

AD-A218 647

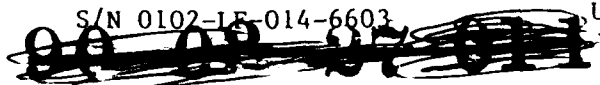
DTIC FILE COPY

2

Unclassified
SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE				Form Approved OMB No 0704-0188	
1a. REPORT SECURITY CLASSIFICATION Unclassified		1b. RESTRICTIVE MARKINGS			
2a. SECURITY CLASSIFICATION AUTHORITY		3. DISTRIBUTION/AVAILABILITY OF REPORT Approved for public release Distribution unlimited			
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE					
4. PERFORMING ORGANIZATION REPORT NUMBER(S) Technical Report #7		5. MONITORING ORGANIZATION REPORT NUMBER(S)			
6a. NAME OF PERFORMING ORGANIZATION Brigham Young University	6b. OFFICE SYMBOL (if applicable)	7a. NAME OF MONITORING ORGANIZATION Office of Naval Research			
6c. ADDRESS (City, State, and ZIP Code) Department of Chemistry Provo, UT 84602		7b. ADDRESS (City, State, and ZIP Code) Department of the Navy Arlington, VA 22217-5000			
8a. NAME OF FUNDING / SPONSORING ORGANIZATION Office of Naval Research	8b. OFFICE SYMBOL (if applicable) ONR	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER N000014-88-K-0115			
8c. ADDRESS (City, State, and ZIP Code) 800 No. Quincy Street Arlington, VA 22217-5000		10. SOURCE OF FUNDING NUMBERS			
		PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
11. TITLE A Comparison of the Temperature Dependent ¹ H NMR and Empirical Force Field Techniques in Determining Enantiomeric Recognition of Organic Ammonium Salts by Chiral Di- and Tetraalkyl-Substituted Pyridino-18-Crown-6 Ligands					
12. PERSONAL AUTHOR(S) J. S. Bradshaw, C. Y. Zhu, S. Lifson and R. M. Izatt					
13a. TYPE OF REPORT Interim	13b. TIME COVERED FROM _____ TO _____	14. DATE OF REPORT (Year, Month, Day) Feb. 20, 1990		15. PAGE COUNT	
16. SUPPLEMENTARY NOTATION					
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB-GROUP			
19. ABSTRACT (Continue on reverse if necessary and identify by block number) Complexation of the (R)- and (S)- forms of α -(1-naphthyl)ethylammonium perchlorate by chiral pyridino-18-crown-6 ligands 1-6 (Figure 1) has been studied by the temperature dependent ¹ H NMR technique. ¹ At low temperatures, the peaks in the ¹ H NMR spectra of the complexes attributable to the hydrogen atoms on the CH ₂ groups attached to the pyridine rings (centered at about δ 4.5), or the methyl hydrogens in the cases of 5 and 6, separated into two peaks of equal intensities. The low temperature peak separations were 40-140 Hz. At high temperatures, the appearance of a single peak is caused by a fast intermolecular or intramolecular face to face guest exchange. The kinetic parameters for the dissociation of these complexes were calculated as reported. ¹ Table I shows the differences in ΔG_c^\ddagger for the dissociation of the complexes of 1-6 with (R) and (S)- α -(1-naphthyl)ethylammonium perchlorate. It (continued on back)					
20. DISTRIBUTION/AVAILABILITY OF ABSTRACT <input type="checkbox"/> UNCLASSIFIED/UNLIMITED <input type="checkbox"/> SAME AS RPT. <input type="checkbox"/> DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION		
22a. NAME OF RESPONSIBLE INDIVIDUAL Dr. Harold Guard		22b. TELEPHONE (Include Area Code) (202) 696-4409		22c. OFFICE SYMBOL	

90 03 02 004



is evident from these differences in the ΔG_C^\ddagger values in Table I that these chiral ligands exhibit enantiomeric recognition.

Also in Table I, these $\Delta\Delta G_C^\ddagger$ values are compared with those calculated from the conformational equilibrium energies of the complexes.^{2,3} These calculated energies included those for the ion-ligand interactions and the strain energy of the ligands that are the main components of ΔG_C^\ddagger . They are therefore the main contributors to $\Delta\Delta G_C^\ddagger$. The other components that are temperature or solvent dependent are smaller and not much different for the (R) and (S) complex and therefore are mostly cancelled out in the calculated $\Delta\Delta G_C^\ddagger$ values.^{1,2} Consequently, the calculated energy difference represents approximately the $\Delta\Delta G_C^\ddagger$ value.

