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Synthesis and Properties of Two Tetrapus Host Molecules with Fluorinated Chains

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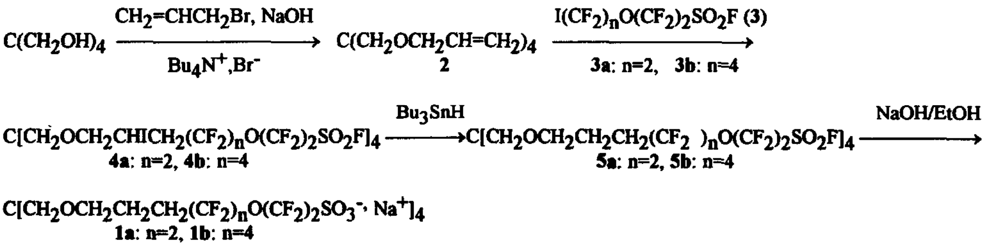
Abstract: Two tetrapus molecules, **1a** and **1b**, were synthesized. They each possess fluorinated tentacles with anionic termini, i.e., $CH_2O(CH_2)_3(CF_2)_2O(CF_2)_2SO_3^-Na^+$ for **1a** and $CH_2O(CH_2)_3(CF_2)_4O(CF_2)_2SO_3^-Na^+$ for **1b**. Cationic and anionic naphthalene fluorescence probes with $CH_2CH_2O(CH_2)_{10}$-chains (FP^+ and FP^-) were used to study host-guest interactions between partners of the following pairs, i.e., **1a** and FP^+, **1a** and FP^-, **1b** and FP^+, **1b** and FP^-. Our results demonstrate that electrostatic attraction is a powerful factor in facilitating the host-guest interactions between the tetrapus and the long-chain probes.

Perhaps modern-day host-guest or supramolecular chemistry can claim to reign over the greatest number of the most exotic molecular species or assemblages.[1] Among them are species coined as octopuses and tetrapuses.[2] On the other hand, the nature of the interaction between hydrocarbon and fluorocarbon chains is also of current interest.[3] Therefore, the present work is dedicated to the synthesis and property studies of two tetrapus molecules carrying four fluorinated chains with anionic termini, namely, tetra (1H,1H,3H,3H,4H,4H,5H,5H-2,8-bisoxa-perfluoro decyl sulfonic sodium) methane (**1a**), and tetra (1H,1H,3H,3H,4H,4H,5H,5H-2,10-bisoxa-perfluoro dodecyl sulfonic sodium) methane (**1b**). Other than the objective of finding out whether fluorinated chains can effectively entrap guest molecules with a hydrocarbon chain, we would also like to find out whether electric charge[4] can play an important role in host-guest interactions involving tetrapus host, since it was very recently established that electrostatic attraction is a deciding factor for the formation of electrostatically stabilized aggregate (ESAg), a species which occupies the structural niche next to and higher than that of the simple aggregate (Ag).[5]

The present work reports the synthesis of 1a and 1b according to Scheme I.

Scheme 1.



$$C(CH_2OH)_4 \xrightarrow[Bu_4N^+,Br^-]{CH_2=CHCH_2Br,\ NaOH} \underset{2}{C(CH_2OCH_2CH=CH_2)_4} \xrightarrow[\mathbf{3a}:\ n=2,\ \mathbf{3b}:\ n=4]{I(CF_2)_nO(CF_2)_2SO_2F\ (3)}$$

$$\underset{\mathbf{4a}:\ n=2,\ \mathbf{4b}:\ n=4}{C[CH_2OCH_2CHICH_2(CF_2)_nO(CF_2)_2SO_2F]_4} \xrightarrow{Bu_3SnH} \underset{\mathbf{5a}:\ n=2,\ \mathbf{5b}:\ n=4}{C[CH_2OCH_2CH_2CH_2(CF_2)_nO(CF_2)_2SO_2F]_4} \xrightarrow{NaOH/EtOH}$$

$$\underset{\mathbf{1a}:\ n=2,\ \mathbf{1b}:\ n=4}{C[CH_2OCH_2CH_2CH_2(CF_2)_nO(CF_2)_2SO_3^{-}\cdot Na^+]_4}$$

$NpCH_2CH_2O(CH_2)_{10}R$: FP^+, $R = N^+Me_3, Br^-$; FP^-, $R = CO_2^-,Na^+$; Np = α-naphthyl

Two previously described surfactants,[5b] namely, the cationic ω-[2-(α-naphthyl)- ethoxyl]decyl ammonium bromide (FP^+),and the anionic ω-[2-(α-naphthyl)ethoxyl] undecanoate (FP^-), were used as the fluorescence probes. The extent of host-guest interaction was monitored by the excimer fluorescence intensity (Ie) when two FP molecules were encapsulated inside the tetrapus tentacles.

