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Modular Synthesis of pH-Sensitive Fluorescent Diaza[4]helicenes

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Configurationally stable diaza[4]helicenes have been prepared in two steps by using a particularly facile N–N bond-cleavage reaction. The synthetic procedure uses hydrazine (NH_2NH_2) for the introduction of a single nitrogen atom. The strategy is general, modular and highly tolerant to functional groups. A mechanistic rationale is proposed for the spontaneous N–N bond-cleavage reaction. The resulting helical quinacridines are dyes that present absorption and emission properties that can be modulated as a function of pH; the pink quinacridine and green protonated forms ($pK_a \approx 9.0$) display distinct optical features in the near-IR region. Single enantiomers were obtained by chiral stationary phase HPLC resolution. The absolute configurations were assigned by comparison of the ECD spectra of the conjugated acids with those of known dialkylquinacridinium derivatives. A rather high racemization barrier was measured by means of variable-temperature ECD experiments ($\Delta G^{\ddagger} = 30.7 \pm 4.0$ kcal mol^{-1} at 140 °C).

Introduction

Azahelicenes are helical derivatives made of *ortho*-fused aromatic rings containing at least one nitrogen atom. Like their all-carbon analogues,[1] they possess distinctive twisted conformations that result from steric repulsions between the terminal aromatic rings or their substituents. Syntheses are mostly based on photochemical,[2] transition-metal-catalysed trimerization[3] and cross-coupling strategies.[2b,4] Azahelicenes are utilized for a variety of applications due to the presence of both an inherently chiral geometry and nitrogen donor atom(s). In fact, studies of azahelicenes have been reported in many different fields,[2j,5] including solid-state self-assembly,[2g,6] asymmetric catalysis,[4i,7] chemosensors[5h,8] and enantioselective biomolecular recognition. In terms of optical properties, these moieties usually absorb light in the UV spectral domain and, to the best of our knowledge, there are few reports of fluorescent azahelicenes.[4c,9] Herein, in a new development made possible by the use of hydrazine as nucleophile and a subsequent surprisingly facile N–N bond-cleavage reaction, we report the general synthesis of configurationally stable [4]helical quinacridines **1** (Figure 1; R = alkyl, aryl, benzyl, allyl, NH_2). These derivatives are pH-sensitive dyes and fluorophores. The neutral **1** and protonated **1**·H$^+$ conjugates ($pK_a \approx 9.0$) present well-separated absorption and fluorescent signatures allowing facile distinction of the entities. Furthermore, the *P* and *M* enantiomers were separated and they present a rather large barrier to racemization ($\Delta G^{\ddagger} > 30.7 \pm 4.0$ kcal mol^{-1} at 140 °C).

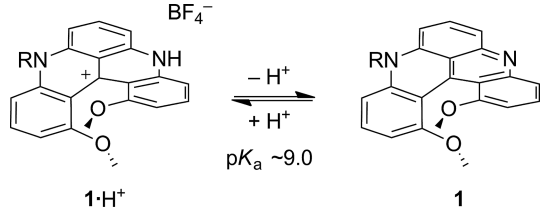

Figure 1. Colourful 1,13-dimethoxyquinacridine **1** (pink) and its conjugated acid **1**·H$^+$ (green). The *M* enantiomers are shown arbitrarily (R = alkyl, aryl, benzyl, allyl, NH_2).

Results and Discussion

Permanently charged cationic dialkyldiaza[4]helicenes of type **2** have previously been studied[10] (Scheme 1) for their interesting stereochemical, biological, supramolecular and photophysical properties.[11] Compounds of type **2** are prepared by treatment of the tris(2,6-dimethoxyphenyl)methyl cation (**3**) with primary amines. The products of ring closures are obtained by sequences of nucleophilic aromatic substitutions (S_NAr) of MeO substituents by nitrogen nucleophiles. Although acridinium cations **4** are usually afforded at 20 °C, elevated temperatures (90–120 °C) are necessary to form quinacridinium ions **2**. Recently, Takui, Morita and co-workers relied on an analogous three-step protocol to form cation **5** containing unsubstituted nitrogen

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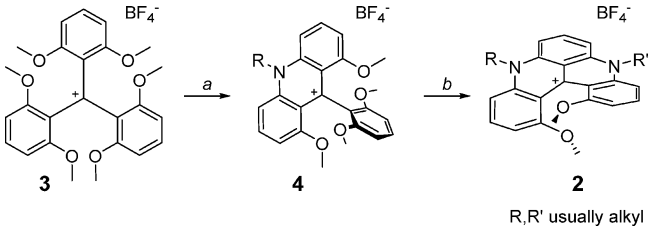
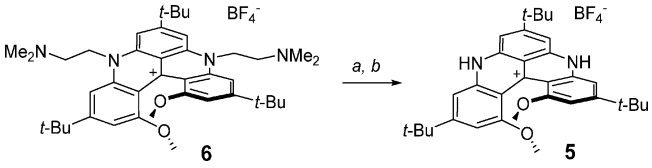
atoms.[10a] First, compound **6** was prepared by using *N*,*N*-dimethylethylenediamine as nucleophile and a precursor cation similar to **3**. Then the aminoalkyl side-chains were removed through a Hoffmann elimination sequence (Scheme 2).



