

DETERMINATION OF COMPLEX STABILITIES WITH NEARLY INSOLUBLE HOST MOLECULES.

PART I. SPECTROPHOTOMETRIC DETECTION

HANS-JÜRGEN BUSCHMANN*, ERNST CLEVE, ULRIKE DENTER AND ECKHARD SCHOLLMEYER
Deutsches Textilforschungszentrum Nord-West eV, Frankenring 2, D-47798 Krefeld, Germany

The determination of stability constants by measuring the increase in solubility of a nearly insoluble host molecule due to complex formation with a soluble guest is discussed. If the host molecule absorbs in the UV–visible region, spectrophotometric measurements are easily performed to obtain the stability constants. The solubilities of the crown ether dibenzo-18-crown-6 and of the cryptand (222BB) in aqueous solutions and the molar absorptivities of these ligands and their complexes with alkali and alkaline earth metal cations were determined. The increase in solubility of these ligands due to complex formation with cations was used to calculate the stabilities of the complexes formed. Even under the assumption that neither the molar absorptivities nor the solubilities are known, the calculated stability constants agree very well with those obtained using the measured values of the molar absorptivities and solubilities. The accuracy of the stability constants even increases with decreasing solubility of the ligands.

INTRODUCTION

Many experimental techniques are used to study the reactions between host and guest molecules in solution. All these techniques have already been described in the literature in detail. Most commonly potentiometric,^{1,2} conductimetric,³ spectrophotometric^{4,5} and calorimetric^{6,7} titrations are used. However, any other experimental technique which allows the determination of the concentration of at least one species in solution or the change of one parameter due to the complex formation is suitable.

Most of the synthetic host molecules, such as calixarenes and other cyclophanes, are only soluble in some organic solvents. Their ability to form complexes with different salts not soluble in these solvents can be measured by extraction of the salts from an aqueous phase to the organic phase due to complex formation.^{8,9} A calculation of the complex stability in the organic solvent is not possible without the knowledge of the solubilities of the host and guest molecules in both solvents, the partition coefficients between both solvents of all species and the formation constants for ion pairs of the salt in the organic solvent.

Further possibilities concerning the determination of complex stabilities from the increase in the solubility

due to complex formation of insoluble guest molecules in aqueous solutions have been reported in the literature.^{10,11} However, this 'opposite' reaction, e.g. the increase in solubility of a nearly insoluble host molecule due to complex formation, has been reported in only few cases.^{12–14} This method shows some important advantages which have not been realized up to now. Owing to their low solubility, the host molecules are needed in only very small amounts to study complexation reactions. If the host molecules absorb in the UV–visible range the changes in the extinction due to the formation of complexes can be measured easily.

From the spectral data the stability constant of the complex can only be calculated if all molar absorptivities and the solubility of the host are known. However, even if these conditions are not fulfilled, it seems to be possible to calculate the stability constant from the experimental data using some assumptions. To prove the validity of these assumptions, it is necessary to study the complex formation of some ligands that are hardly soluble in a given solvent. On the other hand, the ligands should be soluble enough that stability constants have already been determined using different experimental techniques. A few stability constants for the reactions of the macrocyclic ligand dibenzo-18-crown-6 and the macrobicyclic cryptand (222BB) with cations in aqueous solutions have already been reported.^{15,16}

* Author for correspondence.

EXPERIMENTAL

The crown ether dibenzo-18-crown-6 (DB18C6) (Merck) and the cryptand (222BB) (Merck) were used as purchased (see Figure 1).

The salts NaCl, KCl, RbCl, CsCl, CaCl₂, SrCl₂ and BaCl₂ were of the highest purity commercially available. Doubly distilled water was used as the solvent.

To solutions of the salts (2×10^{-3} – 2×10^{-2} mol l⁻¹) the solid ligand was added. The amount of the ligand was so high that all solutions examined contained the solid ligand. The time for dissolution of the ligands was varied between 2 and 4 weeks in the case of the ligand DB18C6 and between 4 and 10 h for the cryptand (222BB) to ensure the complete dissolution of the ligands. Before extinction measurements the saturated solutions were passed through a membrane filter (polycarbonate, 0.4 μm). Owing to the high solubility of the cryptand (222BB), the solutions were diluted prior to the measurement. All solutions were thermostated at 25 °C. An example of these measurements is given in Figure 2.

