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Structure of supramolecular complex of flexible molecular tweezers and planar guest in solution

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Abstract—Flexible molecular receptors having three aromatic chromophores can bind electron deficient planar guests both in the crystalline state and in solution. The crystalline complex has a triple-decker type donor–acceptor–donor sandwich arrangement in which the guest located between the two terminal aromatic chromophores of the host. Two orientations of the guest, parallel and cross, with respect to the phenanthrene ring of the host were predicted by a molecular mechanics calculation. The former structure was found in the crystalline state. Although the latter was predicted to be less stable, the observed complexation induced shift of the guest supports this orientation in solution. When the terminal naphthalene ring of the host was changed to a benzene ring, the stoichiometry of the crystalline complex changed either to 1:2 or 2:1 depending on the guest.

1. Introduction

Host–guest chemistry constitutes an important and rapidly growing research area.[1] Many structurally interesting hosts have been synthesized for studying the nature of the binding interactions between hosts and guests. Molecular tweezers,[2] containing two aromatic chromophores connected by a spacer are interesting host since they can bind a guest by squeezing with their arms. On designing molecular tweezers for uncharged planar π-guests, it is believed that pre-organization and rigidity are important requisites since π-stacking interactions[3] in an organic solvent are generally weak. The strong binding of the planar guests was reported in the rigid molecular tweezers,[4] and in some flexible systems.[5]

We have reported that a flexible molecular tweezers type host can be constructed with the dioxa[2.2]orthocyclophanes **1**, (5,8-dihydro-1,4-dibenzo[b,f]dioxocine)[6,7] as a basic skeleton. This was known to have three important conformers (twist-boat, screw, and chair) which are interconverting to each other quite rapidly in solution. In the crystalline state, a derivative of **1** takes the twist-boat conformation in which the two aromatic rings have a nearly perpendicular arrangement.[8] The perpendicular arrangement of the two aromatic rings as was found in Kagan's ether[9] is a good building block for constructing receptors[10] that bind aromatic guests with both face-to-face and face-to-edge interactions.[11] Thus, the compound **2**[6] having two units of the dioxa[2.2]orthocyclophane within the molecule should be a good candidate for the molecular tweezers because the distance between two terminal aromatic rings is ideal (ca. 7 Å) for π–π stacking with a guest when it has a *syn* conformation.[12] However, **2** did not work as molecular tweezers for various electron acceptors in solution and **2** itself has rod-like double screw forms in the crystalline state. The cavity size of **2**, if it took the tweezers type *syn* conformation of the two terminal benzenes in solution should be too small to bind any guests. To expand the cavity size we synthesized compound **3** in which one of the two terminal benzenes of **2** was replaced by the phenanthrene ring. Compound **4** having both the naphthalene and phenanthrene rings was also prepared.

Recently it was found that **4** can bind π-electron deficient guests such as tetracyanoquinodimethane **5** (TCNQ), pyromellitic dianhydride **6** (PDA), tetracyanobenzene **7** (TCNB) effectively to form a 1:1 complex both in solution and in the crystalline state.[13] It was also found that if one of the two binding chromophores was as small as a benzene ring as in **3**, a 1:1 complex formation was not observed in the crystalline state, hence, the cavity size of the tweezers plays an important role in effective binding of the guest. In this paper we reported the detailed mechanism of guest binding for these hosts.

Keywords: molecular tweezer; host–guest chemistry; molecular mechanics; X-ray analysis; chemical shift simulation.

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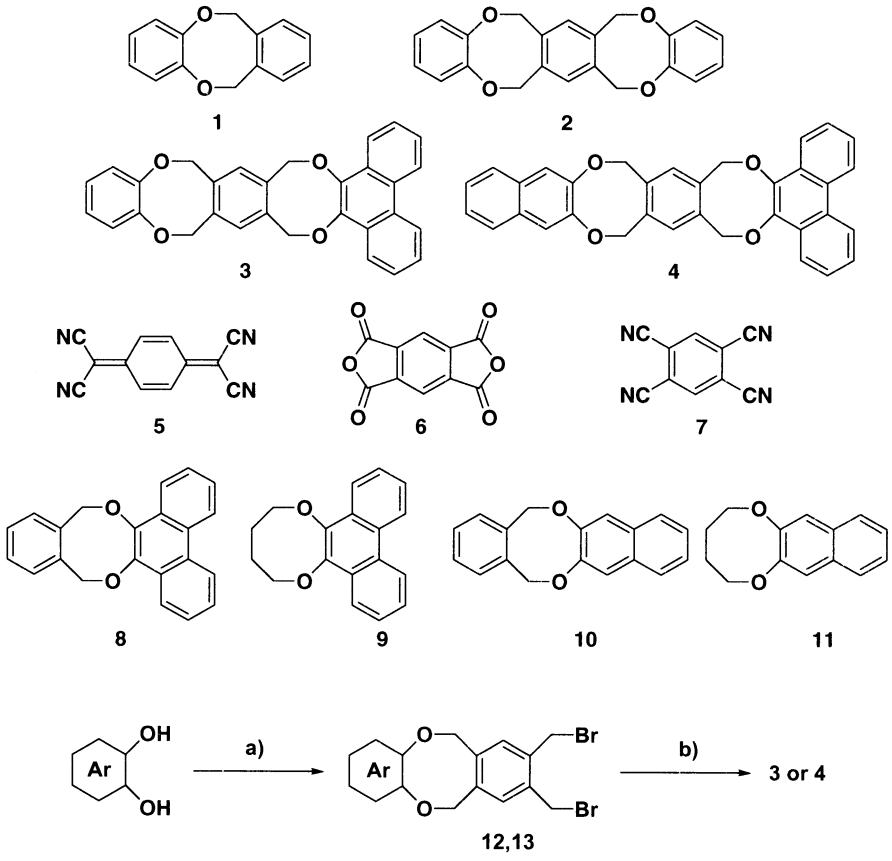

Scheme 1. a) 1,2,4,5-tetrakis(bromomethyl)benzene, Cs_2CO_3, acetone, for **12**: Ar=benzene, 32% for **13**: Ar=naphthalene 28%. b) 9,10-dihydroxyphenanthrene, Cs_2CO_3, acetone, for **3**: Ar=benzene, 53% for **4**: Ar=naphthalene 37%.

