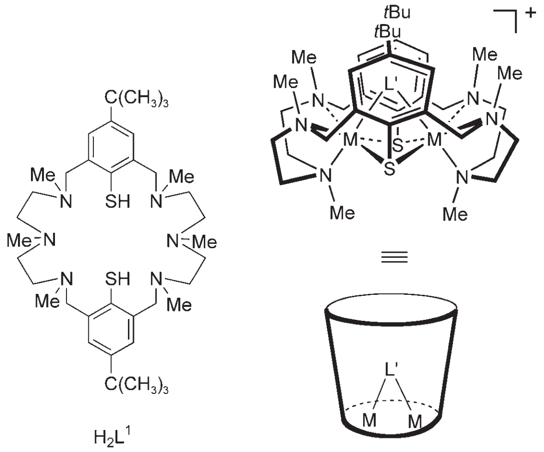
DOI: 10.1002/ange.200500683

# Diels–Alder Reactivity of Binuclear Complexes with Calixarene-like Structures**

*Steffen Käss, Thomas Gregor, and Berthold Kersting**

*Dedicated to Professor Heinrich Vahrenkamp on the occasion of his 65th birthday*

The Diels–Alder reaction is one of the most useful reactions in organic synthesis.[1] As a consequence, a large number of strategies have been developed to control the course and rate of this transformation.[2] Recently, it has been found that the outcome of some cycloadditions can be altered remarkably when performed inside the cavity of cyclodextrines,[3,4] self-assembled molecular capsules,[5–7] or coordination cages.[8–10] This fact intrigued us greatly and awoke our interest in the Diels–Alder reactivity of the "calixarene-like" $[M_2(\mu\text{-}L')(L^1)]^+$ complexes bearing unsaturated carboxylate coligands L′ (Scheme 1).[11] We report herein the synthesis and



$H_2L^1$

$[M_2(\mu\text{-}L')(L^1)]^+$ (M = $Ni^{2+}$, $Zn^{2+}$)
L' = α,β-unsaturated carboxylate ligand

**Scheme 1.** Structures of $H_2L^1$ and its metal complexes. Compound labels are given in Schemes 2–4. The cavity representation of the complexes has been used for reasons of clarity. It should not be confused with the one used for the cyclodextrins.

---

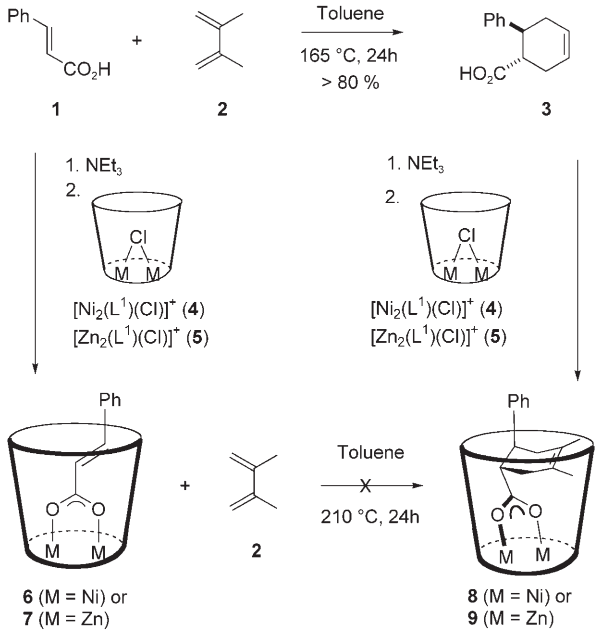
[*] S. Käss, T. Gregor, Prof. Dr. B. Kersting
Institut für Anorganische Chemie
Universität Leipzig
Johannisallee 29, 04103 Leipzig (Germany)
Fax: (+49) 341-973-6199
E-mail: b.kersting@uni-leipzig.de

[**] This work was supported by the Deutsche Forschungsgemeinschaft (KE 585/3-1,2,3).

