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General One-Pot, Three-Step Methodology Leading to an Extended Class of *N*-Heterocyclic Cations: Spontaneous Nucleophilic Addition, Cyclization, and Hydride Loss

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A new class of phenanthridinium derivative has been isolated from the reaction of 2-bromoethyl-phenanthridinium bromide with a range of primary amines in excellent yields. The reaction pathway is unprecedented and proceeds via three cascade steps: nucleophilic attack of a primary amine on the iminium moiety of a heteroaromatic ring system and cyclization to form a five-membered ring, followed by hydride loss to yield a rearomatized dihydro-1*H*-imidazo[1,2-*f*]phenanthridinium derivative. A range of NMR phase transfer experiments were carried out to elucidate the mechanistic pathway, and the methodology has been further developed by means of a biphasic system using *N*-bromosuccinimide as a co-oxidizing agent. The method has also been extended to other *N*-heterocyclic cation derivatives such as quinolinium and quinazolinium.

Introduction

Heterocyclic rings are present as fundamental components in the skeleton of more than half of the biologically active compounds produced by nature.[1] With this in mind there have been great efforts to discover and optimize new reactions that will facilitate the construction of heterocycles.[1–3] A facile route to a new family of heterocycles opens the possibility of finding further types of biologically active units that can be used in the generation of libraries of compounds. Also, improvements in screening methods in the pharmaceutical industry have encouraged the development of highly flexible synthetic procedures. Therefore, new methodologies that increase the structural complexity while decreasing the number of synthetic steps are very attractive. Efficient syntheses leading to *N*-heteroaromatic cations are especially interesting as these moieties can have a high affinity for DNA.[4] In this respect, molecules containing a phenanthridinium core are one important subset of heteroaromatic cations[5] with applications as drugs,[6] DNA targeting agents,[7] dyes,[8] and probes.[9]

Herein we report the discovery of a one-pot, three-step system involving the reaction of a range of primary amines with 2-bromoethyl-phenanthridinium bromide and leading to an unprecedented class of **d**ihydro-**i**midazo-**p**henanthridinium (DIP) compounds, **6a−l**, that exhibit DNA affinity and high cytotoxic activity.[10] The first in the new class of DIP compounds was discovered serendipitously while trying to functionalize the side chain of 2-bromoethyl-phenanthridinium bromide by substitution with a primary amine (see Scheme 1, Path B). Rather than the expected reaction, it was found that the α position of the phenanthridinium moiety had been attacked and that the system had undergone an oxidation step forming a quaternary ammonium salt; further studies revealed the new class of DIP compounds and the generality of the reaction system that is the subject of this paper. Further, the intricate mechanism of this tandem reaction is discussed (synthetic method A) and the application of this synthetic methodology to other *N*-heteroaromatic systems is investigated. Finally, the methodology is developed via the use of a co-oxidizing agent in a biphasic system (method B).

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SCHEME 1.   Method A: Two Possible Reaction Pathways Leading to Framework 6
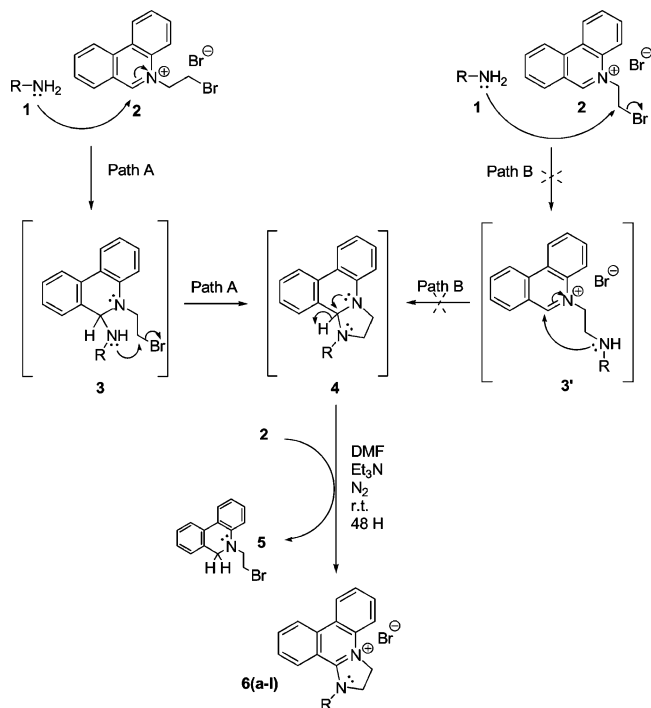
Results and Discussion

Method A. The electrophilic starting material **2** is easily prepared by reaction of phenanthridine with an excess of 1,2-dibromoethane. The subsequent one-pot reaction leads to the DIP cytotoxic compounds **6a**−**l** presented in Table 1. Note that the reaction is general for all types of primary amine, maintains the stereochemistry, and allows the construction of molecules with high structural complexity in a single synthetic step. The reaction could proceed via two different pathways: (i) a route involving nucleophilic addition of the primary amine at the α position of the phenanthridinium derivative **2**, followed by a five-membered ring cyclization and oxidative hydride loss (Path A, Scheme 1), or (ii) a route involving nucleophilic substitution of the primary amine on the ethyl-bromide chain of **2**, followed by a five-membered ring cyclization and oxidation step via hydride loss (Path B, Scheme 1).

The isolation and characterization of molecule **5** (Scheme 1) is in accordance with the proposed in situ oxidation step. Note that this process does not interfere with the purification of **6**, as byproduct **5** remains in solution during precipitation of the final product. Furthermore, because of the high yields obtained with the primary amines studied, the in situ oxidation step appears to be irreversible.[11] Several driving forces can explain the efficiency of this redox reaction. First, the positive charge on the quaternary ammonium ion in **6** is stabilized by the mesomeric donor effect of the tertiary amine. This idea is supported by single-crystal X-ray analysis[12] of [$C_{22}H_{19}N_2O$]Br (**6h**), which clearly shows conjugation between the two nitrogen atoms, see Figure 1. The shortening of the carbon−nitrogen bond N2−C33 com-

pared to N2−C31 and N2−C41 indicates partial double bond character. The similar bond lengths N2−C33 and C33−N1 indicate that the bonding electron density is shared evenly between these three atoms. Second, it can be assumed that the dihydro-imidazole component of **6** has less steric strain than the imidazolidine moiety of **4**. Thus the release of steric strain resulting from hydride loss is a significant driving force. Finally, the central heterocycle regains aromatic character during reoxidation and so restores conjugation between the two adjacent aromatic cycles.

Although the redox chemistry of *N*-heterocyclic hydride donors derived from acridine, quinoline, pyridine, and phenanthridine is well established,[13] there appears to be no reference to a hydride transfer system such as that proposed between **4** and **2** (Scheme 1). In the published systems, the equilibrium tends to be driven by destabilizing effects on the heteroaromatic cation, which enhances its oxidizing power. In this case, the equilibrium is driven to the formation of **6** by mesomeric stabilization of product **6** rather than by electron-withdrawing destabilization of starting material **2**.

Intermediate **4** (Scheme 1) was isolated (**4d**, using isopropylamine) via a phase transfer reaction in an NMR tube whereby the reaction is initiated in a biphasic solvent system of D_2O and $CDCl_3$ (1:1).[14] Compound **4d** was characterized in the organic layer because of its insolubility in aqueous media, thus preventing subsequent hydride transfer with molecule **2**; NMR studies reveal the singlet corresponding to the hydride leaving position is located at 4.81 ppm (see Supporting Information). To form intermediate **4**, the five-membered ring formation seen in Path A would involve a highly favorable 5-*exo-tet* cyclization, whereas Path B would occur via an unfavorable 5-*endo-trig* cyclization.[15] Therefore, studies were undertaken to elucidate whether Path A or Path B dominates during the ring closure.

To Examine Path A. Investigations into the formation of **4** led to the characterization of intermediate **3l** using a hindered primary amine (Scheme 2). This hindrance was thought to explain the low yield of **6l** (Table 1). An NMR phase transfer reaction was conducted with (*R*)-(+)-1-(4-methoxyphenyl)ethylamine acting as both the nucleophile and base. The α addition yields **3l** without further cyclization to **4l** as the proton of the sterically crowded quaternary amine of intermediate **3l′** cannot be

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(11) Electrochemical experiments undertaken in acetonitrile show that the oxidation of molecule **4** into **6** is irreversible.

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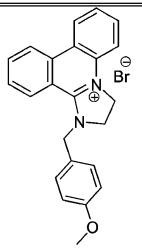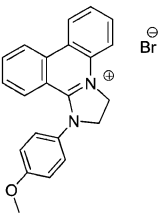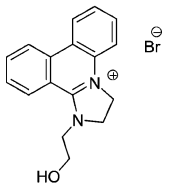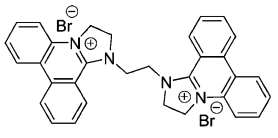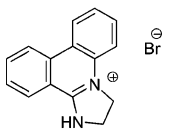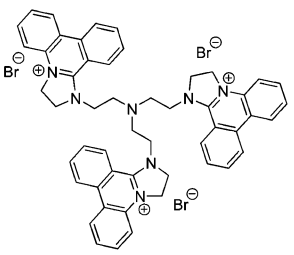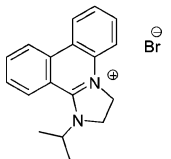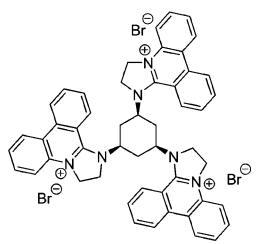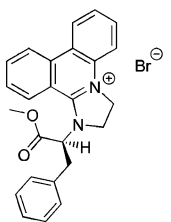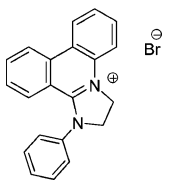
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(14) These types of hydride donor intermediates can only be isolated under these conditions because of their unstable nature. This trapping technique is set up by placing the reaction mixture (in D_2O) into the NMR tube on top of a second immiscible, more dense solv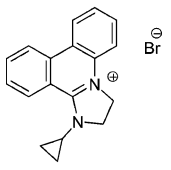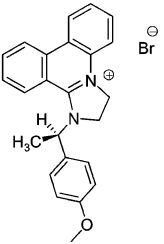ent, in this case $CDCl_3$. Shaking of the tube causes the intermediate, which is much more soluble in $CDCl_3$, to be transferred to the $CDCl_3$ layer and allows the spectrum of the intermediate to be recorded. We believe this approach is unprecedented.

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TABLE 1. DIP Frameworks Obtained via Method A

Entry	Structure	Primary amine **1(a-l)**	Yield (%) (based on amine)	Entry	Structure	Primary amine **1(a-l)**	Yield (%) (based on amine)
6a		4-Methoxybenzylamine	95	**6h**		4-Methoxyaniline	74
6b		Ethanolamine	98	**6i**		Ethylene diamine	98
6c		Ammonia	61	**6j**		*tris*(2-Aminoethyl)amine	95
6d		Isopropylamine	82				
6e		Cyclopropylamine	78	**6k**		*cis*-1,3,5-Triaminocyclohexane	91
6f		L-methoxycarbonyl-phenylalanine	63	**6l**		R-(+)-1-(4-Methoxyphenyl)-ethylamine	22
6g		Aniline	73				

removed by the hindered base. For the same steric reasons, triethylamine is not able to trigger the cyclization process. However it was observed that the use of ammonia, obtained in situ by adding ammonium chloride

to the previous triethylamine solution, appears small enough to gain access to the sterically demanding complex, deprotonating the quaternary ammonium salt and leading to the cyclized molecule **4l**.
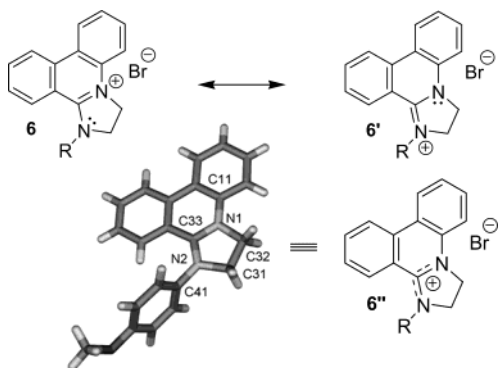
FIGURE 1. Representation of the molecular structure[12] of compound **6h** along with a schematic depiction of the delocalization of the positive charge between both nitrogen centers. Note the lack of planarity between the aromatic groups. Selected bond lengths [Å]: N1−C11 1.392(3), N1−C33 1.342-(3), N1−C32 1.473(3), N2−C33 1.331(3), N2−C41 1.425(3), N2−C31 1.477(3).

Further evidence to differentiate intermediate **3l** from molecule **4l** is given by the addition of bromine, leading to products **7** and **6l**, respectively (Scheme 2).

To examine the α addition step leading to molecule **3**, the bromo leaving group of the side chain of molecule **2** was replaced with nonleaving fluoro and hydroxy groups (**9a** and **9b**, respectively) to prevent cyclization (Scheme 3). The electrophilic nature of the aromatic α positions of **9a** and **9b** were assumed to be similar to that of molecule **2** because of the similar chemical shift of their α position proton in ^{1}H NMR spectroscopy. It was found that reaction of **9a** and **9b** with isopropylamine leads to molecules **10a,b**, and reaction with aniline leads to **11a,b**, characterized in the CDCl$_3$ layer of the NMR phase transfer system.

It is worth noting that reactions involving α addition to a phenanthridinium moiety have been reported with sulfur-based nucleophiles,[16] carbanions,[17] and alcohols.[18] In these cases, the reoxidation step does not occur, possibly because there is insufficient mesomeric stabilization to promote the formation of the positive charge.

