Synthesis and Structure of Molecular Tweezers Containing Active Site Functionality

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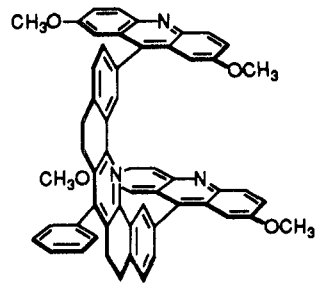
Abstract: A series of molecules has been synthesized in which a functional group is buried inside an aromatic binding cleft. These novel compounds, called "molecular tweezers", have a methyl ester (**6a**, **7–9a**, **10a**), a carboxylic acid (**6b**, **9b**, **10b**, **45**), or a nitrile (**50**) in their clefts. Molecular tweezer **21** has a metal ligand, an annelated terpyridine, oriented toward the binding cleft. The structures of **7–10** have been determined either by X-ray analysis or by molecular modeling techniques and were found to contain different inter-anthracene (acridine) distances and varying degrees of twist in their spacers. As precursors to nucleotide base receptors, these molecules represent four discrete steps toward the development of an optimized receptor for adenine.

Previous reports from this laboratory[1] have described the synthesis, structure, and complexation chemistry of a class of host molecules, called molecular tweezers[2] (e.g. **1**). The critical structural element of these cleft-like receptors is the tetrahydrodibenz[*c*,*h*]acridine spacer, which holds the two acridine rings in an enforced syn orientation with a ca. 7-Å interchromophore separation. As such, receptor **1** efficiently binds π-deficient guests in organic solvents by forming π-sandwich complexes.



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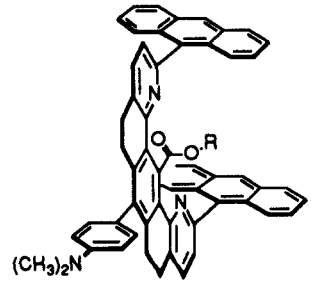
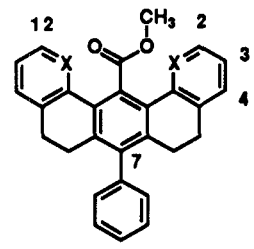
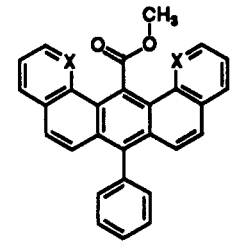


6a : R = CH_3
6b : R = H

In order to increase the molecular tweezers "stickiness"[3] for π-neutral guests, we have sought to incorporate a functional group that might hydrogen bond to the guest. Preliminary studies have shown that spacers **2–5**, containing bay region ester groups, can be efficiently synthesized.[4] X-ray crystal analysis of **3** and **5** showed them to have very different structural features and therefore disparate potentials for the construction of a guest sticky molecular tweezer. In a preliminary report we described the synthesis of **6b**, an efficient receptor of adenine, which is based on spacer **4**.[5] Herein we present full details of this synthesis of **6** along with a new, more efficient, and general synthesis. Also reported are synthetic and structural studies of molecular tweezers based on spacers **2**, **3**, and **5** and molecular tweezers with either a nitrile (**50**) or a terpyridine ligand (**21**) oriented toward the binding cleft. In the following paper full details of the complexation chemistry of molecular tweezer **6b** are described and a comparative binding study with adenine receptors **9b** and **10b** is given.



2: X = CH
4: X = N



3: X = CH
5: X = N

Results and Discussion

Design. The design of the new receptors has as its starting point our earlier molecular tweezers (e.g. **1**) which were known to bind efficiently π-deficient aromatic guests through the formation of π-sandwich complexes. Although these receptors contain a weakly basic nitrogen atom oriented toward the binding cleft, we sought a functional group that could engage in two or more hydrogen bonds and thus increase the binding affinity and selectivity for π-neutral guests. A carboxylic acid was chosen as a suitable group.[6] Even though carboxylic acids can dimerize in nonpolar aprotic media,[7] self-association would be hindered since the group would be buried deep within an aromatic cleft (see Figure 1).

The new spacer design raised several important structural concerns. The previous dibenz[*c*,*h*]acridine spacer was known to have a C-2 to C-12 distance of 7.24 Å,[8] so that chromophores attached at these positions would be held just slightly further apart than the presumed optimum of 6.8 Å. If a functional group were attached to the central atom of the bay region, it was expected that the C-2 to C-12 distance would increase and the spacer might distort as a result of the introduction of severe peri-interactions.[9] For this reason, it was important to determine the C-2 to C-12 distances and the relative orientations of the carboxylic acid and the complexing chromophores in these new molecular tweezers. A model study showed that spacer **3** could be efficiently syn-

(1) (a) Zimmerman, S. C.; VanZyl, C. M. *J. Am. Chem. Soc.* **1987**, *109*, 7894–7896. (b) Zimmerman, S. C.; VanZyl, C. M.; Hamilton, G. S. *J. Am. Chem. Soc.* **1989**, *111*, 1373–1381. (c) Zimmerman, S. C.; Mrksich, M.; Baloga, M. *J. Am. Chem. Soc.* **1989**, *111*, 8528–8530.

(2) Chen, C.-W.; Whitlock, H. W., Jr. *J. Am. Chem. Soc.* **1978**, *100*, 4921–4922.

(3) Adams, S. P.; Whitlock, H. W. *J. Am. Chem. Soc.* **1982**, *104*, 1602–1611. Sheridan, R. E.; Whitlock, H. W., Jr. *Ibid.* **1986**, *108*, 7120–7121. Sheridan, R. E.; Whitlock, H. W., Jr. *Ibid.* **1988**, *110*, 4071–4073. A related host for aromatic carboxylates: Echavarren, A.; Galán, A.; Lehn, J.-M.; de Mendoza, J. *Ibid.* **1989**, *111*, 4994–4995.

(4) Zimmerman, S. C. *Tetrahedron Lett.* **1988**, *29*, 983–986.

(5) Zimmerman, S. C.; Wu, W. *J. Am. Chem. Soc.* **1989**, *111*, 8054–8055.

(6) Crown ethers with convergent carboxylic acids: Newcomb, M.; Moore, S. S.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6405–6410. Bell, T. W.; Cheng, P. G.; Newcomb, M.; Cram, D. J. *Ibid.* **1982**, *104*, 5185–5188. Rigid spacers with converging carboxylic acids: Rebek, J., Jr.; Nemeth, D. *J. Am. Chem. Soc.* **1985**, *107*, 6738–6739.

(7) Pimentel, G. C.; McClellan, A. L. *The Hydrogen Bond*; Freeman: San Francisco, 1960. Davis, M. M.; Paabo, M. *J. Org. Chem.* **1966**, *31*, 1804–1810.

(8) Mason, R. *Proc. R. Soc. London, Ser. A* **1960**, *258*, 302–318.

(9) Cf.: Pascal, R. A., Jr.; McMillan, W. D.; Van Engen, D. *J. Am. Chem. Soc.* **1986**, *108*, 5652–5653.

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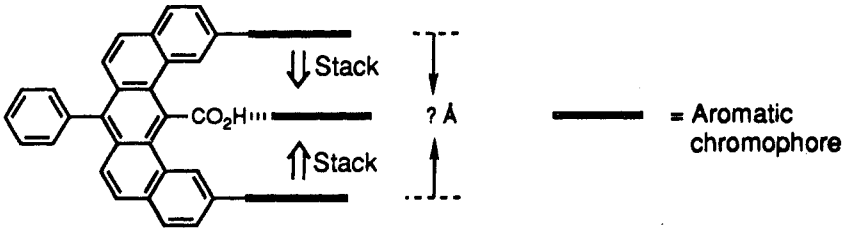
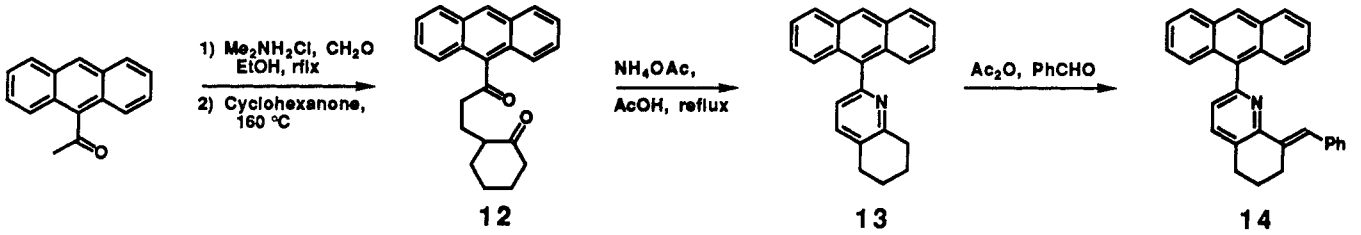


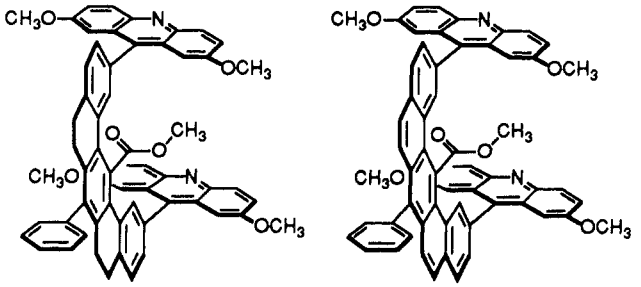
Figure 1. Schematic representation of a molecular tweezer with a carboxylic acid at the central bay-region position of the spacer unit. The guest is an aromatic compound capable of forming one or more hydrogen bonds to the carboxylic acid.

Scheme I

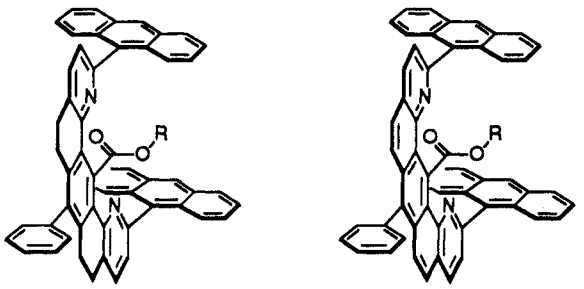


thesized, but it had a large twist (40°) from end-to-end and a C-2 to C-12 distance of 8.2 Å.[4] The severity of the peri-interactions was found to be lessened in spacer **5** where nitrogen atoms occupy the peri-positions (1 and 13). Thus, the twist in **5** was only 22° and the C-2 to C-12 distance was 7.5 Å. According to these studies, a molecular tweezer based on spacer **5** would have the most favorable structural features. Still, incorporating spacers **2–4** into molecular tweezers (i.e. **7–10**) would provide a unique opportunity to examine a series of receptors with differing interchromophore distances and chromophore overlap.

Synthesis. Substantial quantities of **7–10** would be needed for structural and binding studies. For this reason, the synthesis of these new receptors needed to be short, efficient, and easily



7 **8**



9a : R = CH_3 **10a** : R = CH_3
9b : R = H **10b** : R = H

scaled-up. Ideally, the chromophores at C-2 and C-12 would be attached to the spacer at the end of the synthesis so that their properties could be varied easily. Our reported synthesis of **6** met none of these criteria.[5] An alternative route to **9**, an analogue of **6a**, has proven to be shorter and more versatile. Molecular tweezers **7** and **8** were synthesized in a few, easily scaled-up steps starting from inexpensive materials.

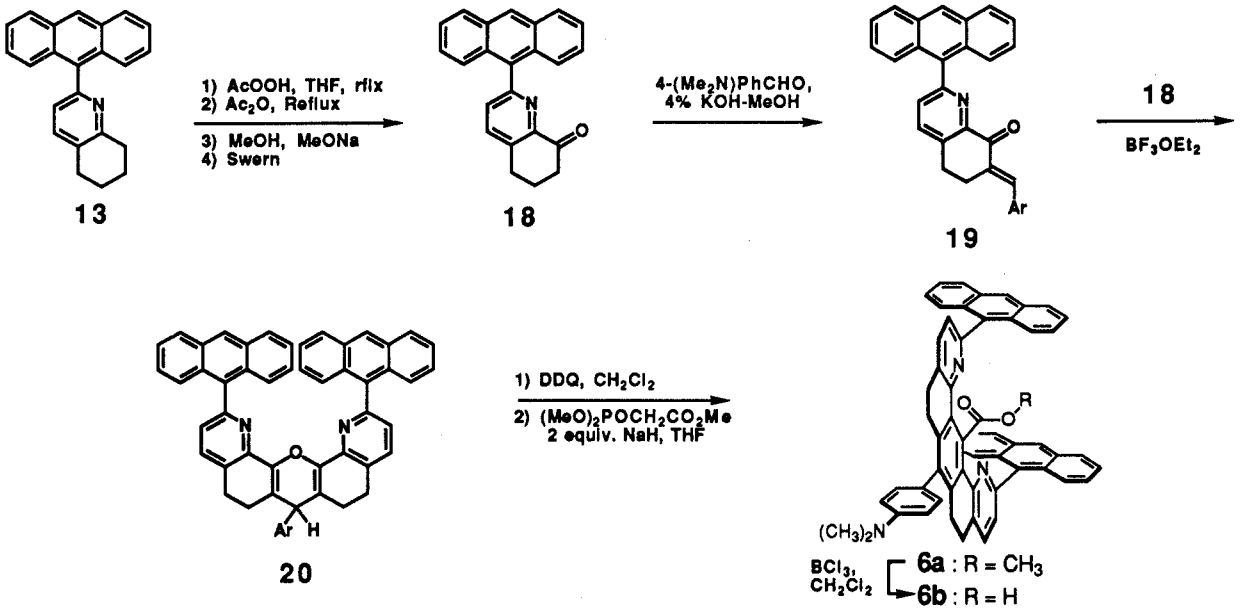
(a) Synthesis of 6a: A Molecular Tweezer with an Active Site Ester. Our previously described synthesis of **6a**[5] began with 9-acetylanthracene which was converted into its Mannich base **11** with use of standard conditions (Scheme I).[10] Refluxing **11** in 3 equiv of cyclohexanone afforded 1,5-diketone **12**,[11] and this was reacted with ammonium acetate in refluxing acetic acid[12] to afford tetrahydroquinoline **13** in 57% yield for the three steps. Although the addition of cupric acetate[13] gave **13** in higher yield, the reaction proved to be more difficult to work up on a very large scale. Oxidation of the benzylic position in **13** was effected by refluxing with benzaldehyde in acetic anhydride.[14] The product benzylidene (**14**) could be obtained in 69% yield, but its ozonolysis was problematic in that competitive oxidation of the anthracene ring occurred.

Rather than pursuing alternative methods for oxidatively cleaving the arylidene in **14**, a four-step lateral oxidation was applied to **13**.[14] Toward this end, **13** was converted into its *N*-oxide (**15**) with peracetic acid, and this was refluxed in acetic anhydride to afford the benzylic acetate **16** (Scheme II). Hydrolysis to quinolinol **17** followed by Swern oxidation[15] afforded quinolone **18** in 55% yield for the four steps. Treatment of **18** with 4-(dimethylamino)benzaldehyde and base afforded the corresponding arylidene **19** in 85% yield. This particular aldehyde was used since it gave the best yield in the subsequent coupling reaction with **18** in boron trifluoride etherate. Surprisingly, the boron trifluoride etherate mediated coupling reaction produced pyran **20** in 72% yield, rather than the expected pyrylium salt.[16] The production of **20** proved to be helpful since the intermediate pyrylium salts in the synthesis of the earlier molecular tweezers (e.g. **1**) could not be isolated,[1a,b] while **20** could be purified readily by chromatography.

Treatment of **20** with DDQ effected its conversion to the pyrylium salt, which was directly condensed with trimethyl phosphonoacetate in the presence of 2 equiv of sodium hydride.[4,5,17]

(10) Maxwell, C. E. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 305.
(11) Gill, N. S.; James, K. B.; Lions, F.; Potts, K. T. *J. Am. Chem. Soc.* **1952**, *74*, 4923–4928.
(12) Thummel, R. P.; Jahng, Y. *J. Org. Chem.* **1985**, *50*, 2407–2412.
(13) Bell, T. W.; Rothenberger, S. D. *Tetrahedron Lett.* **1987**, *28*, 4817–4820.
(14) Cf.: Thummel, R. P. In Pyridine and Its Derivatives; Newkome, G. R., Ed.; Advances in Heterocyclic Chemistry; Wiley: New York, 1984; Vol. 15, Part 5, Chapter 2.
(15) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660.
(16) (a) Katritzky, A. R., Ed. *Pyrylium Salts*; Academic Press: New York, 1982. (b) Katritzky, A. R.; Thind, S. S. *J. Chem. Soc. Perkin Trans. 1* **1980**, 1895–1900.
(17) Griffin, D. A.; Staunton, J. *J. Chem. Soc., Chem. Commun.* **1975**, 675–676.
(18) Constable, E. C. *Adv. Inorg. Chem. Radiochem.* **1986**, *30*, 69–121.

