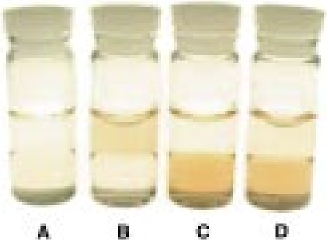

Figure 3. Color changes observed upon exposing aqueous solutions of chloride ions to dichloromethane phases containing 2,2′-bis(3-hydroxy-1,4-naphthoquinone) (1×10^{-3} M). A) Control experiment. The aqueous phase is distilled water (pH 7.41). B) The aqueous phase contains NaCl at a concentration of 1×10^{-1} M. C) The aqueous phase contains NaCl (1×10^{-1} M) and benzo[15]crown-5. D) The aqueous phase is Gulf of Mexico sea water (pH 7.34) and benzo[15]crown-5.

ability to sense qualitatively in a naked-eye-detectable fashion chloride anions is not limited to laboratory samples but was also found to work for sea water obtained from the Gulf of Mexico.[14] This observation leads us to suggest that this particular species could prove useful as a chloride anion sensor.[15]

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[1] a) *Supramolecular Chemistry of Anions* (Eds.: A. Bianchi, K. Bowman-James, E. Garcia-Espana), Wiley-VCH, New York, **1997**; b) F. P. Schmidtchen, M. Berger, *Chem. Rev.* **1997**, *97*, 1609–1646, and references therein.

[2] a) A. W. Czanik, *Acc. Chem. Res.* **1994**, *27*, 302–308. b) A. P. de Silva, H. Q. N. Gunaratne, T. Gunnlaugsson, A. J. M. Huxley, C. P. McCoy, J. T. Rademacher, T. E. Rice. *Chem. Rev.* **1997**, *97*, 1515–1566; c) K. P. Xiao, P. Buhlmann, S. Nishizawa, S. Amemiya, Y. Umezawa, *Anal. Chem.* **1997**, *69*, 1038–1044; d) P. D. Beer, *Acc. Chem. Res.* **1998**, *31*, 71–80; e) K. Niikura, A. Metzger, E. V. Anslyn, *J. Am. Chem. Soc.* **1998**, *120*, 8533–8534; f) H. Miyaji, P. Anzenbacher, Jr., J. L. Sessler, E. R. Bleasdale, P. A. Gale, *Chem. Commun.* **1999**, 1723–1724.

[3] *Comprehensive Supramolecular Chemistry* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, K. S. Suslick), Pergamon, Oxford, **1996**.

[4] a) S. S. Yamamura, M. A. Wade, J. H. Sikes, *Anal. Chem.* **1962**, *34*, 1308–1312; b) S. Nishizawa, R. Kato, T. Hayashita, N. Teramae, *Anal. Sci.* **1998**, *14*, 595–597.

[5] J. J. Lavigne, E. V. Anslyn, *Angew. Chem.* **1999**, *111*, 3903–3906; *Angew. Chem. Int. Ed.* **1999**, *38*, 3666–3669.

[6] a) P. A. Gale, L. J. Twyman, C. I. Handlin, J. L. Sessler, *Chem. Commun.* **1999**, 1851–1852; b) C. B. Black, B. Andrioletti, A. C. Try, C. Ruiperez, J. L. Sessler, *J. Am. Chem. Soc.* **1999**, *121*, 10438–10439.

[7] a) H. Miyaji, W. Sato, J. L. Sessler, V. Lynch, *Tetrahedron Lett.* **2000**, *41*, 1369–1373; b) H. Miyaji, W. Sato, J. L. Sessler, *Angew. Chem.* **2000**, *112*, 1847–1850; *Angew. Chem. Int. Ed.* **2000**, *39*, 1777–1780.

[8] J. L. Sessler, T. D. Mody, D. A. Ford, V. Lynch, *Angew. Chem.* **1992**, *104*, 461–464; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 452–455.

[9] The binding constants (K_a) with various anions were estimated from the shifts in the absorption spectra of 1,2-diaminoanthraquinone, with $F^- = 3820$, $Cl^- = 310$, $Br^- = 85$, $I^- = 20$, $H_2PO_4^- = 1270$, and $HSO_4^- = 25\,M^{-1}$ in dichloromethane. Errors < 10%.