Scheme 1. Synthesis of permanently charged quinacridinium salts **2** from acridinium derivatives **4**. Reagents and conditions: a) R-NH_2 (2.5 equiv.), *N*-methylpyrrolidone (NMP), 20–50 °C, 30 min; b) R′-NH_2 (25 equiv.), 110 °C, NMP, 1.5 h.



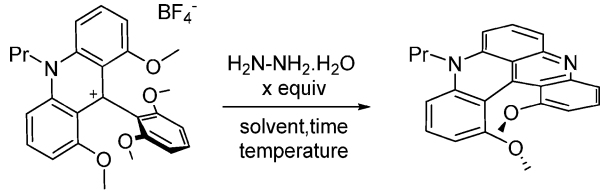
Scheme 2. Reagents and conditions: a) 1. MeI, MeOH, 110 °C; 2. *t*BuOK, DMF, 20 °C; 3. aq. HBF_4, 20 °C, 100%; b) 1. aq. HBF_4, MeOH, 70 °C; 2. Aq. Na_2CO_3, CH_2Cl_2, 20 °C, 94%.

Despite the efficiency of this method, an alternative one-step protocol was sought for the introduction of "naked" nitrogen atoms. Ammonia and sulfamic acid were tested without success by using cation **4a** (R = *n*Pr) as substrate.[12] Hydrazine (NH_2NH_2) was then considered as a substitute due to its availability, reasonable cost, lower volatility and higher nucleophilicity.[13] The often-difficult cleavage of the N–N bond[14] was a problem not to be underestimated, but it was decided to consider it only later. The reaction between acridinium **4a** and NH_2NH_2 (64–65% solution in water, 25 equiv. NMP, 110 °C) was thus attempted. To our satisfaction, the reaction occurred as planned and the desired quinacridine **1a** was obtained directly (Table 1, entry 1, 50% yield), the cleavage of the N–N bond occurring seemingly during the formation of the helical adduct.

Care was taken to ensure that this facile N–N bond cleavage was a general observation and the reaction conditions were optimized accordingly. The results are summarized in Table 1. With NMP as solvent, a longer reaction time was beneficial (85% yield, entry 2). DMSO and DMF performed equally well, however, as the reactions were easier to purify in DMF, this solvent was further studied.[15] The yields were improved by performing the reaction at 90 °C and in red-tinted glassware to limit exposure to light (92%, entry 6). A decrease in the amount of hydrazine, however, was detrimental (Table 1, entry 7).

With the optimized reaction conditions in hand (Table 1, entry 6), a series of acridinium ions **4** were then tested as substrates. The results are summarized in Table 2. In short, the reaction is general and other alkyl, aryl and benzyl side-chains are compatible (entries 1–5). Heteroatoms are also

Table 1. Optimization of the reaction conditions for the direct synthesis of quinacridine **1a**.

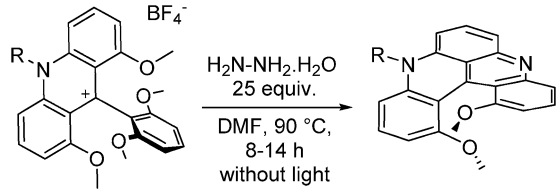


Entry	Solvent	*T* [°C]	NH_2NH_2 [equiv.]	Time [h]	Yield [%][a]
1	NMP	110	25	8	50
2	NMP	110	25	14	85
3	DMSO	110	25	14	80
4	DMF	110	25	14	85
5	DMF	90	25	14	83
6[b]	DMF	90	25	8	92
7	DMF	90	10	8	70

[a] Isolated yields. [c] Reaction performed in red-tainted glassware.

tolerated either as substituents on the side-chains (entries 6–8) or bound directly to the acridine nitrogen atom (entry 9).[16] Only in the case of **4k** containing an allyl moiety was the reaction unsuccessful, the allyl group being systematically reduced to a propyl chain during the reaction to form **1a** in good yield (90%) instead of **1k**.[17] This result will be discussed later.