Experimental Section

Infrared spectra were recorded on a IR-440 or Carl Zeiss specord-75 spectrometers. ^1H-NMR spectra were recorded on Varian EM-360A(60MHz) or Varian XL-200(200MHz) instruments, and the ^{19}F-NMR spectra were recorded on a EM-360L (60 MHz) instrument. All reagents were used without additional purification, unless specified in the procedure. The mass spectra were recorded on a Finnigan-4201 or Finnigan-8430 instrument.

Emission spectra in water at 298 K were recorded by a Perkin-Elmer LS-50 fluorescence spectrometer using the excitation wavelength of 284 nm. Both FP^+ and FP^- have fluorescence λ_{max}'s at 337 nm (monomer) and 400 nm (excimer), thus the latter was used to monitor excimer formation from FP^+ or FP^-. When the probes FP^+ and FP^- were used in the concentration range of 10^{-7}-10^{-5} M in H_2O, they only show 337 nm emission, and the emission intensity was in direct proportion to the concentration, thus both probes FP^+ and FP^- are in the monomeric state in this concentration range.

Compounds **1a** and **1b** are amphiphilic, they possess long hydrophobic chains with hydrophilic SO_3^- end groups. In water they can form micelles and cmc values were evaluated by surface tension measurements to be $(7.0 \pm 0.5) \times 10^{-3}$M for **1a**, and $(1.0 \pm 0.2) \times 10^{-3}$M for **1b**. Similarly, the cmc values of the fluorescence probes[5b] were measured to be $(5.0 \pm 0.2) \times 10^{-3}$M for FP^+, and $(2.0 \pm 0.1) \times 10^{-3}$M for FP^-.

Synthesis of **2**

A mixture of 40 g (1 mol) NaOH, 48 g (0.4 mol) allyl bromide, 6.8 g (50 mmol) pentaerythritol and 6.5 g (20 mmol) Bu_4NBr was stirred at room temperature for 5 h; then the solution was further stirred at 55°C for 24 h. It was extracted with ether (60 ml x 3), and the ethereal solution was dried over Na_2SO_4. After removal of the solvent, the residue was purified by chromatography to give 12.9 g (87%) of **2**. bp 126-128°C/8 torr; Anal. calcd. for $C_{17}H_{28}O_4$: C, 68.92%, H, 9.46%. Found: C, 69.33 %, H, 9.25 %; IR (film): 2800-3100, 1640 cm^{-1}; ^1H-NMR (CCl_4): δ 3.3(s, 8 H), 3.8 (d, 8 H), 4.8-5.3 (m, 8 H), 5.4-6.1 ppm (m, 4 H); M/Z: 297 (M^++1), 239 (M^+-57).

Synthesis of **4**

A mixture of 2.96 g (10 mmol) **2**, 17.0 g (40 mmol) **3a**, 4 g (40 mmol) $NaHCO_3$, 90 ml CH_3CN and 30 ml H_2O was stirred at 10°C while 8 g $Na_2S_2O_4$ was added in several portions within 1 h. The reaction was followed by ^{19}F-NMR monitoring and was shown to be complete in 1 h. The solution was extracted with ether (30 ml x 3), the combined ethereal solution was washed with water and then dried over Na_2SO_4. After removal of ether,the residue was purified by chromatography (petroleum ether/acetone = 20:1 as eluent) to give 6.7 g (yield 80%) **4a**. Anal. calcd. for $C_{33}H_{28}F_{36}S_4O_{16}I_4$: C, 19.80%, H, 1.40%, F, 34.21. Found: C, 19.84 %, H, 1.27 %, F, 34.97%; IR (film): 2860 -2950, 1460 and 1190 cm^{-1}; ^{1}H-NMR: δ 4.38 (m, 4 H), 3.68 (d, 8 H), 3.56 (s, 8 H), 3.2-2.5 ppm (m, 8 H); ^{19}F-NMR (CCl_4): δ 82.3 (8 F, 4 OCH_2CF_2S), 87.3 (8F,4 OCF_2CF_2C), 114.3 (8 F, 4 CF_2S), 117.8 (8 F, 4 CF_2CH_2), -121.0 (4 F, 4 SO_2F) ppm; M/Z: 1745 (M$^+$-2I-1), 1617 (M$^+$-3I-1), 1491 (M$^+$-4I-1).