[10] The change in color for 1,8-diaminoanthraquinone was smaller than for 1,2-diaminoanthraquinone. For example, the color of a solution of 1,8-diaminoanthraquinone in dichloromethane (1×10^{-4} M) changed from orange ($\lambda_{max} = 487$ nm) to red ($\lambda_{max} = 503$ nm) upon the addition of 500 equivalents of fluoride ions.

[11] J. J. Lavigne, S. Savoy, M. B. Clevenger, J. E. Ritchi, B. McDoniel, S.-J. Yoo, E. V. Anslyn, J. T. McDevitt, J. B. Shear, D. Neikirk, *J. Am. Chem. Soc.* **1998**, *120*, 6429–6430.

[12] As a result of a strong interaction with the crown ether and a resulting color change in the absence of anions, 1,2-diaminoanthraquinone could not be used for such extraction-type experiments.

[13] Chloride, rather than fluoride, ions were chosen for these tests since this larger anion is less basic and less prone to modulate the pH of the aqueous phase. Since changes in pH can affect the color of the indicators in this study, rigorous efforts were made to maintain the pH (through, for example, the use of dilute samples) as well as to control any differences in color that changes in pH could induce.

[14] Collected at Corpus Christi, Texas, USA in June of **1999**.

[15] While fluorescence-based chloride sensors are known, colorimetric indicators for this anionic analyte are rare. See, for example, A. S. Verkman, *Am. J. Physiol.* **1990**, *259*, C375-C388. See also ref. [2f].

Resolution and Kinetic Stability of a Chiral Supramolecular Assembly Made of Labile Components**

Andreas J. Terpin, Marco Ziegler, Darren W. Johnson, and Kenneth N. Raymond*

The importance of chirality for recognition processes in nature is impressively exemplified by the different tastes of (*R*)- and (*S*)-asparagine,[1] and the vastly different pharmacological effects of the two enantiomers of thalidomide.[2] Chirality is not the exclusive domain of organic chemistry, many metals can also serve as centers of chirality.[3] The most frequent case is an octahedral arrangment of three bidentate ligands around a metal center to form Δ or Λ absolute configurations. Chirality at metal centers has been found to play an important role in nature, for example, for the siderophore-mediated iron uptake in many organisms.[4]

Δ/Λ Isomerization of tris-bidentate complexes of the labile high-spin ferric ion or its closely related gallium(III) analogues is rapid in aqueous solution. Tris(catecholate)gallium(III) complexes, model compounds of iron siderophores, usually racemize fast. Racemization rates of 10(1) s^{-1} for a mononuclear complex[5] and 0.10(1) s^{-1} for a dinuclear helix[6] were determined by NMR studies. The isomerization was found to

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[**] Coordination Number Incommensurate Cluster Formation, Part 18. Financial support of this work was provided by NSF CHE-9709621 and by NSF and NATO-NSF exchange grants INT-9603212 and SRG 951516, respectively. We thank the Alexander-von-Humboldt Foundation for a Fellowship to A.T., and a Humboldt Research Award for Senior U.S. Scientists to K.R., and the Miller Foundation for a fellowship to M.Z. The authors gratefully acknowledge the assistance of Dr. F. J. Hollander and Dr. D. L. Caulder in selecting and mounting a suitable single crystal, and Prof. Julie A. Leary, Dr. Ulla N. Andersen, and J. J. Miranda for measuring mass spectra. Part 17: M. Ziegler, J. J. Miranda, U. N. Andersen, D. W. Johnson, J. A. Leary, K. N. Raymond, *Angew. Chem.*, in press.

be unimolecular and to proceed through a Bailar twist mechanism. The combination of two chiral metal centers to form a helicate substantially slows the isomerization rate as a result of strong mechanical coupling through the rigid ligands.

