Cyclobisintercaland Macrocycles: Synthesis and Physicochemical Properties of Macrocyclic Polyamines Containing Two Crescent-Shaped Dibenzophenanthroline Subunits

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A general access to isomeric dibenzo[*b,j*]phenanthrolinedicarboxaldehydes is described. These pentacyclic planar quinacridine compounds exhibit crescent-shaped forms that fulfill the geometrical requirements of providing broad overlap of nucleobase pairs or triplets. The dialdehyde derivatives have been condensed with various polyamines to give macrocyclic dimeric structures, cyclobisintercalands, of variable size, charge, and shape. The related water-soluble monomeric quinacridines were prepared from the dialdehydes by grafting ammonium groups. The physicochemical properties of the monomeric quinacridines and of the macrocyclic bis-quinacridines have been investigated by spectroscopic methods (UV−vis, fluorescence, NMR). The results show that some of these macrocyclic compounds could exist as semiclosed conformers suitable to accommodate a pair of nucleotides.

Introduction

Noncovalent interactions between aromatic systems contribute significantly to the stabilization of secondary and tertiary structures of biological macromolecules and thus play a crucial role in many physiological processes both on a structural and functional point of view. *Inter alia* the aromatic stacking is one of the basis components of the canonical B-helix structure of the DNA along with the Watson−Crick base pairing.[1] This interaction is also directly involved in the anchoring of DNA duplexes by many natural cytostatic agents such as antibiotics and antitumor drugs and by numerous synthetic DNA binders.[2] All these compounds display a common structural feature, i.e., coplanar hydrophobic moieties able to overlap with the heterocyclic nucleobases. Their binding to the targeted helical DNA segment may lead to serious local distortions from the normal geometry; one of the most striking example is the binding of quinoxaline antibiotics which induces Hoogsteen base pairing instead of the Watson−Crick hydrogen bonding.[2a] Interestingly π-stacking appears to govern both the stability of the double-helix structure and its conformational variability.

Despite the large number of studies aimed at clarifying the exact nature of the interaction between aromatic groups, there is still much debate on this subject.[3,4] However, some electronic and structural effects of interest for molecular design are well established. Among them, extension of the aromatic surface area is commonly admitted to appreciably enhance the attraction between π-systems in aqueous medium. This effect, which is more likely to be due to increased solvophobic effects, has been frequently documented by experiments based on simple chemical modifications.[5]

In the context of supramolecular chemistry and molecular recognition studies, this structural effect has been widely applied for the design of artificial receptors able to bind a variety of substrates, in particular nucleotides.[6] To this end, in the course of our studies on anion recognition, we developed the cyclobisintercaland type of receptors[7] (built on two intercalative units linked by polyammonium chains), tailored to trap aromatic substrates bearing anionic groups by the simultaneous interplay between electrostatic attraction and "sandwiching" of the guest by π-stacking. Indeed the members of the series possessing naphthalene and acridine units bridged by diethylenetriamine moieties displayed remarkably high affinities for nucleotides in water ($10^6\ M^{-1} < K_{assoc} < 10^8\ M^{-1}$).[7b,c] Moreover considerable enhancements of the stability of the complexes have been observed when the size of the intercalative unit was increased, pointing to the importance of the π-stacking interaction in the binding.[7c] Furthermore a major at-

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tractive property of these receptors is their pronounced solubility in water near the physiological pH (up to 10^{-2} M at pH 6−7), by contrast with most macrocyclic aromatic systems which frequently exhibit poor solubility in aqueous media.

Up to now, most of the molecular receptors have been built to trap a single nucleotide (1/1 complexes), but the recognition of nucleobase pairs by systems able to bind two nucleotides through the formation of 2/1 stoichiometric associations has not been achieved, despite its fundamental and applied interest. However, several model compounds bearing a nucleobase in their framework perform the recognition of the complementary base[8] and more recently a new conceptual approach which rests on the insertion of a molecular wedge between two nucleobases (matched or not) by formation of two hydrogen-bonding arrays has been proposed.[9] In addition to the dominant Watson−Crick type pairing mode, a number of base associations involving other hydrogen-bonding patterns (Hoogsteen, reverse Hoogsteen, homo-base pairing)[10] also play a significant role in the formation of ordered oligonucleotide structures such as duplexes,[11a−c] triplexes,[11d,e] and tetraplexes.[11f−h] Due to their biological relevance, the structural and functional aspects of these pairings are the focus of intensive investigations, further stimulated by potential therapeutic applications.[11−13]

Our approach to the binding of a base pair rests on the search for molecular units exhibiting extended aromatic surface areas able to stabilize canonical and nonusual nucleobase associations through increased π-interactions. Simple geometric considerations and literature examination[10−16] led us to design an angular pentacyclic molecular pattern which possesses a suitable shape and size for overlapping with either Watson−Crick or Hoogsteen matched base pairs, or base triplets (Figure 1). Recently planar aromatic compounds that adopt the crescent-shaped geometry, such as coralyne[14] and benzo[*e*]pyridoindole derivatives (BePIs),[15] have been shown to induce significant stabilization of triple helices as well as reorganization of a Watson−Crick duplex into a Hoogsteen duplex.[15b] These effects arise in part from enhanced hydrophobic effects and aromatic stacking interactions.

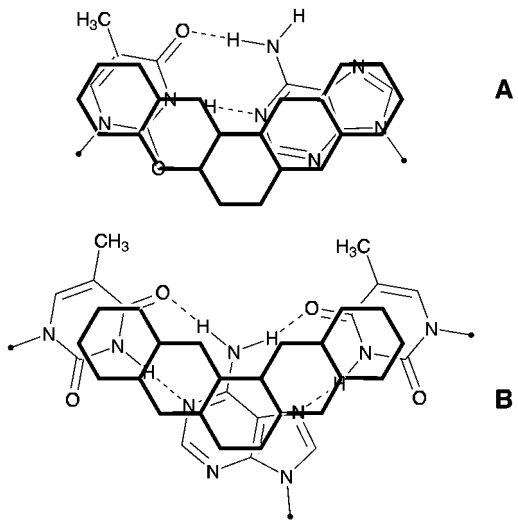

Figure 1. (A) Overlap of G-C base pair held in the Watson−Crick mode by a planar crescent-shaped pentacyclic unit; (B) overlap of a T-A×T base triplet held in the Watson−Crick × Hoogsteen mode by a planar crescent-shaped pentacyclic unit.

Among the fused aromatic compounds, and in accordance with the geometric requirements shown in Figure 1, the dibenzo[*b*,*j*]phenanthrolines, i.e., quinacridines[17] appeared to be good candidates. We report here the preparation of a series of these heterocyclic compounds through a versatile and general procedure and their use as monomeric synthons for building cyclobisintercaland-type receptors of large size. The physicochemical properties of the monomeric dibenzophenanthrolines and of the corresponding dimeric macrocycles have been investigated by spectroscopic methods (RMN, UV−vis absorption, and fluorescence spectroscopies). The comparative analysis of the results suggests that these macrocyclic molecules could provide suitable hydrophobic microenvironments for the complexation of pairs of nucleotides.

Synthesis

The quinacridines are the parent aromatic compounds of the quinacridones,[18] which received attention 30 years ago owing to their remarkable crystalline polymorphism and dyestuff properties, while more recently their use as organic semiconductors has renewed the interest.[18c] However there are only very few examples in the literature of those fully aromatic planar pentacyclic systems that can exist in linear or angular form.[19] The most recent approach to some angular quinacridines was proposed in 1985[19f] but is limited to the introduction of substituents at the *para* positions to the nitrogen atoms (see Chart 1).

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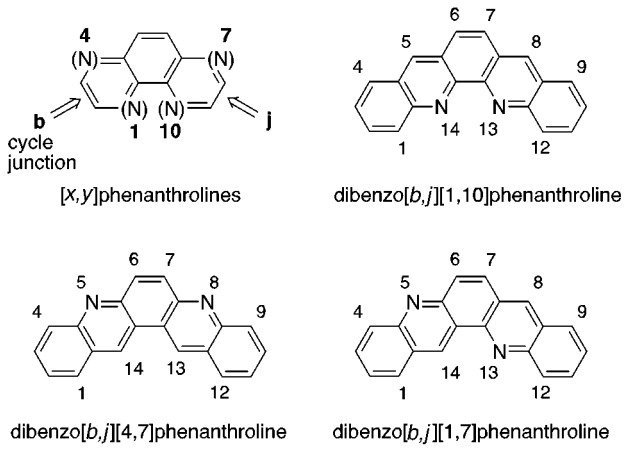
Chart 1[a]



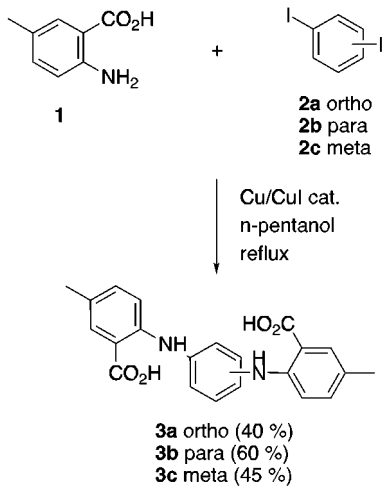
[a] Nomenclature and numbering system for [*x*,*y*]-phenanthroline and dibenzo[*b*,*j*][*x*,*y*]phenanthroline rings (according to CAS, the phenanthroline nomenclature is used for the position of the two ring N in the dibenzophenanthroline skeleton).

In our previous work on cyclobisintercaland receptors,[7] symmetrical aromatic dialdehydes have proven to be suitable intermediates for the preparation of both water soluble monomers by grafting hydrophilic polyammonium chains and dimeric macrocyclic systems through condensation with a diamine. These key compounds are generated by direct oxidation of the dimethyl precursors. In the case of quinacridines the prerequisite dimethyl derivatives bearing the methyl groups on the external benzo rings were not accessible by the existing methods. Therefore a methodology has been developed that offers the possibility of introducing methyl substituents at suitable positions but also of varying the relative places of the two ring nitrogens.

Preparation of Quinacridinedicarboxaldehydes. The quinacridines may be considered as condensed acridines or as dibenzophenanthrolines, and thus the synthetic routes to these structures are related to both acridine and phenanthroline chemistry. A particularly attractive approach would involve the Friedländer condensation[20] of cyclohexanediones with *o*-aminobenzaldehydes. Unfortunately, reacting 2-amino-5-methylbenzaldehyde with 1,2-cyclohexanedione provided the desired 6,7-dihydrodibenzophenanthroline in poor yield, likely due to self-condensation of the starting aminoaldehyde; furthermore this intermediate appeared particularly resistant to oxidation by classical reagents.[21]

These unsuccessful attempts prompted us to devise another strategy transposed from the synthesis of substituted acridine rings.[7c] It is based on the double condensation of diiodobenzene derivatives **2** with 5-methylanthranilic acid (**1**) (Ullmann−Goldberg condensation) (Scheme 1). Mixtures of mono- and disubstituted products were systematically obtained, but the compounds were easily separated by precipitation in hydroalcoholic media. However mention should be made of the requirement for iodo derivatives to reach acceptable yields (40−60%) of the disubstituted compounds, especially in the less reactive ortho series where the use of 1,2-dibromobenzene leads to the exclusive formation of the monocondensed product. Modifications of the reaction conditions such as variation of the solvent or activation of the copper catalyst[22] failed to improve the yield of the double condensation. The possibility of reacting the three (ortho, meta, para) isomers of diodobenzene is at the basis of the versatility of the method that allows the construction of a family of dibenzo[*b*,*j*]phenanthrolines with [1,10], [1,7] and [4,7] patterns.[19f]

