In recent years, the best-developed intramolecular C–H insertion reactions have been rhodium-catalyzed reactions of diazo carbonyl compounds, which are believed to occur via intermediate rhodium carbene complexes.[10] In a comparison of the methods, useful complementarity exists between the iron carbene and the rhodium-catalyzed reactions. From the point of view of synthetic strategy, the rhodium-catalyzed ring closures proceed with carbon–carbon bond formation α to a carbonyl group, whereas the iron-based reactions result in ring closure β to a carbonyl group. Also, the iron carbene reactions produce cyclopentane rings bearing a substituent incorporated stereoselectively at a position γ to a carbonyl group, a position that is not normally subject to direct introduction of substituents. Another attractive feature of the iron-based reactions is the ease and directness with which fairly complex substrates are available from simple starting materials.

Further, in-depth studies of the iron carbene insertion reaction are clearly necessary to define the scope of this new method. The effects of other saturated and unsaturated side-chain substituents as well as heteroatomic substituents will be explored.

Acknowledgment. We thank Dr. James T. Carey, Prof. Anthony Serianni, and Donald Schifferl for extensive help with NMR data, Dr. T. K. Mishra of the Carnegie-Mellon NMR Laboratory for obtaining 620-MHz ^{1}H NMR data, and Dr. Bruce Plashko for mass spectrometric measurements. We are also very grateful to the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, for providing generous financial support of this research.

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Highly Efficient Complexation of a π-Acceptor by a Molecular Tweezer Containing Two π-Donors: The Role of Preorganization

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The stacking of aromatic systems has relevance to many areas of chemistry. For example, it has found recent use as a binding element in host–guest chemistry.[2] We have described a new class of hosts (e.g., *molecular tweezer* **1**) which contain two acridine chromophores held syn cofacially by a rigid dibenz[*c*,*h*]acridine spacer.[3,4] In chloroform, the acridines acted as π-donor chromophores to "cooperatively" sandwich a π-deficient (acceptor) aromatic guest.[5] While efficient π-sandwiching is common when driven by the hydrophobic effect,[6] it has not been well documented in cases where electron donor–acceptor (EDA) interactions are the primary binding force.[7-9] In this communication we report

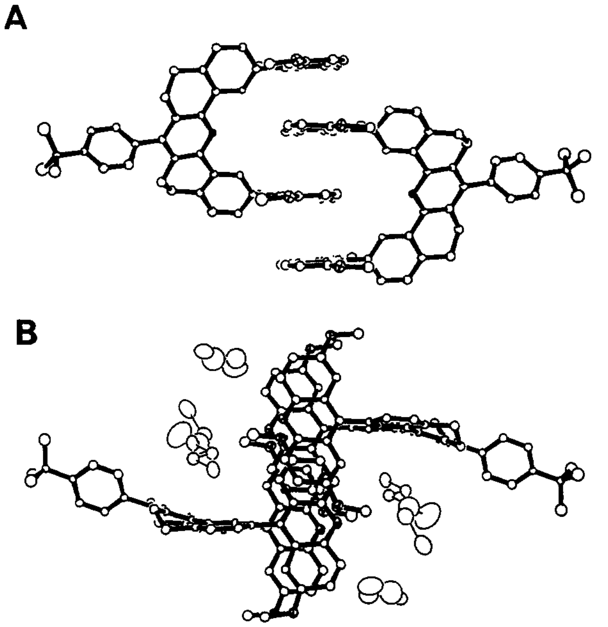

Figure 1. Side (A) and top (B) views of crystal packing of molecular tweezer **4**. Solvent molecules (dichloroethane) have been omitted in A for clarity.

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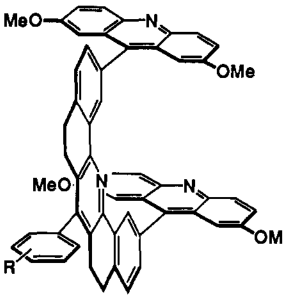
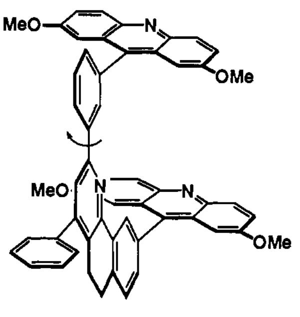


