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ION-DIPOLE ASSOCIATION CHROMATOGRAPHY ON ION EXCHANGER IN NON-AQUEOUS MEDIA. SEPARATION AND CHARACTERIZATION OF CROWN ETHERS AND RELATED COMPOUNDS

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A silica gel-bound sulfonate type cation exchanger was used as a stationary phase in organic media for the chromatographic separation of crown ethers through the ion-dipole interaction. Crown ethers were retained on the column depending on the nature of metals on the ion exchanger, while the open-chain homologues showed only a limited affinity to the column. The chromatography was useful for the analysis and characterization of crown ethers and related compounds.

In the course of our study on the synthesis of functionalized crown ethers, difficulties were frequently encountered in separating and analyzing the reaction mixture which contained several crown ether derivatives and their open-chain homologues. Ordinary liquid Chromatography on silica gel or organic gel was useful, but was oftentimes inadequate to attain a good separation. In this communication, a new type of chromatography is described, in which the ion-dipole interaction between the analyte and the cationic site of the stationary phase (metal loaded cation exchanger) is taken advantage of. This chromatography, schematically shown in Figure 1, is especially suitable to the analysis and characterization of crown ethers and related compounds which are electrically neutral and interact reversibly with metal ions (serve as ligands to the metal).

A column (4 mm x 300 mm) packed with IEX-510SP (silica gel-bound sulfonate type cation exchanger, Toyo Soda Manufacturing Co.) was operated on HLC-802 high performance liquid chromatograph (Toyo Soda) fitted with UV and RI detectors at a flow rate of 1.4 ml/min of eluting solvent (methanol or THF). Ordinary crown ethers as well as azo-crown ethers **1** - **3**1) were analyzed.

Figure 2 shows typical chromatograms of **3**. This crown ether isomerizes under UV or visible light from the "*trans*" to "*cis*" configuration with respect to the azo group, and the ability of the *trans* isomer to complex with alkali metal ions appeared to be lost on isomerization.1) The isomers are barely resolved on an ordinary organic gel, while a complete resolution is achieved on the IEX-510SP column.2) 2,2'-Dimethoxyazobenzene, which lacks the affinity to metal ions, appears at the same position as the *cis* isomer on the ion exchanger column, and it is clear that the highly strained crown ether ring of **3** in the *cis* configuration does not allow the interaction with metal ions.

The retention of the analytes in the present chromatography is solely based on the complexation interaction with the metal ion on the ion exchanger stationary phase. Table 1 lists the retention times of some of the analytes on the column loaded with various univalent cations. The retention times

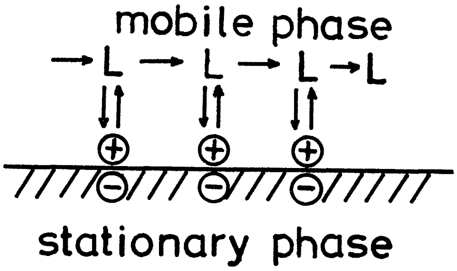
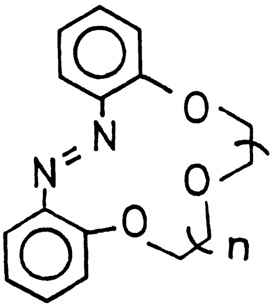


Fig.1. Mechanism of ion-dopole association chromatography



1 (n=1)
2 (n=2)
3 (n=3)

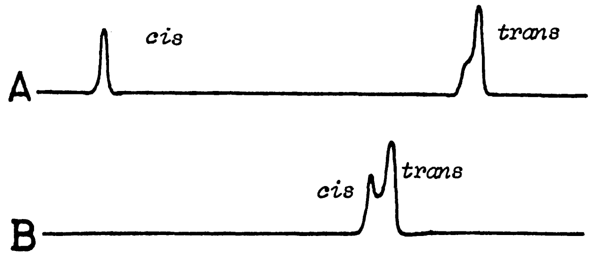


Fig.2. Chromatography of photo-isomerized **3** on ion exchanger gel (Na^+type) (A) and polystyrene gel (B). solvent methanol

are in parallel with the complexation tendency of the crown ethers with alkali metals.[1,3] No retention is observed with the column loaded with tetramethylammonium.[4] The elution of the analytes of excessively large retention times can be facilitated by a gradient technique, in which the metal salts, preferably iodides, is added to the eluting solvent.

It is noteworthy that the interaction between lithium and crown ethers is clearly indicated in Table 1. The complex formation between lithium and crown ethers usually takes place to only a limited extent, and it is difficult to treat the equilibrium by ordinary means. Obviously, the present chromatography gives a valuable tool in treating such weak interactions, and the information on the stability of the complexes can be readily derived from the retention data. A small sample size that the HPLC analysis requires makes the method especially useful in characterizing precious compounds whose supply is limited.

Table 1. Retention times of crown ethers on IEX-510SP column (min)[a]

cation loaded	1[b]	2[b]	3[b]	benzo-15-C-5
$(CH_3)_4N^+$	2.3	3.3	3.3	3.8
Li^+	2.5	8.0	14.8	8.8
Na^+	3.2	20.0	21.5	30.0
K^+	2.5	11.5	56.5	29.0

a) solvent, methanol b) *trans* isomers

The application of the principle is not limited to analytical chromatography. Macroporous cation exchange resin such as AG MP-50 (Bio·Rad) in the K^+ form was useful for a preparative purpose. Crown ethers were separated from the open-chain homologues which lack affinity to metal ions. It is quite possible that the chromatography of this type finds more versatile use in the analysis and characterization of "ligands" by changing the cation on the ion exchanger where a weak interaction of the ligand and the cationic site can be expected in organic media.[5]

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References

1) M. Shiga, M. Takagi, and K. Ueno, Chem. Lett., **1980**, 1021.

2) A shoulder on the main (*trans* isomer) peak may suggest the presence of still other isomers for **3**. Other crown ethers including benzo-type normal crown ethers do not show such an anomaly.

3) J. J. Christensen, D. J. Eatough, and R. M. Izatt, Chem. Rev., **74**, 351 (1974).

4) A small variation in retention times for the $(CH_3)_4N^+$ loaded column may be due to some residual alkali metal ions in the column. The ion exchange by $(CH_3)_4N^+$ was checked by the flame photometry of alkali metals, but there still remained a possibility that a complete exchange was not attained.

5) J. Y. K. Hsieh, D. K. Welch, and J. G. Turchotte, Anal. Chim. Acta, **123**, 41 (1981).

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