Larger supramolecular clusters based on metal–ligand interactions have been designed,[7–10] many of which are intrinsically chiral. In particular, tetrahedral $[\mathrm{M}_4\mathrm{L}_6]$ assemblies have been prepared from C_2-symmetric bis-catecholate or bis-hydroxamate ligands and octahedral metal ions, which form trigonally symmetric vertices (Figure 1).[11–15] In $[\mathrm{Ga}_4\mathbf{1}_6]$ the metal vertices are bridged by a ligand that does not discriminate between the Λ-Δ or Λ-Λ configuration across an edge but does discriminate against the Bailar-twist transition state required for inversion.[11, 12] The result is the formation in solution of all possible isomers (with point group symmetry): $\Delta\Delta\Delta\Delta$ (T), $\Delta\Delta\Delta\Lambda$ (C_3), $\Delta\Delta\Lambda\Lambda$ (S_4), and their mirror images. In contrast, the tetrahedral complex $[\mathrm{Ga}_4\mathbf{2}_6]$ has strongly coupled metal centers, such that if one metal center initially has a Λ configuration, the metal center across an edge from it must necessarily also be Λ. In this case the result is the formation of a racemic mixture of homoconfigurational clusters ($\Lambda\Lambda\Lambda\Lambda$ or $\Delta\Delta\Delta\Delta$).[13] The activation energy for interconversion of a tris(catecholate)gallium(III) center from Λ to Δ is 67(1) kJ mol^{-1}.[6] If the tetrahedral structure is truly rigid and the metal centers cannot racemize independently from each other, the activation barrier for isomerizing a $[\mathrm{M}_4\mathrm{L}_6]$ cluster through a Bailar-twist mechanism would be expected to be much higher. Herein we report the resolution of $[\mathrm{Ga}_4\mathbf{2}_6]$ and show that the enantiomers are indeed exceedingly stable towards racemization.

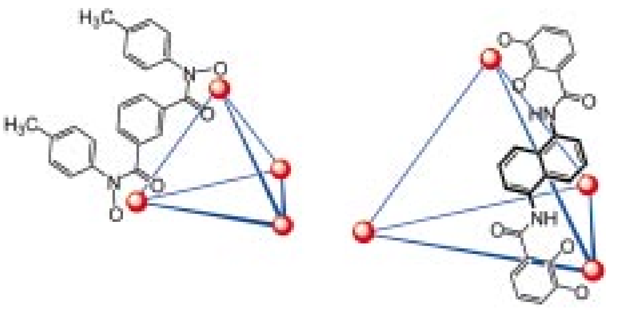

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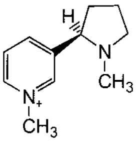
Figure 1. Tetrahedral clusters $[\mathrm{Ga}_4\mathbf{1}_6]$ and $[\mathrm{Ga}_4\mathbf{2}_6]$ formed by bis-catecholate ligands and Ga$^{\mathrm{III}}$ ions at the corners of a tetrahedron.

Complete resolution of the chiral anionic cluster is accomplished in the presence of the chiral N-methylnicotinium cation (Nic) derived from natural (−)nicotine and designed to interact stereospecifically with the vertices of the tetrahedron. Interestingly, the cation is encapsulated in the cavity of the cluster $[(\mathrm{Nic})\subset\mathrm{Ga}_4\mathbf{2}_6]^{11-}$, as shown by the large upfield shift of the resonances of the cation in the ^{1}H spectrum (Figure 2), which is characteristic of encapsulation and has been observed previously for related clusters and guests.[13, 16] The encapsulated chiral cation is an ideal probe to determine the diastereomeric excess (de) of the resolved cluster. The NEt_4^+ ion readily displaces the chiral guest to form enantiopure $\Delta\Delta\Delta\Delta$- and $\Lambda\Lambda\Lambda\Lambda$-$[\mathrm{Et}_4\mathrm{N}]_{11}[(\mathrm{Et}_4\mathrm{N})\subset\mathrm{Ga}_4\mathbf{2}_6]$ clusters with complete retention of chirality of the metal centers. Remarkably, an alkaline, aqueous solution of $\Delta\Delta\Delta\Delta$-$[(\mathrm{Et}_4\mathrm{N})\subset\mathrm{Ga}_4\mathbf{2}_6]^{11-}$ retained its enantiopurity for at least eight months, and even extended boiling of the solution did not lead to racemization![17]