To Examine Path B. Investigations into this potential pathway were accomplished by examining the 5-*endo-trig* cyclization process leading from **3′** to **4** (Scheme 1). Isolated from a biphasic system, the imidazolidine ring of **4d** was protonated, leading to **12d** after oxidative opening of the five-membered ring, rearomatization being the driving force (Scheme 4).[17] Treatment of **12d** with NaHCO$_3$ leads to the stable molecule **3d′**. Note that the deprotonation reaction was once again carried out using an NMR phase transfer procedure to avoid intermolecular α addition during the concentration stage of a standard workup. Molecule **3d′** does not undergo intramolecular cyclization to yield **4d** and remains stable for several days, although intermolecular α addition is evident after 1 week. Treatment of **3d′** with the stronger base triethylamine leads to the reversible addition of a hydroxide (pseudo-base **13d**), which transfers to the

CDCl$_3$ layer in the NMR experiment. Although **4d** and **13d** have relatively similar chemical shifts, the lower TLC Rf value of **13d**, as well as its sensitivity to ninhydrin, is in accordance with the presence of a secondary amine.

The feasibility of the reaction leading to **3′g,h** (Scheme 1) with aromatic amines was also investigated. No substitution reaction occurred under the same conditions using aniline or *p*-methoxyaniline with 1,2-dibromoethane, which was assumed to have reactivity similar to that of the bromo-ethyl side chain of molecule **2**. Therefore, the formation of compounds **6g,h** cannot be explained by the first substitution step of Path B. From this evidence we can eliminate Path B and confidently propose Path A as the most likely mechanistic route leading to molecule(s) **6g,h**.

Finally, the dependence of the final hydride loss on the presence of the five-membered ring was investigated. Having previously established that a five-membered ring is not formed in the reaction of isopropylamine with molecule **9b** (a hydroxy analogue of starting material **2**; see Scheme 3), we found that the oxidation step does not occur, possibly because the rate of the oxidation reaction is much slower than α elimination back to **9b**. Under our standard experimental conditions, starting material **9b** was recovered almost quantitatively (Scheme 5A). Therefore, it is proposed that the formation of the five-membered ring in intermediate **4** prevents the reverse reactions and allows the slow in situ oxidation step yielding compound **6** to take place (Scheme 5B).

Other Heterocyclic Systems. To explore the application of this methodology to other aromatic systems, the synthesis of a reported 2,3-dihydro-1*H*-imidazo[1,2-*a*]quinolinium bromide derivative[19] was investigated with the view of simplifying the synthesis of existing molecules. Product **15a** (Scheme 6) was isolated in a 70% yield by employing our one-pot reaction methodology.

Reaction with *p*-methoxyaniline leads to the final product **15b** (Scheme 6). The low yield was not improved by heating or by the use of a stronger oxidizing agent. It was therefore proposed that steric effects were of importance (Figure 2). The reaction of molecule **14** with the less nucleophilic amine aniline leads to the nonoxidized molecule **14′c**. Contrary to the phenanthridinium-based derivatives, rearomatization of the quinolinium-based derivatives does not occur in this case. This can be explained in terms of the electron-withdrawing effects undergone by the heterocyclic systems. The phenanthridinium-based derivatives are not subject to withdrawing effects from the phenyl group of **6g,h**, as steric interactions prevent the two ring systems from being coplanar (Figure 2). This is confirmed by the crystal structure of [C$_{22}$H$_{19}$N$_2$O]·Br (**6h**) (Figure 1). The phenyl ring of this phenanthridinium derivative is therefore removed from the conjugated system, and the nitrogen lone pair is used in the mesomeric stabilization of the quaternary ammonium charge rather than being withdrawn into the phenyl ring. The smaller quinolinium derivatives do not effect any steric restrictions that prevent conjugation between the phenyl ring and the quinolinium system, as shown in Figure 2. The aromatic moieties of molecule **14′b** therefore exhibit significant withdrawing effects on the two nitrogen atoms, making their electrons less available to trigger the hydride loss. This withdrawing

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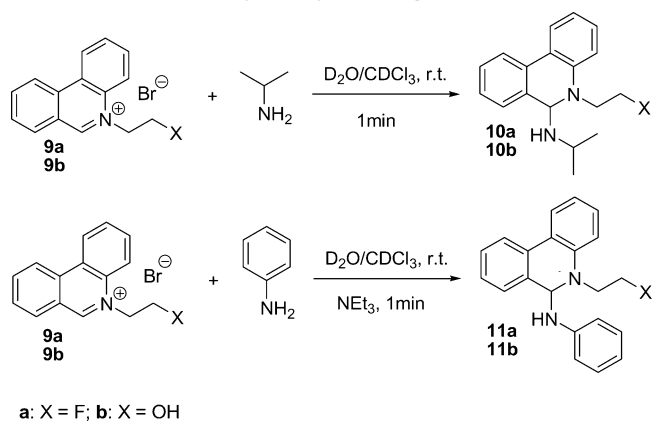
(17) Wimmer, T. L.; Day, F. H.; Bradsher, C. K. *J. Org. Chem.* **1975**, *40* (9), 1198−1201.

(18) Acheson, R. M.; Bond, G. J. F. *J. Chem. Soc.* **1956**, 246−250.

SCHEME 2. Isolation of Intermediate 3l
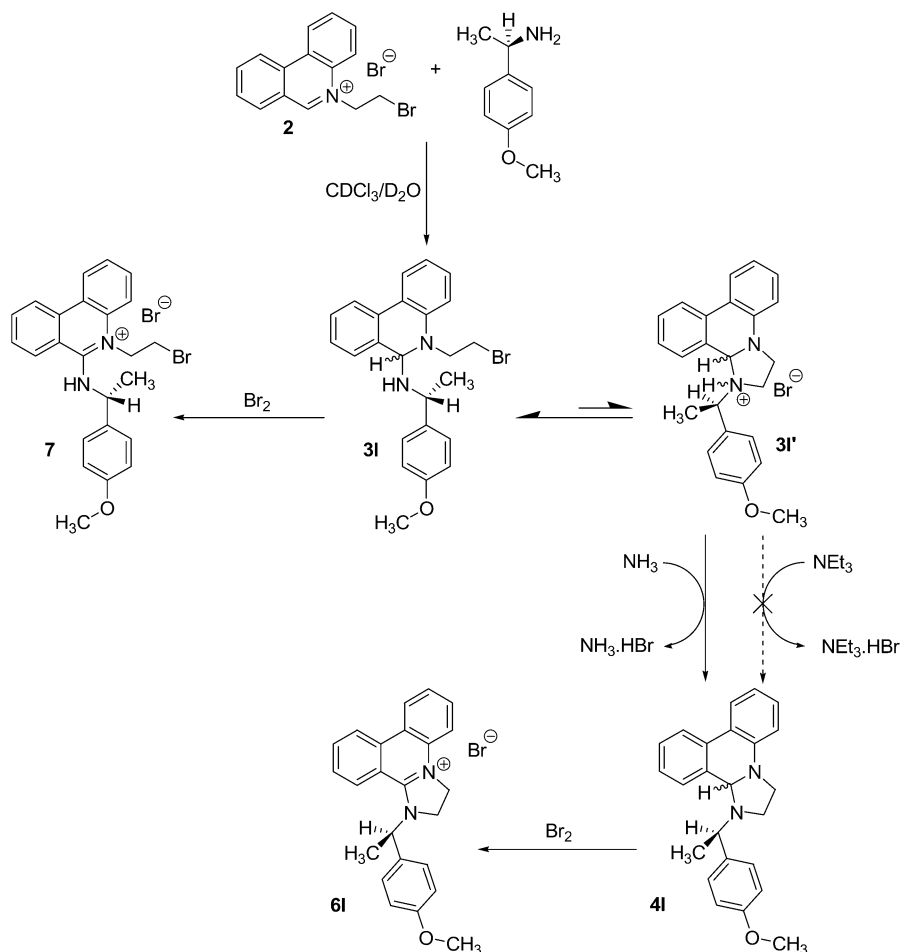
SCHEME 3. NMR Phase Transfer Experiment with Fluoro and Hydroxy Analogues of Molecule 2

a: X = F; b: X = OH

SCHEME 4. Investigation of the 5-*endo-trig* Cyclization of Path B[a]
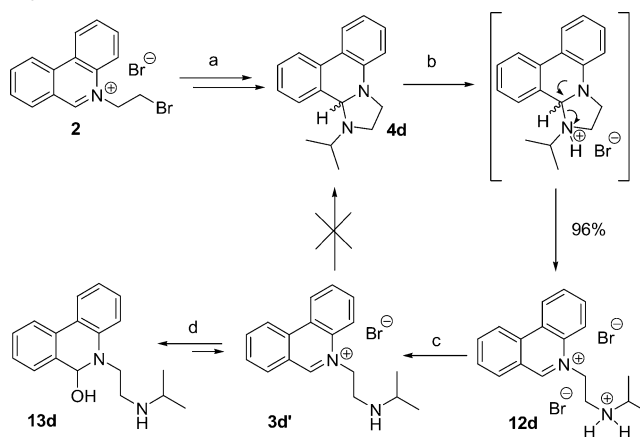
[a] Reagents and conditions: (a) water/chloroform, isopropyl-amine, NaHCO₃, rt, N₂, 3 h. (b) HBr 48%. (c) NMR experiment, NaHCO₃. (d) triethylamine.

effect also lowers mesomeric charge stabilization of the quaternary ammonium product.

Method B. Although the presented tandem reaction (Method A) is simple and effective, it consumes a second equivalent of the starting heteroaromatic cation as a hydride acceptor in the final oxidization step. Intermediate **4** (Scheme 1) can be isolated in the organic phase of a biphasic system and then further reacted in one pot with a co-oxidizing agent such as *N*-bromosuccinimide (NBS) to obtain product **6** (Scheme 7A). This is a simple, efficient procedure that allows recovery of the pure

product by filtration. This methodology can be applied to quinazolinium derivative **16** (Scheme 7B). Note that for steric reasons the N-alkylation of quinazoline only occurs on position 3, leading to starting material **16**. Also, the first nucleophilic addition occurs selectively at position 4 of the quinazolinium starting material **16**, as α addition on position 2 would lead to an anti-aromatic

SCHEME 5. Importance of the Five-Membered Ring Formation

A)

B)
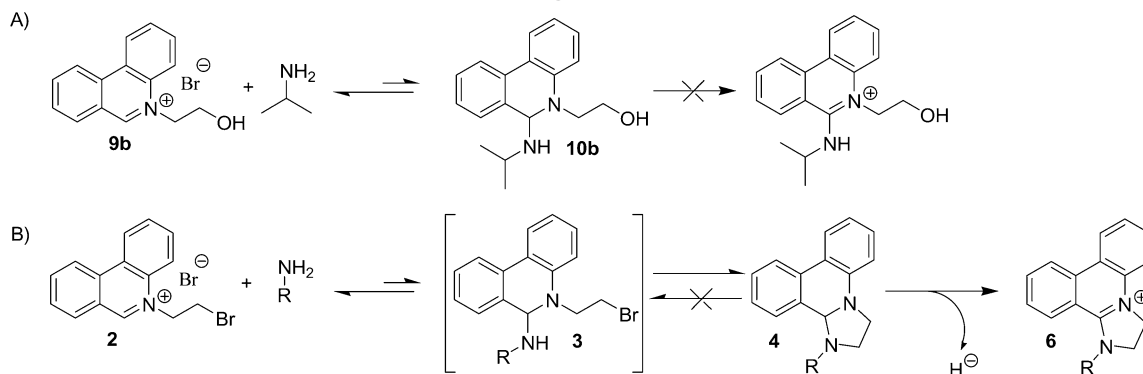
SCHEME 6. Tandem Reaction (Method A) Using a Quinolinium Derivative[a]

15a: R = methoxybenzyl; 70%
15b: R = p-methoxyaniline; 54%
14'c: R = phenyl; 33%
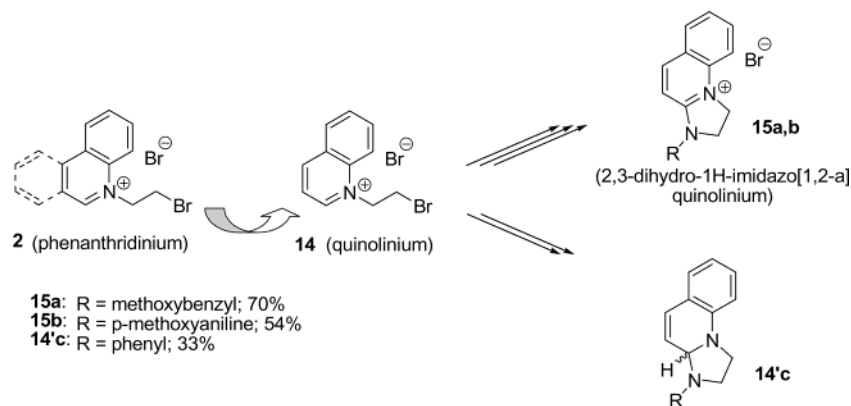
[a] Reagents and conditions: primary amine, DMF, triethylamine, N$_2$, rt, 48 h.