Scheme II



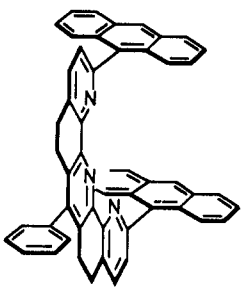
13 18 19 20

This remarkable reaction, which has been discussed in detail,[16a] produced molecular tweezer **6a** in 40–50% yields. The corresponding carboxylic acid **6b** was obtained in 40% yield by treatment of **6a** with boron trichloride. Although **6b** proved to be an efficient receptor for adenine,[5] it was anticipated that the fully oxidized spacer would provide an even more suitable disposition of the complexing functionality. Unfortunately, oxidation of the spacer in **6a** with DDQ was unsuccessful due to competitive oxidation of the (dimethylamino)phenyl substituent. Other attempted oxidations also proved to be unsuccessful. The problem was overcome by application of an improved synthesis (vide infra).

(b) Analogues of 6: An Alternative Route to 9 and 10. A more efficient and versatile approach to close analogues of **6** is outlined in Scheme III. Treatment of 5,6,7,8-tetrahydro-2-quinolone (**22**) with phosphorus tribromide produced bromide **23** in 46% yield, with lower yields obtained on a larger scale (>15 g). The four-step lateral oxidation procedure (vide supra) produced bromoquinolone **27** in 50% yield. Treatment of **27** with benzaldehyde and base afforded benzylidene **28** in 83% yield. Coupling of **27** and **28** in boron trifluoride etherate provided pyran **29**, which was oxidized to the pyrylium salt with DDQ and condensed with trimethyl phosphonoacetate in the presence of sodium hydride to afford **30** in 26% yield. Spacer **30**, was the key intermediate to which different complexing chromophores might be attached. For example, coupling of **30** with 9-anthrylmagnesium bromide in the presence of nickel(II) acetonylacetate formed molecular tweezer **9a** in 69% yield along with 17% of the monoaddition product. That the ester group in **30** survives treatment with a Grignard reagent in refluxing benzene is a clear indication of its steric hindrance.

Attempted oxidation of spacer **30** with excess DDQ in refluxing chlorobenzene produced a 1:1:1, inseparable mixture of fully aromatic spacers **31**, **39**, and **40** in low yield. Presumably, nucleophilic displacement of bromide from **30** initiates a nucleophilic exchange reaction with the chlorides of DDQ.[20] Reacting the mixture of spacers with 9-anthrylmagnesium bromide in the presence of nickel(II) acetonylacetate produced **10** in ca. 55% yield. This suggested that the dichloride spacer **40** would be a suitable precursor to **9** and **10**. In contrast to the difficulty in obtaining bromide **23** in large quantity (vide supra), the reaction of 5,6,7,8-tetrahydro-2-quinolone (**22**) with phorphorus oxychloride produced **32** in 90% yield on a 25-g scale (Scheme III). Indeed, the overall (unoptimized) yield for the 11-step synthesis of **9** is 10% for the chloro and 3% for the bromo series (Scheme III). Beyond the higher efficiency and generality of the approach, it provides access to the fully oxidized molecular tweezer **10**. Thus, DDQ oxidation of **38** in refluxing bromobenzene afforded dichloride **40** in 41% yield. Reaction of **40** with 9-anthrylmagnesium bromide in the presence of nickel(II) acetonylacetate produced **10a** in ca. 45% yield along with the mono-coupled product in 46% yield.

(c) Synthesis of 21: A Molecular Tweezer with a Metal Binding Site. The well-precedented conversion of pyrylium salts, pyrans, and 1,5-diketones to pyridines made **20** an obvious precursor to an annelated terpyridine ligand.[6a,12,13] In the event, treatment of **20** with ammonium acetate afforded **21** in 54% yield. Terpyridine



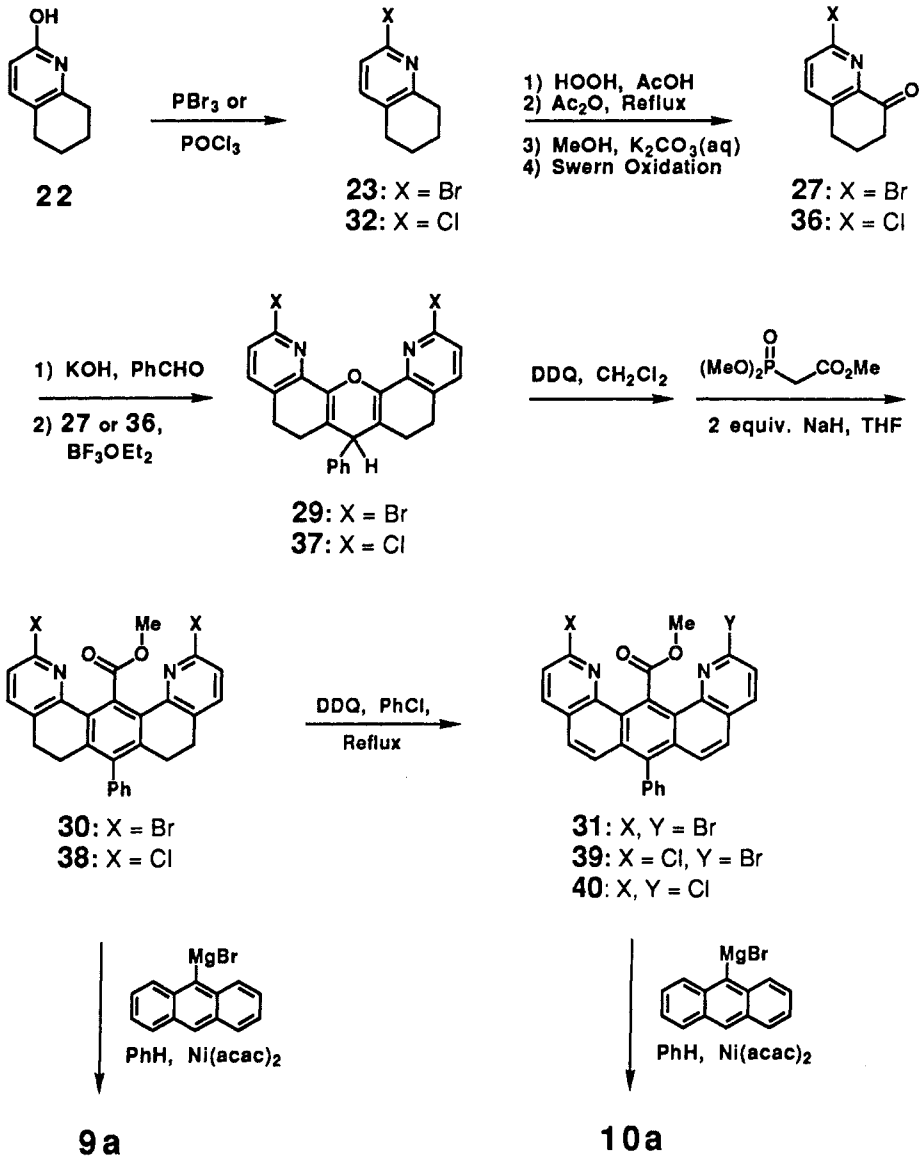
21

has a rich complexation chemistry[18] and Thummel has shown that the annelated terpyridine spacer in **21** is a better ligand for ruthenium trichloride than terpyridine itself.[19] Thus, the vacant coordination site of a metal might converge on the binding cleft thereby increasing the binding affinity of a coordinating aromatic guest. The development of catalytic systems based on **21** can be envisaged as well.

(d) Synthesis of Highly Twisted Molecular Tweezers 7 and 8 with Active Site Esters. The synthesis of **7** and **8** proved to be quite straightforward (Scheme IV). As previously described, dibromide **41** was obtained in 6 steps from bromobenzene and succinic anhydride.[4] At low temperature **41** underwent bromide–lithium exchange with 2 equiv of *n*-butyllithium and the resulting dianion smoothly added to 2,7-dimethoxy-10-(2-methoxyethoxy)-9-acridone (**42**).[22] Treatment of the addition product with acid afforded molecular tweezer **7** in 65% yield. Alternatively,

(19) Hegde, V.; Jahng, Y.; Thummel, R. P. *Tetrahedron Lett.* **1987**, *28*, 4023–4026.
(20) Roberts, R. M. G. *J. Organomet. Chem.* **1976**, *110*, 281–289.
(21) Newman, M. S.; Seshadri, S. *J. Org. Chem.* **1962**, *27*, 76–78. Fieser, L. F.; Seligman, A. M. *J. Am. Chem. Soc.* **1938**, *60*, 170–177.
(22) Zeng, Z.; Zimmerman, S. C. *Tetrahedron Lett.* **1988**, *29*, 5123–5124.

Scheme III



dibromide **41** was oxidized with DDQ to produce the fully unsaturated spacer **43**, which underwent bromide–lithium exchange and addition to **42** to afford molecular tweezer **8** in 50% yield. Although this expeditious (7 step) route to **7** proceeded in only 8% overall yield, gram quantities of **7** could be obtained readily.

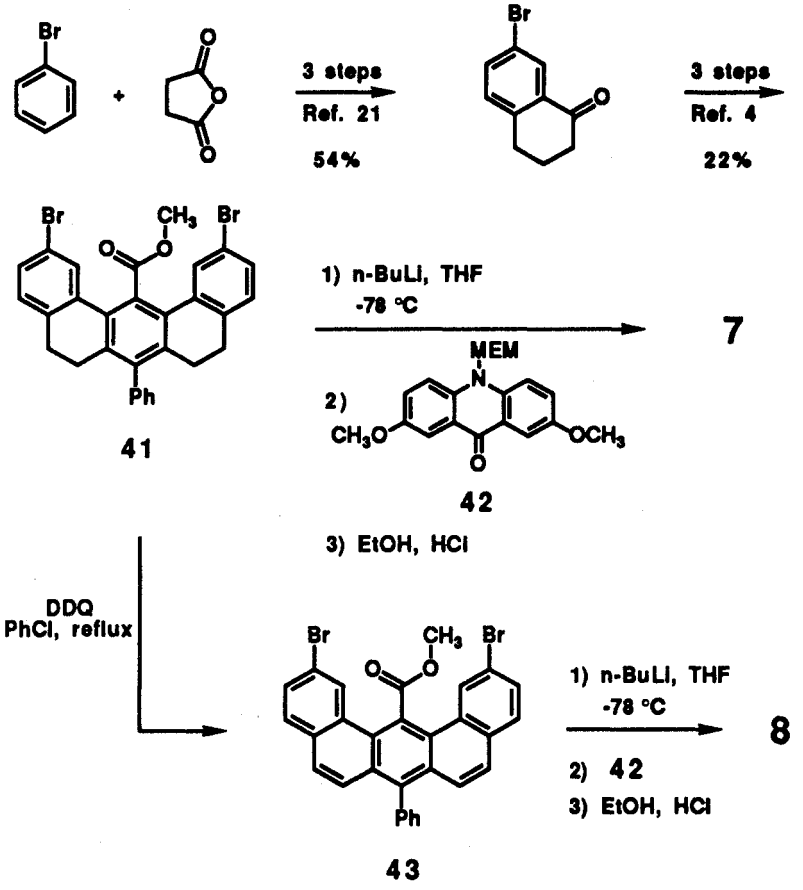
Conversion of ester **7** to the corresponding carboxylic acid proved troublesome. Boron trichloride, which was successful in converting ester **6a** into acid **6b**, converted **7** primarily into ketone **44**, with only a small amount of a product which was tentatively identified as the carboxylic acid **45** (Scheme V). The ^{1}H NMR spectrum of this material in $CDCl_3$ contained broad resonances, indicating the presence of a zwitterion and/or a mixture of aggregates. The IR spectrum was consistent with the presence of a zwitterion, and the ^{1}H NMR spectrum in basic DMSO-d_6 contained sharp resonances that were consistent with the carboxylate salt of **45**. Two higher yielding routes to **45** were developed. In the first, the ester in **7** was hydrolyzed in 84% yield with sodium cyanide in DMSO. The second route involved conversion of methyl ester **41** into the corresponding methoxyethoxymethyl (MEM) ester (Scheme VI). Remarkably, it was found that the hindered ester in **41** could be converted into acid **46** in 82% yield by treatment with lithium triethylborohydride. The mechanism of this reaction has not been investigated and to our knowledge this is the first example of an ester hydrolysis by this powerful reducing agent. Esterification of **46** with (methoxyethoxy)methyl chloride afforded ester **47** which underwent lithium–bromide exchange, addition to **42**, and hydrolysis to form **45** in 33% yield.

In order to avoid proton transfer and/or hydrogen bonding to the acridine nitrogen, efforts were made to attach anthracene chromophores to dibromide **41**. In the first approach, **41** was subjected to lithium–bromide exchange and then treated with cerium trichloride followed by anthrone (Scheme VII). Although the unstable molecular tweezer **48** was obtained in 60% yield, the reaction proved to be irreproducible. The second approach involved conversion of dibromide **41** into the corresponding diiodide **49** (62%). Subsequent coupling with 9-anthrylmagnesium bromide with catalytic nickel(II) acetonylacetate afforded **48** as a mixture with the monoaddition product. The relatively high instability of **48** precluded its isolation in pure form. In related molecular tweezers it has been found that this instability results from oxidation of the anthracene moieties and can be greatly inhibited by substitution in the 10-position.[23] Thus, substituted analogues of **48** have the potential for increased stability and might be suitable precursors to the corresponding carboxylic acids.

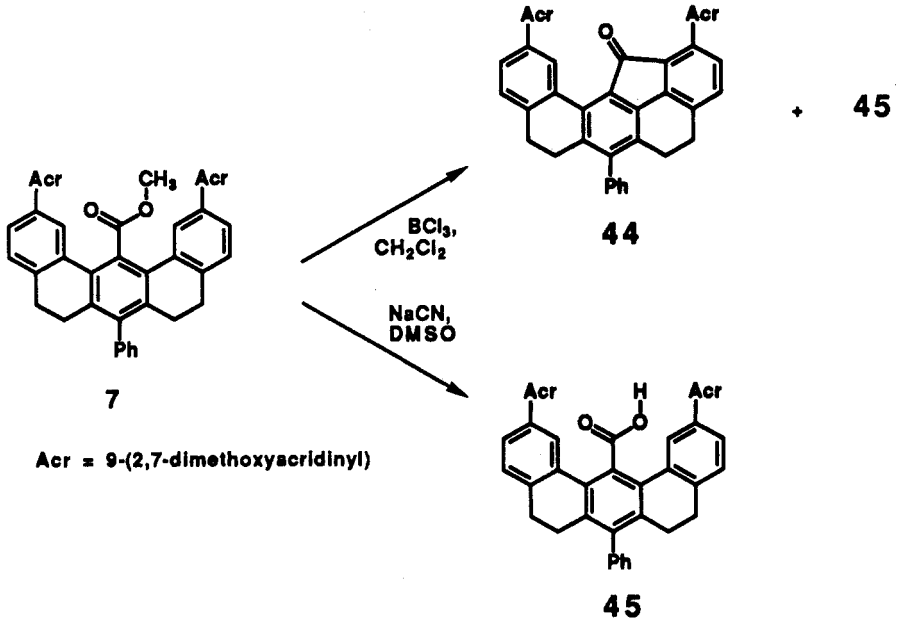
(e) Synthesis of Molecular Tweezer 50 with an Active Site Nitrile. The generality of the approach in Scheme IV was demonstrated by the synthesis of molecular tweezer **50** which contains a nitrile in the cleft. As shown in Scheme VIII, pyrylium salt

(23) Zeng. Z. Unpublished results.
(24) Meyers, A. I.; Garcia-Munoz, G. *J. Org. Chem.* **1964**, *29*, 1435–1438.