Scheme 1



Two different synthetic pathways had to be used to obtain the three isomeric dimethylquinacridines **5a**−**c** (Schemes 2 and 3) due to the particular behavior of the ortho-condensed product (**3a**) compared to the para and meta isomers (**3b,c**). Treatment of compounds **3b** and **3c** with phosphorus oxychloride ($POCl_3$)[17] provided dichloroquinacridines **4b**,**c** (Scheme 2) in moderate yields as compared to those observed with single acridine derivatives.[7c] In principle the cyclization could lead to an angular or a linear structure, but no trace of the latter was detected in both cases. The mechanism of the ring closure proceeds through the formation of a mixed anhydride followed by intramolecular acylation and elimination of hydrochloric acid.[17] The exclusive formation of an angular structure could be explained by the intervention of the half-closed intermediate depicted in Scheme 4: in this hypothetical intermediate, double bonds would lie in fixed positions so that the only orientation for the second cyclization would be toward the angular form. A similar rationale can be applied to the meta isomer. The predominant formation of the angular isomer (>95%) has also been observed in the preparation of *p*-quinacridones.[18,19c]

Several attempts to induce the closure of *o*-dianthranilic acid **3a** by phosphorus oxychloride gave dark and complex mixtures. This led us to apply another cyclization method using concentrated sulfuric acid that converted **3a** to quinacridone (**4a**) (Scheme 3). Subsequent reduction by $LiAlH_4$ respectively (**4b**,**c** Scheme 3) or Na in refluxing pentanol (**4a**, Scheme 4) afforded in the three cases a mixture containing the dimethylquinacridine **5** along with hydrogenated derivatives. The fully aromatized compounds **5** were finally obtained in pure form by reoxidation under mild conditions ($FeCl_3$). Oxidation of the dimethyl intermediates **5** to the dialdehydes **6** was carried out in hot naphthalene with controlled amounts

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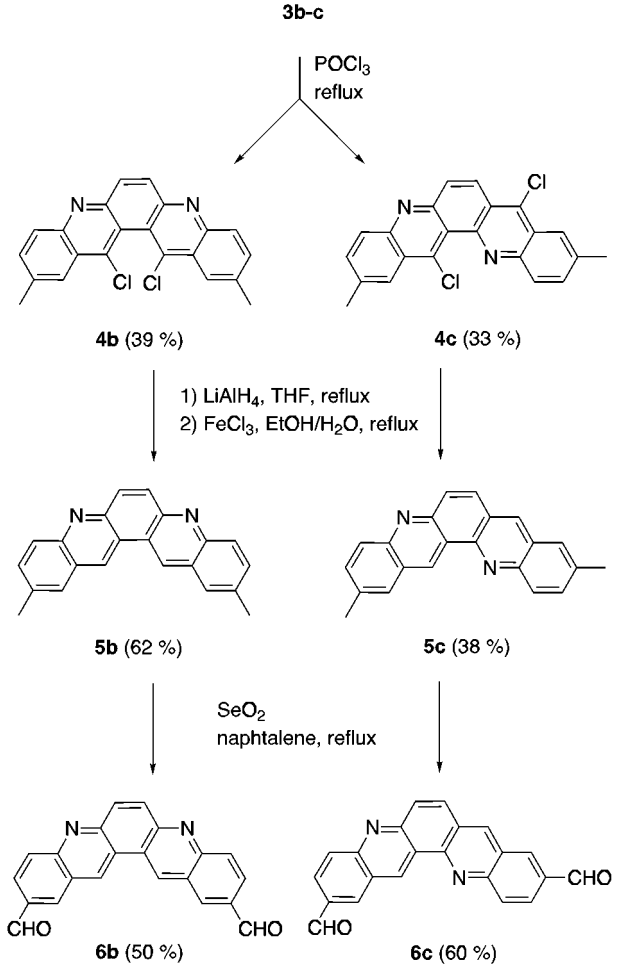
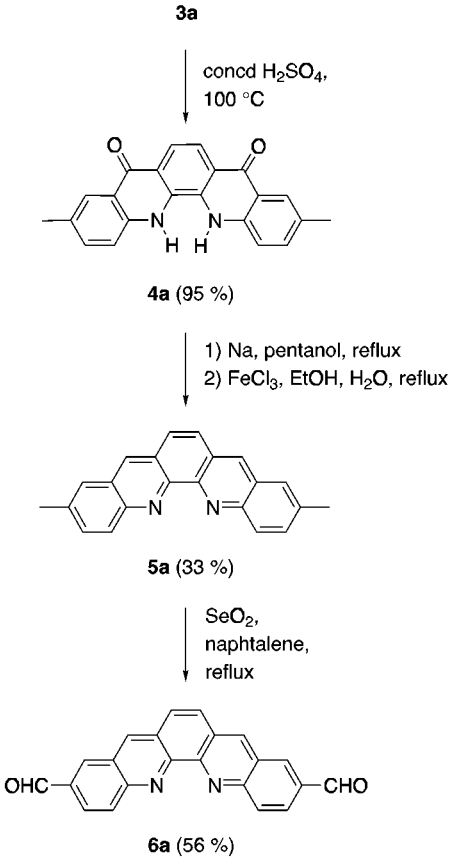
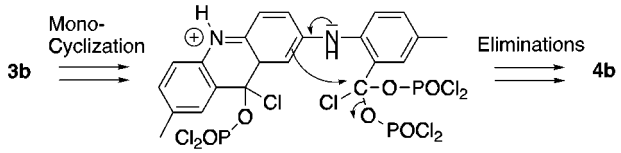
Scheme 2



Scheme 3



Scheme 4. Proposed Intermediate for the Formation of Crescent-Shaped Polycycles



of selenium dioxide; the use of naphthalene as solvent has been mentioned in an earlier report[7c] and afforded a considerable improvement in the oxidation of aromatic methyls as the reaction did not proceed at all in the usual solvents such as dioxane.[23]

Preparation of Macrocyclic Bisquinacridines. The macrocyclic structures were readily obtained via the efficient 2 + 2 condensation between dialdehydes and diamines. Indeed, and despite the low solubility of the aromatic dialdehydes used in earlier work,[7] macrocyclization generally occurred in good yields under moderate dilution conditions ([dialdehyde] = 10^{-3} M). In the present case only compounds **6a** and **6b** appeared suitable to be engaged in cyclization experiments for symmetry reasons: the reaction proceeds unambiguously with dialdehydes **6a** and **6b** both of C_{2v} symmetry; on the contrary the unsymmetrical dialdehyde **6c** offers two modes for cyclization which would give mixtures of isomeric macrocycles.

1. Condensation with Diethylenetriamine. Using diethylenetriamine groups as bridging moieties allows the building of cyclobisintercalands of suitable size and flexibility to accommodate aromatic substrates. Indeed evidence that such receptors might adopt a semiclosed conformation with aromatic units in parallel plans creating a cavity where the anionic aromatic guest is inserted has been recently provided by X-rays analysis of a complex between a bisnaphthalene cyclointercaland and the terephthalate dianion.[24] Furthermore the pK_a values of the three amino groups of diethylenetriamine (3.5, 8.0, 9.0) are compatible with the presence of a unique or largely predominant tetracationic form of the receptor at pH 6. Thus, condensation of **6a** and **6b** respectively with diethylenetriamine afforded after reduction with $NaBH_4$ the macrocycles **7a** and **7b** in reasonable yields (Scheme 5). Protonation by aqueous HCl gave the water-soluble forms **7a,HCl** and **7b,HCl** which are schematically represented by their tetraprotonated forms predominant at pH 6 (Figure 2).

2. Use of Other Polyamines. To investigate the versatility of the method and to obtain analoguous macrocycles of larger size, different overall charge, and conformation, various polyamines were reacted with dialdehyde **6a**. The oxygenated analogue of diethylenetriamine, [2,2′-oxybis(ethylamine)], provided macrocycle **8** which displays physicochemical properties very similar to those of **7a** (Scheme 5). Attempts to use longer polyamines met with some difficulties. Indeed complex mixtures of products were generated upon reaction of **6a** with dipropylenetriamine whereas cyclization with its analogue methylated on the central nitrogen atom pro-

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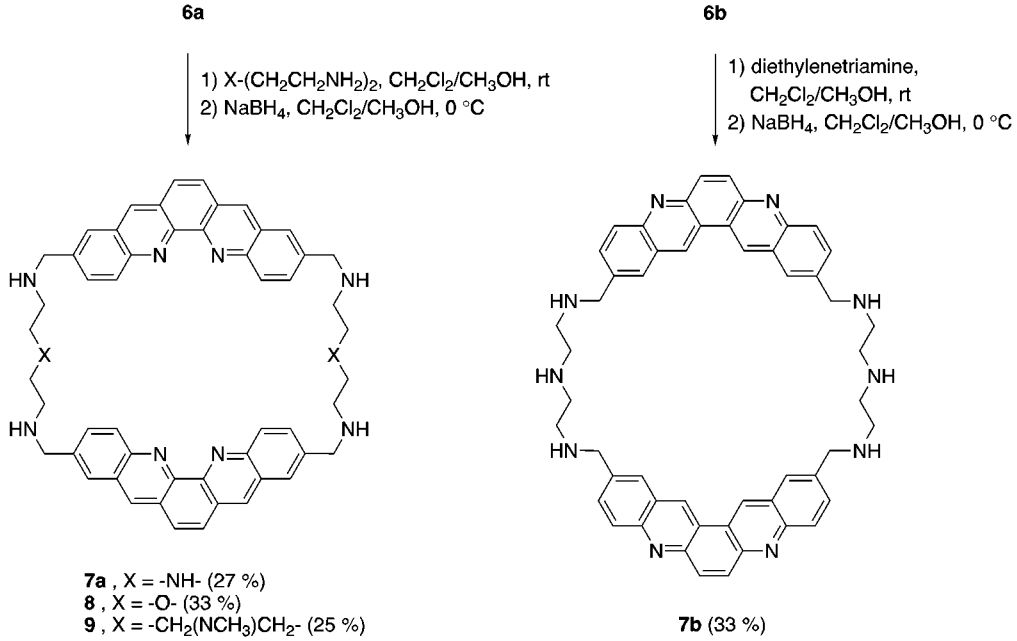
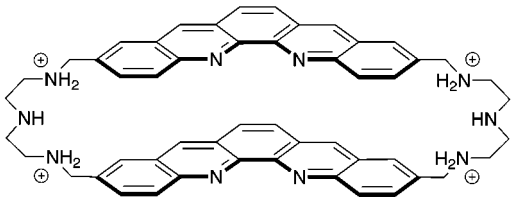
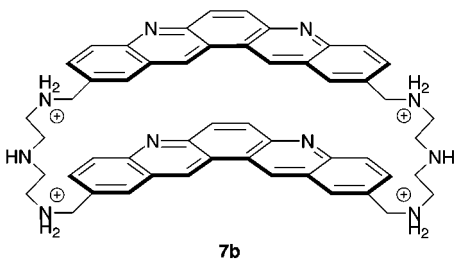
Scheme 5



duced macrocycle **9** in reasonable yield and purity. This dramatic difference in reactivity between the two polyamines might be interpreted in terms of formation of cyclic aminals that prevents macrocyclization from occurring normally (Scheme 6), the *N*-methylated system deprived from the hydrogen atom on the central amine being unable to produce such intermediates. The formation of aminal derivatives was demonstrated by reacting **6a** with propylenediamine which gave the corresponding 6-membered ring diaminal (**10**, Scheme 6) that was characterized by ^{1}H NMR. Such isomeric forms of macrocyclic tetraimines have been described[25] and seem to occur also with ethylene or propylenepolyamines according to a 5(or 6)-endo-trig attack.[26] However these examples are related to macrocyclic systems of small size containing subunits such as benzene or pyridine. In our case the formation of 5-membered ring aminals with diethylenetriamine has never been observed and might be disfavored by the steric hindrance of the large aromatic moieties. On the other hand, the formation of aminals from propylenepolyamines which might be favored by the higher flexibility of the chains and the stability of the 6-membered ring hinders the macrocyclization step.



7a



7b

Figure 2. Schematic representation of macrocycles **7a** and **7b** in their tetraprotonated forms at pH 6.