Table 2. Scope of the reaction (first approach).



Entry	Substrate	R	Product	Yield [%][a]
1	**4b**	methyl	**1b**	97
2	**4c**	hexyl	**1c**	82
3	**4d**	hexadecyl	**1d**	80
4	**4e**	phenyl	**1e**	94
5	**4f**	benzyl	**1f**	78
6	**4g**	$CH_2CH_2NMe_2$	**1g**	89
7	**4h**	CH_2CH_2OH	**1h**	85
8	**4i**	$CH_2CH_2OCH_2CH_2OH$	**1i**	88
9	**4j**	NH_2	**1j**	85
10	**4k**	allyl	**1k**	0[b]

[a] Isolated yields. [b] Instead of the desired product **1k**, adduct **1a** (R = *n*Pr) was obtained in good yield (90%).

Product **1e** was found to be moderately soluble in a 4:1 mixture of hexane and dichloromethane. Single crystals were obtained that were analysed by X-ray diffraction. Cation **1e** adopts a twisted helical conformation typical of this type of [4]helicene.[11e,11f] No particular structural modification due to the presence of the "naked" sp^2 N atom (N2, Figure 2) was noticed.

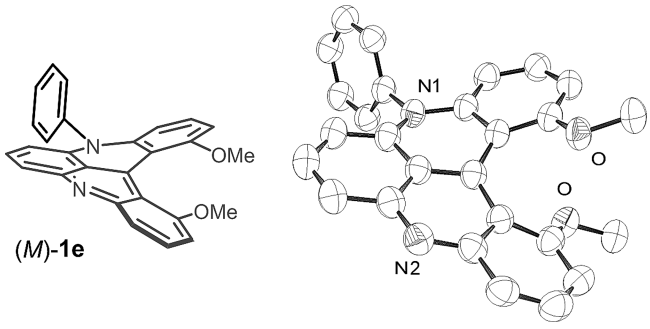
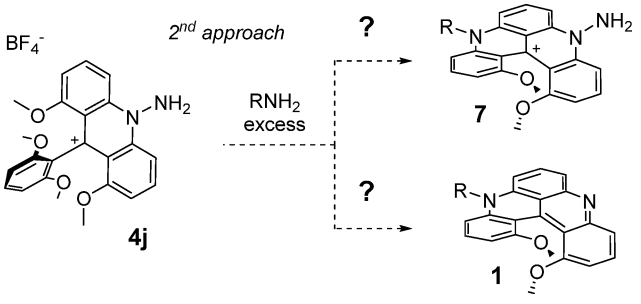


Figure 2. Ortep view of the crystal structure of **1e** (one molecule of CH_2Cl_2 has been omitted). The thermal ellipsoids are drawn at the 50% probability level.

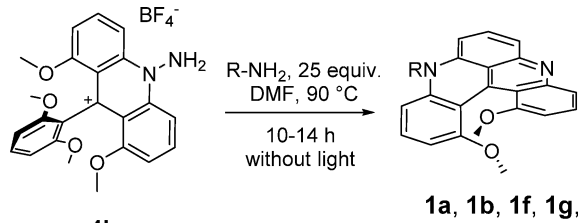
Despite this positive result, a second (one-step) approach was considered to shorten the synthetic strategy, obtain some mechanistic information and to be able to work with unsaturated side-chains (e.g., allyl). This approach used salt [**4j**][BF_4] (Table 2, entry 9) as a single precursor for all derivatives of type **1**. As outlined in Scheme 3, it was considered that **4j** ought to react with primary amines to afford quinacridinium salt **7** or, ideally, quinacridines **1** as final products if the spontaneous N–N bond cleavage was to occur again.



Scheme 3. Second convergent synthetic approach to quinacridines.

To our satisfaction, the salt [**4j**][BF_4] reacted with *n*-propyl- and methylamine (25 equiv.) at 90 °C to afford directly quinacridine **1a** and **1b**, respectively, in excellent yields (90 and 91%, Table 3, entries 1 and 2). The reactions with benzyl-, 2-(*N*,*N*′-dimethylamino)ethyl- and allylamines were then attempted knowing that competing oxidation, elimination and hydrogenation reactions might occur with such amines.[18] Satisfactorily, adducts **1f**, **1g** and **1k** were obtained in yields of 88, 84 and 60%, respectively. This time, in the reaction with allylamine, no evidence for the reduction of the side-chain was found. Functional group tolerance was further confirmed by the reaction of [**4j**][BF_4] with regular hydrazine (entry 6). Amino-substituted quinacridine **1j** (85%) was obtained without traces of a second deamination reaction. Ethanolamine also reacted with [**4j**][BF_4] to afford the expected product **1h** (Table 3, entry 5).

