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INTRAMOLECULAR COMPLEX FORMATION BETWEEN FLEXIBLE MOLECULAR TWEEZERS AND WEAK ELECTRON ACCEPTOR

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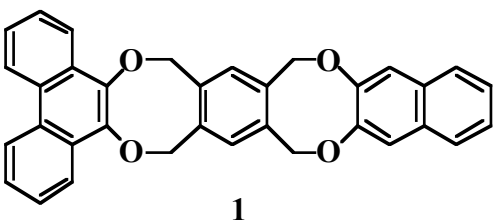
Abstract- A flexible receptor having three aromatic chromophores can bind a weak electron acceptor which is linked covalently to the receptor with alkyl chain of an appropriate length. The receptor has tweezers type conformation when the acceptor was entrapped within the cavity. Sandwich type donnor-acceptor-acceptor arrangement was realized in solution.

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 spacer are suitable receptors for planar guests since they can hold the guest with the two aromatic arms through π-stacking interactions.[3] The two aromatic arms of the host can bind the electron acceptor guests with charge transfer interaction forming a sandwich type layered complexes.[4] Although rigid tweezers,[5] having a preorganized face-to-face arrangement of the two aromatic chromophores are favorable for strong binding, flexible tweezers[6] have the adaptability for the variation of guests. In our previous papers, we reported that the flexible tweezers (**1** and **2**) based on dioxa[2.2]orthocyclophane[7] can bind strong p-electron deficient guests to form the triple-decker type donor-acceptor-donor[8] and donor-acceptor-acceptor[9] arrangements in the crystalline state. In a case of a relatively weak electron-accepting guest, however, no intermolecular complex formation with host (**2**) was observed in solution. A large entropic cost[10,11] prevented the formation of the intermolecular complex of **2** and the weak electron acceptors in organic solvents. In order to overcome the unfavorable entropic cost, we linked the guest to the host with an appropriate methylene chain.[12] In this paper, we report on the synthesis, intramolecular complex formation and



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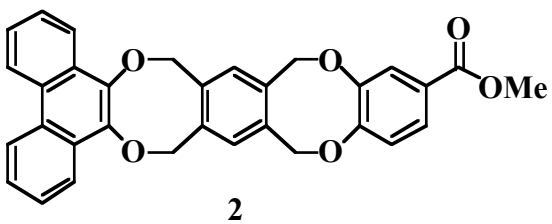


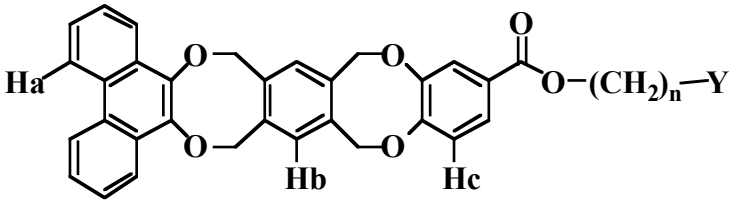
2

molecular structures of these tethered host-guest compounds

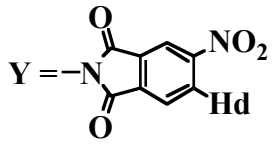
RESULT AND DISCUSSION

Synthesis

As the weak electron acceptor, 2,4,6-tribromoanisole, 4-nitroanisole, 2,4- and 2,5-dinitroanisole, *N*-methylphthalimide, *N*-methyl-4-bromophthalimide, *N*-methyl-3- and 4-nitrophthalimide were selected.[13] These weak electron acceptors were connected with ester linkage to host **2**. Williamson type coupling of carboxylic acid with corresponding ω-bromoalkyl derivative of weak electron acceptors in the presence of K_2CO_3 in DMF gave the desired compounds (**3a**-**3e**, **4a**-**4e**, **5**, **6**, **7**, **8**, **9**, **10**). Reference compounds (**11**, **12**) were prepared to investigate the role of the phenanthrene ring in the formation of an intramolecular complex. Compound (**13**) was also prepared to obtain the precise molecular dimension of the host moiety by an X-ray crystallography. The synthetic route of **2** and **13** is shown in Scheme 1.

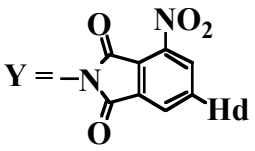


3a: n= 3
3b: n= 4
3c: n= 5
3d: n= 6
3e: n= 10



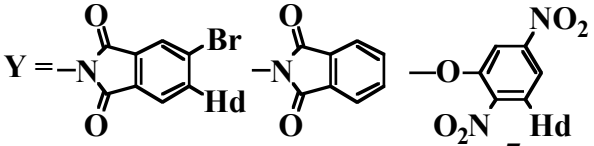
4-Nitrophthalimido

4a: n= 3
4b: n= 4
4c: n= 5
4d: n= 6
4e: n= 10

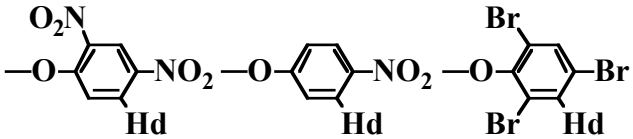


3-Nitrophthalimido

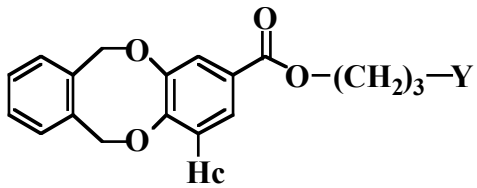
5: n= 3, Y = 4-bromophthalimido
6: n= 3, Y = phthalimido
7: n= 3, Y = 2,5-dinitrophenoxy
8: n= 3, Y = 2,4-dinitrophenoxy
9: n= 3, Y = 4-nitrophenoxy
10: n= 3, Y = 2,4,6-tribromophenoxy



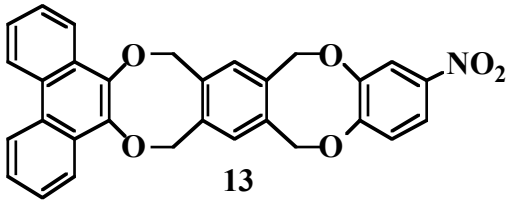
5 **6** **7**



8 **9** **10**



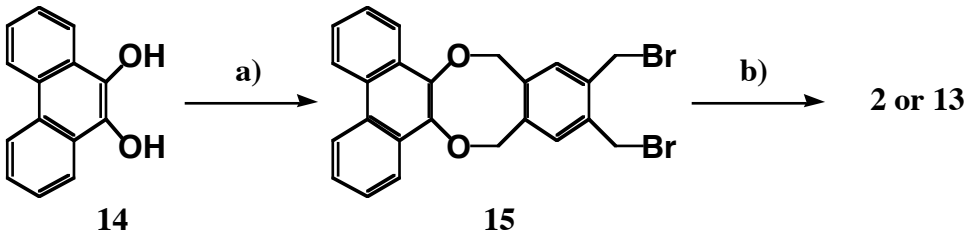
11: Y = 4-nitrophthalimido
12: Y = 3-nitrophthalimido



13

Modeling study of host moiety

A modeling study of **2** as the host moiety was carried out to know the most probable binding structures in solution. The calculation was carried out with AMBER* force field using GB/SA chloroform solvation model[14] in the program package of Macromodel V 6.0.[15] Since the oxygen containing eight-membered



(a) 1,2,4,5-tetrakis(bromomethyl)benzene, Cs_2CO_3, acetone, 25%; (b) for **2**: methyl-3,4-dihydroxybenzene, Cs_2CO_3, acetone, 89%; for **4**: 4-nitrocatecol, Cs_2CO_3, acetone, 60%

Scheme 1

ring has three conformers,[7a] twist-boat (*b*), screw (*s*), and chair (*c*), 9 structures (*bb, bs, bc, sb, ss, sc cb, cs*, and *cc*) are possible for the host moiety. For the effective binding of a planar p-guest, there should be at least one perpendicular arrangement of the two neighboring aromatic rings in the host. Hence, 5 conformers having at least one twist-boat conformer were selected, within which *bb, bc*, and *cb* have each two arrangements, *syn* and *anti*, of the two terminal chromophores. In the case of *bb*, they are boat-boat-*syn* (*bbs*) and boat-boat-*anti* (*bba*), respectively. Altogether 8 conformers (*bbs, bba, bs, bcs, bca, sb, cbs*,