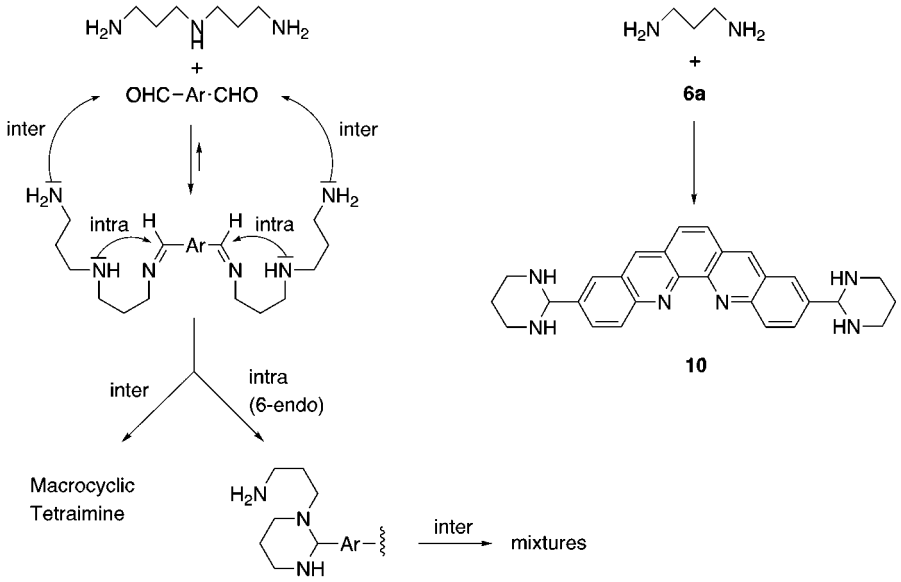
Preparation of Water-Soluble Monomeric Quinacridines. As mentioned in the introduction, derivatives of the parent quinacridine unit are of much interest in investigating the π-stacking effect with various biological targets. Furthermore they are also required as models to interpret properly the spectroscopic properties of the dimeric macrocyclic assemblies. So far, monomeric quinacridinediimines have been synthesized by using a large excess of *n*-propylamine (or *N*,*N*-dimethylpropylenediamine) for condensation to dialdehydes **6** (Scheme 7) and then have been converted to the corresponding protonated quinacridines (**11,HCl**) and (**12,HCl**) by the usual procedure. Such compounds constituted of one monomeric unit bearing positive charges mimick half a macrocycle. Furthermore the structural variations exhibited from one series to another could strongly influence intrinsic properties of the aromatic nucleus such as polarizability and electronic density repartition and might have fundamental consequences on their stabilizing effect toward double- or triple-helix structures as has been demonstrated recently.[16b]

Spectroscopic and Physicochemical Properties of Monomeric Quinacridines and Macrocyclic Bisquinacridines. 1. Dimethylquinacridines: Angular versus Linear Structure. The structure of **5a** is obviously angular according to its synthetic pathway whereas the bent form of the monomeric quinacridines **5b,c** is supported by NMR and UV−vis spectroscopic analysis. Considering that the absorption spectra of aromatic heterocyclic compounds closely resemble those

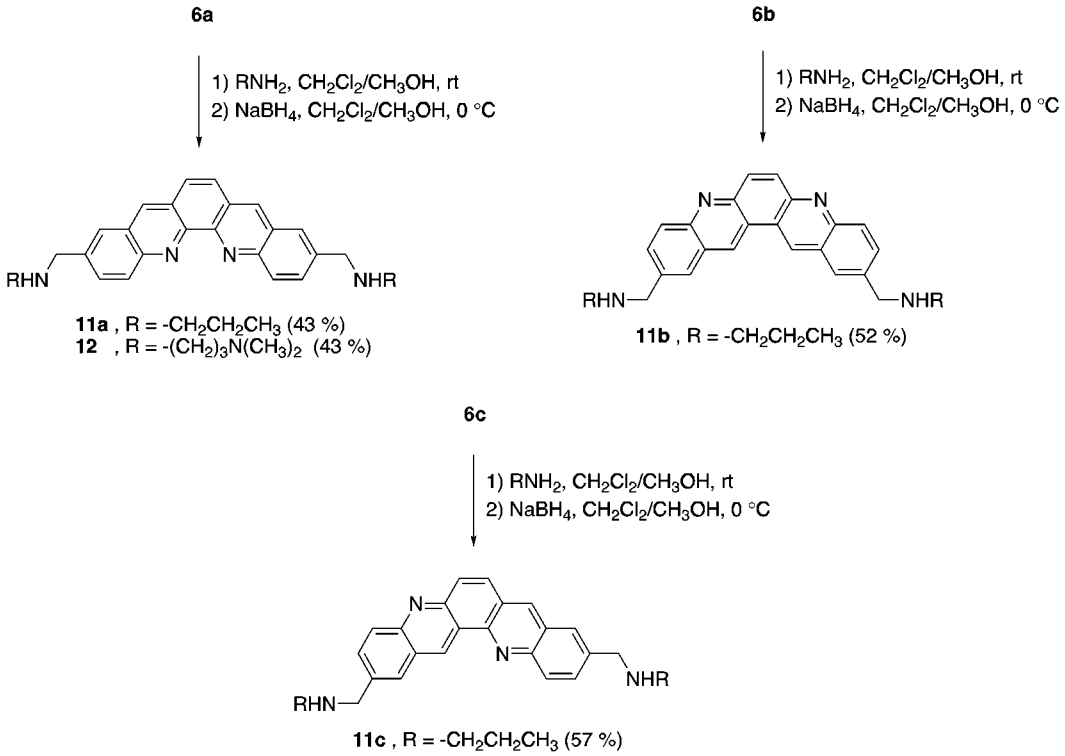
(25) (a) Adams, H.; Bailey, N. A.; Fenton, D. E.; Good, R. J.; Moody, R.; Rodriguez de Barbarin, C. O. *J. Chem. Soc., Dalton Trans.* **1987**, 207. (b) Adams, H.; Bailey, N. A.; Fenton, D. E.; Hempstead, P. D.; Westwood, G. P. *J. Inclusion. Phenom. Mol. Recognit. Chem.* **1991**, *11*, 63. (c) Rockcliffe, D. A.; Martell, A. E.; Reibenspies, J. H. *J. Chem. Soc., Dalton Trans.* **1996**, 167. (d) Adams, H.; Bailey, N. A.; Bertrand, P.; Collinson, S. R.; Fenton, D. E.; Kitchen, S. J. *J. Chem. Soc., Dalton Trans.* **1996**, 1181.

(26) Baldwin J. E., *J. Chem. Soc., Chem. Commun.* **1976**, 734.

Scheme 6. Proposed Formation of 6-Membered Ring Aminals



Scheme 7



of their carbocyclic analogues, a linear quinacridine should be strongly colored like pentacene, a linearly fused pentacyclic molecule which displays a deep blue color.[19c] On the contrary, compounds **5b** and **5c** both exhibit a pale yellow color, their absorption spectra presenting three main bands in the near-UV region with peaks at 314, 332, and 361 nm (**5b**) and 315, 329, and 350 nm (**5c**), similar to that of **5a** (314, 326, and 351 nm).

The ^{1}H NMR spectrum of **5b** shows that the H_{13} and H_{14} protons in the para positions to the nitrogen atoms are equivalent, giving a resonance at 9.35 ppm; this does not allow one to discriminate between the linear or the angular structure of **5b** since the molecules are symmetrical in both cases. However the large downfield shift of the signal indicates a strong interaction between H_{13} and H_{14} that can only arise from the angular form. Finally in the case of **5c**, the observation of two distinct peaks (8.29 and 9.79 ppm) for the protons para to the heteroatoms (H_8 and H_{14}) are in agreement with an unsymmetrical molecule corresponding to a bent aromatic skeleton (H_8 and H_{14} would indeed be equivalent in the linear form of C_{2v} symmetry). Therefore these data demonstrate unambiguously the angular structure of quinacridines **5b** and **5c**.

2. Determination of the pK_a's of Monomeric Compounds 11. Knowledge of the pK_a's of the nitrogen sites of the water-soluble monomeric quinacridines is necessary in order to gain information about the proton distribution at different pH and also to compare it with that of the macrocyclic dimers. To this end we studied the absorption and fluorescence properties of compounds **11** in aqueous solution at various pH.

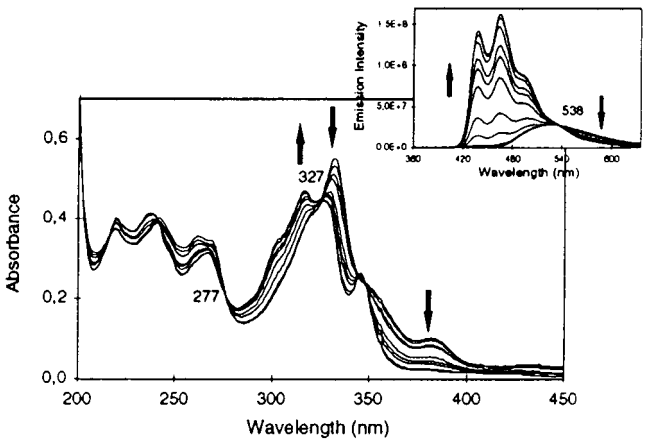


Figure 3. Absorption and (inset) fluorescence spectra (λ_{exc} = 324 nm) of **11a** 1.0 × 10^{-5} M in water (10 mM NaCl) with gradual enhancement of pH from 1.2 to 5.0.

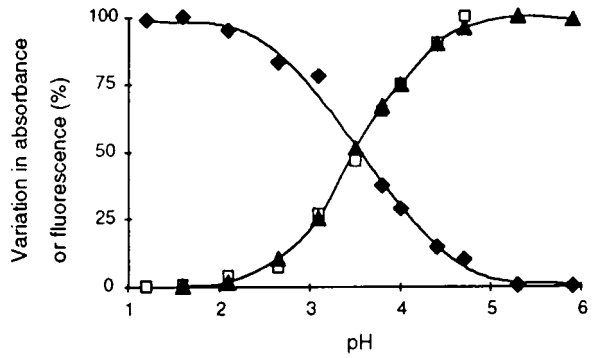


Figure 4. Normalized changes in absorbance of **11a** at 382 (◆) and 320 (□) nm and in fluorescence intensity at 437 nm (▲) as a function of pH.

Strong changes over the entire spectrum of **11a** are observed when the pH is increased from 1.0 to 5.0 (Figure 3): the progressive blue shift of the low-energy band (λ_{max} 332 nm) assigned to $\pi-\pi^*$ transitions is observed as well as the decrease until complete disappearance of the weak band lying near the visible (λ_{max} 382 nm), which is highly characteristic of the phenanthrolinium ion.[27] These variations are accompanied by the remaining of two isosbestic points (277 and 327 nm). On the basis of phenanthrolines' photophysical properties,[27] deprotonation at the ring nitrogen atoms is responsible for these spectral features. Likewise, in the same pH range, the emission fluorescence spectra (inset, Figure 3) show the disappearance of a broad band centered at 525 nm assigned to the protonated form of the dibenzophenanthroline,[27b,c] and the concomitant appearance of a well-structured band with three vibronic shoulders (437, 464, and 496 nm) corresponding to the neutral form of the aromatic nucleus. An isoemissive point is observed at 538 nm.

The variations of intensities of both absorption and fluorescence of **11a** at various wavelengths are represented as a function of pH (Figure 4) and are consistent with the occurrence of one equilibrium process corresponding to the deprotonation of a nitrogen atom of the quinacridine ring. There is no evidence for another protonation process in the pH range examined, in agreement with the low pK_a value of the first N atom in the 1,10-phenanthroline (pK_a = −1.4).[27e] The meta isomer **11c** exhibits a similar qualitative behavior to that of the ortho compound (data not shown).

