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Complexation of Tetracationic Cyclophane with Some Benzene Derivatives: A Theoretical-Computational Study

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Abstract: Complexation of tetracationic cyclophane with a number of benzene derivatives was investigated by means of *ab initio* method at the second-order Møller-Plesset perturbation (MP2) level of theory using 6-311G++(d,p) basis set. A fair correlation was found between the MP2/6-311G++(d,p) calculated binding energies and the experimental ones, which enabled the MP2/6-311G++(d,p) calculation to predict the experimental binding energies for a number of important complexes. A good structure-activity relationship was also found between the MP2/6-311G++(d,p) calculated binding energies and the substituent molar refraction (R_m) and Hammett constants (σ), indicating that the van der Waals force and the electronic interactions constituted the major driving forces for the complexation of tetracationic cyclophane.

Key words: Complexation, Tetracationic cyclophane, Benzene derivatives, MP2/6-311G++(d,p) method

INTRODUCTION

The molecular recognition of tetracationic cyclophane, 1, has drawn great attention recently, due to its important applications in the design and synthesis of electrochemically and chemically switchable rotaxanes, photoactive rotaxanes and other molecular devices [1]. Usually, this type of molecular recognition was investigated with the methods including X-ray, NMR, UV and IR. However, since these methods usually have difficulties in providing a detailed understanding of the energetic and structural properties of the complexes, molecular modeling method becomes important in this field.

To date, though several groups have done some molecular modeling of the molecular recognition of 1, the real application of this approach has not been established yet [2-4]. Also, the driving force leading to the complexation still remains far from clear [5]. Herein, we wish to report a novel method of predicting the binding energy of 1 with symmetric disubstituted benzenes based on the ab initio molecular orbital calculation. We also wish to report the novel structure-activity correlation, which provides important insights into the driving forces of the complexation.

MATERIALS AND METHODS

All the calculations were performed using the GAUSSIAN 98 software [6]. 1 was optimized by MP2/6-311G++(d,p) from the crystalline structure. The inclusion complex was constructed from separately MP2/6-311G++(d,p)-optimized 1 and 1,4-disubstituted benzene derivatives. The energy minima corresponding to centrally symmetric geometries of the host were sought [5]. and no constraints were employed in the optimization. Finally, frequency calculations using MP2/6-311G++(d,p) were performed to confirm the completeness of optimization.

RESULTS AND DISCUSSION

Figure 1 shows the optimized structure of the complex of 1 with benzene, which was characteristic of all the symmetric inclusion complexes of 1. As seen, the optimized complex reflected substantial inclusion of the guest in the central cavity of the host, which well reproduced the experimental observations [7].

Table 1 summarized the calculated binding energies of the complexation of 1 with 1,4-disubstituted benzene derivatives. Plotting the calculated binding energies against the available experimental values of the nine

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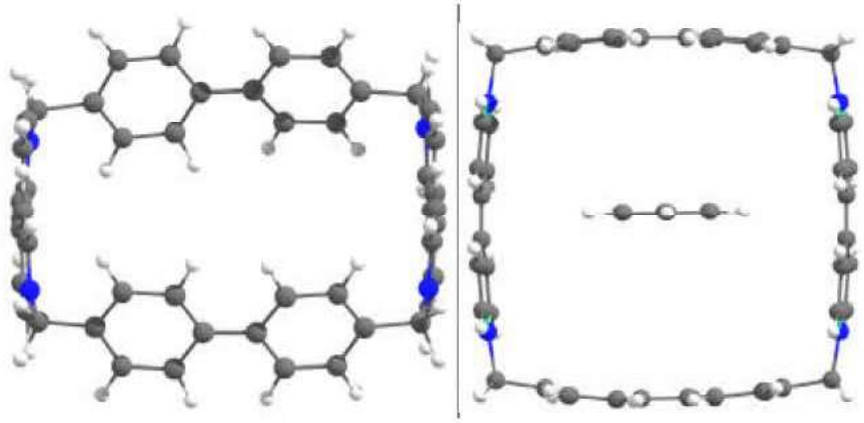