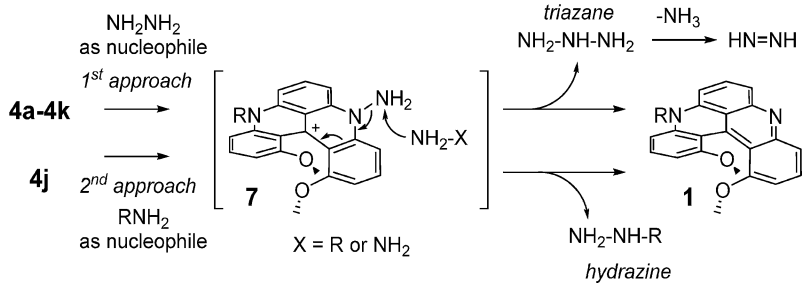
Table 3. Scope of the reaction (second approach).



Entry	R	Product	Yield [%][a]
1	propyl	**1a**	90
2	methyl	**1b**	91
3	benzyl	**1f**	88
4	$CH_2CH_2NMe_2$	**1g**	84
5	CH_2CH_2OH	**1h**	83
6	NH_2	**1j**	85
7	allyl	**1k**	60

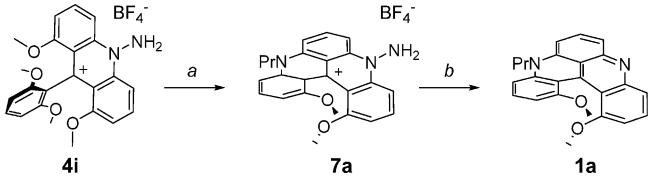
[a] Isolated yields.

This reactivity is explained if the existence of quinacridinium salts **7** as intermediates is considered (Scheme 4). In fact, the addition of hydrazine to "regular" acridinium salts (first approach) or primary amines to **4j** (second approach) generates in both instances derivatives **7**. The difference in the two approaches is only the nature of the nucleophilic reactant in excess in the crude mixtures. Herein it is proposed that the remaining nucleophiles attack the exocyclic amino group of **7** and generate the corresponding quinacridine derivatives. Different byproducts are then generated. In the first approach, a triazane (NH_2NHNH_2) is obtained that decomposes to generate diimide and ammoniac,[19] whereas in the second strategy alkylhydrazines are produced that do not evolve further. If an unsaturated side-chain is present in the molecule, then the second approach is better as it avoids the undesired reduction of the double (triple) bond by the in situ generated HN=NH.



Scheme 4. Mechanistic rationale for the synthesis of quinacridines **1**.

To establish some evidence for this mechanism, a compound of type **7** was prepared and isolated by treatment of acridinium [**4j**][BF_4] with only 5 equiv. of *n*-propylamine, the reaction being monitored by ESI-MS (Scheme 5). Compound **7a** was isolated in 85% yield and then treated with an excess (20 equiv.) of both hydrazine and propylamine to give in both cases the expected product **1a** (90 and 80% yields, respectively).



Scheme 5. Reagents and conditions: a) *n*-propylamine (5 equiv.), DMF, 90 °C, Ar, 8 h, without light, 85%; b) $H_2NNH_2{\cdot}H_2O$ or *n*-propylamine (20 equiv.), DMF, 90 °C, Ar, 3 h, without light, 100% conversion, 90 and 80% yields, respectively.

With these results in hand, the resolution of one of the helical quinacridines was pursued. In a first set of experiments, racemic **1a** (R = Pr) was treated with common enantiopure acids (e.g., tartaric acid, dibenzoyltartaric acid, mandelic acid).[3d] However, conditions that would induce a selective precipitation of a diastereomeric salt were not found. A semi-preparative chromatographic resolution of *rac*-**1f** (R = Benzyl) on a chiral stationary phase was then attempted.[20] Successful conditions were found by using a Chiralpak IB® column and a mixture of *n*-hexane and 2-propanol (60:40) as eluent with 0.1% of ethanolamine as additive. Starting with 25 mg of *rac*-**1f** and after several runs (see the Supporting Information), 10.0 mg (*ee* >99%, 40% yield) and 8.0 mg (*ee* 99%, 32% yield) were afforded in the first and second eluted fractions, which correspond to the dextro- and levorotatory enantiomers of **1f**, respectively ($[\alpha]_{365}$ = +16500 and –16000, respectively, CH_3CN, 10^{-4} M). The electronic circular dichroism (ECD) spectra (250–700 nm) of the two fractions are displayed in Figure S1 in the Supporting Information).

