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# Thermodynamic Parameters for Polyether Adducts with Neutral Molecules

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Thermodynamic parameters for the interaction of neutral molecules with cyclic and acyclic polyethers in benzene solvent have been determined by calorimetry. Although triethylene glycol dimethyl ether loses more entropy upon adduct formation with malononitrile than does 12-crown-4, similar enthalpies of formation indicate that the electron-donating abilities of the oxygen atoms of cyclic or acyclic ethers are comparable. Thus, no macrocyclic effect is observed for 12-crown-4 when compared to its analogous acyclic ether. The interactions of malononitrile and acetonitrile with ethers seem to depend on the collective action of the oxygen atoms in the ethers. Dimethyltin dichloride binds to a specific oxygen site.

## Introduction

Since the discovery of macrocyclic polyethers in 1967,[1] most thermodynamic studies have been directed toward their complexing ability with cations in aqueous or methanol solvent. Investigations of adduct formation by these polyethers with neutral species are quite recent. As late as the early 1980s paper reporting the first thermodynamic data for cyclic polyethers with neutral guests were only beginning to appear.[2] Consequently, most of what is understood about interactions between these macroethers and neutral guests comes by inference from studies with cation guests.

Crown ethers were originally thought to select cations for binding depending on the relative guest–host cavity sizes. Recent data suggest that the selective ability of hosts may depend more on the spatial arrangement of binding sites than on size.[3] Early results also seemed to indicate that the formation of crown ether–cation complexes were enthalpy driven. Presently, however, both an enthalpy and entropy effect are believed to be operative depending on the system. Also reported was a macrocyclic effect which referred to an enhancement by several orders of magnitude in equilibrium constant for binding to cyclic polyethers relative to their acyclic analogues.[4] These studies and others indicated that the oxygen atoms of a crown ether could act synergistically, as collective donors to a guest molecule. Elbasyouny et al. have found considerable flexibility for 18-crown-6.[5] The most stable conformation has approximate $D_{3d}$ symmetry with a polar cavity. The noncoplanar dipoles are directed toward the interior of the ring forming a collective dipolar field. The complexation of cations by 18-crown-6 is assumed to be in part due to the interactions between the electrostatic field of the ion and the cavity of the crown ether.

One of the early studies on complexation to neutral species was the X-ray diffraction study by Elbasyouny et al. They found that neutral guest molecules with compatible hydrogen atom arrangements rendered acidic by neighboring polar groups were particularly able to complex with crown ethers.[5] ${}^1$H NMR and IR spectroscopic evidence pointed to downfield shifts and higher wavenumber readings upon complexation, indicative of hydrogen-bonding type interaction. Elbasyouny et al. also completed a solid-state study of 18-crown-6/cyanoacetic acid/water which indicated that the COOH, $H_2O$, *and* $CH_2$ hydrogens participated in hydrogen bonding with crown ether in a solvated complex. Both solutions[2] and solid-state[5] studies indicate that malononitrile

$[CH_2(CN)_2]$ hydrogens interact with the crown ether. In the solid state two malonitrile molecules complex to each crown ether, with two oxygens from opposite sides of the ring hydrogen bonded to the four methylene hydrogens. Dipole–dipole interactions also participate in complex stabilization. Because substances like dimethyl malonate and methoxy- and phenylacetonitrile do not form similar complexes, the presence of a permanent dipole moment in the guest molecule may be necessary for a stable complex when the hydrogen bond involves a carbon acid.[5]

This investigation was undertaken to study the complexing behaviors of crown ethers and straight-chain ethers wtih neutral guests which had the potential to exhibit different bonding behaviors. Malononitrile and acetonitrile may interact with the collective dipolar field provided by crown ethers. In contrast, dimethyltin dichloride appears to bind to a specific oxygen atom, thus participating in a localized donor–acceptor interaction.

## Experimental Section

Several calorimeters have been built in these laboratories over the past years. These calorimeters use the Parr solution calorimeter Model 1451 thermistor bridge but have been modified for electrical calibration. One of these calorimeters has been constructed to operate in an HE-43-2 DriLab constructed by Vacuum Atmospheres. The DriLab contains the calorimeter, a balance, and all necessary accoutrements so that the entire analysis from solution preparation to data collection may be carried out in a dry atmosphere. A Tronac Model 450 isoperibol calorimeter equipped with an ampule crushing device has been used extensively in the past and will continue to serve for those analyses for which it is appropriate. Data collection has been previously described.[6]

