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Synthesis of a Molecular Tweezer Containing Pentafluorophenyl Groups and Investigation of the π–π Stacking Interaction for a Pentafluorophenyl Group in a Polar Organic Solvent

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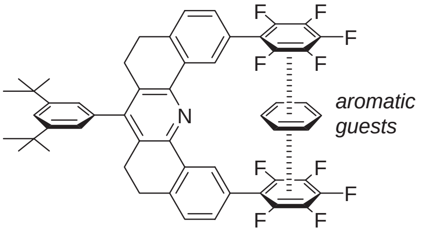
A molecular tweezer having two bidentate pentafluorophenyl (C_6F_5) groups was synthesized, and the π–π stacking ability of the C_6F_5 groups toward benzene derivatives in a polar organic solvent was evaluated. The structure of the molecular tweezer was revealed to be dimeric in the crystalline state by X-ray analysis. Association constants (K_a) between the molecular tweezer and aromatic guests in THF were found to be roughly correlated with the quadrupole moment (Q_{zz}) of the guests, suggesting that the quadrupole–quadrupole contribution plays a significant role in the π–π interaction even in a polar organic solvent.

Much interest has been focused on the π–π interaction between fluorinated benzenes and electron-rich aromatic rings in designing advanced materials.[1] For example, a mixture of hexafluorobenzene (HFB) and benzene forms a 1:1 co-crystal with a face-to-face stacked arrangement,[2] while benzene itself prefers an edge-to-face arrangement.[3] The pentafluorophenyl (C_6F_5) group[1,4] is interesting because of its electron-withdrawing property,[5] and also because of the π–π stacking ability, as demonstrated by X-ray analysis.[1,6] Although the π–π interaction is an interesting phenomenon, the utility of the perfluoroaromatic group has seldom been demonstrated in an organic reaction,[7,8] because the extent of the interaction in polar organic solvents has not been well established.[9,10] The interaction not likely to be strong in polar organic solvents,[9] because the interaction was reported to originate from the quadrupole–quadrupole contribution,[1,2b,11] i.e. an electrostatic contribution. As a preliminary examination for elucidation of the magnitude of the π–π interaction, we attempted to evaluate the association constants (K_a) between anisole and HFB or pentafluorobenzene (PFB) in $CDCl_3$; however, they were hard to access by the NMR titration.[12] Therefore, we newly designed the tweezer molecule **1** (Fig. 1a) having two C_6F_5 groups, which may have a higher affinity for aromatic guests by sandwiching them even in organic solvents.



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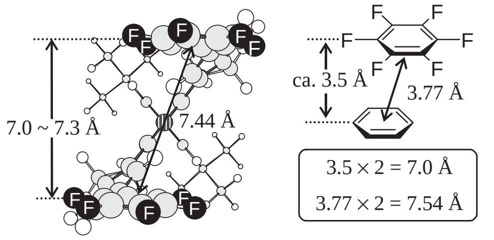
a) Design of molecular tweezer.



b) Optimization of **1** by DFT calculation.

c) Distance between HFB and benzene-d_6 based on X-ray structure.

Fig. 1. Design of molecular tweezer **1**.

Among the molecular tweezers reported,[13] compound **2** reported by Zimmerman et al.[14,15] (Fig. 2) is attractive because the distance of the two acridine groups is ca. 7–8 Å,[14b] which is suitable for capturing aromatic guest compounds. This distance is close to that between HFB and benzene in the crystal structure (Fig. 1c).[2c] DFT calculations of the structure **1** at B3LYP/6-31G* level by using Gaussian 03W[16] showed that the distance between the two C_6F_5 groups is 7.44 Å (centroid–centroid) or 7.0–7.3 Å (plane–plane) (Fig. 1b), these values can match the ones for the host–guest interaction.

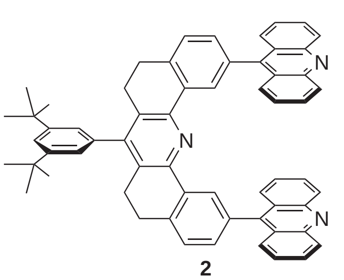


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Fig. 2. Molecular tweezer **2** reported by Zimmerman et al.