The molar absorptivities of the pure ligands were obtained from solutions with known concentrations. To these, salts were added in a higher concentration than the ligand to ensure complete complex formation in order to obtain the molar absorptivities of the complexes.

The solubilities of the ligands were calculated from the extinctions of solutions saturated with the ligands using the estimated molar absorptivities.

All spectrophotometric measurements were made with a Varian Cary 5E spectrophotometer.

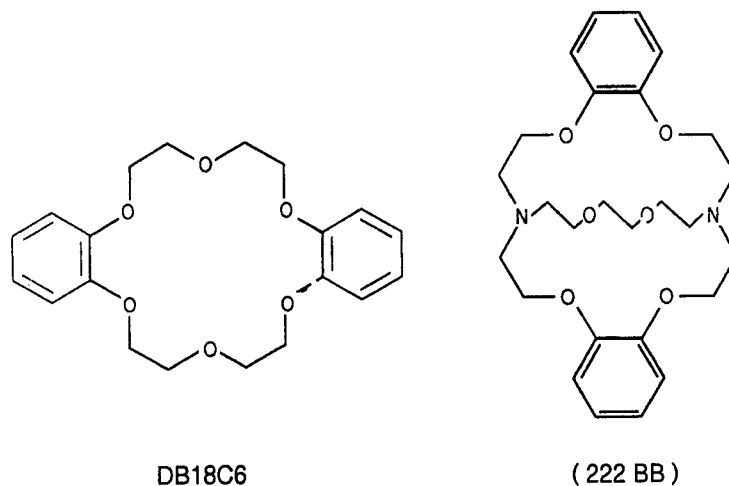


Figure 1. Structures of the ligands dibenzo-18-crown-6 (DB18C6) and cryptand (222BB)

RESULTS AND DISCUSSION

Mathematical models for the treatment of the experimental data

The formation of a 1 : 1 complex between a guest G and a host molecule H can be described using the equation



The corresponding stability constant K is given by

$$K = \frac{[GH]}{[G][H]} \quad (2)$$

The total concentration of the host, C_H , and of the

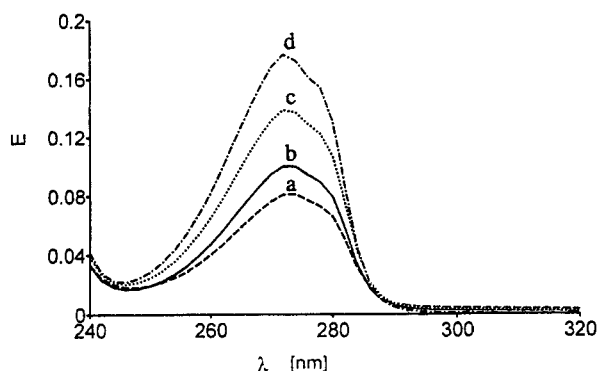


Figure 2. UV spectra of saturated solutions of the ligand DB18C6 in the presence of different concentrations of KCl in aqueous solution at 25 °C: (a) 2×10^{-3} ; (b) 8×10^{-3} ; (c) 2×10^{-2} ; (d) 3.2×10^{-2} M

guest molecule, C_G , are given by the material balances

$$C_H = [H] + [GH] \quad (3)$$

$$C_G = [G] + [GH] \quad (4)$$

If the solid host molecules are always in contact with the solution containing dissolved host molecules and the guest molecules, the actual concentrations of the host molecules $[H]$ in equations (2) and (3) can be substituted by the solubility $[H]_{sol}$, which is a constant for a given host.