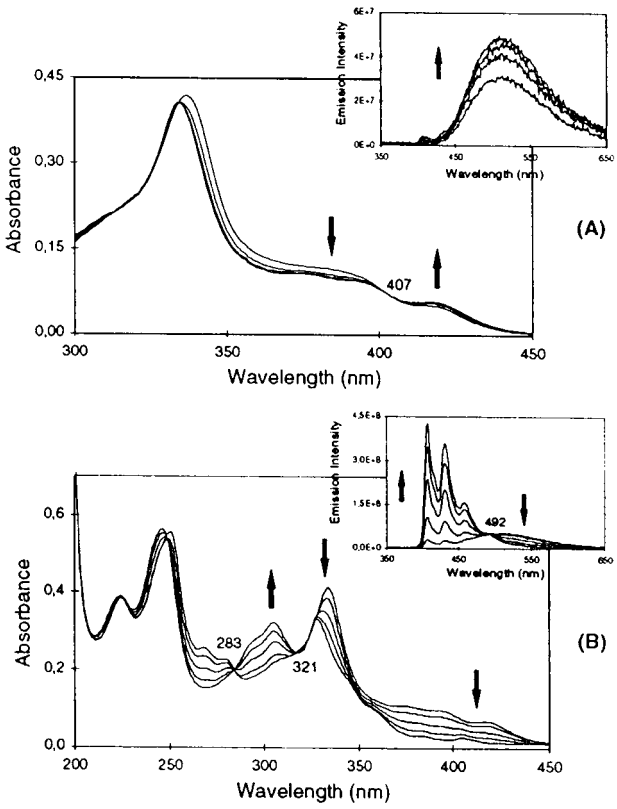


Figure 5. Absorption and (inset) fluorescence spectra (λ_{exc} = 327 nm) of **11b** 1.0 × 10^{-5} M in water (10 mM NaCl) with gradual enhancement of pH: (A) from 1.2 to 2.4; (B) from 2.4 to 5.0.

The same trends are observed for the *p*-quinacridine **11b** but with some discrepancies as compared with the ortho isomer: two distinct families of isosbestic points are detected from the absorption spectra, which are correlated to two pH ranges, i.e., 407 nm (pH 1.2−2.4; Figure 5A) and 283 and 321 nm (pH 2.4−5.0; Figure 5B). The fluorescence variations show also the existence of two pH regions: below pH 2.4 a significant albeit weak increase of the red-shifted emission is noted (Figure 5A, inset), whereas enhancement of pH up to 5.0 induces the disappearance of the red-shifted band and the appearance of the fine structure of the deprotonated quinacridine ring with an isoemissive point remaining at 492 nm (Figure 5B, inset). These data indicate that two equilibria involving three species take place below pH 5.0 which are attributable to the deprotonation of the two ring nitrogen atoms. This is in accordance with the higher pK_a value of the N1 nitrogen of the 4,7-phenanthroline (pK_a = 2.5),[27e] with respect to that of the [1,10]-phenanthroline. However the weak intensity of the spectral variations occurring below pH 2.4 is likely to reflect the small proportion of the fully protonated species thus accounting for the low basicity of N1 in the quinacridine ring.

(27) (a) Badger, G. M.; Walker, I. S. *J. Chem .Soc.* **1956**, 122. (b) Henry, M. S.; Hoffman, M. Z. *J. Phys. Chem.* **1979**, *83*, 618. (c) Armaroli, N.; De Cola, L.; Balzani., V.; Sauvage, J.-P.; Dietrich-Buchecker, C. O.; Kern, J.-M.; Sauvage, J.-P. *J. Chem. Soc., Faraday Trans.* **1992**, *88*, 553. (d) Dietrich-Buchecker, C. O.; Sauvage, J.-P; Armaroli, N.; Ceroni, P.; Balzani., V. *New J. Chem.* **1996**, *20*, 801. (e) Perkampus, H.-H.; Köhler, H. *Z. Elektrochem.* **1960**, *64*, 365.

Table 1. Ground State pK_a Values and Assignments for Monomeric Quinacridines

compound	pK_a[a] N1 (ring)	N2 (ring)	N3, N4 (sidearms)
11a (o)	*b*	3.5 (3.6)	8.9 (9.0)[e]
11b (p)	<1.0[c]	3.5 (3.3)	8.2 (8.5)[e]
11c (m)	*b*	3.3 (3.5)	8.5 (8.7)[e]
[1,10]phen (o)[d]	−1.4	4.9	
[4,7]phen (p)[d]	2.5	5.3	
[1,7]phen (m)[d]	0.75	4.3	

[a] pK_a values have been determined according to the equation pK_a = [pH − log(A_a − A/A − A_b)] where $A_{a,b}$ are the absorption (or fluorescence) intensity of the acid and basic forms and A the absorption (or fluorescence) intensity at an intermediate pH; the values in parentheses are obtained from fluorescence data. [b] Nonmeasurable in the pH range examined. [c] Estimated from the weak spectral variations, see text. [d] See ref 27e. [e] Average values, see text.

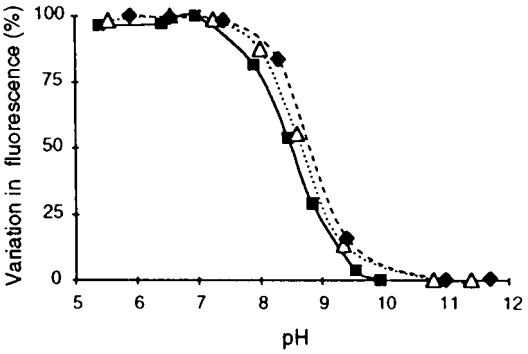


Figure 6. Normalized changes in fluorescence intensity of compounds **11a** at 437 nm (◆) (λ_{exc} = 324 nm); **11b** at 407 nm (Δ) (λ_{exc} = 327 nm), and **11c** at 425 nm (■) (λ_{exc} = 327 nm) in the pH range 7.0−10.0.

The pK_a's of monomers **11** determined from the spectral variations are listed in Table 1. The good correlation between the pK_a values determined from either the absorption or the emission spectral changes of **11** might be interpreted in terms of slow rates of the proton exchange in the excited state relative to the rate of the fluorescence decay.[27c] The comparison of the pK_a values of the nitrogen atoms of compounds **11** with those of the related phenanthrolines indicates a lower basicity of at least 1 pK_a unit for N2 nitrogen in the three series and for N1 nitrogen in the case of **11b**. The influence of the external benzo cycles on the pK_a is known to be weak, and such a difference might be essentially attributed to the electroattracting effect of the ammonium substituents.

Between pH 5.0 and 7.0 a leveling off of the spectral variations is recorded for the three isomeric quinacridines, whereas a spectacular drop in the emission intensities is recorded above pH 7.0 without modification of the spectral shapes (Figure 6). This strong decrease in fluorescence (90%) can be essentially attributed to a quenching effect via photoinduced electron transfer (PET) from the benzylic nitrogen lone pairs to the quinacridine ring excited state as is commonly observed for amino-substituted substituted aromatic compounds.[28] More moderate decrease in absorption (30−40%) of compounds **11** was observed at basic pH which may be explained in terms of a π-stacking effect between the neutral molecules formed by the deprotonation of the linkers. These changes are characteristic of the deprotonation of the amino side chains and lead to average pK_a values around 8.5−9 for the two N atoms (N3, N4) (Table 1).

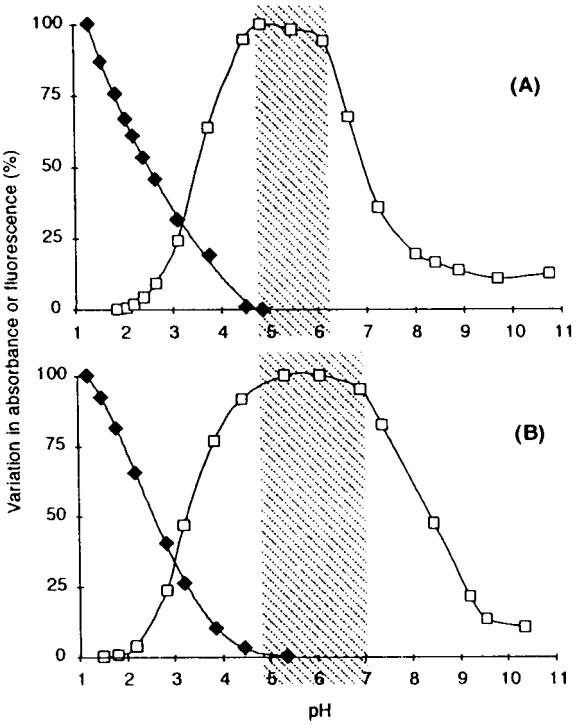


Figure 7. Normalized changes in absorbance and in fluorescence intensity (λ_{exc} = 324 nm) of macrocycles **7a** and **9** (1.0×10^{-5} M) as a function of pH: (A) compound **7a**, absorbance at 386 nm (◆) and fluorescence intensity at 443 nm (□); (B) compound **9**, absorbance at 383 nm (◆) and fluorescence intensity at 444 nm (□).

In summary the determination of the pK_a values and the leveling off of the spectral intensities between pH 5.0 and 7.0 demonstrate that compounds **11** exist in their side-chain diprotonated form in this pH range.

3. Determination of the pK_a of the Macrocyclic Bisquinacridines 7−9. The macrocyclic bisquinacridines contain multiple protonation sites which render difficult the determination of the pK_a's by spectroscopic methods. However the comparison of the spectroscopic properties of the macrocycles with those of the monomers, as a function of pH, with the help of our previous works on other cyclobisintercalands,[7] gives an indication of the dominant species in given pH domains.

Indeed the pH dependence of both absorption and fluorescence spectra of macrocycle **7a** appeared roughly similar to that of the corresponding monomer **11a** (Figure 7A). A pH region between 2.5 and 3.5 corresponding to the deprotonation of the ring nitrogen atoms is clearly determined from these variations. The central NH of diethylenetriamine is known to have a remarkably weak basicity (pK_a = 2.5−3.0), and only slight spectral variations are expected to result from its deprotonation. This phenomenon is thus supposed to be hidden by the strong changes induced by the deprotonation of the quinacridine nuclei. The drop in fluorescence intensities at basic pH induced by the deprotonation of the four benzylic nitrogens of **7a** takes place between pH 6.5 and 8.0, shifted by about 1 unit toward the acidic pH as compared to monomer **11a** (Figure 7A); this indicates the lower basicity of the benzylic NHs in the macrocyclic structure

(28) (a) De Silva, A. P.; De Silva, S. A. *J. Chem. Soc, Chem. Commun.* **1986**, 1709. (b) Czarnik, A. W. *Acc. Chem. Res.* **1994**, *27*, 302.

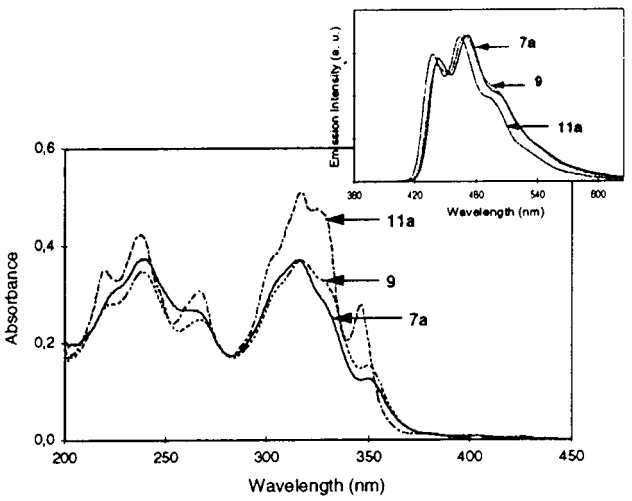


Figure 8. Absorption spectra and (inset) normalized emission spectra of **11a** (—•—) (8×10^{-6} M) (λ_{exc} = 316 nm) and macrocycles **7a** (—) (4×10^{-6} M) (λ_{exc} = 315 nm) and **9** (- - -) (4×10^{-6} M (λ_{exc} = 316 nm) in 1 mM cacodylate buffer (pH 6.0; 4 mM NaCl, 20 °C). For the sake of clarity the absorption and emission spectra of **8** which are similar to those of **7a** have been omitted.

as already observed for other cyclobisintercalands.[7b,c] Therefore, on the basis of these results we may expect that the tetraprotonated form of macrocycle **7a** will predominate in the pH range 5.0−6.0 which is confirmed by the plateau of the spectral intensities in this region (Figure 7A). The same pH domains are deduced from the titration curve of macrocycle **8** (data not shown).