FIGURE 2. Molecular models of the *p*-methoxyaniline derivatives of phenanthridinium **6h** (left) and quinolinium **15b** (right) showing the differences in hydrogen proximity (marked in black and labeled) when the two aromatic systems are restricted to being coplanar.

intermediate. The regioselectivity of both steps has been confirmed by NOE NMR experiments and single-crystal X-ray crystallography of **17** (data not shown).
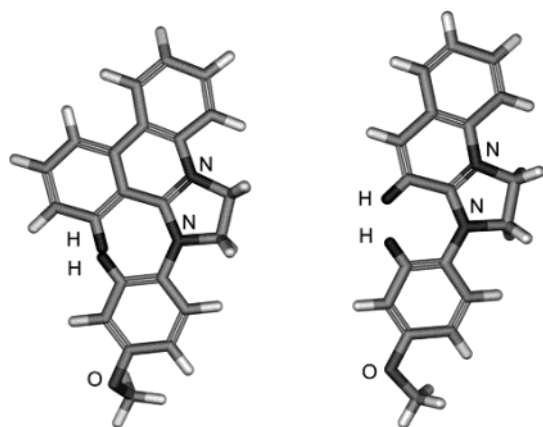
It was found that Method B could not be extended to the synthesis of quinolinium derivatives. The hydride donor **14′** disproportionates in the organic layer before NBS can be added, leading to the oxidation product **15a** and the reduction product **14″** (Scheme 8). The double bond of the heterocycle moiety of **14′** (shown in bold in Scheme 8) is more labile, as it does not belong to an

aromatic system as in the case of phenanthridinium intermediates **4(a−l)** (Scheme 1) or does not undergo mesomeric stabilization as in the case of the quinazolinium intermediate (Scheme 7B). Similar disproportionation reactions between dihydro-thiazolo-isoquinoline derivatives have been reported.[17]

It was also found that Method B is limited to water-soluble amines because of the biphasic reaction conditions. The previously discussed DMF monophasic Method A allows efficient synthesis of dimeric and trimeric molecules via polyamines (cf. molecules **6i−k** in Table 1), whereas a biphasic methodology is not suitable with polyamines because of the production of water-insoluble intermediates that remain in the organic layer and prevent further reaction. A monophasic protocol involving a co-oxidizing agent is under investigation for the synthesis of polymeric systems.

Although methodologies have been reported for the synthesis of a number of dihydro-imidazo-pyridinium frameworks (for instance, dihydro-imidazo-benzo[*f*]quinolinium[20] and dihydro-imidazo-quinolinium[19] derivatives), they tend to be more complicated multistep procedures that lead to poor overall yields. Moreover, each of these procedures requires a hydroxide at the α position of the *N*-heterocycle. Also note that the dihydro-imidazole moiety of these derivatives is either nonfunctionalized[20] or functionalized at the beginning of the multistep synthetic route,[19] rendering the derivatization difficult.

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(20) Yamazaki, T. *J. Heterocycl. Chem*. **1979**, *16*, 517−523.

SCHEME 7. Method B: Modified Procedure Using NBS on Phenanthridinium Derivative (A) and Quinazolinium Derivative (B)[a]

A)

B)

R = p-methoxybenzyl
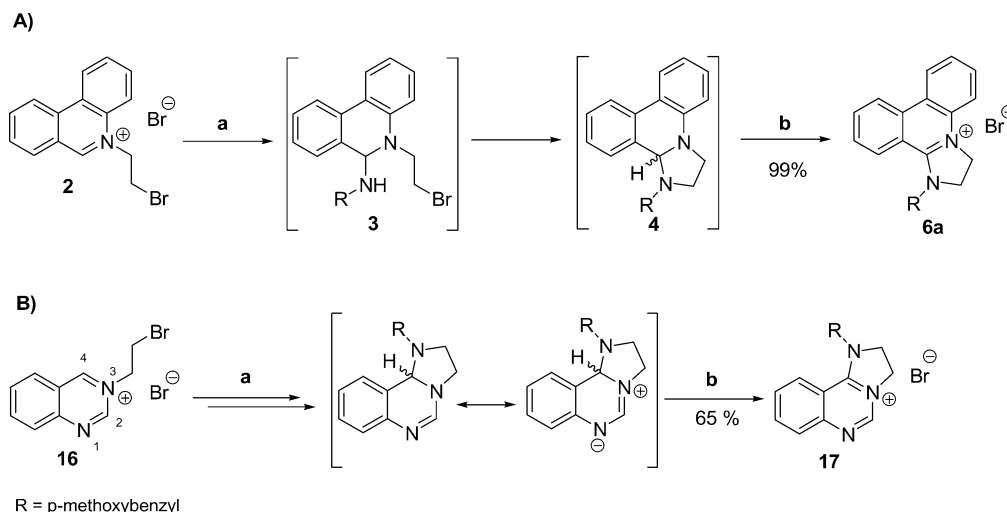
[a] Reagents and conditions: (a) R-NH$_2$, NaHCO$_3$, ethyl acetate/water, rt, N$_2$, 3 h. (b) Aqueous wash, NBS, rt, N$_2$, overnight in the dark.

SCHEME 8. Disproportionation of Quinolinium Derivatives during Method B[a]

R = p-methoxybenzyl
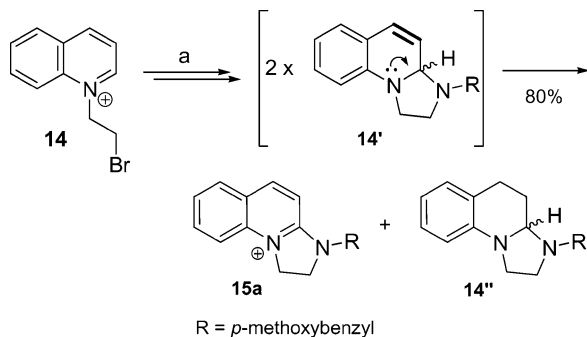
[a] Reagents and conditions: (a) R-NH$_2$, NaHCO$_3$, ethyl acetate/water, rt, N$_2$, 3 h.

Conclusions

In summary, we have shown that combination of a primary amine with 2-bromoethyl-pyridinium derivatives (phenanthridinium, quinolinium and quinazolinium) results in a novel, generic and effective method for the synthesis of dihydro-imidazo-pyridinium (DIP) compounds. The mechanism of reaction is fully understood in the case of the phenanthridinium derivatives and has allowed the development of a biphasic protocol in the case of phenanthridinium and quinazolinium derivatives. It has been shown that our methodology can use a range of primary amines and heteroaromatic systems as starting materials. As there are examples of biologically active DIP frameworks derived from phenanthridine,[10] quinoline,[19] isoquinoline,[22] and quinazoline, this novel one-pot procedure allows a great deal of synthetic flexibility and offers the possibility of synthesizing a large library of potentially bioactive compounds. This reaction system opens up a vast number of possibilities. As such, we are presently examining chiral nonenzymatic redox trans-

formations using **4**,[23–25] as well as application of this tandem reaction for the synthesis of six-membered ring tetrahydro-pyrido-pyridinium via 3-bromopropyl-pyridinium derivatives.

Experimental Section

2-Bromoethyl-phenanthridinium Bromide (2). Phenanthridine (5.44 g; 30.4 mmol) was dissolved in 1,2-dibromoethane (114.2 g; 52 mL; 608 mmol) and stirred at 100 °C for 5 days. During that time, any precipitate formed was filtered. After each filtration, the precipitate was rinsed with an additional 5 mL of 1,2-dibromoethane, and the mother liquor was stirred at 100 °C until the next filtration. The reaction was complete when no more precipitate formed. The precipitates were combined and washed thoroughly with ethyl acetate to give **2** (7.92 g; 21.6 mmol) as a beige powder in a 95% yield: mp 234–235 °C (dec); ^{1}H NMR (D$_2$O, 400 MHz) δ 9.81 (s, 1H), 8.72 (d, 1H, J = 7.2 Hz), 8.63 (d, 1H, J = 7.2 Hz), 8.37 (d, 1H, J = 7.2 Hz), 8.26 (d, 1H, J = 7.2 Hz), 8.18 (t, 1H, J = 7.2 Hz), 7.98 (t, 1H, J = 7.2 Hz), 7.90 (m, 2H), 5.37 (t, 2H, J = 5.8 Hz), 4.05 (t, 2H, J = 5.8 Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 155.27 (CH), 139.03 (CH), 135.59 (C), 133.18 (CH), 132.78 (C), 132.58 (CH), 130.85 (CH), 130.72 (CH), 126.57 (C), 125.13 (CH), 123.32 (C), 123.00 (CH), 118.91(CH), 58.87 (CH$_2$), 29.41(CH$_2$); IR (KBr, cm^{-1}) 2947 (w), 1620 (m), 763 (s), 717 (m); MS (ES) 288.1 (M $-$ Br) (100), 206.2 (8). Anal. Calcd for C$_{15}$H$_{13}$NBr$_2$: C, 49.32; H, 3.59; N, 3.84. Found: C, 49.15; H, 3.48; N, 3.76.

[5-(2-Bromo-ethyl)-5,6-dihydro-phenanthridin-6-yl]-[1-(4-methoxy-phenyl)-ethyl]-amine (3l). In an NMR tube, compound **2** (38 mg; 0.103 mmol) was dissolved in D$_2$O (0.6 mL). CDCl$_3$ (0.6 mL) was added followed by (R)-(+)-1-(4-methoxyphenyl)ethylamine (15.65 mg; 0.103 mmol) used as a reactant and as a base. The solution was shaken energetically for 1 min to allow the phase transfer process to occur. ^{1}H and ^{13}C NMR spectra of the organic layer were taken, characterizing **3l**. MS spectroscopy does not show the molecular peak, as the cyclization seems to occur inside the spectrometer, but one of the peaks clearly shows the presence of the bromo-ethyl side chain of one of the fragments. ^{1}H NMR (CDCl$_3$, 400 MHz)

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δ 8.61 (d, 1H, J = 8.0 Hz), 8.42 (d, 1H, J = 8.0 Hz), 8.37 (d, 1H, J = 8.0 Hz), 8.03 (t, 1H, J = 8.0 Hz), 7.7 (m, 3H), 7.57 (t, 1H, J = 8.0 Hz), 7.36 (d, 2H, J = 7.2 Hz), 6.96 (d, 2H, J = 7.2 Hz), 6.02 (q, 1H, J = 6.8 Hz), 5.37 (m, 1H), 4.85 (m, 2H), 4.39 (s, 1H), 4.16 (m, 1H), 3.82 (s, 3H), 2.05 (d, 3H, J = 6.8 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 159.97 (C), 153.33 (C), 144.62 (C), 136.20 (C), 135.33 (CH), 132.88 (C), 132.04 (CH), 129.12 (CH), 127.84 (CH), 125.91 (CH), 124.23 (CH), 123.39 (CH), 122.57 (CH), 120.44 (C), 116.39 (CH), 114.96 (CH), 112.10 (CH), 58.07 (CH$_3$), 55.45 (CH), 47.23 (CH$_2$), 45.93 (CH$_2$), 19.71 (CH$_3$). MS (FAB) 357.3 (M − Br) (30), 288.1 (12), 287.1 (2), 286.1 (12), 223.2 (10), 206.1 (12), 180.1 (30), 135.1 (100), 102.4 (25).

1-Isopropyl-1,2,3,12b-tetrahydro-imidazo[1,2-*f*]phenanthridine (4d). In an NMR tube, **2** (10 mg; 0.027 mmol) was dissolved in D$_2$O (0.6 mL). CDCl$_3$ (0.6 mL) was added followed by isopropylamine (2.3 μL; 1.60 mg; 0.027 mmol) used as a reactant and as a base. The NMR tube was shaken energetically for 1 min to allow the phase transfer process to occur. ^{1}H and ^{13}C NMR spectra were taken of the CDCl$_3$ layer and the organic layer was then isolated for MS and IR analysis. R_f = 0.5 in ethyl acetate; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.77 (d, 1H, J = 7.8 Hz), 7.74 (d, 1H, J = 7.2 Hz), 7.47 (d, 1H, J = 6.4 Hz), 7.35 (m, 2H), 7.25 (d, 1H, J = 7.6 Hz), 6.92 (t, 1H, J = 7.6 Hz), 6.73 (d, 1H, J = 7.8 Hz), 4.73 (s, 1H), 3.47 (m, 1H), 3.25 (m, 4H), 1.25 (d, 3H, J = 6.4 Hz), 1.12 (d, 3H, J = 6.4 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 144.34 (C), 135.76 (C), 132.00 (C), 129.34 (CH), 127.88 (CH), 127.66 (CH), 124.13 (CH), 123.85 (CH), 123.39 (C), 123.32 (CH), 119.07 (CH), 113.45 (CH), 76.72 (CH), 51.68 (CH), 46.86 (CH$_2$), 45.07 (CH$_2$), 22.63 (CH$_3$), 17.21 (CH$_3$); solution IR with KBr windows (cm^{-1}) 3680 (m), 3022 (s), 2968 (w), 2436 (w), 2398 (s), 1602 (w), 1522 (m), 1480 (m), 1426 (m), 1387 (w), 1136 (w), 1219 (s); MS (CI) 265.2 (M + 1) (20), 195.1 (5), 180.1 (12), 127.1 (10), 119.1 (32), 102.2 (22), 89.1 (100).