4b was similarly prepared. yield 73%. Anal. calcd. for $C_{41}H_{28}F_{52}S_4O_{16}I_4$: C, 20.50%, H, 1.17%, F, 41.17%. Found: C, 20.43 %, H, 1.01 %, F, 41.40 %; IR (film): 2860-2950, 1470 and 1200 cm^{-1}; ^{1}H-NMR(CCl_4): δ 4.38 (m, 4H), 3.65 (d, 8H), 3.65 (s, 8H), 3.2-2.4 ppm (m, 8H); ^{19}F-NMR ($CDCl_3$): δ -121.0 (4F, 4 SO_2F), 82.8-83.8 (16F, d, 4 CF_2CF_2), 113.3 (8 F, 4 CF_2S), 114.3 (8 F, 4 CF_2CH_2), 124.3-125.8 ppm (16 F, d, other 16 F).

Synthesis of 5

A mixture of 4.8 g (2 mmol) 4b, 2.56 g (9 mmol) Bu_3SnH in 20 ml ether was stirred at room temperature while the reaction was followed by ^{19}F-NMR monitoring and was shown to be complete in 10 h. After removal of the ether, the residue was purified by chromatography to give 2.05 g (yield, 54%) **5b**. Anal. calcd. for $C_{41}H_{32}F_{52}S_4O_{16}$: C, 25.95%, H, 1.69%, F, 52.11%. Found: C, 25.96%, H, 1.60 %, F, 52.03 %; IR(film): 2700-3000, 1460, and 1240-1200 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.50 (t, 8H), 3.40 (s, 8H), 2.20 (m, 8H), 1.90 ppm (m, 8 H); ^{19}F-NMR ($CDCl_3$): δ -122.0 (4F, 4 FSO_2), 82.3-83.3 (16F, d, 4 CF_2OCF_2), 112.8 (8F, 4 CF_2S), 114.8(8F, 4 CF_2CH_2), 123.8-125.5 ppm (16F, d, other 16 F); M/Z: 1896 (M$^+$), 1813 (M$^+$-SO_2F).

5a was similarly prepared. yield: 51%. Anal. calcd. for $C_{33}H_{32}F_{36}S_4O_{16}$:C, 26.47%, H, 2.14%, F, 45.72%. Found: C, 26.87 %, H, 2.10 %; F, 46.38 %; IR(Film): 2800-3000, 1460 and 1260-1100 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 3.48 (t, 8H), 3.40 (m, 8 H), 2.20 (m, 8 H), 1.90 ppm (m, 8H); ^{19}F-NMR ($CDCl_3$): δ -121.0 (4F, 4 SO_2F), 82.8-87.8 (16F, 4 CF_2S), 118.8 (8F, 4 CF_2CH_2) ppm. M/Z: 1496 (M$^+$), 1413 (M$^+$-SO_2F).

Synthesis of 1

A mixture of 2.32g (1.23 mmol) **5b**, 0.48g (12 mmol) NaOH in 10 ml EtOH was stirred at room temperature. ^{19}F-NMR showed that the reaction was complete in 2 h. After removal of the EtOH, the residue was extracted with boiling EtOAc (30 ml x 3), The ester solution was filtered and the filtrate was evaporated under reduced pressure to give a colorless solid which was recrystallized from anhydrous EtOH to give 2.29 g (91%) **1b**. Anal. calcd. for $C_{41}H_{40}F_{48}S_4O_{24}Na_4.4H_2O$: C, 23.21%, H, 1.89%, F, 43.02%. Found: C, 24.27 %, H, 1.62 %, F, 44.24 %; IR (KBr): 1345 and 1160 cm^{-1}. ^{1}H-NMR (acetone-d$_6$): δ 3.7-3.3 (m, 16 H), 2.4-2.1 (m, 8 H), 1.9-1.7 ppm (m, 8 H); ^{19}F-NMR (acetone-d6): δ 82.3-84.3 (16 F, 4 CF_2OCF_2), 115.3 (8 F, 4 CF_2CH_2), 118.8 (8 F, 4 CF_2S), 123.8-125.5 ppm (16 F, d, other 16 F).