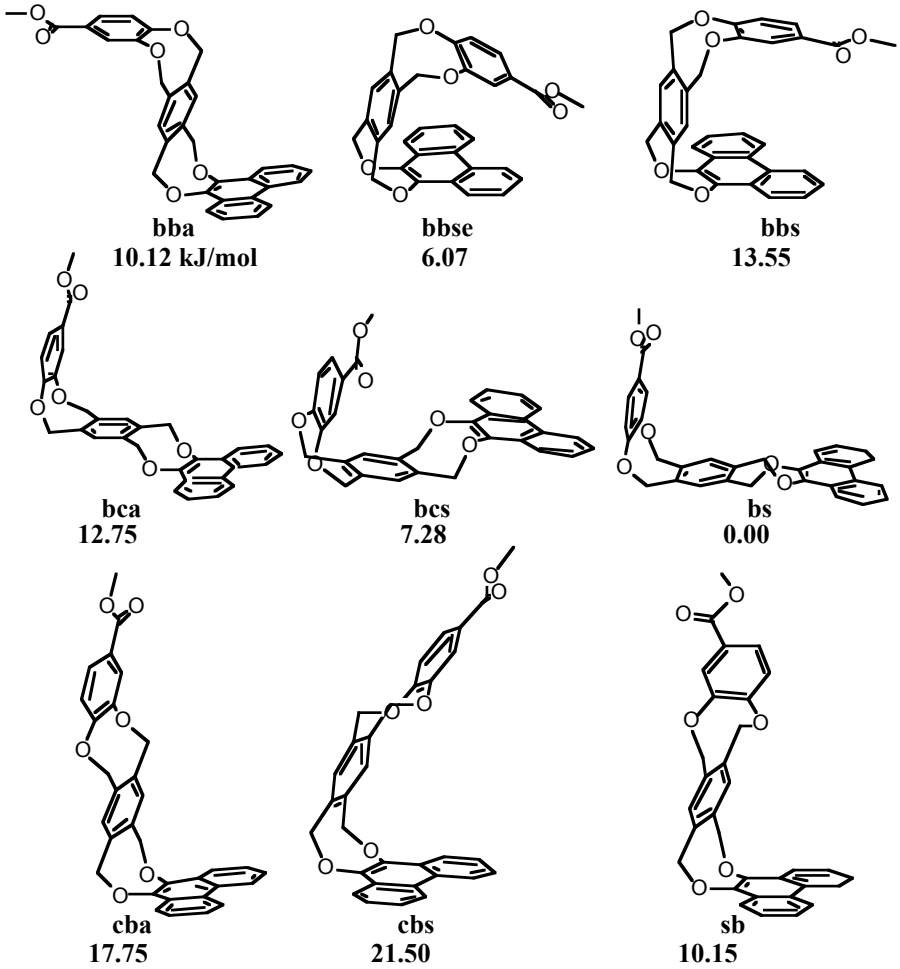


Figure 1. Structures of **2** with relative steric energies.

and *cba*) were taken into consideration and their relative steric energies were calculated. The calculation disclosed that there are two conformers in *bbs* form which differs the arrangement of the two terminal chromophores with respect to each other. One is skewed and the other is eclipsed. The former has skew arrangement around the axis connecting the two centroids of the two oxygen carrying 6-membered aromatic rings and the latter has eclipsed arrangement. The steric energy of the latter is smaller than the former. The structures thus obtained are shown in Figure 1 together with their relative steric energies.

X-ray Study of host moiety

An X-ray crystallographic analysis of **13** was carried out in order to know the structure of the host moiety. As can be seen in ORTEP drawing, **13** does not have a conformation of face-to-face *syn* arrangement of the two terminal aromatic rings (Figure 2). The two terminal chromophores are *anti* with each other to have *bba* form. Two neighboring aromatic chromophores of the host have roughly perpendicular arrangement. The dihedral angles between each terminal aromatic ring and the central durene ring are 88.4 ° for the benzoate and 73.3° for phenanthrene, respectively. The two terminal chromophores are not parallel to each other and have the dihedral angle of 33.7 °. The perpendicular arrangement of the neighboring chromophores should be a prerequisite for an efficient binding of a planar guest. Both the p-p stacking charge transfer interaction and CH-p type face-to-edge interactions[16] should be effective for guest binding.

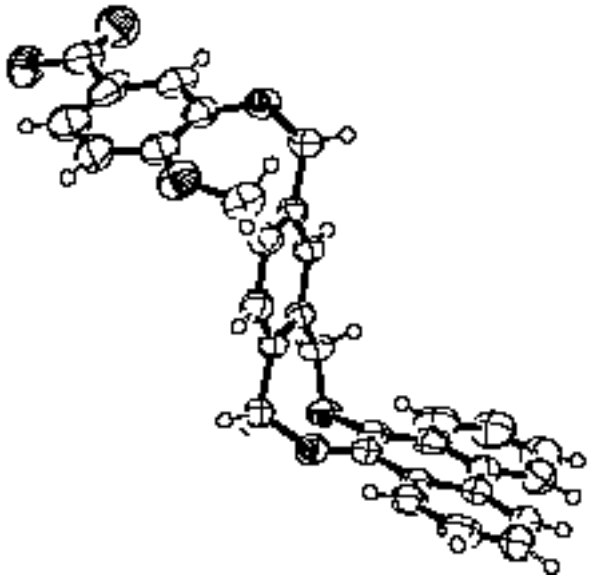


Figure 2. ORTEP drawing of **13**.

NMR measurement

The nmr chemical shift differences of the aromatic protons in these tethered compounds with respect to the references gave information of the extent of the intramolecular interaction between the host and guest moieties in solution. The up-field shift of an aromatic proton from that of the reference compound should be a good sign for the interaction such as p-p stacking as was found in [m.m]cyclophanes.[17] In these tethered compounds, there are roughly two conformers, open and closed forms. In the closed form as was

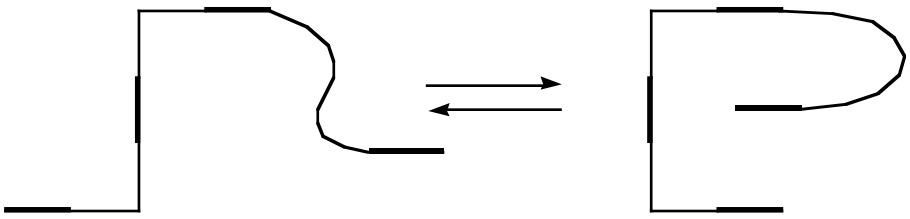


Figure 3. Open and closed forms in tethered compound.

shown in Figure 3, the aromatic proton of the guest should have large up-field shift because of the influence of the ring current effect of the three aromatic chromophores of the host. It is obvious that the entropy of the open form is far larger than closed one.[18] The entropy changes are primarily a consequence of losses of internal rotation of the tether moiety in the closed form. The equilibrium between the open and closed forms should shift in favor of the latter when lowered the temperature, since the latter has smaller entropy. Hence, the NMR measurements at lower temperature should give more prominent shift changes because of the increase of the population of the smaller entropy conformers.

The temperature dependent changes of the chemical shift of **3a** are shown in Figure 4. The up-field shifts of Ha, Hc, and Hd are clearly seen when lowered the temperature. The gradient of Hd is largest of the three. On the other hand, Hb moved to the down-field. Table 1 shows the changes of the chemical shift of the aromatic protons in the tethered compounds together with the chemical shift values of the reference compounds. The largest up-field shift was observed at Hd proton of **3a** at –60 °C. Up-field shift of Hd was also observed in compounds (**4a**) and (**5**). Up-field shift of both Ha and Hc and down-field shift of Hb were commonly observed in compounds (**3a**, **4a**, **5**, and **6**). The shift difference of Ha is largest in **3a** and decreases in the order of **3a**>**4a**>**5**>**6**. The same trend was observed also in Hc and Hd. This order is consistent with the electron accepting ability of the guests as was indicated by the LUMO energy levels.[13] The down field-shift of Hb of these compounds was also consistent to this order. It was thus clear that the stronger the electron accepting ability of the guest the larger contribution of the closed form in the dynamic equilibrium of the close/open forms in solution.