2. Result and discussion

2.1. Synthesis

The receptors (**3**,**4**) were synthesized by the successive coupling of 1,2,4,5-tetrakis(bromomethyl)benzene with the corresponding aromatic diols and with 9,10-dihydroxyphenanthrene using Cs_2CO_3 in acetone (Scheme 1).

2.2. X-Ray study of the host–guest complexes

X-Ray crystallographic analyses were carried out in order to know the precise structures of these complexes. As expected, the host clearly has a tweezers type conformation with face-to-face *syn* arrangement of the two terminal aromatic rings in **4·5** (Fig. 1). The two terminal chromophores lie parallel with each other. The distances between the least-squares plane of the two aromatic arms of **4·5** is 6.54 Å. The guest is suitably positioned with stacking interactions to the terminal chromophores and an edge-to-face interaction to the central durene bridge. The distances between the least-squares plane of the two aromatic arms and the guest of **4·5** are 3.31 Å (from naphthalene) and 3.24 Å (from phenanthrene), respectively. Two hydrogens of **5** are pointing to the central durene ring at distances of 2.74 and 2.70 Å, suggesting a favorable distance for the attractive interaction between the hydrogen of the guest and the durene ring of **4**.

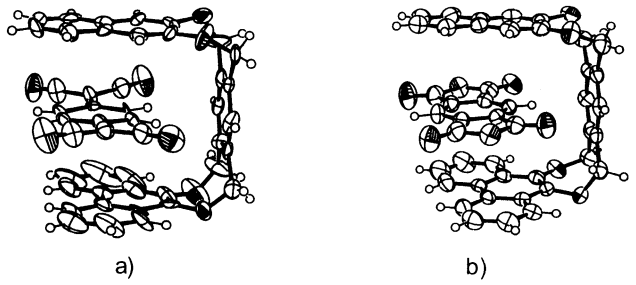

Figure 1. Ortep drawing of (a) **4·5** and (b) **4·6**.

Quite similar stacking mode between **4** and **6** was observed in the crystal of complex **4·6**. It has almost the same face-to-face interactions (interplanar distances of 3.32, 3.33 Å between phenenthrene, naphtharene and guest, respectively) and edge-to-face interaction (a hydrogen of the guest pointing at nearly centroid of the durene unit at a distance of 2.78 Å).

In spite of the close similarity of the structures in **4·5** and **4·6**, relative arrangement of the two terminal aromatic rings in these complexes is quite different. As can be seen in Fig. 2, the two terminal arenes of the complex **4·6** are rotated with each other in opposite direction around the axis connecting the two centroids of the two oxygen carrying six-membered rings. In accord with this rotation, the central durene also rotates to have inclination of the line connecting

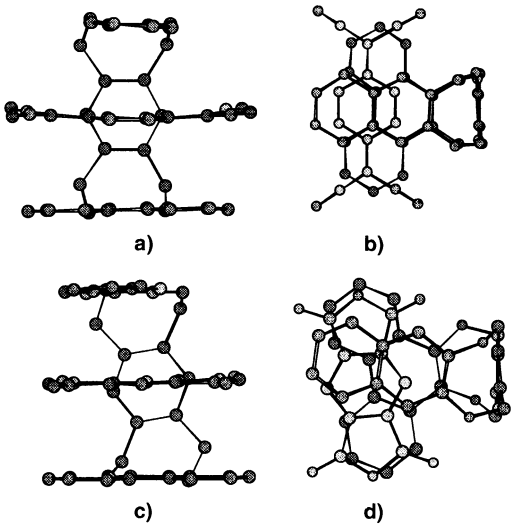

Figure 2. Front (a,c) and top (b,d) views of **4·5** (a,b) and **4·6** (c,d).

the two unsubustituted carbons of the durene ring with respect to the least-squares plane of the phenanthrene ring by ca. 12° (Fig. 2c). On the other hand, the two terminal aromatic rings of **4·5** do not rotate and the two oxygen carrying six-membered rings of the arenes are superimposed when viewed along the perpendicular direction of one of the two terminal arenes (Fig. 2b). Accordingly, no rotation of the central durene moiety was observed.

The binding behavior of the host is quite different if one of the two binding chromophores was as small as benzene ring. Unexpectedly, the 1:1 complex formation was not observed in the crystalline state and the conformer of the host is different from the tweezers form. It gave 2:1 complex, and the conformation of host **3** in the crystalline complex $\mathbf{3}_2\cdot\mathbf{5}$ is 'L' character type conformation, (Fig. 3) in which the phenanthrene and central durene are perpendicular with each other. In the complex, the two phenanthrene chromophores fold the guest with the triple-decker sandwich type arrangement, in which the two hosts grasp the guest both by face-to-face and face-to-edge interactions. While the two arenes (phenenthrene and durene) of **3** contribute significantly for holding the guest, the terminal benzene does not.

The same host holds guest **6** in 1:2 fashion in the crystalline state (Fig. 4). In this complex, host **3** takes 'Z' character form in which three aromatic chromophores form two perpendicular corners. Each corner can hold the guest

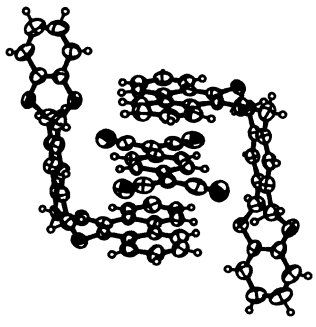

Figure 3. Ortep drawing of $\mathbf{3}_2\cdot\mathbf{5}$.

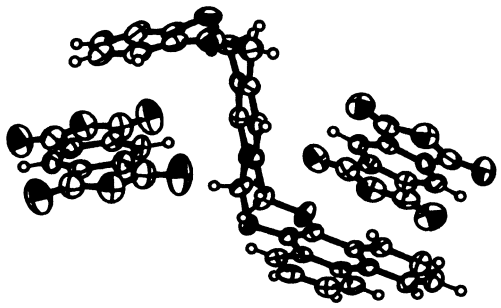

Figure 4. Ortep drawing of $\mathbf{3}\cdot\mathbf{6}_2$.

both by the face-to-face and face-to-edge interactions to form 1:2 crystalline complex.