If only the host molecule and the complex formed absorb at a given wavelength the experimentally measured extinction E for a constant optical path length d is given by

$$E/d = \varepsilon_1 [H]_{sol} + \varepsilon_2 [GH] \quad (5)$$

with ε_1 is the molar absorptivity of the host molecule and ε_2 that of the complex. Using equations (2) and (4), equation (5) can be transformed into

$$E = \varepsilon_1 [H]_{sol} + \varepsilon_2 \frac{K [H]_{sol}}{1 + K [H]_{sol}} C_G \quad (6)$$

Since the first term in equation (6) is constant, it can be substituted by

$$E_0 = \varepsilon_1 [H]_{sol}$$

and also the ratio n of the two molar absorptivities, $n = \varepsilon_2/\varepsilon_1$, can be used to rewrite equation (6):

$$E = E_0 + \frac{K}{1 + K [H]_{sol}} n E_0 C_G \quad (7)$$

Equation (7) can be transformed into

$$(E/E_0) - 1 = \frac{nK}{1 + K [H]_{sol}} C_G \quad (8)$$

Thus, plotting $(E/E_0) - 1$ as a function of the total concentration of the guest C_G , one expects a straight line with slope b . From this slope the stability constant of the complex formed in solution can be calculated:

$$K = \frac{b}{(\varepsilon_2/\varepsilon_1) - b [H]_{sol}} \quad (9)$$

If the unknown parameters, i.e. the two molar absorptivities and the solubility of the host molecule, can be determined from independent experiments, the stability constant is obtained without any problems. However, using almost insoluble host molecules these measurements are not possible or cannot be executed with reasonable accuracy. In this case it is possible to use equation (9) to calculate stability constants if the following assumptions are valid: (a) the molar absorptivities of the host molecule, ε_1 , and the complex formed, ε_2 , are nearly identical and (b) the term $b [H]_{sol}$ is smaller than 1. In this case the slope b is identical with the stability constant K . However, even if both assumptions are incorrect, b does not deviate from K to a large extent. In Figure 3 the influence of varying the ratio of the molar absorptivities and the product of the solubility and slope for a given value of b on the stability constant is demonstrated.

Variation of the ratio $\varepsilon_2/\varepsilon_1$ from 0.5 up to 2 changes the value of the stability constant by less than 10%. Also, an increase in the value of $b [H]_{sol}$ from 0.5 has no large influence on the value of the calculated stability constant. Only under extreme conditions such as $\varepsilon_2/\varepsilon_1 = 0.5$ and $b [H]_{sol} = 0.5$ with both terms nearly equal does the slope b differ considerably from the stability constant.

Since the value of $b [H]_{sol}$ has to be smaller than 1 and

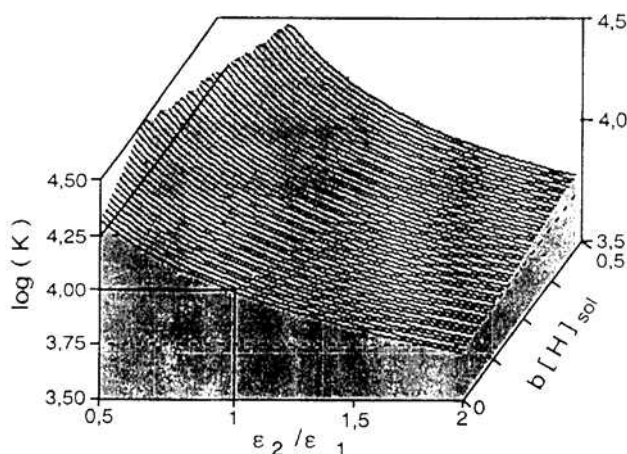


Figure 3. Influence of the variation of the ratio of the molar absorptivities $\varepsilon_2/\varepsilon_1$ and of the product $b [H]_{sol}$ on the calculated stability constant K using equation (9) for a given value of $b = 10\,001 \text{ mol}^{-1}$

the solubility of the host molecule cannot be influenced, an upper limit for the slope b exists.

