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New Synthetic Receptor Derived from Bridged Anthracenes

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May 31, 1991

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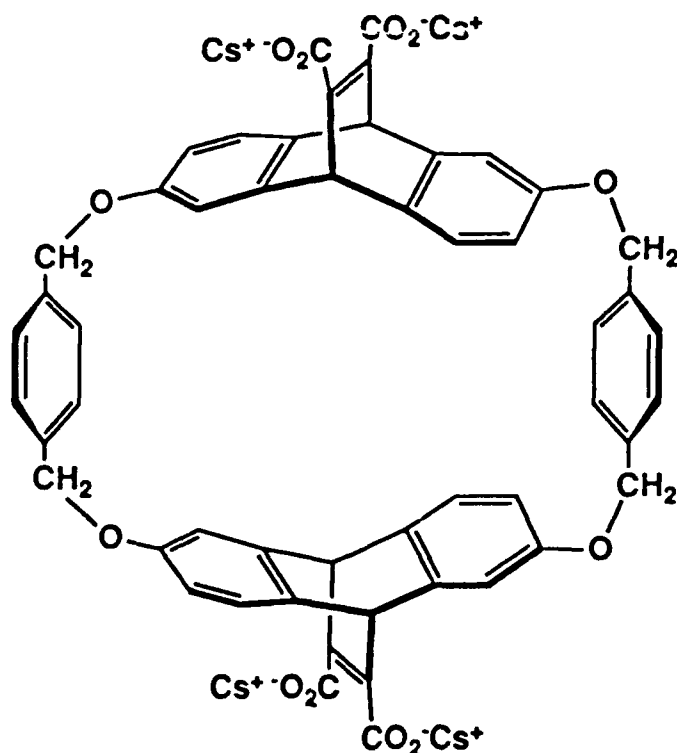
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FINAL TECHNICAL REPORT  
ONR CONTRACT N00014-88-K-0259

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The major goal of the present contract was to develop new insights into the forces responsible for the association of organic molecules so often seen in biological systems (eg., enzyme-substrate, antibody-antigen, neuroreceptor-neurotransmitter interactions). To this end, a series of water-soluble organic molecules with well-defined hydrophobic binding sites was prepared, and the binding characteristics of several structures were evaluated.



a typical receptor of the type developed in the present work

The most significant discovery of the investigations was the demonstration of the importance of the "cation- $\pi$ " (or, alternatively, "ion-dipole") interaction in producing tight, oriented binding of a wide variety of "onium" type guests. High

field NMR was the primary tool used to establish the cation- $\pi$  interaction as a potent force for binding in both aqueous (technical report number 1) and organic media (technical report number 2). In addition, detailed studies revealed the primarily enthalpic nature of the phenomenon and the dangers of overly simplified analyses of binding data (technical report number 3). It seems quite likely that similar binding forces are of critical importance in a variety of biological receptors, especially many that are involved in several aspects of neurochemistry, and future efforts will seek to strengthen this connection.

In addition, the cation- $\pi$  interaction has been exploited to develop a novel catalytic system (technical report number 4). It was demonstrated that a certain type of alkylation chemistry, in which a partial positive charge is developed in the transition state, is substantially accelerated by our synthetic receptors. The system is truly catalytic, exhibiting turnover and appropriate competitive inhibition behaviors. This is a novel example of taking a binding force that was discovered in "ground state" systems and using it to preferentially bind transition states. Future work will seek to expand upon and exploit this concept to produce powerful catalysts for useful organic transformation.

#### PUBLICATIONS PRODUCED

"Hydrophobic" Binding of Water-Soluble Guests by High-Symmetry, Chiral Hosts. An Electron-Rich Receptor Site with a General Affinity for Quaternary Ammonium Compounds and Electron-Deficient  $\pi$  Systems. M.A. Petti, T.J. Sheppard, R.E. Barrans, Jr., and D.A. Dougherty, *J. Am. Chem. Soc.* 1988, 110, 6825-6840.

Ion-Dipole Effect as a Force for Molecular Recognition in Organic Media. D.A. Stauffer and D.A. Dougherty, *Tetrahedron Lett.* 1988, 29, 6039-6042.

Biomimetic Catalysis of an  $S_N2$  Reaction Resulting from a Novel Form of Transition-State Stabilization. D.A. Stauffer, R.E. Barrans, Jr., and D.A. Dougherty, *Angew. Chem. Int. Ed. Engl.* 1990, 29, 915-918.

Concerning the Thermodynamics of Molecular Recognition in Aqueous and Organic Media. Evidence for Significant Heat Capacity Effects. D.A. Stauffer, R.E. Barrans, Jr., and D.A. Dougherty, *J. Org. Chem.*, 1990, 55, 2762-2767.

## TECHNICAL REPORTS

Technical Report No.1 - "'Hydrophobic' Binding of Water-Soluble Guests by High-Symmetry, Chiral Hosts. An Electron-Rich Receptor Site with a General Affinity for Qarternary Ammonium Compounds and Electron-Deficient  $\pi$  Systems." M.A. Petti, T.J. Shepodd, R.E. Barrans, Jr., and D.A. Dougherty.

Technical Report No. 2 - "Ion-Dipole Effect as a Force for Molecular Recognition in Organic Media." D.A. Stauffer and D.A. Dougherty.

Technical Report No. 3 - Concerning the Thermodynamics of Molecular Recognition in Aqueous and Organic Media. Evidence for Significant Heat Capacity Effects." D.A. Stauffer, R.E. Barrans, Jr., and D.A. Dougherty

Technical Report No. 4 - "Biomimetic Catalysis of an  $S_N2$  Reaction Resulting from a Novel Form of Transition-State Stabilization." D.A. Stauffer, R.E. Barran, Jr., and D.A. Dougherty.