here. Furthermore, it could also be applicable to MALDI-TOF MS as a possible means of moderating metastable decomposition and enhancing mass resolution.

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Chiral Molecular Recognition in Intercalated Zirconium Phosphate

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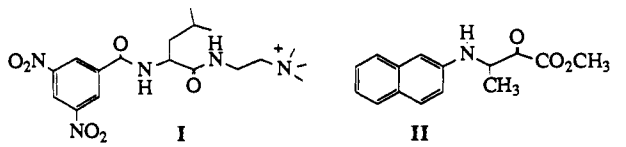
One of the challenges of modern inorganic and analytical chemistry is the synthesis of microporous solids that bind molecular analytes selectively and reversibly. The practical implications of such materials are very significant for separations and catalysis. For example, size- and shape-selective sorption and reactivity in the case of zeolites form the basis of a catalytic hydrocarbon chemistry that is carried out on an enormous scale. In recent years, layered metal phosphates and phosphonates have received considerable attention as metal–organic analogues of zeolitic solids,[1-8] because their structures can in principle be tailored, and there are now a few examples of interlayer molecular recognition in these materials. Small "templating" molecules can be introduced in some cases at interlayer coordination sites during the synthesis, and subsequently removed in order to create shape-selective binding pockets for aliphatic alcohols or amines.[9-11] These examples of shape-selective intercalation in the solid state are nevertheless rather primitive in comparison with the elegant host/guest chemistry that has been developed for purely molecular systems. The latter use multipoint noncovalent interactions in concert not only to bind analytes with a high degree of specificity but also to effect complex and often biomimetic reactivity.[12]

In terms of shape selectivity, enantioselective binding of molecules from a racemic mixture is significantly more demanding than binding of an achiral molecule. Both enantiomers possess chemically identical functional groups and are resolved by multipoint binding to a chiral host possessing complementary functionality. It is generally accepted that at least three points of contact between host and guest are required for enantioselectivity.[13] Because of this requirement, enantiomeric excesses achieved in the intercalation reactions of chiral microporous solids, most notably smectite clays,[14] have been modest. To our knowledge similar attempts to resolve enantiomers using zeolite beta one polymorph of which crystallizes[15] in the chiral space group $P4_122$, have as yet been unsuccessful.

While chiral molecules, particularly amino acids[16] and cyclodextrins,[17] have been studied as intercalants in metal phosphates, there have been no previous reports of enantioselective binding in these materials. We report here an approach that combines the ultrahigh internal surface area and structural versatility of these solids with the enantioselectivity of a well-studied chiral selector group. The chiral selector (I) and racemic analyte (II) molecule used in this study are structurally nearly identical to those



studied by Pirkle and co-workers,[18] the difference being that the (*S*)-(+)-*N*-(3,5-dinitrobenzoyl)-L-leucine derivative I contains a cationic quaternary ammonium group at the end of the molecule remote from the π-stacking and hydrogen-bonding sites. I was intercalated into microcrystalline α-$Zr(HPO_4)_2 \cdot H_2O$ by reaction with tetrabutylammonium hydroxide, followed by the iodide salt of I. The bulky tetrabutylammonium ion swells the layers, causing the solid to disperse in water; because of its poor electrostatic interaction with the anionic layers, this cation acts as a good "leaving group", being quantitatively displaced by I up to a loading of approximately 0.5 mmol/g. Introduction of an aqueous solution of I causes immediate flocculation of the solid, and X-ray powder diffraction patterns show a single phase in which the layer spacing is 19 Å, compared to 7.6 Å for the parent solid. Exposure of this solid to acetonitrile solutions of the racemic analyte II causes, at high concentrations, the immediate formation of an orange I·II charge-transfer complex within the solid.