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

structures of a series of such complexes and demonstrate the remarkable effect of the binding pocket on the regioselectivity of the Diels–Alder reaction between sorbinic acid and acrylonitrile.

The observation that α,β-unsaturated carboxylate ligands can be readily incorporated in the binding pocket of our complexes[12] led us to focus our first investigation on the Diels–Alder reaction between the cinnamate ion in **6** and 2,3-dimethylbutadiene (**2**). The reaction between cinnamic acid **1** and **2** proceeds readily in solution with toluene at 165 °C to give the corresponding adduct **3** (Scheme 2).[13] However, the reaction of **6** with a large excess of **2** in solution with toluene did not occur, even when heated in a sealed glass tube at 210 °C for 24 h.[14] The same behavior was observed for the dizinc complex **7**.



***Scheme 2.*** Preparation of **6**–**9**.

It has been possible to synthesize the expected products **8** and **9** of the above reactions by substituting the bridging chlorides in complexes **4** and **5** for triethylammonium cinnamate (Scheme 2) and to determine the X-ray crystal structure of complex **8** (Figure 1). This structure revealed the presence of an unusual conformation of cyclohexene derivative **3**, with both the phenyl and carboxylate residues in axial positions. In general, the substituents in cyclohexene rings assume equatorial positions.[15] The bisaxial arrangement in **8** is presumably enforced by the limited space in the binding pocket, which can be described by the distances between H38a···H33c (9.226 Å, diameter of the pocket) and C48···Ni1 (6.820 Å, depth of the pocket).[16] It is likely that these steric constraints also inhibit the Diels–Alder reaction of the coordinated cinnamate ion in **6**.

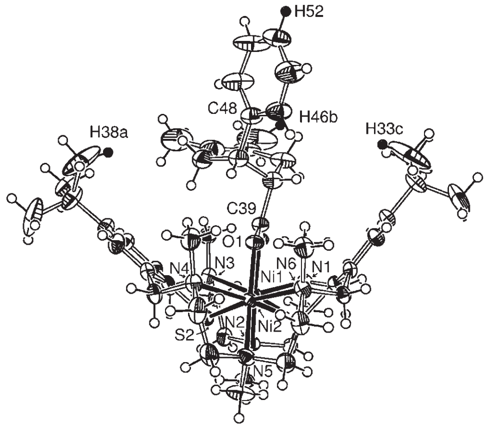
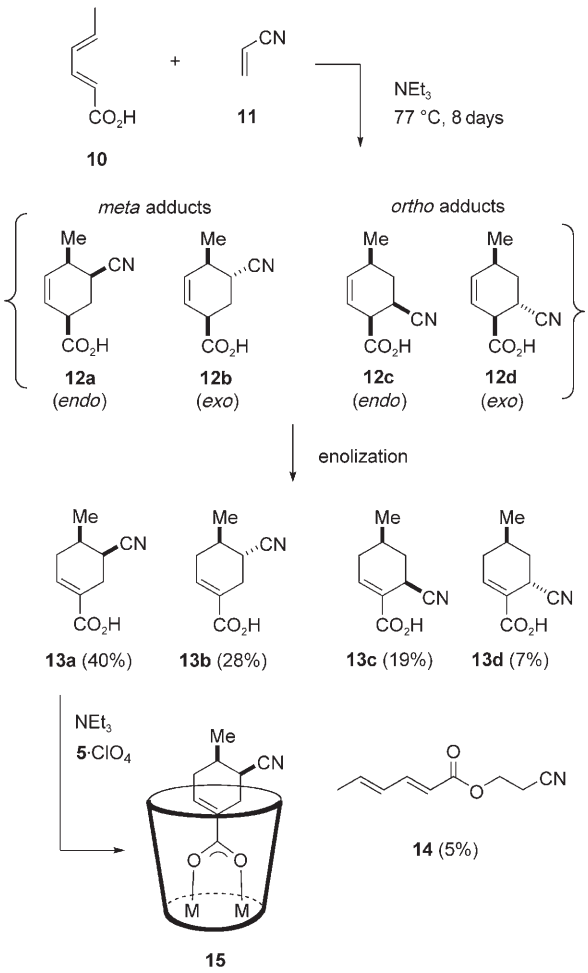


***Figure 1.*** Structure of the dinickel complex **8**, with thermal ellipsoids drawn at the 30% probability level. Bond lengths and angles are given in the Supporting Information.

