here a diastereomeric excess of 70% is observed.*

The ^{1}H NMR spectrum of [Cp*Ru(2-ethylbutadiene)$(H_2O){\subset}Ga_4L_6]^{11-}$ illustrates how every signal of the major diastereomer is accompanied by a much smaller signal for the minor diastereomer

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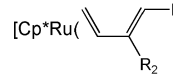
Table 1. Observed Diastereoselectivities in the Encapsulation Reactions[a]

[Cp*Ru()(H$_2$O)⊂Ga$_4$L$_6$]$^{11-}$		compound	de(%)
R^1 = H,	R^2 = Me	**5**	4
R^1 = H,	R^2 = Et	**6**	70
R^1 = H,	R^2 = *i*-Pr	**7**	26
R^1 = H,	R^2 = *n*-Pr	**8**	64
R^1 = Me,	R^2 = H	**9**	15
R^1 = Et,	R^2 = H	**10**	18
R^1 = *n*-Pr,	R^2 = H	**11**	17

[a] The de values were determined by integration of the ^{1}H NMR spectra and have an estimated ±3% error

(Figure 2). We suspect that this product distribution is the thermodynamic ratio, since heating the sample to 90 °C does not change the diastereomeric excess. To the best of our knowledge, diastereomeric excesses larger than 60% for inclusion of chiral guest molecules into chiral, self-assembled cavities have not been observed previously.[3g−k]

Other Cp*Ru(diene)−nanovessel complexes also show diastereoselectivity; their diastereomeric excesses are given in Table 1. Note that the diastereomeric excess observed for [Cp*Ru(2-*i*-propylbutadiene)(H$_2$O)⊂Ga$_4$L$_6$]$^{11-}$ (**7**) and the 1-substituted complexes are fairly low, indicating that the encapsulation process is controlled not only by the guest's size but also by its shape. In any case, the values in Table 1 establish a key property: the host assembly recognizes one enantiomer of the chiral ruthenium complex relative to the other with high selectivity, reflecting the guest molecule's close fit into the cavity.

The observation of chiral recognition of an organometallic complex by the host cavity prompted attempts to resolve the chiral ruthenium complexes with the resolved assembly. One equivalent of Λ,Λ,Λ,Λ-[Ga$_4$L$_6$]$^{12-}$ in aqueous solution was combined with an ethereal solution containing two equivalents of Cp*Ru(2-ethylbutadiene)Cl.[9] The resulting mixture was stirred for 2 h, and the layers were separated. The ^{1}H NMR spectrum of the aqueous layer confirmed the formation of the host−guest complex **6** with the above-mentioned diastereomeric excess of 70%. The intense CD spectrum of this solution originates from the host-assembly, corroborating the formation of Λ,Λ,Λ,Λ-**6**, a host−guest complex in which the resolved host has fully retained its chirality and primarily encapsulates one enantiomer of the chiral ruthenium complex. The ethereal layer, which still contained one equivalent of Cp*Ru(2-ethylbutadiene)Cl, however, remained CD silent. The repetition of this experiment with only one equivalent Cp*Ru(2-ethylbutadiene)Cl revealed an interesting result: formation of the host−guest complex was quantitative, and the isolated product gave rise to the same strong CD signal as observed in the previous experiment, again implying that the assembly has retained its chirality. The diastereomeric excess displayed in the ^{1}H NMR spectrum still amounted to 70%, which requires racemization of the ruthenium complex at some stage of the encapsulation reaction.[11] This encapsulation reaction is therefore an example of a dynamic resolution of enantiomers.

In summary, it has been demonstrated that the chiral metal−ligand assemblies have a high potential for asymmetric recognition processes, illustrating the assemblies' large influence on the bound substrate. Moreover, a dynamic resolution of the reactive catalyst precursor was accomplished by utilizing the resolved supramolecular assembly. The present results highlight the potential of chiral assemblies to mediate catalytic organometallic reactivity asymmetrically. This would extend the known application of host−guest reactivity[12] and is currently being pursued in our laboratory.

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Supporting Information Available: Experimental details and spectroscopic data for ruthenium complexes and **2**−**11** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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