The crystallographic study of the host–guest complexes has disclosed that at least one perpendicular arrangement of the neighboring chromophores should be a prerequisite for the efficient binding of the planar guest. Both the charge transfer type π–π stacking interaction between the terminal aromatic chromophore(s) and a guest and CH-π type face-to-edge interactions[14] should be the main contributor for the efficient guest binding.

2.3. Binding behavior in solution

Simple aromatics such as benzene and naphthalene showed no propensity for binding, while π electron deficient systems such as **5**–**7** were complexed in solution, hence electron donor–acceptor interaction plays an important role in the binding. New broad charge transfer bands[15] were observed (for **4**; 520 (**5**), 520 (**6**), 460 (**7**) nm, respectively) in $CHCl_3$. A 1:1 stoichiometry of the complex was determined by a continuous variation method using the CT-band in all cases.

The stoichiometry of the complex was further supported by ^{1}H NMR measurement in $CHCl_3$. By titrating a solution of guest with that of a host using the complexation induced shift (CIS) of the guest, a standard hyperbolic curve could be constructed. The association constants were determined by the direct fitting using a nonlinear least squares procedure with damping Gauss–Newton algorithm.[16] They are shown in Table 1 together with those of the reference

Table 1. Association constants in $CDCl_3$ at 26°C

	3	4	8	9	10	11
5	35(3)	130(2)	190(70)	56(4)	–	–
6	60(7)	1000(100)	95(13)	34(2)	46(11)	1.4(5)
7	73(2)	1000(110)	41(11)	27(4)	12(3)	10(1)

Table 2. Complexation induced shift of fully bound guest (ppm)

	3	4	8	9	10	11
5	1.34(6)	1.64(2)	0.28(1)	0.24(6)	–	–
6	1.10(4)	1.30(3)	0.43(1)	0.36(1)	0.10(3)	0.46(1)
7	1.07(1)	1.35(6)	0.46(1)	0.70(6)	0.33(1)	0.27(1)

hosts. The same fitting procedure also gave the CIS value of the fully bound guest (Table 2).

The association constants of **4** are all larger than that for **3**, reflecting the better donor–acceptor interaction between the host and guest, because the former has larger terminal aromatic chromophore than **3** has. The association constants of host **3** with **6** and **7** are almost identical to those of reference host **8**. The host of $\mathbf{3}_2\cdot\mathbf{5}$ in the crystalline state has L character form and the terminal benzene ring does not contribute in the guest binding. Hence, the similarity of the association constants suggested that the terminal benzene ring of **3** does not contribute for the guest binding also in solution. However, the structure of these complexes in solution should be quite different with each other, because the CIS values of **3**·**6** and **3**·**7** are far larger than that of **8**·**6** and **8**·**7**, respectively. Since the binding constants of reference host **9** toward **6** and **7** are not so different from that of host **8**, it suggested that the 9,10-dioxyphenenthrene ring itself is the main contributor for the guest binding in host **3**. The binding constants of reference host **10** toward **6** and **7** are also not so different to that of host **9**. It is interesting that the product of the two binding constants ($ka_{9\cdot6} \cdot ka_{10\cdot6}$) is close to that of host **4**. This might be an evidence for the cooperative contribution of both of the terminal aromatic chromophores, phenanthrene and naphthalene, for the guest binding of **4** in solution. The same is true for the binding of **7**, though the product of the two binding constants is one third of that for **4**.

It is known that the association constant of flexible molecular tweezers and an electron deficient guest is solvent dependent. In order to know the solvent effect for the host–guest complexation, ^{1}H NMR titration was carried out in acetone-d_6, however, neither **3** nor **4** showed any propensity for binding any guests. This result showed that the polarity of the solvent has a very important role in the guest binding.

2.4. Modeling study of complex 4·6

In order to know the structure of the complex in solution, the modeling study of **4**·**6** was carried out with AMBER* force field using GB/SA chloroform solvation model[17] in the program package of Macromodel V6.5.[18] Since the low mode search algorithm[19] is known to be efficient to generate all the possible structures of a host–guest complex we applied the method to obtain the most probable structures of the complex. The 5000 initial structures of the complex were generated and then optimized. The structures thus obtained are shown in Fig. 5.

The most stable structure (**c1**) predicted by this calculation is almost identical to that found in the crystalline state. The two terminal arenes of the host rotated with each other around the axis connecting the two controids of the two oxygen carrying six-membered rings. The long axis of the guest is parallel to that of phenanthrene ring. The second stable structure (**c2**) has eclipsed orientation of the two terminal chromophores of the host as is found in the crystalline structure of **4**·**5**. The energy difference of the two is 2.7 kcal mol^{-1}. Following to these two is the structure (**c3**, 5.6 kcal mol^{-1} from **c1**) similar to the most stable one. The

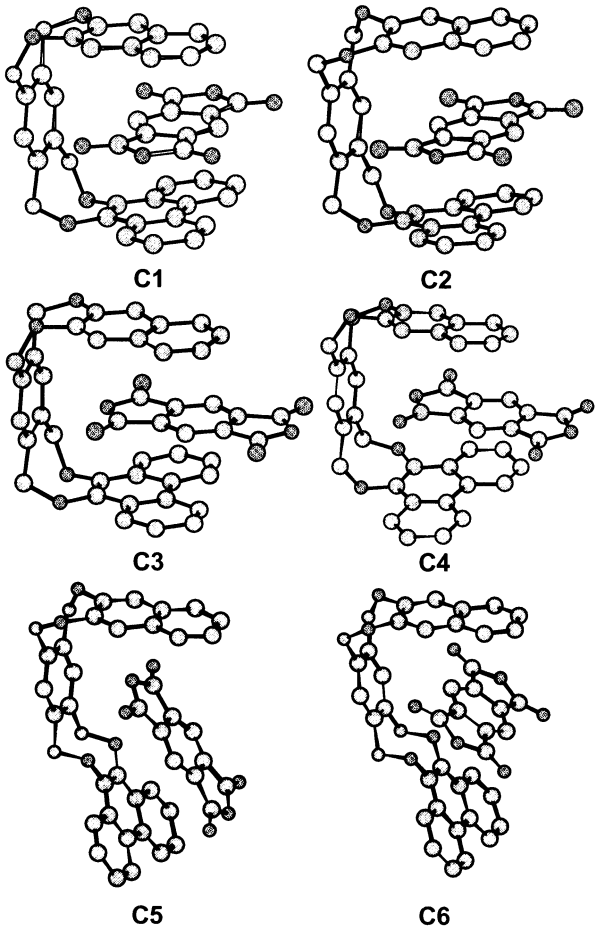

Figure 5. Calculated structures of **4**·**6**.