The intercalation reaction of II is very selective for its (*S*)-(−)-isomer, as shown in Figure 1. The reaction shows an interesting dependence on the concentration of racemic II in solution,

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(1) Mikulski, C. M.; Karayannis, N. M.; Minkiewicz, J. V.; Pytlewski, L. L.; Labes, M. M. *Inorg. Chim. Acta* **1969**, *3*, 523.
(2) (a) Yamanaka, S. *Inorg. Chem.* **1976**, *15*, 2811. (b) Yamanaka, S.; Koizumi, M. *Clays Clay Miner.* **1975**, *23*, 477. (c) Yamanaka, S.; Tsujimoto, M.; Tanaka, M. *J. Inorg. Nucl. Chem.* **1979**, *41*, 605. (d) Yamanaka, S.; Matsunaga, M.; Hattori, M. *J. Inorg. Nucl. Chem.* **1981**, *43*, 1343.
(3) (a) Alberti, G.; Costantino, U.; Alluli, S.; Tomassini, J. *J. Inorg. Nucl. Chem.* **1978**, *40*, 1113. (b) Alberti, G.; Costantino, U.; Giovagnotti, M. L. L. *J. Chromatogr.* **1979**, *180*, 45. (c) Casciola, M.; Costantino, U.; Fazzini, S.; Tosoratti, G. *Solid State Ionics* **1983**, *8*, 27. (d) Alberti, G. *Acc. Chem. Res.* **1978**, *11*, 163.
(4) (a) Dines, M. B.; DiGiacomo, P. *Inorg. Chem.* **1981**, *20*, 92. (b) Dines, M. B.; DiGiacomo, P.; Callahan, K. P.; Griffith, P. C.; Lane, R.; Cooksey, R. E. In *Chemically Modified Surfaces in Catalysis and Electrocatalysis*; Miller, J., Ed.; ACS Symposium Series 192; American Chemical Society: Washington, DC, 1982; p 223. (c) Dines, M. B.; Griffith, P. C. *Inorg. Chem.* **1983**, *22*, 567. (d) Dines, M. B.; Cooksey, R. E.; Griffith, P. C. *Inorg. Chem.* **1983**, *22*, 1003. (e) Dines, M. B.; Griffith, P. C. *Polyhedron* **1983**, *2*, 607.
(5) (a) Johnson, J. W.; Jacobson, A. J.; Brody, J. F.; Lewandowski, J. T. *Inorg. Chem.* **1984**, *23*, 3844. (b) Huan, G.; Jacobson, A. J.; Johnson, J. W.; Corcoran, E. W., Jr. *Chem. Mater.* **1990**, *2*, 91. (c) Johnson, J. W.; Brody, J. F.; Alexander, R. M.; Pilarski, B.; Katritzky, A. R. *Chem. Mater.* **1990**, *2*, 198.
(6) (a) Cheng, S.; Peng, G.-Z.; Clearfield, A. *Ind. Eng. Chem. Prod. Res. Dev.* **1984**, *23*, 219. (b) Wan, B.-Z.; Anthony, R. G.; Peng, G. Z.; Clearfield, A. *J. Catal.* **1986**, *101*, 19. (c) Clearfield, A. In *Design of New Materials*; Clearfield, A., Cocke, D. A., Eds.; Plenum: New York, 1987; p 121. (d) Peng, G.-Z.; Clearfield, A. *J. Inclusion Phenom.* **1988**, *6*, 49. (e) Clearfield, A. *Chem. Rev.* **1988**, *88*, 125. (f) Yang, C.-Y.; Clearfield, A. *React. Polym.* **1987**, *5*, 13. (g) Colon, J. L.; Yang, C. Y.; Clearfield, A.; Martin, C. R. *J. Phys. Chem.* **1988**, *92*, 5777. (h) Clearfield, A. *Comments Inorg. Chem.* **1990**, *10*, 89.