1a was similarly prepared. yield: 95%. Anal. calcd. for $C_{33}H_{40}F_{32}S_4O_{24}Na_4.4H_2O$: C, 23.02%, H, 2.33%, F, 35.35%. Found: C, 24.12 %, H, 2.20 %, F, 35.71 %; IR (KBr): 1348, 1158 cm^{-1}; ^{1}H-NMR (acetone-d_6): δ 3.6-3.4 (m, 16H), 2.4-2.1 (m, 8H), 1.9-1.7 ppm (m, 8H); ^{19}F-NMR (acetone-d_6): δ 82.3-87.8 (16 F, 4 CF_2OCF_2), 118.8 ppm (16 F, 4 CF_2CH_2, 4 CF_2S).

Results and Discussion

Schneider has shown that electrostatic attraction in aqueous solution may contribute 1.2 kcal/mol per ion pair of free energy,[4] and we have very recently demonstrated that in the concentration domain of 10^{-7} to 10^{-4} M, ESAg's (electrostatically stabilized aggregates) will form only from oppositely-charged molecules with flexible long-chains of roughly eight to sixteen CH_2's.[5a,b] Spectroscopically, ESAg formation can be quantitatively assessed by monitoring the formation of intermolecular excimers of fluorescence probes FP^+ or FP^-, which have λ_{max}'s at 337 nm (monomer) and 400 nm (excimer).[5b] The same technique, therefore, is applicable to a quantitative study of the host-guest interaction between the tetrapus **1** and fluorescence probe (FP^+ or FP^-). In almost all of our previous studies, it was found that the naphthalene-excimer formation was preceded by preassociation, which was brought about by hydrophobic lipophilic interactions (HLI).[5b,6] Therefore, in the present work, excimer formation would suggest that a considerable number of host molecules had entrapped two FP probes inside each tetrapus cavity.

Figures 1 and 2 are the fluorescence spectra of FP^+ and FP^- in aqueous solution. ([FP] = 1.0 x 10^{-5}M, in monomeric state) with increasing amounts of **1a** ([**1a**] = 0 - 1.0 x 10^{-4}M). The first notable feature of Figure 1 is the red shift of the λ_{max} of monomeric FP from 337 to approximately 350-360 nm when increasing amounts of **1a** are added. As mentioned in the experimental section, the monomeric λ_{max} in water is 337 nm, but in n-hexane it is red-shifted to 360 nm. Evidently, curves g and h suggest that practically all FP^+ molecules are encapsulated if sufficient amounts of **1a** are used ([**1a**] = 0.4 or 1.0 x 10^{-5}M). This conclusion is amply comfirmed by the six fluorescence spectra of increasing concentrations of FP^+ at a constant [**1a**] of 1.0 x 10^{-5}M (Figure 3), since all the monomeric λ_{max}'s are at about 357 nm, as shown in Figure 3. In other words, in the **1a** : FP^+ molar ratio range of 1 : 0.2 to 1:1, practically all the FP^+ molecules dwell in the tetrapus cavity.