difference is the orientation of the guest. The guest of **c3** was rotated 90° from **c1**. Since the cleft of the host is not so deep that the guest is not fully buried in this cleft and almost one third of it is exposed outside. In this orientation the contact area between the host and guest is smaller than that of the parallel orientation and hence, it is less stable than the fully buried one. Again the eclipsed arrangement of the two terminal chromophores in **c4** (7.4 kcal mol^{-1} from **c1**) is less stable than **c3**, but the structural characteristics are very similar. The two terminal chromophores of **c5** (8.0 kcal mol^{-1} from **c1**) are not parallel to each other and phenanthrene unit bent outward. In this structure, the guest stacks on the phenanthrene unit with the perpendicular arrangement, as was found in **c3** and **c4**. The guest rotated 90° in **c6** (9.0 kcal mol^{-1} from **c1**) structure.

It is noteworthy that the relative stability of these structures mainly comes from the difference of the van der Waals interaction and Coulomb interaction of the partial charge of the individual atom in the binding partners. Charge transfer type interaction between the electron donor and acceptor should be operative in the actual case, however, such type of interaction cannot be included in the force field calculations. Hence, the relative stability of the structures predicted in this calculation not always corresponds to the actual stability in solution.

Using these structures, the theoretical CIS of the guest was

estimated. The CIS value of the individual structures was calculated with magnetic anisotropy due to the ring current effect of the three aromatic rings. The calculated up-field shifts of these structures are 3.58, 3.75, 1.65, 1.71, and 1.36 ppm for **c1**, **c2**, **c3**, **c4**, and **c5**, respectively.

2.5. Structure of the complexes in solution

The essential aspect of molecular recognition is to understand nature of the interaction of molecules. Presumably, there should be a specific arrangement of the two molecules at which the energy is lower than any other orientations. Hence, it is very important to elucidate the precise structures of a host–guest complex in solution to understand the nature of the interaction between the binding partners. However, the structure elucidation of the host–guest complex is rather elusive because the structure found in the crystalline state does not always correspond to that in solution. Solvent molecules play an important role in controlling the relative arrangement of the interacting pair. We have found that NMR chemical shift simulation method[20] is very efficient and reliable to know the relative population of dynamically equilibrating conformational change of a flexible macrocyclic compound.

From the binding study it was ascertained that the three aromatic chromophores in the hosts worked cooperatively, since the binding constant of **4** toward **6** is nearly equal to the product of that for **9** and **10**. Moreover, the modeling study suggested that the tweezers form of the host is the most favorable for binding a guest. Actually, the molecular mechanics calculations predicted that the most stable structure of the complex is **c1** and the second one is **c2**. Although they differ in the relative arrangement of the two terminal chromophores (skewed and eclipse), they are essentially identical with respect to the orientation of the guest. Actually, the calculated CIS values of the guest are quite similar (3.58 ppm for **c1**, 3.75 ppm for **c2**). Reflecting the perpendicular arrangement of the guest, the calculated CIS values of **c3** and **c4** are small (1.65 ppm for **c3** and 1.71 ppm for **c4**) when compared to the former cases.

It is well known that the stability of supramolecular complexes depends on attractive interactions between the host and guest and on solvation of the binding partners. Since the host and guest were separately solvated in solution, the desolvation of the host and guest is requisite in the association process. The desolvation process should be energetically up-hill and hence, an association took place only when the energy gain between the host and guest interaction exceeds this unfavorable energy. Thus, the extent of solvation and desolvation of the binding partners play an important role in the structure of the supramolecular complex.

Both in structures **c1** and **c2**, the guest was fully buried in the cleft of the host, since the molecular size of the guest is almost identical to that of one of the terminal chromophores of the host, and hence, the guest was completely shielded from the solvent molecules. On the other hand, in structure **c3** and **c4**, the depth of the cleft is not enough for the perpendicularly arranged guest, and hence, a part of the molecule is left shielded from the binding arms of the host. The exposed part is the one of the two polar moieties (acid anhydride moiety) of the guest and the solvent molecules can interact to this moiety.[21] This solvation of the guest should be stabilizing interaction. In other words, both **c3** and **c4** have extra solvation energy of the entrapped guest when compared to the cases of the fully buried guest (**c1** and **c2**). Thus, it is not unreasonable to assume that the latter two are more stable than the former structures due to the extra solvation of the guest. It is rather difficult to verify the reversal of the relative stability of these structures in solution. However, the close similarity to the observed CIS value (1.30 ppm) to that of the calculated one (1.65 and 1.71 ppm for **c3** and **c4**, respectively) is a good experimental proof to the reversal of the relative stability of the calculated structures.

The reversal of the stability for the perpendicular guest (**c3** and **c4**) with respect to the parallel (**c1** and **c2**) in chloroform solution is thus explained by the difference of the extent of solvation on the buried guest in the host cavity. The fact that both **3** and **4** did not show any propensity to form supramolecular complex with any of these acceptor in acetone is the further experimental proof that the solvation/desolvation play a very important role not only in the binding strength but also the relative arrangement between the host and guest.

3. Conclusion

Flexible molecular receptors (**3,4**) having three aromatic chromophores can bind electron deficient π-system such as **5** or **6** both in the crystalline state and in solution. The crystallographic analysis disclosed that both complexes **4·5** and **4·6** have a triple-decker type donor–acceptor–donor sandwich arrangement in which the guest located between the two terminal aromatic chromophores of the host. When the terminal aromatics naphthalene ring of **4** was changed to a benzene ring, the stoichiometry of the crystalline host–gust complex changed either to 1:2 or 2:1 depending on the guest. In the 1:2 complex (**3**·$\mathbf{6}_2$) the host has Z character conformation. The host of its form has two perpendicular corners and each corner can hold the guest to form 1:2 complex in the crystalline state. On the other hand, in the 2:1 complex ($\mathbf{3}_2$·**5**), the host has L character conformation. Combination of the two L character hosts makes the box type cavity in which the guest was encapsulated with both face-to-face and face-to-edge interactions. Two orientations of the guest, parallel and cross, with respect to the phenanthrene ring of the host were predicted in the triple-decker complex **4·6** by a molecular mechanics calculation. The former structure was found in the crystalline state and predicted to be more stable than that of the cross orientation. Since the depth of the cavity of the receptor is not enough for the cross arrangement, a part of the guest was not covered by the two terminal chromophores of the host. Although the latter was predicted to be less stable, the observed complexation shift of the guest supports this orientation in solution. The solvation to the exposed part of the guest should give extra stabilization of the complex in solution.

