



NMR Studies of Host–Guest Complexes of Anionic Cyclophanes with Dopamine and Its Analogues in Aqueous Media

CLAUDIA VIRUÉS, ENRIQUE F. VELÁZQUEZ*, MICHIKO B. INOUE and MOTOMICHI INOUE
Departamento de Investigación en Polímeros y Materiales, Universidad de Sonora, Apdo. Postal 130, Hermosillo, Sonora 83000, México

(Received: 19 May 2003; in final form: 14 October 2003)

Key words: cyclophanes, dopamine, host–guest complexes, NMR

Abstract

NMR studies were carried out on the complexation of dopamine, tyramine and phenethylamine with cyclophanes that incorporate two phenylene groups in the macrocyclic framework and four pendant carboxylate arms: the cyclophanes studied were 2,9,18,25-tetraoxo-4,7,20,23-tetrakis(carboxymethyl)-1,4,7,10,17,20,23,26-octaaza[10.10]paracyclophane (**1**), its 2,5-dimethyl-*p*-phenylene derivative (**2**) and tetramethyl-*p*-phenylene derivative (**3**). The formation constants of the 1:1 host–guest complexes, $K = [\text{HG}]/[\text{H}][\text{G}]$, were determined as: 17–23 for the complexes of **1** with the aromatic amines; 20 for **2**–dopamine complex, 12–14 for **2**–tyramine and 3–8 for **2**–phenethylamine; 16 for **3**–dopamine, 6 for **3**–tyramine and 4 for **3**–phenethylamine. The formation constants of the complexes of the methyl-substituted cyclophanes, **2** and **3**, show a clear increase in the order phenethylamine < tyramine < dopamine, whereas the stabilities of the complexes of **1** are less dependent on the nature of the guest molecules. The introduction of methyl groups increases the selectivity towards dopamine, although the stabilities of the complexes are decreased by the steric effect of the methyl groups. The benzene rings of the host and guest molecules are stacked face-to-face in a slipped manner. Transannular interaction in this stack and an electrostatic interaction between the NH_3^+ group of the guest and the $-\text{CO}_2^-$ group of the host are the major binding forces for complexation.

Introduction

Supramolecular assemblies of molecules held together by non-covalent bonds or weak intermolecular forces have been reported for a class of synthetic macrocycles which incorporate phenylene groups as an integral part of the macrocyclic ring framework; these macrocycles are known as cyclophanes [1–10]. In this type of supramolecular complexes, or host–guest complexes, cyclophanes function as hosts to selectively bind or include an apolar ring of an aromatic molecule. Of special interest to us are the water-soluble cyclophanes that recognize highly bio-active organic molecules in aqueous media. One of our principal target organic guest molecules is dopamine, which belongs to a family of catecholamine neurotransmitters. A major binding force of a cyclophane in aqueous media arises from hydrophobic (or solvent-exclusion) effects. Since this force is weak, introduction of electrostatic binding sites is required to enhance selective complexation capability; hydrogen bonding is ineffective in aqueous media. In our previous paper, we reported that dopamine and tyramine were selectively recognized by a cyclophane that involved two diphenylmethane or diphenyl ether groups as an integral part of the cavity and four carboxylate groups as pendant arms [11]. Thus, it has been confirmed that the combined effect of the $-\text{CO}_2^-$ arms

and the aromatic cavity leads to selective molecular recognition towards the aromatic amines. The structures of the resulting host–guest complexes, however, have not been well elucidated, because of the complicate conformation of the cyclophane framework. For this reason, we have designed simpler cyclophanes, which are shown in Figure 1: cyclophane **1** that consists of two *p*-phenylene groups, its dimethyl-*p*-phenylene derivative (**2**) and tetramethyl-*p*-phenylene derivative (**3**). The simplification of the macrocyclic framework is expected to facilitate the determination of geometrical relation between host and guest molecules in their complexes; the size of the cavity is reduced, still sufficient for encapsulating a guest amine molecule. Methyl groups in cyclophanes **2** and **3** enhance the hydrophobicity of the cavity and also the steric constraint in the macrocyclic framework. These effects are supposed to influence the capability of forming inclusion complexes and hence the selectivity towards specific guest molecules. This paper reports ^1H NMR studies of host–guest complexes of these cyclophanes with dopamine, tyramine and phenethylamine in D_2O media; the formation constants have been determined for the host–guest complexes, and geometrical relation between the constituent molecules has been proposed on the basis of the ring-current effect on chemical shift.

