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The complexation of amino alcohols and amino acids by the crown ether 18C6 and the cryptand (222) in methanol

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Abstract

The complex formation between certain amino alcohols and amino acids and the crown ether (18-crown-6) and the cryptand (222) in methanol was studied by calorimetric titrations. In the case of the amino alcohols, no influence of the number of methylene groups upon the complex formation with both ligands is observed. After protonation of one amino alcohol, the value of the reaction enthalpy with 18-crown-6 is doubled. In comparison with amino alcohols, amino acids form more stable complexes with both ligands. However, favorable enthalpic changes during the complex formation are compensated for by unfavorable entropic contributions. The amino groups of the amino acids are already protonated. Even in methanol as solvent, the amino acids examined exist in their zwitterionic form. © 1998 Elsevier Science B.V.

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1. Introduction

The formation of hydrogen bonds plays an important role in nature [1]. The double helix of DNA is formed by hydrogen bonds between base pairs. This process is highly selective and only a limited number of base pairs is possible.

Artificial receptors for the complexation of molecules which are able to form hydrogen bonds have also been reported [2]. Pedersen [3,4] demonstrated that derivatives of 18-crown-6 form stable complexes with alkylammonium ions. In the meantime, the complex formation between the ligand 18-crown-6 and the cryptand (222) and ammonium and substituted ammonium ions has been studied in detail in methanol [5–7]. However, only few results are available in other solvents and with other ligands [8]. The complexation of ammonium ions by macrotricyclic cryptands has also been reported [9,10]. Few results have been published for the complexation of molecules with uncharged amino groups [11,12].

Amino acids are among the most important classes of natural chemical compounds. They form complexes with 18-crown-6 and the cryptand (222) [13,14] and also with other macrocyclic ligands [15]. The stability of the complexes formed with naturally occurring amino acids depends strongly upon the degree of the protonation [15]. Due to complex formation, the solubility of the amino acids in organic solvents is enhanced [16]. Macrocyclic and macrobicyclic ligands are able to transport amines and amino acids through liquid membranes [17,18].

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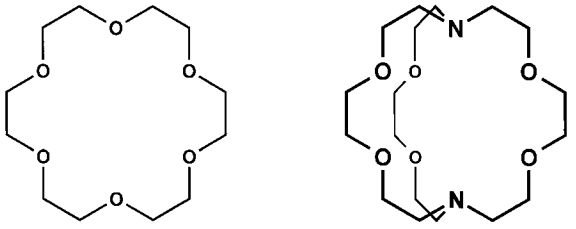

Fig. 1. Chemical structures of the ligands used.

In order to obtain more information about the complexation of amino compounds by macrocyclic and macrobicyclic ligands, the reaction between amino alcohols and amino acids and 18-crown-6 and the cryptand (222) was studied by calorimetric titrations.

2. Experimental

The ligand 18-crown-6 (18C6) and the cryptand (222), see Fig. 1 (all Merck) were used without further purification. The amino compounds ethanolamine, 4-amino-1-butanol, 6-amino-1-hexanol, ß-alanine (ß-ala), 5-amino-pentanoic acid (pent) and 8-amino-octanoic acid (oct) (all Fluka) were of the highest purity commercially available. The protonated 6-amino-1-butanol was prepared by the addition of hydrochloric acid to an aqueous solution of this amine. After neutralization, an aqueous solution of $NaBPh_4$ (Fluka) was added. The precipitating ammonium tetraphenylborate salt was washed with water and recrystallized from a mixture of water and acetone.

Anhydrous methanol (H_2O content <0.005%, Merck) was used as solvent.

All stability constants and thermodynamic parameters were determined from calorimetric titrations using a Tronac Model 450 calorimeter. During the titration, a solution of the ligands 18C6 or (222) (0.06–0.08 mol/l) is added continuously to a solution of a guest molecule ($4–5\times10^{-3}$ mol/l). The heat Q produced during the titration is related to the reaction enthalpy after correction of all non-chemical effects by the following equation:

$$Q = \Delta n \times \Delta H$$

The number of the complexes formed during the titration Δn depends on the stability constant. The mathematical treatment of the experimental data has been described in the literature in detail [19–21]. The accuracy of the results obtained from calorimetric titrations compared with other experimental techniques has already been shown [22]. All titrations are performed at least three times.