(7) (a) Lee, C. S.; Myers, L. K.; Valentine, K. G.; Thompson, M. E. *J. Chem. Soc., Chem. Commun.* **1992**, 201. (b) Burwell, D. A.; Valentine, K. G.; Timmermans, J. H.; Thompson, M. E. *J. Am. Chem. Soc.* **1992**, *114*, 4144. (c) Burwell, D. A.; Valentine, K. G.; Thompson, M. E. *J. Magn. Reson.*, in press.
(8) Mallouk, T. E.; Lee, H. *J. Chem. Educ.* **1990**, *67*, 829. (b) Cao, G.; Hong, H.-G.; Mallouk, T. E. *Acc. Chem. Res.*, in press.
(9) Johnson, J. W.; Jacobson, A. J.; Butler, W. M.; Rosenthal, S. E.; Brody, J. F.; Lewandowski, J. T. *J. Am. Chem. Soc.* **1989**, *111*, 381.
(10) Cao, G.; Mallouk, T. E. *Inorg. Chem.* **1991**, *30*, 1434.
(11) Frink, K. J.; Wang, R.-C.; Colon, J. L.; Clearfield, A. *Inorg. Chem.* **1991**, *30*, 1439.
(12) For recent reviews, see: (a) Rebek, J., Jr. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 245. (b) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1304. (c) Whitesides, G. M.; Mathias, J. P.; Seto, C. *Science* **1991**, *254*, 1312.
(13) (a) Dalgliesh, C. E. *J. Chem. Soc.* **1952**, 3940. (b) Baczuk, R. J.; Landrum, G. K.; Dubois, R. J.; Dehm, H. C. *J. Chromatogr.* **1971**, *60*, 351. (c) Prikle, W. H.; Sikkenga, D. L. *J. Org. Chem.* **1975**, *40*, 3430. (d) Pirkle, W. H.; Burke, J. A.; Wilson, S. R. *J. Am. Chem. Soc.* **1989**, *111*, 9222.
(14) Yamagishi, A. *J. Coord. Chem.* **1987**, *16*, 131.
(15) Treacy, M. M. J.; Newsam, J. M. *Nature* **1988**, *332*, 249.
(16) (a) Kijima, T.; Sekikawa, Y.; Ueno, S. *J. Inorg. Nucl. Chem.* **1981**, *43*, 849. (b) Kijima, T.; Ueno, S.; Goto, M. *J. Chem. Soc., Dalton Trans.* **1982**, 2499.
(17) (a) Kijima, T.; Tanaka, J.; Goto, M.; Matsui, Y. *Nature* **1984**, *310*, 45. (b) Kijima, T.; Tanaka, J.; Goto, M.; Matsui, Y. *Nature* **1985**, *316*, 280. (c) Kijima, T.; Matsui, Y. *Nature* **1986**, *322*, 533. (d) Kijima, T. *J. Inclusion Phenom.* **1986**, *4*, 333. (e) Kijima, T. *J. Inclusion Phenom.* **1990**, *9*, 171.
(18) Pirkle, W. H.; Pochapsky, T. *Chem. Rev.* **1989**, *89*, 347.