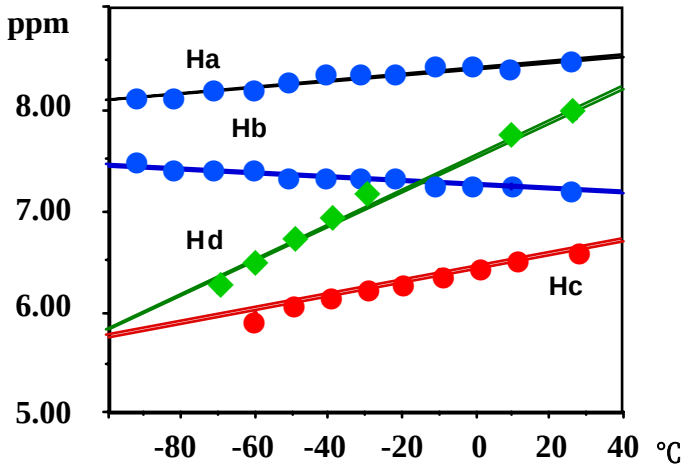


Figure 4. Temperature dependent chemical shift of **3a**.

In order to know a role of the phenanthrene ring in the intramolecular complex formation, tethered compounds (**11**) and (**12**) were prepared and their chemical shift behaviors toward the temperature change were examined. Hd protons of both **11** and **12** did not change at all even at –60 °C (Table 1). This means that the phenanthrene ring is requisite for the formation of closed form. The π-π stacking interaction between the phenenthrene and the electron-accepting guests is thus essential for the intramolecular complex formation. The phthalimide functionality is efficient for the formation of the closed form, however, phenols are not effective even in the dinitro derivatives whose LUMO energy levels are lower than that of *N*-methyl-3-bromophthalimide. No large chemical shift change was observed even in the aromatic proton of the guest moiety of **7**, **8**, **9**, and **10**. In these compounds, the chemical shift of the

aromatic protons of the host moiety (Ha, Hb, and Hc) did not change also from the reference compound even at the low temperature. The behavior of the chemical shift changes in these compounds suggested a negligible contribution of the closed form to the dynamic equilibrium. The chemical shift change might be explained due to the change of relative population within the open form, since there should be a significant amount of conformers in the open than and their populations are temperature dependent.

Modeling study of closed form of 6

In order to know the structure of the closed form in solution, the modeling study of **6** was carried out. The low mode search algorithm[19] was selected to generate all the possible structures. The 3000 initial structures were generated and then optimized with AMBER* force field. The structures are shown in Figure 5.

The structure of the host moiety of the most stable structure (**c1**) has tweezers type conformation with face-to-face syn arrangement of the two terminal aromatic rings. The two terminal chromophores lie parallel and have skewed arrangement to each other (*bbs*-skew). The guest was suitably accommodated in this cleft. Both the p-p stacking and face-to-edge interactions are operative in binding the guest. In this

Table 1. Selected Chemical Shift Changes in Tethered Compounds and Chemical Shifts of Reference Compounds

		Ha	Hb	Hc	Hc (**11,12**)	Hd (**3a, 11**)	Hd (**4a, 12**)	Hd (**5**)	Hd (**8**)	Hd (**9**)	Hd (**10**)
Reference	25°C	8.58	7.17	6.89	6.85	8.58	8.08	7.86	8.46	8.08	7.58
3a	25°C	-0.14*	0.05	-0.33		-0.69					
	-60°C	-0.39	0.21	-0.89		-2.12					
4a	25°C	-0.08	0.03	-0.22			-0.50				
	-60°C	-0.14	0.14	-0.63			-1.10				
5	25°C	-0.04	0.00	-0.12				-0.46			
	-60°C	-0.09	0.06	-0.28				-0.61			
6	25°C	-0.03	-0.01	-0.09							
	-60°C	-0.04	0.03	-0.13							
7	25°C	-0.01	0.00	0.00							
	-60°C	0.01	0.05	0.01							
8	25°C	-0.02	0.00	0.00					-0.08		
	-60°C	0.00	0.04	0.00					-0.05		
9	25°C	-0.01	-0.02	0.01						0.08	
	-60°C	0.01	0.02	0.02						0.13	
10	25°C	0.00	-0.02	0.01							0.06
	-60°C	0.00	0.02	0.03							0.10
11	25°C				0.01	-0.09					
	-60°C				0.02	-0.04					
12	25°C				0.01		0.01				
	-60°C				0.03		0.02				

*) - sign denotes up-field shift

structure, the guest lied on the phenanthrene to have maximum overlap with it. This π–π stacking interaction should be the major contributor to the formation of the closed form in solution.

Quite similar triple-decker stacking interaction was observed in the second structure (**c2**). Its energy difference form **c1** is 2.0 kJ/mol. Again, the maximum overlap between the guest and phenanthrene was observed in the structure. In **c2**, the host moiety has *bbs*-eclipsed conformation and the two oxygen carrying 6-membered rings of the two terminal chromophores are superimposed when viewed along the perpendicular direction of one of the two terminal arenes of the host. Other structures of the closed form having the host conformation other than *bbs*-skew or *bbs*-eclipse are **c3** and **c4**. They have *bs* or *bcs* conformer in the host moiety. In these structures π–π stacking interaction between the guest and phenanthrene was observed. However, they are less stable by 15.5 and 19.8 kJ/mol from **c1**, respectively. The instability of these structures may come from the lesser contact area between the host and guest moieties. In both structures the mean squares plane of the guest is almost perpendicular to that of the benzoate ring and has poor overlap with durene ring of the host moiety. There are quite many structures in between **c2** and **c3**. They have either *bbs*-skew or *bbs*-eclipse form of the host moiety but have different orientations of ester functionality,different chain conformations, and different orientations of the guest with respect to the host phenanthrene.

Structure of closed form in solution

The temperature-dependent chemical shift movements of the aromatic protons gave a good clue for the

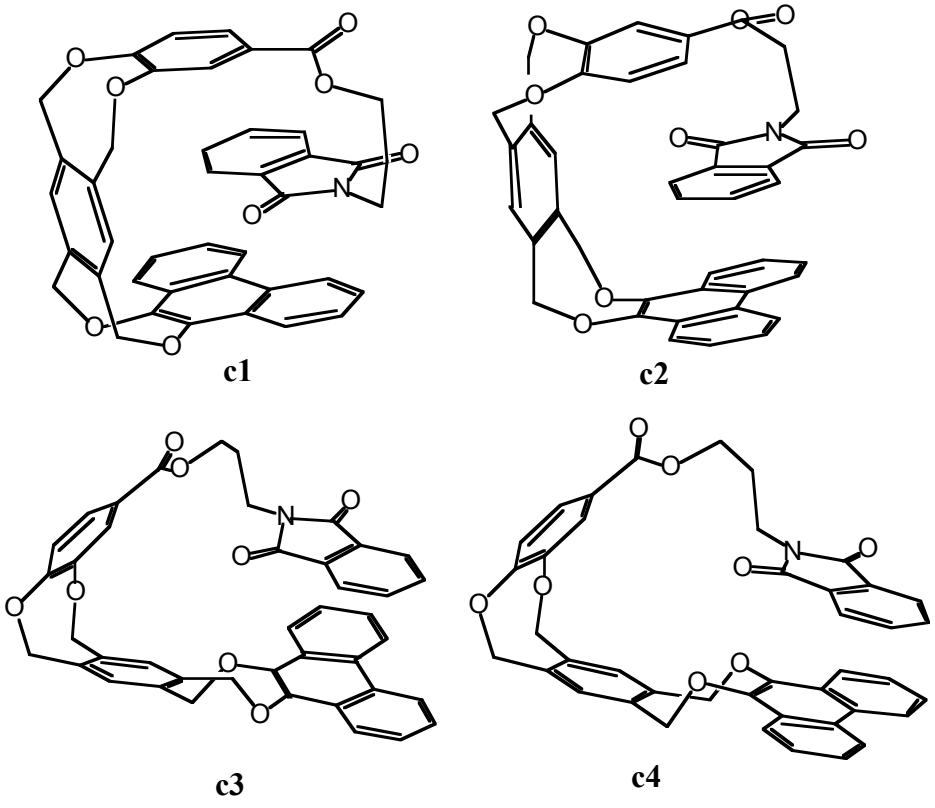


Figure 5. Structures of closed form for **6**.

structure elucidation. The chemical shift simulation[20] is also the method of choice. If the precise arrangement of the interacting two aromatic rings is known, the resulting induced chemical shift change of the aromatic protons can be easily estimated by the influence of the ring current effect[21] of the interacting counterpart.