The second important feature of Figure 1 is that decreasing intensities of FP^+ monomer fluorescence are always accompanied by increasing intensities of FP^+ excimer fluorescence. In fact, Figure 2 for the anionic probe FP^- also shows the same feature, but to a much lesser degree. If we let the ratio R = Ie/(Ie+Im), where Ie and Im are the fluorescence intensities at λ_{max}'s of the excimer and monomer respectively (cf. Figure 1 and 2), and plot R against log [**1a**] as shown in Figure 4, then we can readily obtain the critical coaggregate concentrations or CoCAgC values[5b] for the (**1a** and FP) systems. As previously mentioned, ESAg's[5] are premicelles to cationic/anionic (+/-) mixed micelles composed of comparable amounts of oppositely charged surfactants. Therefore, if the CoCAgC values for comparable amounts of oppositely charged surfactants are measured in the concentration domain of 10^{-6} - 10^{-4}M (10^{-3}M), they would correspond to the cmc values of (+/-) mixed micelles which are known to be much smaller than the cmc values of micelles composed of similarly charged surfactants.[7] It should be noted, however, that by our-previous definition the CoCAgC values (cf. ref. 8) are always measured at a constant concentration of the probe, e.g., FP. The CoCAgC for the (**1a** and FP^+) system is $(6.6\pm0.1) \times 10^{-7}$M; this is the smallest CoCAgC value on record for ESAg formation, e.g., for the ($S16^+$ + FP^-) system, it is 5.0×10^{-6}M, and for ($S12^-$ and FP^+), 1.0×10^{-4}M.[5b] On the other hand, for the (**1a** and FP^-) system, it is 6.3×10^{-5}M, a value two orders of magnitude larger! The aforesaid observation might be taken as a dramatic demonstration of the importance of electrostatic attraction, a notion heavily emphasized in the formulation of the ESAg concept.[5] It might be visualized that this electrostatic attractive force will keep the FP^+ probe molecules inside the tetrapus cavity by anchoring together oppositely charged termini and thus helping the hydrophobic force to coil-up the FP^+ hydrocarbon chains which can then readily stay inside the tetrapus cavity as "guests".Without this electrostatic force, as in the (**1a** and FP^-) system, the host-guest

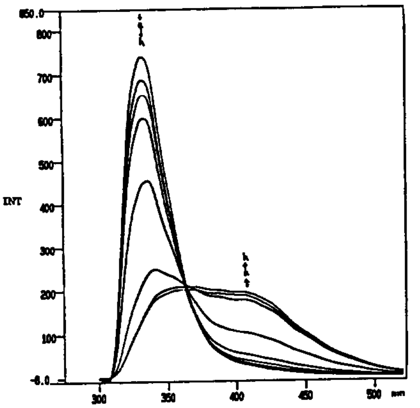


Figure 1. The effect of the concentration of **1a** on the fluorescence spectra of FP^+, $[FP^+] = 1.0 \times 10^{-5}$ M. Values of [**1a**] (10^{-6} M) are: a. 0; b. 0.1; c, 0.2; d. 0.4; e. 1.0; f. 2.0; g. 4.0; h. 10.0

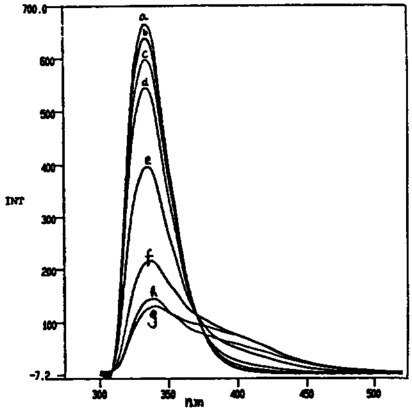


Figure 2. The effect of the concentration of **1a** on the fluorescence spectra of FP^-, $[FP^-] = 1.0 \times 10^{-5}$ M. Values of [**1a**] (10^{-6} M) are: a. 0; b. 1.0; c. 2.0; d. 4.0; e. 10.0; f. 20.0; g. 40.0; h. 100.0

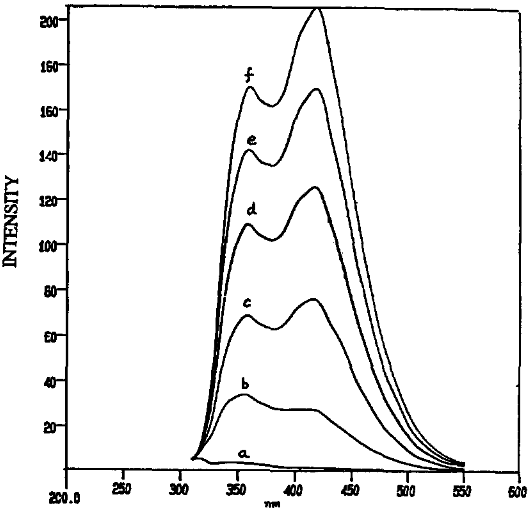


Figure 3. The emission spectra of FP^+ in H_2O with [**1a**] = 1.0×10^{-5} M, [FP^+] (10^{-6} M): a. 0; b. 2.0; c. 4.0; d. 6.0; e. 8.0; f. 10.0.