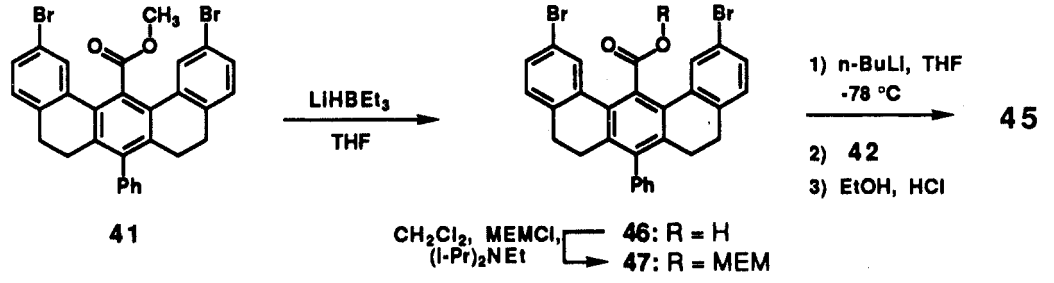
Scheme IV



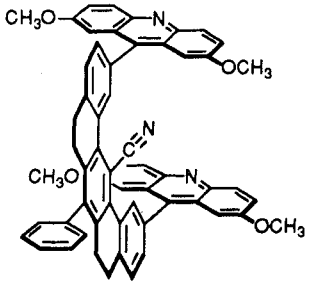
Scheme V



Scheme VI



51 underwent condensation with (dimethylphosphono)acetonitrile



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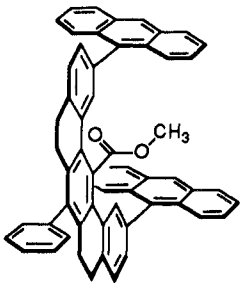

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and base to afford nitrile **52**. Treatment of **52** with *n*-butyllithium effected lithium–bromide exchange and coupling with acridone **42** afforded molecular tweezer **50** in 65% yield. Despite its steric hindrance, conversion of the nitrile in **50** to amides, amidines, and related functionality can be envisaged.

In summary, molecular tweezers containing active site esters (**6a**, **7–9a**, **10a**), carboxylic acids (**6b**, **9b**, **10b**, **45**), and nitriles (**50**), and a terpyridine spacer (**21**), have been synthesized. Although the overall (unoptimized) yields are modest, the synthetic sequences that have been developed are short and readily allow >500-mg quantities of the molecular tweezers to be obtained.

Structure of Molecular Tweezers 7–10. The X-ray structure of molecular tweezer **1** showed it to possess a nearly perfect cofacial orientation of the acridine rings with a 6.8-Å separation, features which were regarded as most desirable for sandwich complexation of aromatic guests (see Figure 2).[1c] However, as noted previously, a larger interchromophore separation may not necessitate a sacrifice of complexation efficiency since rotations around the aryl–aryl bonds have the effect of reducing the interchromophore separation.[1b] This ability of these receptors to self-adjust their cleft dimensions makes the "molecular tweezer" moniker apropos. As seen in Figure 3, an arbitrarily chosen interchromophore distance of 7.8 Å (at maximum separation) can close to the presumed optimum of 6.8 Å by 30° rotations about the spacer–chromophore bonds. Of course, a reduced overlap between the chromophores accompanies these rotations.

In the new molecular tweezers (e.g. **6**) it was assumed that the optimum conformation for binding complementary guests would have the carboxylic acid and the two anthracene chromophores in nearly parallel planes with an ca. 3.4-Å separation between adjacent planes. However, a model study showed the presence of the bay region functional group could markedly increase the C-2 to C-12 distance and cause the spacer to distort from planarity into a helical shape.[4] Thus, it was important to determine not only the ground-state conformations of molecular tweezers **7–10**, but also the degree to which their inherent flexibilities might allow access to conformations suitable for complexation. These issues were addressed through a combination of X-ray structural analysis and molecular modeling.

(a) Structure of Spacers 2–5. The structures of spacers **3** and **5** have been determined by X-ray analysis.[4] The structure of spacer **2** can be inferred from that of molecular tweezer **7**, whose X-ray structure has been determined (vide infra). No direct structural information is available for **4**, despite the fact that its related molecular tweezer, acid **6**, is the most thoroughly studied receptor. Therefore, molecular modeling techniques were used to determine the structure of **4**, after their accuracy was tested by comparison with the X-ray data of **3** and **5**. It was assumed in these calculations that the esters and their corresponding carboxylic acids will have very similar structures.

The PC Model program was used for the calculations and was found to reproduce the bond distances and angles of the X-ray data remarkably well, while somewhat larger differences were found in dihedral angles (data not shown). Since small differences in bond and dihedral angles can accumulate to produce large overall differences between the calculated and X-ray conformations, it is preferable to focus on those structural parameters that give the molecular tweezers their gross structure. These parameters include the C-2 to C-12 distance which defines the maximum interchromophore separation in the molecular tweezers and the spacer twist angle which largely determines the extent of interchromophore overlap. Finally, the dihedral angle between the ester group and the spacer will affect how well the guest is able to hydrogen bond to the corresponding carboxylic acid.

Table I. Comparison of Conformations in Spacer Units **2–5**

spacer	method[a]	C-2 to C-12 distance, Å	spacer twist angle, deg	ester to spacer dihedral angle, deg
2	A	8.29	36	58
2	B	8.21	35	61
3	A	8.20	24	68
3 (7)	B	8.20	19	70
4	A	7.66	22	74
5	A	7.63	3	85
5	B	7.52	11	78

[a] Method A: PC Model calculation. Method B: X-ray crystal structure.

Table II. Upfield ^{1}H NMR Chemical Shift (ppm) of Methyl Esters in Molecular Tweezers **7–10** and **48**

molecular tweezer	chemical shift of methyl ester	spacer	chemical shift of methyl ester	Δδ, ppm
48	2.72	**41**	3.91	1.19
7	2.72	**41**	3.91	1.19
8	2.73	**43**	4.35	1.62
9	1.71	**30**	4.14	2.43
10	1.42	**31**	4.64	3.22

As seen in Table I, the calculated C-2 to C-12 distances agree extremely well (<2%) with the corresponding X-ray data. Larger differences are seen in the comparisons between the spacer–ester dihedral angles, but the agreement is still quite good (<9%). The amount of twist in the spacers is reproduced well for **2**, but only partially for **3**, while the calculated structure for spacer **5** is substantially more planar than seen in the X-ray structure. Overall, the calculated structures are in good agreement with the X-ray data.

The ease with which the ester groups can rotate from their optimum conformation was determined with use of the dihedral driver function with 5° increments and geometry optimization. The resultant data (Figure 4) contain two interesting features. The rotation of the ester group in spacers **3–5** led to a discontinuity in energy due a new local minima whose structure could be described as crescent shaped. These conformations were not seen in any of the X-ray structures and are not expected to play any significant role since they are of much higher energy than the helical conformation. It can also be seen from Figure 4 that some flexibility is present in the spacers since rotations of ±20° from the optimum ester dihedral angle in **2** and **3** and ±30° from the optimum in **4** and **5** cost less than 2 kcal mol^{-1} in energy.

(b) Structure of Molecular Tweezers 7–10. The structure of molecular tweezer **7** was determined by X-ray analysis. As seen in Figure 5, the spacer is so highly twisted that there is no vertical overlap between the acridine rings. The calculated structures for **7–9a** and **10a** are shown in Figure 6. The helical twist observed in the spacers is reflected in the increasing amount of interchromophore overlap along the series **7** → **8** → **9** → **10**. This calculated increase in chromophore overlap and decrease in C-2 to C-12 distance is supported by the observed ^{1}H NMR chemical shifts of the methyl ester resonances. Thus, relative to the appropriate synthetic precursor, the upfield chemical shift of the methyl ester resonances in **7–10** increase in the order **7** < **8** < **9** < **10**. While the anthracene and acridine rings might be expected to exhibit different degrees of anisotropic shielding, the ^{1}H NMR chemical shifts of the methyl ester in **7** and **48** are identical.

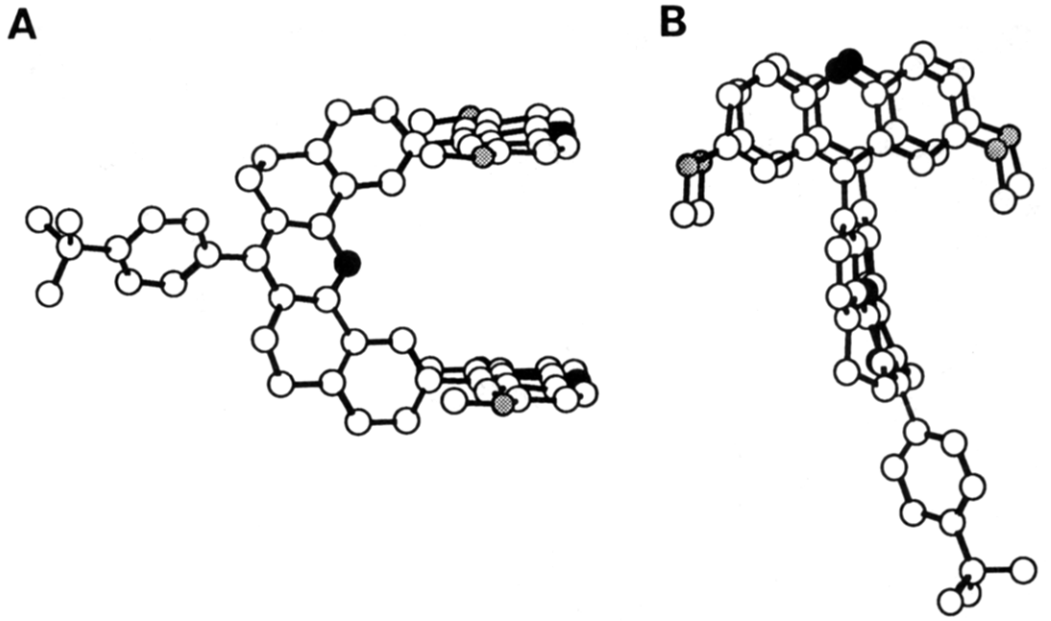


Figure 2. Side (A) and top (B) view of the X-ray structure of **1** (4-*tert*-butylphenyl analogue).

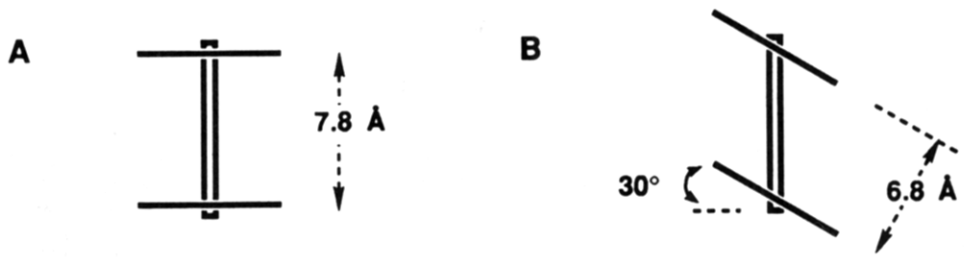
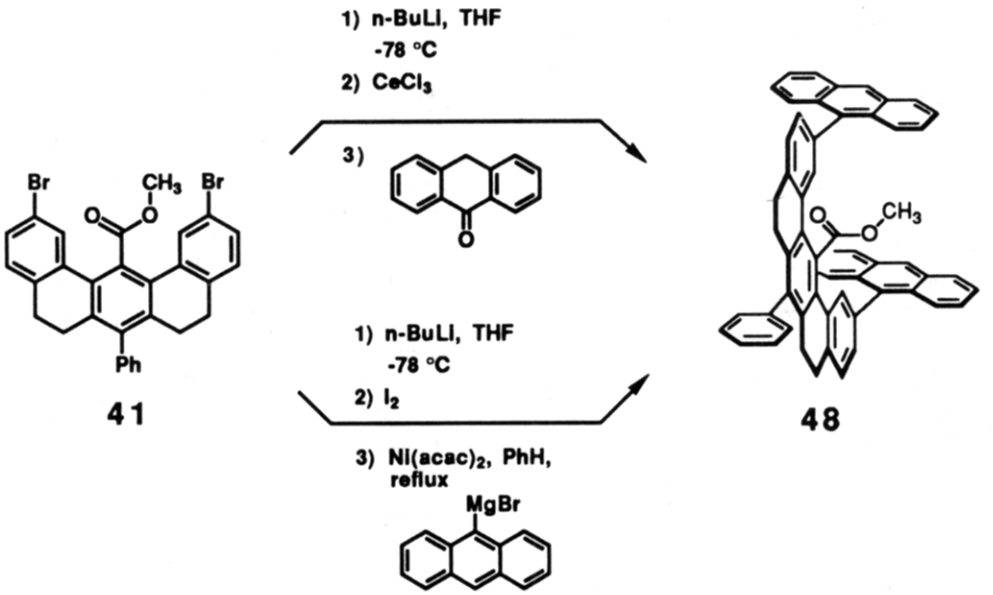


Figure 3. Schematic representation of the relationship between spacer–chromophore dihedral angle and interchromophore angle.

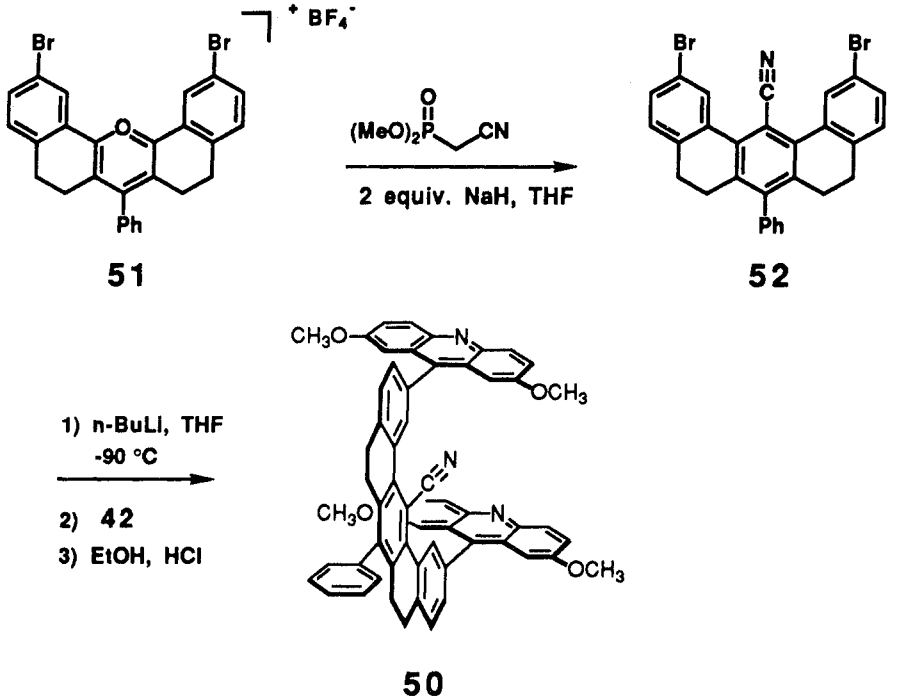
Scheme VII



Dihedral driver calculations for the anthracene to spacer bond again indicate a moderate degree of flexibility. The preferred dihedral angle of ca. 90° can be changed by ±20° in **7** and **8**, ±30° in **9**, and ±40° in **10** with less than a 2 kcal mol^{-1} cost in energy. However, this flexibility is insufficient to allow molecular tweezers **7** and **8** to organize their binding clefts for simultaneous hydrogen bonding and π-sandwich complexation. The acridine rings in these systems can close to within only 7.7 Å and there is minimal overlap between the chromophores. In contrast, **9** and **10** are sufficiently flexible to allow their anthracene rings and ester group to occupy parallel planes separated by the presumed optimum of 3.4 Å between adjacent planes (i.e. inter-anthracene separation of 6.8 Å) with only a minimum energy investment.

In summary, it has been found that the C-2 to C-12 distances range from 8.2 to 7.5 Å and increase in the order **10** < **9** < **8** < **7**. Additionally, the lowest energy conformations of the spacers are nonplanar with helical twists of between 40° and 2° from end-to-end. This means that the degree of chromophore overlap

Scheme VIII



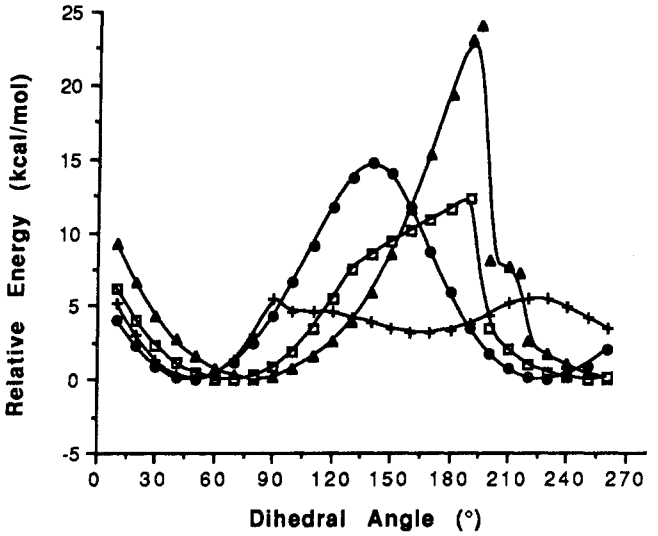


Figure 4. Relative energy of geometry optimized molecular tweezers **7** (●), **8** (+), **9a** (□), and **10a** (▲) as a function of ester-to-spacer dihedral angle.

increases in the order **7** < **8** < **9** < **10**. Molecular mechanics calculations suggest that the potential barrier for rotations around the ester-to-spacer bond and around the aryl–aryl bonds is relatively flat within 20–40° of the optimum, suggesting that molecular tweezers **7–10** have a moderate degree of flexibility.