Treatment of experimental data

The solubility of the crown ether DB18C6 was determined as $(1.7 \pm 0.1) \times 10^{-5} \text{ mol l}^{-1}$ and that of the cryptand (222BB) as $(8.2 \pm 0.1) \times 10^{-4} \text{ mol l}^{-1}$. These results are in good agreement with published data for DB18C6 (2×10^{-5} and $1.28 \times 10^{-5} \text{ mol l}^{-1}$)^{12,17} and the cryptand (222BB) ($6.22 \times 10^{-4} \text{ mol l}^{-1}$).¹³

In Figure 4, the extinctions of solutions saturated with the ligand DB18C6 as a function of the salt concentration are shown. Owing to the complex formation, the concentration of the ligand in solution increases. By extrapolation to zero salt concentration, the value of E_0 can be calculated. E_0 is also directly obtained from the extinction of a saturated solution of the pure ligand. It is possible that the two methods give different values of E_0 . Two explanations are possible. The aqueous solutions of the salts behave differently in the solvation of the ligands compared with the pure solvent or other reactions are possible such as protonation of the ligand. Owing to the interactions of the ligand with protons, the solubility also increases. In the presence of salt concentrations that are relatively high compared with the concentration of the protons, the interactions with the protons have no significant influence on the solubility of the ligands. In both cases the value of E_0 obtained by extrapolation should be used for further calculations.

For both ligands and the corresponding complexes with salts the molar absorptivities are summarized in Table 1. For the ligand DB18C6 no significant differences between the molar absorptivities of the ligand and the complexes are observed with the exception of the complex with Ba^{2+} . Only the complexes of the cryp-

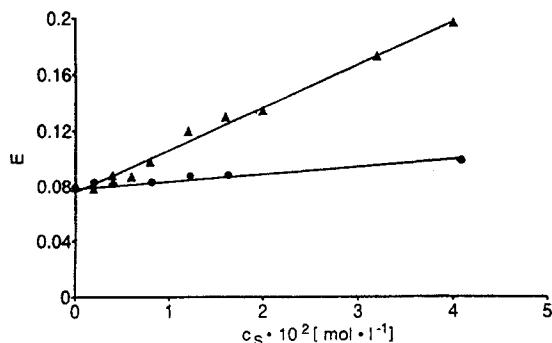


Figure 4. Changes in the extinction E at 274 nm of saturated solutions of the ligand DB18C6 as a function of the salt concentration c_s in aqueous solutions at 20 °C. Salt: (\blacktriangle) KCl; (\bullet) CsCl

Table 1. Molar absorptivities ϵ ($1 \text{ mol}^{-1} \text{ cm}^{-1}$) at 274 nm of the ligands DB18C6 and (222BB) and of the salt complexes in aqueous solutions at 25 °C

| Cation | DB18C6 | (222BB) |
|------------------|----------------|---------------|
| — | 4682 ± 68 | 5046 ± 14 |
| Na^+ | 4780 ± 276 | 4759 ± 40 |
| K^+ | 4760 ± 308 | 4912 ± 16 |
| Rb^+ | 4961 ± 241 | 5056 ± 34 |
| Cs^+ | 4980 ± 197 | 5026 ± 8 |
| Ca^{2+} | 4795 ± 232 | 4877 ± 85 |
| Sr^{2+} | 4578 ± 235 | 3877 ± 71 |
| Ba^{2+} | 4232 ± 156 | 4084 ± 42 |

tand (222BB) with Sr^{2+} and Ba^{2+} possess lower molar absorptivities when compared with other complexes and the free ligand.

Since the molar absorptivities of the ligand DB18C6, ϵ_1 , and of all complexes formed, ϵ_2 , and the solubility of this ligand are known, it is possible to calculate the stability constants of the complexes straightforwardly from the measured extinctions of the solutions saturated with the ligand using the material balances.

Another possibility for the calculation of the stability constants is to use equation (8): by plotting $(E/E_0) - 1$ as a function of the total salt concentration C_G , one obtains a straight line with slope b . The stability of the complex formed is then given by equation (9). Now it is possible to discuss the proposed method for the reactions of the ligand DB18C6 under the assumption of unknown molar absorptivities of the ligand and the complexes formed and the solubility of the ligand.

The stability constants for the complexation reactions of the crown ether DB18C6 with alkali and alkaline earth metal cations in aqueous solutions calculated in different ways are summarized in Table 2. Even without the use of the known molar absorptivities and the solubility of the ligand, correct values of the stability constants are calculated using equations (8) and (9). The agreement with already published stability constants is very good.