Analysis of calorimetric data utilizes a least-squares technique.[7] In general, the heat change for *n* reactions in the reaction vessel can be given by

$$Q = \sum_{i=1}^{n} n_{i,p} \Delta H_i$$

where $n_{i,p}$ is the number of moles of product *i* and is a function of the equilibrium constant for reaction *i*. The best values of $K_i$ and $\Delta H_i$ are calculated by a least-squares analysis of the equation. The error square sum over the *m* data points is given by

$$U(K_i, \Delta H_i) = \sum_{p=1}^{m} (Q_p - \sum_{i=1}^{n} (n_{i,p} \Delta H_i))^2$$

where the subscript *p* is over all data points and *i* is over all reactions. The best values for *K* and $\Delta H$ for a given determination are those which minimize $U(K_i, \Delta H_i)$. The complete solution of

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the least-squares equations involves five steps: (1) assumption of initial $K$ values, (2) calculation of concentration of each species using the assumed $K$, (3) calculation of the best $\Delta H$ corresponding to each $K$, (4) evaluation of $K$ and $\Delta H$ values to establish how well the data are fit, and (5) recalculation of steps 2–4 using new $K$ values until the best set of $K$ and $\Delta H$ values is found. A least-squares error analysis given by Rosseinsky and Kellawi[8] is used to determine the errors in the thermodynamic parameters for 1:1 equilibria determined by calorimetric analysis.

Because of the possibility of competing equilibria (equilibria other than 1:1 adduct formation), programs utilizing least-squares schematic mapping techniques have been developed to handle up to six simultaneous equilibria involving virtually any species (such as 1:1, 1:2, 2:2, and 2:1 adducts, as well as associated acid and base and solvated acid and base). The programs permit equal or weighted least-squares fitting of the data and also present the option of holding one or more equilibrium constants or enthalpies constant while obtaining the best-fit constants for other equilibria. These programs are similar to those described by Abraham et al.[9] and by Mullens et al.[10] In order to maximize the utility of these programs, data must be obtained with a wide range of initial concentrations and varying acid/base molar ratios. A standard state of 1 M was used.

All reagents were purchased in the highest purities available. Care was taken to maintain as dry an atmosphere as possible both for solution preparation and for calorimetric analysis. Reagents were monitored for the presence of water by near-IR spectroscopy. Aldrich HPLC grade benzene solvent was used without further purification. Malononitrile was sublimed under reduced pressure. All other reagents were used as received.

## Results and Discussion

**Interaction of Acetonitrile with Crown Ethers.** Two previous investigations have reported thermodynamic parameters for the interaction of acetonitrile with 18-crown-6 in benzene solvent.[2,11] Only one of these studies reported an enthalpy,[2] and that was only for the 1:1 adduct. We undertook a reexamination of this system to calibrate our methods and to provide additional thermodynamic data. Our results, along with those previously reported, are given in Table I. All three studies agree that the equilibrium constants are equal to or less than 1 for 1:1 and 1:2 (1 crown ether:2 acetonitrile) adducts. One investigation reported self-association of acetonitrile;[11] the other did not.[2] We find self-association of acetonitrile with the self-association dimer constant equal to 0.3 ± 0.1, an enthalpy for dimer formation of −3.0 ± 0.4 kJ mol$^{-1}$, and an enthalpy of solution at infinite dilution for acetonitrile of +1.80 kJ mol$^{-1}$.

Acetonitrile interacts with crown ethers through the $CH_3$ structure element. Interactions of this type have been studied in some detail by Elbasyouny et al.,[5] who conclude that the binding is due to dipole–dipole forces aided by "a hydrogen atom arrangement that is complementary to the crown ether and in which the hydrogens are rendered acidic by a neighboring polar group". The 1:2 complex found by all investigators probably is due to bonding by acetonitrile to both faces of the crown ether. The enthalpy and entropy changes measured in our work further indicate a similar interaction for binding of the second acetonitrile. Models show that 18-crown-6 can adopt a conformation which presents three oxygen atoms to each acetonitrile molecule, making for a good "fit" on either face of the 18-crown-6.

The sodium ion adduct with 18-crown-6 has a formation constant about 10 times that for 15-crown-5.[12] This interaction is of an ion–dipole nature and depends on the collective action of the oxygen atoms in the crown. We attempted to isolate adduct

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**TABLE I: Thermodynamic Parameters for Polyether Adducts with Neutral Molecules (298 K, Benzene Solvent)**

### Acetonitrile

|  | 18-crown-6$^a$ | 18-crown-6$^b$ | 18-crown-6$^c$ | 15-crown-5$^a$ |
|---|---|---|---|---|
| $K_{11}{}^d$ | 0.29 ± 0.05 | 1.0 ± 0.2 | 0.5 ± 0.05 | ~0 |
| $-\Delta H_{11}{}^e$ | 25 ± 2 |  | 25 |  |
| $-\Delta S_{11}{}^f$ | 94 ± 7 |  | 90 ± 1 |  |
| $K_{12}$ | 0.40 ± 0.05 | 0.26 ± 0.04 |  |  |
| $-\Delta H_{12}$ | 54 ± 4 |  |  |  |
| $-\Delta S_{12}$ | 189 ± 13 |  |  |  |