Conclusions

Expeditious routes have been developed for the synthesis of novel compounds wherein a functional group is "buried" within an aromatic cleft. Four of these compounds contain ester groups that can be converted into carboxylic acids and might be expected to complex aromatic compounds with complementary hydrogen-bonding arrays. X-ray analysis, combined with simple molecular mechanics calculations, suggests that these four molecules have regular variations in structure that represent discrete steps toward an optimized binding cleft. The ability of some of these molecular tweezers to act as receptors for nucleotide bases is the subject of the accompanying article.

Experimental Section

General Methods. The following solvents were freshly distilled prior to use: tetrahydrofuran (THF) from sodium benzophenone ketyl, methanol (CH_3OH) from magnesium turnings, methylene chloride (CH_2Cl_2) from calcium hydride, dimethylformamide (DMF), predried over 4 Å molecular sieves, from barium oxide. Dimethyl sulfoxide (DMSO) and triethylamine were distilled over calcium hydride and stored under a nitrogen atmosphere. All other solvents and reagents were of reagent grade quality and used without further purification. Analytical TLC was performed on 0.2 mm silica 60 coated plastic sheets (EM Science) with F-254 indicator. Flash chromatography was performed on Merck 40-63 μm silica gel. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected.

^1H and ^{13}C NMR spectra were recorded on a General Electric QE-300 instrument unless otherwise stated. Spectra were obtained in chloroform-*d*. Chemical shifts are reported in parts per million (ppm) with TMS as an internal reference, and coupling constants are reported in hertz (Hz). Infrared spectra were recorded on a Perkin-Elmer 1320 spectrometer. Mass spectra were obtained on a Finnigan-At CH-5 or Finnigan-MAT-731 spectrometer. Elemental analyses were performed at the University of Illinois School of Chemical Sciences. Some molecular tweezers were found to remain small quantities of the recrystallization/precipitation solvent as evidenced by the ^1H NMR and elemental analysis. The elemental analysis is reported for the partial solvate which best fit the combustion data. The X-ray analysis data were collected on an Enraf-Nonius CAD4 automated κ-axis diffractometer and analyzed with SHELXS-86.

1-(9-Anthracenyl)-3-(dimethylamino)-1-propanone (11). To a mixture of 50.0 g (0.23 mol) of 9-acetylanthracene, 9.0 g (0.1 mol) of paraformaldehyde, 24.5 g (0.3 mol) of dimethylammonium chloride, and 100 mL of 95% ethanol was added 1.2 mL of concentrated aqueous HCl, and the solution was heated to reflux for 32 h. The reaction was cooled to room temperature and partitioned between 250 mL of 2 N HCl and 300 mL of ether. The ether layer was washed once with 100 mL of 2 N HCl. The combined aqueous layers were cooled to 0 °C, basified with solid sodium carbonate, and extracted with 10% 2-propanol–chloroform. The organic layer was dried over Na_2SO_4 and concentrated to give 48.8 g (78%) of **11** as a colorless oil which was judged to be >95% pure by ^1H NMR: ^1H NMR δ 8.48 (s, 1 H, H-10′), 8.03 (d, $J_{3',4'}$ = 9.7, 2 H, H-4′, H-5′), 7.85 (d, $J_{1',2'}$ = 9.3, 2 H, H-1′, H-2′), 7.51–7.46 (m, 4 H, H-2′, H-3′, H-6′, H-7′), 3.24 (t, J = 7.2, 2 H, NCH_2), 2.90 (t, J = 7.2, 2 H, $COCH_2$), 2.28 (s, 6 H, NCH_3); ^{13}C NMR δ 209.29, 131.02, 128.74, 128.23, 126.94, 126.71, 126.57, 125.47, 124.39, 53.86, 45.49, 44.58; MS (EI, 70 eV), m/z (relative intensity) 277 (M^+, 12); exact mass calcd for $C_{19}H_{19}NO$ m/z 277.146 62, found 277.147 12.

1-(9-Anthracenyl)-3-(2-oxo-1-cyclohexyl)-1-propanone (12). A solution of 48.8 g (0.17 mol) of **11** and 51.8 g (0.46 mol) of cyclohexanone was heated to reflux for 20 min. The remaining cyclohexanone was

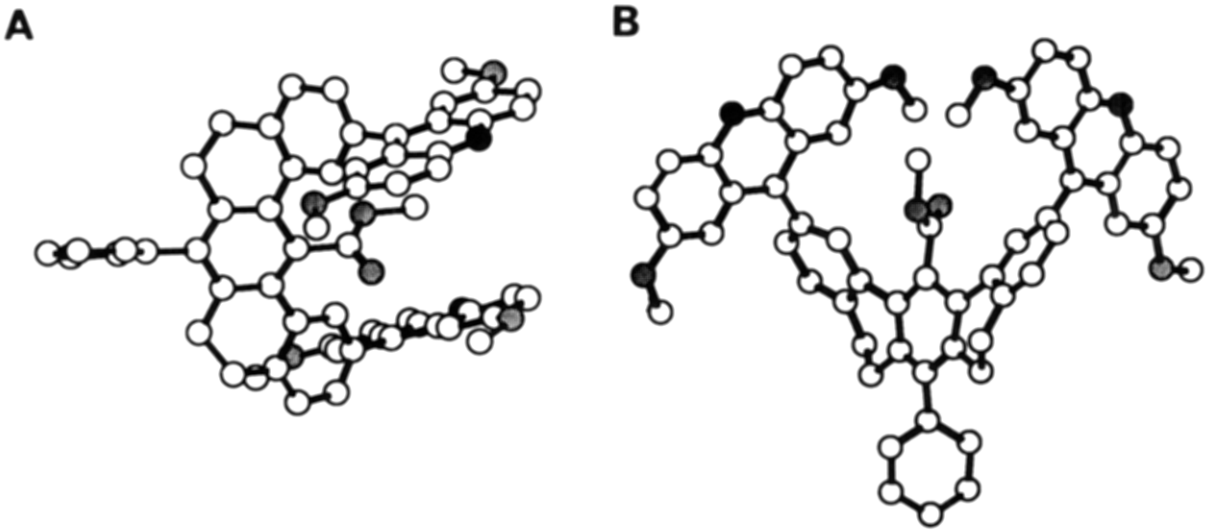


Figure 5. Side (A) and top (B) view of the X-ray structure of **7**. Note: View B is a different perspective form that of the calculated structures in Figure 6.

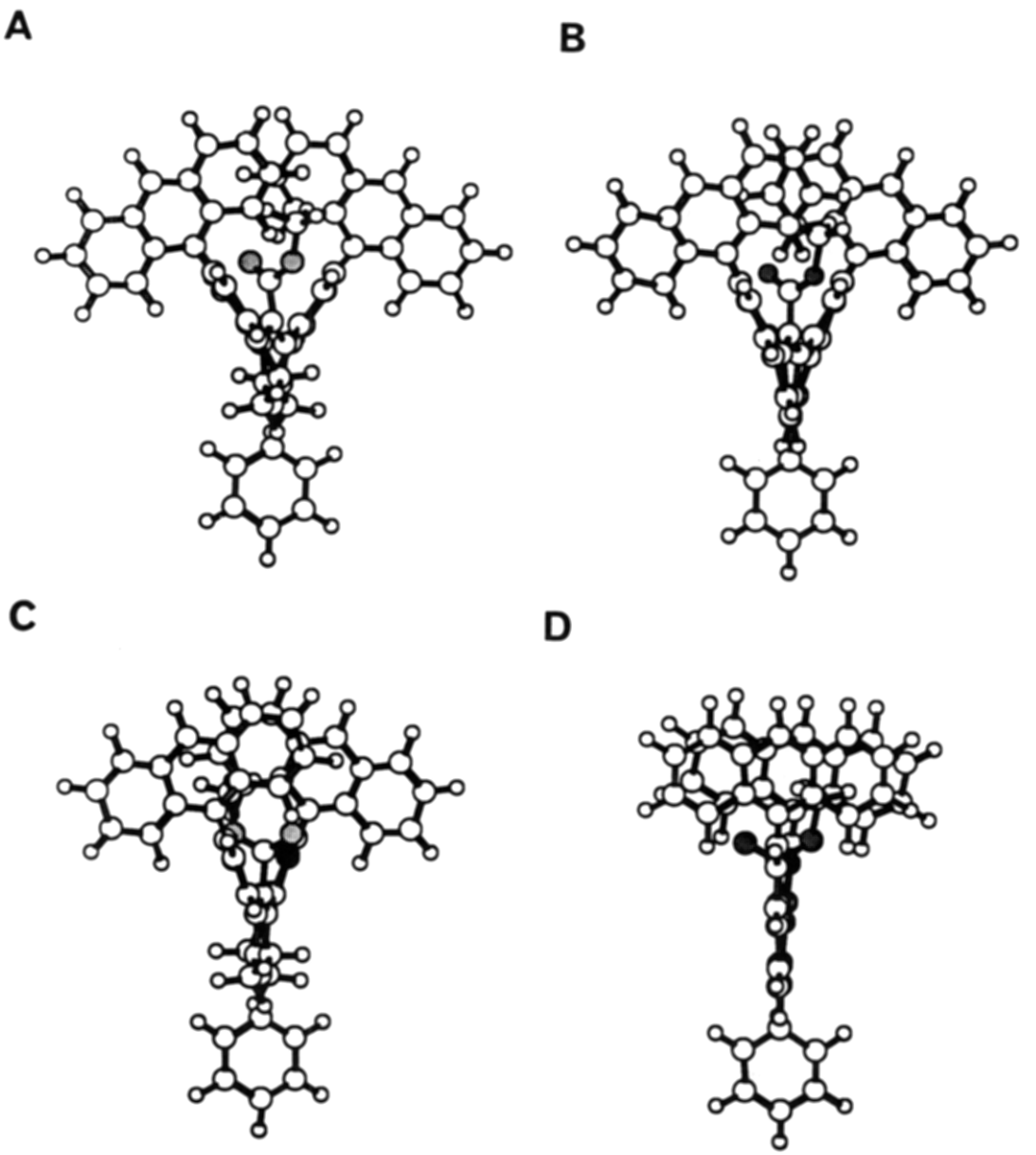


Figure 6. Top view of the calculated minimum energy conformation of **7** (A), **8** (B), **9a** (C), and **10a** (D) (see text for details).

removed at reduced pressure to afford 58.1 g (100%) of **12** as a colorless oil which was judged to be >95% pure by ^{1}H NMR: ^{1}H NMR δ 8.44 (s, 1 H, H-10′), 8.00 (d, $J_{3',4'}$ = 7.9, 2 H, H-4′, H-5′), 7.77 (d, $J_{1',2'}$ = 8.1, 2 H, H-1′, H-8′), 7.52–7.43 (m, 4 H, H-2′, H-3′, H-6′, H-7′), 3.22–2.97 (m, 2 H, H-2), 2.48–2.42 (m, 1 H, H-4), 2.40–2.22 (m, 3 H, H-8, H-5$_{ax}$), 2.18–2.02 (m, 2 H, H-5$_{eq}$, H-6$_{ax}$), 1.92–1.81 (m, 2 H, H-3), 1.73–1.62 (m, 2 H, H-7), 1.51–1.43 (m, 1 H, H-6$_{eq}$); ^{13}C NMR δ 212.61, 210.33, 130.97, 128.72, 128.10, 127.94, 126.69, 125.42, 124.29, 123.83, 40.80, 49.73, 43.98, 42.16, 34.43, 28.06, 25.05; MS (EI, 70 eV), m/z (relative intensity) 330 (M$^+$, 24). 205 (100); exact mass calcd for $C_{23}H_{22}O_2$ m/z 330.161 96, found, 330.162 96.

2-(9-Anthracenyl)-5,6,7,8-tetrahydroquinoline (13). To a solution of 25.0 g (76 mmol) of diketone **12** in 150 mL of acetic acid was added 17.5 g (0.23 mol) of ammonium acetate. The reaction mixture was heated to reflux for 24 h, cooled to 0 °C, and made basic with a 20% aqueous solution of NaOH. After extraction with chloroform, the organic layers were dried over magnesium sulfate and the solvent was evaporated to leave a deep yellow solid. Flash chromatography (5% EtOAc–carbon tetrachloride) afforded 13.4 g (57%) of **13** as light yellow powder: mp 152 °C dec; ^{1}H NMR δ 8.43 (s, 1 H, H-10′), 7.95 (d, $J_{3',4'}$ = 8.3, 2 H, H-4′, H-5′), 7.63 (d, $J_{1',2'}$ = 8.6, 2 H, H-1′, H-8′), 7.44 (d, $J_{3,4}$ = 7.6, 1 H, H-4), 7.39–7.27 (m, 4 H, H-2′, H-3′, H-6′, H-7′), 7.16 (d, $J_{3,4}$ = 7.6, 1 H, H-3), 3.04 (t, J = 6.2, 2 H, H-8), 2.82 (t, J = 6.1, 2 H, H-5), 1.84 (m, 4 H, H-6, H-7); ^{13}C NMR δ 157.31, 154.73, 136.75, 135.35, 131.31, 130.56, 130.05, 128.24, 127.08, 126.18, 125.35, 124.80, 123.70, 32.49, 28.52, 23.00, 22.59; MS (EI, 70 eV), m/z (relative intensity) 309 (M$^+$, 24), 308 (100), exact mass calcd for $C_{23}H_{19}N$ m/z 309.151 75, found 309.150 65.

2-(9-Anthracenyl)-5,6,7,8-tetrahydroquinoline 1-Oxide (15). To a stirred solution of 7.0 g (22.6 mmol) of **13** in 80 mL of THF was added slowly 8.5 mL (45.2 mmol) of 35% peracetic acid. The reaction was refluxed for 5 h, cooled to room temperature, diluted with chloroform, and washed with 4 N KOH. The aqueous layer was extracted once with chloroform. The combined organic layers were dried over Na_2SO_4 and concentrated to give **15** as a light yellow solid. This material was sufficiently pure for use in the next reaction: mp 219 °C dec; ^{1}H NMR δ 8.52 (s, 1 H, H-10′), 8.01 (d, $J_{3',4'}$ = 7.8, 2 H, H-4M, H-5′), 7.50 (d, $J_{1',2'}$ = 8.3, 2 H, H-1′, H-8′), 7.44–7.34 (m, 4 H, H-2′, H-3′, H-6′, H-7′), 7.18 (d, $J_{3,4}$ = 8.0, 1 H, H-4), 7.12 (d, $J_{3,4}$ = 8.0, 1 H, H-3), 3.04 (t, J = 6.3, 2 H, H-8), 2.88 (t, J = 6.0, 2 H, H-5), 2.00–1.92 (m, 2 H, H-7), 1.88–1.83 (m, 2 H, H-6); ^{13}C NMR δ 149.51, 144.82, 135.63, 131.28, 129.99, 128.58, 128.32, 127.90, 126.34, 125.73, 125.15, 125.07, 124.99, 28.68, 24.85, 21.96, 21.64; MS (EI, 70 eV), m/z (relative intensity) 325 (M$^+$, 69), 297 (100), 295 (84); exact mass calcd for $C_{23}H_{19}NO$ m/z 325.146 64, found 325.146 74.