3. Results and discussion

The results for the complexation of amino alcohols and amino acids by the ligands 18C6 and (222) are summarized in Table 1.

The stability constants for the complexation of amino alcohols by both ligands are nearly identical. However, the values of the reaction enthalpies and entropies are quite different. The values of reaction enthalpies for the reaction with the ligand (222) are more than 10 kJ/mol smaller when compared with 18C6. This reduction in the values of the reaction enthalpies is compensated for by the reaction entropies. Comparable observations have been reported for the complexation of naturally occurring amino acids. With both ligands, the number of methylene groups between the amino- and hydroxy group has no influence on the stability constants and thermodynamic parameters. In case of the ligand 18C6, there is nearly no difference between the values of the reaction enthalpies for the complexation of *n*-butylamine, amino alcohols and deprotonated amino acids, like, e.g. l-ala, within the experimental error.

The protonation of 6-amino-1-hexanol nearly doubles the value of the reaction enthalpy for the complex formation with 18C6. This value is identical with those observed for the complexation of amino acids. The chemical structure of the amino acids also influences the complex formation as it can be seen by comparing the results of ß-ala and l-ala. Obviously, the number of methylene groups between the amino and carboxylic groups has an influence on the reaction enthalpies with 18C6. With increasing number of methylene groups, the values of the reaction enthalpies increase. In contrast, the value of the reaction entropies decreases with increasing number of

Table 1
Stability constants (log K, K in l/mol) and thermodynamic parameters ΔH and $T\Delta S$ (kJ/mol) for the complexation of different amino alcohols and amino acids by the ligands 18C6 and (222) in methanol at 25°C

ligand	Amine	log K	$-\Delta H$	$T\Delta S$
18C6	n-$NH_2C_4H_9$	2.60±0.05 [a]	31.5±0.3 [a]	−16.7±0.6 [a]
	$NH_2(CH_2)_2OH$	2.31±0.10	29.7±2.1	−16.6±2.7
	$NH_2(CH_2)_4OH$	2.47±0.41	35.9±2.5	−21.9±4.9
	$NH_2(CH_2))_6OH$	2.66±0.12	33.8±0.1	−18.7±0.8
	l-ala$^-$		34.1±2.0 [b]	
	$^+NH_3(CH_2)_6OH$	2.81±0.22	60.4±0.7	−44.4±1.9
	l-ala	3.24±0.01 [b]	46.2±2.6 [b]	−27.8±2.7 [b]
	ß-ala	4.19±0.24	52.2±1.1	−28.4±2.5
	pent	3.56±0.06	62.4±0.5	−42.20±0.9
	oct	3.53±0.08	69.6±0.6	−49.5±1.0
222	$NH_2(CH_2)_2OH$	2.55±0.09	17.4±1.3	−2.9±1.8
	$NH_2(CH_2)_4OH$	2.61±0.10	20.8±1.5	−5.9±2.0
	$NH_2(CH_2))_6OH$	2.59±0.08	17.5±0.9	−2.8±1.4
	l-ala	3.11±0.09 [b]	16.0±0.8 [b]	1.6±1.2 [b]
	ß-ala	4.83±0.05	39.7±0.9	−12.2±1.1
	pent	3.69±0.07	40.7±1.2	−19.7±1.6
	oct	4.14±0.04	38.1±0.7	−14.6±0.9

[a] From Ref. [11].
[b] From Ref. [15].

methylene groups. As a result, the stability constants hardly vary.

The same interpretation is valid for the reactions with the macrobicyclic ligand (222). The values of the reaction enthalpies with amino acids are higher when compared with the amino alcohols. Again, the self-protonation of the amino group is responsible. The number of methylene groups between the amino and the carboxylic groups has no influence on reaction enthalpies with (222).

The most important factor for the formation of complexes of amino alcohols and amino acids with macrocyclic and macrobicyclic ligands is the protonation of the amino groups. Due to self-protonation of the amino groups of the amino acids, the measured values of the reaction enthalpy are higher. However, this is compensated by entropic contributions.

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