In the case of macrocycle **9** a similar behavior is observed at acidic pH (2.5−3.5) with respect to **7a** (Figure 7B). On the other hand the deprotonation of the propylene linkers arises at a higher pH range (7.0−9.0), in agreement with the higher basicity of the free dipropylenetriamine (8 < pK_a's <10). One may conclude that **9** exists mainly as an hexaprotonated species between pH 5.0 and 7.0.

The pH dependence of the absorbance of macrocycle **7b** similarly indicates the predominance of the tetracationic form near neutrality (pH 6.0). The fluorescence changes are more difficult to interpret owing to the particular photoreactivity of compound **7b** (see next section).

4. Spectroscopic Data and Molecular Shapes. A comparative study of the spectroscopic properties of the monomers and the dimers has been carried out at pH 6.0 in order to evaluate the extent of intramolecular interactions between the two quinacridine units in the macrocyclic structures. Our purpose was to gain information on the conformation of the macrocyclic compounds in the pH domain where they exist in a unique form and where biological substrate binding experiments are to be conducted.

The absorption spectra of cyclic compounds **7**−**9** (Figures 8 and 9) display similar behavior as compared to their related monomers: the $\pi-\pi^*$ band centered at 315 nm is not shifted but the fine structure is affected and presents a strong hypochromism ($\epsilon_{dimer} \ll 2\epsilon_{monomer}$) (Table 2). These spectral features, which have been observed for other cyclobisintercalands,[7] are characteristic of bichromophoric systems;[29] they are attributed to weak intramolecular interactions between the quinacridine nuclei and reflect a more or less mutual parallel orientation of the two rings. On the other hand, the absence of a bathochromic shift shows that there is no significant electronic interaction between the aromatic units.[29c,d]

Examination of fluorescence data indicates some differences between the ortho and the para series. The emission spectra of macrocycles **7a**, **8**, and **9** display a shape similar to that of monomer **11a** (Figure 8, inset) with a slight red shift of the band already observed in related systems; by contrast they exhibit much lower quantum yields (Table 2). In accordance with the hypochromism of the absorption, these data support the existence of intramolecular interactions between the aromatic rings in the excited state and are thus representative of the dimeric macrocyclic structure. On the other hand, the emission spectrum of **7b** shows important distortions from the shape of monomeric compound **11b** (Figure 9, inset): the monomer emission has almost completely disappeared at the expense of a broad band strongly red-shifted (474 nm) which exhibits a very low quantum yield [Φ_F(**11b**)/Φ_F(**7b**) = 40] (Table 2). This band is ascribable to an excimer emission as excitation spectra scanned at various wavelengths are similar to the absorption spectrum of **7b**. The stabilization of an

Table 2. Molar Extinction Coefficients (ϵ) and Fluorescence Quantum Yields (Φ_F) of Monomers 11a−c and Macrocyclic Bisquinacridines 7−9 Measured in Cacodylate Buffer 1 mM (pH 6.0, 4 mM NaCl, 20 °C)

compound	(λ_{max}/nm)	ϵ/dm^3 mol^{-1} cm^{-1} ($\times 10^{-4}$)	Φ_F[a]
11a	316, 324	6.2, 5.8	0.10
11b	305, 327	4.2, 4.6	0.25
11c	312, 327	3.9, 5.0	0.12
7a	315, 327	9.1, 7.2	0.03
8	315, 327	8.5, 7.1	0.04
9	316, 327	8.9, 8.2	0.04
7b	299, 324	6.2, 4.6	0.006

[a] Determined using quinine disulfate in 0.05 N H_2SO_4 (Φ_F = 0.55) and anthracene in ethanol (Φ_F = 0.27) as references.

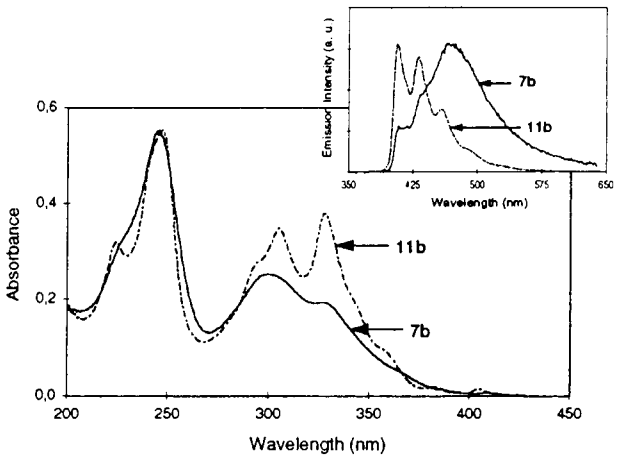
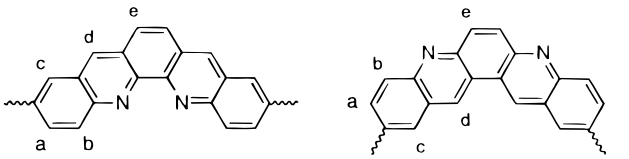


Figure 9. Absorption spectra and (inset) normalized emission fluorescence spectra of **11b** (— • —) (8×10^{-6} M) (λ_{exc} = 327 nm) and **7b** (—) (4×10^{-6} M) (λ_{exc} = 324 nm) in 1 mM cacodylate buffer (pH 6.0; 4 mM NaCl, 20 °C).

(29) (a) Castellan, A.; Desvergne, J.-P.; Bouas-Laurent, H. *Nouv. J. Chem.* **1979**, *3*, 231. (b) Hinschberger, J.; Desvergne, J.-P.; Bouas-Laurent, H.; Marsau, P. *J. Chem. Soc., Perkin Trans. 2* **1990**, 93. (c) Bouas-Laurent, H.; Castellan, A.; Daney, M.; Desvergne, J.-P.; Guinand, P.; Marsau, P. Riffaud, M. H. *J. Am. Chem. Soc.* **1986**, *108*, 315. (d) Misumi, S.; Otsubo, T. *Acc. Chem. Res.* **1978**, *11*, 251.

(30) De Schryver, F. C.; Collart, P.; Vandendriessche, J.; Goedeweeck, R.; Swinnen, A.; Van der Auweraer, M. *Acc. Chem. Res.* **1987**, *20*, 159.

Table 3. NMR Chemical Shifts (ppm) of Monomeric and Macrocyclic Dimeric Quinacridines at pH 6.0



	D_2O, pH 6.0[a]				
compd	Ha ($\Delta\delta$)[b]	Hb ($\Delta\delta$)	Hc ($\Delta\delta$)	Hd ($\Delta\delta$)	He ($\Delta\delta$)
11a	7.79	8.28	8.0	8.53	7.53
7a	7.59	7.96	7.37	7.12	6.62
	(−0.20)	(−0.32)	(−**0.63**)	(−**1.41**)	(−**0.91**)
8	7.45	7.98	7.79	7.43	7.09
	(−0.34)	(−0.30)	(−0.30)	(−**1.10**)	(−**0.44**)
9	7.52	8.05	7.40	8.24	7.40
	(−0.27)	(−0.23)	(−**0.60**)	(−0.29)	(−0.13)
11b	7.03	7.42	7.70	8.25	7.39
7b[c]					

[a] All solutions are 5 mM in D_2O, and the pH was adjusted to 6.0 with pyridine-d_5/CF_3COOD buffer. [b] $\Delta\delta$ = difference of chemical shifts between the macrocyclic dimer and the related monomer. [c] Nonmeasurable, see text.

excimer is strongly dependent on the overlap between the two chromophores.[30] This result suggests, therefore, that within the lifetime of the excited state, **7b** exists as a flattened conformation with at least partial stacking of the aromatic units. Moreover repeated scans on a sample of **7b** at pH 6.0 induce dramatic changes of the emission spectrum both in shape and intensity, revealing the occurrence of photoinduced processes. No significant variation of the fluorescence of **11b** is observed in the same conditions and the behavior of **7b** under irradiation may be attributed to photochemical reactivity resulting from the macrocyclic structure.

Additional information about interchromophoric interactions in the macrocycles is provided by ^1H NMR spectral data: a comparative study of the proton resonances for cyclic and monomeric quinacridines has been carried out in D_2O at pH 6.0 where the macrocycles and the monomers contain uncharged quinacridine moieties and at acidic pH (<1.0) where the compounds are fully protonated.

At pH 6.0, the aromatic proton resonances are strongly shifted upfield in the spectrum of **7a**, with respect to that of **11a**, especially for Hc−e (Table 3). Similarly strong shieldings are recorded for anologue **8** but the trend is much weaker for macrocycle **9**. Such results are coherent with the occurrence of some interaction between the two quinacridine units for the tetracationic forms of **7a** and **8**. These interactions are diminished evidently for **9** due to the higher length of the two amino linkers and to the hexaprotonation of the bridges which should enhance the interchromophoric distance. This behavior can be interpreted in terms of conformational flexibility of these dimeric molecules and allows for the prediction that a semiclosed conformation[24] would be favored in water near the neutrality for the macrocycles possessing diethylenetriamine linkers whereas a more open structure is likely to exist for the dimers bridged by propylenetriamine chains. However an increase in concentration of **7a** from 1 to 8 mM induces a continuous shielding of all aromatic protons, and the same concentration dependence is recorded for monomer **11a**. Though the magnitude of this effect is weak (−0.4 ppm at the maximum), it is nonetheless indicative of self-association of quinacridine **11a** and bisquinacridine **7a** at millimolar concentration

Table 4. NMR Chemical Shifts (ppm) of Monomeric and Dimeric Quinacridines at Acidic pH

	D_2O/TFA, pH 0.3[a]				
compd	Ha ($\Delta\delta$)[b]	Hb ($\Delta\delta$)	Hc ($\Delta\delta$)	Hd ($\Delta\delta$)	He ($\Delta\delta$)
11a	8.20	8.60	8.45	9.37	8.08
7a	7.91	8.21	8.15	8.95	7.75
	(−0.29)	(−0.39)	(−0.30)	(−0.42)	(−0.33)
11b	8.49	8.63	8.87	10.83	8.92
7b	8.40	8.44	8.72	10.60	8.77
	(−0.09)	(−0.19)	(−0.15)	(0.23)	(−0.15)

[a] All solutions are 3 mM in D_2O, and the pH was adjusted to 0.3 with CF_3COOD. [b] $\Delta\delta$ = difference of chemical shifts between the macrocyclic dimer and the related monomer.

which contributes to the shielding observed for the macrocycles. However, aggregation of quinacridines in water has never been detected at lower concentrations and it seems to be a phenomenon of marginal importance, in contrast to the high tendency of planar aromatic cations to aggregate in aqueous media.[16,31]

Analysis of macrocycle **7a** at more acidic pH in D_2O/DCl reveals some difficulties due to large broadening of the signals. This effect detectable from pH 3.5 is more pronounced as the pH decreases to give completely unresolved spectra around pH 1.0 while no precipitation was observed. On the contrary, a well-resolved spectrum of **7a** is recorded in a mixture of D_2O/CF_3COOD (pH = 0.3). Compounds **8** and **9** exhibit the same behavior, but this effect, which may be attributed to proton exchange processes, has never been observed with monomer **11a** or with other cyclobisintercalands. These results may indicate the formation of associations displaying proton exchange when the counteranion is chloride. Downfield shifts of all aromatic proton signals of **11a** and **7a** are observed at acidic pH as expected from protonation of the ring nitrogens. On the other hand the magnitudes of the $\Delta\delta$ values are considerably reduced as compared to those recorded at pH 6.0 (Table 4). This illustrates the decrease of the stacking effects between the quinacridine units both inter- and intramolecularly due to the repulsion between the supplementary positive charges on the side chains and on the aromatic moieties of the molecules.

