

Figure 2. Stereopair representations of a TMA cation in a sodalite cage (upper) and in a gmelinite cage (lower) generated by using interactive molecular graphics. The aluminosilicate cages are represented as straight lines connecting bonded atoms (Si/Al and O). The orientation of the TMA cation in the sodalite cage is taken from ref 9. Drawing radii are C 1.77 Å, H 1.17 Å.

at the pulsed neutron source IPNS-I of Argonne National Laboratory.¹⁶ (Both CAS and QENS are inverted-geometry spectrometers and spectra are measured in neutron energy loss mode.¹⁷ The instrumental resolutions, $\Delta E/E$, for CAS and QENS are 0.03 and 0.015 respectively.) Selected regions of the INS spectra for the two materials are compared with that of TMA-Br (recorded at 16 K on CAS) in Figure 1. The frequencies of the modes displayed in Figure 1 are compared with those observed in the halide salts¹⁸ in Table I.

The results of an ab initio molecular orbital calculation for an isolated TMA cation are also included in Table I. From the STO-3G basis set,¹⁹ the vibrational frequencies of the free ion were determined from its harmonic force field calculated by analytical evaluation of the second derivatives of the Hartree-Fock energy with respect to the nuclear coordinates.²⁰ The STO-3G equilibrium structure of the TMA cation with tetrahedral symmetry [$R(\text{C}-\text{N}) = 1.527$ Å, $R(\text{C}-\text{H}) = 1.089$ Å, $\angle\text{H}-\text{C}-\text{H} = 110.4^\circ$] was used in the calculation. The STO-3G predictions for the torsional and bending harmonic frequencies in Table I are expected to be reasonably accurate based on comparison of STO-3G²¹ and experimental²² vibrational frequencies for a related molecule, trimethylamine. For trimethylamine, the two STO-3G torsional frequencies are about 3% higher than the observed gas-phase torsional frequencies, while the two bending frequencies are about 10% higher. Hence, the theoretical results indicate that the torsional frequencies of the TMA ion in the gmelinite cage of zeolite omega are approaching those of the free ion. This is illustrated in Figure 1 where the theoretical torsional and bending frequencies are indicated, all scaled downward by 6% so that the experimental and theoretical bending modes approximately match (the theoretical frequencies in Table I are unscaled).

Consistent with earlier Raman results,¹³ the bending modes vary little in energy from one material to another. The splitting between

the two torsional modes is also fairly constant and in good agreement with the theoretical calculation. The positions of the torsional modes, that importantly are Raman inactive, however, are clearly very sensitive to the nature of the TMA environment. The marked frequency lowering (compared to the halide salts) for both torsional modes that occurs when the TMA cations are occluded in sodalite (LTA) or gmelinite (MAZ) cages (Figure 2) reveals that the interactions between the TMA cations and the zeolites are much weaker than those between TMA and the halide ions. Preliminary observation by INS of rotational diffusion of TMA at room temperature in both ZK-4 and omega samples is also consistent with weak TMA-zeolite interaction. The torsional frequencies are lower for the TMA ion in the gmelinite cage than in the slightly smaller sodalite cage. The isolated TMA ion represents a cage of infinite dimension, and its torsional frequencies are lower still. This general trend parallels the trend in ¹³C NMR chemical shifts with cage size,^{10,11} although the results of a broader series of measurements (currently under way) are required in order to quantify the relative importance of direct cage size effects and framework composition or nonframework cation influences.

The lack of selection rules and the very high sensitivity to modes involving hydrogen atom motion make inelastic neutron scattering a very useful probe of the dynamics, particularly the torsional modes, of organic species occluded within zeolites. It will be interesting to extend the present studies to INS measurements both of TMA cations during the process of zeolite crystallization and of TMA ions in cages larger than the gmelinite cage in order to probe further the approach of the torsional frequencies to the free ion values.

Acknowledgment. We thank S. K. Sinha and M. T. Melchior for helpful discussions and all the staff of IPNS for their support, input, and encouragement.

Molecular Recognition: New Shapes for Asymmetric Microenvironments

Julius Rebek, Jr.,* Ben Askew, Pablo Ballester, and Maria Doa

Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260

Received January 2, 1987

Asymmetric synthesis is a widely pursued goal in modern organic chemistry. A number of systems which feature C_2 symmetry elements in their ligands, such as Sharpless' epoxidation reagent,¹ Noyori's catalysts,² and Masamune's boranes,³ are so successful that there is much confidence placed in the use of such symmetry elements in reagent and catalyst design.⁴ This shape may be well suited for distinguishing between the two faces of a π system, but it is not obvious that C_2 symmetry offers advantages or is even appropriate for the recognition of single asymmetric centers. Whether such recognition involves minimizing steric effects involving large, medium, and small groups (eq 1) or maximizing donor (D) and acceptor (A) attractions (eq 2) between substrate and receptor, *three* domains appear to offer a better fit than the *two* inherent in structures of C_2 symmetry. Accordingly, we have prepared structures in which three groups are spatially arranged in the desired sense.