Synthesis of [5-(2-Bromo-ethyl)-5,6-dihydro-phenanthridin-6-yl]-[1-(4-methoxy-phenyl)-ethyl]-amine (4l). The D$_2$O layer of the NMR tube containing **3l** was removed, and a clean D$_2$O layer was added followed by an excess of TEA (40 μL; 0.28 mmol). The solution was shaken energetically for 1 min, and a ^{1}H NMR spectrum of the CDCl$_3$ solution was taken characterizing the unreactive mixture of starting material **3k** and the excess of TEA. Ammonium chloride (15 mg; 0.28 mmol) was added, and the NMR tube shaken vigorously for 1 minute. ^{1}H and ^{13}C NMR and mass spectra of the organic layer were taken, characterizing **4l**: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.45 (d, 1H, J = 8.0 Hz), 8.19 (d, 2H, J = 8.0 Hz), 7.69 (t, 2H, J = 8.0 Hz), 7.51 (t, 1H, J = 8.0 Hz), 7.37 (t, 1H, J = 8.0 Hz), 7.22 (d, 1H, J = 8.0 Hz), 7.17 (d, 2H, J = 6.4 Hz), 6.76 (d, 2H, J = 6.4 Hz), 4.36 (m, 1H), 4.31 (s, 1H), 3.75 (s, 3H), 3.70 (q, 1H, J = 6.8 Hz), 2.86 (m, 1H), 2.76 (m, 1H), 1.27 (d, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 161.67 (C), 158.59 (C), 137.41 (C), 137.15 (C), 133.64 (C), 132.51 (CH), 129.55 (CH), 128.83 (CH), 127.96 (CH), 127.86 (CH), 125.42 (CH), 123.39 (CH), 122.40 (CH), 121.60 (CH), 119.45 (C), 115.15 (CH), 113.83 (CH), 57.53 (CH$_3$), 55.27 (CH), 44.58 (CH$_2$), 42.98 (CH$_2$), 30.96 (CH), 24.41 (CH$_3$); MS (FAB) 357.3 (M + 1) (100), 341.3 (10), 307.3 (5), 289.2 (4), 221.2 (15), 180.1 (15), 135.1 (70), 105.3 (4).

5-(2-Bromo-ethyl)-5,6-dihydro-phenanthridine (5). During the preparation of **6a**, the mother liquor from the DMF/ether (1:5) solution was kept and washed thoroughly with water. The organic layer was then washed with brine and dried over MgSO$_4$. The solvent was removed under vacuum to give a dark residue. Column chromatography (silica, DCM) afforded **5** (140 mg; 0.485 mmol) as a beige powder in a 50% yield. R_f = 0.75 in 100% ethyl acetate; mp 99−100 °C; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.64 (d, 1H, J = 7.60 Hz), 7.60 (d, 1H, J = 7.60 Hz), 7.22 (t, 1H, J = 7.60 Hz), 7.13 (t, 2H, J = 7.60 Hz), 7.01 (d, 1H, J = 7.60 Hz), 6.77 (t, 1H, J = 7.60 Hz), 6.62 (d, 1H, J = 7.60 Hz), 4.27 (s, 2H), 3.64 (t, 2H, J = 7.80 Hz), 3.44 (t, 2H, J = 7.80 Hz); ^{13}C NMR (CDCl3, 100 MHz) δ 145.02 (C), 132.71 (C), 132.19 (C), 129.68 (CH), 128.55 (CH), 128.22 (CH), 125.96 (CH), 124.44 (CH), 124.22 (C), 123.59 (CH), 119.19 (CH),

112.51 (CH), 53.38 (CH$_2$), 53.26 (CH$_2$), 27.78 (CH$_2$); IR (KBr, cm^{-1}) 3429 (s), 2924 (w), 1716 (w), 1628 (s), 1601 (s), 1525 (w), 1493 (s), 1442 (s), 1340 (m), 1290 (m), 1269 (s), 1196 (s), 1022 (m), 758 (s), 725 (m), 615 (m); MS (FAB) 289 (M + H) (100), 222.1 (7), 194.1 (35), 180.1 (22), 166.1 (6), 152.1 (4), 107.2 (2), 85.7 (1), 58.1 (7). Anal. Calcd for C$_{15}$H$_{14}$NBr: C, 62.51; H, 4.89; N, 4.86. Found: C, 62.30; H, 4.96; N, 4.75.

General DMF Monophasic Procedure for the Synthesis of Molecules 6(a−h), 6l, 15a,c, and 17 (Method A). 2-Bromo-ethyl-pyridinium bromide derivative (**2**, **14**, or **17**) (1.9 mmol) was suspended in DMF (20 mL). Primary amine **1a−h** (0.95 mmol) and TEA (530 μL; 3.8 mmol) were added successively to the stirred solution. After stirring for 48 h at room temperature under nitrogen, the final product and TEA hydrobromide salt were precipitated from the solution with diethyl ether (100 mL) and recovered by filtration. The precipitate was washed thoroughly with diethyl ether and triturated with 1 mL of water to remove the TEA salt, yielding, after drying, the corresponding dihydro-imidazo-pyridinium bromide derivative (**6a−h**), **6l**, **15a,c**, or **17**.

General Biphasic Procedure using NBS as a Co-oxidizing Agent for the Synthesis of 6a and 17 (Method B). A 10% NaHCO$_3$ aqueous solution (20 mL) was prepared and ethyl acetate (40 mL) added along with 3 drops of TEA. The biphasic solution was cooled to 0 °C and the primary amine (2.1 mmol) added followed by 2-bromo-ethyl-pyridinium derivative **2** or **17** (1.9 mmol). The reaction mixture was stirred under nitrogen at room temperature for 3 h. The organic layer was separated, washed with water (2 × 40 mL), and placed into a round-bottom flask covered with aluminum foil. *N*-Bromosuccinimide (374 mg; 2.1 mmol) was added to the stirred solution at 0 °C, and the reaction mixture stirred at room temperature for 3 h in the dark. The precipitate was filtered and washed with diethyl ether to yield the corresponding DIP framework **6a** or **17**. More details and characterization data for the products and intermediates can be found in Supporting Information.

1-(4-Methoxy-benzyl)-2,3-dihydro-1*H*-imidazo[1,2-*f*]-phenanthridin-4-ylium Bromide (6a). **6a** was obtained as an white off powder in a 95% yield (380 mg; 0.9 mmol; Method A) and 99% yield (792 mg; 1.88 mmol; Method B): mp 245−246 °C (dec); ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.52 (d, 1H, J = 8.2 Hz), 8.36 (d, 1H, J = 8.2 Hz), 8.21 (d, 1H, J = 8.2 Hz), 7.93 (t, 1H, J = 8.2 Hz), 7.69 (t, 1H, J = 8.2 Hz), 7.56 (t, 1H, J = 8.2 Hz), 7.51 (m, 2H), 7.32 (d, 2H, J = 8.2 Hz), 6.91 (d, 2H, J = 8.2 Hz), 5.41 (s, 2H), 5.04 (t, 2H, J = 10.6 Hz), 4.68 (t, 2H, J = 10.6 Hz), 3.76 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 160.26 (C), 154.91 (C), 136.30 (C), 135.79 (CH), 133.25 (C), 132.25 (CH), 129.49 (CH), 128.34 (CH), 127.94 (CH), 126.28 (CH), 125.29 (C), 124.42 (CH), 123.96 (CH), 120.93 (C), 116.38 (CH), 115.91 (C), 115.40 (CH), 55.81 (CH$_3$), 55.36 (CH$_2$), 52.54 (CH$_2$), 47.72 (CH$_2$); IR (KBr, cm^{-1}) 3431 (s), 2924 (w), 2360 (w), 1612 (s), 1576 (s), 1514 (m), 1456 (m), 1304 (m), 1248 (m), 1026 (m), 814 (m), 754 (m); MS (FAB) 341.2 (M − Br) (35), 232 (10), 157.1 (56), 121.2 (13), 79.7 (100). Anal. Calcd for C$_{23}$H$_{21}$N$_2$OBr·0.5H$_2$O: C, 64.19; H, 5.15; N, 6.51. Found: C, 64.87; H, 5.47; N, 6.95.

1-(2-Hydroxy-ethyl)-2,3-dihydro-1*H*-imidazo[1,2-*f*]-phenanthridin-4-ylium Bromide (6b). **6b** (320 mg; 0.93 mmol) was obtained as a pale yellow crystalline solid in a 98% yield: mp 270−271 °C (dec); ^{1}H NMR (D$_2$O, 400 MHz) δ 8.23 (d, 2H, J = 8.2 Hz), 8.11 (d, 1H, J = 8.2 Hz), 7.86 (t, 1H, J = 8.2 Hz), 7.64 (t, 2H, J = 8.2 Hz), 7.43 (t, 1H, J = 8.2 Hz), 7.20 (d, 1H, J = 8.2 Hz), 4.35 (t, 2H, J = 11 Hz), 4.22 (t, 2H, J = 11 Hz), 4.09 (t, 2H, J = 5.2 Hz), 4.03 (t, 2H, J = 5.2 Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 153.47 (C), 135.59 (CH), 134.59 (C), 132.13 (C), 131.63 (CH), 129.30 (CH), 127.68 (CH), 125.67 (CH), 123.63 (CH), 123.29 (CH), 119.59 (C), 115.42 (CH), 114.73 (C), 59.10 (CH$_2$), 52.54 (CH$_2$), 51.45 (CH$_2$), 45.80 (CH$_2$); IR (KBr, cm^{-1}): 3433 (s), 2922 (w), 2360 (w), 1603 (s), 1576 (s), 1520 (w), 1456 (m), 1387 (w), 1302 (m), 1265 (m), 1084 (m), 874 (w), 758 (m); MS (FAB) 265.2 (M − Br) (100), 219.1

(12), 178.1 (5), 154.1 (2), 136.1 (2). Anal. Calcd for $C_{17}H_{17}N_2$-OBr: C, 59.14; H, 4.96; N, 8.11. Found: C, 58.67; H, 4.78; N, 7.92.

2,3-Dihydro-1H-imidazo[1,2-f]phenanthridin-4-ylium Bromide (6c). 6c (250 mg; 0.83 mmol) was obtained as a yellow powder in a 61% yield: mp 392−394 °C (dec); ^{1}H NMR (D$_2$O, 400 MHz) δ 7.83 (d, 1H, J = 8.0 Hz), 7.79 (d, 1H, J = 8.0 Hz), 7.66 (t, 1H, J = 8.0 Hz), 7.46 (m, 3H), 7.28 (t, 1H, J = 8.0 Hz), 6.93 (d, 1H, J = 8.0 Hz), 4.13 (t, 2H, J = 10.8 Hz), 3.91 (t, 2H, J = 10.8 Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 154.69 (C), 135.75 (CH), 133.18 (C), 131.65 (C), 129.56 (CH), 126.26 (CH), 125.65 (CH), 123.40 (CH), 123.01 (CH), 119.25 (C), 115.45 (CH), 113.64 (C), 47.62 (CH$_2$), 43.04 (CH$_2$); IR (KBr, cm^{-1}) 3435 (s), 3028 (m), 2997 (m), 2950 (m), 2773 (w), 2684 (w), 2050 (w), 1626 (s), 1608 (s), 1585 (s), 1469 (m), 1454 (m), 1358 (m), 1294 (m), 1267 (w), 1169 (w), 1022 (w), 754 (s); MS (EI+) 220 (M − Br) (10), 219.3 (12), 142.3 (8), 112.2 (5), 100.2 (15), 86.2 (100), 56.1 (50). Anal. Calcd for $C_{15}H_{13}N_2Br$: C, 59.82; H, 4.35; N, 9.30. Found: C, 59.39; H, 4.23; N, 9.03.

1-Isopropyl-2,3-dihydro-1H-imidazo[1,2-f]phenanthridin-4-ylium Bromide (6d). 6d (267 mg; 0.78 mmol) was obtained as a yellow powder in a 82% yield: mp 250−251 °C (dec); ^{1}H NMR (CD$_3$OD, 400 MHz) δ 8.81 (d, 1H, J = 8.4 Hz), 8.62 (d, 1H, J = 8.4 Hz), 8.58 (d, 1H, J = 8.4 Hz), 8.12 (t, 1H, J = 8.4 Hz), 7.90 (t, 1H, J = 8.4 Hz), 7.82 (t, 1H, J = 8.4 Hz), 7.62 (m, 2H), 5.23 (q, 1H, J = 6.6 Hz), 4.76 (t, 2H, J = 10.5 Hz), 4.38 (t, 2H, J = 10.5 Hz), 1.62 (d, 6H, J = 6.6 Hz); ^{13}C NMR (CD$_3$OD, 100 MHz) δ 155.03 (C), 137.64 (C), 136.76 (CH), 134.96 (C), 133.02 (CH), 130.74 (CH), 129.55 (CH), 126.95 (CH), 125.81 (CH), 125.29 (CH), 122.21 (C), 117.52 (C), 116.98 (CH), 52.50 (CH), 47.51 (CH), 45.16 (CH$_2$), 21.22 (CH$_3$); IR (KBr, cm^{-1}) 3433 (s), 2981 (w), 2015 (w), 1610 (m), 1597 (m), 1574 (s), 1550 (s), 1556 (w), 1303 (m), 1169 (w), 1126 (w), 1068 (w), 758 (m); MS (FAB) 263.2 (M − Br) (100), 221.1 (6), 154.1 (12), 137.1 (6), 89.6 (2), 77.7 (1). Anal. Calcd for $C_{18}H_{19}N_2Br$·0.25 H$_2$O: C, 62.17; H, 5.65; N, 8.90. Found: C, 62.27; H, 6.01; N, 8.95.