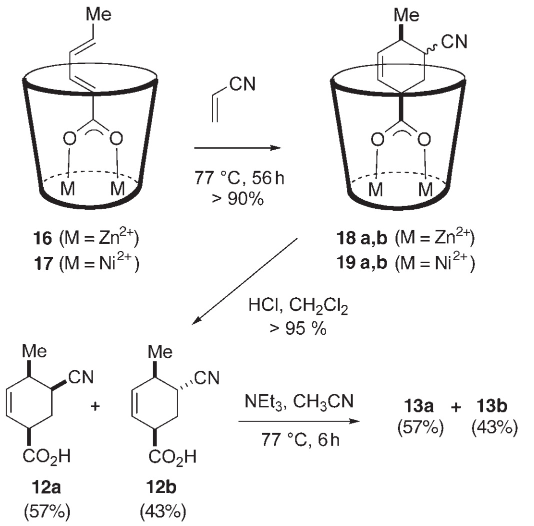
The above findings prompted us to study a Diels–Alder reaction between a coordinated dienoate ligand and an external alkene. We chose to study the reaction between sorbinic acid **10** and acrylonitrile **11** (Scheme 3). The reaction of the free acid was investigated first. This reaction is rather slow (pseudo first-order rate constant $k' = 4.8\times10^{-6}\ \mathrm{s}^{-1}$, $\tau_{1/2} \approx 2$ days) and produces a mixture of the four possible Diels–



***Scheme 3.*** Preparation of **13a**–**15**. Numbers in parentheses refer to the yields of the isolated products.

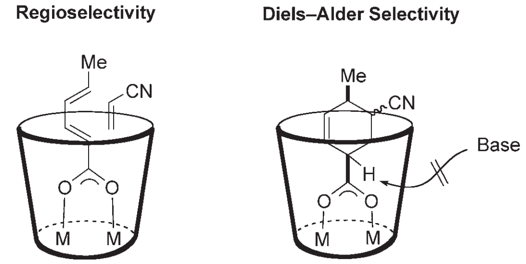
Alder adducts **12a**–**d** and the by-product **14**. All acids **12a**–**d** isomerize under the basic reaction conditions to give the corresponding α,β-unsaturated derivatives **13a**–**d**. It was possible to separate **13a**, **13b**, and **13d** by fractional crystallization and to determine their structures by $^1$H and $^{13}$C NMR spectroscopic and X-ray crystallographic studies.[14] This analysis confirmed unambiguously the assignment of the regiochemistry as represented in Scheme 3. Complex **15** (prepared by a simple coligand exchange reaction) served as a reference compound.

We then looked at the Diels–Alder reaction between the coordinated dienoate ligand in **16** and acrylonitrile (Scheme 4). Surprisingly, this reaction was already complete after 56 hours (pseudo first-order rate constant $k' = 1.4 \times 10^{-5}$ s$^{-1}$, $\tau_{1/2} \approx 0.5$ days) and gave only two products **18a** and **18b** in nearly quantitative yield in a ratio of 57:43, as revealed by NMR spectroscopy. The dinickel complex **17** behaved in a similar manner, thus producing **19a** and **19b**. To establish the structures of the coligands, **18a** and **18b** (or **19a** and **19b**) were decomposed under mild acidic conditions. In both cases, this gave the hydrochloride of the macrocycle ($H_2L^1 \cdot 6HCl$), a metal(II) salt (M = Zn$^{II}$ or Ni$^{II}$), and the free acids **12a** and **12b**. The latter isomerized in the presence of a base to the α,β-unsaturated derivatives **13a** and **13b**, respectively. This approach proved the structures of **12a** and **12b** and their complexes. Thus, in striking contrast to the low regioselectivity observed in the background reaction, the Diels–Alder reaction between coordinated **10** and acrylonitrile proceeds with strict "*meta*" regioselectivity. In addition, there are no detectable by-products, such as **14**.