2-(9-Anthracenyl)-8-hydroxy-5,6,7,8-tetrahydroquinoline (17). A mixture of **15** and 80 mL of acetic anhydride was refluxed for 2 h and the remaining acetic anhydride was removed at reduced pressure to afford a dark brown solid. The ^{1}H NMR spectrum showed this material to be **16** of ca. 90% purity. A solution of **16** was dissolved in 40 mL of THF and transferred by canula to 2.3 g (0.1 mol) of sodium dissolved in 120 mL of methanol under a nitrogen atmosphere. The reaction mixture was stirred overnight at room temperature and ca. half of the solvent was removed at reduced pressure. The reaction was quenched with 200 mL of water, extracted with 10% 2-propanol–chloroform (3 × 150 mL), dried over $MgSO_4$, and concentrated to give a black solid. The solid was purified by flash chromatography (7% EtOAc–CH_2Cl_2) to yield 4.9 g of **17** (67% from **13**) as colorless microcrystals: mp 209 °C dec; ^{1}H NMR δ 8.50 (s, 1 H, H-10′), 8.02 (d, $J_{3',4'}$ = 8.4, 2 H, H-4′, H-5′), 7.63–7.56 (m, 3 H, H-1′, H-8′, H-4), 7.45–7.20 (m, 5 H, H-2′, H-3′, H-6′, H-7′, H-3), 4.80 (t, J = 6.5, 1 H, H-8), 4.13 (s, 1 H, OH), 3.00–2.84 (m, 2 H, H-5), 2.34–2.27 (m, 1 H, H-7$_{ax}$), 2.10–2.02 (m, 1 H, H-7$_{eq}$), 1.97–1.79 (m, 2 H, H-6); ^{13}C NMR δ 158.15, 154.92, 137.13, 134.78, 131.27, 130.14, 129.93, 128.42, 127.44, 125.91, 125.72, 125.45, 125.03, 68.82, 30.53, 28.23, 19.46; MS (EI, 70 eV), m/z (relative intensity) 325 (M$^+$, 64); exact mass calcd for $C_{23}H_{19}NO$ m/z 325.146 62, found 325.146 72.

2-(9-Anthracenyl)-5,6,7,8-tetrahydro-8-quinolone (18). To a stirred solution of 2.0 mL (23 mmol) of oxalyl chloride in 10 mL of CH_2Cl_2 at −70 °C was added slowly 3.3 mL (46 mmol) of DMSO and the solution stirred for 10 min. To this was added a solution of 4.0 g (12.3 mmol) of **17** in 50 mL of CH_2Cl_2. A yellow precipitate formed. The reaction was stirred for 5 min, and 10 mL (72.0 mmol) of triethylamine was added. After being warmed to room temperature the solution was partitioned between water and CH_2Cl_2. The water layer was washed once with CH_2Cl_2, and the combined organic layers were dried over magnesium sulfate and concentrated to leave a brown solid. Flash chromatography (7% EtOAc–CH_2Cl_2) afforded 3.9 g (98%) of quinolone **18** as a yellow solid: mp 214 °C dec; ^{1}H NMR 8.53 (s, 1 H, H-10′), 8.03 (d, $J_{3',4'}$ = 8.4, 2 H, H-4′, H-5′), 7.88 (d, $J_{3,4}$ = 7.9, 1 H, H-4), 7.60 (d, $J_{3,4}$ = 7.9, 1 H, H-3), 7.52–7.41 (m, 4 H, H-1′, H-3′, H-6′, H-8′), 7.36–7.31 (m, 2 H, H-2′, H-7′), 3.21 (t, $J_{5,6}$ = 6.1, 2 H, H-5), 2.92 (t, $J_{6,7}$ = 6.1, 2 H, H-7), 2.35 (quintet, $J_{5,6}$ = $J_{6,7}$ = 6.1, 2 H, H-6); ^{13}C NMR δ 196.34, 157.39, 148.14, 139.40, 137.81, 134.20, 131.07, 129.99, 128.20, 127.46, 125.72, 125.61, 125.01, 124.86, 39.75, 28.90, 22.49; MS (EI, 70 eV), m/z (relative intensity) 323 (M$^+$, 100), 322 (92); exact mass calcd for $C_{23}H_{17}NO$ m/z 323.130 99, found 323.129 79.

2-(9-Anthracenyl)-7-(4-(dimethylamino)benzylidene)-8-quinolone (19). To a mixture of 500 mg (1.55 mmol) of quinolone **18** and 370 mg (2.50 mmol) of 4-(dimethylamino)benzaldehyde was added 10 mL of a 4% methanolic solution of potassium hydroxide. The reaction mixture was stirred at 75 °C for 3.5 h, cooled, dissolved in chloroform, and washed with 10% aqueous potassium carbonate solution. The organic layer was dried over $MgSO_4$ and filtered, and the solvent was removed at reduced pressure. The residue was purified by flash chromatography (1:4 EtOAc–carbon tetrachloride) to yield 600 mg (85%) of **19** as red-orange prisms: mp >250 °C dec; ^{1}H NMR δ 8.53 (s, 1 H, H-10′), 8.04 (d, $J_{3',4'}$ = 8.0, 2 H, H-4′, H-5′), 8.00 (s, 1 H, H-9), 7.85 (d, $J_{3,4}$ = 7.8, 1 H, H-4), 7.58 (t, $J_{3,4}$ = 7.8, $J_{2'',3''}$ = 8.1, 3 H, H-3, H-2″), 7.52–7.42 (m, 4 H, H-1′, H-3′, H-6′, H-8′), 7.37–7.32 (m, 2 H, H-2′, H-7′), 6.78 (d, $J_{2'',3''}$ = 8.1, 1 H, H-3″), 3.36 (t, J = 6.3, 2 H, H-5), 3.15 (t, J = 6.3, 2 H, H-6), 3.06 (s, 6 H, NMe$_2$); ^{13}C NMR δ 185.52, 157.50, 150.47, 139.30, 137.33, 136.62, 132.74, 132.04, 131.06, 130.67, 130.03, 129.36, 128.11, 127.34, 125.88, 125.48, 124.77, 123.12, 111.35, 110.83, 39.89, 27.76, 26.56; MS (EI, 70 eV), m/z (relative intensity) 454 (M$^+$, 100); exact mass calcd for $C_{32}H_{26}N_2O$ m/z 454.204 50, found 454.205 52.

2,12-Bis(9-anthracenyl)-7-(4-(dimethylamino)phenyl)-5,6,8,9-tetrahydro-1,13-diazadibenz[*a*,*j*]xanthene (20). A mixture of 89 mg (0.28 mmol) of quinolone **18**, 125 mg (0.28 mmol) of benzylidene **19**, and 0.7 mL of boron trifluoride etherate was heated to 100 °C. Upon consumption of starting material (4–9 h, TLC), the reaction was cooled to room temperature, diluted with CH_2Cl_2, washed vigorously with a saturated aqueous sodium bicarbonate solution, and dried over Na_2SO_4, and the solvent was removed at reduced pressure. Flash chromatography (1:9 EtOAc–CH_2Cl_2) afforded 150 mg (72%) of unstable pyran **20**, which was judged to be ca. 90% pure by ^{1}H NMR: ^{1}H NMR δ 8.43 (s, 2 H, H-10′), 7.92 (t, $J_{3',4'}$ = $J_{5',6'}$ = 9.1, 4 H, H-4′, H-5′), 7.63 (q, $J_{3',4'}$ = $J_{5',6'}$ = 9.1, $J_{2',3'}$ = $J_{6',7'}$ = 4.1, 4 H, H-3′, H-6′), 7.47 (d, $J_{3,4}$ = 7.5, 2 H, H-4), 7.35 (d, $J_{2'',3''}$ = 8.6, 2 H, H-2″), 7.24–7.19 (m, 2 H, H-1′ or H-8′), 7.13 (d, $J_{3,4}$ = 7.5, 2 H, H-3), 7.15–7.11 (m, 2 H, H-1′ or H-8′), 6.92–6.86 (m, 2 H, H-2′ or H-7′), 6.71 (d, $J_{2'',3''}$ = 8.6, 2 H, H-3″), 6.64–6.59 (m, 2 H, H-2′ or H-7′), 4.09 (s, 1 H, H-7), 2.95 (s, 6 H, NMe$_2$), 3.00–2.79 (m, 4 H, H-5), 2.34–2.05 (m, 4 H, H-6); ^{13}C NMR (500 MHz) δ 154.94, 149.44, 149.07,142.62, 135.13, 133.83, 131.13, 130.92, 129.78, 129.59, 129.18, 127.50, 127.30,126.55, 126.31, 125.24, 124.75, 124.61, 115.91, 112.21, 46.58, 40.35, 27.02, 24.94; MS (EI, 70 eV), m/z (relative intensity) 759 (M$^+$, 3), 741 (100); exact mass calcd for $C_{55}H_{41}N_3O$ m/z 759.324 96, found 759.323 94.

Methyl 2,12-Bis(9-anthracenyl)-7-(4-(dimethylamino)phenyl)-5,6,8,9-tetrahydro-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylate (6a). To a stirred solution of 150 mg (0.2 mmol) of pyran **6a** in 5 mL of CH_2Cl_2 was added 45 mg (0.20 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). After 30 min the solvent was removed at reduced pressure to give a green solid. In a separate flask, 120 μL (0.74 mmol) of trimethyl phosphonoacetate was added to a suspension of 24 mg (1.0 mmol) of dry sodium hydride in 10 mL of THF. After 10 min, the pyrylium salt was added to the THF solution and the mixture was stirred for 2 h at room temperature. The mixture was diluted with CH_2Cl_2, washed with saturated aqueous sodium chloride solution, dried over Na_2SO_4, and concentrated to give a brown solid. Flash chromatography (CH_2Cl_2) afforded 89 mg (55%) of **6a** as a yellow solid: mp >250 °C dec; ^{1}H NMR δ 8.35 (s, 2 H, H-10′), 7.89 (d, $J_{3',4'}$ = 8.4, 4 H, H-4′, H-5′), 7.59–7.51 (m, 6 H, H-4, H-3′, H-4′), 7.33–7.10 (m, 12 H, H-3, H-1′, H-2′, H-7′, H-8′, H-2″), 6.88 (d, $J_{2'',3''}$ = 7.6, 2 H, H-3″), 3.04 (s, 6 H, NMe$_2$), 2.82 (m, 4 H, H-5), 2.79 (m, 4 H, H-6); ^{13}C NMR (500 MHz) δ 154.83, 152.21, 149.59, 139.99, 135.78, 134.68, 131.66, 131.28, 131.16, 130.08, 130.02, 128.04, 127.90, 127.82, 126.92, 126.72, 126.58, 125.60, 125.09, 124.69, 112.23, 49.84, 40.55, 28.00, 27.61; MS (EI, 70 eV), m/z 813 (M$^+$); exact mass calcd for $C_{57}H_{43}N_3O_2$ m/z 813.335 51, found 813.335 64.

2,12-Bis(9-anthracenyl)-7-(4-(dimethylamino)phenyl)-5,6,8,9-tetrahydro-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylic Acid (6b). To a solution of 140 mg (0.17 mmol) of ester **21** in CH_2Cl_2 cooled to −20 °C was added 1.0 mL of boron trichloride solution in hexane (1.0 M). The solution was stirred at room temperature for 30 min and heated to 40–50 °C for 6 h. The mixture was cooled to room temperature, diluted with CH_2Cl_2, vigorously washed with saturated sodium bicarbonate solution, dried over Na_2SO_4, filtered, and concentrated at reduced pressure to afford a yellow solid. Flash chromatography (CH_2Cl_2) afforded 55 mg (40%) of **6b** as a light yellow powder: ^{1}H NMR δ 8.50 (s, 2 H, H-10′),

8.03 (d, $J_{3',4'}$ = 8.5, 4 H, H-4′, H-5′), 7.69–7.63 (m, 6 H, H-4, H-3′, H-6′), 7.45–7.40 (m, 4 H, H-2′, H-7′), 7.27 (d, $J_{2'',3''}$ = 8.3, 2 H, H-2″), 7.18–7.11 (m, 6 H, H-3, H-1′, H-8′), 6.85 (d, $J_{2'',3''}$ = 8.3, 2 H, H-3″), 3.05 (s, 6 H, NMe_2), 2.81 (t, $J_{5,6}$ = 3.4, 4 H, H-5), 2.75 (t, $J_{5,6}$ = 3.4, 4 H, H-6); MS (FD, −4 kV), *m/z* (M^+, 783). Anal. Calcd for $C_{56}H_{41}N_3O_2 \cdot 1.5CH_2Cl_2$: C, 75.94; H, 4.79; N, 4.54; Cl, 11.27. Found: C, 75.68, H, 4.69; N, 4.35; Cl, 11.00.

2-Bromo-5,6,7,8-tetrahydroquinoline (23). To a stirred solution of 15 g (0.11 mol) of 5,6,7,8-tetrahydro-2-quinolone[24] in 150 mL of dry DMF was added 100 g of phosphorus tribromide (0.37 mol) under a nitrogen atmosphere at 0 °C. The solution was heated to 110 °C overnight. The mixture was cooled, poured into cold 2 N sodium hydroxide, and extracted with ether. The organic layer was dried over $MgSO_4$ and the solvent was removed at reduced pressure. The residue was purified by flash chromatography (1:1 petroleum ether–CH_2Cl_2) to afford 9.9 g (46%) of **23** as a light green oil: ^{1}H NMR δ 7.20 (s, 2 H, H-3, H-4), 2.90 (t, $J_{5,6}$ = 6.0, 2 H, H-5), 2.71 (t, $J_{7,8}$ = 6.1, 2 H, H-8), 1.89–1.77 (m, 4 H, H-6, H-7); MS (EI, 70 eV), *m/z* 213 (M^+). Anal. Calcd for $C_9H_{10}NBr$: C, 50.91; H, 4.75; N, 6.60; Br, 37.67. Found: C, 50.53; H, 4.75; N, 6.52; Br, 38.04.

2-Chloro-5,6,7,8-tetrahydroquinoline (32). A mixture of 48.1 mL (0.52 mol) of $POCl_3$ and 25.6 g (0.17 mol) of 5,6,7,8-tetrahydro-2-quinolone was refluxed under nitrogen overnight. The mixture was cooled, poured into cold 2 N NaOH, and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (1:2 petroleum ether–CH_2Cl_2) to afford 26.1 g (90%) of **32** as a colorless oil: ^{1}H NMR δ 7.31 (d, $J_{3,4}$ = 8.0, 1 H, H-4), 7.03 (d, $J_{3,4}$ = 8.0, 1 H, H-3), 2.88 (t, $J_{7,8}$ = 6.3, 2 H, H-8), 2.72 (t, $J_{5,6}$ = 6.1, 2 H, H-5), 1.90–1.75 (m, 4 H, H-6, H-7); ^{13}C NMR δ 158.13, 147.64, 139.54, 131.03, 121.15, 32.21, 28.03, 22.66, 22.37; MS (EI, 70 eV), *m/z* (relative intensity) 169 (M^+, 32), 167 (M^+, 100). Anal. Calcd for $C_9H_{10}NCl$: C, 64.48, H, 6.01; N, 8.36; Cl, 21.15. Found: C, 64.40; H, 6.01; N, 8.33; Cl, 21.27.

2-Bromo-5,6,7,8-tetrahydroquinoline *N*-Oxide (24). A solution of 7.20 g (34.0 mmol) of **23** and 30 mL of 35% peracetic acid in 80 mL of THF was refluxed under a nitrogen atmosphere until TLC showed starting material to be absent. The solution was cooled and made basic with a saturated aqueous solution of sodium bicarbonate. The organic layer was separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure, and the residue was purified by flash chromatography (EtOAc) to afford 5.77 g (75%) of **24** as a white solid: mp 112.5–114.0 °C; ^{1}H NMR δ 7.45 (d, $J_{3,4}$ = 8.3, 1 H, H-4), 6.89 (d, $J_{3,4}$ = 8.3, 1 H, H-3), 2.97 (t, $J_{7,8}$ = 6.4, 2 H, H-8), 2.75 (t, $J_{5,6}$ = 6.0, 2 H, H-5), 1.89 (m, 2 H, H-7), 1.76 (m, 2 H, H-6); ^{13}C NMR δ 150.37, 135.00, 129.74, 126.52, 126.03, 28.31, 25.77, 21.77, 21.33; MS (EI, 70 eV), *m/z* (relative intensity) 227 (M^+, 65), 229 (M^+, 63); exact mass calcd for $C_9H_{10}BrNO$ *m/z* 226.994 62, found 226.995 68.