4. Experimental

Melting points are uncorrected. ^{1}H NMR spectra were recorded at 270 and 500 MHz, and ^{13}C NMR spectra were recorded at 67.5 and 125 MHz. ^{1}H and ^{13}C chemical shifts were measured in ppm relative to internal Me_4Si, and coupling constants are expressed in Hz.

4.1. Titration

NMR titrations were performed at 500 MHz on a JEOL Lamda500 instrument at ambient temperature (approximately 26°C) by treating 500 μL of guest (1 mM in $CDCl_3$) with aliquots of host (15 mM in $CDCl_3$) and monitoring the changes in the chemical shift. Nonlinear least squares regression curve fitting was used to determine the binding constants, along with the final chemical shift of each of the monitored protons.

4.1.1. 9,13,18,22-Tetraoxa-9,10,12,13,18,19,21,22-octahydrobenzo-9′,10′-phenanthro[*e*,*e*′]benzo[1,2-*a*:4,5-*a*′]-dicyclooctene (3). A mixture of phenanthrenequinone (280 mg, 1.34 mmol) and a catalytic amount of palladium–carbon in 5 ml of THF was stirred under H_2 for one day at room temperature. The reaction mixture was filtered under Ar and the filtrate was added dropwise to a mixture of **12** (470 mg, 1.18 mmol) and cesium carbonate (1.2 g, 3.69 mmol) in 350 ml of acetone at refluxed temperature. The mixture was refluxed for 2 h and was filtered. The solvent was removed under reduced pressure, residue was purified by silicagel column chromatography ($CHCl_3$) and then by GPC ($CHCl_3$) to afford 280 mg (53% yield) of **3**; colorless powder, mp 216–217°C; IR (KBr): 1280 1240 cm^{-1}; ^{1}H NMR (270 MHz $CDCl_3$): δ 8.59–8.55 (m, 2H), 8.27–8.23 (m, 2H), 7.64–7.25 (m, 4H), 7.04 (s, 2H), 6.91–6.87 (m, 4H), 5.63 (s, 4H), 5.33 (s, 4H); ^{13}C NMR (67.5 MHz $CDCl_3$): δ 149.587, 140.344, 136.096, 136.066, 129.618, 128.595, 127.983, 126.761, 125.539, 123.706, 122.483, 121.918, 74.892, 674. 47; MS (70 eV, EI): *m*/*z* (%): 446 (8) [M$^+$]; $C_{30}H_{22}O_4$ (446.1): calcd C 80.70, H 4.97. found: C 80.57, H 5.00.

4.1.2. 9,13,20,24-Tetraoxa-9,10,12,13,20,21,23,24-octahydro-3′,4′-naphtho-9′,10′-phenanthro[*e*,*e*′]benzo[1,2-*a*:4,5-*a*′]dicyclooctene (4). A mixture of phenanthrenequinone (110 mg, 0.52 mmol) and a catalytic amount of palladium–carbon in 5 ml of THF was stirred under H_2 for one day at room temperature. The reaction mixture was filtered under Ar and the filtrate was added dropwise to a mixture of **13** (120 mg, 0.28 mmol) and cesium carbonate (400 mg, 1.23 mmol) in 150 ml of acetone at refluxed temperature. The mixture was refluxed for 3 h and was filtered. The solvent was removed under reduced pressure, residue was purified by silicagel column chromatography ($CHCl_3$) and then by GPC ($CHCl_3$) to afford 50 mg (37% yield) of **4**; colorless powder, mp 262–263°C; IR (KBr) 1286, 1240 cm^{-1}; ^{1}H NMR (270 MHz $CDCl_3$): δ 8.59–8.55 (m, 2H), 8.26–8.23 (m, 2H), 7.69–7.53 (m, 6H), 7.41 (s, 2H), 7.33–7.30 (m, 2H), 7.07 (s, 2H), 5.43 (s, 4H), 5.37 (s, 4H); ^{13}C NMR (67.5 MHz $CDCl_3$): δ 149.931, 140.243, 136.148, 130.663, 129.563, 128.585, 128.004, 126.751, 126.675, 125.529, 124.857, 122.488, 121.908, 118.164, 74.891, 74.800; MS (70 eV, EI): *m*/*z* (%): 496 (10). IR (KBr); $C_{34}H_{24}O_4$ (496.2): calcd C 82.24, H 4.87. found: C 82.32, H 5.09.

4.1.3. 5,6,7,8-Tetrahydro-1,4-9′,10′-phenanthro[*b*]dioxocin (9). A mixture of phenanthrenequinone (500 mg, 2.40 mmol) and a catalytic amount of palladium–carbon in 5 ml of THF was stirred under H_2 for one day at room temperature. The reaction mixture was filtered under Ar and the filtrate was added dropwise to a mixture of 1,4-dibromoburane (550 mg, 2.54 mmol) and cesium carbonate (1.90 g, 5.85 mmol) in 100 ml of acetone at refluxed temperature. The mixture was refluxed for 3 h and was filtered. The solvent was removed under reduced pressure, residue was purified by silicagel column chromatography ($CHCl_3$) and then by GPC ($CHCl_3$) to afford 400 mg (63% yield) of **9**; colorless powder, mp 100–102°C; IR (KBr) 1259 cm^{-1}; ^{1}H NMR (270 MHz $CDCl_3$): δ 8.62–8.20 (m, 2H), 8.27–8.23 (m, 2H), 7.63–7.56 (m, 4H), 4.60 (bs, 4H), 2.04 (bs, 4H); ^{13}C NMR (67.5 MHz $CDCl_3$): δ 139.665, 129.019, 128.005, 126.654, 125.304, 122.427, 122.175, 72.354, 27.453; MS (70 eV, EI): *m*/*z* (%): 264 (27) [M$^+$]; HRMS (EI) for $C_{18}H_{16}O_2$: *m*/*z* (calcd) M$^+$=264.1150; *m*/*z* (obsd) =264.1146.