(16) Lander, G. H.; Brown, B. S., Eds. *IPNS-I Users Handbook*; Intense Pulsed Neutron Source, Argonne National Laboratory: IL, 1982.

(17) Windsor, C. G. *Pulsed Neutron Scattering*; Taylor and Francis: London, 1981; Chapter 9.

(18) Ratcliffe, C. I.; Waddington, T. C. *J. Chem. Soc., Faraday Trans. 2* **1976**, *72*, 1935.

(19) Hehre, W. J.; Stewart, R. F.; Pople, J. A. *J. Chem. Phys.* **1969**, *51*, 2657.

(20) Schlegel, H. B.; Binkley, J. S.; Pople, J. A. *J. Chem. Phys.* **1984**, *80*, 1976.

(21) Curtiss, L. A. 1986, unpublished work.

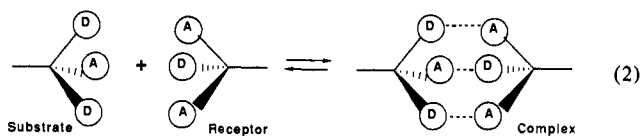
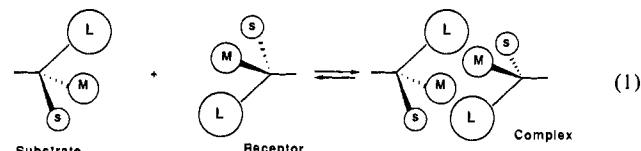
(22) Cybin, S. J.; Gebhardt, O. *J. Mol. Struct.* **1972**, *12*, 215.

(1) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974-5976. For discussions see: Kagan, H. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1985, Vol. 5, Chapter 1. Finn, M. G.; Sharpless, K. B. *Ibid.* Chapter 8.

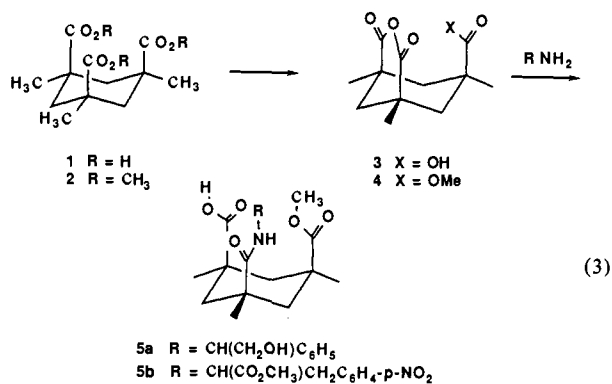
(2) (a) Noyori, R. et al. *J. Am. Chem. Soc.* **1980**, *102*, 7932. Noyori, R. *Pure Appl. Chem.* **1981**, *53*, 2315. (b) For asymmetric recognition in chromatography and its origins in multisite binding, see: Pirkle, W. H.; Pochapsky, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 5627-5628.

(3) Masamune, S.; Kim, B. M.; Petersen, J. S.; Sato, T.; Veenstra, S. J. *J. Am. Chem. Soc.* **1985**, *107*, 4549-4551.

(4) Kagan, H. B.; Dang, T. P. *J. Am. Chem. Soc.* **1972**, *94*, 6429-6433. Kelly, T. R.; Whiting, A.; Chandrakumar, N. S. *Ibid.* **1986**, *108*, 3510-3512.

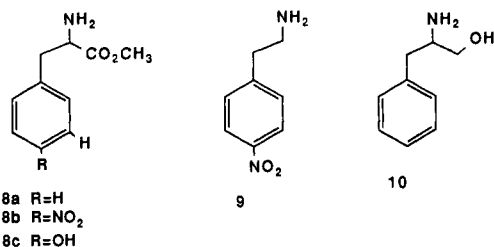


The scaffolding for the new structures is provided by Kemp's triacid **1**. In this structure the three carboxyl groups are constrained to the triaxial conformation by dint of the larger A values of the equatorial methyl groups. New structures in which three groups protrude from a single face of a molecule are rapidly assembled from conventional derivatization of **1** (Eq 3).