2-Chloro-5,6,7,8-tetrahydroquinoline *N*-Oxide (33). With use of the procedure described for **24**, 35.0 g of **32** afforded a crude residue which was purified by flash chromatography (EtOAc) to afford 38 g (100%) of 2-chloro-5,6,7,8-tetrahydroquinoline *N*-oxide as a white solid: mp 100–102 °C; ^{1}H NMR δ 7.29 (d, $J_{3,4}$ = 8.3, 1 H, H-4), 6.96 (d, $J_{3,4}$ = 8.3, 1 H, H-3), 2.97 (t, $J_{7,8}$ = 6.4, 2 H, H-8), 2.76 (t, $J_{5,6}$ = 6.1, 2 H, H-5), 1.90 (m, 2 H, H-7), 1.76 (m, 2 H, H-6); ^{13}C NMR δ 150.44, 139.00, 134.20, 125.86, 122.88, 28.35, 25.48, 21.69, 21.41; MS (EI, 70 eV), *m/z* (relative intensity) 185 (M^+, 12), 183 (M^+, 38). Anal. Calcd for $C_9H_{10}ClNO$: C, 58.87; H, 5.49; N, 7.63; Cl, 19.31. Found: C, 58.87; H, 5.48; N, 7.60; Cl, 19.32.

8-Acetoxy-2-bromo-5,6,7,8-tetrahydroquinoline (25). A solution of 4.37 g (19 mmol) of **24** in 75 mL of acetic anhydride was heated at 110 °C for 5 h. The excess acetic anhydride was removed under reduced pressure. The residue was dissolved in CH_2Cl_2, washed with sodium bicarbonate, and dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography (20% EtOAc–petroleum ether) to give 4.02 g (78%) of **25** as a white solid: mp 78.0–79.0 °C; IR (KBr) 1740, 1235 cm^{-1}; ^{1}H NMR δ 7.32 (t, 2 H, H-3, H-4), 5.85 (t, $J_{7,8}$ = 4.2, 1 H, H-8), 2.85–2.66 (m, 2 H, H-5), 2.10 (s, 3 H, CH_3CO_2), 2.19–1.83 (m, 4 H, H-6, H-7); ^{13}C NMR δ 170.18, 154.34, 139.69, 139.27, 132.96, 127.67, 70.44, 28.51, 27.78, 21.43, 17.96; MS (FI, 75 °C), *m/z* 271 (M^+), 269; exact mass calcd for $C_{11}H_{12}BrNO_2$ *m/z* 269.005 19, found 269.004 76. Anal. Calcd for $C_{11}H_{12}BrNO_2$: C, 48.91; H, 4.48; N, 5.19; Br, 29.58. Found: C, 48.93; H, 4.73; N, 5.14; Br, 29.42.

8-Acetoxy-2-chloro-5,6,7,8-tetrahydroquinoline (34). With use of the procedure described for **25**, 57 g of **33** was converted into an oil which was purified by flash chromatography (20% EtOAc–petroleum ether) to afford 69 g (98%) of **34** as a light yellow oil: ^{1}H NMR δ 7.43 (d, $J_{3,4}$ = 8.1, 1 H, H-4), 7.19 (d, $J_{3,4}$ = 8.1, 1 H, H-3), 5.84 (t, $J_{7,8}$ = 4.3, 1 H, H-8), 2.89–2.67 (m, 2 H, H-5), 2.10 (s, 3 H, CH_3COO–), 2.21–1.79 (m, 4 H, H-6, H-7); ^{13}C NMR δ 170.10, 153.64, 148.72, 139.97, 132.50, 123.84, 70.39, 28.54, 27.69, 21.36, 18.03; MS (EI, 70 eV), *m/z* (relative intensity) 227 (M^+, 2), 225 (M^+, 5). Anal. Calcd for $C_{11}H_{12}ClNO_2$: C, 58.55; H, 5.36; N, 6.21; Cl, 15.71. Found: C, 58.38; H, 5.37; N, 6.21; Cl, 15.92.

2-Bromo-8-hydroxy-5,6,7,8-tetrahydroquinoline (26). A solution of 4.02 g (14.9 mmol) of **25** in 50 mL of CH_3OH and 50 mL of a 10% aqueous solution of potassium carbonate was stirred at room temperature for 5 h. The mixture was extracted with CH_2Cl_2 five times. The combined organic layer was dried over Na_2SO_4, the solvent was removed at reduced pressure, and the residue was flash chromatographed (1:2 EtOAc–petroleum ether) to produce 3.33 g (98%) of **26** as a white solid: mp 60.5–62.0 °C; IR (KBr) 3532 cm^{-1}; ^{1}H NMR δ 7.24 (s, 2 H, H-4, H-3), 4.67 (s, $J_{7,8}$ = 6.4, 1 H, H-8), 3.79 (br s, 1 H, OH), 2.79–2.63 (m, 2 H, H-5), 2.21–2.13 (m, 1 H, cis H-7), 1.99–1.86 (m, 1 H, trans H-7), 1.82–1.70 (m, 2 H, H-6); ^{13}C NMR δ 159.36, 139.65, 138.76, 131.11, 126.74, 68.40, 30.33, 27.87, 19.00; MS, *m/z* (FD, 10 ma) 229, 227 (M^+); exact mass calcd for $C_9H_{10}BrNO$ *m/z* 226.994 62, found 226.994 67. Anal. Calcd for $C_9H_{10}BrNO$: C, 47.39; H, 4.42; N, 6.14; Br, 35.03. Found: C, 47.48; H, 4.65; N, 65.14; Br, 34.95.

2-Chloro-8-hydroxy-5,6,7,8-tetrahydroquinoline (35). With use of the procedure described for **26**, 30 g of **34** was converted into a crude product that was purified by flash chromatography (EtOAc) to afford 23 g (90%) of **35** as a light yellow oil: ^{1}H NMR δ 7.39 (d, $J_{3,4}$ = 8.1, 1 H, H-4), 7.14 (d, $J_{3,4}$ = 8.1, 1 H, H-3), 4.70 (dd, $J_{7,8}$ = 7.0, 1 H, H-8), 3.79 (s, 1 H, OH), 2.80–2.70 (m, 2 H, H-5), 2.27–2.18 (m, 1 H, H-7, cis to OH), 2.03–1.95 (m, 1 H, H-7, trans to OH), 1.90–1.74 (m, 2 H, H-6); ^{13}C NMR δ 158.61, 148.32, 139.89, 130.63, 122.95, 68.43, 30.33, 27.80, 19.08; MS (EI, 70 eV), *m/z* (relative intensity) 185 (M^+, 1), 183 (M^+, 3). Anal. Calcd for $C_{39}H_{10}ClNO$: C, 58.87; H, 5.49; N, 7.63; Cl, 19.31. Found: C, 58.55; H, 5.49; N, 7.57; Cl, 19.23.

2-Bromo-5,6,7,8-tetrahydro-8-quinolone (27). With use of the general procedure of Swern,[15] 3.25 g of **26** gave a crude product that was purified by flash chromatography (1:2 EtOAc–petroleum ether) to afford 2.84 g (88%) of **27** as a white solid: mp 108–110 °C; IR (KBr) 1707 cm^{-1}; ^{1}H NMR δ 7.59 (d, $J_{3,4}$ = 8.1, 1 H, H-4), 7.50 (d, $J_{3,4}$ = 8.1, 1 H, H-3), 2.99 (t, $J_{5,6}$ = 6.1, 2 H, H-5), 2.79 (t, $J_{6,7}$ = 6.6, 2 H, H-5), 2.19 (m, 2 H, H-6); ^{13}C NMR δ 194.96, 148.68, 141.30, 140.30, 140.08, 131.88, 39.26, 28.55, 22.34; MS (EI, 70 eV), *m/z* (relative intensity) 227 (M^+, 77), 225 (M^+, 79); exact mass calcd for C_9H_8BrNO *m/z* 224.978 97, found 224.979 01. Anal. Calcd for C_9H_8BrNO: C, 47.82; H, 3.57; N, 6.20; Br, 35.34. Found: C, 47.88; H, 3.62; N, 6.17; Br, 35.33.

2-Chloro-5,6,7,8-tetrahydro-8-quinolone (36). With use of the general procedure of Swern,[15] 22.9 g of **35** gave a crude product that was purified by flash chromatography (50% EtOAc–petroleum ether) and then recrystallized from EtOAc and petroleum ether to afford 21.6 g (96%) of **36** as white needles: mp 127–129 °C; ^{1}H NMR δ 7.68 (d, $J_{3,4}$ = 8.1, 1 H, H-4), 7.42 (d, $J_{3,4}$ = 8.1, 1 H, H-3), 3.03 (t, $J_{6,7}$ = 6.1, 2 H, H-7), 2.79 (t, $J_{5,6}$ = 6.6, 2 H, H-5), 2.20 (m, 2 H, H-6); ^{13}C NMR δ 195.08, 150.70, 147.94, 140.68, 139.66, 128.17, 39.29, 28.45, 22.41; MS (EI, 70 eV), *m/z* (relative intensity) 183 (M^+, 16), 181 (M^+, 54). Anal. Calcd for C_9H_8ClNO: C, 59.52; H, 4.44; N, 7.71; Cl, 19.52. Found: C, 59.53; H, 4.44; N, 7.74; Cl, 19.41.

7-Benzylidene-2-bromo-5,6,7,8-tetrahydro-8-quinolone. A mixture of 5.51 g (24.6 mmol) of quinolone, 10.0 mL (98.4 mmol) of benzaldehyde, and 1.18 g of KOH in 14 mL of water and 70 mL of CH_3OH was stirred at room temperature overnight. The mixture was filtered and the solid was crystallized from EtOAc to give 6.51 g (85%) of 7-benzylidene-2-bromo-5,6,7,8-tetrahydro-8-quinolone as green cubic crystals: mp 175–177 °C; ^{1}H NMR δ 7.96 (s, 1 H, H-9), 7.59 (d, $J_{3,4}$ = 8.1, 1 H, H-4), 7.51 (d, $J_{3,4}$ = 8.1, 1 H, H-3), 7.45–7.39 (m, 5 H, PhH), 3.17 (m, 2 H, H-5), 2.94 (t, 2 H, H-5), 2.19 (m, 2 H, H-6); ^{13}C NMR δ 184.94, 149.95, 141.93, 139.69, 139.01, 138.66, 135.39, 134.42, 131.79, 130.11, 129.18, 128.69, 27.50, 26.33; MS (EI, 70 eV), *m/z* (relative intensity) 315 (M^+, 55), 314 (M −1, 100), 313 (M^+, 54), 312 (M − 1, 98). Anal. Calcd for $C_{16}H_{12}BrNO$: C, 61.17; H, 3.85; N, 4.46; Br, 25.43. Found: C, 61.27; H, 3.85; N, 4.44; Br, 25.52.

7-Benzylidene-2-chloro-5,6,7,8-tetrahydro-8-quinolone. A mixture of 5.86 g (32.2 mmol) of 2-chloro-5,6,7,8-tetrahydro-8-quinolone, 13.2 mL (0.129 mol) of benzaldehyde, and 1.79 g of KOH in 21 mL of water and 105 mL of CH_3OH was stirred at room temperature overnight. The mixture was filtered and the solid recrystallized from EtOAc to give 6.3 g (72%) of green cubic crystals: ^{1}H NMR δ 7.94 (s, 1 H, H-9), 7.65 (d, $J_{3,4}$ = 8.1, 1 H, H-4), 7.44–7.37 (m, 6 H, H-3, PhH), 3.17 (m, 2 H, H-5), 2.96 (t, $J_{5,6}$ = 6.9, 2 H, H-5); ^{13}C NMR δ 184.94, 151.19, 149.08, 139.99, 138.83, 138.16, 135.24, 134.37, 129.97, 129.04, 128.55, 127.95, 27.28, 26.25; MS (EI, 70 eV), *m/z* (relative intensity) 271 (M^+, 19), 270 (M − 1, 41), 269 (M^+, 56), 268 (M − 1, 100). Anal. Calcd for $C_{16}H_{12}ClNO$: C, 71.25; H, 4.48; N, 5.19; Cl, 13.14. Found: C, 71.41; H, 4.47; N, 5.06; Cl, 12.97.

Methyl 2,12-dibromo-7-phenyl-5,6,7,8-tetrahydro-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylate (30). A mixture of 1.25 g (5.53 mmol) of **27** and 1.67 g (5.53 mmol) of 7-benzylidene-2-bromo-5,6,7,8-tetrahydro-8-quinolone was stirred in 3.4 mL of boron trifluoride etherate at 110 °C for 0.5 h. The mixture was cooled to room temperature, dissolved in chloroform, and washed vigorously with aqueous saturated sodium bicarbonate solution. The organic layer was dried over Na_2SO_4 and the solvent was removed at reduced pressure. The residue was purified by flash chromatography (10% EtOAc–CH_2Cl_2) to afford crude pyran which was used without further purification. A mixture of pyran and DDQ (1 equiv) in 50 mL of CH_2Cl_2 was stirred at room temperature for 5 h or until pyran disappeared (TLC). The solvent was removed and the residue was dried under vacuum. In a separate flask, 2.1 mL (13 mmol) of trimethyl phosphonoacetate was added to a stirred slurry of 0.73 g (29.5 mmol) of sodium hydride in 100 mL of dry THF, and the mixture was stirred for 1 h at room temperature. The pyran was added in one lot to this thick white slurry. The reaction mixture was refluxed for 4 h, cooled to room temperature, quenched with 1 N aqueous HCl, extracted with CH_2Cl_2, and dried over Na_2SO_4. After the solvent was removed at reduced pressure, the residue was purified by flash chromatography (CH_2Cl_2) to afford 0.66 g (21%) of **30** as a white solid: mp >280 °C; ^{1}H NMR δ 7.45 (m, 3 H, H-3′, H-4′, H-5′), 7.33 (AB q, 4 H, H-3, H-4, H-10, H-11), 7.13 (dd, $J_{2',3'}$ = 8.0, $J_{2',4'}$ = 1.3, 2 H, H-2′, H-6′), 3.14 (s, 3 H, $-CO_2CH_3$), 2.69 (m, 4 H, H-6, H-8), 2.55 (m, 4 H, H-5, H-9); MS (EI, 70 eV), *m*/*z* (relative intensity) 578 (16), 576 (31), 574 (17); exact mass calcd for $C_{28}H_{20}Br_2N_2O_2$ *m*/*z* 573.989 24, found 573.989 03. Anal. Calcd for $C_{28}H_{20}Br_2N_2O_2$: C, 58.36; H, 3.50; N, 4.86; Br, 27.73. Found: C, 58.42; H, 3.52;, N, 4.80; Br, 27.84.

Methyl 2,12-Dichloro-7-phenyl-5,6,8,9-tetrahydro-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylate (38). By the procedure described for **30**, 1.00 g of 2-chloro-5,6,7,8-tetrahydro-8-quinolone and 1.48 g of 7-benzylidene-2-chloro-5,6,7,8-tetrahydro-8-quinolone afforded a crude product that was purified by chromatography (CH_2Cl_2) to afford 1.0 g (37%) of **38** as a white solid: mp >300 °C; ^{1}H NMR δ 7.45–7.42 (m, 5 H, H-4, H-10, H-3′, H-4′, H-5′), 7.15 (m, 4 H, H-3, H-11, H-2′, H-6′), 4.08 (s, 3 H, CO_2CH_3), 2.72 (m, 4 H, H-6, H-8), 2.55 (m, 4 H, H-5, H-9); MS (EI, 70 eV), *m*/*z* (relative intensity) 490 (M^+, 4.2), 488 (M^+, 17.1), 486 (M^+, 27.4). Anal. Calcd for $C_{28}H_{20}Cl_2N_2O_2$: C, 69.00; H, 4.14; N, 5.75; Cl, 14.55. Found: C, 69.12; H, 4.19; N, 5.76; Cl, 14.39.

Methyl 2,12-Dichloro-7-phenyl-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylate (40). A mixture of 453 mg of **38** and 2.11 g of DDQ was refluxed under nitrogen in bromobenzene for 20 h. The mixture was allowed to cool to room temperature and passed through a dry column of silica gel, eluting with CH_2Cl_2. The fractions containing product were combined and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2) to afford 183 mg (41%) of **40** as a yellow powder: mp >300 °C; ^{1}H NMR δ 8.12 (d, $J_{3,4}$ = 8.4, 2 H, H-4, H-10), 7.64–7.58 (m, 9 H, H-3, H-4, H-10, H-11, H-3′, H-4′, H-5′), 7.43–7.39 (m, 2 H, H-2′, H-6′), 4.58 (s, 3 H, CO_2CH_3); MS (EI, 70 eV), *m*/*z* (relative intensity) 486 (M^+, 7), 484 (M^+, 31), 482 (M^+, 45). Anal. Calcd for $C_{28}H_{16}Cl_2N_2O_2$: C, 69.58; H, 3.34; N, 5.80; Cl, 14.67. Found: C, 69.43; H, 3.49; N, 5.81; Cl, 14.50.