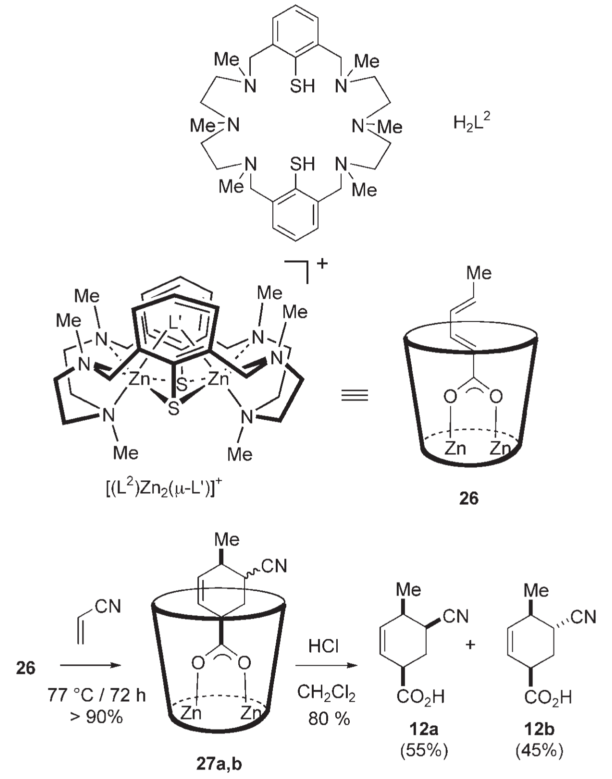
*Scheme 4.* Preparation of complexes **18a,b**, **19a,b**, Diels–Alder products **12a,b**, and α,β-unsaturated acids **13a,b**. Numbers in parentheses refer to the yields of the isolated products.

This regioselectivity and the fact that the Diels–Alder adducts **12a,b** do not isomerize in the binding pocket of the complexes can be attributed to the directing and protecting effect of the binding cavity, as schematically represented in Scheme 5.



*Scheme 5.* Directing and protecting effect of the binding cavity.

Finally, to investigate the role played by the *tert*-butyl substituents of $(L^1)^{2-}$, we investigated the reactivity of the analogous complex $[Zn_2\{(2E,4E)\text{-hexa-2,4-dienoate}\}(L^2)]^+$ **26** of macrocycle $(L^2)^{2-}$ lacking *tert*-butyl groups (Scheme 6).



*Scheme 6.* Structure of $H_2L^2$ and reactivity of its dizinc complex **26**.

The reaction of **26** with acrylonitrile and the subsequent decomposition of the intermediate complexes **27a,b** produced the acids **12a,b** as the sole reaction products again in a similar 55:45 ratio. The pseudo first-order rate constant $k'$ was determined to be $8.2 \times 10^{-6}$ s$^{-1}$ ($\tau_{1/2} \approx 1$ day). This rate is slower than the reaction between **16** and acrylonitrile ($\tau_{1/2} \approx 0.5$ days), but still significantly faster than the background reaction ($\tau_{1/2} \approx 2$ days). Thus, the *tert*-butyl substituents do not affect the regiochemistry of this particular Diels–Alder reaction, but they clearly increase its rate. The observed trend is indicative of a small stabilization of the transition state by hydrophobic effects ($\Delta\Delta G^{\ddagger} \approx 3$ kJ mol$^{-1}$; $k'_{\text{complex}}/k'_{\text{background}} = \exp(\Delta\Delta G^{\ddagger}/RT)$). This result would be consistent with our earlier observation that complexes bearing less polar carboxylate anions have higher stability constants.[17]