* Author for correspondence. E-mail: evlzqz@guaymas.uson.mx

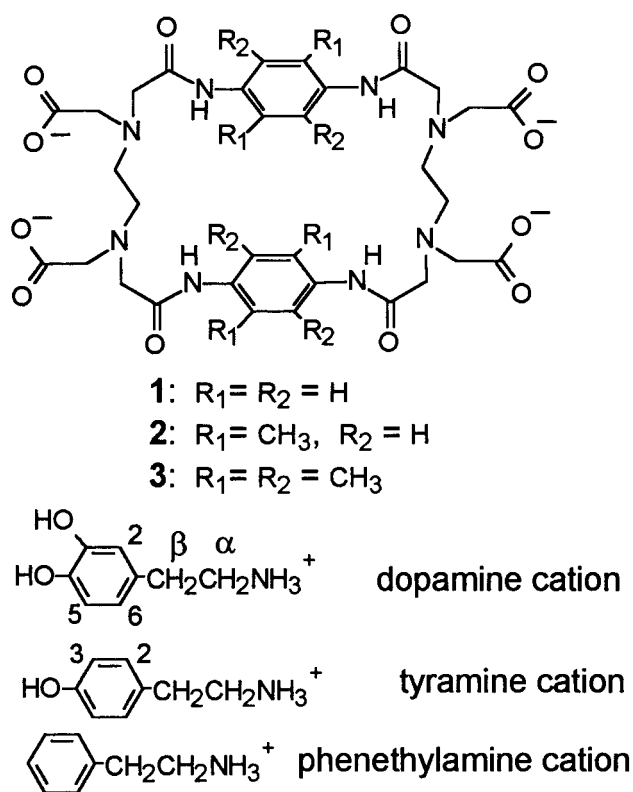


Figure 1. Host and guest molecules studied in this work.

Experimental

The macrocycles were synthesized by the methods reported previously [12, 13]. The products isolated as the Li salts were purified further by the use of a silica gel 60 (230–400 mesh) column with an ethanol/water (8:2) eluent. The purity was checked by 1H NMR. The Li salts were converted to the corresponding acids by the use of dilute HCl at $pH \sim 2$. Dopamine hydrochloride and tyramine hydrochloride were supplied from Sigma and phenethylamine hydrochloride from Aldrich; they were used without further purification.

1H NMR spectra were obtained with a Bruker AM400 spectrometer operating at 400 MHz at a probe temperature of $30^\circ C$. The internal reference was sodium 4,4-dimethyl-4-silapentane-1-sulfonate (DSS), the concentration of which was kept as low as possible so that possible electrostatic effects with sample compounds were minimized. In titrations, the total concentration of host $[H]_t$ was kept constant at 5×10^{-3} M, and the total guest concentration $[G]_t$ was changed up to 50×10^{-3} M. Stock solutions were prepared by dissolving appropriate host and guest compounds in 99.9% D_2O , and the pD was adjusted to 8.0 ± 0.1 by the use of solid Na_2CO_3 . Sample solutions were prepared by mixing the stock solutions in appropriate ratios, and the pD values were confirmed. The pD values were obtained on the basis of the relation, $pD = pH_{measured} + 0.44$, from pH values measured with a glass electrode that was calibrated with aqueous standard buffers [14]. Dopamine is sensitive to atmospheric oxygen in solution. The sample solutions were,

Table 1. NMR chemical-shift differences, Δ_H , of probe protons of the hosts (total concentration $[H]_t$ 5×10^{-3} M) in the presence of the guests ($[G]_t$ 35×10^{-3} M), the chemical-shift differences, Δ_{HC} , calculated for host signals of host–guest complexes, and the formation constants $K(M^{-1}) = [HG]/[H][G]$