The computer-calculated $\Delta\Delta G_C^\ddagger$ values for the complexes of ligands 1, 3, 4 and 6 with the salt were about the same as those determined by the ¹H NMR method. The calculated $\Delta\Delta G_C^\ddagger$ values for the complexes of 2 and 5 were significantly higher than the determined values. Based on this significant, though less than thorough, agreement between the determined and calculated values of $\Delta\Delta G_C^\ddagger$ for some of these complexes, the force field calculations were further extended to many other variants of the same family of molecules such as 7 and 8. The calculations were used to estimate the expected capacity of these variants for enantiomeric recognition, and helped to choose which variants should be synthesized and which should not. Thus, the variant with R₁ = t-butyl is predicted to yield high enantiomeric recognition, and is currently being prepared in our laboratory. Other variants where R₁ = other alkyl groups were shown to be less promising, and are not being prepared.

The computer-generated stereoviews of the ligand-ion complexes complemented the calculated $\Delta\Delta G_C^\ddagger$ values by exposing visually the nature of the ion-ligand interactions and the source of the enantiomeric recognition. Figure 2 represents stereoviews of the two diastereoisomeric ion complexes with ligand 8 each viewed from two perpendicular directions. It is seen that for the (R)-enantiomer, the t-butyl substituent contacts the methyl part of the salt, the naphthyl substituent of the salt contacts the pyridine, and the three NH bonds are properly oriented towards their respective ligating groups, thus optimizing the salt-ligand electrostatic interaction. The (S) enantiomeric salt appears to be less favorably bound to the ligand. The naphthyl substituent of the salt repels the t-butyl substituent of the ligand, thus introducing distortion and strain in the complex, and the NH bonds are not well oriented towards their respective ligating group, thus weakening the salt-ligand interaction.

1. Davidson, R. B.; Bradshaw, J. S.; Jones, B. A.; Dalley, N. K.; Christensen, J. J.; Izatt, R. M. Izatt, R. M.; Morin, F. G.; Grant, D. M. J. Org. Chem. 1984, 49, 353.
2. Lifson, S.; Felder, C. E.; Shanzer, A. J. Am. Chem. Soc. 1983, 105, 3866.
3. Lifson, S.; Felder, C. E.; Shanzer, A.; Libman, J. in "Progress in Macrocyclic Chemistry," Vol. 3, Izatt, R. M.; Christensen, J. J. Eds., Wiley Interscience, New York, pp. 241-308, 1987.

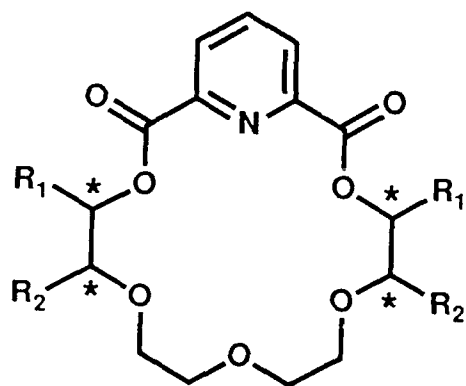
Table I. Differences in Free Energies of Activation ($\Delta\Delta G_c^\ddagger$, kcal/mol) [$\Delta G_c^\ddagger(R) - \Delta G_c^\ddagger(S)$] for the Interaction of Various Chiral Macrocyclic Ligands with (R)- and (S)- α -(1-Naphthyl)ethylammonium Perchlorate (A in Table I) as Determined Experimentally (NMR) and as Calculated from Empirical Energy Functions^a.

Ligand	$\Delta\Delta G_c^\ddagger$	
	Determined	Calculated
(S,S)-1	1.1 ^b	0.7
(S,S)-2	1.3	2.5
(S,S)-3	0.1 ^b	0.1
(S,S)-4	1.6 ^b	1.7
(R,R)-5	0.8	1.7
(R,R,R,R)-6	0.9	0.9
7,R = t-butyl (Y = O)		2.5
8,R = t-butyl (Y = H ₂)		2.2

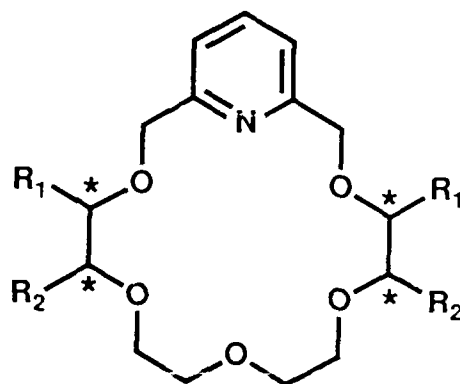
^aEmpirical calculations as reported in references 2 and 3. ^bData from reference 1.