Here, the molecular tweezer **1** was successfully synthesized via introduction of a couple of C_6F_5 groups into dibromo pre-

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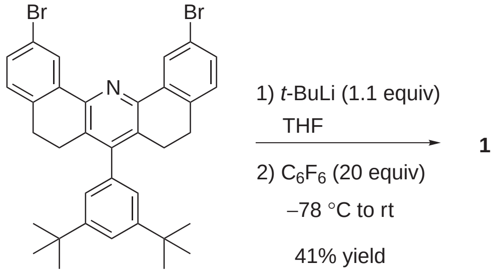
cursor **3**, which had been reported by Zimmerman et al. (Scheme 1)[14d] However, the introduction of C_6F_5 group into **3** was not easy. Although one of the most useful methods for aryl–aryl coupling is the Suzuki–Miyaura reaction,[17] the reaction between **3** and pentafluorophenylboronic acid with $[Pd(PPh_3)_4]$, and K_2CO_3 did not proceed.[18] Next, we examined the S_NAr reaction of the dianion from **3** toward HFB.[19] Thus, the dibromide **3** was treated with *n*-BuLi at −78 °C in THF, and the resulting dianion was allowed to react with 20 equivalent of HFB; however, the desired product **1** was not obtained. Finally, we changed the base to *t*-BuLi, which was found to be effective to promote the reaction, successfully giving the product **1** in 41% yield.

The structure of the compound **1** confirmed by X-ray analysis (Fig. 3)[20] was consistent with the calculated one (Fig. 1), especially as for the distance between the two C_6F_5 groups (Fig. 3: centroid–centroid = 7.29 Å and plane–plane = 6.6–6.9 Å). However, the structure was revealed to be an undesirable dimeric one, in which the pyridine ring of the one molecule is locked into the slit between the two C_6F_5 groups of the other molecule. These results suggest that the dimeric structure may weaken the association with aromatic guests.

Association constants (K_a) between the tweezer **1** and aromatic guests were measured by NMR titrations in ^{19}F NMR analysis at 27 °C. Unfortunately, we here encountered the low solubility of **1** in organic solvents. THF was the best solvent among those examined, although the solubility of **1** in THF is still low.[21] Addition of the guest molecule of *N*,*N*,*N*′,*N*′-tetramethyl-1,4-phenylenediamine (TMPD) to a 0.0076 M THF solution of **1** resulted in a upfield shift of the fluorine atoms at the *o*-position (Fig. 4a).[22,23] The K_a value was calculated to be 0.73 (±0.09) M^{-1} (Table 1, Entry 1) from the titration data by using the nonlinear least-squares method. The K_a values for other guests, such as 1,3,5-trimethoxybenzene, 1,3-dimethoxybenzene, *N*,*N*-dimethylaniline, anisole, and benzene, were also measured in a similar manner (Figs. 4b–f; Table 1, Entries 2–6),[24] although that for benzene was too small to detect. In contrast, K_a values for HFB could be detected only for TMPD and 1,3,5-trimethoxybenzene (Table 1); however, those for PFB could not. Thus, K_a values for **1** were found to be higher than those for HFB and PFB. The facts showed that the two C_6F_5 groups effectively sandwich the aromatic guests examined (Entries 2–5).



3

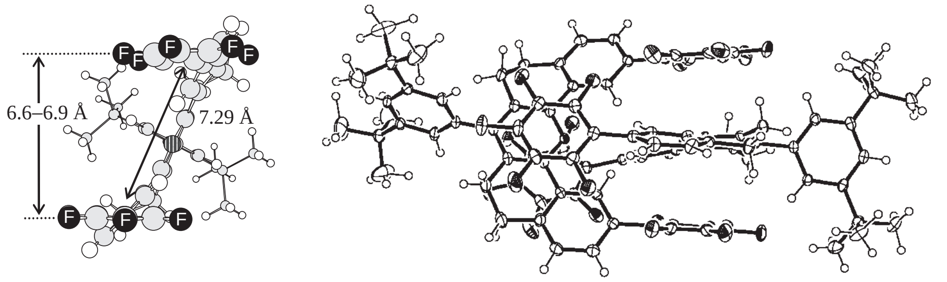
Scheme 1. Synthesis of molecular tweezer **1**.