Host	Proton	Guest	Δ_H^a	$\Delta_{HC}^{b,c}$	K^c
1	arH	Dopamine	−0.043	−0.099(2)	23(2)
		Tyramine	−0.036	−0.090(2)	20(2)
		Phenethylamine	−0.027	−0.074(2)	17(2)
2	arH	Dopamine	−0.026	−0.064(2)	20(2)
		Tyramine	−0.022	−0.077(2)	12(1)
		Phenethylamine	−0.011	−0.050(2)	8(2)
	CH ₃	Dopamine	−0.024	−0.062(5)	20(3)
		Tyramine	−0.022	−0.067(4)	14(2)
		Phenethylamine	−0.014	−0.154(2)	3(1)
3	CH ₃	Dopamine	−0.017	−0.044(2)	16(2)
		Tyramine	−0.016	−0.094(4)	6(1)
		Phenethylamine	−0.010	−0.088(2)	4(1)

^a $\Delta_H = \delta_H([G]_t = 35 \times 10^{-3} M) - \delta_H([G]_t = 0)$, $pD = 8.0$ and $T = 30^\circ C$.

^b Shifts referenced to δ_H at $[G]_t = 0$, or $\Delta_{HC} = \delta_H([G]_t = \infty) - \delta_H([G]_t = 0)$.

^c Numbers in parentheses are estimated errors in the least significant digits.

however, stable during the NMR experiments; no coloration was appreciable after the NMR data collection.

Results and discussion

NMR titration and complexation

The NMR studies of complex formation have been carried out at pD 8 for the following reasons: (1) the solubilities of the host cyclophanes decrease rapidly with decreasing pD at $pD < 8$; (2) the guest amines are completely protonated to be in the cationic form at $pD \leq 8$; (3) dopamine is unstable at higher pD ; (4) complexation at pD close to the physiological pH is important for biologically interesting compounds. Around pD 8, the cyclophanes undergo acid dissociation, which results in a large shift in the NMR signals of the aliphatic protons, as reported previously [12, 13]. On the other hand, the signals of protons attached to phenylene groups show a very small pD dependence. The aromatic protons were, therefore, used as probes for studying the complexation. For methyl-substituted cyclophanes, **2** and **3**, the protons of CH_3 bonded to phenylene groups were also used as probes. The pD values of sample solutions were adjusted to 8.0 within a deviation of ± 0.1 ; an error in chemical shift due to a mismatch of pD was small, and was corrected by the use of δ vs. pD curves reported for these cyclophanes [12, 13].

The aromatic proton signals of the host cyclophanes shifted upfield in the presence of the aromatic amines. Table 1 shows the chemical-shift differences, Δ_H , that are the δ values in the presence of the guest amines, with reference to the values in the absence of the amines: $\Delta_H = \delta_H([G]_t = 35 \times 10^{-3} M) - \delta_H([G]_t = 0)$ at $[H]_t = 5 \times 10^{-3}$ M, where $[G]_t$

Table 2. NMR chemical-shift differences, Δ_G , of guest protons (total concentration $[G]_t$ 5×10^{-3} M) in the presence of hosts **1**, **2** and **3** ($[H]_t$ 35×10^{-3} M), and the chemical-shift differences, Δ_{GC} , calculated for host–guest complexes (pD = 8.0, $T = 30$ °C)

	Δ_G^a			Δ_{GC}^b		
	1	2	3	1	2	3
Dopamine ^c						
ar 2	−0.059	−0.027	−0.015	−0.137	−0.068	−0.043
ar 5	−0.045	−0.031	−0.019	−0.104	−0.078	−0.054
ar 6	−0.067	−0.052	−0.027	−0.157	−0.131	−0.077
α -CH ₂	−0.059	−0.048	−0.031	−0.137	−0.119	−0.089
β -CH ₂	−0.064	−0.043	−0.022	−0.148	−0.107	−0.065
Tyramine ^c						
ar 2	− ^d	−0.034	−0.021	–	−0.111	−0.125
ar 3	−0.045	−0.024	−0.017	−0.113	−0.080	−0.098
α -CH ₂	−0.055	−0.041	−0.028	−0.138	−0.136	−0.167
β -CH ₂	−0.059	−0.034	−0.020	−0.147	−0.111	−0.118
Phenethylamine ^c						
ar	−0.046	−0.016	−0.014	−0.127	−0.103	−0.112
α -CH ₂	−0.049	−0.028	−0.023	−0.136	−0.176	−0.190

^a $\Delta_G = \delta_G([H]_t = 35 \times 10^{-3} \text{ M}) - \delta_G([H]_t = 0)$.

^b Shifts referenced to δ_G at $[H]_t = 0$, or $\Delta_{GC} = \delta_G([H]_t = \infty) - \delta_G([H]_t = 0)$.