The up-field shift of the guest proton should be largest in **c1** because of the shielding effects due to the surrounding three aromatic rings. Both Ha and Hc have to show up-field shifts of similar amount to each other. The chemical shift of Hb, however, should have down-field movement because Hb is placed in the deshielding region of the guest aromatic ring. The characteristic feature of these chemical shift movements of **c1** should be observed also in **c2**. Both Hd and Ha should have up-field shift movements in **c3** and **c4** because of the stacking arrangement of the guest and phenanthrene, however, both Hb and Hc have to be shifted to the lower field because they are placed within the deshielding cone of the guest benzene ring.

The observed behavior of the chemical shift movements in **3a**, **4a**, **5**, and **6** is consistent with the theoretical shift movements in **c1** and **c2** but not compatible to those of **c3** and **c4**. Thus, the chemical shift movements of all the aromatic protons can be clearly explained by the formation of the intramolecular complex with the triple-decker sandwich arrangement of the three aromatic rings as in **c1** and **c2**. In other words, the guest moiety was entrapped within the tweezers shaped host in the closed form. Of course, the observed shift values reflect the population of the closed form in the equilibrium. The bigger the contribution of the closed form the larger the shift values in solution.

Chain length effect

The formation of the closed form is related to a ring formation by an intramolecular cyclization.[22] It is known that the yield of the cyclization is dependent on the chain length. In many instances, the formation of medium size rings (8- to 11-membered) is the most difficult.[23] In order to understand the effect of the chain length on the ease of the formation of the closed form in the equilibrium, we prepared series of compounds (**3a**–**3e**, **4a**–**4e**) having the host and guest moieties linked with different chain length. Intuitively, the probability of the two chromophores coming closer enough for the formation of the closed form should decrease as the chain gets longer. In terms of entropy, this implies the negative contribution of ΔS owing to reduction of freedom of internal rotation of the chain when disordered open-chain converted into the closed form.

The NMR chemical shift differences of the aromatic protons at –60 °C in the series of **3a**–**3e** with respect to the references are given in Figure 6. Protons Ha, Hc, and Hd show up-field shift. The shift difference of Hd is largest in **3a** and decreases with the number of the methylene in the chain. It is rather surprising that shift in **3c** (n=5) is larger than that of **3b** (n=4) and the graph shows a zigzag line. The same trends are shown in both Ha and Hc and also in Hb though the shift magnitudes are negative. It is known that n=3 (trimethylene chain) is the special number[24] to have the largest interaction between the two

chromophores linked by an appropriate methylene chain. Since the magnitude of the chemical shift difference corresponds to the population of the closed form, **3c** has larger population of the closed form t han **3b** though the entropy change in closed/open forms in **3c** should be more negative than in s**3b**. The same chemical shift behavior including zigzag lines with respect to the chain length was observed in the series of compounds (**4a-4e**), though the magnitudes of the shift differences are smaller.

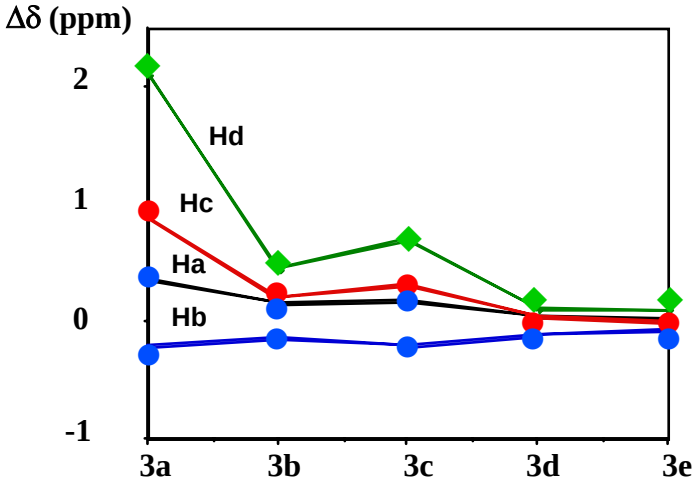


Figure 6. Chain length dependence of chemical shift difference in **3a-3e**.

CONCLUSION

This paper presents the synthesis of the flexible molecular tweezers having the covalently linked weak electron accepting guest and the formation of the intramolecular triple-decker complex of donor-acceptor-acceptor arrangement. The behavior of the temperature-dependent chemical shift movement of the aromatic protons was consistent to the formation of the intramolecular complexes whose structures were predicted by molecular mechanics calculations. Efficiency of the intramolecular complex formation is dependent both on the electron accepting ability of the guest and chain length which links the host and guest moieties.

EXPERIMENTAL

Preparation of the tethered compounds

A mixture of **2** and 10 eq of lithium hydroxide monohydrate in MeOH/THF/H_2O = 1/3/1 was refluxed for 3 h and treated with 1N-HCl. The mixture was extracted with ethylacetate, and the organic layer was washed with brine, and dried (Na_2SO_4). The solvent was removed under reduced pressure to afford carboxylic acid (95%). ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.59-8.57 (m, 2H), 8.26-8.23 (m, 2H), 7.74 (d, 1H, J= 1.5 Hz), 7.62-7.57 (m, 5H), 7.16 (s, 1H), 7.00 (s, 1H), 6.92 (d, 1H, J=8.5 Hz), 5.66 (s, 2H), 5.62 (s, 2H), 5.49 (s, 2H), 5.34 (s, 2H); IR 3300-2800, 1692, 1254 cm^{-1}. MS M^+ m/z 490; HRMS for $C_{31}H_{22}O_6$: m/z (calcd) M^+=490.1416; m/z (obsd) =490.1422.

A mixture of carboxylic derivative and 1 eq of corresponding bromoalkyl derivatives of weak electron acceptor and 1.5 eq of K_2CO_3 in 30 mL of DMF was stirred one day at 80°C. The reaction mixture was poured into 50 mL of ethyl acetate. The organic layer was washed with 1N-HCl, saturated $NaHSO_4$ and brine, dried (Na_2SO_4). The solvent was removed under reduced pressure, residue was purified by silica gel column chromatography ($CHCl_3$) and then by GPC ($CHCl_3$) to afford tethered derivatives.

Tethered compound (3a) (n=3)

75% yield. yellow powder, mp 216-219°C; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.42-8.36 (m, 3H), 8.21-8.16 (m, 2H), 7.82 (dd, 1H, J=1.5, 8.5 Hz), 7.81-7.43 (m, 5H), 7.20 (s, 1H), 7.19-7.16 (m, 2H), 7.08 (s, 1H),

6.52 (d, 1H, J=8.5 Hz), 5.70 (s, 2H), 5.68 (s, 2H), 5.45 (s, 2H), 5.33 (s, 2H), 4.32 (t, 2H, J=6.0 Hz), 3.89 (t, 2H, J= 6.5 Hz), 2.16 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.993, 165.811, 165.268, 153.647, 151.044, 147.464, 140.155, 139.369, 136.717, 136.526, 135.848, 134.497, 132.883, 131.413, 129.098, 128.605, 128.477, 128.320, 127.953, 127.718, 126.880, 126.702, 125.963, 125.520, 125.472, 124.785, 124.368, 123.726, 122.327, 122.270, 122.034, 121.744, 120.738, 118.107, 75.981, 74.805, 74.102, 72.768, 62.899, 36.400, 26.978; IR 1718, 1539, 1344 cm^{-1}. MS M^+ m/z 722; HRMS for $C_{42}H_{30}N_2O_{10}$: m/z (calcd) M^+=722.1900; m/z (obsd) =722.1904.