4.1.4. 5,8-Dihydro-1,4-2′,3′-naphthobenzo[*b*]dioxocin (10). A mixture of 1,2-bis(bromomethyl)benzene (500 mg, 1.89 mmol), 2,3-dihydroxynaphthalene (300 mg, 1.88 mmol) in 30 ml of acetone was added dropwise to a suspension of cesium carbonate (1.52 g, 4.68 mmol) in 100 ml of acetone at refluxed temperature. The mixture was refluxed for 1 h and was filtered. The solvent was removed under reduced pressure, residue was purified by silicagel column chromatography (10% ethylacetate/hexane) to afford 130 mg (26% yield) of **10**; colorless powder, mp 178–179°C; IR (KBr) 1260 cm^{-1}; ^{1}H NMR (270 MHz $CDCl_3$): δ 7.68–7.65 (m, 2H), 7.44 (s, 2H), 7.34–7.30 (m, 2H), 7.28–7.22 (m, 4H), 5.46 (s, 4H); ^{13}C NMR (67.5 MHz $CDCl_3$): δ 150.175, 135.827, 130.663, 128.921, 128.524, 126.675, 124.780, 118.118, 75.487; MS (70 eV, EI): *m*/*z* (%): 262 (33) [M$^+$]; HRMS (EI) for $C_{18}H_{14}O_2$: *m*/*z* (calcd) M$^+$=262.0994; *m*/*z* (obsd) =262.0993.

4.1.5. 5,6,7,8-Tetrahydro-1,4-2′,3′-naphtho[*b*]dioxocin (11). A mixture of 1,4-dibromobutane (130 mg, 0.60 mmol), 2,3-dihydroxynaphthalene (100 mg, 0.63 mmol) in 30 ml of acetone was added dropwise to a suspension of cesium carbonate (500 mg, 1.53 mmol) in 30 ml of acetone at refluxed temperature. The mixture was refluxed for 2 h and was filtered. The solvent was removed under reduced pressure, residue was purified by silicagel column chromatography ($CHCl_3$) to afford 120 mg (90% yield) of 11; colorless oil; IR (KBr) 1225 cm^{-1}; ^{1}H NMR (270 MHz $CDCl_3$): δ 7.68–7.65 (m, 2H), 7.33–7.30 (m, 2H), 7.16 (s, 2H), 4.19 (bs, 4H), 2.16 (bs, 4H); ^{13}C NMR (67.5 MHz $CDCl_3$): δ 150.146, 129.538, 126.273, 124.029, 109.403, 69.248, 26.173; MS (70 eV, EI): *m*/*z* (%): 214 (100) [M$^+$]; HRMS (EI) for $C_{14}H_{14}O_2$: *m*/*z* (calcd) M$^+$=214.0994; *m*/*z* (obsd)= 214.0986.

4.1.6. 2,3-Bis(bromomethyl)-6,11-dioxa-5,12-dihydrobenzo[*e*]benzo[1,2-*e*]cyclooctene (12). A mixture of 1,2,4,5-tetrakis(bromomethyl)benzene (1 g, 2.2 mmol), catechol (0.24 g, 2.1 mmol) and cesium carbonate (1.8 g,

5.3 mmol) in 500 ml of acetone was stirred for a day and was filtered. The solvent was removed under reduced pressure, residue was purified by silicagel column chromatography ($CHCl_3$) and then by GPC ($CHCl_3$) to afford 0.29 g (32% yield) of **12**; colorless powder, mp 87–89°C; IR (KBr): 1248 cm^{-1}; ^1H NMR (270 MHz $CDCl_3$): δ 7.19 (s, 2H), 7.04–6.92 (m, 4H), 5.36 (s, 4H), 4.60 (s, 4H); ^{13}C NMR (67.5 MHz $CDCl_3$): δ 149.885, 136.515, 161.557, 126.744, 123.779, 74.139, 29.136; MS (70 eV, EI): *m/z* (%): 396 (22) [$M-2^+$], 398 (43) [M^+], 400 (21) [$M+2^+$]. $C_{16}H_{14}O_2{}^{79}Br_2$: calcd 395.9361, found 395.9334, $C_{16}H_{14}O_2{}^{79}Br^{81}Br$: calcd 397.9341, found 397.9341, $C_{16}H_{14}O_2{}^{81}Br_2$: calcd 399.9323, found 399.9290 (MS).

4.1.7. 2,3-Bis(bromomethyl)-6,13-dioxa-5,14-dihydro-2′,3′-naphtho[*e*]benzo[1,2-*e*]cyclooctene (13). A mixture of 1,2,4,5-tetrakis(bromomethyl)benzene (200 mg, 0.24 mmol), and 2,3-dihydroxynaphthalene (26 mg, 0.16 mmol) and cesium carbonate (170 mg, 0.52 mmol) in 100 ml of acetone was stirred for a day and was filtered. The solvent was removed under reduced pressure, residue was purified by silicagel column chromatography ($CHCl_3$) and then by GPC ($CHCl_3$) to afford 23 mg (28% yield) of **13**; colorless powder, mp 188–189°C; IR (KBr): 1247 cm^{-1}; ^1H NMR (270 MHz $CDCl_3$): δ 7.70–7.65 (m, 2H), 7.46 (s, 2H), 7.30–7.35 (m, 2H), 7.20 (s, 2H), 5.40 (s, 4H), 4.60 (s, 4H); ^{13}C NMR (67.5 MHz $CDCl_3$): δ 150.091, 137.302, 136.591, 131.435, 130.648, 126.744, 125.002, 118.149, 74.853, 29.098; MS (70 eV, EI): *m/z* (%): 446 (3) [$M-2^+$], 448 (7) [M^+], 450 (3) [$M+2^+$]. $C_{20}H_{16}O_2Br_2$ (447.9): calcd C 53.60, H 3.60. found: C 53.57, H 3.78.