^c For labeling, see Figure 1.

^d Overlapped with host signals.

^e Averaged value for aromatic protons; β -CH₂ signal was overlapped with host signals.

and $[H]_t$ are the total concentrations of the guest and host, respectively. The signals of the guests also shifted upfield in the presence of the hosts as shown in Table 2, which lists the chemical-shift differences, $\Delta_G = \delta_G(\text{at } [H]_t = 35 \times 10^{-3} \text{ M}) - \delta_G([H]_t = 0)$ at $[G]_t = 5 \times 10^{-3} \text{ M}$. These observations suggest the formation of host–guest complexes. Figures 2 and 3 show the chemical-shift differences Δ_H of the host signals as functions of guest concentration in the range $[G]_t$ 0 – $50 \times 10^{-3} \text{ M}$ at $[H]_t = 5 \times 10^{-3} \text{ M}$. The observation of saturation curves shows that the host–guest complexes have a definite composition. When host and guest are in equilibrium with their 1:1 complex, the formation constant of the complex, $K = [HG]/[H][G]$, can be calculated by Lang’s method [15]. Since $[H]_t$ is constant, Lang’s equation is given by:

$$[G]_{ti}/\Delta_{Hi} = \{[G]_{ti} + [H]_t - (\Delta_{Hi}/\Delta_{HC})[H]_t\} \times (1/\Delta_{HC}) + 1/(K \cdot \Delta_{HC}). \quad (1)$$

Here $[G]_{ti}$ is the total concentration of the guest in the i th sample, Δ_{Hi} is the δ value of the host in the i th sample, with reference to the value in the absence of the guest, i.e., $\Delta_{Hi} = \delta_H([G]_{ti}) - \delta_H(0)$, and Δ_{HC} is the chemical-shift difference of the host signal of the complex, or $\Delta_{HC} = \delta_H(\infty) - \delta_H(0)$. The parameters K and Δ_{HC} were determined by repeating linear least-squares calculations until the linear fits of Equation (1) converged [11, 15]. The obtained values are collected in Table 1. The Lang plots showed a straight line without any systematic deviation for every host–guest combination, giving evidence for the formation of the 1:1 complexes. The probe signals of hosts **2** and **3** in the presence of phenethylamine showed very small changes in Δ_{Hi} with $[G]_{ti}$, and consequently the parameters determined

had a large relative error; in fact, the formation constants determined by two probe signals for the complexes of **2** gave a large difference (Table 1). However, Lang’s plots show a linear relation without a systematic deviation, despite a relatively large standard deviation, suggesting that phenethylamine also forms 1:1 host–guest complexes with **2** and **3**. The solid lines in Figures 2 and 3 are Δ_{Hi} vs. $[G]_{ti}$ curves that were calculated with the K and Δ_{HC} values shown in Table 1; they fit the experimental data quite well for every host–guest combination.

The chemical-shift difference Δ_{GC} of a guest signal in a host–guest complex was calculated by the use of the formation constant of the complex and the shift difference Δ_G observed at given host and guest concentrations on the basis of the relation $\Delta_{GC} = \Delta_G[G]_t/[HG]$. The Δ_{GC} values obtained are shown in Table 2. In the calculations for the complexes of **2**, the formation constants were assumed to be the averages of the values determined by two probe signals, i.e., aromatic proton and CH₃ proton signals. The Δ_{GC} values of the phenethylamine complexes with **2** and **3** are tentative, because the formation constants are very small and have a large relative error due to the small chemical-shift differences.

Host–guest interaction

At pD 8, at which the NMR experiments were carried out, the carboxylate groups of the hosts are in the anionic form [12, 13], and the amino groups of the aromatic amines are completely protonated: $pK_a = 9.83$ for phenethylamine; 9.3 and 10.9 for tyramine [16]. The complexes are, therefore, supposed to be stabilized by an electrostatic interaction between an NH_3^+ group in a guest molecule and CO_2^- groups in a host molecule, together with interaction