Tethered compound (3b) (n=4)

78% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.47-8.42 (m, 2H), 8.31-8.27 (m, 2H), 8.21-8.15 (m, 2H), 7.61-7.49 (m, 6H), 7.41 (dd, 1H, J=2.1, 8.4 Hz), 7.16 (s, 1H), 7.04 (s, 1H), 6.73 (d, 1H J=8.4, Hz), 5.68 (s, 2H), 5.62 (s, 2H), 5.45 (s, 2H), 5.33 (s, 2H), 4.24 (t, 2H, J=6.3 Hz), 3.75 (t, 2H, J=6.6 Hz), 1.82 (m, 4H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 163.066, 162.792, 162.471, 150.858, 148.264, 144.777, 136,948, 136.834, 133.614, 133.568, 133.232, 133.018, 131.439, 129.989, 128.394, 125.907, 125.434, 125.373, 124.824, 124.778, 123.816, 123.641, 123.229, 122.550, 122.489, 121.710, 121.665, 120.947, 119.368, 118.849, 118.819, 118.094, 115.240, 72.892, 71.580, 71.480, 70.000 60.890, 35.206, 22.990, 21.800; IR 1716, 1538, 1343 cm^{-1}. MS M^+ m/z 736; HRMS for $C_{43}H_{32}N_2O_{10}$: m/z (calcd) M^+=736.2059; m/z (obsd) =736.2024.

Tethered compound (3c) (n=5)

66% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.46-8.43 (m, 2H), 8.36 (d, 1H, J=1.8 Hz), 8.25-8.16 (m, 3H), 7.61-7.49 (m, 6H), 7.39 (dd, 1H, J=1.8, 8.4 Hz), 7.19 (s, 1H), 7.04 (s, 1H), 6.75 (d, 1H, J=8.4 Hz), 5.67 (s, 2H), 5.63 (s, 2H), 5.47 (s, 2H), 5.33 (s, 2H), 4.21 (t, 2H, J=6.0 Hz), 3.70 (t, 2H, J=7.2 Hz), 1.74 (m, 4H), 1.42 (br m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 166.069, 165.840, 165.558, 153.717, 151.191, 147.735, 139.930, 139.792, 136.756, 136.588, 136.161, 135.978, 134.452, 132.987, 131.560, 128.867, 128.745, 128.386, 127.791, 126.791, 126.669, 126.189, 125.563, 125.423, 124.856, 124.617, 123.862, 122.351, 121.855, 121.039, 118.231, 75.932, 74.566, 74.490, 72.929, 63.999, 38.287, 28.033, 27.613, 22.860; IR 1716, 1539, 1343 cm^{-1}. MS M^+ m/z 750; HRMS for $C_{44}H_{34}N_2O_{10}$: m/z (calcd) M^+=750.2213; m/z (obsd) =750.2244.

Tethered compound (3d) (n=6)

70% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.51-8.48 (m, 2H), 8.45 (d, 1H, J=1.8 Hz), 8.39 (dd, 1H, J=1.8, 6.3 Hz), 8.23-8.18 (m, 2H), 7.77 (d, 1H, J=6.3 Hz), 7.63 (d, 1H, J=1.2 Hz), 7.61-7.50 (m, 5H), 7.15 (s, 1H), 7.00 (s, 1H), 6.85 (d, 1H, J=8.7 Hz), 5.65 (s, 2H), 5.61 (s, 2H), 5.45 (s, 2H), 5.31 (s, 2H), 4.21 (t, 2H, J=6.6 Hz), 3.70 (t, 2H, J=7.2 Hz), 1.71 (br m, 4H), 1.41 (br t, 4H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 166.130, 165.863, 165.680, 153.762, 151.374, 147.949, 140.227, 139.899, 136.763, 136.458, 136.199, 136.039, 134.490, 133.170, 131.400, 128.974, 128.592,128.439, 128.394, 127.860, 127.799, 126.753, 126.723, 126.227, 125.578, 125.464, 125.060, 124.541, 124.052, 122.381, 121.908, 121.794, 121.161, 118.361,75.848, 74.787, 74.528, 73.155, 64.648, 38.485, 28.445, 28.170, 26.324, 25.622; IR 1716, 1539, 1343 cm^{-1}. MS M^+ m/z 764; HRMS for $C_{45}H_{36}N_2O_{10}$: m/z (calcd) M^+=764.2370; m/z (obsd) =764.2369.

Tethered compound (3e) (n=10)

56% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.58 (d, 1H, J=1.8 Hz), 8.56-8.53 (m, 2H), 8.50 (dd, 1H, J=1.8, 8.1 Hz), 8.27-8.21 (m, 2H), 7.93 (d, 1H, J=8.1 Hz), 7.70 (d, 1H, J=2.1 Hz), 7.69-7.52 (m, 5H), 7.14 (s, 1H), 7.00 (s, 1H), 6.90 (d, 1H, J=8.7 Hz), 5.64 (s, 2H), 5.61 (s, 2H), 5.45 (s, 2H), 5.32 (s, 2H), 4.23 (t, 2H, J=6.6 Hz), 3.70 (t, 2H, J=7.5 Hz), 1.68 (br m, 4H), 1.29 (br s, 12H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 163.204, 162.921, 162.838, 150.797, 148.546, 145.120, 137.368, 137.238, 133.698, 133.415, 133.163, 131.592, 130.394, 128.143, 126.052, 125.625, 125.480, 124.915, 124.877, 123.771, 123.244, 122.580, 122.534, 122.328, 121.558, 121,214, 119.444, 118.910, 118.849, 118.208, 115.4921, 72.846, 71.854, 71.747, 70.305, 61.981, 35.702, 26.294, 26.309, 26.149, 26.012, 25.653, 25.386, 23.738, 22.937; IR 1717, 1539, 1343 cm^{-1}. MS M^+ m/z 820; HRMS for $C_{49}H_{44}N_2O_{10}$: m/z (calcd) M^+=820.2996; m/z (obsd) =820.2993.

Tethered compound (4a) (n=3)

77% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.49-8.45 (m, 2H), 8.24-8.19 (m, 2H), 7.68 (dd, 1H,

J=1.0, 8.0 Hz), 7.62-7.48 (m, 6H), 7.36-7.33 (m, 2H), 7.17 (s, 1H), 7.04 (s, 1H), 6.67 (d, 1H, J=8.5 Hz), 5.68 (s, 2H), 5.65 (s, 2H), 5.46 (s, 2H), 5.32 (s, 2H), 4.31 (t, 2H, J=6.0 Hz), 3.88 (t, 2H, J=7.0 Hz), 2.16 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.650, 165.342, 162.788, 153.671, 147.696, 144.708, 140.017, 139.899, 136.785, 136.771, 136.273, 134.861, 134.89, 133.717, 131.449, 128.694, 128.459, 128.441, 128.103, 127.972, 127.928, 126.800, 126.764, 126.509, 126.111, 125.572, 125.522, 124.804, 124.494, 123.455, 122.441, 122.78, 121.890, 121.830, 120.967, 76.003, 74.604, 74.549, 72.902, 62.622, 36.315, 27.078; IR 1718, 1541, 1354 cm^{-1}. MS M^+ m/z 722; HRMS for $C_{42}H_{30}N_2O_{10}$: m/z (calcd) M^+=722.1900; m/z (obsd) =722.1893.