1-Cyclopropyl-2,3-dihydro-1H-imidazo[1,2-f]phenanthridin-4-ylium Bromide (6e). 6e (250 mg; 0.74 mmol) was obtained as a white off powder in a 78% yield: mp 129−130 °C (dec); ^{1}H NMR (D$_2$O, 400 MHz) δ 8.84 (d, 1H, J = 8.4 Hz), 8.20 (d, 1H, J = 8.0 Hz), 8.84 (d, 1H, J = 8.0 Hz), 8.10 (d, 1H, J = 8.0 Hz), 7.85 (t, 1H, J = 8.0 Hz), 7.64 (m, 2H), 7.42 (t, 1H, J = 8.0 Hz), 7.17 (d, 2H, J = 8.0 Hz), 4.25 (t, 2H, J = 11 Hz), 4.11 (t, 2H, J = 11 Hz), 3.26 (qt, 1H, J = 3.5 Hz), 1.21 (m, 2H), 1.03 (m, 2H); ^{13}C NMR (D$_2$O, 100 MHz) δ 155.05 (C), 155.05 (C), 135.52 (CH), 134.87 (C), 132.43 (C), 131.55 (CH), 129.24 (CH), 128.88 (CH), 125.69 (CH), 123.55 (CH), 123.40 (CH), 119.98 (C), 115.46 (CH), 102.52 (C), 49.95 (CH$_2$), 45.77 (CH$_2$), 31.51(CH), 10.49 (2×CH$_2$); IR (KBr, cm^{-1}) 3427 (s), 3024 (w), 2358 (w), 1610 (m), 1595 (m), 1575 (s), 1548 (s), 1454 (m), 1356 (w), 1307 (m), 1045 (w), 762 (m); MS (FAB) 261.1 (M − Br) (100), 219.1 (6), 154 (12), 136 (11), 120.1 (2), 89.5 (2), 77.7-(1). Anal. Calcd for $C_{18}H_{17}N_2Br$: C, 64.35; H, 5.02; N, 8.21. Found: C, 64.68; H, 5.02; N, 8.09.

1-(1-Methoxycarbonyl-2-phenyl-ethyl)-2,3-dihydro-1H-imidazo[1,2-f]phenanthridin-4-ylium Bromide (6f). 6f (550 mg; 1.2 mmol) was obtained as a hygroscopic white powder in a 63% yield: mp 137−138 °C; ^{1}H NMR (D$_2$O, 400 MHz) δ 8.13 (d, 1H, J = 8.0 Hz), 8.03 (d, 1H, J = 8.0 Hz), 7.87 (d, 1H, J = 8.0 Hz), 7.82 (t, 1H, J = 8.0 Hz), 7.62 (t, 1H, J = 8.0 Hz), 7.59 (t, 1H, J = 8.0 Hz), 7.44 (t, 1H, J = 8.0 Hz), 7.22 (d, 1H, J = 8.0 Hz), 7.05 (d, 2H, J = 6.4 Hz), 6.82 (m, 3H), 5.90 (dd, 1H, J = 15.6 and 4 Hz), 4.48 (m, 1H), 4.30 (m, 2H), 4.19 (m, 1H), 3.84 (s, 3H), 3.50 (dd, 1H, J = 15.6 and 4 Hz), 3.24 (dd, 1H, J = 15.6 and 11.2 Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 135.96 (CH), 135.10 (C), 135.05 (C), 131.72 (CH), 131.5 (C), 129.22 (CH), 129.00 (CH), 127.80 (CH), 127.01 (CH), 126.64 (CH), 124.06 (CH), 123.51 (CH), 121.00 (CH), 120.00 (C), 115.97 (CH), 114.6 (C); IR (KBr, cm^{-1}) 3433 (s), 1739 (s), 1610 (s), 1572 (s), 1534 (s), 1453 (m), 1265 (m), 753 (s); MS (FAB) 383.5 (M − Br) (100), 307.3 (12), 233.2 (5), 219.2 (5), 154.1

(22), 137.1 (15). Anal. Calcd for $C_{25}H_{23}BrN_2O_2$·H$_2$O: C, 62.38; H, 5.23; N, 5.82. Found: C, 62.27; H, 5.32; N, 5.95.

1-Phenyl-2,3-dihydro-1H-imidazo[1,2-f]phenanthridin-4-ylium Bromide (6g). 6g (260 mg; 0.695 mol) was obtained as a yellow powder in a 73% yield: mp 355−356 °C (dec); ^{1}H NMR (CD$_3$OD, 400 MHz) δ 8.85 (d, 1H, J = 8.4 Hz), 8.75 (d, 1H, J = 8.4 Hz), 8.05 (t, 1H, J = 8.4 Hz), 7.93 (t, 1H, J = 8.4 Hz), 7.81 (d, 1H, J = 8.4 Hz), 7.71 (m, 6H), 7.45 (m, 2H), 5.04 (t, 2H, J = 10.4 Hz), 4.69 (t, 2H, J = 10.4 Hz); ^{13}C NMR (CD$_3$-OD, 100 MHz) δ 154.87 (C), 144.05 (C), 141.02 (CH), 137.69 (CH), 137.07 (CH), 134.63 (C), 133.20 (CH), 132.60 (CH), 132.02 (CH), 129.94 (CH), 129.24 (CH), 128.47 (CH), 126.45 (CH), 125.76 (CH), 122.72 (C), 120.46 (C), 117.43 (CH), 117.00 (C), 56.19 (CH$_2$), 48.76 (CH$_2$); IR (KBr, cm^{-1}) 3434 (s), 3047 (w), 1612 (m), 1599 (m), 1575 (s), 1545 (s), 1485 (w), 1440 (m), 1309 (s), 1171 (w), 935(w), 758 (s); MS (FAB) 297 (M − Br) (100), 269 (2), 230 (8), 219 (4), 178 (4), 154 (6), 136 (5), 107.2 (1), 77.6 (2). Anal. Calcd for $C_{21}H_{17}N_2Br$·0.5H$_2$O: C, 65.30; H, 4.70; N, 7.25. Found: C, 65.71; H, 4.53; N, 7.11.

1-(4-Methoxy-phenyl)-2,3-dihydro-1H-imidazo[1,2-f]-phenanthridin-4-ylium Bromide (6h). 6h (285 mg; 0.7 mmol) was obtained as a pale green powder in a 74% yield: mp 368−369 °C (dec); ^{1}H NMR ((CD$_3$)$_2$SO, 400 MHz) δ 8.90 (d, 1H, J = 8.0 Hz), 8.80 (d, 1H, J = 8.0 Hz), 0.05 (t, 1H, J = 8.0 Hz), 7.91 (t, 1H, J = 8.0 Hz), 7.82 (d, 1H, J = 8.0 Hz), 7.67 (m, 3H), 7.58 (t, 1H, J = 8.0 Hz), 7.35 (d, 1H, J = 8.0 Hz), 7.24 (d, 2H, J = 8.0 Hz), 4.92 (t, 2H, J = 9.8 Hz), 4.56 (t, 2H, J = 9.8 Hz), 3.88 (s, 3H); ^{13}C NMR ((CD$_3$)$_2$SO, 100 MHz) δ 160.42 (C), 152.98 (C), 135.59 (CH), 135.36 (C), 133.03 (C), 131.90 (CH), 131.88 (CH), 129.02 (CH), 128.51 (CH), 128.50 (CH), 127.29 (CH), 125.98 (CH), 124.64 (CH), 124.43 (CH), 120.63 (C), 120.62 (C), 116.45 (CH), 116.30 (CH), 115.77 (C), 56.02 (CH$_3$), 55.01 (CH$_2$), 47.09 (CH$_2$); IR (KBr, cm^{-1}) 3435 (s), 29232 (w), 2360 (w), 1610 (s), 1577 (s), 1554 (m), 1512 (m), 1456 (w), 1298 (w), 1251 (s), 1028 (m), 764 (m); MS (FAB) 327.1 (M − Br) (100), 307.1 (20), 289.1 (10), 261.1 (2), 219.1 (2), 154 (80), 136 (50), 107.3 (16), 89.5 (14), 77.6 (12), 65.8 (5), 52 (5). Anal. Calcd for $C_{22}H_{19}N_2OBr$·H$_2$O: C, 62.13; H, 4.98; N, 6.59. Found: C, 62.21; H, 4.46; N, 6.60.

Ethylenediamine Derivative (6i). 2-Bromo-ethyl-phenanthridinium bromide (**2**) (700 mg; 1.9 mmol) was suspended in DMF (20 mL). Ethylenediamine (31.8 μL; 0.48 mmol) and TEA (530 μL; 3.8 mmol) were added successively to the stirred solution. After stirring for 48 h at room temperature under nitrogen, the final product and TEA hydrobromide salt were precipitated from the solution with diethyl ether (100 mL) and recovered by filtration. The precipitate was washed thoroughly with diethyl ether and triturated with 1 mL of water to remove the TEA salt, yielding, **6i** (295 mg; 0.47 mmol) as a yellow powder in a 98% yield: mp > 400 °C; ^{1}H NMR ((CD$_3$)$_2$SO, 400 MHz) δ 8.70 (d, 2H, J = 8.0 Hz), 8.66 (d, 2H, J = 8.0 Hz), 8.62 (d, 2H, J = 8.0 Hz), 8.01 (t, 2H, J = 8.0 Hz), 7.87 (t, 2H, J = 8.0 Hz), 7.78 (t, 2H, J = 8.0 Hz), 7.66 (m, 4H), 4.76 (s, 4H), 4.68 (t, 4H, J = 10.6 Hz), 4.50 (t, 4H, J = 10.6 Hz); IR (KBr, cm^{-1}) 3435 (s), 1612 (m), 1597 (m), 1574 (s), 1554 (s), 1456 (w), 1311 (m), 1265 (m), 762 (m); MS (FAB) 234 ((M − 2Br)/2) (5), 232 (10), 214 (5), 198 (1), 157 (35), 137 (5), 102.4 (2), 79.6 (100), 61.8 (5). Anal. Calcd for $C_{32}H_{28}N_4Br_2$·H$_2$O: C, 59.46; H, 4.68; N, 8.67. Found: C, 59.80; H, 4.42; N, 8.31.

Tris(2-aminoethyl)amine Derivative (6j). 2-Bromo-ethyl-phenanthridinium bromide (**2**) (1 g; 2.72 mmol) was suspended in DMF (50 mL). Tris(2-aminoethyl)amine (68 μL; 0.454 mmol) and TEA (763 μL; 5.44 mmol) were added successively to the stirred solution. After stirring for 48 h at room temperature under nitrogen, the final product and TEA hydrobromide salt were precipitated from the solution with diethyl ether (100 mL) and recovered by filtration. The precipitate was washed thoroughly with diethyl ether and triturated with 1 mL of water to remove the TEA salt, yielding **6j** (430 mg; 0.43 mmol) as a yellow powder in a 95% yield: mp 326−327 °C; ^{1}H NMR ((CD$_3$)$_2$SO, 400 MHz) δ 8.61 (d, 3H, J = 8.0 Hz), 8.51 (d, 3H, J = 8.0 Hz), 8.43 (d, 3H, J = 8.0 Hz),

7.94 (t, 3H, *J* = 8.0 Hz), 7.82 (m, 6H), 7.57 (t, 3H, *J* = 8.0 Hz), 7.51 (d, 3H, *J* = 8.0 Hz), 4.57 (t, 6H, *J* = 10.0 Hz), 4.44 (t, 6H, *J* = 10.0 Hz), 4.35 (m, 6H), 3.35 (m, 6H); ^{13}C NMR ((CD$_3$)$_2$SO, 100 MHz) δ 153.55 (C), 135.43 (C), 134.81 (CH), 132.72 (C), 131.78 (CH), 129.50 (CH), 127.69 (CH), 125.67 (CH), 124.31 (CH), 124.08 (CH), 119.79 (C), 116.09 (C), 115.25 (CH), 51.76 (CH$_2$), 51.46 (CH$_2$), 49.19 (CH$_2$), 46.25 (CH$_2$); IR (KBr, cm^{-1}) 3435 (s), 2925 (w), 2358 (w), 1610 (s), 1575 (s), 1456 (m), 1384 (w), 1304 (m), 1267 (m), 1106 (w), 750 (w), 717 (w), 667 (w). Anal. Calcd for C$_{51}$H$_{48}$Br$_3$N$_7$: C, 61.34; H, 4.84; Br, 24.00; N, 9.82. Found: C, 61.11; H, 4.90; N, 9.62.

***cis*-1,3,5-Triaminocyclohexane Derivative (6k).** 2-Bromo-ethyl-phenanthridinium bromide **(2)** (1 g; 2.72 mmol) was suspended in DMF (30 mL). *cis*-1,3,5-Triaminocyclohexane (58 mg; 0.45 mmol) and TEA (763 μL; 5.44 mmol) were added successively to the stirred solution. After stirring for 48 h at room temperature under nitrogen, the final product and TEA hydrobromide salt were precipitated from the solution with diethyl ether (100 mL) and recovered by filtration. The precipitate was washed thoroughly with diethyl ether and ethyl acetate and then triturated with 1 mL of water to remove the TEA salt, yielding **6k** (400 mg; 0.41 mmol) as a yellow powder in a 91% yield: mp 360 °C; ^{1}H NMR ((CD$_3$)$_2$SO, 400 MHz) δ 9.11 (d, 3H, *J* = 8.4 Hz), 8.91 (d, 3H, *J* = 8.4 Hz), 8.73 (d, 3H, *J* = 8.0 Hz), 8.18 (t, 3H, *J* = 5.1 Hz), 8.04 (t, 3H, *J* = 5.1 Hz), 7.86 (t, 3H, *J* = 5.1 Hz), 7.70 (d, 3H, *J* = 8.0 Hz), 7.64 (t, 3H, *J* = 5.1 Hz), 5.93 (m, 3H), 4.79 (t, 6H, *J* = 6.9 Hz), 4.53 (t, 6H, *J* = 6.9 Hz), 2.82 (q, 3H, *J* = 11.6 Hz), 2.6 (d, 3H, *J* = 11.6 Hz); ^{13}C NMR ((CD$_3$)$_2$SO, 100 MHz) δ 156.31 (CH), 135.53 (CH), 135.25 (C), 133.11 (CH), 131.82 (CH), 130.40 (CH), 129.17 (CH), 125.80 (C), 124.68 (CH), 124.23 (C), 120.41 (CH), 116.32 (C), 115.85 (CH), 52.66 (CH$_2$), 46.25 (CH$_2$), 45.54 (CH), 32.43 (CH$_2$); IR (KBr, cm^{-1}) 3421 (s), 1610 (s), 1570 (s), 1533 (s), 1452 (m), 1386 (w), 1304 (s), 1263 (m), 1155 (m), 1122 (m), 783 (m), 754 (s), 717 (m), 669 (m); MS (FAB) 247.14 ((M − 3Br)/3) (5), 232.1 (11), 219.11 (10), 214.08 (2), 157.1 (45), 79.7 (100). Anal. Calcd for C$_{51}$H$_{45}$Br$_3$N$_6$: C, 62.40; H, 4.62; N, 8.56. Found: C, 62.30; H, 4.71; N, 8.64.