Compound **7b** exhibits very poor solubility in D_2O whatever the pH. In this case significant intermolecular interactions between the macrocyclic molecules are thus likely to take place in addition to the strong intramolecular interactions indicated by the fluorescence properties. However, **7b** is soluble in the D_2O/CF_3COOD mixture which emphasizes the ability of this medium to prevent intermolecular associations. As already observed for **7a**, the spectrum of **7b** at acidic pH shows only modest shifts of the proton resonances of the macrocycle with respect to those of the monomer **11b** (Table 4); this confirmed the weak interactions between the two quinacridine units when the macrocycles are fully protonated.

The marked differences in physicochemical properties between the macrocycles containing *o*-quinacridine units (**7a** and **8**) and compound **7b** built from *p*-quinacridine moieties leads to a conclusion of the existence of different conformations with various interchromophoric distance. These structural differences could induce interesting binding preferences in particular toward biological species such as nucleotides and nucleic acids.

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Conclusion

The efficient synthesis of substituted angular quinacridines described here is applicable to the preparation of a large number of substituted compounds and requires only cheap and accessible starting materials. It should be possible to further expand the versatility of this approach to the synthesis of analogues bearing protonatable pendant chains in various positions by using functional dihalogenated derivatives or differently substituted aminobenzoic acids. The dichloro intermediates offer also an opportunity to build functionalized quinacridines. Finally the possibility of obtaining monocondensed anthranilic acids as major products in the Ullmann−Goldberg reaction when a dibromobenzene is used instead of a diiodo derivative makes this route attractive for the preparation of unsymmetrically substituted quinacridines.

The availability of isomeric quinacridines **11** will be very helpful for the systematic study of the steric and electronic requirements for the stabilization of ordered nucleic structures such as duplexes and triplexes through a putative intercalative mode. Furthermore the potential of compounds **11** to induce damages in DNA by means of photochemically triggered cleavages is currently under examination.

The cationic macrocyclic bisquinacridines containing cavities of large size and variable charge, shape, and hydrophobic character provide a tool for the recognition of nucleobases associated through various H-bonding patterns. By analogy to macrocyclic bisacridines that have been shown to discriminate between single-stranded and double-stranded DNA sequences,[32] these compounds could also selectively recognize nucleic acids secondary structures such as loops or bulges.

In addition the space delineated by the macrocyclic bisquinacridine framework could be appropriate for combining catalytic and binding functionalities; to this end one may consider complexing metal ions or attaching functional groups to the macrocycle for inducing a catalytic event on the bound substrate. Such perspectives represent attractive developments for the future.

Experimental Section

All commercially available chemicals were reagent grade and used without further purification. THF and dioxane were distilled over classical drying agents before use. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 200 spectrometer. Attributions were made by two-dimensional experiments (Cq = quaternary carbon). NMR spectra of D_2O solutions were monitored using DSS as the reference; solutions at pH = 6.0 have been obtained using a pyridine-d_5/CF_3CO_2D buffer (6.5×10^{-2} M). UV−vis experiments were monitored on a Beckmann DU 640 spectrophotometer. Fluorescence measurements were performed on a Spex Fluoromax spectrophotometer equipped with a Hamamatsu R928 photomultiplier (PM), using a thermostated cell holder; the data were corrected for the response of the PM. Melting points were determined on a Electrothermal 9100 apparatus. IR spectra were obtained on a Bruker Vector 22 FT-IR spectrometer. Mass spectrometry was performed at the Laboratoire de Chimie Structurale Organique et Biologique, Université Pierre et Marie Curie (Paris). The microanalyses were performed at the Service Régional de Microanalyse de l'Université Pierre et Marie Curie.

5,5′-Dimethyl-2,2′-(1,2-phenylenediamino)bisbenzoic Acid (3a). A mixture of 1,2-diiodobenzene (8.73 g, 26.5 mmol), 2-amino-5-methylbenzoic acid (10.00 g, 66.2 mmol), copper bronze (420 mg, 6.6 mmol), CuI (1.01 g, 5.3 mmol), K_2CO_3 (9.14 g, 66.2 mmol), and *n*-pentanol (100 mL) was stirred under reflux for 24 h. After the solvent was removed in vacuo, methanol was added and the solution was filtered through Celite. Methanol was evaporated by 75%, and an equal volume of water was added. The solution was treated dropwise with concentrated hydrochloric acid until a precipitate appeared. The dark precipitate was filtered and stirred vigorously in ethyl ether (300 mL); the suspension was filtered and the precipitate again stirred in ether (the operation was repeated twice). Combined ether fractions were distilled off until a slightly colored precipitate appeared. A yellow solid was then obtained after filtration. The crude product was recrystallized from ethanol and water yielding 4.0 g (40%) of a pale yellow powder: mp 220 °C; ^{1}H NMR (DMSO-d_6) δ 2.19 (s, 6 H), 6.93 (d, J = 8.5 Hz, 2 H), 7.08 (m, 2 H), 7.15 (dd, J = 8.5 and 2 Hz, 2 H), 7.38 (m, 2 H), 7.65 (d, J = 2 Hz, 2 H), 9.40 (s, 2 H), 12.8 (br s, 2 H) ppm; IR (Nujol mull) 3344, 3328, 3300−3000, 1660 cm^{-1}. Anal. Calcd for $C_{22}H_{20}N_2O_4$: C, 70.20; H, 5.36; N, 7.44. Found: C, 70.05; H, 5.36; N, 7.38.

3b and **3c** were obtained in the same manner from 1,4-diiodobenzene and 1,3-diiodobenzene, respectively.

5,5′-Dimethyl-2,2′-(1,4-phenylenediamino)bisbenzoic acid (3b): pale yellow powder (yield 60%); decomposition ≥ 275 °C; ^{1}H NMR (DMSO-d_6) δ 2.20 (s, 6 H), 7.08 (d, J = 8.5 Hz, 2 H), 7.17 (2 s, 4 H), 7.20 (dd, J = 8.5 and 1.5 Hz, 2 H), 7.68 (d, J = 1.2 Hz, 2 H) ppm; ^{13}C (DMSO-d_6) δ 19.9 (CH_3), 112.4 (Cq), 114.0 (CH), 122.7 (CH), 125.7 (Cq), 131.5 (CH), 134.9 (CH), 136.2 (Cq), 145.4 (Cq), 169.8 (Cq) ppm; IR (Nujol mull) 3323, 2729, 2627, 2547, 1667, 1584 cm^{-1}. Anal. Calcd for $C_{22}H_{20}N_2O_4 \cdot 0.5H_2O$: C, 68.56; H, 5.49; N, 7.27. Found: C, 68.48; H, 5.37; N, 6.91.

5,5′-Dimethyl-2,2′-(1,3-phenylenediamino)bisbenzoic acid (3c): yellow powder (yield 45%); decomposition ≥ 260 °C; ^{1}H NMR (DMSO-d_6) δ 2.22 (s, 6 H), 6.79−6.83 (dd, J = 8 and 2 Hz, 2 H), 6.99 (s, 1 H), 7.20−7.24 (m, 5 H), 7.69 (s, 2 H) ppm.

13,14-Dihydrodibenzo[*b,j*][1,10]phenanthroline-5,8-dione (4a). 3a (10.39 g, 27.6 mmol) was stirred with 95% sulfuric acid (150 mL) at 100 °C for 1 h. The cool mixture was slowly poured into cold water (250 mL). The orange precipitate was filtered off and washed with boiling water and 1 mM KOH until the pH of the filtrate became 3−4. The product was washed with ethanol and ether and dried under vacuum at 70 °C, yielding 9.0 g (95%) of a yellow powder (hygroscopic): mp > 400 °C; ^{1}H NMR (DMSO-d_6) δ 2.46 (s, 6 H), 7.67 (s, 4 H), 7.99 (s, 2 H), 8.07 (s, 2 H), 11.62 (br s, 2 H) ppm; IR (Nujol mull) 3375−3000, 1668, 1632 cm^{-1}; MS (EI+, I = 4.5 V), m/z 340 ($M^{+\bullet}$).

13,14-Dichloro-2,11-dimethyldibenzo[*b,j*][4,7]phenanthroline (4b). 3b (1.0 g, 2.66 mmol) and $POCl_3$ (10 mL, 0.106 mol) were refluxed under nitrogen for 3.5 h. $POCl_3$ was removed under vacuum, CH_2Cl_2 (50 mL) was added, and the dark solution was slowly poured into cold 15% NH_4OH (30 mL). The organic layer was decanted, and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The organic solutions were mixed, dried over sodium sulfate, and evaporated. The brown product was recrystallized from $CHCl_3$, yielding 388 mg (39%) of yellow prisms: mp 252 °C; ^{1}H NMR ($CDCl_3$) δ 2.66 (s, 6 H), 7.72 (dd, J = 8.5 and 1.7 Hz, 2 H), 7.81 (s, 2 H), 8.15 (d, J = 8.5 Hz, 2 H), 8.26 (s, 2 H) ppm; ^{13}C ($CDCl_3$) δ 22.0, 120.7, 123.6, 124.9, 129.0, 132.8, 133.3, 138.1, 141.0, 146.6, 150.0 ppm; UV−vis (CH_2Cl_2) λ (ϵ) 249 (42 000), 325 (57 000), 376 (14 000) (M^{-1} cm^{-1}). Anal. Calcd for $C_{22}H_{14}N_2Cl_2 \cdot 0.1CHCl_3$: C, 68.39; H, 3.64; N, 7.22. Found: C, 68.35; H, 3.56; N, 7.28.

13,14-Dichloro-2,10-dimethyldibenzo[*b,j*][1,7]phenanthroline (4c). 4c was obtained in the same manner as above for **4b**: yellow crystals (yield: 33%); mp 260 °C; ^{1}H NMR ($CDCl_3$/CD_3OD) δ 2.45 (s, 3 H), 2.47 (s, 3 H), 7.49 (d, J = 2.8 Hz, 1 H), 7.54 (d, J = 2.8 Hz, 1 H), 7.66 (d, J = 9.8 Hz, 1 H), 7.88 (d, J = 8.7 Hz, 1 H), 7.93 (s, 1 H), 8.05 (d, J = 8.8 Hz, 1 H), 8.18 (d, J = 9.9 Hz, 1 H), 8.28 (s, 1 H) ppm.

3,10-Dimethyldibenzo[*b,j*][1,10]phenanthroline (5a). Dry **4a** (3.04 g, 8.9 mmol) and *n*-pentanol (350 mL) were

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heated to reflux. Sodium (8.18 g, 356 mmol) was added in small portions, and the solution was refluxed for about 10 h after the end of the addition. The pentanol was removed under vacuum, and the residue was taken up in CH_2Cl_2 and water. The emulsion was filtered in order to recover the unreacted quinacridone. The biphasic filtrate was decanted, and after being washed with water, 1 N HCl, and H_2O again, the organic solution was dried over $MgSO_4$ and evaporated, giving a red powder containing **5a** and a hemireduced compound (major product). This mixture was reoxidized as follows: it was refluxed in ethanol (120 mL), and $FeCl_3$ (5.1 g, 19 mmol) dissolved in water (60 mL) was slowly added. The solution was refluxed for about 15 h, 15% NH_4OH was added to the cooled solution, and the black precipitate was filtered and washed with methanol. The alcoholic solvents were removed under vacuum from the filtrate, and water was then extracted with dichloromethane. The organic layer was dried over Na_2SO_4 and evaporated, giving a brown product that was recrystallized from $CHCl_3$, yielding 912 mg (33%) of yellow crystals: mp 330−335 °C; ^{1}H NMR ($CDCl_3/CD_3OD$ 5/1) δ 2.56 (s, 6 H, $CH_{3(3/10)}$), 7.59 (s, 2 H, $H_{(6/7)}$), 7.67 (dd, J = 9 and 2 Hz, 2 H, $H_{(2/11)}$), 7.72 (d, J = 2 Hz, 2 H, $H_{(4/9)}$), 8.43 (d, J = 9 Hz, 2 H, $H_{(1/12)}$), 8.47 (s, 2 H, $H_{(5/8)}$) ppm; ^{13}C NMR ($CDCl_3/CD_3OD$ 5/1) δ 21.9 (CH_3), 126.5 (CH), 126.7 (CH), 127.7 (Cq), 128.4 (Cq), 130.0 (CH), 133.2 (CH), 135.0 (CH), 137.6 (Cq), 146.9 (Cq), 147.1 (Cq) ppm; UV−vis ($CHCl_3$) λ_{max} (ϵ) 244 (52 000), 270 (16 000), 314 (39 000), 326 (50 000), 351 (23 000) nm (M^{-1} cm^{-1}); fluorescence ($CHCl_3$, λ_{exc} = 326 nm) λ_{em} 422, 448, 479, 511 nm. Anal. Calcd for $C_{22}H_{16}N_2$: C, 85.69; H, 5.23; N, 9.08. Found: C, 85.53; H, 5.20; N, 9.01.