Methyl 2,12-Bis(9-anthracenyl)-7-phenyl-5,6,8,9-tetrahydro-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylate (9a). To a solution of 942 mg (3.5 mmol) of 9-bromoanthracene in 120 mL of dry Et_2O was added an excess amount of magnesium chips, 10 drops of 1,2-dibromoethane, and an iodine crystal. The mixture was heated to reflux and kept at 50 °C for 1 h. The resulting solution or suspension was transferred to a mixture of 401 mg (0.7 mmol) of **30** and 9.4 mg of $Ni(acac)_2$ in 200 mL of dry benzene and 20 mL of ether at 0 °C. The solution was stirred at 0 °C for 1 h and refluxed for 24 h. The solution was allowed to cool to room temperature, acidified with 1 N HCl, and filtered. The aqueous layer was separated, extracted with $CHCl_3$, dried over Na_2SO_4, filtered, and concentrated at reduced pressure to afford a yellow solid. Flash chromatography (1:3 petroleum ether–CH_2Cl_2) afforded 395 mg (73%) of **9a** as a yellow powder: ^{1}H NMR δ 8.38 (s, 2 H, H-10′), 7.92 (d, 4 H, $J_{3',4'}$ = 8.4, H-4′, H-5′), 7.58 (d, $J_{3,4}$ = 7.6, 2 H, H-4, H-10), 7.56–7.47 (m, 7 H, H-3′, H-6′, H-3″, H-4″, H-5″), 7.36–7.31 (m, 6 H, H-2′, H-7′, H-2″, H-6″), 7.24–7.16 (m, 4 H, H-1′, H-8′), 7.14 (d, 2 H, $J_{3,4}$ = 7.6, H-3, H-11), 2.86 (m, 4 H, H-6, H-8), 2.72 (m, 4 H, H-5, H-9), 1.70 (s, 3 H, CO_2CH_3); MS (FAB, Xe) 771 (M + H); exact mass calcd for $C_{56}H_{39}N_2O_2$ *m*/*z* 771.3011, found 771.3000.

Methyl 2,12-Bis(9-anthracenyl)-7-phenyl-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylate (10a). By the same procedure described for **9a**, 867 mg (3.2 mmol) of 9-bromoanthracene and 310 mg (0.64 mmol) of **40** were coupled to afford a yellow solid. Flash chromatography (1:2 petroleum ether–CH_2Cl_2) afforded 219 mg (45%) of **10a** as yellow powder: ^{1}H NMR δ 8.40 (s, 2 H, H-10′), 8.27 (d, 2 H, $J_{3,4}$ = 8.0, H-4, H-10), 7.93 (m, 4 H, H-4′, H-5′), 7.61 (d, 2 H, $J_{3,4}$ = 8.0, H-3, H-11), 7.58–7.17 (m, 21 H, H-5, H-6, H-8, H-9, H-1′, H-2′, H-3′, H-6′, H-7′, H-8′, H-2″, H-3″, H-4″, H-5″, H-6″), 1.43 (s, 3 H, CO_2CH_3); MS (FAB) 767 (M + H); exact mass calcd for $C_{56}H_{35}N_2O_2$ *m*/*z* 767.2698, found 767.2690.

2,12-Bis(9-anthracenyl)-7-phenyl-5,6,8,9-tetrahydro-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylic Acid (9b). To a solution of 282 mg (0.37 mmol) of ester **9a** in 50 mL of CH_2Cl_2 cooled to 0 °C was added 3.7 mL of boron trichloride in hexane (1.0 M). The solution was refluxed under nitrogen overnight. The mixture was cooled to room temperature, diluted with CH_2Cl_2, vigorously washed with saturated $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated at reduced pressure to afford a yellow solid. Flash chromatography (CH_2Cl_2) afforded 137 mg (50%) of **9b** as yellow powder: ^{1}H NMR δ 8.51 (s, 2 H, H-10′), 8.05 (d, 4 H, $J_{3',4'}$ = 8.5, H-4′, H-5′), 7.68–7.64 (m, 6 H, H-4, H-10, H-3′, H-6′), 7.52–7.41 (m, 7 H, H-2′, H-7′, H-3″, H-4″, H-5″), 7.31–7.28 (m, 4 H, H-3, H-11, H-2″, H-6″), 7.18–7.13 (m, 4 H, H-1′, H-8′), 2.84 (m, 4 H, H-6, H-8), 2.67 (m, 4 H, H-5, H-9); MS (FAB) 757 (M + H), 739 (M − OH), 713 (M + H − CO_2). Anal. Calcd for $C_{55}H_{36}N_2O_2 \cdot 1.4CH_2Cl_2$: C, 77.35; H, 4.47; N, 3.20; Cl, 11.33. Found: C, 77.33; H, 4.60; N, 3.11; Cl, 11.51.

2,12-Bis(9-anthracenyl)-7-phenyl-1,13-diazadibenz[*a*,*j*]anthracene-14-carboxylic Acid (10b). To a solution of 219 mg (0.29 mmol) of **10a** in 60 mL of CH_2Cl_2 cooled to 0 °C was added 2.9 mL of boron trichloride in hexane (1.0 M). The solution was refluxed under nitrogen overnight. The mixture was cooled to room temperature, diluted with CH_2Cl_2, vigorously washed with saturated $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated at reduced pressure to afford a yellow solid. Flash chromatography (25% petroleum ether–CH_2Cl_2) afforded 144 mg (67%) of **10b** as a yellow powder: ^{1}H NMR δ 8.44 (s, 2 H, H-10), 8.30 (d, 2 H, $J_{3,4}$ = 8.0, H-4, H-10), 7.96 (d, 4 H, $J_{3',4'}$ = 8.5, H-4′, H-5′), 7.74–7.66 (m, 13 H, H-5, H-6, H-8, H-9, H-3′, H-6′, H-2″, H-3″, H-4″, H-5″, H-6″), 7.52 (d, 2 H, $J_{3',4'}$ = 8.0, H-3, H-11), 7.39–7.34 (m, 4 H, H-2″, H-7′), 7.25–7.20 (m, 4 H, H-1′, H-8′); MS (FAB) 753 (M + H), 735 (M − OH), 709 (M + H − CO_2); exact mass calcd for $C_{55}H_{33}N_2O_2$ *m*/*z* 753.254 10, found 753.250 70. Anal. Calcd for $C_{55}H_{32}N_2O_2$: C, 87.74; H, 4.28; N, 3.72. Found: C, 87.17; H, 4.41; N, 3.58.

Methyl 2,12-Dibromo-7-phenyl-5,6,8,9-tetrahydrobenz[*a*,*j*]anthracene-14-carboxylate (41). A mixture of 11.0 g (35 mmol) of 7-bromo-1-tetralone and 7.91 g (35 mmol) of 7-bromo-2-benzylidene-1-tetralone were combined with 18 mL of $BF_3 \cdot Et_2O$ under nitrogen and stirred at 100 °C for 5 h. The reaction mixture was allowed to cool to room temperature and dry ether (400 mL) was added to the solid residue and the mixture allowed stirred overnight. The suspension was filtered and the solid was washed with ether. The solid pyrylium salt **51** (ca. 60% pure) was added to a thick slurry generated by stirring a mixture of 13.7 g (148 mmol) of sodium hydride and 12 g (66 mmol) of trimethyl phosphonoacetate in 400 mL of dry THF for 1 h at room temperature. The mixture was stirred at room temperature for 5 h and quenched with 1 N aqueous HCl solution. The mixture was extracted with CH_2Cl_2 and the organic layer dried over Na_2SO_4. After the solvent was removed at reduced pressure, the residue was purified by flash chromatography (4:1 CH_2Cl_2–petroleum ether) to afford 5.19 g (26%) of **41** as a white solid: mp 253–254 °C; ^{1}H NMR δ 7.57 (d, $J_{1,3}$ = 1.6, 2 H, H-1, H-13), 7.60–7.56 (m, 3 H, H-3′, H-4′, H-5′), 7.35 (dd, $J_{1,3}$ = 1.6, $J_{3,4}$ = 8.1, 2 H, H-3, H-11), 7.17 (dd, $J_{2',3'}$ = 7.9, $J_{2',4'}$ = 1.5, 2 H, H-2′, H-6′), 7.13 (d, $J_{3,4}$ = 8.1, 2 H, H-4, H-10), 3.91 (s, 3 H, $-COOCH_3$), 2.62 (t, $J_{5,6}$ = 6.9, 4 H, H-6, H-8), 2.46 (t, $J_{5,6}$ = 6.9, 4 H, H-5, H-9); ^{13}C NMR δ 171.07, 139.88, 138.25, 137.65, 136.87, 134.77, 130.14, 129.9, 128.45, 128.29, 128.18, 128.10, 127.84, 127.50, 119.08, 52.42, 27.86, 27.24. IR (KBr) 1725 cm^{-1}; MS (EI, 70 eV), *m*/*z* (relative intensity) 576 (50), 574 (100), 572 (50); exact mass calcd for $C_{30}H_{22}Br_2O_2$ *m*/*z* 571.998 75, found 571.998 38.

2,12-Dibromo-7-phenyl-5,6,8,9-tetrahydrobenz[*c*,*h*]xanthylium Tetrafluoroborate (51). A small amount of **51** was purified and characterized: ^{1}H NMR δ 8.58 (d, $J_{1,3}$ = 1.6, 2 H, H-1, H-13), 7.93 (dd, $J_{1,3}$ = 1.6, $J_{3,4}$ = 8.1, 2 H, H-3, H-11), 7.68 (m, 3 H, H-3′, H-4′, H-5′), 7.48 (m, 4 H, H-4, H-10, H-2′, H-6′), 3.01 (t, $J_{5,6}$ = 7.48, 4 H, H-6, H-8), 2.87 (t, $J_{5,6}$ = $J_{8,9}$ + 6.92, 4 H, H-5, H-9); ^{13}C NMR δ 166.3, 164.0, 141.3, 138.3, 138.2, 132.8, 132.0, 131.6, 131.2, 129.9, 129.3, 128.0, 121.6, 25.8, 24.7; MS (EI, 70 eV), *m*/*z* (relative intensity) 312 (M^+, 55), 314 (M^+, 54); exact mass calcd for $C_{27}H_{19}Br_2O$ *m*/*z* 516.980 36, found 516.961 81.

10-((2-Methoxyethoxy)methyl)-2,7-dimethoxy-9-acridone (42). To a mixture of 2.60 g (10 mmol) of 2,7-dimethoxyacridone and 0.38 g (16 mmol) of sodium hydride was added 50 mL of DMF at 0 °C. The solution was allowed to warm to room temperature and stirred until it was homogeneous. After mixture was cooled to 0 °C, 1.7 mL (15 mmol) of (2-methoxyethoxy)methyl chloride was then added slowly at 0 °C and the mixture was stirred for 2 h. The mixture was quenched with water, unreacted acridone was filtered off, and the filtrate was extracted with

CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure, and the residue was flash chromatographed (5% CH_3OH–CH_2Cl_2) to afford 2.74 g (78%) of **42** as a yellow solid: mp 116–118 °C; IR (KBr) 1599 cm^{-1}; ^1H NMR δ 7.91 (d, $J_{1,3}$ = 3.5, $J_{3,4}$ = 9.4, 2 H, H-3, H-6), 5.79 (s, 2 H, H-1′), 3.94 (s, 6 H, $-OCH_3$), 3.80 (t, 2 H, $J_{2',3'}$ = 3.8, H-2′), 3.61 (t, $J_{2',3'}$ = 3.8, 2 H, H-3′), 3.41 (s, 3 H, H-4′); ^{13}C NMR δ 177.05, 154.53, 136.60, 124.17, 122.14, 116.87, 106.11, 76.85, 72.10, 67.07, 59.04, 55.63; MS (EI, 70 eV), *m/z* 343 (M^+); exact mass calcd for $C_{19}H_{21}NO_5$ *m/z* 343.141 96, found 343.142 75. Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.71; H, 6.20; N, 4.06.

Methyl 2,12-Dibromo-7-phenylbenz[*a*,*j*]anthracene-14-carboxylate (43). To a solution of 166 mg (0.29 mmol) of **41** in 4 mL of chlorobenzene was added 654 mg (2.88 mmol) of DDQ. The mixture was heated to reflux for 2 days. After being cooled to room temperature, the mixture was separated by flash chromatography (1:3 CH_2Cl_2–petroleum ether) to afford 133.0 mg (81%) of **43** as a yellow powder: mp 254–256 °C; ^1H NMR δ 8.59 (s, 2 H, H-1, H-13), 7.74 (s, 4 H, H-5, H-6, H-8, H-9), 7.50–7.40 (m, 3 H, H-3′, H-4′, H-5′), 7.54 (dd, $J_{3,4}$ = 9.2, 2 H, H-3, H-11), 7.43 (dd, $J_{3,4}$ = 9.2, 2 H, H-4, H-10), 7.41–7.37 (m, 2 H, H-2′, H-6′), 4.35 (s, 3 H, $COOCH_3$); MS (EI, 70 eV), *m/z* (relative intensity) 572 (59), 570 (100), 568 (47); exact mass calcd for $C_{30}H_{18}Br_2O_2$ *m/z* 567.967 45, found 567.967 37.

Methyl 2,12-Bis(2,7-dimethoxyacridin-9-yl)-7-phenyl-5,6,8,9-tetrahydrodibenz[*a*,*j*]anthracene-14-carboxylate (7). To a solution of 517 mg (0.90 mmol) of **41** in 50 mL of THF cooled to −78 °C was added 1.28 mL (1.98 mmol) of *n*-butyllithium in hexane. The resulting solution was stirred for 0.5 h and was transferred via canula to a solution of 928 mg (2.70 mmol) of acridone **42** in 100 mL of THF at −78 °C. The mixture was stirred for 3 h and was quenched with a saturated aqueous solution of ammonium chloride. The solution was extracted with CH_2Cl_2 and dried over Na_2SO_4, and the solvent was removed at reduced pressure. The remaining solid was dissolved in 100 mL of 1:1 ethanol–2 N aqueous HCl and was stirred at 50 °C overnight. The solution was cooled to room temperature, neutralized with 2 N aqueous NaOH, and filtered to remove insoluble acridone, and the solution was extracted with CH_2Cl_2. After the solution was dried over Na_2SO_4, the solvent was removed at reduced pressure, and the solid was purified by flash chromatography (40% EtOAc–CH_2Cl_2) to afford 520 mg (65%) of **7** as yellow powder: mp >270 °C; ^1H NMR δ 8.10 (d, $J_{3',4'}$ = 9.4, 4 H, H-4′, H-5′), 7.52 (m, 3 H, H-3″, H-4″, H-5″), 7.44 (d, $J_{3,4}$ = 7.7, 2 H, H-3, H-11), 7.35 (dd, $J_{3',4'}$ = 9.4, $J_{1',3'}$ = 2.6, 2 H, H-3′, H-6′), 7.34 (s, 2 H, H-1, H-13), 7.31 (m, 2 H, H-2″, H-6″), 7.21 (d, $J_{3,4}$ = 7.7, 2 H, H-4, H-10), 6.67 (d, $J_{1',3'}$ = 2.6, 4 H, H-1′, H-8′), 3.67 (s, 12 H, $-OCH_3$), 2.82 (t, $J_{5,6}$ = 3.2, 4 H, H-6, H-8), 2.72 (s, 3 H, CO_2CH_3), 2.64 (t, $J_{5,6}$ = 3.2, 4 H, H-5, H-9); ^{13}C NMR δ 170.49, 156.93, 144.20, 142.37, 140.82, 139.43, 138.82, 138.55, 135.00, 134.18, 131.86, 131.05, 129.33, 129.01, 128.67, 128.17, 127.90, 127.61, 127.56, 126.43, 123.54, 102.08, 55.36, 52.16, 29.22, 28.42; IR (KBr) 1717 cm^{-1}; MS (FD, 26 ma) 890 (M^+), exact mass calcd for $C_{60}H_{47}N_2O_6$ *m/z* 891.3434, found 891.3458.

