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6. AUTHOR(S)

Alexander Y. Nazaraenko, Peter Huszthy, Jerald S. Bradshaw, John D. Lamb and Reed M. Izatt

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MOLECULAR RECOGNITION AS SHOWN BY THE SOLVENT EXTRACTION OF (R)- AND (S)-[α-(1-NAPHTHYL)ETHYL]AMMONIUM PICRATE OR ORANGE 2 BY CHIRAL PYRIDINO-CROWN ETHERS

Alexander Y. Nazarenko, Peter Huszthy, Jerald S. Bradshaw, John D. Lamb
and Reed M. Izatt

Abstract

A solvent extraction technique was used to determine equilibrium constants for the reaction of [α-(1-naphthyl)ethyl]ammonium ions [(R)- and (S)-isomers] with chiral substituted pyridino-18-crown-6 ligands in a water-chloroform system. Selectivity coefficients and stability constants for the interaction in chloroform solutions were calculated. The selectivity patterns are similar to those found by the ^1H NMR technique. Thus, this method may be a simple and rapid way to determine enantiomeric recognition.

Introduction

Although solvent extraction of metal ions with crown ethers has been widely studied, few studies involving the solvent extraction of organic cations with crown compounds have been reported. Amines and amino acids have been extracted into dichloroethane or chloroform as protonated cations using picrate [1,2], Methanil Yellow [3,4] or Orange 2 [5] as counter-ions. The selectivity of crown ethers for various types of amines could be improved by using the solvent extraction method [1,5].

We report here the solvent extraction of (R)- and (S)-[α-(1-naphthyl)ethyl]ammonium picrate (NapEtHPic) with several chiral pyridino-crown ether ligands. Picrate ion was selected as the counter ion because of its absorptivity in the near UV region and also because it is convenient to compare the results with data from many other picrate salts studied earlier. For ligands with a large absorbance in the near UV region, the Orange 2 anion was used instead of picrate.

Experimental Section

Crown ethers 1-9 (Figure 1) were synthesized and purified as described previously [6]. (R)- and (S)- Isomers of [α-(1-naphthyl)ethyl]ammonium ion (NapEtH$^+$) were used as the perchlorate salts. Standard solutions of macrocycles in chloroform and NapEtHClO$_4$ in water were used. Phosphate buffer [7] with total phosphate concentration of 0.05 mol/l and a pH value of 5.7 was used in all experiments.

A typical extraction procedure was as follows: 2 ml of an aqueous solution containing 0.5-3 x 10^{-4} M picrate, 1-3 x 10^{-4} M NapEtHClO$_4$ and buffer solution was mixed with 2 ml of chloroform containing 1-5 x 10^{-4} M of the crown compound. After equilibrium had been reached, the absorbance in the organic phase was measured. This value was corrected in all cases by a blank test - the absorbance of the same solutions, but without crown compound or amine. The experiment was carried out with both (R)- and (S)-isomers simultaneously at nearly the same concentrations to reduce possible errors in selectivity coefficients.

Results and Discussion

The conditional equilibrium constants and selectivity coefficients are shown in Table 1. The log K$_1$ values for complexes of tetramethyl-substituted 1 with (R)- and (S)-NapEtH$^+$ were

the same within a narrow standard deviation. Dimethyl-substituted chiral diester crown **2** exhibited recognition for one of the enantiomers of NapEtH$^+$ as shown by the log $K_{R/S}$ value of 0.47 (Table 2). This value is very near the Δ log K value as determined by the ^{1}H NMR technique [7]. The ^{1}H NMR derived Δ log K values were 0.42 in methanol and 0.44 in methanol/chloroform : 1/9. Substitution of sulfur atoms for the carbonyl oxygens of **2** to form **3** gave a slight decrease in K_1 as well as in selectivity (log $K_{R/S}$ = 0.38). Chiral ligands **4** and **7** exhibited no extractive selectivity for the enantiomers of NapEtH$^+$ as was also observed by the ^{1}H NMR technique [6d,7]. Chiral ligands **5, 6** and **8** exhibited the largest log K_1 values and were selective with log $K_{R/S}$ values of 0.31, 0.42 and 0.47, respectively. These selectivity coefficients compare favorably with the ^{1}H NMR data observed in methanol/chloroform : 1/1 [7].

The use of Orange 2 instead of picrate ion increased log K_2 (Table 1) but slightly decreased log K_1 (Table 2). The reason for this phenomenon may be steric repulsion between the comparatively large sulfonate group of the anion and the macrocyclic molecule. The selectivity coefficients when using Orange 2 ion associates are similar to those with picrate.

CONCLUSION

In the ligand separated ion pair [NapEtH$^+$L-R] a protonated amine cation is bonded to the macrocycle molecule with three hydrogen bonds, one of which is directed to the pyridine nitrogen atom [Gc]. These bonds fix the geometry of complex cation, and they are nearly the same for both enantiomers. As a result, the weak Van der Waals interactions remain the main source of chiral recognition. The low total energy of recognition effect which was observed in this study ($\Delta\Delta G$ = 0.7 kcal/mol and ΔH about 1 kcal/mol) confirm this explanation. In general, it is hard to expect a much higher recognition for chiral amines without functional groups.