To establish the absolute configurations of these separated enantiomers, (+)-**1f** and (–)-**1f** were transformed into their conjugated acids, namely (+)-[**1f**·H^+][BF_4] and (–)-[**1f**·H^+][BF_4].[21] Their ECD spectra were then compared with that of classical enantiopure cations of type **2**. In fact, it was considered that the protonation of quinacridines **1** ought to generate species with chiroptical properties similar to those of permanently charged quinacridiniums **2**, as was indeed the case, as seen in Figure 3. The ECD spectra of [(*P*)-**2a**][BF_4] and [(*M*)-**2a**][BF_4] (R = R′ = Pr) are presented in the top panel, in which the configurations were unambiguously assigned by VCD spectroscopy and X-ray crystallography in the presence of a chiral auxiliary of known configuration.[10e,10f] These spectra are virtually superposable on those of (+)-[**1f**·H^+][BF_4] and (–)-[**1f**·H^+][BF_4] displayed in the bottom panel.[22] As such, it is safe to consider that the first and second fractions eluted from the Chiralpak IB® column correspond to (+)-(*P*)- and (–)-(*M*)-**1f**, respectively. Interestingly, strong differences are observed in the ECD spectra of enantiopure **1f** and [**1f**·H^+][BF_4]; the dextro- and levorotatory series are compared in Figure S2 in the Supporting Information.

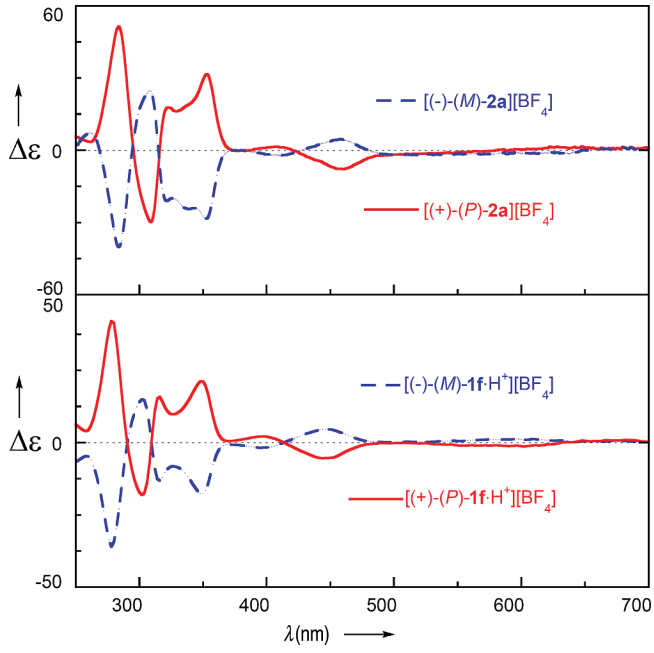


Figure 3. Top: ECD spectra of (*P*)-[**2a**][BF_4] (red solid line) and (*M*)-[**2a**][BF_4] (blue dashed line). Bottom: ECD spectra of (+)-[**1f**·H^+][BF_4] (red solid line) and (–)-[**1f**·H^+] (blue dashed line) derived from (+)- and (–)-[**1f**], respectively. Solutions in CH_3CN (20 °C, 5×10^{-6} M).

Finally, an attempt was made to determine the racemization barrier by ECD, monitoring a single wavelength every 5 s (357 nm, see the Supporting Information). It was necessary to heat dibutyl sulfoxide solutions of (+)-(*P*)-**1f** at 130 °C to start observing a decrease in the Cotton effect. After 1000 s, a loss of only 20% enantiomeric purity was observed at this temperature. Samples were then heated at 140 and 150 °C and analysed for the same period of time. At 160 °C, the start of the decomposition was observed. Measurements were thus not taken at this or higher temperatures. Kinetic constants were calculated and activation parameters determined (E_a, A, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ and $\Delta G^{\ddagger}$, see the Supporting Information). The racemization of **1f** ($\Delta G^{\ddagger}$ = 30.7 ± 4.0 kcal mol^{-1} at 140 °C) occurs more quickly than that of [**2a**][BF_4], for which a rather high barrier was measured ($\Delta G^{\ddagger}$ = 41.3 kcal mol^{-1} at 200 °C).[10f] Clearly, the absence of an alkyl substituent on a nitrogen atom gives a large degree of flexibility. The very high positive value for the entropy tends to indicate that this transformation involves a strong involvement of solvent and/or an ion-pairing reorganization. The racemization barrier for **1f** remains, however, slightly higher than that reported for analogous derivative **5** ($\Delta G^{\ddagger}$ = 28.4 kcal mol^{-1}, 28 °C).[10a]

With these compounds in hand, care was taken to study and characterize the optical properties.