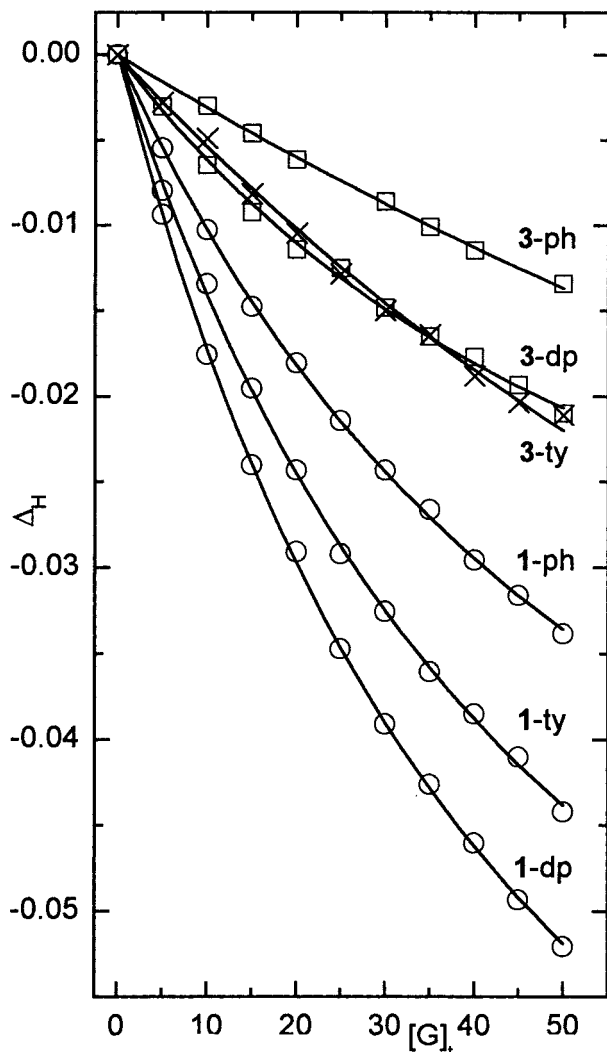


Figure 2. NMR chemical-shift differences Δ_H (with reference to the chemical shifts in the absence of guests) of aromatic proton of host **1** and methyl proton of host **3** as functions of the total concentrations $[G]_t$ of dopamine (dp), tyramine (ty) and phenethylamine (ph): $\Delta_H = \delta_H([G]_t) - \delta_H(0)$. The total concentration of the hosts $[H]_t = 5.0 \times 10^{-3}$ M, pD = 8.0 and $T = 30$ °C. The solid curves were calculated with Δ_{HC} and K values shown in Table 1.

between aromatic groups. The presence of the electrostatic interaction was confirmed by the fact that the α -CH₂ protons of the guests showed upfield shifts in the presence of the hosts (Table 2). The formation constants of the complexes of host **1** with the three guest amines are practically identical, suggesting that the OH groups in the guest amines do not significantly contribute to the stability of the complexes. At pD 8, phenol group is not capable of having an electrostatic interaction because phenol proton is not dissociated, and hydrogen bonding is insignificant in an aqueous solution due to the strong solvation of water.

The NMR shifts of the aromatic protons of the guest amines upon complexation are attributable to the influence from the ring current of the neighboring host molecule. The ring current of a benzene ring produces an angle-dependent magnetic field in its neighborhood. A dipole model shows that the chemical shift is given by [17]:

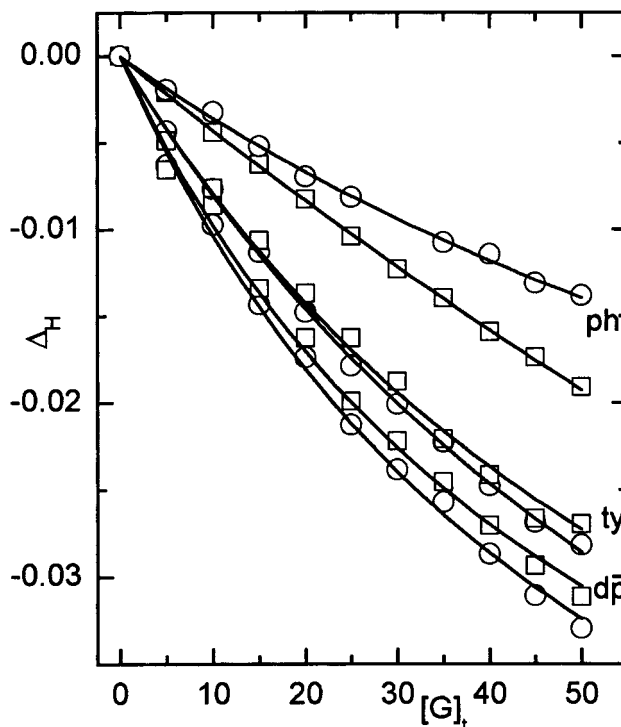


Figure 3. NMR chemical-shift differences Δ_H (with reference to the chemical shifts in the absence of guests) of aromatic proton (circle) and methyl proton (square) of host **2** as functions of the total concentrations $[G]_t$ of dopamine (dp), tyramine (ty) and phenethylamine (ph): $\Delta_H = \delta_H([G]_t) - \delta_H(0)$. $[H]_t = 5.0 \times 10^{-3}$ M, pD = 8.0, and $T = 30$ °C. The solid curves were calculated with Δ_{HC} and K values shown in Table 1.

$$\delta_{rc} \text{ (in ppm)} = 27.6(1 - 3 \cos^2 \theta)/r^3. \quad (2)$$

Here, r is the distance (in Å) between the resonant proton and the center of the benzene ring, and θ is the angle between the r vector and the normal to the ring center. Since both host and guest show upfield shifts (or the δ values decrease) upon complex formation, the aromatic protons of a constituent molecule are located in a region of $\theta < 55^\circ$ from the normal to the benzene-ring center of the counter constituent molecule, and hence the host and guest molecules are stacked on each other basically in a face-to-face manner (rather than a face-to-edge manner). Since a guest proton is susceptible to field produced by two phenylene groups of host **1**, half the Δ_{GC} value of the relevant proton is equal to the δ_{rc} value induced by one of the two phenylene rings of the host molecule in the complex. When the van der Waals contact 3.4 Å is assumed for the face-to-face stack in the complexes of host **1** [18], the r and $\cos \theta$ of a resonant guest proton are given by the distance d , along the phenylene-ring plane, from the normal to the phenylene-ring center of the host: $r = [3.4^2 + d^2]^{1/2}$ and $\cos \theta = 3.4/r$. For **1**-dopamine complex, the substitution of $\delta_{rc} = \Delta_{GC}/2$ in Equation (2) gave $d = 3.8$ Å for aromatic proton 2 in dopamine; 4.0 Å for proton 5; 3.7 Å for proton 6 (for labeling, see Figure 1). The same d values were obtained on the contour map of δ_{rc} based on a double-loop model [19]. These d values indicate the time-averaged positions of the aromatic protons, because the guest molecule reorients rapidly in solution resulting in a

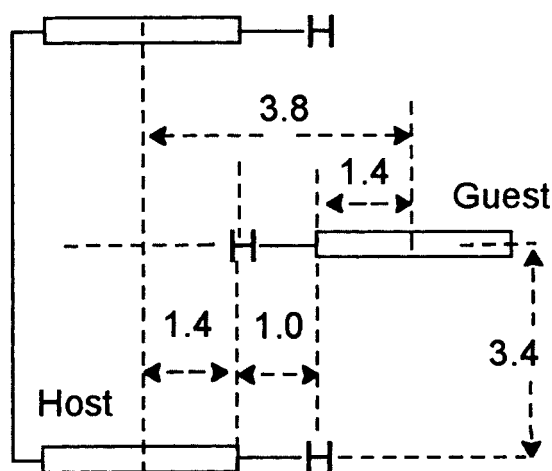


Figure 4. Time-averaged stack proposed for the complexes of host **1**. The aromatic rings of the host and guest molecules are stacked with the van der Waals contact. Benzene ring radius and C–H bond distance are shown in Å.

rapid relocation of the protons attached to the phenyl group. Since the time-averaged positions of all aromatic protons in the guest molecule are practically identical (3.7–4.0 Å), the relocation of all aromatic protons is supposed to occur around a common center, which is most probably the center of the benzene ring to which the protons are attached. In this case, the mean value (3.8 Å) of d gives the position of the benzene-ring center of the guest with respect to the ring center of the host; the benzene rings of host and guest molecules are slipped away from each other by a distance of $d = 3.8$ Å along their molecular planes, as schematically illustrated in Figure 4. In this mode of stack with a slip distance of 3.8 Å, an aromatic proton of guest dopamine resides at a position above a phenylene carbon atom of host **1**. This position is occupied by all aromatic protons in the same probability, with a certain life time, in such a way that the ring center of the guest molecule is kept at $d = 3.8$ Å. When a proton resides above an aromatic carbon atom, an H– π interaction is operative between the atoms, leading to the stabilization of the face-to-face stack. This mode of stacking is consistent with an electrostatic calculation, which reported that a face-to-face stack is stable only in the slipped form [20]. For the complexes of **1** with tyramine and phenethylamine, the time-averaged distances were obtained as $d = 3.9$ Å, suggesting that the mode of host–guest stack is identical with that in the dopamine complex.