Since the solubility of the cryptand (222BB) is more than one order of magnitude higher when compared with the crown ether DB18C6, more values of the stability constants with this ligand are available in the literature.¹⁸⁻²⁰ In Figure 5, the extinctions of solutions saturated with the cryptand (222BB) as a function of the salt concentration are shown. All results are given in Table 3. From the increase in solubility of the cryptand (222BB) due to complex formation, the stability constants of the complexes formed can be calculated directly since all molar absorptivities and the solubility of the ligand have been determined. These values are in most cases in accordance with the published stability constants. However, using equations (8) and (9) only in

Table 2. Stability constants, $\log[K(\text{l mol}^{-1})]$, for complex formation of the crown ether DB18C6 with different cations in aqueous solutions at 25 °C calculated using different assumptions

| Cation | Log K^a | Log K^b | Log K^c | Log K^d | Log K |
|------------------|-------------|-----------|-----------|-----------|---------------------------------------|
| Na ⁺ | 1.09 ± 0.05 | 1.09 | 1.07 | 1.09 | 1.16 ^e 1.1 ^f |
| K ⁺ | 1.58 ± 0.03 | 1.78 | 1.56 | 1.60 | 1.67 ^e 1.6 ^f |
| Rb ⁺ | 1.06 ± 0.10 | 1.02 | 0.99 | 0.89 | 1.08 ^e |
| Cs ⁺ | 0.81 ± 0.07 | 0.88 | 0.85 | 0.74 | 0.83 ^e |
| Ca ²⁺ | 0.53 ± 0.28 | — | — | 0.47 | <1 ^e |
| Sr ²⁺ | 0.78 ± 0.13 | 0.73 | 0.70 | 0.75 | 0.99 ^e |
| Ba ²⁺ | 1.74 ± 0.06 | — | 1.76 | 1.75 | 1.96 ^e |

^a Calculated using the estimated values of the molar absorptivities of the ligand, ϵ_1 , and of the complexes formed, ϵ_2 , and the solubility of the ligand.

^b Calculated using equation (8) under the assumptions that ϵ_1 , ϵ_2 and E_0 are known.

^c Calculated using equation (8) under the assumptions that ϵ_1 and ϵ_2 are unknown and E_0 is known.

^d Calculated using equation (8) under the assumptions that ϵ_1 , ϵ_2 and E_0 are unknown.

^e From Ref. 17.

^f From Ref. 13.

some cases can reliable stability constants be obtained. Thus the assumptions made for calculating the stability constants are not valid.

Using the molar absorptivities of the ligands and complexes, the ratio of both values can easily be calculated. For both ligands the stability constants of the complexes formed can be obtained directly from the measurement of the extinction of salt solutions saturated with the corresponding ligands. Hence the product $K[\text{H}]_{\text{sol}}$ can be calculated exactly. The results for both ligands are given in Table 4.

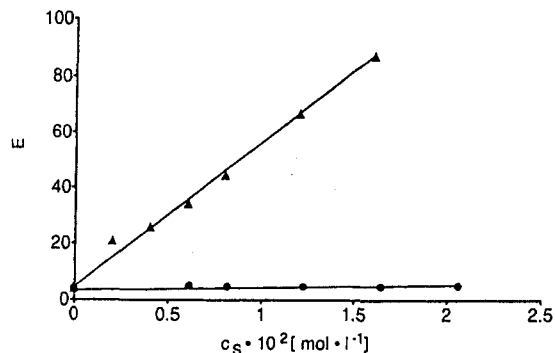


Figure 5. Changes in the extinction E at 274 nm of saturated solutions of the cryptand (222BB) as a function of the salt concentration C_s in aqueous solutions at 25 °C. Salt: (\blacktriangle) KCl; (\bullet) CsCl