In the case of two pyridine groups (macrocycle **1**), there are two possible orientations of the chiral amine leading to a loss in recognition. In partly separated ion pairs, the direct interaction of protonated amine with the anion makes the contract between chiral species weak, resulting in poor recognition. The procedure being used in this study appears to be a convenient and simple technique to study chiral recognition using small amounts (ca 1-3 mg) of the ligand.
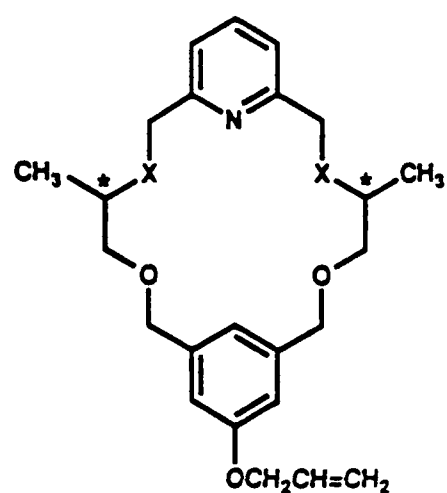
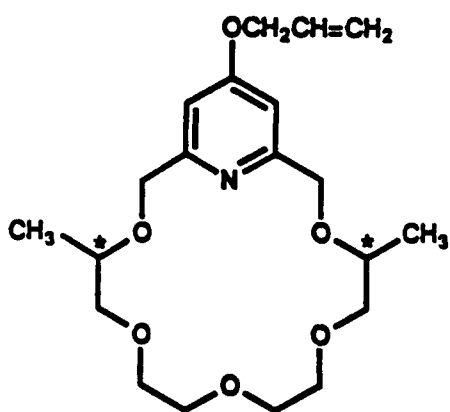# Figure 1. Chiral Macrocyclic Ligands Used in this Study
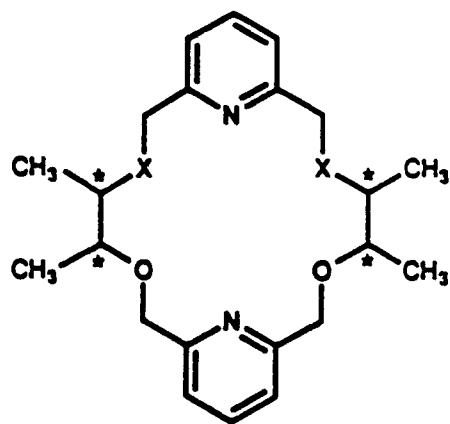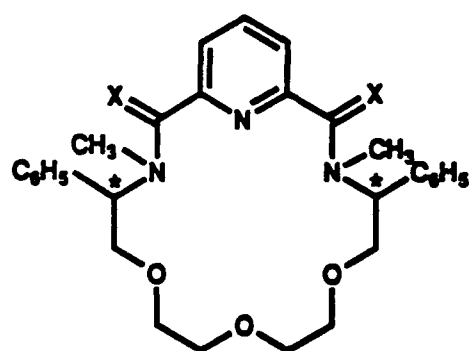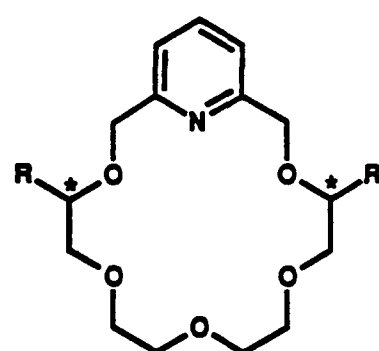

1, (R,R,R,R)
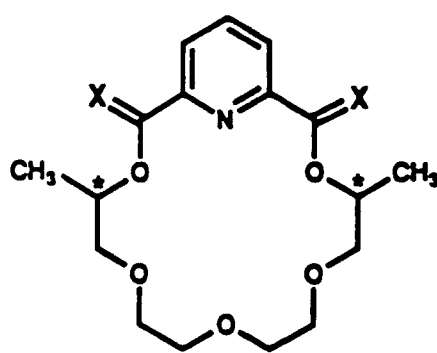
2, X = O (S,S)
3, X = S (S,S)
5, X = H₂ (S,S)

4, (S,S)

6, (S,S)

7, X = O (S,S)
9, X = H₂ (S,S)

8, R = (CH₂)₂CH=CH₂ (S,S)

Table 1. Extraction constants K_2 for NapEtHR complexes, at 25°C (standard deviation in parenthesis).

	pH	I^a	$\log K^b_{c2}$	$\log f^c$	$\log K_2/K_{c2}$	$\log K_2$
Picrate	3	0.001	2.03(3)	0.03	0.00	2.06
	5.8	0.05	1.80(4)	0.16	0.17	2.13
Orange 2	3	0.001	3.07(10)	0.03	0.00	3.10
778	5.8	0.02	2.84(4)	0.11	0.17	3.08

[a] activity coefficient from the Davies equation.

[b] correction term on unprotonated form of NapEt.

[c] corrected on activity coefficient term.

Table 2. Equilibrium constants of NapEtHLR associates formation in a water-chloroform system at 25°C (pH = 5.8, I = 0.05).[a]

Ligand	Log K^c		log $k_{R/S}$
	(R)-	(S)-	
1	6.39(5)	6.39(5)	0.00(7)
2	5.80(6)	5.42(5)	0.38(8)
3	6.13(3)	5.65(3)	0.48(5)
4	5.60(3)	5.59(4)	0.01(5)
4[b]	5.42(3)	5.41(5)	0.01(7)
5	7.64(4)	7.33(5)	0.31(7)
6	7.72(4)	7.30(6)	0.42(7)
7	4.48(3)	4.48(3)	0.00(4)
8	6.97(4)	6.50(5)	0.47(7)
8[b]	6.55(3)	6.14(9)	0.41(10)
9[b]	5.16 (5)	4.9(1)	0.2(1)

[a]standard deviation in parentheses.

[b]value for Orange 2 complex, otherwise R = picrate ion.

[c]K_{c1} is a conditional equilibrium constant.

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