0002-7863/92/1514-7574$03.00/0

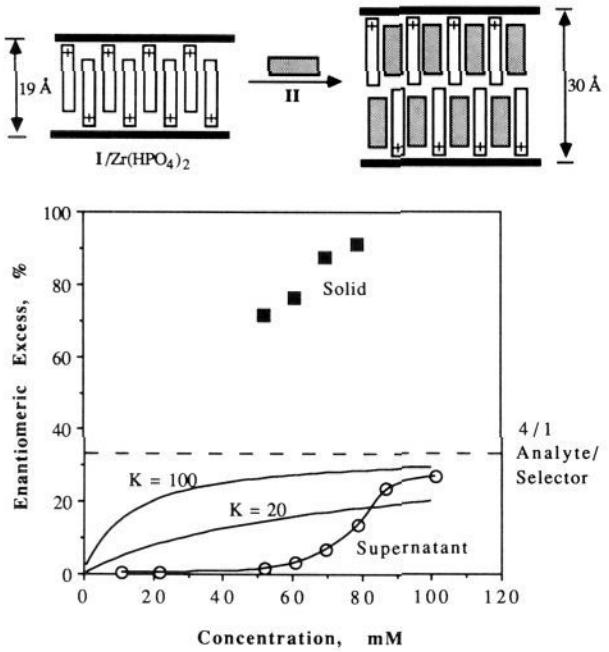

Figure 1. Top: Schematic representation of layer expansion in the intercalation of zirconium phosphate/I by II. Bottom: Enantiomeric excess vs concentration of racemic II in acetonitrile. The dashed line represents the maximum theoretical solution ee for a 4/1 molar ratio of II/I. For comparison, two calculated Langmuir isotherms with $K = 20$ and 100 M^{-1} are shown. The composition of the 19-Å solid phase before intercalation was $Zr[(TBA)_{0.138}(I)_{0.093}H_{0.77}PO_4]_2 \cdot xH_2O$.

there being essentially no intercalation below 50 mM, and almost stoichiometric reaction to form the I·II complex at 100 mM concentration. The experiments shown were carried out with a 4/1 molar ratio of II/I, to allow comparison of the binding curve, expressed as enantiomeric excess (ee),[19] to the Langmuir adsorption isotherms calculated for (*S*,*S*)-I·II complex formation constants of 100 and 20 M^{-1}. This formation constant, measured previously for the same diastereomeric complex lacking the remote quaternary ammonium group, is approximately 100 M^{-1} in fluid solution.[20] While the binding at low concentration is clearly non-Langmuirian, at high concentrations of analyte the observed solution ee's approach the 100 M^{-1} curve. We postulate that the observed concentration threshold for intercalation reflects the work needed to separate the layers from a 19-Å spacing, which represents an interdigitated arrangement of chiral selector molecules, to 30 Å for the I·II intercalated phase.

The intercalation of II is completely and rapidly reversed by simply exposing the solid to pure acetonitrile, and analysis of these solutions shows that the ee exceeds 90% for the fully loaded solid. This result is consistent with chromatographically measured separation factors (α) in excess of 10 for similar molecules[21] and demonstrates that the enantioselectivity of the chiral selector is unimpaired by intercalation into zirconium phosphate; therefore, it is reasonable to expect that other chiral selectors should retain their activity as well as in this host solid. Since the internal surface area of zirconium phosphate and similar layered ion exchangers is on the order of 1000 m^2/g, approximately an order of magnitude higher than that of commercially available chiral stationary phases, these materials may potentially be of interest for preparative chiral separations, operating in either a batchwise or chromatographic mode. These possibilities are currently under investigation.

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(19) Concentrations of (*S*)- and (*R*)-II were measured by HPLC, using a Regis DNB-phenylglycine Pirkle column with UV detection at 242 nm. Enantiomeric excess (ee) is defined as

$$ee = \left|\frac{[R] - [S]}{[R] + [S]}\right| \times 100\%$$

At the 4/1 molar ratio used to generate the plot in Figure 1, 33% ee is the maximum solution ee attainable. Solid ee's were determined by reversing the intercalation reaction in acetonitrile and measuring the concentrations of (*R*)- and (*S*)-II in the supernatant solutions.

(20) Pirkle, W. H.; Pochapsky, T. C. *J. Am. Chem. Soc.* **1987**, *109*, 5975.

(21) Pirkle, W. H.; Pochapsky, T. C.; Mahler, G. S.; Corey, D. E.; Alessi, D. M.; Reno, D. S. *J. Org. Chem.* **1986**, *51*, 4991. The α value reflects roughly the ratio of formation constants for (*S*,*S*)-I·II and (*S*,*R*)-I·II.

Tentacle Porphyrins: DNA Interactions

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Cationic porphyrins exhibit diverse binding modes with nucleic acids.[1-3] Initial interest in porphyrin–DNA interactions arose in conjunction with photodynamic therapy,[4] but more recent interest in porphyrin–nucleic acid interactions stems from porphyrin antiviral (including HIV-1)[5-8] and anticancer activity[9] and from their utility as nucleic acid structural probes; e.g., metallo derivatives selectively cleave nucleic acids.[10-12] Thus, a greater understanding of the fundamental factors that influence porphyrin–nucleic acid binding not only has value in elucidating the relationship of structure to nucleic acid binding but may also be useful in developing therapeutic agents and biological probes.