Tethered compound (4b) (n=4)

77% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.56-8.52 (m, 2H), 8.25-8.20 (m, 2H), 8.10 (dd, 1H, J=1.2, 8.4 Hz), 7.91 (dd, 1H, J=1.2, 7.5 Hz), 7.76 (dd, 1H, J=7.5,8.4Hz), 7.67 (d, 1H, J=2.1 Hz), 7.61-7.53 (m, 5H), 7.13 (s, 1H), 7.00 (s, 1H), 6.86 (d, 1H, J=8.4 Hz), 5.64 (s, 2H), 5.61 (s, 2H), 5.59 (s, 2H), 5.32 (s, 2H), 4.27 (t, 2H, J=6.0 Hz), 3.76 (t, 2H, J=6.9 Hz), 1.80 (m, 4H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.471, 165.619, 162.857, 153.892, 147.964, 140.235, 140.174, 136.687, 136.519, 136.130, 135.154, 134.459, 133.895, 133.216, 131.240, 128.615, 128.462, 128.386, 127.913, 127.875, 126.822, 126.761, 126.349, 125.555, 125.517, 124.838, 124.693, 122.450, 121.878, 121.847, 121.184, 75.917, 74.764, 74.703, 73.116, 63.976, 38.287, 26.072, 24.966; IR 1718, 1541, 1352 cm^{-1}. MS M^+ m/z 736; HRMS for $C_{43}H_{32}N_2O_{10}$: m/z (calcd) M^+=736.2059; m/z (obsd) =736.2014.

Tethered compound (4c) (n=5)

69% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.54-8.51 (m, 2H), 8.25-8.20 (m, 2H), 7.93 (dd, 1H, J=1.2, 7.8 Hz), 7.87 (dd, 1H, J=1.2, 7.8 Hz), 7.70-7.51 (m, 7H), 7.14 (s, 1H), 7.00 (s, 1H), 6.85 (d, 1H, J=8.7 Hz), 5.65 (s, 2H), 5.62 (s, 2H), 5.44 (s, 2H), 5.31 (s, 2H), 4.23 (t, 2H, J=6.3 Hz), 3.71 (t, 2H, J=7.2 Hz), 1.74 (m, 4H), 1.45 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.756, 165.672, 162.865, 153.801, 147.994, 144.866, 140.174, 140.067, 136.702, 136.519, 136.115, 135.039, 134.528, 133.879, 131.232, 128.615, 128.447, 128.294, 127.913, 127.867, 126.753, 126.257, 125.563, 125.510, 125.029, 124.594, 123.633, 122.427, 121.870, 121.840, 121.145, 75.901, 74.734, 74.635, 73.162, 64.312, 38.417, 28.132, 27.827, 23.188; IR 1718, 1541, 1357 cm^{-1}. MS M^+ m/z 750; HRMS for $C_{44}H_{34}N_2O_{10}$: m/z (calcd) M^+=750.2213; m/z (obsd) =750.2221.

Tethered compound (4d) (n=6)

74% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.56-8.53 (m, 2H), 8.25-8.20 (m, 2H), 8.01 (dd, 1H, J=0.9, 6.6 Hz), 7.98 (dd, 1H, J=0.9, 6.6 Hz), 7.78 (t, 1H, J=6.6 Hz), 7.67 (d, 1H, J=2.1 Hz), 7.62-7.52 (m, 5H), 7.13 (s, 1H), 6.99 (s, 1H), 6.89 (d, 1H, J=8.7 Hz), 5.64 (s, 2H), 5.60 (s, 2H), 5.44 (s, 2H), 5.31 (s, 2H), 4.22 (t, 2H, J= 6.6Hz), 3.70 (t, 2H, J= 6.9Hz), 1.70 (m, 4H), 1.41 (m, 4H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.794, 165.756, 162.888, 153.808, 148.063, 144.943, 140.311, 140.166, 136.687, 136.458, 136.100, 135.100, 134.536, 134.009, 131.179, 128.569, 128.470, 128.356, 127.921, 127.875, 126.822, 126.753, 126.273, 125.563, 125.517, 125.166, 124.579, 123.717, 122.443, 121.901, 121.840, 121.580, 121.184, 75.871, 74.826, 74.696, 73.223, 64.701, 38.577, 28.498, 28.170, 26.423, 25.591; IR 1718, 1541, 1354 cm^{-1}. MS M^+ m/z 764; HRMS for $C_{45}H_{36}N_2O_{10}$: m/z (calcd) M^+=764.2370; m/z (obsd) =764.2374.

Tethered compound (4e) (n=10)

62% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.56-8.53 (m, 2H), 8.26-8.21 (m, 2H), 8.04-8.01 (m, 2H), 7.80 (t, 1H, J=7.8 Hz), 7.69 (d, 1H, J=2.4 Hz), 7.62-7.53 (m, 5H), 7.12 (s, 1H), 6.98 (s, 1H), 6.90 (d, 1H, J=8.4 Hz), 5.64 (s, 2H), 5.60 (s, 2H), 5.43 (s, 2H), 5.30 (s, 2H), 4.23 (t, 2H, J=6.9 Hz), 3.68 (t, 2H, J=7.5 Hz), 1.67 (m, 4H), 1.29 (m, 12H); ^{13}C-NMR (75MHz $CDCl_3$) δ 165.817, 162.872, 153.785, 148.124, 144.943, 140.334, 140.212, 136.657, 136.413, 136.070, 135.070, 134.574, 134.085, 131.095, 128.577, 128.478, 128.317, 127.921, 127.875, 126.807, 126.753, 126.234, 125.563, 125.517, 125.334, 124.541, 123.755, 122.443, 121.893, 121.840, 121.519, 121.184, 75.833, 74.833, 74.726, 73.284, 64.991, 38.737, 29.330, 29.284, 29.162, 29.002, 28.658, 28.277, 26.728, 25.590; IR 1718, 1541, 1357 cm^{-1}. MS M^+ m/z 820; HRMS for $C_{49}H_{44}N_2O_{10}$: m/z (calcd) M^+=820.2996; m/z (obsd) =820.2990.

Tethered compound (5)

60% yield. colorless oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.55-8.52 (m, 2H), 8.25-8.22 (m, 2H), 7.85 (s, 1H), 7.62-7.45 (m, 6H), 7.47 (d, 1H, J=7.6 Hz), 7.44 (dd, 1H, J=1.5, 7.6 Hz), 7.15 (s, 1H), 7.02 (s, 1H), 6.78 (d,

1H, J=8.5 Hz), 5.66 (s, 2H), 5.64 (s, 2H), 5.45 (s, 2H), 5.32 (s, 2H), 4.30 (t, 2H, J=6.0 Hz), 3.85 (t, 2H, J=6.5 Hz), 2.13 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 167.387, 166.876, 165.478, 153.921, 147.979, 140.268, 140.140, 136.790, 136.676, 136.579, 136.287, 134.549, 133.535, 131.228, 130.420, 128.791, 128.701, 128.538, 128.492, 127.982, 127.963, 126.783, 126.742, 126.477, 126.210, 125.560, 125.531, 124.693, 124.668, 124.430, 122.482, 122.438, 121.915, 121.882, 121.083, 75.958, 74.796, 74.694, 73.165, 62.461, 35.634, 27.444; IR 1714 cm^{-1}. MS M-1$^+$, M+1$^+$ m/z 755, 757; HRMS for $C_{42}H_{30}NO_8Br$: m/z (calcd) M-1$^+$=755.1155, M+1$^+$=757.1144; m/z (obsd) M-1$^+$=755.1147, M+1$^+$=757.1103.

Tethered compound (6)

60% yield. colorless oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.56-8.53 (m, 2H), 8.27-8.21 (m, 2H), 7.76-7.73 (m, 2H), 7.67 (d, 1H, J=2.7 Hz), 7.63-7.49 (m, 7H), 7.14 (s, 1H), 7.00 (s, 1H), 6.80 (d, 1H, J=8.4 Hz), 5.65 (s, 2H), 5.62 (s, 2H), 5.44 (s, 2H), 5.31 (s, 2H), 4.31 (t, 2H, J=6.0 Hz), 3.85 (t, 2H, J=6.6 Hz), 2.14 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 168.221, 165.543, 153.862, 147.929, 140.204, 140.174, 136.657, 136.527, 136123, 134.459, 133.841, 131.911, 131.217, 128.539, 128.478, 127.936, 127.905, 126.738, 126.280, 125.533, 125.502, 124.731, 123.129, 122.450, 122.435, 121.870, 121.062, 75.924, 74.749, 74.703, 73.101, 62.328, 35.204, 27.628; IR 1710 cm^{-1}. MS M$^+$ m/z 677; HRMS for $C_{42}H_{31}NO_8$: m/z (calcd) M$^+$=677.2050; m/z (obsd) =677.2010.