1-[1-(4-Methoxy-phenyl)-ethyl-2,3-dihydro-1*H*-imidazo-[1,2-*f*]phenanthridin-4-ylium Bromide (6l). **6l** (260 mg; 0.6 mmol) was obtained as a dark green powder in a 22% yield: mp 107–108 °C (dec); ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.55 (d, 1H, *J* = 8.0 Hz), 8.35 (d, 1H, *J* = 8.0 Hz), 8.29 (d, 1H, *J* = 8.0 Hz), 7.95 (t, 1H, *J* = 8.0 Hz), 7.69 (t, 1H, *J* = 8.0 Hz), 7.64 (t, 1H, *J* = 8.0 Hz), 7.59 (d, 1H, *J* = 8.0 Hz), 7.50 (t, 1H, *J* = 8.0 Hz), 7.28 (d, 2H, *J* = 8.8 Hz), 6.88 (d, 2H, *J* = 8.8 Hz), 5.93 (q, 1H, *J* = 6.8 Hz), 5.31 (m, 2H), 4.85 (m, 2H), 4.09 (m, 1H), 3.75 (s, 3H), 1.98 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 159.96 (C), 153.32 (C), 136.17 (CH), 132.85 (C), 132.01 (CH), 129.56 (C), 129.18 (CH), 128.00 (CH), 127.88 (CH), 125.93 (CH), 124.28 (CH), 123.45 (CH), 120.45 (C), 116.36 (CH), 115.34 (C), 114.96 (CH), 58.06 (CH), 55.46 (CH$_3$), 47.23 (CH$_2$), 45.94 (CH$_2$), 19.74 (CH$_3$); IR (KBr, cm^{-1}) 3431 (w), 3371 (w), 1610 (w), 1596 (w), 1571 (s), 1537 (s), 1508 (s), 1437 (m), 1299 (s), 1032 (m), 1019 (m), 749 (s), 714 (s), 664 (s); MS (FAB+) 355.3 (M − Br) (100), 329.4 (10), 221.2 (40), 219.1 (20), 135.1 (50); MS (FAB+) 355.3 (M − Br) (100), 329.4 (10), 221.2 (40), 219.1 (20), 135.1 (50). Anal. Calcd for C$_{24}$H$_{23}$BrN$_2$O·H$_2$O: C, 63.58; H, 5.56; N, 6.18. Found: C, 63.29; H, 5.63; N, 6.08. **6l** was also obtained by adding bromine (10 μL; 0.2 mmol) to the biphasic NMR solution used to make **4l**. Despite its ionic character, molecule **6l** does not move into the D$_2$O layer because of its greater lipophilicity.

5-(2-Bromo-ethyl)-6-[1-(4-methoxy-phenyl)-ethylamino]-phenanthridinium Bromide (7). A new NMR solution of **3k** was prepared, and bromine (10 μL; 0.2 mmol) was added. The NMR tube was shaken energetically for 1 min. Despite its ionic character, molecule **7** does not move into the D$_2$O layer because of its greater lipophilicity. ^{1}H and ^{13}C NMR and mass spectra of the organic layer were taken characterizing **7**: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 8.42 (d, 1H, *J* = 8.4 Hz), 8.26 (d, 2H, *J* = 8.4 Hz), 7.95 (t, 1H, *J* = 8.4 Hz), 7.74 (d, 1H, *J* = 8.4

Hz), 7.67 (t, 1H, *J* = 8.4 Hz), 7.50 (m, 2H), 7.28 (d, 2H, *J* = 8.4 Hz), 6.89 (d, 2H, *J* = 8.4 Hz), 5.98 (q, 1H, *J* = 6.8 Hz), 5.13 (m, 1H), 4.76 (m, 1H), 4.66 (m, 1H), 4.04 (m, 1H), 3.75 (s, 3H), 1.97 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 159.38 (C), 153.70 (C), 135.52 (CH), 133.29 (C), 131.80 (CH), 131.03 (C), 129.55 (CH), 128.46 (CH), 128.42 (CH), 125.60 (CH), 124.68 (CH), 124.24 (CH), 120.47 (CH), 116.25 (CH), 115.94 (C), 114.65 (CH), 57.10 (CH), 55.56 (CH$_3$), 46.34 (CH$_2$), 45.51 (CH$_2$), 19.66 (CH$_3$); MS (FAB) 435.26 (M − Br) (40), 434.26 (12), 433.26 (40), 355.3 (100), 307.2 (35), 221.2 (65), 154.1 (60), 135.1 (95).

2-Fluoro-ethyl-phenanthridinium Bromide (9a). To prepare 2-fluoroethyltosylate, 2-fluoroethanol (1 g; 15.6 mmol) was dissolved in dry pyridine (15 mL) under nitrogen. The solution was stirred at 0 °C and *p*-toluene sulfonyl chloride (6.5 g; 34.1 mmol) was added slowly to the solution over a period of 30 min, keeping the temperature below 5 °C. The solution was then stirred at 0 °C for another 4 h before quenching by slow addition of ice (15 g) and then water (20 mL). Ethyl acetate (50 mL) was added, and the organic layer was separated and washed with water. Excess pyridine was removed by washing the organic layer with a 1 M HCl solution until the aqueous layer became acidic. The excess tosyl chloride was removed by washing the organic layer with an aqueous solution of Na$_2$CO$_3$ (pH ≈ 10). The organic layer was then washed with brine, dried over MgSO$_4$, and concentrated under vacuum to obtain 2-fluoroethyltosylate (3.29 g; 15 mmol) as an oil in a 96% yield: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.81 (d, 2H, *J* = 8.0 Hz), 7.38 (d, 2H, *J* = 8.0 Hz), 4.65 (t, 1H, *J* = 4.2 Hz), 4.53 (t, 1H, *J* = 4.2 Hz), 4.32 (t, 1H, *J* = 4.2 Hz), 4.25 (t, 1H, *J* = 4.2 Hz), 2.48 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 145.53 (C), 133.05 (C), 130.32 (CH), 128.37 (CH), 81.78 (CH$_2$), 80.06 (CH$_2$), 68.91 (CH$_2$), 68.70 (CH$_2$), 22.05 (CH$_3$); MS (EI) 218.2 (M + 1) (50), 185.2 (8), 155.1 (100), 139.1 (5), 107.1 (8), 91.1 (100), 65.1 (30), 63.1 (10). Phenanthridine (690 mg; 3.84 mmol) was added to a solution of 2-fluoroethyltosylate (1.68 g; 7.68 mmol) in DMF (10 mL) and stirred at 100 °C for 48 h. The solution was then concentrated to a brown oil and precipitated by addition of acetone (10 mL) followed by diethyl ether (60 mL). The precipitate was recovered by filtration, washed with diethyl ether, and dried under vacuum to obtain the tosylate salt of **9a** (1.52 g; 3.84 mmol) as an off white powder in a quantitative yield. Finally, the tosylate salt was passed through an anionic exchange column (Dowex 1X-850) preloaded with a saturated NaBr solution and flushed with distilled water. The compound was eluted with distilled water. The resulting aqueous solution was washed twice with ethyl acetate before being concentrated under vacuum to obtain **9a** (1.12 g; 3.68 mmol) as a pale yellow powder in a 96% yield: mp 239–240 °C (dec); ^{1}H NMR (D$_2$O, 400 MHz) δ 9.80 (s, 1H), 8.79 (d, 1H, *J* = 8.0 Hz), 8.71 (d, 1H, *J* = 8.0 Hz), 8.36 (d, 1H, *J* = 8.0 Hz), 8.29 (d, 1H, *J* = 8.4 Hz), 8.21 (t, 1H, *J* = 7.2 Hz), 8.01 (t, 1H, *J* = 7.2 Hz), 7.94 (m, 2H), 5.40 (t, 1H, *J* = 4.4 Hz), 5.33 (t, 1H, *J* = 4.4 Hz), 5.12 (t, 1H, *J* = 4.4 Hz), 5.00 (t, 1H, *J* = 4.4 Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 155.22 (CH), 138.89 (CH), 135.09 (C), 133.08 (C), 132.96 (CH), 132.60 (CH), 130.85 (CH), 130.70 (CH), 126.20 (C), 124.88 (CH), 123.37 (C), 122.79 (CH), 119.18 (CH), 82.08 (CH$_2$), 80.39 (CH$_2$), 58.17 (CH$_2$), 57.98 (CH$_2$); IR (KBr, cm^{-1}) 3404 (m), 1534 (m), 1460 (m), 1447 (m), 1371 (m), 1265 (s), 1165 (s), 1048 (s), 1031 (s), 764 (s), 718 (m); MS (FAB) 226.2 (M − Br) (100), 199.2 (10), 180.1 (25), 101.4 (20); MS (FAB) 226.2 (M − Br) (100), 199.2 (10), 180.1 (25), 101.4 (20).

2-Hydroxy-ethyl-phenanthridinium Bromide (9b). Phenanthridine (2 g; 11.17 mmol) was added to a solution of 2-bromoethanol (3.2 mL; 44.8 mmol). The reaction mixture was refluxed for 4 h under N$_2$. After cooling, crystallization was aided by the addition of ether. After 2 h, the crystals were recovered by filtration and washed with ether to produce **9b** (3.10 g; 10.13 mmol) as a beige powder in a 90% yield: mp 239–240 °C (dec); ^{1}H NMR (D$_2$O, 400 MHz) δ 9.71 (s, 1H), 8.81 (d, 1H, *J* = 8.0 Hz), 8.74 (d, 1H, *J* = 8.0 Hz), 8.37 (d, 1H,

$J = 8.0$ Hz), 3.32 (d, 1H, $J = 8.0$ Hz), 8.22 (t, 1H, $J = 8.0$ Hz), 7.97 (m, 3H), 5.11 (t, 2H, $J = 5.0$ Hz), 4.14 (t, 2H, $J = 5.0$ Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 156.71 (CH), 140.70 (CH), 136.62 (C), 134.88 (CH), 134.68 (CH), 132.81 (CH), 127.93 (C), 126.75 (C), 125.09 (C), 124.65 (CH), 121.33 (CH), 62.31 (CH$_2$), 61.19 (CH$_2$); IR (KBr, cm^{-1}) 3232 (s), 1624 (s), 1581 (w), 1535 (m), 1446 (s), 1423 (m), 1346 (m), 1261 (s), 1157 (s), 1084 (s), 1033 (s), 899 (s), 867 (m), 756 (s), 717 (s), 609 (s); MS (ES) 224.1 (M − Br) (100), 222.1 (25), 210.1 (10), 206.1 (40), 194.1 (8), 193.1 (18), 182.1 (10), 181.1 (80), 180.1 (100).

[5-(2-Fluoro-ethyl)-5,6-dihydro-phenanthridin-6-yl]-isopropyl-amine (10a). In an NMR tube, **9a** (10 mg; 0.032 mmol) was dissolved in D$_2$O (0.6 mL). CDCl$_3$ (0.6 mL) was added, followed by isopropylamine (5.4 μL; 0.064 mmol) used as a reactant and as a base. The NMR tube was energetically shaken for 1 min to allow the phase transfer process to occur. A ^{1}H NMR spectrum of the CDCl$_3$ solution was taken, characterizing **8a**: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.80 (d, 1H, $J = 8.4$ Hz), 7.70 (d, 1H, $J = 8.4$ Hz), 7.3 (t, 1H, $J = 4.6$ Hz), 7.23 (d, 1H, $J = 6.4$ Hz), 7.19 (d, 1H, $J = 7.2$ Hz), 7.14 (d, 1H, $J = 7.2$ Hz), 6.87 (m, 2H), 5.74 (s, 1H), 4.66 (m, 1H), 4.57 (m, 1H), 4.47 (m, 1H), 3.95 (m, 1H), 3.75 (m, 1H), 0.90 (d, 6H).