Methyl 2,12-Bis(2,7-dimethoxyacridin-9-yl)-7-phenylbenz[*a*,*j*]-anthracene-14-carboxylate (8). To a solution of 133 mg (0.23 mmol) of **43** in 5 mL of THF at −78 °C was added 0.32 mL (0.51 mmol) of *n*-butyllithium in hexane. The resulting solution was stirred for 0.5 h and was transferred via canula to a solution of 240.2 mg (0.7 mmol) of **42** in 10 mL of THF at −78 °C. The mixture was stirred for 3 h and was quenched with a saturated solution of ammonium chloride at −78 °C. The mixture was extracted with CH_2Cl_2 and dried over Na_2SO_4, and the solvent was evaporated at reduced pressure. The residue was dissolved in 20 mL of 1:1 ethanol–2 N aqueous HCl and was stirred at 50 °C overnight. The solution was cooled to room temperature, neutralized with 2 N aqueous NaOH, and filtered (acridone). The filtrate was extracted with CH_2Cl_2 and dried over Na_2SO_4, and the solvent was removed at reduced pressure. The residue was purified by flash chromatography (1:1 EtOAc–CH_2Cl_2) to afford 105.5 mg (51%) of **43** as a yellow powder: ^1H NMR δ 8.34 (s, 2 H, H-1, H-13), 8.10 (t, 6 H, H-4″, H-5″, H-5, H-9), 7.74 (d, $J_{3,4}$ = 7.2, 2 H, H-3, H-11), 7.67–7.57 (m, 7 H, H-4, H-6, H-8, H-10, H-3″, H-4″, H-5″), 7.50 (dd, $J_{2'',3''}$ = 7.5, $J_{2'',4''}$ = 2.0, 2 H, H-2″, H-6″), 7.35 (dd, $J_{3',4'}$ = 9.5, $J_{1',3'}$ = 2.5, 2 H, H-3′, H-6′), 6.64 (d, $J_{1',3'}$ = 2.5, 4 H, H-1′, H-8′), 3.59 (s, 12 H, $-OCH_3$), 2.73 (s, 3 H, CO_2CH_3); ^{13}C NMR δ 174.11, 157.21, 144.24, 141.93, 139.68, 138.71, 132.6, 132.90, 131.48, 131.4, 131.03, 130.28, 129.45, 129.29, 128.90, 128.73, 128.09, 127.72, 127.6, 127.52, 126.42, 126.0, 123.92, 101.87, 55.29, 52.42; MS (FAB, Xe) 887 ($M^+ + H$); exact mass calcd for $C_{60}H_{43}N_2O_6$ *m/z* 887.312 09, found 887.311 20.

2,12-Bis(2,7-dimethoxyacridin-9-yl)-7-phenyl-5,6,8,9-tetrahydrobenz-[*a*,*j*]anthracene-14-carboxylic Acid (45). A suspension of 101 mg (0.11 mmol) of **7** and 111 mg (2.22 mmol) of sodium cyanide in 8 mL of DMSO was stirred under nitrogen at 90 °C for 3 days when the solution became homogeneous. The mixture was poured into the water and was neutralized with 1 N aqueous HCl. Chloroform was added and the organic layer was washed with water three times. The organic layer was dried over Na_2SO_4 and the solvent was removed at reduced pressure. The residue was purified by flash chromatography (1:1 EtOAc–CH_2Cl_2) to give 83.3 mg (84%) of **45** as a yellow powder: ^1H NMR (sodium salt in DMSO-d_6) δ 8.69 (s, 2 H, H-1, H-13), 8.02 (d, $J_{3',4'}$ = 9.3, 4 H, H-4′, H-5′), 7.47–7.50 (m, 3 H, H-3″, H-4″, H-5″), 7.42 (dd, $J_{3',4'}$ = 9.3, $J_{1',3'}$ = 2.47, 2 H, H-3′, H-6′), 7.39 (d, $J_{3,4}$ = 7.6, 2 H, H-3, H-11), 7.33 (d, $J_{2'',3''}$ = 7.5, 2 H, H-2″, H-6″), 7.11 (d, $J_{3,4}$ = 7.6, 2 H, H-4, H-10), 6.99 (d, $J_{1',3'}$ = 2.2, 4 H, H-1′, H-8′), 3.71 (s, 12 H, OCH_3), 2.67 (t, $J_{5,6}$ = 6.0, 4 H, H-6, H-8), 2.45 (t, $J_{5,6}$ = 6.0, 4 H, H-5, H-9); MS (FD, 30 ma) 876 (M^+). Anal. Calcd for $C_{59}H_{44}N_2O_6 \cdot 0.12CH_2Cl_2$: C, 80.04; H, 5.03; N, 3.16; Cl, 0.96. Found: C, 79.73; H, 5.00; N, 3.08; Cl, 0.64.

2,12-Dibromo-7-phenyl-5,6,8,9-tetrahydrobenz[*a*,*j*]anthracene-14-carboxylic Acid (46). To a solution of 101 mg (0.18 mmol) of **41** in 5 mL of THF at 0 °C was added 0.88 mL (0.85 mmol) of a solution of lithium triethylborohydride in THF and the mixture was stirred overnight at room temperature. The reaction was quenched with cold water and a mixture of 2 mL of 1 N aqueous sodium hydroxide and 1 mL of 30% aqueous hydrogen peroxide. After being stirred for 0.5 h, the mixture was acidified with a 1 N aqueous HCl solution and extracted with ether. The ethereal solution was dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (5% EtOAc–CH_2Cl_2) to afford 81.0 mg (82%) of **46** as a white solid: ^1H NMR δ 7.80 (s, 2 H, H-1, H-13), 7.46–7.40 (m, 3 H, H-3′, H-4′, H-5′), 7.34 (d, $J_{3,4}$ = 8.0, 2 H, H-3, H-11), 7.16 (d, $J_{2',3'}$ = 7.3, 2 H, H-2′, H-6′), 7.12 (d, $J_{3,4}$ = 8.0, 2 H, H-4, H-10), 2.61 (t, $J_{5,6}$ = 6.4, 4 H, H-6, H-8), 2.44 (t, $J_{5,6}$ = 6.4, 4 H, H-5, H-9); ^{13}C NMR δ 174.27, 140.88, 139.07, 138.58, 137.74, 135.50, 131.24, 130.43, 129.54, 129.21, 128.93, 128.66, 127.62, 127.35, 120.10, 28.76, 28.16; MS (EI, 70 eV), *m/z* (relative intensity) 558 (50), 560 (100), 562 (50); exact mass calcd for $C_{29}H_{20}Br_2O_2$ *m/z* 557.983 10, found 557.981 91.

(2-Methoxyethoxy)methyl 2,12-Dibromo-7-phenyl-5,6,8,9-tetrahydrobenz[*a*,*j*]anthracene-14-carboxylate (47). To a solution of 100 mg (0.18 mmol) of **46** in 10 mL of CH_2Cl_2 at 0 °C was added 60 μL (0.32 mmol) of *N*,*N*-diisopropylethylamine and the mixture was stirred for 0.5 h. To this was added 37 μL (0.32 mmol) of (methoxyethoxy)methyl (MEM) chloride and the mixture was stirred for 1 h. Cold water was added and the mixture was made basic with 1 N aqueous NaOH. The mixture was extracted with CH_2Cl_2 and dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (2:3 petroleum ether–CH_2Cl_2) to afford 95.5 mg (83%) of **47** as a white solid: mp 133–135 °C; ^1H NMR δ 7.65 (d, $J_{1,3}$ = 1.5, 2 H, H-1, H-13), 7.45–7.37 (m, 3 H, H-3′, H-4′, H-5′), 7.34 (dd, $J_{1,3}$ = 1.5, $J_{3,4}$ = 8.2, 2 H, H-3, H-11), 7.16 (dd, $J_{2',3'}$ = 6.6, 2 H, H-2′, H-6′), 7.12 (d, $J_{3,4}$ = 8.2, 2 H, H-4, H-10), 5.37 (s, 2 H, H-1″), 3.47 (t, $J_{2'',3''}$ = 4.4, 2 H, H-2″), 3.46 (t, $J_{2'',3''}$ = 4.4, 2 H, H-3″), 3.34 (s, 3 H, H-4″), 2.61 (t, $J_{5,6}$ = 6.4, 4 H, H-6, H-8), 2.45 (t, $J_{5,6}$ = 6.4, 4 H, H-5, H-9); ^{13}C NMR δ 170.76, 140.80, 138.94, 138.59, 137.83, 135.73, 131.11, 130.25, 129.06, 129.24, 128.73, 128.61, 128.01, 127.67, 119.97, 92.59, 71.36, 70.01, 59.03, 28.70, 28.09; MS (EI, 70 eV), *m/z* (relative intensity) 646 (7), 648 (14), 650 (7); exact mass calcd for $C_{33}H_{28}Br_2O_4$ *m/z* 646.035 53, found 648.032 36.

Methyl 2,12-Diiodo-7-phenyl-5,6,8,9-tetrahydrodibenz[*a*,*j*]-anthracene-14-carboxylate (49). To a solution of 496.2 mg (0.86 mmol) of **41** in 50 mL of dry THF was added 1.72 mL (1.90 mmol) of *n*-butyllithium in hexane at −78 °C and the solution was stirred for 0.5 h. To this was added via canula a solution of 1.12 g (4.3 mmol) of iodine in 20 mL of THF and the solution was stirred for 2 h. A solution of 1.5 g of sodium thiosulfate in 10 mL of water was added and the mixture was stirred at room temperature for 0.5 h. The mixture was extracted with CH_2Cl_2, the organic layer was dried over Na_2SO_4, and the solvent was removed at reduced pressure. The residue was recrystallized from EtOAc to afford 358 mg (62%) of **49** as a white powder: ^1H NMR δ 7.76 (d, $J_{1,3}$ = 1.5, 2 H, H-1, H-13), 7.55 (dd, $J_{1,3}$ = 1.5, $J_{3,4}$ = 8.0, 2 H, H-3, H-11), 7.45–7.40 (m, 3 H, H-3′, H-4′, H-5′), 7.17 (dd, $J_{2',3'}$ = 6.3, $J_{2',4'}$ = 1.6, 2 H, H-2′, H-6′), 7.00 (d, $J_{3,4}$ = 8.0, 2 H, H-4, H-10), 3.94 (s, 3 H, CO_2CH_3), 2.62 (m, 4 H, H-6, H-8), 2.46 (m, 4 H, H-5, H-9); ^{13}C NMR δ 171.97, 140.79, 139.20, 138.49, 136.26, 135.97, 135.21, 130.93, 129.62, 129.41, 129.35, 128.75, 128.38, 127.71, 91.20, 52.61, 28.89, 28.11; MS (EI, 70 eV), *m/z* (relative intensity) 668 (M^+, 100); exact mass calcd for $C_{30}H_{22}I_2O_2$ *m/z* 667.971 29, found 667.969 99.

2,12-Dibromo-7-phenyl-5,6,8,9-tetrahydrobenz[*a*,*j*]anthracene 14-Cyanide (52). To a stirred slurry of 367 mg (14.9 mmol) of sodium hydride in 50 mL of dry THF was added 1.9 mL (11.5 mmol) of diethyl (cyanomethyl)phosphonate. The mixture was stirred for 1 h at room temperature and 1.0 g (3.2 mmol) of 2,12-dibromo-7-phenyl-5,6,8,9-tetrahydrodibenz[*c*,*h*]xanthylium tetrafluoroborate (**51**) was added and the mixture refluxed for 4 h. After the mixture was cooled to room temperature, the reaction was quenched with 1 N aqueous HCl and the

mixture was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and the solvent was removed at reduced pressure. The residue was purified by flash chromatography (1:3 CH_2Cl_2-petroleum ether) to afford 743.3 mg (83%) of **52** as a light yellow solid: mp >244 °C; ^1H NMR δ 8.48 (d, $J_{1,3} = J_{11,13} = 1.5$, 2 H, H-1, H-13), 7.48-7.41 (m, 5 H, H-3, H-11, H-3', H-4', H-5'), 7.16-7.12 (m, 4 H, H-4, H-10, H-2', H-6'), 2.62 (t, $J_{5,6} = 6.6$, 4 H, H-6, H-8), 2.43 (t, $J_{5,6} = 6.6$, 4 H, H-5, H-9); ^{13}C NMR δ 143.9, 138.7, 138.3, 138.1, 137.3, 134.1, 131.6, 130.7, 130.0, 128.7, 127.9, 120.2, 120.1, 104.0, 28.7, 27.5; MS (EI, 70 eV), m/z (relative intensity) 539 (4), 541 (7), 543 (3); MS (FAB, Xe) exact mass calcd for $C_{29}H_{20}Br_2N$ m/z 541.998 75, found 541.992 80.

2,12-Bis(2,7-dimethoxy-9-acridinyl)-7-phenyl-5,6,8,9-tetrahydrobenz[*a*,*j*]anthracene 14-Cyanide (50). To a solution of 105 mg (0.19 mmol) of **52** in 40 mL of THF at -90 °C was added 0.42 mL (0.394 mmol) of *n*-butyllithium in hexane. The resulting solution was stirred for 0.5 h and was transferred via canula to a solution of 199 mg (0.58 mmol) of **52** in 10 mL of THF at -78 °C. The mixture was stirred for 3 h and was quenched with a saturated aqueous solution of ammonium chloride at -78 °C. The mixture was extracted with CH_2Cl_2 and dried over Na_2SO_4, and the solvent was removed at reduced pressure. The residue was purified by flash chromatography (1:4 EtOAc-CH_2Cl_2) to afford 112 mg (65%) of **50** as a light green powder: ^1H NMR δ 8.25 (d, $J_{1,3} = 1.1$, 2 H, H-1, H-13), 8.06 (d, $J_{3',4'} = 9.4$, 4 H, H-4', H-5'), 7.58-7.51 (m, 3 H, H-3'', H-4'', H-5''), 7.48 (d, $J_{3,4} = 7.5$, 2 H, H-3, H-11), 7.36-7.27 (m, 8 H, H-4, H-10, H-3', H-6', H-2'', H-6''), 6.78 (d, $J_{1',3'} = 2.7$, 4 H, H-1', H-8'), 2.86 (t, $J_{5,6} = 6.5$, 4 H, H-6, H-8), 2.61 (t, $J_{5,6} = 6.5$, 4 H, H-5, H-9); MS (FAB, Xe), m/z 858 (M + H), exact mass calcd for $C_{59}H_{43}N_3O_4$ m/z 858.333 16, found 858.331 50.

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Complexation of Nucleotide Bases by Molecular Tweezers with Active Site Carboxylic Acids: Effects of Microenvironment

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Abstract: In chloroform-*d* molecular tweezer **1** forms a 1:1 complex (Job plot) with 9-propyladenine (**4**). Changes in the UV-visible absorption spectrum of **1** upon addition of **4** and the changes **1** and **4** induce in each other's ^1H NMR spectrum are consistent with those of a complex comprised of hydrogen bonds and π-stacking interactions. The microenvironment around the carboxylic acid group in **1** markedly alters its complexation behavior relative to a simple carboxylic acid such as butyric acid (Lancelot, G. *J. Am. Chem. Soc.* **1977**, *99*, 7037-7042). The association constants for the **1-4** and butyric acid-**5** complexes are 25 000 M^{-1} (298 K) and 160 M^{-1} (303 K), respectively. Butyric acid prefers a type 1 hydrogen bonding pattern while **1** adopts a type 7 pattern. The nucleotide base selectivities follow the order G > C > A > U for butyric acid and A > G $\gg$ C > U for **1**. The presence of protic solvents markedly decreases the strength of the complex between **1** and **4**. Two analogues of **1** have also been studied, molecular tweezer **2** and **3**. Both lack the dimethylamino substituent found in **1**, while **3** has a spacer unit that is fully oxidized. The association constants for the **2-4** and **3-4** complexes are 14 000 and 120 000 M^{-1}, respectively.

Noncovalent interactions are of fundamental importance to all biological processes. This has inspired the study of host-guest chemistry whose goals include the development of artificial enzymes and the understanding of complexation phenomena.[1] While the small, usually nonpeptidic, organic hosts bear little resemblance to natural "receptors" such as enzymes and antibodies, they have several distinct advantages. They provide a more manageable degree of structural complexity. Furthermore, hosts with different functional group orientations, varying degrees of flexibility, and modified electronic properties can be synthesized and compared. Additionally, synthetic receptors are often soluble in several solvents, and because these molecules are constructed of covalent bonds they maintain their structural integrity in a wide range of media. Well-chosen changes in structure and solvent provide invaluable insights into molecular recognition phenomena.

Our interest in this area has been with receptors, called "molecular tweezers",[2] which complex aromatic guests through π-sandwiching[3] and, more recently, through π-sandwiching combined with hydrogen bonding.[4,5] These latter receptors were inspired by two quite different areas of research. The first involves the study of bichromophoric molecules that can bind to DNA by bis-intercalation.[6] The second area is the study of protein-DNA recognition.[7] It was proposed several years ago that amino acid side chains might recognize DNA bases and base-pairs through π-stacking and hydrogen-bonding interactions. The most selective

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