Tethered compound (7)

83% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.67 (d, 1H, J=3.0 Hz), 8.52-8.51 (m, 2H), 8.25 (dd, 1H, J=2.5, 9.5 Hz), 8.23-8.19 (m, 2H), 7.65 (d, 1H, J=2.0 Hz), 7.60-7.52 (m, 5H), 7.10 (s, 1H), 7.02 (d, 1H, J=9.0 Hz), 6.95 (s, 1H), 6.87 (d, 1H, J=9.0 Hz), 5.61 (s, 2H), 5.56 (s, 2H), 5.41 (s, 2H), 5.28 (s, 2H), 4.46 (t, 2H, J=6.0 Hz), 4.24 (t, 2H, J=6.0 Hz), 2.28 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.497, 156.403, 154.082, 148.160, 140.266, 140.170, 140.021, 138.680, 136.708, 136.295, 136.212, 134.504, 131.109, 128.944, 128.603, 128.439, 128.434, 127.911, 127.881, 126.781, 126.253, 125.559, 125.564, 124.633, 124.628, 122.439, 121.869, 121.856, 121.812, 121.343, 114.097, 75.815, 74.750, 74.678, 73.287, 67.248, 60.821, 28.388; IR 1711, 1526, 1342 cm^{-1}. MS M$^+$ m/z 714; HRMS for $C_{40}H_{30}N_2O_{11}$: m/z (calcd) M$^+$=714.1850; m/z (obsd) =714.1866.

Tethered compound (8)

69% yield. yellow oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.53-8.51 (m, 2H), 8.23-8.20 (m, 2H), 7.86-7.78 (m, 3H), 7.66 (d, 1H, J=1.5 Hz), 7.60-7.52 (m, 5H), 7.09 (s, 1H), 6.95 (s, 1H), 6.88 (d, 1H, J=8.5 Hz), 5.61 (s, 2H), 5.57 (s, 2H), 5.41 (s, 2H), 5.28 (s, 2H), 4.45 (t, 2H, J=6.0 Hz), 4.28 (t, 2H, J=6.0 Hz), 2.28 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.506, 154.062, 152.156, 150.143, 148.131, 140.305, 140.172, 136.714, 136.348, 136.158, 134.480, 131.146, 128.561, 128.460, 128.455, 127.923, 127.879, 126.771, 126.759, 126,314, 126.035, 125.580, 125.534, 124.657, 124.645, 122.432, 121.887, 121.825, 121.313, 115.331, 109.599, 75.845, 74.789, 74.675, 73.239, 67.037, 60.838, 28.344; IR 1712, 1544, 1346 cm^{-1}. MS M$^+$ m/z 714; HRMS for $C_{40}H_{30}N_2O_{11}$: m/z (calcd) M$^+$=714.1850; m/z (obsd) =714.1871.

Tethered compound (9)

61% yield. colorless powder, mp 148-149℃; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.57-8.54 (m, 2H), 8.25-8.21 (m, 2H), 8.16 (d, 2H, J=7.2 Hz), 7.68 (d, 1H, J=1.8 Hz), 7.63-7.52 (m, 5H), 7.12 (s, 1H), 6.96 (s, 1H), 6.90 (d, 3H, J=7.2 Hz), 5.63 (s, 2H), 5.59 (s, 2H), 5.43 (s, 2H), 5.30 (s, 2H), 4.45 (t, 2H, J=6.0 Hz), 4.16 (t, 2H, J=6.0 Hz), 2.25 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.619, 163.673, 154.060, 148.178, 141.509, 140.380, 140.273, 136.725, 136.725, 136.283, 136.222, 134.490, 131.117, 128.569, 128.470, 127.936, 127.905, 126.776, 126.288, 125.876, 125.594, 125.555, 124.754, 124.640, 122.465, 121.893, 121.832, 121.344, 114.355, 75.871, 74.833, 74.749, 73.315, 65.304, 61.260, 28.513; IR 1701, 1593, 1340 cm^{-1}. MS M$^+$ m/z 669; HRMS for $C_{40}H_{31}NO_9$: m/z (calcd) M$^+$=699.1999; m/z (obsd) =699.1957.

Tethered compound (10)

54% yield. colorless powder, mp 152-153℃; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.58-8.55 (m, 2H), 8.27-8.22 (m, 2H), 7.72 (d, 1H, J=2.1 Hz), 7.63 (s, 2H), 7.61-7.54 (m, 5H), 7.13 (s, 1H), 6.98 (s, 1H), 6.89 (d, 1H, J=8.7 Hz), 5.63 (s, 2H), 5.59 (s, 2H), 5.43 (s, 2H), 5.30 (s, 2H), 4.45 (t, 2H, J=6.0 Hz), 4.16 (t, 2H, J=6.0 Hz), 2.25 (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.657, 153.976, 152.526, 148.124, 141.509, 140.403, 136.710, 136.405, 136.161, 135.016, 134.497, 131.186, 128.501, 127.951, 127.913, 126.769, 126.357,

125.578, 125.540, 125.006, 124.701, 122.473, 121.908, 121.855, 121.252, 118.994, 117.491, 75.871, 74.833, 74.749, 73.315, 65.304, 61.260, 28.513; IR 1711 cm^{-1}. MS M-3^+, M-1^+, M+1^+, M+3^+m/z 858, 860, 862, 864; HRMS for $C_{40}H_{29}O_7Br_3$: m/z (calcd) MS M-3^+=857.9463, M-1^+=859.9446, M+1^+=861.9431, M+3^+=863.9425; m/z (obsd) M-3^+=857.9460, M-1^+=859.9471, M+1^+=861.9458, M+3^+=863.9431.

Preparation of tethered compounds (11) and (12)

A mixture of 1,2-bis(bromomethyl)benzene (1.6 g, 6.1 mmol) and methylprotocatechuate (1.3 g, 6.5 mmol) in 30 mL of acetone was added dropwise to a suspension of cesium carbonate (5.0 g, 15 mmol) in 30 mL of acetone at refluxed temperature. The reaction mixture was refluxed for 2 h and was filtered. The solvent was removed under reduced pressure, residue was purified by silica gel column chromatography (50% Hexane/$CHCl_3$) to afford 1.3 g (81%) of cyclophane methyl ester; colorless powder, mp 112-113℃; ^{1}H-NMR (300 MHz $CDCl_3$) δ 7.74 (d, 1H, J=1.8 Hz), 7.62 (dd, 1H, J=1.8, 8.4 Hz), 7.30-7.26 (m, 3H), 7.13 (br t, 1H), 6.94 (d, 1H, J=8.4 Hz); ^{13}C-NMR (75 MHz $CDCl_3$) δ 166.344, 154.258, 136.153, 134.406, 130.461, 128.951, 128.523, 128.050, 126.204, 124.937, 124.670, 121.245, 76.420, 73.986, 51.92; IR 1716, 1304 cm^{-1}. MS M^+ m/z 270; HRMS for $C_{16}H_{14}O_4$: m/z (calcd) M^+=270.0892; m/z (obsd) =280.0872.

A mixture of cyclophane methyl ester (500 mg, 1.8 mmol) and lithium hydroxide monohydrate (780 mg, 18 mmol) in 7 mL of MeOH/THF/H_2O = 3/3/1 was refluxed for 1 h. The reaction mixture was poured into 150 mL of ethyl acetate. The organic layer was washed with 1N-HCl and brine, and then dried (Na_2SO_4). The solvent was removed under reduced pressure to afford 470 mg (99%) of carboxylic acid. colorless powder; ^{1}H-NMR (300 MHz $CDCl_3$) δ 7.80 (d, 1H, J=2.4 Hz), 7.68 (dd, 1H, J=2.4, 8.1 Hz), 7.29-7.26 (m, 3H), 7.14 (br s, 1H), 6.96 (d, 1H J=8.1 Hz); ^{13}C-NMR (75 MHz $CDCl_3$) δ 155.067, 148.414, 136.161, 134.215, 130.622, 129.027, 128.546, 127.959, 127.020, 125.433, 123.648, 121.344, 73.902; IR 2917, 1687 cm^{-1}. MS M^+ m/z 256; HRMS for $C_{15}H_{12}O_4$: m/z (calcd) M^+=256.0736; m/z (obsd) =256.0771.