The enhanced K_a values for the molecular tweezer **1** made it possible to assess the affinity of the C_6F_5 group for aromatic groups. To evaluate these results quantitatively, we calculated the quadrupole moments tensor (Q_{zz}) for the guest compounds at the HF/6-31G**//B3LYP/6-31G* level by using Gaussian 03W.[16,25] The values for $\Delta\Delta G^\circ$ are defined by the difference in ΔG° values for the guests relative to that for anisole, which were calculated from K_a values as shown in Table 1. We found a good correlation between Q_{zz} for the guests and K_a (Table 1), as shown in Fig. 5. Thus, the K_a values increase as the Q_{zz} values decrease. This correlation suggests that the π–π interactions originate from the quadrupole–quadrupole (i.e. electrostatic) contribution even in organic solvents and that charge-transfer contribution is less important, as reported previously.[26]

In conclusion, we designed and synthesized a molecular tweezer **1** containing bidentate C_6F_5 groups. The structural property and its ability for the π–π interaction in a polar organic solvent were elucidated. The NMR titration experiments suggest that the π–π intereaction in THF originates essentially from the quadrupole–quadrupole interaction.

Experimental

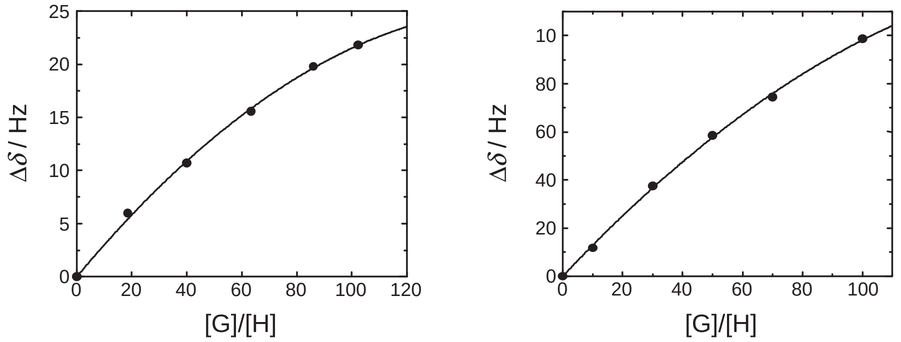
7-(3,5-Di-*t*-butyldiphenyl)-2,12-bis(pentafluorophenyl)-5,6,8,9-tetrahydrodibenzo[*c*,*h*]acridine (1). To a solution of dibromide **3**[14d] (283 mg, 0.45 mmol) in dry THF (12 mL) was added *t*-BuLi (1.50 M in hexane, 0.72 mL, 1.08 mmol) at −78 °C. After this mixture had been stirred for 0.5 h, 2.0 mL (18.0 mmol) of C_6F_6 was added, and then the resulting mixture was stirred for 84 h. The solvent was removed under reduced pressure, and then $CHCl_3$ was added. This mixture was washed with water, and dried over Na_2SO_4. After the solution was concentrated under reduced pressure, the residue was recrystallized from $CHCl_3$ and MeOH to give **1** (148 mg, 41% yield) as a white powder: mp >300 °C (dec.); ^1H NMR (500 MHz, $CDCl_3$) δ 1.38 (s, 18H), 2.72–2.77 (m, 4H), 2.87–2.92 (m, 4H), 7.05 (d, $J = 1.8$ Hz, 2H), 7.30 (m, 4H), 7.47 (t, $J = 1.8$ Hz, 1H), 8.59 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$, except for C_6F_5 carbon) δ 25.6, 27.8, 31.5, 35.0, 121.2, 122.9, 124.8, 127.2, 127.8, 129.3, 130.2, 135.2, 136.3,