4.2. Crystal structure determinations

4.2.1. X-Ray diffraction analysis of 3·6 complex. The crystal data for **3·6** complex are as follows; Monoclinic, space group *P*21 with a=8.284 (4), b=30.644 (5), c=7.823 (5) Å, β=98.859 (5)°, V=1962 (2) Å^3, and Z=4. The empirical formula is $(C_{30}H_{22}O_4)(C_{10}H_2O_6)_2$, molecular weight is 882, and calculated density is 1.49 g cm^{-3}. The three-dimensional intensity data were collected by the use of graphite-monochromated Cu-Kα radiation (λ= 1.54178 Å) on a Rigaku AFC-4 automatic four-circle diffractometer up to a maximum 2θ of 110°. Of 2089 total unique reflections, 1580 were considered observed at the level of $|F_o| > 2.0\sigma|F_o|$. The structure was solved by the direct method (Sir97).[22] All non-hydrogen atoms were located on the initial E synthesis. Hydrogen atoms were found from the difference fourier map and included in the further calculations. Full matrix least squares refinements with anisotropic 66 non-hydrogen atoms and 26 isotropic hydrogens converged to a conventional R factor of 0.032.

4.2.2. X-Ray diffraction analysis of 3·5 complex. The crystal data for **3·5** complex are as follows; Triclinic, space group *P*1 with a=11.888 (3), b=11.919 (2), c=11.935 (2) Å, α=103.74 (2), β=105.87 (2), γ=108.67 (2)°, V=1439.6 (5) Å^3, and Z=2. The empirical formula is $(C_{34}H_{22}O_4)_2(C_{12}H_4N_4)(C_3H_6O_2)$, molecular weight is 1154, and calculated density is 1.33 g cm^{-3}. The three-dimensional intensity data were collected by the use of graphite-monochromated Cu-Kα radiation (λ=1.54178 Å) on a Rigaku AFC-4 automatic four-circle diffractometer up to a maximum 2θ of 110°. Of 5135 total unique reflections, 4242 were considered observed at the level of $|F_o| > 2.0\sigma|F_o|$. The structure was solved by the direct method (Sir97). All non-hydrogen atoms were located on the initial E synthesis. Hydrogen atoms were found from the difference fourier map and included in the further calculations. Full matrix least squares refinements with anisotropic 88 non-hydrogen atoms and 54 isotropic hydrogens converged to a conventional R=0.049, $w2R$=0.173.

4.2.3. X-Ray diffraction analysis of 4·6 complex. The crystal data for **4·6** complex are as follows; Monoclinic, space group $P2_1/a$ with a=22.801 (3), b=14.767 (2), c=10.859 (1) Å, β=91.86 (1)°, V=3654.5 (8) Å^3, and Z=4. The empirical formula is $(C_{34}H_{22}O_4)_2(C_{10}H_2O_6)_3$, molecular weight is 1646, and calculated density is 1.49 g cm^{-3}. The three-dimensional intensity data were collected by the use of graphite-monochromated Cu-Kα radiation (λ=1.54178 Å) on a Rigaku AFC-4 automatic four-circle diffractometer up to a maximum 2θ of 110° Of 5135 total unique reflections, 4242 were considered observed at the level of $|F_o| > 2.0\sigma|F_o|$. The structure was solved by the direct method (Sir97). All non-hydrogen atoms were located on the initial E synthesis. Hydrogen atoms were found from the difference fourier map and included in the further calculations. Full matrix least squares refinements with anisotropic 116 non-hydrogen atoms and 54 isotropic hydrogens converged to a conventional R factor of 0.0652.

4.2.4. X-Ray diffraction analysis of 4·5 complex. The crystal data for **4·5** complex are as follows; Orthorhombic, space group $Pc2_1/n$ with a=17.212(2), b=37.939 (2), c=15.462 (1) Å, V=10096(4) Å^3, and Z=12. The empirical formula is $(C_{34}H_{22}O_4)(C_{12}H_4N_4)$, molecular weight is 700, and calculated density is 1.38 g cm^{-3}. The three-dimensional intensity data were collected by the use of graphite-monochromated Cu-Kα radiation (λ=1.54178 Å) on a Rigaku AFC-4 automatic four-circle diffractometer up to a maximum 2θ of 110° Of 5339 total unique reflections, 3682 were considered observed at the level of $|F_o| > 2.0\sigma|F_o|$. The structure was solved by the direct method (Sir97). All non-hydrogen atoms were located on the initial E synthesis. Hydrogen atoms were found from the difference fourier map and included in the further calculations. Full matrix least squares refinements with anisotropic 54 non-hydrogen atoms and 28 isotropic hydrogens converged to a conventional R=0.054, $w2R$=0.175.

References

1. (a) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1304. (b) Cram, J.-D. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1417. (c) Rebeck, Jr., J. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 245.
2. (a) Zimmerman, S. C. *Bioorganic Chemistry Frontiers*, Vol. 2; ;1991 p 33. (b) Chen, C.-W. W.; Whitlock, H. *J. Am. Chem. Soc.* **1978**, *100*, 4921.
3. (a) Hunter, C. A.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5525. (b) Adams, H.; Carver, F. J.; Hunter, C. A.; Morales, J. C.; Seward, E. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1542. (c) Hamilton, A. D.; Van Eugen, D. *J. Am. Chem. Soc.* **1987**, *109*, 5035.