Nic

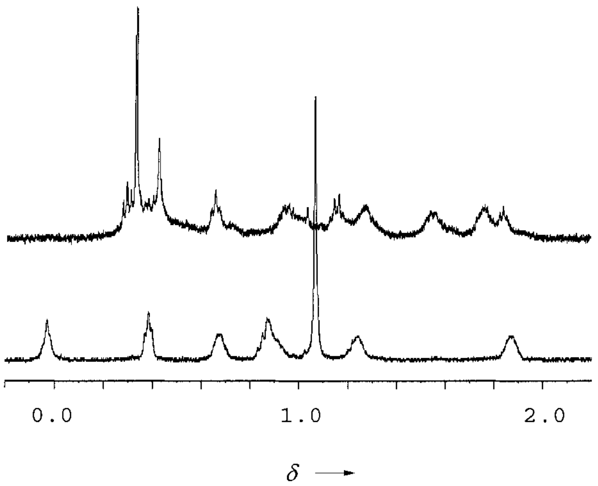


Figure 2. NMR spectra (D_2O) of the resolved tetrahedral clusters $\Delta\Delta\Delta\Delta$-$[(\mathrm{Nic})\subset\mathrm{Ga}_4\mathbf{2}_6]^{11-}$ (bottom) and $\Lambda\Lambda\Lambda\Lambda$-$[(\mathrm{Nic})\subset\mathrm{Ga}_4\mathbf{2}_6]^{11-}$ (top) showing the strongly upfield shifted resonances of the encapsulated chiral guest (Nic).

The absolute configuration and enantiopurity of the clusters was determined from their CD spectra (Figure 3): the $\pi-\pi^*$ transitions in the catechol moiety at each metal center give rise to a strong exciton couplet from which the absolute configuration can be determined.[18]

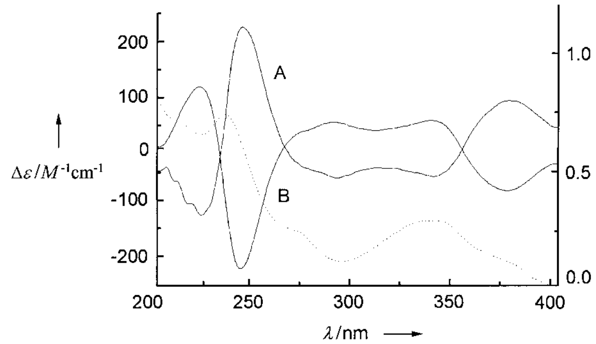


Figure 3. CD and absorption spectrum of the resolved tetranuclear cluster $[(\mathrm{Nic})\subset\mathrm{Ga}_4\mathbf{2}_6]^{11-}$: $\Lambda\Lambda\Lambda\Lambda$ (A) and $\Delta\Delta\Delta\Delta$ (B) forms.

An X-ray crystallographic analysis[19] of $\Delta\Delta\Delta\Delta$-$[(\mathrm{Et}_4\mathrm{N})\subset\mathrm{Ga}_4\mathbf{2}_6]$ confirmed the absolute configuration at the metal center (Figure 4). The gallium ions are coordinated in a distorted octahedral fashion (average Ga–O bond length 1.966 Å, with a twist angle at the Ga center of 40.2° and Ga ··· Ga distances of 12.663 Å). These values are very similar to those found in the crystal structure of the same compound in racemic form.[13]

Chirality at octahedral metal centers can be imposed by chiral ligands,[3] and a tetrahedral bis-catecholate cluster with

Figure 4. Crystal structure of $\Delta\Delta\Delta\Delta$-[$(Et_4N)\subset Ga_4\mathbf{2}_6$] (stereoview). View along the twofold axis of the molecule showing its overall crystallographic *T*-symmetry. The disorder of the naphthyl backbone and counterions have been omitted for clarity.

exclusive Λ configurations at the Ga^{III} metal centers has been reported.[20] To the best of our knowledge, the $\Delta\Delta\Delta\Delta$- and $\Lambda\Lambda\Lambda\Lambda$-$[Et_4N]_{11}[(Et_4N)\subset Ga_4\mathbf{2}_6]$ clusters are the first examples of enantiopure, nonracemizing clusters formed quantitatively from achiral labile components.[21] Like a wooden house, the rigidity of this molecular tetrahedron results from not the individual components but the way they are assembled. Dissociation of one board followed by reattachment does not change the structure.

In summary, we have shown that a racemic mixture of homoconfigurational tetrahedral clusters with labile metal ions can be resolved into its $\Delta\Delta\Delta\Delta$ and $\Lambda\Lambda\Lambda\Lambda$ enantiomers, which are stable towards racemization even though related mononuclear or dinuclear metal complexes (helicates) racemize quickly. "Mechanical stiffness" that prevents racemization is provided through the interconnection of all four labile metal centers in a rigid three-dimensional tetrahedral arrangment. We are currently investigating the use of such chiral capsules for enantioselective catalysis and diastereoselective encapsulation of other chiral molecules.