Synthesis of 2-(6-Isopropylamino-6*H*-phenanthridin-5-yl)-ethanol (10b). Molecule **9b** (10 mg; 0.033 mmol) was reacted with isopropylamine (5.66μL; 0.066) using the same NMR phase transfer methodology than for the isolation of **10a**. ^{1}H and ^{13}C NMR and mass spectra of the CDCl$_3$ solution were taken, characterizing **10b**: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.79 (d, 1H, $J = 8.0$ Hz), 7.75 (dd, 1H, $J = 7.6$ and 1.2 Hz), 7.40 (d, 1H, $J = 7.6$ Hz), 7.36 (dt, 1H, $J = 7.6$ and 1.6 Hz), 7.27 (dt, 1H, $J = 7.6$ and 1.2 Hz), 7.18 (dt, 1H, $J = 7.6$ and 1.6 Hz), 6.83 (dt, 1H, $J = 7.6$ and 1.2 Hz), 6.72 (d, 1H, $J = 8.0$ Hz), 5.69 (s, 1H), 3.95 (m, 2H), 3.84 (m, 1H), 3.51 (m, 1H), 3.01 (sept, 1H, $J = 6.2$ Hz), 1.00 (d, 6H, $J = 6.2$ Hz); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 154.58 (C), 141.86 (C), 130.38 (C), 129.44 (CH), 129.06 (CH), 127.49 (CH), 126.48 (CH), 123.25 (CH), 122.15 (CH), 120.49 (C), 119.06 (CH), 113.81 (CH), 87.70 (CH), 63.11 (CH$_2$), 48.11 (CH$_2$), 42.11 (CH), 25.94 (CH$_3$); MS (CI) 281.38 (M − H$^-$) (1), 266.34 (M − OH) (5), 224.3 (30), 193.2 (8), 180.2 (7), 57.1 (100).

[5-(2-Fluoro-ethyl)-5,6-dihydro-phenanthridin-6-yl]-phenyl-amine (11a). Molecule **9a** (10.4 mg; 0.034 mmol) was reacted with aniline (3.1μL; 0.034 mmol) and TEA (9.4 μL; 0.068 mmol) using the same NMR phase transfer methodology than for the isolation of **10a**. ^{1}H and ^{13}C NMR spectra of CDCl$_3$ layer were taken, characterizing **11a**: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.84 (d, 1H, $J = 7.6$ Hz), 7.79 (d, 1H, $J = 7.6$ Hz), 7.33 (t, 1H, $J = 7.6$ Hz), 7.22 (t, 1H, $J = 7.6$ Hz), 7.12 (d, 1H, $J = 7.6$ Hz), 7.07 (t, 1H, $J = 7.6$ Hz) 6.90 (t, 1H, $J = 7.6$ Hz), 6.80 (d, 1H, $J = 7.6$ Hz), 6.65 (m, 5H), 5.87 (s, 1H), 4.6 (t, 1H, $J = 6.0$ Hz), 4.48 (t, 1H, $J = 6.0$ Hz), 3.80 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 146.26 (C), 141.05 (C), 132.96 (C), 129.31 (CH), 128.31 (CH), 127.24 (CH), 125.93 (CH), 123.89 (CH), 122.74 (CH), 121.67 (C), 120.59 (C), 119.02 (CH), 118.96 (CH), 118.64 (CH), 115.26 (CH), 113.90 (CH), 113.19 (C), 72.05 (CH), 49.89 (CH$_2$), 46.20 (CH$_2$).

2-(6-Phenylamino-6*H*-phenanthridin-5-yl)-ethanol (11b). Molecule **9b** (11.8 mg; 0.039 mmol) was reacted with aniline (3.54 μL; 0.039 mmol) and TEA (10.9 μL; 0.078 mmol) using the same NMR phase transfer methodology as for the isolation of **10a**. ^{1}H and ^{13}C NMR spectra of the organic layer were taken, characterizing **11b**: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.79 (d, 1H, $J = 7.6$ Hz), 7.75 (d, 1H, $J = 7.6$ Hz), 7.40 (d, 1H, $J = 7.6$ Hz), 7.36 (t, 1H, $J = 7.6$ Hz), 7.27 (t, 1H, $J = 7.6$ Hz), 7.18 (t, 1H, $J = 7.6$ Hz), 7.08 (m, 2H), 6.83 (t, 1H, $J = 7.6$ Hz), 6.72 (d, 1H, $J = 7.6$ Hz), 6.68 (t, 1H, $J = 7.6$ Hz), 6.62 (d, 2H, $J = 7.6$ Hz), 5.68 (s, 1H), 3.95 (m, 2H), 3.82 (m, 1H), 3.50 (m, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 153.60 (C), 146.26 (C), 141.89 (C), 130.40 (C), 129.47 (CH), 129.30 (CH), 129.08 (CH), 127.51 (CH), 126.51 (CH), 123.27 (CH), 122.26 (CH), 120.51 (C), 119.08 (CH), 118.64 (CH), 115.12 (CH), 113.84 (CH), 87.72 (CH), 63.13 (CH$_2$), 48.14 (CH$_2$).

Hydrobromide Salt of 5-(2-Isopropylamino-ethyl)-phenanthridinium Bromide (12d). 2 (700 mg; 1.9 mmol) was suspended in 20 mL of water and 20 mL of chloroform. To the stirred solution was added isopropylamine (162.4 μL; 1.9 mmol) followed by NaHCO$_3$ (2 g; 23.8 mmol). The solution was left stirring at room temperature under nitrogen for 2 h. The aqueous layer was removed, and the organic solution was washed with water (2 × 20 mL) yielding **4d** in solution (1.9 mmol; 20 mL). Next, 20 mL of HBr 48% was added to the solution of **4d** and the solution was stirred overnight at room temperature. Water (30 mL) was added to the newly formed yellow precipitate, and the aqueous layer separated and washed twice with ethyl acetate. The aqueous solution was then concentrated under vacuum to 2 mL and precipitated by adding acetone. The precipitate was filtered and washed with ethyl acetate to yield **12d** (780 mg; 1.8 mmol) as an off white powder in a 96% yield: mp 285−286 °C; ^{1}H NMR (D$_2$O, 400 MHz) δ 9.96 (s, 1H), 9.00 (2, 1H, $J = 8.0$ Hz), 8.91 (d, 1H, $J = 8.0$ Hz), 8.48 (d, 1H, $J = 8.0$ Hz), 8.35 (m, 2H), 8.11 (t, 1H, $J = 8.0$ Hz), 8.07 (d, 1H, $J = 8.0$ Hz), 8.02 (t, 1H, $J = 8.0$ Hz), 5.44 (t, 2H, $J = 7.0$ Hz), 3.80 (t, 2H, $J = 7.0$ Hz), 3.45 (sept, 1H, $J = 6.5$ Hz), 1.25 (d, 6H, $J = 6.5$ Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 164.50 (C), 156.17 (CH), 139.47 (CH), 136.17 (C), 133.23 (CH), 132.87 (CH), 131.08 (CH), 130.93 (CH), 127.10 (C), 125.61 (CH), 124.05 (C), 123.34 (CH), 118.76 (CH), 54.17 (CH), 52.44 (CH$_2$), 43.04 (CH$_3$), 18.42 (CH$_2$); IR (KBr, cm^{-1}) 2676 (m), 1627 (s), 1532 (m), 1450 (s), 1148 (m), 1037 (m), 904 (m), 872 (m), 762 (s), 719 (s); MS (CI+) 267.2 (M − 2Br + H$^-$) (100), 265.2 (60), 195.1 (15), 180.1 (25). Anal. Calcd for C$_{18}$H$_{22}$-Br$_2$N$_2$: C, 50.13; H, 5.20; N, 6.57. Found: C, 50.20; H, 5.03; N, 6.44.

5-(2-Isopropylamino-ethyl)-phenanthridinium Bromide (3d′). **12d** (12 mg; 0.027 mmol) was dissolved in D$_2$O (0.6 mL). CDCl$_3$ (0.6 mL) was added, followed by NaHCO$_3$ (3.4 mg; 0.04 mmol). The NMR tube was energetically shaken for 1 min before reading the CDCl$_3$ layer, which appeared to be free from five-membered ring adduct. The D$_2$O layer was transferred to another NMR tube. ^{1}H and ^{13}C NMR was done, characterizing **12d**: ^{1}H NMR (D$_2$O, 400 MHz) δ 9.86 (s, 1H), δ 8.92 (d, 1H, $J = 8.0$ Hz), δ 8.84 (d, 1H, $J = 8.0$ Hz), δ 8.45 (d, 1H, $J = 8.0$ Hz), δ 8.37 (d, 1H, $J = 8.0$ Hz), δ 8.32 (t, 1H, $J = 8.0$ Hz), δ 8.05 (m, 3H), δ 5.24 (t, 2H, $J = 6.6$ Hz), δ 3.49 (t, 2H, $J = 6.6$ Hz), δ 3.08 (qt, 1H, $J = 6.4$ Hz), δ 1.1 (d, 6H, $J = 6.4$ Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 138.94 (CH), δ 138.59 (CH), δ 138.51 (C), δ 132.95 (CH), δ 132.59 (CH), δ 130.76 (CH), δ 129.15 (CH), δ 125.26 (CH), δ 125.04 (CH), δ 123.14 (C), δ 119.05 (CH), δ 115.90 (C), δ 107.06 (C), δ 49.68 (CH$_2$), δ 44.21 (CH$_2$), δ 20.37 (CH$_3$), δ 19.89 (CH).

5-(2-Isopropylamino-ethyl)-5,6-dihydro-phenanthridin-6-ol (13d). CDCl$_3$ (0.6 mL) was added to the NMR tube containing **3d′** in D$_2$O (0.6 mL). TEA (4 μL; 0.027 mmol) was added, and the NMR tube was energetically shaken for 1 min. ^{1}H and ^{13}C NMR was performed, characterizing **13d**: $R_f = 0$ in ethyl acetate; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.71 (d, 1H, $J = 7.5$ Hz), δ 7.65 (d, 1H, $J = 7.5$ Hz), δ 7.38 (d, 1H, $J = 7.5$ Hz), δ 7.27 (t, 2H, $J = 7.5$ Hz), δ 7.17 (t, 1H, $J = 7.5$ Hz), δ 6.82 (t, 1H, $J = 7.5$ Hz), δ 6.64 (d, 1H, $J = 7.5$ Hz), δ 4.80 (s, 1H), δ 3.39 (t, 1H, $J = 5.5$ Hz), δ 3.16 (m, 4H), δ 1.16 (d, 3H, $J = 6.5$ Hz), δ 1.03 (d, 3H, $J = 6.5$ Hz); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 135.39 (C), δ 131.80 (C), δ 128.97 (CH), δ 127.51 (CH), δ 127.29 (CH), δ 123.78 (CH), δ 123.48 (CH), δ 122.95 (CH), δ 121.68 (C), δ 121.22 (C), δ 118.70 (CH), δ 113.09 (CH), δ 76.36 (CH), δ 51.32 (CH), δ 46.51 (CH$_2$), δ 44.73 (CH$_2$), δ 22.26 (CH$_3$), δ 16.86 (CH$_3$).

1-(2-Bromo-ethyl)-quinolinium Bromide (14). Quinoline (3.00 g; 23.22 mmol) was reacted with 1,2-dibromoethane following the same protocol as for the synthesis of molecule **2**. Molecule **14** (7 g; 22.05 mmol) was obtained as a beige powder in a 95% yield: mp 289−290 °C (dec); ^{1}H NMR (D$_2$O, 400 MHz) δ 9.24 (d, 1H, $J = 8.4$ Hz), 9.12 (d, 1H, $J = 8.4$ Hz), 8.87 (d, 1H, $J = 8.4$ Hz), 8.33 (d, 1H, $J = 8.4$ Hz), 8.20 (t, 1H, $J = 8.4$ Hz), 7.98 (m, 2H), 5.41 (t, 2H, $J = 5.8$ Hz), 4.05 (t, 2H, $J = 5.8$

Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 149.80 (C), 149.20 (CH), 138.08 (C), 136.66 (CH), 131.43 (CH), 130.68 (CH), 130.55 (CH), 121.59 (CH), 118.08 (CH), 58.59 (CH$_2$), 29.28 (CH$_2$); IR (KBr, cm^{-1}) 3437 (s), 3045 (w), 2981 (m), 2947 (m), 1624 (s), 1599 (m), 1585 (m), 1525 (s), 1489 (w), 1450 (m), 1400 (m), 1363 (s), 1242 (s), 1126 (m), 1161 (m), 1144 (m), 1049 (w), 874 (w), 816 (m), 800 (m), 775 (s); MS (FAB) 237 (M − Br) (98), 236 (100), 209.9 (2), 172 (2), 156 (12), 129.1 (6), 107.2 (2), 89.5 (2), 72.7 (1), 59.9 (1). Anal. Calcd for C$_{11}$H$_{11}$NBr$_2$: C, 41.67; H, 3.49; N, 4.42. Found: C, 41.75; H, 3.50; N, 4.51.