1: R = 3,5-di-t-Bu
4: R = 4-t-Bu



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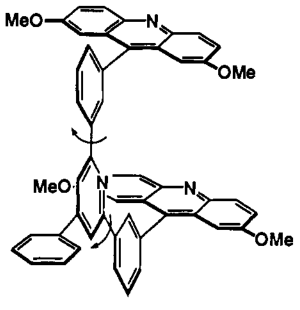

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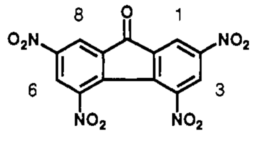

TENF

the magnitude of the cooperativity in the complex between molecular tweezers **1**–**3** and 2,4,5,7-tetranitrofluorenone (TENF). The new molecular tweezers **2** and **3** have spacer units that possess one and two free rotations, respectively. While *preorganization* has been shown to be critical in the binding of ionic guests,[10] its importance in the complexation of neutral molecules has not been well documented.[11-14]

Molecular tweezers **1**–**4** were prepared by addition of 2,7-dimethoxy-10-[(2-methoxyethoxy)methyl]acridone to the corresponding dilithio spacers.[15,16] Full appreciation of the structure of **4** (**1**) was achieved by a single-crystal X-ray diffraction study.[17] As seen in Figure 1, the acridines are held syn cofacially with a nearly perfect overlap when viewed along an axis orthogonal to the acridine ring. The ability of molecular tweezer **4** (**1**) to complex aromatic guests is apparent from the packing arrangement which indicates infinite arrays generated by each molecular tweezer partially sandwiching one acridine ring of an adjacent molecule.

Table I. Association Constants, Thermodynamic Parameters, and $\Delta\delta_{max}$ Values Obtained from the ^1H NMR Titration of 2,4,5,7-Tetranitrofluorenone (TENF) with Molecular Tweezers **1**–**3** and **5**[a]

compd	$\Delta\delta_{max}$,[b] ppm H-1(8)[c]	$\Delta\delta_{max}$,[b] ppm H-3(6)	K_{assoc},[d] M^{-1}	$-\Delta H°$[e,f]	$-\Delta S°_{288}$[e]	$-\Delta G°_{288}$[e]
1	>1.3	0.33	3400	6.3	5.6	4.7
2	>1.3	0.32	700	5.8	6.9	3.8
3	>1.3	0.32	170	4.7	6.3	2.9
5	1.2	0.60	≈3			<1

[a] Association constants and complexation shifts were determined from H-3 of TENF by using the methods described in ref 3. All duplicate runs agreed within 30%, most within 10%. For **5**, only ca. 40% saturation could be achieved, and the data were analyzed by using the Hildebrand–Benesi method.[18] [b] For protons of TENF. [c] Peak became obscured. [d] At 288 K. [e] Kilocalories per mole. [f] Enthalpies of binding were determined from the slopes of four-point van't Hoff plots. Duplicate determinations agreed within 10%.

The complexation of 2,4,5,7-tetranitrofluorenone (TENF) by **1**–**3** and 2,7-dimethoxy-9-phenylacridine (**5**) was monitored in chloroform-*d* solution by ^1H NMR. The complexation shifts ($\Delta\delta_{max}$) and association constants in Table I allow the following observations and conclusions to be made:

(1) Flexibility does not alter the complex geometry substantially. In the complex with **1**–**3**, the protons of TENF have nearly identical upfield shifts: $\Delta\delta_{max}$ H-3(6) = 0.3 ppm; $\Delta\delta_{max}$ H-1(8) > 1.3 ppm. This indicates oriented inclusion complexes where the fluorenone carbonyl is pointed toward but to one side of the spacer units.[3]

(2) Increased rigidity results in more stable complexes. An approximately 4-fold increase in K_{assoc} is experienced for each single-bond rotation that is frozen out (i.e., **3** → **2** → **1**). Thus, the effect of increasing rigidity is additive ($\Delta\Delta G°_{3\to1} = 2\Delta\Delta G°_{3\to2} = 1.8$ kcal mol^{-1}). The origin of this additivity is unclear given that the $-\Delta H°$ values do not increase in as regular a way. Furthermore, the $-\Delta S°_{288}$ value increases from **3** to **2** but decreases from **2** to **1**. Ordinarily, the tightest complex pays the highest price in entropy.[19]

(3) The two acridine rings in **1**–**3** show extraordinary "cooperativity" in sandwiching TENF. The association constant for **1** is ca. 10^3-fold larger than that for **5**.

