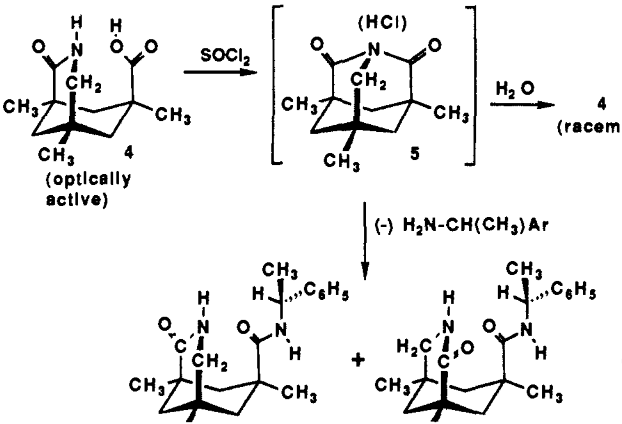
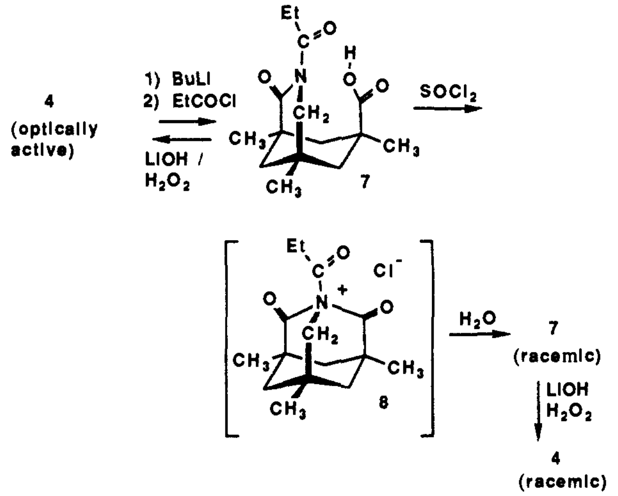
optically active (*S*)-α-phenylethylamine gave the diastereomeric lactam amides **6** (eq 2). A symmetrical intermediate cannot be avoided by this evidence.[8] One possibility is the tricyclic **5**, a decidedly nonplanar imide.[9] It could arise from an acylium ion, but even the cyclization of the acylium species is less than optimal from a stereoelectronic point of view.[10]



(2)

Finally, the participation of an even less nucleophilic nitrogen, a neighboring imide, was observed. The optically active lactam acid **4** was treated first with BuLi and then with propionyl chloride (eq 3) to give the imide acid **7**. This, on mild hydrolysis,[11] regenerated optically active lactam acid **4**. However, treatment of the *N*-propionyl lactam **7** with SOCl$_2$ followed by quenching with H$_2$O *gave racemic 7*. Mild hydrolysis of this material gave racemic **4**. The intermediate that summarizes these results most economically is the unusual structure **8**.



(3)

In summary, the relief of strain or other factors[12] involved in neighboring-group participation on this rigid template results in some bizarre intermediates. Lactams and imides become involved in a "face" sense rather than the "edge" or in-plane sense usually required by their lone pairs, and even carboxyl carbons undergo reactions involving unusual stereoelectronics.

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[8] Labeling experiments bear this out. Quenching of **5** with H$_2{}^{18}$O gave the label only in the acid. Resubmission of this material to SOCl$_2$ then H$_2$O *gave label in the lactam* as well as the acid, as determined by ^{13}C NMR spectroscopy: Vederdas, J. C. *J. Am. Chem. Soc.* **1980**, *102*, 374–376. Chloro derivatives of **5** are also likely intermediates, particularly since the initial reaction of **4** with SOCl$_2$ is at the lactam function.

[9] For studies on nonplanar (bridgehead) lactams, see: Pracejus, H.; Kehlen, M.; Kehlen, H.; Matschiner, H. *Tetrahedron* **1965**, *21*, 2257–2270. For imides, see: Brouillette, W. J.; Einspahr, H. M. *J. Org. Chem.* **1984**, *49*, 5113–5116. For a recent review, see: Greenberg, A. *Structure and Reactivity*; Liebman, J. F., Greenberg, A., Eds.; VCH Publishers, Inc.: New York, 1988; Chapter 4, p 138–179.

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Bifunctional Zinc–Imidazole and Zinc–Thiophenol Catalysts

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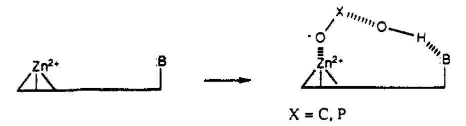
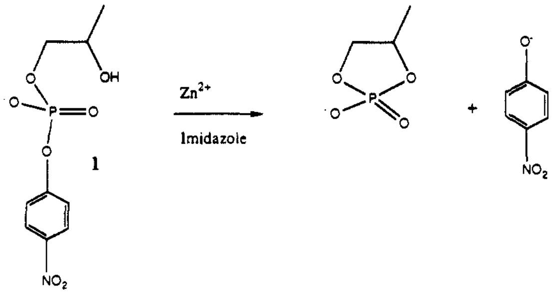
Many enzymes perform bifunctional catalysis using a metal ion and a basic group. Electron flow from base to metal occurs through the atoms of the transition state for the reaction catalyzed. For attack of a hydroxyl group on the central atom of a carboxylic acid derivative or of a phosphate derivative, the bridge has an H, two O's, and the carbon or phosphorus atom (eq 1).