3-Phenyl-1,2,3,3a-tetrahydro-imidazo[1,2-a]quinoline (14′c). 14 (700 mg; 2.21 mmol) was dissolved in DMF (20 mL). Aniline (100 μL; 1.10 mmol) and TEA (615 μL; 4.42 mmol) were added successively to the stirred solution. After stirring for 48 h at room temperature under nitrogen, the solution was diluted with ethyl acetate (80 mL) and washed thoroughly with water. The organic layer was then brined and dried over MgSO$_4$ before being concentrated to a brown dark residue. The compound was purified by column chromatography (silica beforehand loaded with TEA). The column was eluted with a DCM/TEA (95:5) solution to obtain the acid- and air-sensitive compound **14′c** (90 mg; 0.63 mmol) as a brown crystal in a 33% yield: R_f = 0.7 in DCM; mp 130−132 °C; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 6.95 (m, 2H), 6.83 (d, 1H, J = 8.8 Hz), 6.66 (t, 2H, J = 7 Hz), 6.56 (t, 1H, J = 7.4 Hz), 6.48 (d, 1H, J = 8.0 Hz), 6.35 (dd, 2×0.5H, J = 10.0 and 2.4 Hz), 5.45 (dd, 2×0.5H, J = 10 and 2.4 Hz), 5.23 (s, 0.5H), 4.96 (s, 0.5H), 4.56 (d, 2×0.5H, J = 6.0 Hz), 4.41 (d, 2×0.5H, J = 6.0 Hz), 3.77 (m, 1H), 3.62 (m, 1H), 3.00 (t, 1H, J = 14.2 Hz), 2.72 (dd, 1H, J = 10.6 and 4.8 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 171.55 (C), 142.66 (C), 140.34 (C), 130.11 (CH), 129.75 (CH), 128.08 (CH), 127.59 (CH), 127.49 (CH), 126.62 (CH), 124.89 (CH), 122.01 (C), 119.75 (CH), 116.88 (CH), 110.83 (CH), 109.98 (CH), 104.24 (CH), 60.79 (CH$_2$), 51.95 (CH$_2$), 28.71 (CH$_2$), 25.15 (CH$_2$); IR (KBr, cm^{-1}) 1723 (w), 1598 (s), 1493 (s), 1455 (m), 1266 (m), 1164 (m), 909 (m), 825 (w), 745 (s), 724 (s); MS (FAB) 249.2 (M − Br) (30), 121.2 (5), 180.2 (20), 145.2 (15), 83 (100), 77.1 (6), 47 (18).

3-(4-Methoxy-benzyl)-1,2,3,3a,4,5-hexahydro-imidazo-[1,2-a]quinoline (14″). A 7.5% Na$_2$CO$_3$ aqueous solution (20 mL) was prepared and ethyl acetate (40 mL) added along with 3 drops of TEA. The biphasic solution was cooled to 0 °C, and *p*-methoxybenzylamine (274 μL; 2.1 mmol) added followed by 2-bromo-ethyl-quinolinium **14** (604 mg; 1.9 mmol). The reaction mixture was stirred under nitrogen at room temperature overnight. The aqueous layer was sublimed using a freeze-drier and the resulting powder triturated several times with chloroform. The chloroform solution was concentrated to saturation, precipitated with ether and filtered, to yield **15a** (315 mg; 0.85 mmol) after ether wash, as white crystals in a 90% yield. The organic layer was washed twice with water and concentrated under vacuum. The product was purified by column chromatography (ethyl acetate/TEA (95:5)) to yield **14″** (280 mg; 0.8 mmol) as an orange oil in a 84% yield: R_f = 0.8 in ethyl acetate; ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.64 (d, 2H, J = 8.4 Hz), δ 7.17 (d, 2H, J = 8.4 Hz), δ 6.81 (m, 4H), δ 4.65 (s, 2H), δ 3.73 (m, 5H), δ 3.48 (m, 2H), δ 3.39 (t, 2H, J = 8.0 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 206.93 (C), δ 161.68 (C), δ 160.93 (CH), δ 153.66 (C), δ 131.79 (C), δ 130.01 (CH), δ 129.81 (CH), δ 129.17 (CH), δ 113.91 (CH), δ 110.77 (CH), δ 64.42 (CH$_2$), δ 55.31 (CH), δ 51.66 (CH$_2$), δ 30.93 (CH$_3$), δ 28.38 (CH$_2$), δ 27.19 (CH$_2$), δ 26.32 (CH$_2$); IR (KBr, cm^{-1}) 1626 (m), 1601 (s), 1509 (s), 1454 (m), 1374 (m), 1301 (m), 1243 (s), 1173 (m), 1110 (w), 1025 (s), 815 (m), 788 (w), 752 (s); MS (CI) 295.2 (M + H) (70), 256.2 (100), 192.2 (3), 164.2 (4), 137.1 (10), 121.1 (30).

3-(4-Methoxy-benzyl)-2,3-dihydro-1H-imidazo[1,2-a]-quinolinium Bromide (15a). Quinolinium derivative **14** (1 g; 3.15 mmol) was reacted with 4-methoxybenzylamine (0.216 g; 205 μL; 1.57 mmol) using the same protocol as for the synthesis of **6a−h**. **15a** (405 mg; 1.09 mmol) was obtained as an off white powder in a 70% yield: mp 259−260 °C (dec); ^{1}H

NMR (CDCl$_3$, 400 MHz) δ 8.34 (d, 1H, J = 9.6 Hz), 7.83 (t, 2H, J = 8.0 Hz), 7.55 (d, 1H, J = 8.0 Hz), 7.49 (t, 1H, J = 8.00 Hz), 7.40 (d, 1H, J = 9.60 Hz), 7.34 (d, 2H, J = 8.80 Hz), 6.91 (d, 2H, J = 8.8 Hz), 4.99 (t, 2H, J = 10.4 Hz), 4.42 (t, 2H, J = 10.4 Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 159.11 (C), 154.51 (C), 145.65 (CH), 136.06 (C), 134.21 (CH), 130.10 (CH), 130.00 (CH), 126.86 (C), 125.46 (CH), 122.41 (C), 114.88 (CH), 114.80 (CH), 107.46 (CH), 55.78 (CH$_3$), 49.11 (CH$_2$), 47.93 (CH$_2$), 46.48 (CH$_2$); IR (KBr, cm^{-1}) 3433 (s), 2997 (w), 2939 (w), 2677 (w), 1631 (s), 1579 (m), 1512(m), 1448 (w), 1361 (w), 1304 (m), 1238 (s), 1178 (m), 1024 (m), 771 (m); MS (FAB) 292.1 (M − Br) (100), 260.1 (4), 184 (1), 169 (12), 129.1 (4), 121.1 (48), 102.4 (7), 77.6 (2). Anal. Calcd for C$_{19}$H$_{19}$N$_2$OBr· 0.5H$_2$O: C, 58.62; H, 5.16; N, 8.22. Found: C, 58.83; H, 4.97; N, 8.28.

3-(4-Methoxy-phenyl)-2,3-dihydro-1H-imidazo[1,2-a]-quinolin-10-ylium Bromide (15b). Quinolinium derivative **14** (1 g; 3.15 mmol) was reacted with 4-methoxyaniline (0.193 g; 1.57 mmol) using the same protocol as for the synthesis of **6a−h**. **15b** (302 mg; 0.85 mmol) was obtained as a brown powder in a 54% yield: mp 217−218 °C (dec); ^{1}H NMR (D$_2$O, 400 MHz) δ 8.27 (d, 1H, J = 9.2 Hz), δ 7.88 (d, 1H, J = 8.0 Hz), δ 7.85 (t, 1H, J = 8.0 Hz), δ 7.55 (d, 1H, J = 8.0 Hz), δ 7.51 (t, 1H, J = 8.0 Hz), δ 7.41 (d, 2H, J = 8.8 Hz), δ 7.09 (d, 2H, J = 8.8 Hz), δ 6.95 (d, 1H, J = 9.2 Hz), δ 4.83 (t, 3H, J = 10.2 Hz), δ 4.50 (t, 3H, J = 10.2 Hz); δ 3.8 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 160.27 (C), δ 153.93 (C), δ 145.53 (CH), δ 136.01 (C), δ 134.63 (CH), δ 129.79 (CH), δ 129.07 (C), δ 127.03 (CH), δ 125.91 (CH), δ 122.60 (C), δ 115.74 (CH), δ 115.62 (CH), δ 107.60 (CH), δ 55.74 (CH$_3$), δ 52.68 (CH$_2$), δ 47.85 (CH$_2$); IR (KBr, cm^{-1}) 2975 (w), 2934 (w), 2736 (m), 2674 (s), 2491 (m), 2357 (w), 1619 (m), 1471 (s), 1433 (s), 1396 (s), 1069 (w), 1035 (s), 803 (m), 761 (m); MS (FAB) 277.3 (M − Br) (45), 255.3 (10), 176.1 (7), 102.4 (100), 72.8 (5). Anal. Calcd for C$_{18}$H$_{17}$BrN$_2$O·H$_2$O: C, 57.61; H, 5.10; N, 7.47. Found: C, 57.85; H, 5.02; N, 7.37.

3-(2-Bromo-ethyl)-quinazolin-3-ium Bromide (16). Quinazoline (1.13 g; 8.7 mmol) was reacted with 1,2-dibromoethane following the same protocol as for the synthesis of molecule **2**. Molecule **16** (2.36 g; 7.4 mmol) was obtained as a yellow, hygroscopic powder in a 85% yield: mp 116−118 °C; ^{1}H NMR (D$_2$O, 400 MHz) δ 8.41 (s, 1H), δ 7.5 (m, 3H), δ 7.21 (d, 1H, J = 7.6 Hz), δ 6.32 (s, 1H), δ 4.3 (tt, 1H, J = 15.2, 5.6 Hz), δ 4.03 (tt, 1H, J = 15.2, 5.6 Hz), δ 3.78 (t, 2H, J = 5.6 Hz); ^{13}C NMR (D$_2$O, 100 MHz) δ 149.1 (CH), δ 131.3 (CH), δ 129.0 (C), δ 128.8 (CH), δ 128.4 (CH), δ 120.4 (C), δ 117.4 (CH), δ 77.0 (CH), δ 53.6 (CH$_2$), δ 30.3 (CH$_2$); IR (KBr, cm^{-1}) 2971 (w), 2930 (w), 1665 (s), 1628 (w), 1596 (w), 1550 (m), 1492 (s), 1408 (m), 1190 (m), 1024 (s), 896 (m), 758 (s); MS (EI) 237 (M − Br) (5), 184.1 (12), 173.1 (8), 144.1 (9), 130.1 (100), 103.1 (59), 76.1 (36), 50.0 (16). Anal. Calcd for C$_{10}$H$_{10}$Br$_2$N$_2$·H$_2$O: C, 35.74; H, 3.60; N, 8.34. Found: C, 35.50; H, 3.77; N, 8.24.

1-(4-Methoxy-benzyl)-2,3-dihydro-1H-imidazo[1,2-c]-quinazolin-4-ylium Bromide (17). Molecule **16** (720 mg; 2.26 mmol) was reacted with 4-Methoxybenzylamine (343 mg; 2.5 mmol) following Protocol B for the synthesis of molecule **6a**. **17** (0.426 g; 2.2 mmol) was obtained as an orange hygroscopic powder in a 60% yield: mp 83.3 °C; ^{1}H NMR (D$_2$O, 400 MHz) δ 8.43 (s, 1H), δ 8.14 (d, 1H, J = 8 Hz), δ 7.95 (tt, 1H, J = 7.6, 1.2 Hz), δ 7.81 (dd, 1H, J = 13.2, 7.6 Hz), δ 7.56 (dt, 1H, J = 7.6, 1.2 Hz), δ 7.28 (d, 2H, J = 8.4 Hz), δ 6.93 (d, 2H, J = 8.4 Hz), δ 5.22 (s, 2H), δ 4.64 (t, 2H, J = 10 Hz), δ 4.22 (t, 2H, J = 10 Hz), δ 3.71 (s, 3H); ^{13}C NMR (D$_2$O, 100 MHz) δ 159.4 (C), δ 156.3 (C), δ 148.6 (C), δ 143.8 (CH), δ 138.1 (CH), δ 129.7 (CH), δ 128.8 (CH), δ 128.5 (CH), δ 126.6 (C), δ 125.4 (CH), δ 115.1 (CH), δ 114.9 (C), δ 114.7 (CH), δ 112.4 (C), δ 55.7 (CH$_3$), δ 52.3 (CH$_2$), δ 52.0 (CH$_2$), δ 46.4 (CH$_2$); IR (KBr, cm^{-1}) 3427 (s), 2926 (s), 1631 (s), 1581 (s), 1513 (s), 1303 (s), 1248 (s), 1177 (m), 1137 (w), 1028 (m), 832 (w), 773 (m), 675 (m), 540 (m); MS (CI+ mode) 292.2 (M − Br) (3), 172.1 (87), 138.1 (13), 121.1 (100), 100.1 (5), 71.1 (5). Anal. Calcd for C$_{18}$H$_{18}$BrN$_3$O·H$_2$O: C, 55.40; H, 5.17; N, 10.77. Found: C, 55.32; H, 5.26; N, 10.68.

Single-Crystal Structure Determination of 6h. Suitable single crystals were grown and mounted onto the end of a thin glass fiber using Fomblin oil. X-ray diffraction intensity data were measured at 150 K on a Nonius Kappa-CCD diffractometer [λ(Mo Kα) = 0.7107 Å]. Structure solution and refinement was carried out with SHELXS-97[12a] and SHELXL-97[12b] via WinGX.[12c] Corrections for incident and diffracted beam absorption effects were applied using empirical methods.[12d] Crystal data and structure refinement for **6h**: [$C_{22}H_{19}BrN_2O$], M_r = 407.30 g mol^{-1}; colorless lath (0.48 × 0.10 × 0.08 mm^3) was analyzed with a Kappa CCD diffractometer using Mo Kα radiation (λ = 0.71073 Å) at 150(2) K. Monoclinic, space group $P2_1/n$, a = 10.4821(1), b = 14.2325(2), c = 12.5420-(2) Å, α = 90°, β = 106.365(1)°, γ = 90°, V = 1795.29(6) Å^3, Z = 4, ρ = 1.51 g cm^{-3}, μ(Mo Kα) = 2.303 mm^{-1}, F(000) = 831.9, 28924 reflections measured, of which 4123 are independent, 235 refined parameters, R1 = 0.029, wR2 = 0.065. CCDC-213459 contains the supplementary crystallographic data for **6h**. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ; fax (+44) 1223-336-033 or email deposit@ccdc.cam.ac.uk.

Supporting Information Available: Additional details, ^{1}H NMR spectra of the products and intermediates, and crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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