Photophysical Properties

Absorption, pH titration and fluorescence measurements were performed on quinacridines **1b** and **1j** (R = Me and NH_2, respectively) in aqueous solution containing 0.1% DMSO. Protonation strongly affects the electronic structure of the quinacridines and, thus, leads to significant changes in their absorption spectra, as illustrated in Figure 4. For both **1b** and **1j**, the lowest-energy absorption band shifts from 560 to 625 nm and a new band appears at 420 nm. The presence of the hydrazino substituent in **1j** has very little effect on the absorption spectrum of either its neutral or cationic forms, which points to a minor involvement of the exocyclic NH_2 group in the lowest optical transitions. Consequently, a possible acid/base reaction of this group should have only a minor impact on the electronic absorption spectrum.

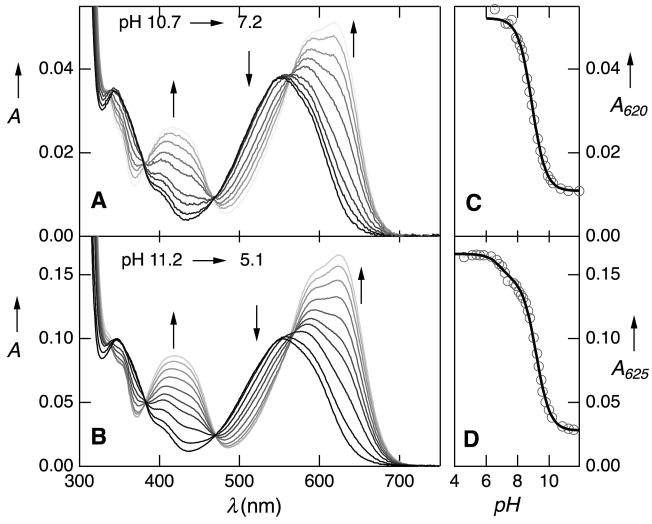


Figure 4. Electronic absorption spectra and titration curves for aqueous solutions of **1b** (A, C) and **1j** (B, D). The solid lines in C and D are the best fits of Equations (S1) and (S2), respectively.

The pH-dependence of the absorbance at 620 nm (**1b**) and 625 nm (**1j**) is depicted in parts C and D of Figure 4 (**1j**). These titration curves were analysed assuming one and two acid/base equilibria for **1b** and **1j**, respectively [see Equations (S1) and (S2) in the Supporting Information], and the best fits were obtained with pK_1 = 8.9 for **1b**·H^+ and pK_1 = 6.9 for **1j**·H^{2+} and pK_2 = 9.1 for **1j**·H^+. The similarity of pK_2 for **1j**·H^+ and pK_1 for **1b**·H^+ points to an average pK_a value of about 9.0 for the equilibrium between quinacridinium and quinacridine conjugates. On the other hand, the pK_1 value found for **1j** can be associated with the NH_2 substituent and, as anticipated above, this equilibrium has a minor effect on the absorption spectrum.

The steady-state absorption and emission spectra of the quinacridine and quinacridinium forms of **1b** and **1j** are shown in Figure 5. The weak feature above 700 nm in the absorption spectrum of **1b** at high pH is a result of the scattering from small particles in suspension, most probably aggregates. Indeed, [4]heliceniums of type **2** have been shown to form dimeric aggregates at modest concentrations in aqueous solution.[11d] Moreover, the quinacridine form that predominates at high pH has a larger aromaticity than quinacridinium and is neutral. Consequently, it can be expected to be less hydrophilic and more prone to the formation of large aggregates.

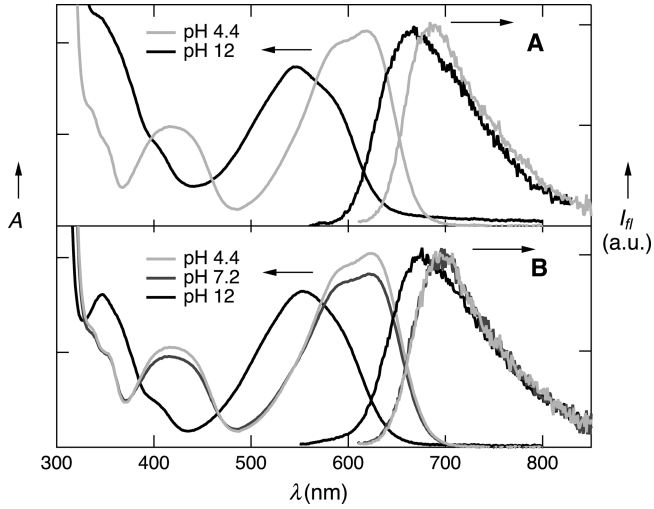


Figure 5. Absorption and emission spectra of (A) **1b** and (B) **1j** in aqueous solutions at various pH.