Fig. 1: Two views of the optimized complex of 1^{4+} with benzidine

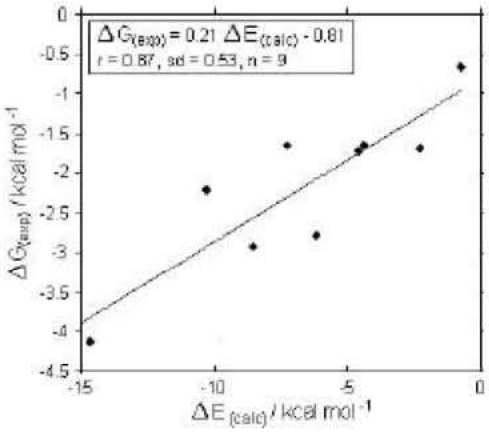
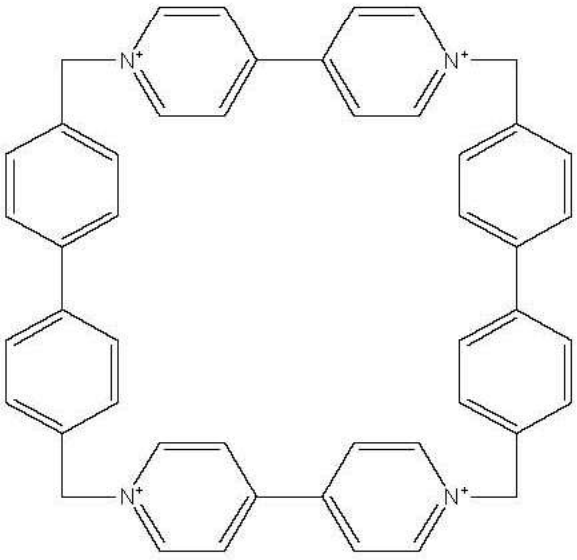


Fig. 2: Plot of the calculated binding energies *versus* the experimental ones



Scheme 1: Chemical structure of cyclobis paraquat-*p*-phenylene)

Table 1: The calculated binding energies of the complexation of 1 with disubstituted benzene derivatives. (kcal/mol)

No.	Guest	ΔE (calc.)	ΔG (exp.)[a]	ΔG (pred.)
1	Benzene	-2.29	-1.68	-1.29
2	$CH_3C_6H_4CH_3$	-4.38	-1.64	-1.73
3	HOC_6H_4OH	-4.58	-1.71	-1.77
4	$NH_2C_6H_4NH_2$	-6.15	-2.79	-2.10
5	$NO_2C_6H_4NO_2$	12.87	-	1.89
6	$CF_3C_6H_4CF_3$	8.90	-	1.06
7	CNC_6H_4CN	12.06	-	1.72
8	FC_6H_4F	3.83	-	0.00
9	$CHOC_6H_4CHO$	1.78	-	-0.44
10	$Me_2NC_6H_4NMe_2$	-10.27	-2.21	-2.97
11	ClC_6H_4Cl	-0.72	-0.65	-0.96
12	$CH_3OC_6H_4OCH_3$	-7.28	-1.64	-2.34
13	4,4'-Biphenol	-8.55	-2.93	-2.61
14	Benzidine	-14.65	-4.12	-3.89

[a]The data were cited from ref [3].

complexes gave a straight line with a fair correlation coefficient of 0.87. (Figure 2) Though this correlation coefficient was not very high, because the present study did not take the solvation effect into consideration due to the technique difficulties, the result was still valuable in predicting the binding energies of 1 with a number of important guests, which remained unavailable due to the experimental limitation. Table 1 listed the predicted binding energies for the guests typically used in the synthesis of rotaxanes. As seen, the predicted values were usually close to the experimental ones, indicating the reliability of the approach. Also, it showed that the binding energies of 1 were strongly dependent of the nature of the guests, which enabled the design of very interesting molecular devices.

Interestingly, a good structure-activity relationship was found between the MP2/6-311G++(d,p) calculated binding energies and the substituent molar refraction constants R_m and Hammett σ constants for the 1,4-disubstituted benzenes [8,9]. The regression fits the following equation,

$$\Delta E\ (calc) = 0.03\, R_m + 14.22\, \sigma - 0.12 \quad (1)$$
$$(r = 0.94,\ sd = 2.84,\ n = 12)$$

The correlation coefficient (0.94) was good enough to indicate a significant dependence of the binding energy on the properties of the substituents. As seen, the regression coefficient of R_m (0.03) was positive, indicating that increasing the size of the substituent disfavored the complexation. This was understandable, since the cavity of 1 was not large and size-fitness was thus important for a good complexation. The regression coefficient of σ (14.22) was also positive. This indicated electron-withdrawing groups would disfavor the complexation, while electron-donating substituent would enhance the complexation. Hence, electrostatic interaction was a driving force for the complexation of 1. Examination of the t-value of the regression indicated that σ parameter had a much larger t-value (8.44) than R_m (0.13). Thus, electrostatic interaction was much more important to the complexation of 1 than the van der Waals forces. This conclusion has been proposed before [10], because 1 was a highly positive charged host molecule. However, the demonstration here by the structure-activity correlation was much more cogent and straightforward.

CONCLUSION

MP2/6-311G++(d,p) was found to be a good theoretical method in modeling the molecular recognition of tetracationic cyclophane. The results could be used to predict the experimental binding energies, which were fundamentally important to rotaxane chemistry but often unavailable experimentally. Structure-activity analysis indicated that the major driving force of the complexation was the electrostatic interaction, followed by the van der Waals interactions.

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