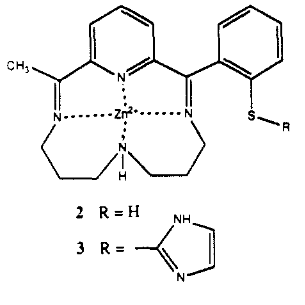
(1)

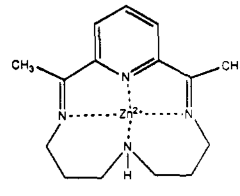
We have described intracomplex catalysis of amide cleavage by a metal ion and a base[1] and bifunctional catalysis of the cyclization of **1** by the combined action of Zn^{2+} or its complexes with free imidazole acting as a base[2] (eq 2). We have now designed and constructed a new class of catalysts, with a metal ion rigidly complexed by a strong multidentate ligand and the auxiliary catalytic group held so that it cannot directly bond to the metal.



(2)

The first examples are catalysts **2** and **3**, with a fixed Zn^{2+} and either a thiophenol/thiophenoxide group or a somewhat more flexibly held imidazole group. Molecular models show that no internal base–metal short circuit is possible and that the catalysts can readily accommodate to the binding of a transition state symbolized in eq 1. The additional catalytic group indeed increases the effectiveness of the Zn^{2+} complex.





4

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[1] Schepartz, A.; Breslow, R. *J. Am. Chem. Soc.* **1987**, *109*, 1814.

[2] Breslow, R.; Huang, D.-L.; Anslyn, E. *Proc. Natl. Acad. Sci. U.S.A.* **1989**, *86*, 1746. In that paper the structure of compound **1** is misprinted; it should be shown as the *p*-nitrophenyl phosphate ester of the *primary* hydroxyl of propylene glycol, as in this paper.

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J. Am. Chem. Soc. **1990**, *112*, 3687-3688

Table I. Pseudo-First-Order Rate Constants for the Catalyzed Cyclization of 0.19 mM Compound **1** in 10% v/v DMSO in Water with 10 mM HEPES[a] Buffer, pH 7.0, 37 °C

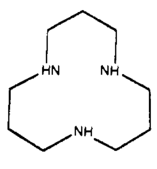
catalyst[b]	k,[c] 10^2 h^{-1}	k_{rel}
4	0.074 ± 0.001	1.0
2	0.690 ± 0.006	9
3	1.50 ± 0.01	20
Zn^{2+} + Im	1.68 ± 0.02	23
Zn^{2+}[d]	1.71 ± 0.12	23
Zn^{2+}·**5** complex[d]	4.64 ± 0.27	63

[a] 4-(2-Hydroxyethyl)-1-piperazineethanesulfonic acid. [b] All at 0.5 mM. [c] Corrected for the small background rate at this pH. [d] In H_2O solvent without DMSO.

For this series we use the Zn^{2+} complex of the macrocycle **4** that was first examined by Rich and Stucky[3] and further studied by Woolley.[4] We have also described the catalysis of some phosphate ester hydrolyses by **4** and various of its derivatives.[5] These are easily prepared by reaction of a 2,6-diacylpyridine with dipropylenetriamine and Zn^{2+} salts, if one of the acyl groups is small so the first condensation reaction is relatively unhindered.

For the synthesis of **2**, lithium thiophenoxide was orthometalated with *tert*-butyllithium, and 1 equiv of this anion was then added to pyridine-2,6-bis(dimethylcarboxamide), followed by 1 equiv of MeLi. The resulting 2-acetyl-6-(*o*-mercaptobenzoyl)pyridine was treated with dipropylenetriamine and $ZnBr_2$ in the standard manner[3-5] to afford **2** as an orange solid, mp 255 °C dec.[7] For the synthesis of **3**, the above intermediate mercapto diketone reacted with 2-fluoroimidazole to attach the imidazole group to the thio, and with the dipropylenetriamine reaction this diketone,[6] mp 186–188 °C, afforded **3**[7] as a light yellow solid, mp 135 °C dec.

We have examined the rate of the reaction of eq 2 with these catalysts and with various other comparison systems. The data are listed in Table I. Uncomplexed Zn^{2+} is more effective than is the deactivated Zn^{2+} in **4**; interestingly, a Zn^{2+} complex of 1,5,9-triazacyclododecane (**5**) is better than zinc alone.



5

The addition of thiophenol or imidazole catalytic groups, in compounds **2** and **3**, increases the effectiveness of **4** by 9- and 20-fold, respectively. Both **2** and **3** show bell-shaped pH vs rate profiles, with rate maxima near pH 9.0, as expected for the bifunctional mechanism.