In our previous paper, we have reported that dopamine and its analogues are recognized by a cyclophane consisting of four phenylene groups from two diphenylmethane groups, which are involved in place of *p*-phenylene groups in the structure shown in Figure 1; the formation constants of the complexes are 40–500 [11]. A similar cyclophane whose cavity consists of two diphenyl ether groups forms slightly less stable complexes with the aromatic amines, the formation constants being 6–20 [11]. Of the same order of magnitude are the formation constants of the complexes of cyclophane **1**, despite that this host involves only two phenylene groups in the macrocyclic framework. A simple

molecular model shows that the two phenylene groups in the host molecule can be apart up to 8 Å, which is close to twice the distance predicted for the van der Waals contact. Probably, the cavity of **1** is suitably defined for encapsulating a guest molecule; in the resulting host–guest complex the guest molecule is supposed to be inserted between the phenylene groups of the host as schematically illustrated in Figure 4.

For the complexes of methyl-substituted cyclophanes, **2** and **3**, the face-to-face distance between the benzene rings of the host and guest is assumed to be the sum of the van der Waals radius of methyl group 2.0 Å and half the thickness of aromatic ring 1.7 Å [18]. From half the ΔG_C values, the positions of aromatic protons of guest molecules in their complexes were determined as: $d = 4.0$ Å (aromatic proton 6), 4.3 Å (ar 5) and 4.4 Å (ar 2) for **2**–dopamine complex; 4.4 Å (ar 6), 4.5 Å (ar 5) and 4.7 Å (ar 2) for **3**–dopamine; $d = 4.1$ Å (ar 2) and 4.3 Å (ar 3) for **2**–tyramine; 4.0 Å (ar 2) and 4.2 Å (ar 3) for **3**–tyramine; $d = 4.2$ Å and 4.1 Å for **2**–phenethylamine and **3**–phenethylamine, respectively. For every host–guest combination, protons attached to a phenyl group have practically identical d values, and hence the d values indicate the position of the center of the benzene ring in the face-to-face stack, as described for the complexes of **1**. The d values of the complexes of **2** and **3** with dopamine are larger than those in the complexes of **1**. The benzene rings of the host and the guest are, therefore, slipped away to a greater extent in the complexes of the methyl-substituted cyclophanes. Since the C–C bond distance is 1.5 Å and the component of the C–H vector in C–CH₃ along the C–C axis is 0.3 Å, CH₃ protons of the host, in the face-to-face stack with a slipped distance of 4.6 Å, take a position above a carbon atom of the guest ring, and an aromatic proton of the guest resides above the midpoint of the C–CH₃ bond of the host. This mode of stack is supposed to be formed in the time-averaged structure of **3**–dopamine complex, in which the mean value of d is 4.5 Å. For the other complexes of **2** and **3**, the d values are slightly smaller, and hence the aromatic rings of the host and guest are slightly closer to each other. In any case of the methyl-substituted cyclophane complexes, an aromatic proton of a guest is placed outside the axis of the *p* orbital of a host ring carbon; in the complexes of cyclophane **1**, on the other hand, an aromatic proton of a guest molecule resides just above a phenylene carbon atom of the host. The H– π interaction between host and guest is, therefore, weaker in the complexes of the methyl-substituted cyclophanes. This is consistent with the fact that the formation constants of the complexes of **2** and **3** are smaller than those of the corresponding complexes of **1**.