Accession For	
NTIS GRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By _____	
Distribution/	
Availability Codes	
Dist. Special	
A-1	

Figure 1. Chiral Pyridino-18-Crown-6 Ligands



- 1, $R_1 = \text{CH}_3$; $R_2 = \text{H}$
(S,S) & (R,R)
- 2, $R_1 = \text{C}_6\text{H}_5$; $R_2 = \text{H}$
(S,S)
- 3, $R_1 = \text{H}$; $R_2 = \text{C}_6\text{H}_5$
(S,S)
- 7, $R_1 = \text{C}(\text{CH}_3)_3$, $R_2 = \text{H}$



- 4, $R_1 = \text{CH}_3$; $R_2 = \text{H}$
(S,S)
- 5, $R_1 = \text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_3$;
 $R_2 = \text{H}$ (R,R)
- 6, $R_1, R_2 = \text{CH}_3$;
(R,R,R,R)
- 8, $R_1 = \text{C}(\text{CH}_3)_3$, $R_2 = \text{H}$

Figure 2. Computer-Generated Stereoviews Obtained From Force Field Calculations of the Complexes of the Proposed (S,S)-Di-t-butyl-Substituted Pyridino-18-Crown-6 with (R)- α -(1-Naphthyl)ethylammonium Perchlorate (Stereoviews A) and With the (S)-Perchlorate (Stereoviews B)

A

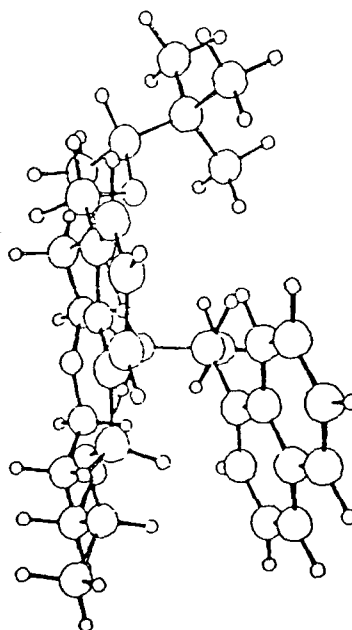
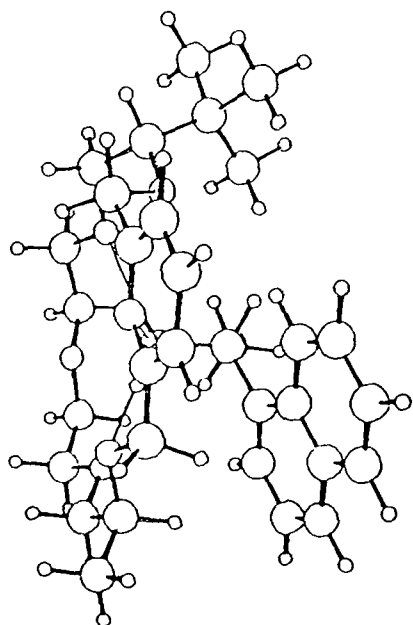
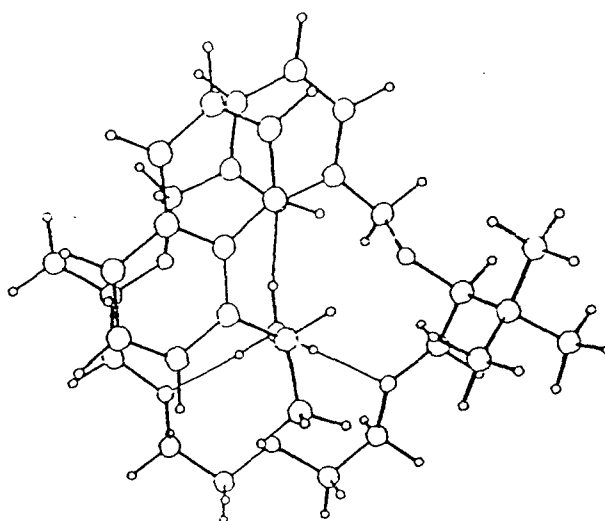
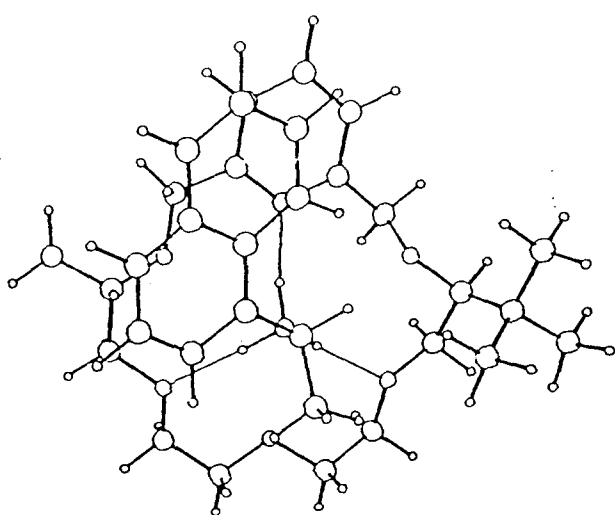


Figure 2. (Continued)

B