The quinacridines **1b** and **1j** fluoresce weakly above 600 nm with quantum yields, Φ_f, of around 5×10^{-3} (Table 4). Upon protonation, their emission bands shift to longer wavelengths with peaks at around 700 nm. However, protonation has a negligible effect on the fluorescence quantum yield, as illustrated in Table 4. The fluorescence spectrum and quantum yield of **1j** with the protonated NH_2 substituent are essentially the same as those of the unprotonated form, as could be expected from the quasi-identical absorption spectra.

Table 4. Fluorescence properties of **1b** and **1j**.

Product	pH	Φ_f [10^{-3}][a]	τ_{f1} [ns][b]	τ_{f2} [ns][b]
1b	4.4	6	0.45 (0.81)	0.92 (0.19)
	12	4	0.48	–
1j	4.4	4	0.35	–
	7.2	3	0.35	–
	12	4	0.35	–

[a] Fluorescence quantum yield (error: $\pm 2 \times 10^{-3}$). [b] An additional decay component with a time constant of >4 ns and a relative amplitude of <0.01 has been omitted.

The fluorescence decays of the various forms of **1b** and **1j** recorded at the maximum emission wavelength by time-correlated single photon counting (TCSPC) upon excitation at 395 nm[23] are depicted in Figure 6. Although marked differences can be seen for the acid and basic forms of **1b** (Figure 6, **A**), the three forms of **1j** exhibit very similar fluorescence dynamics. These time profiles could be well reproduced by the sum of two (**1j**) or three exponential functions (**1b**) convolved with the instrument response function; the resulting time constants are listed in Table 4. A component with a time constant greater than 4 **ns** and a relative amplitude smaller than 0.01 was attributed to impurities

present in very low concentrations (<0.1 %) and will not be further considered.

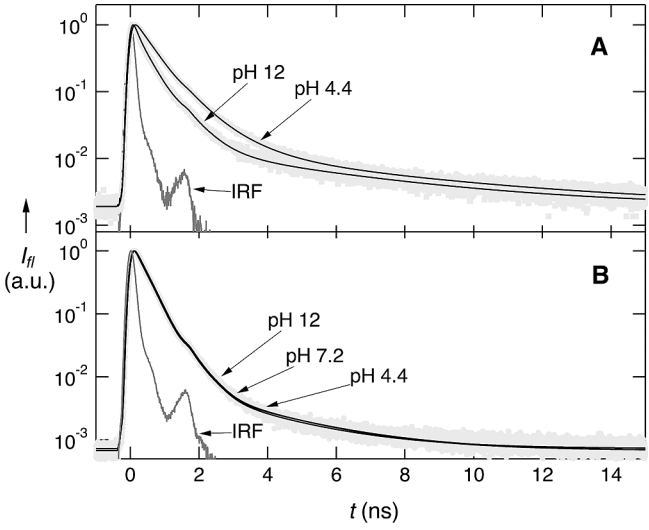


Figure 6. Fluorescence time profiles measured for (A) **1b** and (B) **1j** in water at various pH, instrument response function (IRF) and best fits (black).

The structures of the quinacridiniums **1**·H^+ are very similar to those of [4]heliceniums **2** investigated previously,[11d] which, because of the presence of an alkyl substituent on both N atoms, are not pH sensitive. Therefore a similar interpretation of the biphasic nature of the fluorescence decay of **1b** can be proposed, that is, the faster decay component is attributed to **1b** and the other is assigned to an aggregate. This explanation is supported by further TCSPC measurements on a solution of **1b** diluted by a factor two: the relative amplitude of the slower component was found to decrease from 0.19 to 0.11.

In the case of **1j**, the fluorescence of all three forms decays exponentially with the same time constant. No aggregate formation could be detected under either neutral or basic conditions, which can be explained by the presence of the polar and hydrophilic amino group, which effectively counteracts hydrophobic effects.