A mixture of carboxylic acid (50 mg, 0.19 mmol) and 1 eq of corresponding w-bromoalkylphthalimides and 1.5 eq of K_2CO_3 in 30 mL of DMF was stirred for one day at 80℃. The reaction mixture was poured into 50 mL of ethyl acetate. The organic layer was washed with 1N-HCl, saturated $NaHSO_4$ and brine, and then dried (Na_2SO_4). The solvent was removed under reduced pressure, residue was purified by silica gel column chromatography ($CHCl_3$) and then by GPC ($CHCl_3$) to afford tethered compounds.

Tethered compound (11)

73% yield. colorless powder, mp 153-154℃; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.61 (d, 1H, J=2.1 Hz), 8.48 (dd, 1H, J=2.1, 8.4 Hz), 7.91 (d, 1H, J=8.4 Hz), 7.56 (d, 1H, J=2.4 Hz), 7.49 (dd, 1H, J=2.4, 8.4 Hz), 7.31-7.26 (m, 3H), 7.13 (br t, 1H), 6.82 (d, 1H, J=8.4 Hz), 4.34, (t, 2H, J=6.0 Hz), 3.93, (t, 2H, J=6.6 Hz), 2.19, (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.489, 154.258, 136.374, 136.069, 134.337, 133.414, 130.522, 129.134, 128.989, 128.584, 128.073, 126.097, 124.510, 124.312, 118.620, 76.374, 73.948, 62.481, 36.273, 27.543; IR 1721, 1536, 1342 cm^{-1}. MS M^+ m/z 488; HRMS for $C_{15}H_{12}O_4$: m/z (calcd) M^+=488.1220; m/z (obsd) =488.1214.

Tethered compound (12)

69% yield. colorless oil; ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.04-7.99 (m, 2H), 7.82 (t, 1H, J =7.5 Hz), 7.65 (d, 1H, J=2.1 Hz), 7.50 (dd, 1H, J=2.1, 8.7 Hz), 7.31-7.26 (m, 3H), 7.14 (br t, 1H), 6.83 (d, 1H, J=8.7 Hz) 4.33, (t, 2H, J=6.6 Hz), 3.91, (t, 2H, J=6.6 Hz), 2.18, (m, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 165.680, 165.505, 154.228, 148.300, 136.222, 135.207, 134.430, 134.085, 130.530, 129.012, 128.516, 128.439, 128.088, 126.868, 126.097, 124.670, 124.586, 123.770, 121.145, 76.413, 73.902, 62.381, 36.250, 27.534; IR 1719, 1541, 1356 cm^{-1}. MS M^+ m/z 488; HRMS for $C_{15}H_{12}O_4$: m/z (calcd) M^+=488.1220; m/z (obsd) =488.1216.

Preparation of dioxa[2.2]orthocyclophane derivatives (2) and (13)

A mixture of phenanthrenequinone (50 mg, 0.24 mmol) and a catalytic amount of 10% palladium-carbon in 5 mL of THF was stirred under H_2 for one day at rt. The reaction mixture was filtered under Ar and the filtrate was added dropwise to a mixture of 1,2,4,5-tetrakis(bromomethyl)benzene (320 mg, 0.71 mmol) and cesium carbonate (188 mg, 0.58 mmol) in 50 mL of acetone at reflux temperature. The reaction mixture was refluxed for 1 h and was filtrated. The solvent was removed under reduced pressure and the residual oil was chromatographed on silica gel (3% Ethyl acetate/Hexane) to afford 30mg (25%) yield of

15; colorless powder, mp 201~204℃. ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.61-8.57 (m, 2H), 8.29-8.25 (m, 2H), 7.65-7.57 (m, 4H), 7.25 (s, 2H), 5.64 (s, 4H), 4.59 (s, 4H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 140.662, 137.336, 136.557, 131.484, 128.485, 127.959, 126.822, 125.632, 122.504, 121.916; IR 1209, 1109 cm^{-1}. MS M-2$^+$, M$^+$, M-2$^+$, m/z 496, 498, 500; HRMS for $C_{24}H_{18}O_2Br_2$: m/z (calcd) M-2$^+$ =495.9669, M$^+$ =497.9765, M-2$^+$ =499.9639; m/z (obsd) M-2$^+$ =495.9687, M$^+$ =497.9763, M-2$^+$ =499.9632.

A mixture of **15** and 1.1 eq of related catecol in acetone was added dropwise to a suspension of cesium carbonate (2.5 eq) in acetone at reflux temperature. The reaction mixture was refluxed for 2 h and was filtrated. The solvent was removed under reduced pressure and the residual oil was chromatographed on silica gel (12.5% Ethyl acetate/Hexane) to afford dioxa[2.2]orthocyclophane derivatives (**2**) and (**13**);

Dioxa[2.2]orthocyclophane derivative (13)

60% yield colorless powder; mp 228~230℃. ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.59-8.57 (m, 2H), 8.26-8.22 (m, 2H), 7.92 (d, 1H, J=2.4 Hz), 7.81(dd, 1H, J= 2.4, 9.0 Hz), 7.62-7.56 (m, 4H), 7.17 (s, 1H), 7.01 (s, 1H), 6.94 (d, 1H, J=9.0 Hz), 5.66 (s, 2H), 5.62 (s, 2H), 5.52 (s, 2H), 5.37 (s, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 155.678, 147.910, 142.707, 140.395, 140.281, 137.198, 136.596, 135.978, 133.864, 131.560, 128.577, 128.462, 127.997, 127.936, 126.830, 126.791, 125.624, 122.488, 121.901, 121.840, 121.542, 120.688, 119.436, 76.313, 74.810, 74.696, 73.315; IR 1522, 1334, 1265 cm^{-1}. MS M$^+$ m/z 491; HRMS for $C_{30}H_{21}NO_6$: m/z (calcd) M$^+$=491.1369; m/z (obsd) =491.1365.

Dioxa[2.2]orthocyclophane derivative (2)

89% yield; colorless powder; mp 94~96℃. ^{1}H-NMR (300 MHz $CDCl_3$) δ 8.58-8.57 (m, 2H), 8.26-8.23 (m, 2H), 7.70 (d, 1H J=1.2Hz), 7.62-7.56 (m, 5H), 7.14 (s, 1H), 7.00 (s, 1H), 6.90 (d, 1H, J=8.5 Hz), 5.65 (s, 2H), 5.62 (s, 2H), 5.46 (s, 2H), 5.33 (s, 2H); ^{13}C-NMR (75 MHz $CDCl_3$) δ 166.291, 153.987, 148.186, 140.447, 140.324, 136.776, 136.496, 136.228, 134.592, 131.201, 128.564, 128.556, 128.024, 127.983, 126.784, 126.771, 126.363, 125.593 125.552, 124.995, 124.711, 122.490, 121.946, 121.885, 121.246, 75.949, 74.907, 74.800, 73.287, 51.968; IR 1715, 1289, 1249 cm^{-1}. MS M$^+$ m/z 504; HRMS for $C_{32}H_{24}O_6$: m/z (calcd) M$^+$=504.1573; m/z (obsd) =504.1572.

X-Ray Diffraction Analysis of 13

The crystal data for **13** are follows; Monoclinic space group $P2_1/a$ with a = 14.4750 (4), b = 14.0470 (8), c = 14.926 (8) Å, b = 107.436 (3)°, V =2295.4 (2) Å^3, and Z = 4. The experimental formula is $C_{30}H_{21}NO_{10}$, molecular weight is 491.14 and calculated density is 1.42g·cm^{-3}. The three-dimensional X-Ray data were collected by the use of graphite-monochromated Mo-Ka radiation (λ= 0.71073 Å) on Mac Science DIP2030 diffractometer. Of 4251 total unique reflections, 3195 were considered observed at the level of |Fo| > 3.0 σ|Fo|. The structure was solved by the direct method (Sir97). All non-hydrogen atoms were located on the initial E synthesis. The location of hydrogen atoms were calculated and included in the further calculations Full matrix least square refinements with anisotropic 37 non-hydrogen atoms and 21 isotropic hydrogen converted to a conventional R factor of 0.097.

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