2,11-Dimethyldibenzo[*b,j*][4,7]phenanthroline (5b). 4b (200 mg, 0.53 mmol) in dry THF (10 mL) was added dropwise under nitrogen to a refluxing solution of $LiAlH_4$ (161 mg, 4.2 mmol) in dry THF (5 mL) for 30 min. It was refluxed for 10 h more, and the deep blue solution was allowed to cool at room temperature. The flask was put in an ice bath, and the $LiAlH_4$ in excess was slowly hydrolyzed with 1/1 THF/H_2O. THF was removed in vacuo, aqueous potassium tartrate was added, and the solution was extracted with CH_2Cl_2. After drying over Na_2SO_4, an orange-red solid was obtained, containing a mixture of **5b** and hydrogenated derivatives. This mixture was reoxidized in the same manner as above for **5a** with $FeCl_3$ (0.6 g, 2.1 mmol). The crude product was recrystallized from $CHCl_3$ and CH_3OH, giving 102 mg (62%) of pale yellow needles: mp 345 °C (decomposition); ^{1}H NMR ($CDCl_3/CD_3OD$ 2/1) δ 2.59 (s, 6 H, CH_3), 7.65 (dd, J = 8.5 and 1.7 Hz, 2 H, $H_{(3/10)}$), 7.86 (s, 2 H, $H_{(1/12)}$), 8.07 (d, J = 8.5 Hz, 2 H, $H_{(4/9)}$), 8.07 (s, 2 H, $H_{(6/7)}$), 9.35 (s, 2 H, $H_{(13/14)}$) ppm; ^{13}C NMR δ 21.7 ($CH_{3(2/11)}$), 123.8 (Cq), 126.8 ($CH_{(1/12)}$), 127.0 (Cq), 128.2 ($CH_{(6/7)}$), 130.3 ($CH_{(13/14)}$), 133.3 ($CH_{(4/9)}$), 133.6 ($CH_{(3/10)}$), 137.3 (Cq), 146.7 (Cq), 148.0 (Cq); UV−vis ($CHCl_3$) λ (ϵ) 248 (70 000), 314 (48 000), 332 (54 000), 361 (14 500) nm (M^{-1} cm^{-1}); fluorescence ($CHCl_3$, λ_{exc} = 332 nm) λ_{em} 411, 421, 436, 463, 495 nm. Anal. Calcd for $C_{22}H_{16}N_2$·0.09$CHCl_3$: C, 83.14; H, 5.08; N, 8.78. Found: C, 83.18; H, 5.19; N, 8.43.

2,10-Dimethyldibenzo[*b,j*][1,7]phenanthroline (5c). 5c was obtained in the same manner as above for **5b**: white crystals (yield 38%); mp 230 °C; ^{1}H NMR ($CDCl_3/CD_3OD$) δ 2.49 (s, 3 H, $CH_{3(10)}$), 2.53 (s, 3 H, $CH_{3(2)}$), 7.56 (d, 1 H, $H_{(11)}$), 7.58 (s, 1 H, $H_{(9)}$), 7.60 (d, 1 H, $H_{(3)}$), 7.71 (s, 1 H, $H_{(6)}$), 7.74 (s, 1 H, $H_{(7)}$), 7.79 (s, 1 H, $H_{(1)}$), 8.00 (d, 1 H, $H_{(4)}$), 8.09 (d, 1 H, $H_{(12)}$), 8.30 (s, 1 H, $H_{(8)}$), 9.79 (s, 1 H, $H_{(14)}$) ppm; ^{13}C NMR ($CDCl_3/CD_3OD$) δ 21.7 (2 $CH_{3(2/10)}$), 124.6 (Cq), 125.7 (Cq), 126.7 ($CH_{(9)}$), 127.2 (Cq), 127.6 (Cq), 127.7 ($CH_{(3)}$), 127.9 ($CH_{(1)}$), 128.1 ($CH_{(6)}$), 129.0 ($CH_{(12)}$), 131.4 ($CH_{(7)}$), 133.1 ($CH_{(11)}$), 133.3 ($CH_{(14)}$), 133.8 ($H_{(4)}$), 134.8 ($CH_{(8)}$), 136.7 (Cq), 136.8 (Cq), 146.5 (Cq), 146.9 (Cq), 147.2 (Cq), 150.2 (Cq) ppm; UV−vis ($CHCl_3$) λ (ϵ) 246 (75 000), 315 (50 000), 329 (56 000), 350 (29 000) nm (M^{-1} cm^{-1}); fluorescence ($CHCl_3$, λ_{exc} = 329 nm) λ_{em} 415, 424, 440, 468, 502 nm. Anal. Calcd for $C_{22}H_{16}N_2$·0.2$CHCl_3$: C, 80.25; H, 4.91; N, 8.43. Found: C, 80.16; H, 4.99; N, 8.49.

Dibenzo[*b,j*][1,10]phenanthroline-3,10-dicarboxaldehyde (6a). 5a (507 mg, 1.64 mmol), SeO_2 (401 mg, 3.62 mmol), and naphthalene (10 g) were heated to reflux for 2.5 h. The residue was suspended in CH_2Cl_2/MeOH, decanted, and filtered off. The filtrate was evaporated, and the residue was washed with hexane to remove naphthalene and recrystallized three times from $CHCl_3$ and CH_3OH, yielding 312 mg (56%) of a yellow powder: mp > 400 °C; ^{1}H NMR ($CDCl_3/CD_3OD$ 5/1) δ 7.84 (s, 2 H), 8.30 (dd, J = 9 and 2 Hz, 2 H), 8.59 (d, J = 2 Hz, 2 H), 8.71 (d, J = 9 Hz, 2 H), 8.90 (s, 2 H), 10.22 (s, 2 H); IR (Nujol mull) 1688, 1621 cm^{-1}. Anal. Calcd for ($C_{22}H_{12}N_2O_2$·0.75$CHCl_3$): C, 62.69; H, 2.96; N, 6.40. Found: C, 62.61; H, 3.13; N, 6.51.

Compounds **6b** and **6c** were obtained in the same manner from **5b** and **5c** respectively.

Dibenzo[*b,j*][4,7]phenanthroline-2,11-dicarboxaldehyde (6b): pale yellow powder (yield 55%); decomposition ≥ 350 °C; ^{1}H NMR ($CDCl_3/CD_3OD$ 5/1) δ 8.28−8.34 (1 s + 2 d, 6 H), 8.72 (s, 2 H), 9.78 (s, 2 H), 10.25 (s, 2 H); IR (Nujol mull) 1697, 1615 cm^{-1}. Anal. Calcd for $C_{22}H_{12}N_2O_2$·0.22$CHCl_3$: C, 73.60; H, 3.40; N, 7.73. Found: C, 73.63; H, 3.47; N, 7.59.

Dibenzo[*b,j*][1,7]phenanthroline-2,10-dicarboxaldehyde (6c): yellow powder (yield 60%); mp 320−330 °C (decomposition); ^{1}H NMR (DMSO-d_6) δ 7.99 (d, J = 9.4 Hz, 1 H), 8.30 (m, 4 H), 8.43 (d, J = 9 Hz, 1 H), 8.66 (s, 1 H), 9.09 (s, 1 H), 9.27 (s, 1 H), 10.24 (s, 1 H), 10.25 (s, 1 H), 10.33 (s, 1 H) ppm; IR (Nujol mull) 1696, 1636, 1606 cm^{-1}. Anal. Calcd for $C_{22}H_{12}N_2O_2$·0.6$CHCl_3$: C, 66.54; H, 3.11; N, 6.87. Found: C, 66.14; H, 3.73; N, 6.31.

2,5,8,25,28,31-Hexaaza[9,9](3,10)dibenzo[*b,j*][1,10]phenanthrolinophane (7a). 6a (200 mg, 0.60 mmol) was dissolved in an anhydrous mixture of 4/1 CH_2Cl_2/MeOH (500 mL). Diethylenetriamine (61 mg, 0.60 mmol) dissolved in the same mixture of solvents (50 mL) was added dropwise for 2.5 h at room temperature, and the resulting solution was stirred for 4 h after the end of the addition. The solvents were distilled off to give the tetraimine as a yellow powder (95% crude yield) that was used without further purification. It was dissolved in 1/1 CH_2Cl_2/MeOH (100 mL), and the stirred mixture was cooled to 0 °C. $NaBH_4$ (56 mg, 1.49 mmol) was added, and the solution was stirred at 0 °C for 2.5 h and at room temperature for 30 min. The solvents were removed in vacuo, and the residue was washed with water and recrystallized from $CHCl_3$ and CH_3OH, giving **7a** as a pale powder. **7a,HCl** was obtained in the following manner: 1 N HCl was added to the powder, and the solution was heated and precipitated with ethanol, yielding 95.5 mg (27%) of an orange powder: salt decomposition ≥ 150 °C; ^{1}H NMR (D_2O, pH = 6.0, [**7a**] = 5 mM) δ 3.22 (m, 4 H), 3.44 (m, 4 H), 4.28 (s, 4 H), 6.62 (s, 2 H, $H_{(6/7)}$), 7.12 (s, 2 H, $H_{(5/8)}$), 7.37 (s, 2 H, $H_{(4/9)}$), 7.59 (d, J = 8 Hz, 2 H, $H_{(2/11)}$), 7.96 (d, J = 8 Hz, 2 H, $H_{(1/12)}$); UV−vis (H_2O, pH = 6.0) λ (ϵ) 239 (91 000), 263 (65 000), 315 (91 000), 350 (30 000) nm (M^{-1} cm^{-1}); fluorescence (H_2O, pH = 6.0, λ_{exc} = 315 nm) λ_{em} 444, 472, 502 nm; MS (Electrospray, MeOH/H_2O 1/1) m/z 815.5 ($[C_{52}H_{50}N_{10} + H]^+$), 408.25 ($[C_{52}H_{50}N_{10} + 2\ H]^{2+}/2$). Anal. Calcd for ($C_{52}H_{50}N_{10}$·7HCl·6$H_2O$): C, 53.00; H, 5.90; N, 11.89. Found: C, 53.05; H, 5.96; N, 11.95.