Experimental Section

General: All NMR spectra were measured with a Bruker 500 MHz spectrometer. Chemical shifts are reported as δ downfield from sodium $[D_4]$2,2,3,3-[3-(trimethylsilyl)]propionate. Absorption spectra were recorded on a Hewlett–Packard 8450A UV/Vis diode array spectrophotometer. Circular dichroism (CD) spectra were measured with a Jasco J-500C spectropolarimeter equipped with an IF-500 II A/D converter. Mass spectral data were acquired using a Bruker Apex II actively shielded FT-ICR mass spectrometer equipped with an Analytica electrospray source (off-axis probe). $H_4\mathbf{2}$[13] and *N*-methylnicotinium iodide[24] (NicI) were synthesized according to published procedures. Solvents and commercially available reagents were used without further purification.

Enantiopure tetrahedral clusters: $[Ga(acac)_3]$ (37.0 mg, 0.101 mmol), $H_4\mathbf{2}$ (66.7 mg, 0.155 mmol), and NicI (94.3 mg, 0.310 mmol) were suspended in degassed, dry CH_3OH (20 mL). A 0.508 N KOH solution in CH_3OH (610 µL) was slowly added through a syringe whereupon the ligand dissolved, and a clear solution was obtained. After 1 h, an orange-yellow powder started to precipitate. The precipitate ($\Delta\Delta\Delta\Delta$ form) was collected after 24 h by centrifugation, washed with a small portion of methanol, and dried under high vacuum (55 mg, 100%, *de* > 98%). The remaining methanolic solution was concentrated to about 1 mL and an excess of acetone (20 mL) added to quantitatively precipitate the remaining $\Lambda\Lambda\Lambda\Lambda$-form, which was collected by centrifugation, washed with acetone, and dried under high vacuum (49 mg, 100%, *de* > 98%). Enantiopure Al^{III}, In^{III}, and Fe^{III} complexes were obtained using the same procedure starting with the corresponding $[M(acac)_3]$ salts. The enantiopure $[(Nic)\subset Ga_4\mathbf{2}_6]^{11-}$ clusters precipitated with various unstoichiometric mixtures of Nic and K^+ ions, with quantitative yields of both $\Delta\Delta\Delta\Delta$ and $\Lambda\Lambda\Lambda\Lambda$ enantiomers (50% each). The same cluster was previously found to precipitate with mixtures of Et_4N^+ and K^+ ions.[13] The *de* values were determined by NMR spectroscopy and exceeded 98% in all cases, since no trace of the other diastereomer could be found (Figure 2). The encapsulated Nic ions were exchanged quantitatively against Et_4N^+ by elution with 1 N basic Et_4NCl on a cation exchange column (Amberlite IRC-50) and precipitation of the complex by addition of acetone after elution to yield $\Delta\Delta\Delta\Delta$-$[Et_4N]_{11}[(Et_4N)\subset Ga_4\mathbf{2}_6]$ and $\Lambda\Lambda\Lambda\Lambda$-$[Et_4N]_{11}[(Et_4N)\subset Ga_4\mathbf{2}_6]$. Crystals suitable for analysis by X-ray diffraction were obtained by slow vapor diffusion of acetone into an aqueous solution of $\Delta\Delta\Delta\Delta$-$[(Et_4N)\subset Ga_4\mathbf{2}_6]^{11-}$ with a mixture of K^+/NEt_4^+/Nic ions present.

The following abbreviations have been employed: Nic_fH for free nicotinium protons, Nic_eH for encapsulated nicotinium protons, Ar_nH for the ligand naphthyl protons and Ar_cH for the ligand catecholate protons.