Bifunctional catalysts can be based on structure **5**, whose zinc complex is not deactivated. An additional binding group can be added, as we have done with **4**.[5b] Unnecessary flexibility can be removed, although we have shown that some flexibility must be left in catalyst systems so they can accommodate to the changing geometry of the reaction path.[8] With such improvements we can hope for even better mimics of the zinc–base bifunctional catalysis used by many enzymes.

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(5) (a) Gellman, S.; Petter, R.; Breslow, R. *J. Am. Chem. Soc.* **1986**, *108*, 2388. (b) Breslow, R.; Singh, S. *Bioorg. Chem.* **1988**, *16*, 408.

(6) Characterized by NMR, IR, and mass spectra.

(7) Compound **2** was purified by Sephadex LH-20 chromatography. Anal. Found (calcd for $C_{20}H_{24}N_4SZnBr_{1.4}{\cdot}2H_2O$) C, 42.41 (42.45); H, 4.55 (4.95); N, 9.55 (9.91); Zn, 10.73 (11.56); Br, 19.81 (19.81). ^1H NMR (CD_3OD): δ 8.25–8.00 (3 H, m), 7.90 (1 H, d, J = 7.6 Hz), 7.35 (1 H, dd, J_o = 7.1 Hz, J_m = 2.1 Hz), 7.05–6.90 (2 H, m), 4.34 (1 H, d, J = 12.0 Hz), 4.25–4.10 (1 H, m), 3.92 (1 H, d, J = 11.6 Hz), 3.73 (1 H, t, J = 12.0 Hz), 3.60–3.30 (1 H, m), 3.25–3.15 (1 H, m), 3.10–2.95 (2 H, m), 2.90–2.80 (1 H, m), 2.56 (3 H, s), 2.35–2.15 (1 H, m), 2.1–1.8 (3 H, m). Compound **3** was purified by Sephadex LH-20 chromatography. Anal. Found (calcd for $C_{23}H_{26}N_6SZnBr_2{\cdot}H_2O$) C, 40.55 (40.64); H, 4.72 (4.71); N, 12.64 (12.37); Zn, 8.49 (9.63); Br, 26.18 (23.53). ^1H NMR (CD_3OD): δ 8.15–8.05 (2 H, m), 7.80–7.70 (2 H, m), 7.44–7.25, (3 H, m), 7.40 (1 H, s, H4 of Im), 7.00 (1 H, s, H5 of Im), 4.20–4.05 (4 H, m), 3.65–3.45 (2 H, m), 3.25–2.95, (3 H, m), 2.52 (3 H, s, protons of this methyl group exchange with deuteriums of CD_3OD rapidly), 2.40–2.10 (2 H, m), 2.10–1.95 (2 H, m).

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Supertriptycene, $C_{104}H_{62}$[1]

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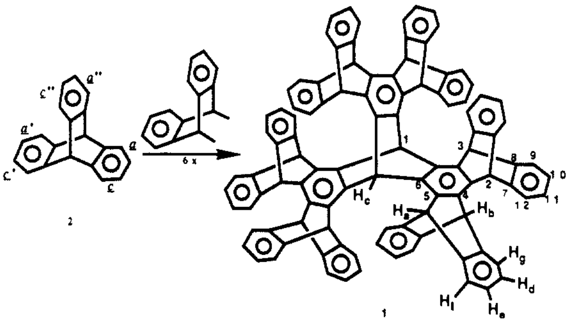
Received November 24, 1989

Recently[2] we analyzed the consequences of fusing 9,10-anthradiyl moieties to the benzenoid bonds of triptycene **2**.[3] Twenty-four iptycenes can be generated in this way, the ultimate structure being the pentadecaiptycene[3] **1**, with six 9,10-anthraidyl groups fused across the *a*, *c*, *a′*, *c′*, *a″*, and *c″* bonds of **2**. This exquisite D_{3h} molecule (Figure 1) is of interest for several reasons. It possesses three symmetrically located intramolecular cavities, each lined with six benzenoid rings. Therefore **1** should act as a unique host. Also, we anticipated that **1** would be exceptionally thermally stable.[2,4] Finally, iptycene **1** represents conceptually the first (and also the only possible) stage of symmetric three-dimensional "expansion" of the triptycene core in a manner similar to that recently developed[5,6] for starburst dendrimers.



We report here a nine-step synthesis of **1** (overall yield 33–43%) that includes an unusual high-yield Diels–Alder reaction between unactivated hydrocarbon participants.

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(1) The Chemical Abstracts name is 5,6,11,12,13,18,19,24,25,26,35,40,41,46-tetradecahydro-35,40[1′,2′]:41,46[1″,2″]-dibenzeno-5,26[1′,2′]:6,11-[1″,2″]:13,18[1‴,2‴]:19,24[1⁗,2⁗]-tetrabenzeno-12,26[6′,7′]-*endo*-pentaphenodinaphtho[2,3-*a*:2′,3′-*c*]trinaphthylene. We thank Dr. Kurt Loening and Dr. Joy E. Merritt, Chemical Abstracts Service, for supplying this name.

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0002-7863/90/1512-3687$02.50/0