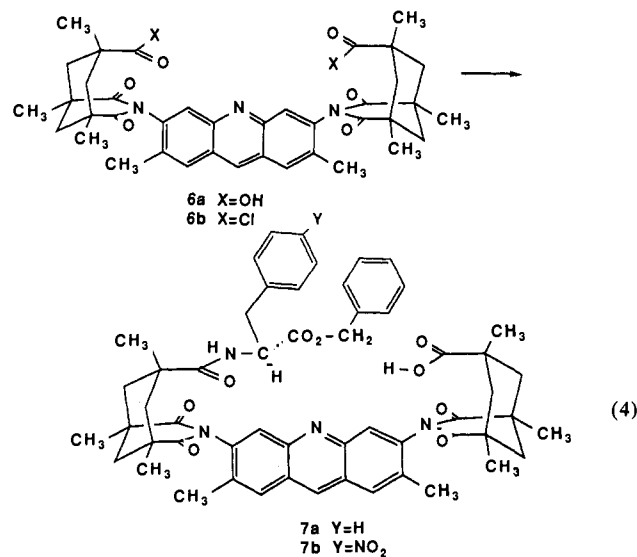
Treatment of the anhydride acid⁵ **3** with CH_2N_2 gave the methyl ester **4**, mp 220–223 °C, from which the diastereomers⁷ of **5a** could be obtained by aminolysis with L-phenylglycinol. The separation of diastereomers was achieved with flash chromatography.⁸ Similarly, the diastereomers of **5b** were obtained and separated from the reaction of **4** with L-p-nitrophenylalanine methyl ester **8b**.

Initial binding experiments revealed these structures to be highly effective chiral solvating agents⁹ for racemic amines. For example, titration of **5a** with a mixture of (+)- and (-)-ephedrine (2:1) showed different chemical shifts in the benzylic protons of the ephedrine (18 Hz) when 6 mol % of **5a** is present.

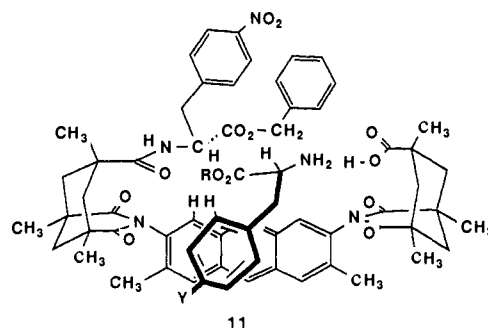


Arranging three attractive forces as suggested in eq 2 is an inherently more difficult problem, but progress is being made by using molecules in the shape of a cleft. In such structures, e.g., **7**, the three domains are represented by the carboxylic acid, the acridine stacking surface, and the bulky phenylalanine derivative,

and these converge to create a chiral cavity. The acid and π surface can bind suitable bases¹⁰ and position them for maximum impact of the chiral microenvironment. Structures **7** are prepared from the diacid chloride⁶ **6b** by treatment with the appropriate phenylalanine derivatives followed by mild hydrolysis (eq 4).



Both binding forces available to **7** play a significant role in the asymmetric recognition of esters of racemic amino acids **8**. For example, stronger bases such as **9** or **10** displace the weaker amino esters **8** from the receptor, but only **9** shows the characteristic *upfield* shifts of its aromatic protons when in contact with **7**. Even excess Et_3N fails to displace **9** from **7**. In competition experiments between comparable bases, both **8b** and **8c** readily displace **8a** from the receptors, and no enantiomeric recognition is observed with **8a**. However, enantiomers of either **8b** or **8c** show large differential shifts when in contact with **7**. When a mixture of **8b** (3:1, L:D) is added in CDCl_3 to 1 equiv of **7b**, $\Delta\nu = 150$ Hz is observed in the NMR spectrum of the meta proton of **8b** with the L isomer shifted *upfield*. Similar results are observed with **7a**, or with **8c** using either receptor. It appears that a dipole in the aromatic ring enhances interactions between aryl subunits in receptor and substrate in these systems. The structural details must await crystallographic analysis, but **11** is proposed on the basis of the current evidence.¹¹ It is possible to line the cleft of **6** with functions complementary to other amino acid side chains, and we will report on these systems elsewhere.



Acknowledgment. We are grateful to the National Science Foundation and the National Institutes of Health for support of this research.

(5) Kemp, D. S.; Petrakis, K. S. *J. Org. Chem.* **1981**, *46*, 514. A new synthesis of **2** is described in ref 6.

(6) Rebek, J., Jr.; Askew, B.; Killoran, M.; Nemeth, D.; Lin, F.-T. *J. Am. Chem. Soc.* **1987**, *109*, 2426–2431.

(7) The sense of asymmetry of the cyclohexyl structure is arbitrarily assigned. The faster moving isomer of **5a** had mp 108–110 °C while the other showed mp 168–170 °C; for **5b**, only the major isomer was isolated, mp 78–79 °C. All new compounds were characterized by a full complement of high-resolution spectra: **7a**, mp 198–201 °C; **7b**, mp 215–220 °C.

(8) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

(9) Weisman, G. R. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1983; Vol. 1, Chapter 8.

(10) Rebek, J., Jr.; Askew, B.; Nemeth, D.; Parris, K. *J. Am. Chem. Soc.* **1987**, *109*, 2432–2434. Rebek, J., Jr.; Nemeth, D. *Ibid.* **1985**, *107*, 6738–6739.

(11) Intermolecular NOE (ref 2b) was observed in the form of a 5% enhancement of the proton lining the cleft of the receptor when the ortho proton of the substrate was irradiated (protons are indicated in **11**).