The introduction of methyl groups into the cyclophane molecules is expected to deepen the hydrophobic cavity to enhance the hydrophobic effect in the host–guest interaction. In contrary to this simple expectation, the stabilities of the complexes decrease in the order host **1** > host **2** > host **3** for every guest molecule, and the depth of the insertion of a guest molecule into a host cavity is significantly smaller (or the d values are larger) in the complexes of the methyl-substituted cyclophanes. Probably, the steric effect

of methyl groups obstacles the encapsulation of a guest molecule, and is dominant over the hydrophobic effect. The formation constants of the complexes of **2** and **3** show a clear increase in the order phenethylamine < tyramine < dopamine, whereas the formation constants of the complexes of **1** are less dependent on the nature of the guest molecules. The phenylene-ring plane in cyclophane **3** is rotated by 60–70° from the least-squares planes of the amide groups due to the steric effect of the methyl groups [13]. As a result of this steric constraint, the macrocyclic framework of **3** is less flexible than that in cyclophane **1**, and the cavity of **3** may be more strictly defined to favor the inclusion of a dopamine molecule although the detailed function is not clear. Thus, the selectivity towards dopamine is enhanced by the introduction of methyl groups.

Acknowledgements

The NMR spectrometer was provided by the Secretaría de Educación Pública de México (Project No. SEP/FOMES/99-26-05). CV thanks the Consejo Nacional de Ciencia y Tecnología de México for a graduate scholarship.

References

1. F. Diederich: *Cyclophanes*, The Royal Society of Chemistry, Cambridge (1991).
2. D.J. Cram and J.M. Cram: *Container Molecules and Their Guests*, Royal Society of Chemistry, Cambridge (1994).
3. F. Vögtle (ed.): *Molecular Recognition: Receptors for Molecular Guests*, Comprehensive Supramolecular Chemistry, Vol. 2, Pergamon, New York (1996).
4. K. Odashima and K. Koga: Cyclophanes in Host–Guest Chemistry. In P.M. Keehn and S.M. Rosenfeld (eds.), *Cyclophanes*, Vol. 2, Academic Press, New York (1983), pp. 629–678.
5. I. Tabushi and K. Yamamura: Water Soluble Cyclophanes as Hosts and Catalysts. In F. Vögtle (ed.), *Topics in Current Chemistry 113, Cyclophanes I* (1983), pp. 145–182.
6. Y. Murakami: Functionalized Cyclophanes as Catalysts and Enzyme Model. In F. Vögtle (ed.), *Topics in Current Chemistry 115, Cyclophanes II* (1983), pp. 107–155.
7. T.H. Webb and C.S. Wilcox: *Chem. Soc. Rev.* **22**, 383 (1993).
8. Y. Murakami, J. Kikuchi, Y. Hisaeda, and O. Hayashida: *Chem. Rev.* **96**, 721 (1996).
9. R.M. Izatt, J.S. Bradshaw, K. Pawlak, R.L. Bruening, and B.J. Tarbet: *Chem. Rev.* **92**, 1261 (1992).
10. R.M. Izatt, K. Pawlak, J.S. Bradshaw, and R.L. Bruening: *Chem. Rev.* **95**, 2529 (1995).
11. M.B. Inoue, E.F. Velazquez, M. Inoue, and Q. Fernando: *J. Chem. Soc. Perkin Trans. 2*, 2113 (1997).
12. M.B. Inoue, E.F. Velazquez, F. Medrano, K.L. Ochoa, J.C. Galvez, M. Inoue, and Q. Fernando: *Inorg. Chem.* **37**, 4070 (1998).
13. M.B. Inoue, M. Inoue, R. Sugich-Miranda, L. Machi, E.F. Velazquez, and Q. Fernando: *Inorg. Chim. Acta* **317**, 181 (2001).
14. K. Mikkelsen and S.O. Nielsen: *J. Phys. Chem.* **64**, 632 (1960).
15. R.P. Lang: *J. Am. Chem. Soc.* **84**, 1185 (1962).
16. J.D. Dean: *Lange's Handbook of Chemistry*, 13th ed., MacGraw-Hill, New York (1985), Table 5–8.
17. R.J. Abraham, S.C.M. Fell, and K.M. Smith: *Org. Magn. Reson.* **9**, 367 (1977).
18. L. Pauling: *The Nature of the Chemical Bonds*, 3rd. ed., Cornell University Press, Ithaca, NY (1960), p. 261.
19. C.E. Johnson, Jr., and F.A. Bovey: *J. Chem. Phys.* **29**, 1012 (1958).
20. C.A. Hunter and J.K.M. Sanders: *J. Am. Chem. Soc.* **112**, 5525 (1990).