$\Delta\Delta\Delta\Delta$-$K_6[Nic]_5[(Nic)\subset Ga_4\mathbf{2}_6]$: ^1H NMR (500 MHz, D_2O): δ = 13.35 (s, 12 H), 7.86 (s, 12 H, Nic_fH), 7.71 (d, 5 H, Nic_fH), 7.66 (d, 5 H, Nic_fH), 7.55 (s, 12 H, Ar_nH), 7.35 (t, 1 H, Nic_eH), 7.31 (d, 12 H, Ar_cH), 7.12 (t, 5 H, Nic_fH), 6.83 (t, 12 H, Ar_nH), 6.75 (d, 12 H, Ar_cH), 6.61 (t, 12 H, Ar_cH), 6.20 (d, 1 H, Nic_eH), 5.21 (d, 1 H, Nic_eH), 4.22 (s, 1 H, Nic_eH), 3.77 (s, 15 H, Nic_fH), 2.97 (t, 5 H, Nic_fH), 2.89 (t, 5 H, Nic_fH), 2.21 (dd, 5 H, Nic_fH), 2.01 (d, 5 H, Nic_fH), 1.88 (s, 15 H, Nic_fH), 1.85 (s, 3 H, Nic_eH), 1.71 (d, 5 H, Nic_fH), 1.68 (dd, 5 H, Nic_fH), 1.32 (m, 5 H, Nic_fH), 0.02 (m, 1 H, Nic_eH), −0.38 (t, 1 H, Nic_eH), −0.83 (m, 1 H, Nic_eH), −0.88 (m, 2 H, Nic_eH), −1.07 (s, 3 H, Nic_eH), −1.28 (m, 1 H, Nic_eH), −1.89 (m, 1 H, Nic_eH); UV/Vis (H_2O, $c = 4.85\times10^{-6}$ M): 229 (15 500), 271 (5400, sh), 340 (12 400), 365 nm (4700); CD (H_2O, $c = 4.85\times10^{-6}$ M): 221 (340), 242 (−680), 288 (150), 337 nm (150), 374 (−240). ESI-FTMS (410 pmol µL^{-1} in methanol, samples prepared with NaOH instead of KOH): Matching isotope distributions of $Na_8[(Nic)\subset Ga_4\mathbf{2}_6]^{3-}$ and $Na_7[(Nic)\subset Ga_4\mathbf{2}_6]^{4-}$ were found; *m*/*z* observed for $Na_8[(Nic)\subset Ga_4\mathbf{2}_6]^{3-}$: 1065.424, 1065.759, 1066.092, 1066.425, 1066.759, 1067.094, calcd for $Ga_4C_{155}H_{101}N_{14}O_{36}Na_8$: 1065.425, 1065.759, 1066.092, 1066.426, 1066.759, 1067.093.

$\Lambda\Lambda\Lambda\Lambda$-$K_6[Nic]_5[(Nic)\subset Ga_4\mathbf{2}_6]$: ^1H NMR (500 MHz, D_2O): δ = 13.10 (s, 12 H), 7.91 (t, 1 H, Nic_eH), 7.81 (d, 12 H, Ar_nH), 7.77 (s, 5 H, Nic_fH), 7.61 (d, 12 H, Ar_nH), 7.55 (d, 5 H, Nic_fH), 7.52 (d, 12 H, Ar_cH), 7.20–7.30 (m, 3 H, Nic_eH), 7.25 (t, 12 H, Ar_cH), 7.08 (t, 5 H, Nic_fH), 6.84 (t, 12 H, Ar_nH), 6.74 (d, 12 H, Ar_cH), 6.57 (t, 12 H, Ar_cH), 4.89 (d, 1 H, Nic_eH), 3.64 (s, 15 H, Nic_fH), 2.87 (t, 5 H, Nic_fH), 2.68 (t, 5 H, Nic_fH), 2.10 (dd, 5 H, Nic_fH), 1.87 (s, 3 H, Nic_eH), 1.86 (d, 5 H, Nic_fH), 1.75 (s, 15 H, Nic_fH), 1.64 (m, 10 H, Nic_fH), 1.38 (m, 5 H, Nic_fH), −0.39 (s, 3 H, Nic_eH), −0.39 (m, 1 H, Nic_eH), −0.75 (m, 1 H, Nic_eH), −1.00 (m, 1 H, Nic_eH), −1.29 (m, 1 H, Nic_eH), −1.18 (m, 1 H, Nic_eH), −1.51 (m, 1 H, Nic_eH), −1.71 (m, 1 H, Nic_eH).

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[1] A. Piutti, *C. R. Hebd. Seances Acad. Sci.* **1886**, *103*, 134.

[2] J. Knabe, W. Rummel, H. P. Buech, N. Franz, *Arzneim. Forsch.* **1978**, *28*, 1048.

[3] A. von Zelewsky, U. Knof, *Angew. Chem.* **1999**, *111*, 312; *Angew. Chem. Int. Ed.* **1999**, *38*, 302.

[4] G. Müller, Y. Isowa, K. N. Raymond, *J. Biol. Chem.* **1985**, *260*, 13 921.