### Malononitrile

|  | THP$^a$ | tegdme$^a$ | 12-crown-4$^a$ | 15-crown-5$^a$ | 18-crown-6$^g$ |
|---|---|---|---|---|---|
| $K_{11}$ | ~0 | 4.1 ± 0.4 | 5.7 ± 0.3 | 12 ± 2 | 150 ± 15 |
| $-\Delta H_{11}$ |  | 21 ± 1 | 16 ± 1 | 26 ± 2 | 59 ± 2 |
| $-\Delta S_{11}$ |  | 58 ± 3 | 40 ± 3 | 67 ± 7 | 156 ± 7 |
| $K_{12}$ |  |  |  |  | 1650 |

### Dimethyltin Dichloride$^a$

|  | THP | dioxane | egdee | tegdme | 15-crown-5 |
|---|---|---|---|---|---|
| $K_{11}$ | 3 ± 1 | 6 ± 1 | 1 ± 0.5 | 13 ± 3 | 30 ± 10 |
| $-\Delta H_{11}$ | 10 ± 2 | 9.2 ± 0.8 | 6 ± 2 | 17 ± 2 | 10 ± 2 |
| $-\Delta S_{11}$ | 23 ± 7 | 16 ± 3 | 20 ± 8 | 36 ± 7 | 6 ± 7 |
| $K_{12}$ | 4 ± 1 | 9 ± 2 |  |  | $5 \times 10^2 \pm 1 \times 10^2$ |
| $-\Delta H_{12}$ | 23 ± 2 | 15 ± 2 |  |  | 27 ± 2 |
| $-\Delta S_{12}$ | 66 ± 7 | 32 ± 7 |  |  | 39 ± 7 |
| $K_{21}$ |  |  |  | 50 ± 10 | $1.7 \times 10^3 \pm 0.2 \times 10^3$ |
| $-\Delta H_{21}$ |  |  |  | 33 ± 4 | 29 ± 4 |
| $-\Delta S_{21}$ |  |  |  | 78 ± 14 | 35 ± 13 |

$^a$This work. $^b$Reference 10. $^c$Reference 4; $K_{12}$ constant reported at 290 and 282 K as 0.54 and 1.36, respectively. $^d$A + B = AB, $K_{11}$; A + 2B = AB$_2$, $K_{12}$; 2A + B = A$_2$B, $K_{21}$; A = acid, B = ether. $^e$In kJ mol$^{-1}$. $^f$In J mol$^{-1}$ K$^{-1}$. $^g$Reference 4.

formation with 15-crown-5 and acetonitrile but were unable to detect sufficient heat to carry out the analysis. This indicates equilibrium constants and enthalpies for 15-crown-5 with acetonitrile less than those found for 18-crown-6 and suggests that this interaction does depend on a collective six-oxygen dipolar field.

**Interaction of Malononitrile with Cyclic and Acyclic Ethers.** deBoer et al.[2] have reported a large equilibrium constant and enthalpy change for the 18-crown-6–malononitrile adduct in benzene solvent. They also report 1:2 (1 crown ether:2 malononitrile) adduct formation. Malononitrile should bind to crown ether analogously to acetonitrile, with a combination of hydrogen bond and dipolar interactions. The hydrogens in malononitrile are more acidic than those of acetonitrile, and malononitrile also has a larger dipole moment than acetonitrile, so it should complex more strongly. The data in Table I show this effect in the equilibrium constants, enthalpies, and entropies for interactions with crown ethers. Because of the increased binding ability of malononitrile, we were able to calorimetrically monitor host–guest complexation with a broad array of ethers.

We investigated the 15-crown-5–malononitrile system in benzene solvent with the results given in Table I. We find only 1:1 adducts for this system which may indicate that the spatial arrangement of oxygens in 15-crown-5 will not permit binding of two malononitriles. The equilibrium constant for the 1:1 complex is about a factor of 10 less than that reported for the 18-crown-6 adduct, in agreement with the general complexing ability of crown ether oxygens when the interaction is of a collective nature. 12-Crown-4 shows a further decrease in equilibrium constant and a less negative enthalpy. The reduction in the number of oxygen atoms in passing from 18-crown-6 to 15-crown-5 to 12-crown-4 seems to be reflected in the equilibrium constants and enthalpies for these adducts with malononitrile.