(4) The enforced syn-cofacial orientation of the acridines in **1** provides no special advantage other than its nearness to the binding conformation. If enthalpically rich solvent molecules were present in the cleft,[20] or if the cleft were poorly solvated,[21] then a much larger increase in K_{assoc} would be seen from **2** to **1** relative to the increase from **3** to **2**. Thus, molecular tweezer **1** is not a high-energy host in search of stabilization from a guest molecule.

While the 1 kcal mol^{-1} loss in complex stability accrued with each new free bond rotation may represent a value specific to the molecular tweezer system,[22,23] the result suggests that rigidity is an important element in receptor affinity for neutral guests. We conclude by noting that highly cooperative π-sandwiching is a general phenomenon not dependent on hydrogen bonding, hy-

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(16) Schemes describing the synthesis of **1**–**5** and a table of "cyclization shifts" which shows open clefts for **1**–**3** are contained in supplementary material. Compounds **1**–**5** gave satisfactory elemental analyses for fractional solvates of the recrystallization solvent. All other spectroscopic data were in accord with the assigned structures.

(17) Crystal data for $C_{61}H_{51}N_3O_4\cdot2.5C_2H_4Cl_2$ at −75 °C: $a = 14.690$ (4) Å, $b = 12.247$ (11) Å, $c = 16.040$ (8) Å, $\alpha = 91.03$ (6)°, $\beta = 101.05$ (3)°, $\gamma = 92.50$ (5)°, $Z = 2$, $\rho_{calcd} = 1.336$ g cm^{-3} and space group P_1 (C_i^1). Of 7454 intensities measured (Mo Kα, 2° < 2θ < 44°), 6909 were processed, and 3096 reflections having $I > 2.58\sigma(I)$ were used in the full-matrix least-squares refinement. The solvent molecules were disordered. Final agreement factors are $R = 0.083$, $R_w = 0.096$.

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(23) The effects of freezing out single-bond rotations on intramolecular reaction rates are controversial: Bruice, T. C.; Pandit, U. K. *J. Am. Chem. Soc.* **1960**, *82*, 5858–5865. Page, M. I.; Jencks, W. P. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 1678–1683. Menger, F. M.; Venkataram, U. V. *J. Am. Chem. Soc.* **1985**, *107*, 4706–4709.

drophobic forces, or a syn orientation of the complexing chromophores. The origin of this cooperativity and applicability to new host–guest complexes is the subject of current investigation.[5]

Acknowledgment. We thank Lance E. Steward for the preparation of **5** and Scott Wilson for assistance with the X-ray analysis. Funding from the NIH (GM 38010) and the NSF (CHE 58202) is gratefully acknowledged. The Monsanto Company is acknowledged for a generous contribution toward the NSF-PYI program.

Supplementary Material Available: Schemes detailing the preparation of **1–5**, a table of "cyclization shifts" for **2–4**, and positional and thermal parameters from the X-ray analysis of compound **4** (9 pages). Ordering information is given on any current masthead page.

Self-Assembly of Bilayer Membranes in Organic Solvents by Novel "Amphiphilic" Compounds[1]

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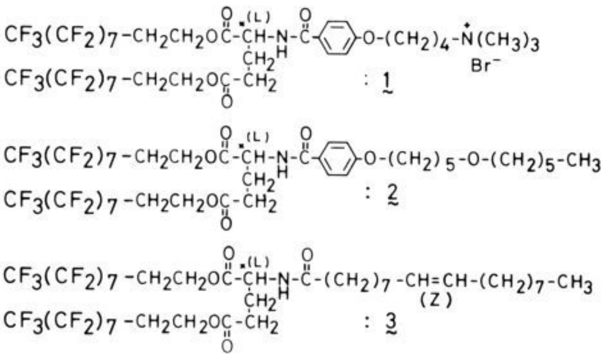
We describe herein spontaneous bilayer formation by perfluoroalkyl derivatives in nonaqueous media. The synthetic bilayer membrane[2] has been shown to be useful as biomembrane models and as novel functional materials, because of its unique molecular organizations and a rich variety of component molecules.[3] The bilayer structure is produced spontaneously when component amphiphiles are dispersed in water. However, it is usually not preserved in organic media, since the hydrophobic interaction is a major driving force for this assembly. Should stable molecular bilayers be produced in organic media, one could expect emergence of a wholly new branch of organic chemistry.