[5] B. Kersting, M. Meyer, R. E. Powers, K. N. Raymond, *J. Am. Chem. Soc.* **1996**, *118*, 7221.

[6] M. Meyer, B. Kersting, R. E. Powers, K. N. Raymond, *Inorg. Chem.* **1997**, *36*, 5179.

[7] D. L. Caulder, K. N. Raymond, *J. Chem. Soc. Dalton Trans.* **1999**, 1185.

[8] R. W. Saalfrank, I. Bernt, *Curr. Opin. Solid State Mater. Sci.* **1998**, *3*, 407.

[9] S. Leininger, B. Olenyuk, P. J. Stang, *Chem. Rev.* **2000**, *100*, 853.

[10] M. Fujita, *Chem. Soc. Rev.* **1998**, *27*, 417.

[11] T. Beissel, R. E. Powers, K. N. Raymond, *Angew. Chem.* **1996**, *108*, 1166; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1084.

[12] T. Beissel, R. E. Powers, T. N. Parac, K. N. Raymond, *J. Am. Chem. Soc.* **1999**, *121*, 4200.

[13] D. L. Caulder, R. E. Powers, T. N. Parac, K. N. Raymond, *Angew. Chem.* **1998**, *110*, 1940; *Angew. Chem. Int. Ed.* **1998**, *37*, 1840.

[14] M. Scherer, D. L. Caulder, D. W. Johnson, K. N. Raymond, *Angew. Chem.* **1999**, *111*, 1690; *Angew. Chem. Int. Ed.* **1999**, *38*, 1588.

[15] D. W. Johnson, K. N. Raymond, unpublished results.

[16] T. N. Parac, D. L. Caulder, K. N. Raymond, *J. Am. Chem. Soc.* **1998**, *120*, 8003.

[17] Clusters with the labile Al^{III}, Fe^{III}, and In^{III} ions were resolved by the same method and also show exceedingly high stability towards racemization.

[18] M. Ziegler, A. von Zelewsky, *Coord. Chem. Rev.* **1998**, *177*, 257.

[19] Crystal structure of $\Delta\Delta\Delta\Delta$-[(Et$_4$N) $\subset$ Ga$_4$**2**$_6$] $\cdot$ x(solvent): Crystal data were collected using a Siemens SMART diffractometer equipped with a CCD area detector[25], crystal size $0.30 \times 0.20 \times 0.15$ mm, $T = -125\,^{\circ}$C, graphite-monochromated Mo$_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), cubic, space group $I23$ (No. 197), $a = 22.572(1)$ Å, $V = 11500.5(9)$ Å^3, $Z = 2$, $\mu = 0.528$ cm^{-1}, $F(000) = 3706$, $\rho_{calcd} = 1.07$ Mg m^{3-}, $2\Theta_{max} = 37.64^{\circ}$. Of the 15524 reflections measured, 1510 were unique ($R_{int} = 0.087$). The structure was solved by direct methods and refined on F^2 using SHELXTL.[26] Data were corrected for Lorentz and polarization effects. A semi-empirical absorption correction was applied using XPREP (ellipsoidal model, $R_{int} = 0.0486$, $T_{max} = 0.812$, $T_{min} = 0.755$).[26] The carbonyl oxygen atom of the ligand is disordered over two positions with 1/2 occupancy, and the naphthalene backbone of the ligand is disordered across an imaginary line connecting the two carbon atoms affixed to the nitrogen atoms of the amide. This disorder was modeled as a twist of this backbone around its center with both orientations having 1/2 occupancy. A disordered NEt$_4{}^+$ ion is present in the cavity of the cluster. The nitrogen atom is located on the 23 special position, and the methylene groups are disordered over two sites with 1/2 occupancy. The methyl carbon atoms were disordered over the threefold axes and 12 sites with 1/3 occupancy. There was also a high degree of disorder among the other cations and solvent molecules present. As a result, only the encapsulated NEt$_4{}^+$ ion was found and constrained to be rigid in the disorder model described. The other 11 cations and solvent molecules are included as "x(solvent)" in the chemical formula and accounted for by a SWAT parameter. As a result of the lack of high angle data (1.2 Å resolution) only the gallium atoms, amide nitrogens, and catecholate oxygen atoms were refined anisotropically. All other atoms were refined isotropically. Hydrogen atoms were included on all appropriate atoms of the ligand that were not disordered but were not refined. Weighting scheme: $1/[\sigma^2(F_o^2) + (0.1763p)^2 + 2.7183p]$, where $p = (F_o^2 + 2F_c^2)/3$. Final $R_1 = 0.0837$ for 1022 reflections with $F_o > 4\sigma(F_o)$ (1162 Friedel unique data, 157 parameters, 6 restraints); for all 1510 data, $wR_2 = 0.269$, GOF = 1.118; Flack[27] parameter = 0.08(8); max/min residual density +0.28/ -0.27 e Å^{-3}. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-145431. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[20] E. J. Enemark, T. D. P. Stack, *Angew. Chem.* **1998**, *110*, 977; *Angew. Chem. Int. Ed.* **1998**, *37*, 932.