Previous studies on the hydrogen bonding of m-cresol to ethers[13] found no evidence for a macrocyclic effect. The enthalpies of attachment of m-cresol to cyclic and acyclic hosts ranging from

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one oxygen atom ethers to six oxygen atom ethers were similar. This indicated that a specific interaction site, presumably an individual oxygen atom, was involved for 12-crown-4, 15-crown-5, and 18-crown-6 as well as the acyclic ethers. Any differences in equilibrium constants for the adducts were attributed to a statistical effect due to differing numbers of oxygen atoms. In contrast, the data in Table I for the binding of malononitrile to various ethers indicate that the enthalpy depends on the number of oxygen atoms available. No detectable heat due to adduct formation was observed upon adding the single oxygen cyclic ether tetrahydropyran (THP) to a benzene solution containing malononitrile. These data suggest that the interaction between malononitrile and the crown ethers is dependent on all of the oxygen atoms.

Comparison of the thermodynamic data for 12-crown-4 and triethylene glycol dimethyl ether (tegdme) (Table I) shows that the equilibrium constants for adduct formation with both ethers are similar. This seems to imply a collective oxygen interaction by tegdme with malononitrile similar to that observed for the crown ethers. The enthalpy change for the tegdme adduct is more negative than that for the 12-crown-4 adduct, but the equilibrium constant is slightly larger for the 12-crown-4 adduct. This indicates a more favorable entropy change for the formation of the 12-crown-4 than for the tegdme adduct with malononitrile. This may result from entropy loss for the acyclic tegdme as it rearranges to accommodate the malononitrile guest. Cyclic 12-crown-4, being conformationally ready to accept a guest, would experience little entropy change upon complexation.

**Interaction of Dimethyltin Dichloride with Cyclic and Acyclic Ethers.** Organotin dihalides are electron pair acceptors and behave as typical Lewis acids toward bases.[6] Thus, specific attachment of these molecules at individual oxygen atoms of the ethers is expected. In proceeding from one- to five-oxygen ethers, a general increase is seen in the equilibrium constants for the 1:1 adducts. For all adducts except tegdme, the enthalpies fall within a range of 6–10 kJ mol$^{-1}$. The differences in equilibrium constants may be partially understood by a simple statistical model[13] which shows that the equilibrium constant is proportional to the number of oxygen atoms in an ether. The equilibrium constant is also influenced by the electron pair donating ability of the oxygens. It is only for dioxane and THP that relative measures of the electron pair donating ability are available. THP, based on $\beta$ values, should be the better donor.[14] This agrees qualitatively with our enthalpy measurements, displayed in Table I.

All these systems show complicated multiple equilibria except possibly ethylene glycol diethyl ether (egdee); and here, because the equilibrium constant and enthalpy are so low, it may not be possible to detect higher adduct formation. For THP and dioxane 1:1 and 1:2 (1 dimethyltin dichloride:2 ether) adducts were found; with tegdme 1:1 and 2:1 (2 dimethyltin dichloride:1 ether) adducts were detected. For 15-crown-5 there is evidence for 1:1, 1:2, and 2:1 adducts.

In these systems binding appears to occur at specific sites; there is no evidence of any collective action of the oxygens of the polyethers. The enthalpy changes for the 1:1 adducts of dimethyltin dichloride are, within error limits, about the same for the single-oxygen ether THP, the double-oxygen ethers dioxane and ethylene glycol diethyl ether (egdee), and 15-crown-5. This is best interpreted to mean that one oxygen atom on each of these ethers serves as a specific interaction site for donation of an electron pair to the organotin compound.

The data for tegdme do not fit in with the other results. The enthalpy change for the tegdme–organotin adduct is clearly more negative than that for the other ethers and is almost double in magnitude. The loss of entropy in adduct formation is greater for tegdme than for the other ethers. There is no evidence for two tegdme molecules binding to a single dimethyltin dichloride species, while for THP, dioxane, and 15-crown-5, adducts containing two ether molecules per organotin molecule are found. This difference in enthalpy between tegdme and the other adducts could be a result of steric hindrance or a possible bidentate binding of the tegdme at two sites on the organotin moiety. This latter interpretation could also account for the nearly doubled enthalpy change observed for the tegdme–dimethyltin dichloride 1:1 adduct.

## Conclusions

We have investigated two different binding mechanisms for neutral guest–polyether adducts. Collective action of the oxygen atoms of the polyether is responsible for binding acetonitrile and malononitrile via dipole–dipole and hydrogen-bonded interactions. In the other case, a Lewis acid guest, localized donor–acceptor interactions occur at each oxygen binding site. For specific interactions, our thermodynamic studies indicate that the binding mechanism is unchanged for cyclic and acyclic polyethers.

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