Considerable evidence exists that porphyrins can intercalate into nucleic acids;[1,2,13-17] the projection of substituents from the

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(1) Fiel, R. J. *J. Biomol. Struct. Dyn.* **1989**, *6*, 1259.
(2) Marzilli, L. G. *New J. Chem.* **1990**, *14*, 409.
(3) Rodriguez, M.; Bard, A. J. *Inorg. Chem.* **1992**, *31*, 1129.
(4) Fiel, R. J.; Howard, J. C.; Mark, E. H.; Datta-Gupta, N. *Nucleic Acids Res.* **1979**, *6*, 3093.
(5) Dixon, D. W.; Marzilli, L. G.; Schinazi, R. *Ann. N. Y. Acad. Sci.* **1990**, *616*, 511.
(6) (a) Asanaka, M.; Kurimura, T.; Toya, H.; Ogaki, J.; Kato, Y. *AIDS* **1989**, *3*, 403. (b) Levere, R. D.; Gong, Y.-F.; Kappas, A.; Bucher, D. J.; Wormser, G. P.; Abraham, N. G. *Proc. Natl. Acad. Sci. U.S.A.* **1991**, *88*, 1756.
(7) Dixon, D. W.; Kim, M. S.; Kumar, V.; Obara, G.; Marzilli, L. G.; Schinazi, R. F. *Antiviral Chemistry & Chemotherapy*, in press.
(8) Sessler, J. L.; Cyr, M. J.; Maiya, B. G.; Judy, M.; Newman, J. T.; Skiles, H. L.; Boriak, R.; Matthews, J. L.; Chanh, T. C. *Proc. SPIE-Int. Soc. Opt. Eng.* **1990**, *1203*, 233.
(9) (a) Ding, L.; Casas, C.; Etemad-Moghadam, G.; Meunier, B. *New J. Chem.* **1990**, *14*, 421. (b) Ding, L.; Etemad-Moghadam, G.; Meunier, B. *Biochemistry* **1990**, *29*, 7868. (c) Ding, L.; Etemad-Moghadam, G.; Cros, S.; Auclair, C.; Meunier, B. *J. Med. Chem.* **1991**, *34*, 900.
(10) (a) Groves, J. T.; Farrell, T. P. *J. Am. Chem. Soc.* **1989**, *111*, 4998. (b) Pratviel, G.; Pitié, M.; Bernadou, J.; Meunier, B. *Nucleic Acids Res.* **1991**, *19*, 6283. (c) Gasmi, G.; Pasdeloup, M.; Pratviel, G.; Pitié, M.; Bernadou, J.; Meunier, B. *Nucleic Acids Res.* **1991**, *19*, 2835. (d) Pitié, M.; Pratviel, G.; Bernadou, J.; Meunier, B. *Proc. Natl. Acad. Sci. U.S.A.* **1992**, *89*, 3967.
(11) Vlassov, V. V.; Deeva, E. A.; Ivanova, E. M.; Knorre, D. G.; Maltseva, T. V.; Frolova, E. I.; Ponomariov, G. V.; Kirillova, G. V. *Nucleosides, Nucleotides* **1991**, *10*, 641.
(12) Le-Doan, T.; Praseuth, D.; Perrouault, L.; Chassignol, M.; Thuong, N. T.; Hélène, C. *Bioconjugate Chem.* **1990**, *1*, 108.
(13) Gibbs, E. J.; Tinoco, I., Jr.; Maestre, M. F.; Ellinas, P. A.; Pasternack, R. F. *Biochem. Biophys. Res. Commun.* **1988**, *157*, 350.
(14) Sari, M. A.; Battioni, J. P.; Dupré, D.; Mansuy, D.; Le Pecq, J. B. *Biochemistry* **1990**, *29*, 4205.

0002-7863/92/1514-7575$03.00/0