4. (a) Zimmerman, S. C.; VanZyl, C. M. *J. Am. Chem. Soc.* **1987**, *109*, 7894. (b) Zimmerman, S. C.; VanZyl, C. M.; Hamilton, G. S. *J. Am. Chem. Soc.* **1989**, *111*, 1373. (c) Zimmerman, S. C.; Wu, W. *J. Am. Chem. Soc.* **1989**, *111*, 8054. (d) Zimmerman, S. C.; Mrksich, M.; Baloga, M. *J. Am. Chem. Soc.* **1989**, *111*, 8028. (e) Sijbesma, R. P.; Kentgens, A. P. M.; Nolte, J. M. *J. Org. Chem.* **1991**, *56*, 3199. (f) Sijbesma, R. P.; Nolte, J. M. *J. Org. Chem.* **1991**, *56*, 3122. (g) Coolen, H. A. C.; van Leeuwen, P. W. N. M.; Nolte, J. M. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 905. (h) Sijbesma, R. P.; Kentgens, A. P. M.; Lutz, E. T. G.; van der Maas, J. H.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1993**, *115*, 8999. (i) Reek, J. N. H.; Elmans, J. A. A. W.; Nolte, R. J. M. *J. Org. Chem. Soc.* **1997**, *62*, 2234. (j) Reek, J. N. H.; Priem, A. H.; Engelkamp, H.; Rowan, A. E.; Elmans, J. A. A. W.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1997**, *119*, 9956. (k) Jansen, R. J.; Rowan, A. E.; de Gelder, R.; Scheeren, H. W.; Nolte, R. J. M. *Chem. Commun.* **1998**, 121. (l) Mink, D.; Deslongchamps, G. *Tetrahedron Lett.* **1996**, *37*, 7035. (m) Mugnus, P.; Morris, J. C.; Lynch, V. *Synthesis* **1997**, 596. (n) Fleischhaur, J.; Harmata, M.; Kahraman, M.; Koslowski, A.; Welch, C. J. *Tetrahedron Lett.* **1997**, *38*, 8655.
5. (a) Chen, C. W.; Withlock, H. W. *J. Am. Chem. Soc.* **1978**, 4921. (b) Allwood, B. L.; Colguhoun, H. M.; Doughty, S. M.; Kohuke, F. H.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J.; Zarzycki, R. J. C. S. *Chem. Commun.* **1987**, 1054. (c) D'Souza, L. J.; Maitra, U. *J. Org. Chem.* **1996**, *61*, 9494. (d) Lamsa, M.; Suorasa, T.; Pursiainen, J.; Huuskonen, J.; Rissanen, K. J. C. S. *Chem. Commun.* **1996**, 1443. (e) Maitra, U.; Rao, P.; Kurmar, U.; Balasubramanian, P. R. *Tetrahedron Lett.* **1998**, *39*, 3255.
6. Kurebayashi, H.; Mine, T.; Harada, K.; Usui, S.; Okajima, T.; Fukazawa, Y. *Tetrahedron* **1998**, *54*, 13495.
7. Kleinpeter, E.; Gabler, M.; Schroth, W. *Monatsh Chem.* **1988**, *119*, 233.
8. (a) Ollis, W. D.; Stoddart, J. F.; Sutherland, I. O. *Tetrahedron* **1974**, *30*, 1903. (b) Jones, P. G.; Bodwell, G.; Hopf, H. Z. *Naturforsch, Teil B* **1990**, *45*, 1213. (c) Elguero, J.; Kartrizky, A. R.; El-Osta, B. S.; Hawlow, P. L.; Simonsen, S. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 312.
9. Kagan, J.; Chen, S.-A.; Agdeppa, Jr., D. A. *Tetrahedron Lett.* **1977**, 4469.
10. (a) Harmata, M.; Murray, T. *J. Org. Chem.* **1989**, *54*, 3761. (b) Harmata, M.; Barnes, C. L. *Tetrahedron Lett.* **1990**, *31*, 1825. (c) Harmata, M.; Barnes, C. L. *J. Am. Chem. Soc.* **1990**, *112*, 5655.
11. (a) Rebeck, Jr., J. *Science* **1987**, *235*, 1478. (b) Jorgensen, W. L.; Serverance, D. L. *J. Am. Chem. Soc.* **1990**, *112*, 4768. (c) Hobza, P.; Selze, H. L.; Schlag, E. W. *J. Am. Chem. Soc.* **1994**, *116*, 3500. (d) Kim, E.; Paulowal, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1998**, *120*, 11192.
12. New chiral molecular tweezers with a bis-Troger's base was reported quite recently: Pardo, C.; Sesmilo, E.; Puebla, E. G.; Monge, A.; Elguero, J.; Fruchier, A. *J. Org. Chem.* **2001**, *66*, 1607.
13. Kuerebayashi, H.; Sakaguchi, M.; Okajima, T.; Haino, T.; Usui, S.; Fukazawa, Y. *Tetrahedron Lett.* **1999**, *40*, 5545.
14. (a) Nishio, M.; Hirota, M. *Tetrahedron* **1989**, *45*, 7201. (b) Nishio, M.; Umezawa, Y.; Hirota, M.; Takeuchi, Y. *Tetrahedron* **1995**, *51*, 8665.
15. Foster, R. *Organic Charge-Transfer Complexes*; Academic: New York, 1969.
16. Connors, K. A. *Binding Constant*; Wiley: New York, 1987.
17. Still, W. C.; Tempczyk, A.; Howly, R. C.; Hendrickson, T. *J. Am. Chem. Soc.* **1990**, *112*, 6127.
18. Mohadomi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comp. Chem.* **1990**, *11*, 440.
19. Kolossvary, I.; Guida, W. C. *J. Am. Chem. Soc.* **1996**, *118*, 5011.
20. (a) Fukazawa, Y.; Ogata, K.; Usui, S. *J. Am. Chem. Soc.* **1988**, *110*, 8692. (b) Okajima, T.; Wang, Z. H.; Fukazawa, Y. *Tetrahedron Lett.* **1989**, *30*, 1551. (c) Fukazawa, Y.; Usui, S.; Tanimoto, K.; Hirai, Y. *J. Am. Chem. Soc.* **1994**, *116*, 8169. (d) Fukazawa, Y.; Yang, Y.; Hayashibara, T.; Usui, S. *Tetrahedron* **1996**, *52*, 2847. (e) Fukazawa, Y.; Hayashibara, T.; Yang, Y.; Usui, S. *Tetrahedron Lett.* **1995**, *36*, 3349. (f) Yang, Y.; Haino, T.; Usui, S.; Fukazawa, Y. *Tetrahedron* **1996**, *52*, 2325. (g) Fukazawa, Y.; Haino, T.; Kondoh, Y. *Tetrahedron Lett.* **1999**, *40*, 3591.
21. (a) Desiraju, G. R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311. (b) Desiraju, G. R. *Acc. Chem. Res.* **1991**, *24*, 290.
22. Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterini, A. G. G.; Burla, M. C.; Polidor, G.; Camalli, M.; Spangna, R. *J. Appl. Cryst.* **1999**, *32*, 115.