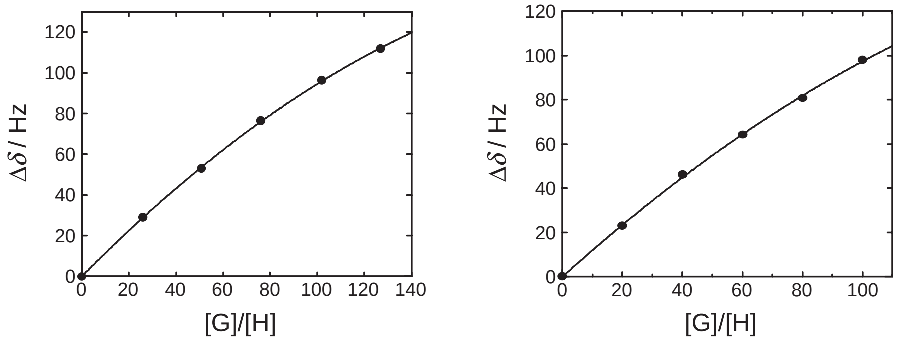
monomeric structure of **1**

dimeric structure of **1**

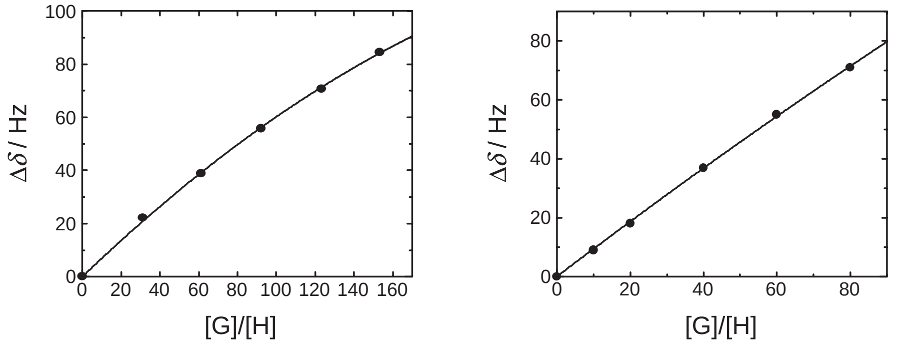
Fig. 3. X-ray analysis of **1**.



a) TMPD b) 1,3,5-trimethoxybenzene



c) 1,3-dimethoxybenzene d) *N*,*N*-dimethylaniline



e) anisole f) benzene

[G]/[H] = (concentration of guest) / (concentration of **1**)

Fig. 4. NMR titration of **1** with aromatic guests by ^{19}F NMR in THF.

138.9, 149.0, 149.2, 150.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ −163.8 (m, 2F), −157.4 (t, $J = 20.9$ Hz, 1F), −144.2 (m, 2F); IR (CCl_4) 716, 772, 804, 864, 883, 920, 931, 991, 1067, 1229, 1250, 1367, 1418, 1441, 1495, 1520, 1558, 1595, 2359, 2851, 2928, 2963 cm^{-1}. Anal. Calcd for $C_{47}H_{35}F_{10}N$: C, 70.23; H, 4.39; N, 1.74%. Found: C, 70.03; H, 4.47; N, 1.77%.

X-ray Analysis of 1. Crystals of **1** were obtained by recrystallization from CH_2Cl_2. Crystal data for **1** (dimeric structure): $C_{94}H_{70}F_{20}N_2$, MW = 1607.57, monoclinic, space group $P2_1/c$, $a = 17.0657(4)$, $b = 12.1689(4)$, $c = 37.045(1)$ Å, $\beta = 100.707(2)^\circ$, $V = 7559.1(4)$ Å^3, $T = 150.2$ K, $Z = 4$, $D_{\mathrm{calcd}} = 1.412$ g cm^{-3}, $R = 0.069$ for 15292 observed reflections [$I > 2.00\sigma(I)$] and 865 variable parameters. All measurements were made on a Rigaku RAXIS-IV imaging plate area detector with Mo Kα radiation. Crystallographic data have been deposited with Cambridge Crystallographic Data Centre: Deposition number CCDC-279883 for compound No. **1**. Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