5,28-Dioxy-2,8,25,31-tetraaza[9,9](3,10)dibenzo[*b,j*][1,10]phenanthrolinophane (8). 2,2′-Oxybis(ethylamine) dihydrochloride (197 mg, 1.11 mmol) and sodium hydroxide (111 mg, 2.78 mmol) were dissolved in anhydrous methanol (10 mL). After 3 h of stirring, the NaCl precipitate was filtered off and methanol was removed in vacuo at room temperature. CH_2Cl_2 was added, NaCl was again removed by filtration, and the solvent was evaporated, yielding 116 mg (100%) of the free amine that was used without further purification. Compound **8** was obtained in two steps in the same manner as above for **7a**, from 2,2′-oxybis(ethylamine) (64 mg, 0.61 mmol) and **6a** (205 mg, 0.61 mmol). **8,HCl** was formed by addition of 1 N HCl and was purified by recrystallization from H_2O and THF to give 113 mg (33%) of an orange powder: decomposition of the salt ≥ 150 °C; ^{1}H NMR (D_2O, pH = 6.0, [**8**] = 5 mM) δ 3.48 (m, 4 H), 3.95 (m, 4 H), 4.12 (s, 4 H), 7.09 (s, 2 H, $H_{(6/7)}$), 7.43 (s, 2 H, $H_{(5/8)}$), 7.45 (d, J = 8 Hz, 2 H, $H_{(2/11)}$), 7.79 (s, 2 H, $H_{(4/9)}$), 7.98 (d, J = 8 Hz, 2 H, $H_{(1/12)}$); UV−vis (H_2O, pH = 6.0) λ (ϵ) 238 (89 000), 266 (63 000), 315 (85 000), 349 (29 000) nm (M^{-1} cm^{-1}); fluorescence (H_2O, pH = 6.0, λ_{exc} = 315 nm) λ_{em} 446, 473, 504 nm; MS (Electrospray, MeOH/H_2O 1/1) m/z 818.0 ($[C_{52}H_{48}N_8O_2 + H]^+$), 409.51 ($[C_{52}H_{48}N_8O_2 + 2\ H]^{2+}/2$), 273.34

($[C_{52}H_{48}N_8O_2 + 3\ H]^{3+}/3$). Anal. Calcd for ($C_{52}H_{48}N_8O_2 \cdot 5HCl \cdot 6.5H_2O$): C, 55.94; H, 5.96; N, 10.04. Found: C, 55.91; H, 6.03; N, 9.64.

6,31-Dimethyl-2,6,10,27,31,35-hexaaza[11,11](3,10)dibenzo[*b,j*][1,10]phenanthrolinophane (9). 9 was obtained in two steps in the same manner as above for **7a**, from 3,3′-diamino-*N*-methyldipropylamine (90 mg, 0.62 mmol) and **6a** (200 mg, 0.59 mmol). **9,HCl** was recrystallized twice from 1 N HCl and THF to give 100 mg (25%) of an orange powder: decomposition of the salt ≥ 150 °C; ^{1}H NMR (D_2O, pH = 6.0, [**9**] = 5 mM) δ 1.87 (m, 8 H), 2.56 (s, 6 H), 2.95 (m, 16 H), 3.46 (s, 8 H), 7.40 (2 s, 8 H, $H_{(6/7)} + H_{(4/9)}$), 7.52 (d, J = 9 Hz, 4 H, $H_{(2/11)}$), 8.05 (d, J = 9 Hz, 4 H, $H_{(1/12)}$), 8.24 (s, 4 H, $H_{(5/8)}$); UV−vis (H_2O, pH = 6.0) λ (ϵ) 238 (83 000), 267 (60 000), 316 (89 000), 326 (81 000), 350 (36 000) nm ($cm^{-1}\ M^{-1}$); fluorescence (H_2O, pH = 6.0, λ_{exc} = 316 nm) λ_{em} 442, 470, 499 nm; MS (Electrospray, MeOH/H_2O 1/1) m/z 900.5 ($[C_{58}H_{62}N_{10} + H]^+$), 450.5 ($[C_{58}H_{50}N_{10} + 2H]^{2+}/2$). Anal. Calcd for ($C_{58}H_{62}N_{10} \cdot 8HCl \cdot 7.5H_2O$): C, 52.54; H, 6.46; N, 10.56. Found: C, 52.62; H, 6.81; N, 10.06.

2,5,8,25,28,31-Hexaaza[9,9](2,11)dibenzo[*b,j*][4,7]phenanthrolinophane (7b). 7b was obtained in two steps in the same manner as above for **7a**, from **6b** (192 mg, 0.57 mmol) and diethylenetriamine (61 mg, 0.59 mmol). Recrystallization of crude **7b** from $CHCl_3$ and MeOH afforded a pale powder that was recrystallized from 1 N HCl to give 111 mg (33%) of **7b,HCl** as a yellow-green powder: salt decomposition ≥ 150 °C; ^{1}H NMR (D_2O/CF_3CO_2D, pH = 0.3) δ 3.74 (m, 16 H), 4.79 (s, 8 H), 8.40 (d, J = 9 Hz, 4 H, $H_{(3/10)}$), 8.44 (d, J = 9 Hz, 4 H, $H_{(4/9)}$), 8.72 (s, 4 H, $H_{(1/12)}$), 8.77 (s, 4 H, $H_{(6/7)}$), 10.60 (s, 4 H, $H_{(13/14)}$) ppm; UV−vis (H_2O, pH = 6.0) λ (ϵ) 245 (135 000), 299 (62 000), 324 (46 000) nm ($M^{-1}\ cm^{-1}$); fluorescence (H_2O, pH = 6.0, λ_{exc} = 324 nm) λ_{em} 409, 434, 469 nm; MS (Electrospray, MeOH/H_2O 1/1) m/z 815.25 ($[C_{52}H_{50}N_{10} + H]^+$), 407.5 ($[C_{52}H_{50}N_{10} + 2H]^{2+}/2$). Anal. Calcd for $C_{52}H_{50}N_{10} \cdot 9HCl \cdot 2.5H_2O$: C, 52.56; H, 5.43; N, 11.79. Found: C, 52.55; H, 5.48; N, 11.26.

3,10-Bis((*n*-propylamino)methyl)dibenzo[*b,j*][1,10]phenanthroline (11a). *n*-Propylamine (330 mg, 5.57 mmol) was added to a clear suspension of **6a** (75 mg, 0.223 mmol) in 4/1 CH_2Cl_2/MeOH (150 mL) at room temperature. The solution was stirred for 2 h, and the solvents were distilled off. The crude diimine was dissolved in methanol (20 mL) and cooled to 0 °C. $NaBH_4$ (21 mg, 0.557 mmol) was added, and the solution was stirred at 0 °C for 2 h and at room temperature for 30 min. The solvents were distilled off, water was added, and the product was extracted with dichloromethane. The organic layer was dried over Na_2SO_4 and evaporated. The 1 N HCl was added, and **11a,HCl** was precipitated with THF. It was recrystallized from 1 N HCl and ethanol, yielding 54 mg (43%) of an orange powder: salt decomposition ≥ 150 °C; ^{1}H NMR (D_2O, pH = 2.1) δ 0.88 (t, 6 H), 1.60−1.71 (m, 4 H), 3.02 (t, 4 H), 4.33 (s, 4 H), 7.57 (s, 2 H, $H_{(6/7)}$), 7.85 (dd, J = 9 and 2 Hz, 2 H, $H_{(2/11)}$), 8.05 (d, J = 2 Hz, 2 H, $H_{(4/9)}$), 8.16 (d, J = 9 Hz, 2 H, $H_{(1/12)}$), 8.78 (s, 2 H, $H_{(5/8)}$) ppm; ^{13}C NMR (D_2O, pH = 2.1) δ 10.5 (CH_3), 19.4 (CH_2), 49.5 (CH_2), 50.5 (CH_2), 126.6 (CH), 127.0 (CH), 127.4 (Cq), 128.0 (Cq), 130.6 (CH), 131.8 (2 Cq), 134.1 (CH), 141.1 (CH), 143.1 (Cq) ppm; UV−vis (H_2O, pH = 6.0) λ (ϵ) 220 (42 000), 238 (52 000), 267 (37 000), 316 (62 000), 324 (58 000), 346 (34 000) nm ($M^{-1}\ cm^{-1}$); fluorescence (H_2O, pH = 6.0, λ_{exc} = 316 nm) λ_{em} 438, 463, 495 nm. Anal. Calcd for ($C_{28}H_{30}N_4 \cdot 3HCl \cdot 2H_2O$): C, 59.21; H, 6.57; N, 9.86. Found: C, 59.19; H, 6.51; N, 9.60.

11b and **11c** were obtained in the same manner from **6b** and **6c**, respectively.

2,11-Bis((*n*-propylamino)methyl)dibenzo[*b,j*][4,7]phenanthroline (11b): yellow powder (yield 52%): salt decomposition ≥ 150 °C; ^{1}H NMR (D_2O, pH = 1.6) δ 0.97 (t, 6 H), 1.60−1.78 (m, 4 H), 3.04 (t, 4 H), 4.14 (s, 4 H), 6.79 (d, J = 8.6 Hz, 2 H, $H_{(3/10)}$), 7.14 (s, 2 H, $H_{(6/7)}$), 7.33 (d, J = 8.5 Hz, 2 H, $H_{(4/9)}$), 7.57 (s, 2 H, $H_{(1/12)}$), 8.26 (s, 2 H, $H_{(13/14)}$) ppm; ^{13}C (D_2O, pH = 1.6) δ 10.6 (CH_3), 19.3 (CH_2), 49.5 (CH_2), 50.3 (CH_2), 121.6 (Cq), 125.3 (Cq), 125.8 (CH), 130.2 (CH), 130.9 (Cq), 132.2 (CH), 133.3 (CH), 133.9 (CH), 143.3 (Cq), 144.7 (Cq) ppm; UV−vis (H_2O, pH = 6.0) λ (ϵ) 247 (68 000), 305 (42 000), 327 (46 000) nm ($M^{-1}\ cm^{-1}$); fluorescence (H_2O, pH = 6.0, λ_{exc} = 327 nm) λ_{em} 407, 432, 459, 490 nm. Anal. Calcd for $C_{28}H_{30}N_4 \cdot 3HCl \cdot 1.3H_2O$: C, 60.56; H, 6.46; N, 10.09. Found: C, 60.54; H, 6.53; N, 9.64.

2,10-Bis((*n*-propylamino)methyl)dibenzo[*b,j*][1,7]phenanthroline (11c): yellow powder (yield 57%); salt decomposition ≥ 150 °C; ^{1}H NMR (D_2O, pH = 2.7) δ 0.85−0.95 (m, 6 H), 1.60−1.74 (m, 4 H), 2.96−3.07 (m, 4 H), 4.19 (s, 2 H), 4.25 (s, 2 H), 7.11 (d, J = 9.4 Hz, 1 H), 7.45−7.62 (m, 6 H), 7.95 (s, 1 H), 8.09 (s, 1 H), 9.12 (s, 1 H) ppm; UV−vis (H_2O, pH = 6.0) λ (ϵ) 223 (35 000), 243 (62 000), 312 (44 000), 327 (55 000), 345 (22 000) nm ($M^{-1}\ cm^{-1}$); fluorescence (H_2O, pH = 6.0, λ_{exc} = 327 nm) λ_{em} 425, 444, 472 nm. Anal. Calcd for $C_{28}H_{30}N_4 \cdot 3.5HCl \cdot 2.2H_2O$: C, 57.02; H, 6.48; N, 9.50. Found: C, 57.01; H, 6.43; N, 8.96.

3,10-Bis[[(3-(dimethylamino)propyl)amino]methyl]dibenzo[*b,j*][1,10]phenanthroline (12). 12 was obtained in the same manner as above for **11a**, from 3-(dimethylamino)-propylamine and **6a**: orange yellow powder (43%); salt decomposition ≥ 150 °C; ^{1}H NMR (D_2O, pH = 3.2) δ 2.13 (m, 4 H), 2.81 (s, 12 H), 3.12−3.21 (m, 8 H), 4.40 (s, 4 H), 7.48 (s, 2 H, $H_{(6/7)}$), 7.78 (d, J = 9 Hz, 2 H, $H_{(2/11)}$), 8.02 (s, 2 H, $H_{(4/9)}$), 8.11 (d, J = 9 Hz, 2 H, $H_{(1/12)}$), 8.64 (s, 2 H, $H_{(5/8)}$) ppm; ^{13}C NMR (D_2O, pH = 3.2) δ 21.5, 43.2, 44.6, 51.1, 54.6, 126.7, 127.6, 127.8, 128.2, 130.6, 130.8, 133.1, 139.8, 143.2, 144.3 ppm. Anal. Calcd for ($C_{32}H_{40}N_6 \cdot 5HCl \cdot 4.4H_2O$): C, 49.90; H, 7.04; N, 10.91. Found: C, 49.87; H, 6.47; N, 10.58.

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