Table 3. Stability constants $\log [K(\text{l mol}^{-1})]$ for complex formation of the cryptand (222BB) with different cations in aqueous solutions at 25 °C calculated using different assumptions

| Cation | Log K^a | Log K^b | Log K |
|------------------|-------------|-----------|---|
| Na ⁺ | 4.13 ± 0.23 | 2.97 | 3.44 ^c |
| K ⁺ | 5.01 ± 0.29 | 3.07 | 4.35 ^c 4.62 ^c |
| Rb ⁺ | 2.60 ± 0.10 | 2.40 | |
| Cs ⁺ | 1.08 ± 0.13 | 0.96 | |
| Ca ²⁺ | 3.23 ± 0.19 | 2.52 | 3.45 ^d 2.66 ^e 3.07 ^f |
| Sr ²⁺ | 4.76 ± 0.43 | 3.03 | 6.38 ^d 5.7 ^e 5.65 ^c 5.65 ^d 5.4 ^e |
| Ba ²⁺ | > 5 | | |

^a Calculated using the estimated values of the molar absorptivities of the ligand, ϵ_1 , and of the complexes formed, ϵ_2 , and the solubility of the ligand.

^b Calculated using equation (8) under the assumptions that ϵ_1 , ϵ_2 and E_0 are unknown.

^c From Ref. 13.

^d From Ref. 18.

^e From Ref. 19.

^f From Ref. 20.

Table 4. Ratio of the molar absorptivities of the complexes, ϵ_2 , with the ligands DB18C6 and (222BB) to that of the pure ligands, ϵ_1 , and the product of the stability constant, K , with the solubility of the ligand $[\text{H}]_{\text{sol}}$ in aqueous solutions at 25 °C

| Cation | DB18C6 | | (222BB) | |
|------------------|-------------------------|----------------------------|-------------------------|----------------------------|
| | ϵ_2/ϵ_1 | $K[\text{H}]_{\text{sol}}$ | ϵ_2/ϵ_1 | $K[\text{H}]_{\text{sol}}$ |
| Na ⁺ | 1.02 | 2.1×10^{-4} | 0.94 | 11.1 |
| K ⁺ | 1.02 | 6.5×10^{-4} | 0.97 | 83.9 |
| Rb ⁺ | 1.06 | 2.0×10^{-4} | 1.00 | 0.33 |
| Cs ⁺ | 1.06 | 1.1×10^{-4} | 1.00 | 0.0099 |
| Ca ²⁺ | 1.02 | 5.8×10^{-5} | 0.97 | 1.4 |
| Sr ²⁺ | 0.98 | 1.0×10^{-4} | 0.77 | 47.2 |
| Ba ²⁺ | 0.90 | 9.3×10^{-4} | 0.81 | > 80 |

For both ligands the ratio of the molar absorptivities of the complexes ϵ_2 and of the ligands ϵ_1 varies between 1.06 and 0.77. Such variations do not influence the calculated stability constants, as already demonstrated. For the ligand DB18C6 all values of $K[\text{H}]_{\text{sol}}$ are much smaller than 1 for all complexes. Owing to the higher values of the stability constants of the complexes formed with the ligand (222BB) and the higher solubility of this ligand compared with the ligand DB18C6, the values of $K[\text{H}]_{\text{sol}}$ are greater than 1 with the excep-

tion of Rb^+ and Cs^+ . Only in the case of these two cations do stability constants calculated using equations (8) and (9) give valid values.

CONCLUSION

These results confirm the possibility of determining stability constants with nearly insoluble host molecules. Hence it becomes possible to examine the complexation behaviour of these ligands quantitatively. Host molecules may be, for example, uncharged ligands such as crown ethers, cryptands or other ligands, and the guest molecules may be cations or uncharged molecules. The advantage of this method is that only small amounts of the host molecules are needed for the determination of the stability constants of the complexes formed.

The validity of the discussed assumptions was verified by studying the complexation reactions of dibenzo-18-crown-6 and the cryptand (222BB) in aqueous solutions. If the solubilities of the ligands are low, the stability constants can easily be calculated from spectrophotometric measurements of saturated ligand solutions in the presence of salts, even without knowing the molar absorptivities of the ligand and the corresponding complexes. This new technique offers the opportunity to study complexation reactions inaccessible with potentiometric, conductimetric or other common techniques normally used.

ACKNOWLEDGEMENT

Financial support by the Minister of Science and Technology of Nordrhein-Westfalen is gratefully acknowledged.

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