Estimation of Association Constants by ^{19}F NMR Titrations. As a typical example, the titration of **1** with 1,3,5-trimethoxybenzene is described here. A 0.0084 M solution of **1** and a 3.0 M solution of 1,3,5-trimethoxybenzene in THF were prepared. A 420 µL portion of the solution of **1** and a 0, 17, 50, 84, 118, or 168 µL por-

Table 1. Measurement of the K_a Values of **1** by NMR Titration in THF[a]

Entry	Guests	K_a for **1** $/\mathrm{M}^{-1}$	$\Delta\Delta G^\circ$ for **1** $/\mathrm{kcal\,mol}^{-1}$ [b]	K_a for HFB[c] $/\mathrm{M}^{-1}$	K_a for PFB[d] $/\mathrm{M}^{-1}$	Q_{zz} of guests /DÅ[e]
1	TMPD[f]	0.73 ± 0.09	-1.1	0.14 ± 0.01	N.D.[g]	-16.30
2	1,3,5-Trimethoxybenzene	0.49 ± 0.06	-0.84	0.10 ± 0.02	N.D.[g]	-12.67
3	1,3-Dimethoxybenzene	0.29 ± 0.02	-0.53	N.D.[g]	N.D.[g]	-10.88
4	*N*,*N*-Dimethylaniline	0.27 ± 0.04	-0.48	N.D.[g]	N.D.[g]	-10.97
5	Anisole	0.12 ± 0.07	0.0	N.D.[g]	N.D.[g]	-9.41
6	Benzene	N.D.		N.D.[g]	N.D.[g]	-8.55

a) Determined by nonlinear curve-fitting method after measuring ^{19}F NMR in THF at 27 °C. b) Relative to ΔG° of anisole. c) Hexafluorobenzene. d) Pentaflurobenzene. e) Quadrupole moments tensors (Q_{zz}) calculated at HF/6-31G**//B3LYP/6-31G* level. f) *N*,*N*,*N*′,*N*′-Tetramethyl-1,4-phenylenediamine. g) Not detected.

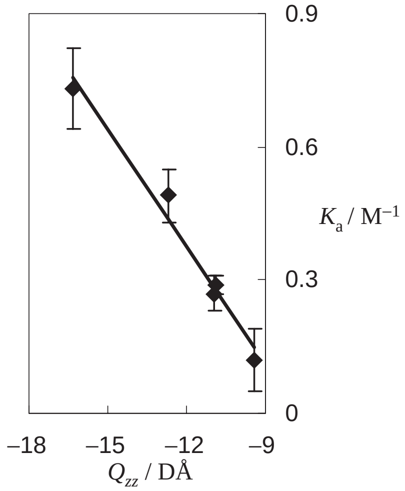


Fig. 5. Correlation between Q_{zz} for guest compounds and K_a for **1**.

tion of the solution of 1,3,5-trimethoxybenzene were combined, and the total volume was increased to 1 mL by adding THF. Each of the resulting solutions was placed in six NMR tubes, and then a capillary containing benzene-d_6 was inserted for an external *d* lock. ^{19}F NMR spectra were taken for each tube. The $\Delta\delta$ values were calculated by subtracting the chemical shift of interest in the spectrum of the mixtures (δ_x) from the appropriate resonance in the spectrum of pure **1** (δ_0). An association constant was calculated by a nonlinear curve-fitting method.

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Supporting Information

^{1}H, ^{13}C, and ^{19}F NMR and IR spectra, cartesian coordinates for **1**, synthetic procedures for precursor **3**, and NMR titration data. This material is available free of charge on the web at http://www.csj.jp/journals/bcsj/.

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22 The K_a values of **1** at other temperatures which were required for estimation of thermodynamic parameters (ΔH° and ΔS°) were difficult due to low solubility of **1** and small association constants.

23 Concentration-induced chemical shift variation in ^{19}F NMR of **1** was measured in THF at the range of 0.01–0.0005 M and found to be only 3 Hz, which is judged to be vanishingly small as compared with those observed for the host–guest complex. Therefore, the influence of the self-association of **1** is considered to be negligible.

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