Some fluorocarbon amphiphiles have been shown to form stable bilayer membranes in water.[4-6] The limited miscibility between the fluorocarbon and hydrocarbon components led to reduced permeation of probe molecules into fluorocarbon vesicles and to controlled phase separation. The limited miscibility was also crucial in recent findings that semifluorinated *n*-alkanes, F-$(CF_2)_n(CH_2)_mH$, possessed bilayer-type crystal structures[7] and that they formed micellar aggregates in toluene and in fluorinated solvents.[8]

Ammonium amphiphile **1** (Chart I) forms stable bilayer vesicles in water.[9] Therefore, we adopted a similar molecular design and synthesized compounds **2** and **3** as components of molecular assemblies to be organized in organic media.[10] The ammonium head group in **1** is replaced by solvophilic units in **2** and **3**. The fluorocarbon tails should provide the solvophobic property.

Chart I



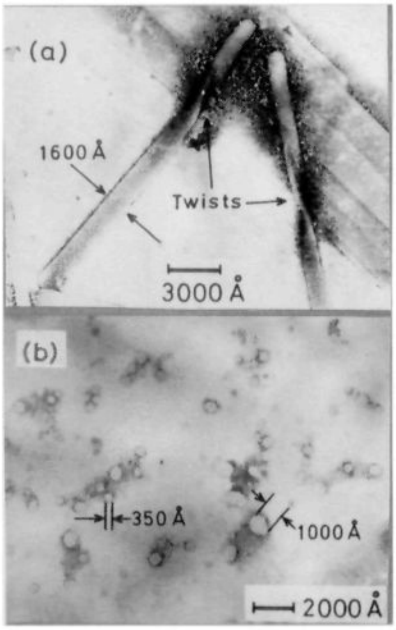


Figure 1. Electron micrographs of **2** in cyclohexane. **2** was poststained with lead(II) bis(acetylacetonate). $[\mathbf{2}] = (0.5 - 1.0) \times 10^{-4}$ M, ca. 17 °C. (a) Twisted tapes. (b) Vesicles.

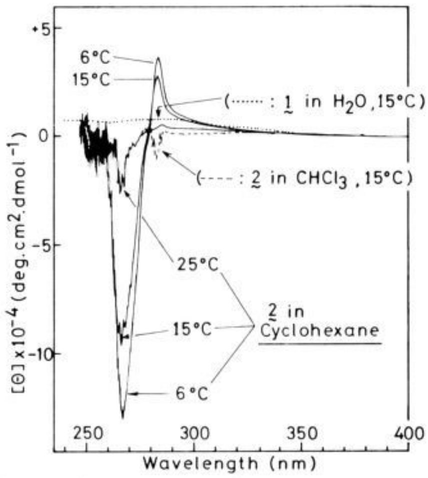


Figure 2. Circular dichroism spectra of **2** in organic solvent and aqueous **1**. $[\mathbf{1}] = [\mathbf{2}] = 1.0 \times 10^{-4}$ M.

Compound **2** gave a colorless, transparent solution in cyclohexane at 6–25 °C upon dispersion by warming.[11] A few drops

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(1) Contribution no. 912 from the Department of Organic Synthesis.

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(9) Kunitake, T.; Tawaki, S.; Nakashima, N. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3235–3242.

(10) Compounds **2** and **3** were prepared from bis(perfluoroalkyl) glutamate and the corresponding acid chlorides, according to the procedures employed for **1**. For **2**: Anal. Found: C, 38.98; H, 3.12; N, 1.08. Calcd for $C_{43}H_{41}O_7NF_{34}$: C, 38.84; H, 3.11; N, 1.05. For **3**: Anal. Found: C, 39.74; H, 3.65; N, 1.09. Calcd for $C_{43}H_{47}O_5NF_{34}$: C, 39.61; H, 3.63; N, 1.07. IR and NMR data are consistent with the respective structures.

(11) **2** was not soluble at all in hexane and decane. It gave clear solutions in hot alcohols, ethylene glycol, CH_3CN, DMF, and DMSO, but crystals precipitated at room temperature. $CHCl_3$, acetone, ethyl ether, dioxane, THF, and CF_2CCl_2 were good solvents.

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