The Diels–Alder reactivity of “calixarene-like” metal complexes supported by the ligands $H_2L^1$ and $H_2L^2$ has been described. The reaction between the coordinated sorbinate coligand and acrylonitrile is controlled by the binding cavity of the complexes and is highly regioselective. The new method is currently only applicable to dienes with anchoring carboxylate groups, but expansion of this approach to a general concept for the control of the regioselectivity of Diels–Alder reactions between unsymmetrical dienes and dienophiles appears to be in reach. We are currently probing the possibility whether the rate of these transformations can be enhanced by enlarging the binding pocket of the complexes.

Received: February 23, 2005
Revised: October 4, 2005

**Keywords:** binuclear complexes · calixarenes · Diels–Alder reaction · regioselectivity · synthetic methods

---

[1] J. Sauer, *Angew. Chem.* **1966**, *78*, 233–252; *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 211–230.
[2] S. Otto, J. B. F. N. Engberts, *Pure Appl. Chem.* **2000**, *72*, 1365–1372.
[3] D. C. Rideout, R. Breslow, *J. Am. Chem. Soc.* **1980**, *102*, 7816–7817.
[4] H. J. Schneider, N. K. Sangwan, *Angew. Chem.* **1987**, *99*, 924–925; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 896–897.
[5] D. J. Cram, M. E. Tanner, R. Thomas, *Angew. Chem.* **1991**, *103*, 1048–1051; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1024–1027.
[6] J. Kang, J. Rebek, Jr., *Nature* **1997**, *385*, 50–52.
[7] T. Ooi, Y. Kondo, K. Maruoka, *Angew. Chem.* **1998**, *110*, 3213–3215; *Angew. Chem. Int. Ed.* **1998**, *37*, 3039–3041.
[8] C. J. Walter, J. K. M. Sanders *J. Chem. Soc. Chem. Commun.* **1993**, 458–460.
[9] T. Kusukawa, M. Yoshizawa, M. Fujita, *Angew. Chem.* **2002**, *114*, 1403–1405; *Angew. Chem. Int. Ed.* **2002**, *41*, 1403–1405.
[10] D. Fiedler, R. G. Bergman, K. N. Raymond, *Angew. Chem.* **2004**, *116*, 6916–6919; *Angew. Chem. Int. Ed.* **2004**, *43*, 6748–6751.
[11] G. Steinfeld, V. Lozan, B. Kersting, *Angew. Chem.* **2003**, *115*, 2363–2365; *Angew. Chem. Int. Ed.* **2003**, *42*, 2261–2263.
[12] B. Kersting, G. Steinfeld, *Inorg. Chem.* **2002**, *41*, 1140–1150.
[13] J. Monnin, *Helv. Chim. Acta* **1958**, *41*, 2112–2119.
[14] For details of the experimental procedures, characterization data, results of kinetic measurements, control experiments, and crystal-structure determinations, see the Supporting Information. CCDC-264275 (**8**·$BPh_4$), -264276 (**13a**), -264277 (**13b**), -264278 (**13d**), -264279 (**15**·$BPh_4$·EtOH), -264280 (**16**·$BPh_4$), and -278590 (**25**·$BPh_4$) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[15] C. Pedone, E. Benedetti, A. Immirzi, G. Allegra, *J. Am. Chem. Soc.* **1970**, *92*, 3549–3552.
[16] The distances between H52 and H46 for the two conformers were calculated to be 9.062 Å (ax,ax) and 10.401 Å (eq,eq) by using the program Chem3D (CambridgeSoft); only the dimensions of the former conformer are compatible with those of the binding pocket of **8**.
[17] B. Kersting, *Angew. Chem.* **2001**, *113*, 4110–4112; *Angew. Chem. Int. Ed.* **2001**, *40*, 3988–3990.