Compared with the non-pH-sensitive [4]helicenes **2**,[11d] the fluorescence quantum yields and lifetimes of **1b** and **1j** are smaller by a factor of around 4. The excited-state dynamics of **2** were found to be dominated by a non-radiative decay to the ground state, the efficiency of which increased with the hydrogen-bond-donating property of the solvent.[11d] Such hydrogen-bond-assisted non-radiative deactivation has been shown to be an efficient quenching mechanism for a large number of organic molecules in aqueous solutions.[24] The faster non-radiative decay found here for **1** could be explained by the presence of the unprotected nitrogen atom that most likely forms hydrogen bonds with water molecules. Comparing **1b** and **1j** (Table 4), the somewhat lower values of Φ_f and τ_{f1} for **1j** speak in favour of a higher efficiency of this non-radiative process because of the presence of the hydrophilic amino group.

Conclusions

A series of pH-sensitive [4]helical quinacridines **1** have been synthesized in two steps from a classical carbenium precursor using hydrazine (NH_2NH_2) for the introduction of a single nitrogen atom. This synthetic procedure is general, modular and highly tolerant to functional groups. A mechanistic rationale has been proposed for the facile N–N bond cleavage that seemingly occurs during the formation of the product.

Single enantiomers of the [4]helicenes were obtained by chiral stationary phase HPLC resolution and assignment of the absolute configuration was realized through a perfect comparison of the ECD spectra of the conjugated acids with those of known quinacridinium derivatives. Moreover, a high racemization barrier ($\Delta G^{\ddagger} = 30.7 \pm 4.0$ kcal mol^{-1} at 140 °C) was measured. This racemization barrier for **1f** is lower than that of [**2a**][BF_4], for which a rather high barrier ($\Delta G^{\ddagger} = 41.3$ kcal mol^{-1} at 200 °C) was measured. However, it remains slightly higher than that reported for the analogous derivative **5** ($\Delta G^{\ddagger} = 28.4$ kcal mol^{-1}, 28 °C).

These helical quinacridines are effective dyes that present interesting absorption and emission properties that can be modulated as a function of pH. Despite a weak fluorescence and relatively modest changes in the emissive properties upon protonation, the large difference in the absorption spectrum could be advantageously used to sense hydrophobic domains of proteins and other biological systems.

Experimental Section

General: Experimental procedures for the synthesis of the targeted [4]helical quinacridines **1a**–**k** are reported below. Characterization data and further protocols can be found in the Supporting Information.

General Procedures for the Synthesis of Cationic Quinacridines 1a–k

Approach 1: Hydrazine monohydrate (7.3 mL, 150 mmol, 25 equiv., 64–65% in water) was added to a solution of the corresponding acridinium salt **4** (6 mmol) in anhydrous DMF (30 mL) in red-tinted glassware. The reaction mixture was degassed with argon and then heated at 90 °C without light for 10 h. After complete consumption of the starting acridinium salt **4** (monitored by ESI-MS analysis), the purple reaction mixture was cooled to 20 °C. The crude product precipitated upon addition of a solution of 50% HBF_4 in water (ca. 80 mL). The solid was filtered, washed several times with water and then dissolved in CH_2Cl_2. Selective precipitation by addition of diethyl ether afforded the title green compounds.

Approach 2: The corresponding primary amine (15.68 mmol, 25 equiv.) was added to a solution of acridinium salt **4j** (300 mg, 627 μmol) in anhydrous DMF (3 mL) in red-tinted glassware. The reaction mixture was degassed with argon and then heated at 90 °C without light for 14 h. After complete consumption of starting acridinium salt **4j** (monitored by ESI-MS analysis), the purple reaction mixture was cooled to 20 °C. The crude product precipitated upon addition of a solution of 50% HBF_4 in water (ca. 10 mL). The solid was filtered, washed several times with water and then dissolved in CH_2Cl_2. Selective precipitation by addition of diethyl ether afforded the title green compounds.

Optical Resolution of Neutral [4]Helical Quinacridine 1f: The two enantiomers of racemic azahelicene **1f** differed significantly in their HPLC retention times on a Chiralcel IB column. Separation was therefore possible under semi-preparative conditions using a 1×25 cm column. Racemic diazahelicene **1f** (25 mg) was resolved by repeated HPLC separation using an Agilent 1100 Series instrument (hexane/2-propanol 6:4 + 0.1% ethanolamine, 0.6 mL/min flow rate, and 1.5 mg injections of the racemate in 900 μL of eluent). Evaporation of the solvents and trituration with diethyl ether afforded (+)-**1f** (10 mg, >99% *ee*) and (–)-**1f** (8 mg, 99% *ee*) as pink amorphous solids.

CCDC-1000626 (for **1e**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supporting Information (see footnote on the first page of this article): General remarks and analysis conditions; synthesis and data; ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS-ESI spectra; X-ray data for compound **1e**; resolution, enantiomeric purity determination, ECD spectra; racemization barrier determination.

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[17] The origin of the reduction will be discussed in the mechanism section.
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