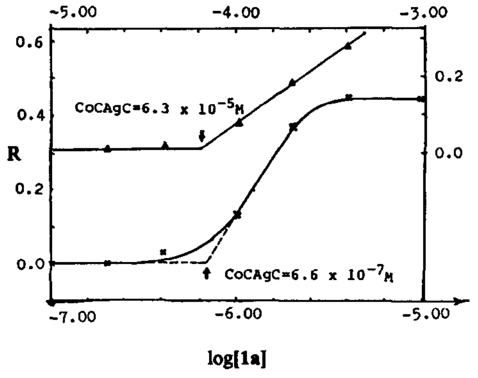


Figure 4. R [I_o / (I_o+I_m)] as a function of the log concentration of **1a**. Values on the left and bottom are for FP^+; values on the right and top are for FP^-.

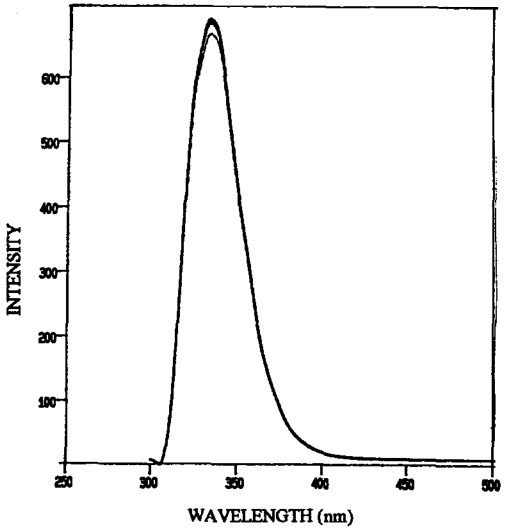


Figure 5. The effect of concentration of **1b** on the fluorescence spectra of FP^-, [FP^-] = 1.0×10^{-5} M. Values of [**1b**] (10^{-3} M) are: 0 - 10.

interaction becomes much weaker. This time perhaps some methylene chains might be dangling outside a lot of the times. Under these circumstances, there is little repulsive interaction between the anionic termini and the negative charge on FP^- because of the presence of Na^+ ions. This state of affairs in conjunction with host-guest interactions involving a preorganized host (tetrapus) make it possible for the (**1a**+FP^-) system to have a CoCAgC value (6.3 x 10^{-5}M) smaller than the CoCAgC values of some simple ESAg systems (cf. examples in ref. 5).

A comparison of the behavior of **1a** with that of **1b** might reveal the effect of four extra CF_2CF_2 segments on the capability of the tetrapus **1** to host a hydrocarbon guest, may it be favorable or unfavorable. In fact, Figure 5 for the (**1b** and FP^-) system shows that the larger-sized tetrapus **1b** no longer welcomes the hydrocarbon guest. This is somewhat of a surprising observation because the extra room provided by the four extra CF_2CF_2 segments might be expected to favor the host-guest interaction. Nonetheless, our results seem to suggest that the affinity between a fluorocarbon and a hydrocarbon chain is either exceedingly small or even negative in nature, a conclusion in accord with the conventional wisdom.[3]

For the (**1b** and FP^+) system, fluorescence spectra and a R vs log[**1b**] plot similar to Figures 1 and 2 were obtained. If the above-mentioned unfavorable effect of the four CF_2CF_2 segments is taken into consideration, we should expect that the CoCAgC value for the (**1b** and FP^+) system would be larger than that of the (**1a** and FP^+) system. Surprisingly, the CoCAgC value of (5.0 ± 0.1) x 10^{-7}M for the former system is almost the same as that of the latter, i.e., (6.6 ± 0.1) x 10^{-7}M. This observation again demonstrates that under certain circumstances electrostatic interactions might become an overpowering effect.

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