CONFORMATIONAL FACTORS IN THE COMPLEXATION OF TETRAOXACROWN ETHERS

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The conformational changes in tetraoxacrown ethers (ring size 12-16) during hypothetical reaction with alkali-metal ions were investigated by the method of penalty functions. An analysis is made of the variation of the selectivity curves of crown ethers, calculated by the method of atom-atom potential functions, with variation in the length of the methylene chains between the donor atoms. It is shown that the important factor for the effective complexation of macroheterocycles is not the formal correspondence between the size of the ion and the cavity of the ligand but the possible adjustment of the macrocycle for complementary combination with the cation with minimal expenditures of conformational energy.

The ability of a macrocyclic ligand to adapt its cavity to ions of various sizes is one of the principal factors which determine the selectivity of the complexation of the ligand. The change in the conformational energy of the macrocycle during substitution of one cation in the complex by another can be taken into account approximately by modeling the coordination polyhedron with optimum size for a given cation. (If account is taken of the fact that the bond between the donor center and the ion during the complexation of a crown ether with alkali-metal cations mainly has ion—dipole character [1], the coordination polyhedron can be modeled by the method proposed in [2, 3].)

In this method the donor atoms of the ligand are fixed at a specific distance \( l_0 \) from the point simulating the position of the cation (PSC) by means of a penalty added to the conformational energy of the ligand \( E_{\text{conf}} \). The target function \( F \) is then constructed and in our case has the following form:

\[
F = E_{\text{conf}} + C_1 (r_1 - r_1^0)^2 + C_2 \sum_{i=1,2} (\alpha_i - \alpha_i^0)^2 + C_3 \sum_{i=1}^n (l_{qi} - l_0)^2 + \sum_{i=1}^{N-n} (d_i - l_0)^2, \quad (d_i < l_0),
\]

where the second and third terms are the penalties imposed for closure of the ring; the fourth is the penalty for departure of the dimensions of the coordination polyhedron from the required value \( l_0 \); the fifth is the penalty which prevents entry of the nondonor atoms of the ligand into the coordination polyhedron; \( C_1, C_2, C_3, \) and \( C_4 \) are empirical constants; \( r_1 \) and \( r_1^0 \) are the real and equilibrium values of the bond length between the first and last atoms of the macrocycle; \( \alpha_i, \alpha_i^0, \) \( \alpha_2^0 \) are the real and equilibrium values of the first two bond angles of the ring; \( l_{qi} \) is the distance from the PSC to donor center \( i \); \( d_i \) is the distance between the PSC and atom \( j \); \( n \) is the number of donor centers; \( N \) is the number of atoms in the ligand molecule. The target function was minimized with respect to the independent torsion angles of the macrocycle and the coordinates of the PSC. The conformational energy of the ligand was calculated by the method of atom-atom potential functions in terms of the Wipff—Weiner—Kollman force field [4].

Fig. 1. The selectivity curves of the ligands: a) 12-Crown-4 (●), 13-crown-4 (O), 14-crown-4 (*); b) 15-crown-4 (O), 16-crown-4 (●), 1,4,7,10-tetraoxacyclotetradecane (*).

By repeating the minimization procedure for F with each new value of $l_0$, varied over a range covering all the interesting cations, we obtained curves for the dependence of the conformational energy of the ligand on the size of the hypothetical coordination polyhedron $l_0$. If such a curve is constructed in relation to the conformational energy level of the ligand in the free state, then each point on this curve ($l_{0j}, E_{conf,j}$) reflects the energy expenditures of the free ligand on adjustment to the conformation, which is presumably characteristic of the complex with the cation $j$ separated from the donor atoms by the distance $l_{0j}$. The minimum on such a curve corresponds to the cation for complexation with which the ligand acquires minimum energy expenditures on conformational rearrangement. Therefore, the indicated relationships can be interpreted as complexation selectivity curves. During the assignment of the length of the coordination bonds ($B - M^{n+}$) to one or the other alkali (or alkaline-earth) cation we used the table given in [3].

In the present article an attempt was made to investigate the effect of the ring size and the length of the methylene chains between the donor atoms in tetraoxacrown ethers on the energy expenditures for conformational adjustment of the ligand to the cation during complexation by means of the described mathematical apparatus. As subjects for investigation we chose the following series of compounds: 1,4,7,10-tetraoxacyclododecane (12-crown-4) (I); 1,4,7,10-tetraoxacyclotridecane (13-crown-4) (II); 1,4,8,11-tetraoxacyclotetradecane (14-crown-4) (III); 1,4,8,12-tetraoxacyclopentadecane (15-crown-4) (IV); 1,5,9,13-tetraoxaclohexadecane (16-crown-4) (V); 1,4,7,10-tetraoxacyclotetradecane (VI). The PSC was close to the macrocycle, taking $l_0$ values from the range of 0.340-0.170 nm which includes the lengths of the coordination bonds with oxygen for the majority of the cations. It should be noted that the form and relative position of the complexation selectivity curve depends on the choice of initial approximation [5]. Therefore, during choice of the initial conformation of the ligand we started from the values of the torsion angles corresponding to the conformation of the macrocycle in the complexes (according to X-ray crystallographic data), or we modeled the conformation with the optimum values of the torsion angles [6, 7]. For the analysis of the change in the form of the macrocycles along the selectivity curves we used harmonic analysis [8], in terms of which the real conformation of the ring is treated as the superimposition of basic conformations (BC) of a strictly defined form.

The selectivity curve of 12-crown-4, obtained from the "maxidentate" initial conformation [9] (Fig. 1a), does not have a clearly defined minimum. The region of the minimum values of $E_{conf}$ extends from 0.21 to 0.34 nm. The conformation of the macrocycle, which has $C_4$ symmetry and consists of the BC of the fourth family to the extent of 95%, does not change appreciably in this range. With decrease in the length of the hypothetical coordination bond $l_0$ the macrocycle, while retaining its symmetry, is "flattened" (Fig. 2), the general nonplanarity and folding amplitudes [8] decrease in line (from 0.147 to 0.120 and from 1.92 to 1.48 rad respectively), the degree of "sphericity" and "convexity" of the macrocycle decreases a little [8] (to 93%), and the fraction of the fourth-family BC decreases to 68%