[21] Other examples of partially resolved assemblies made from moderately labile octahedral metal ions (Ni^{II} and Co^{II}) and achiral ligands are dinuclear triple helicates.[22, 23]

[22] R. Kramer, J. M. Lehn, A. DeCian, J. Fischer, *Angew. Chem.* **1993**, *105*, 764; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 703.

[23] L. J. Charbonniere, G. Bernardinelli, C. Piguet, A. M. Sargeson, and A. F. Williams, *J. Chem. Soc. Chem. Commun.* **1994**, 1419.

[24] J. I. Seemann, J. F. Whidby, *J. Org. Chem.* **1976**, *41*, 3824.

[25] SMART, Area Detector Software Package, **1995**, Siemens Industrial Automation, Inc., Madison, WI, USA.

[26] G. Sheldrick, SHELXTL, Crystal Structure Determination Software Package, **1993**, Siemens Industrial Automation, Inc., Madison, WI, USA.

[27] H. Flack, *Acta Crystallogr. Sect. A* **1983**, *39*, 876.

Catalytic Asymmetric Friedel–Crafts Alkylation of β,γ-Unsaturated α-Ketoesters: Enantioselective Addition of Aromatic C–H Bonds to Alkenes**

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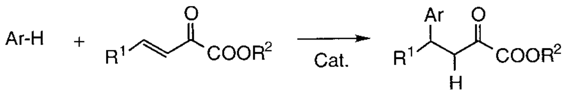
Aromatic compounds are very important molecules in chemistry and the addition of these compounds to alkenes in the Friedel–Crafts alkylation constitutes one of the fundamental reactions in synthetic chemistry.[1]

The catalytic enantioselective addition of aromatic C–H bonds to alkenes leading to formation of a new C–C bond is of considerable interest and remains a long-term challenge for chemists. Such a reaction would provide a simple and attractive method for the formation of optically active aryl-substituted compounds from easily available starting materials. Recently, the first examples of catalytic enantioselective addition reactions of aromatic and heteroaromatic compounds to activated carbonyl compounds,[2] α-dicarbonyl compounds,[3] and imines were reported.[4] However, the development of a catalytic enantioselective version of the corresponding Friedel–Crafts alkylation reaction has, to the best of our knowledge, not been reported, although numerous examples can be given for the non-enantioselective version of this reaction.[1, 5] This paper presents the first catalytic highly enantioselective Friedel–Crafts alkylation, that is, the addition of aromatic C–H bonds to β,γ-unsaturated α-ketoesters catalyzed by chiral Lewis acids [Eq. (1)].



(1)

The reaction of indole (**1a**) with methyl 4-phenyl-2-oxo-3-butenoate (**2a**) can be catalyzed by various metal complexes, and the application of the chiral bisoxazoline (BOX) complexes[6, 7] [{(*S*)-*t*Bu-BOX}M] ((*S*)-**4a**–**c**; M = Cu(OTf)$_2$, Cu(SbF$_6$)$_2$, and Zn(OTf)$_2$, respectively) and [{(*S*)-Ph-BOX}M] ((*S*)-**4d**; M = Cu(OTf)$_2$) gives the optically active Friedel–Crafts alkylation product **3a**. Some representative screening results are presented in Table 1. The Friedel–Crafts alkylation reactions with (*S*)-**4a**–**c** and (*S*)-**4d** proceed with high conversion. For the reaction catalyzed by (*S*)-**4a**, product **3a** is formed with up to 88 % *ee* in CH$_2$Cl$_2$ (entry 3), while 74 % *ee* is found in THF (entry 6). In Et$_2$O, with 2 mol % of the catalyst,

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