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Selective Anti-Markovnikov Cyclization and Hydrofluorination Reaction in Superacid HF/SbF_5: A Tool in the Design of Nitrogen-Containing (Fluorinated) Polycyclic Systems

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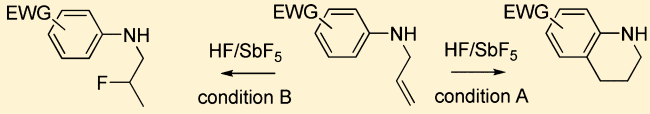
Supporting Information

ABSTRACT: The selective synthesis of tetrahydroquinolines and fluorinated arylamines was performed in superacid HF/SbF_5 through a superelectrophilic ammonium−carbenium activation process. This anti-Markovnikov oriented reaction was applied to the straightforward synthesis of highly valued (fluorinated) nitrogen-containing heterocyclic compounds.



1. INTRODUCTION

Nitrogen heterocycles are widespread molecules in the pharmaceutical and agrochemical industries. In particular, the tetrahydroquinoline ring is a very common scaffold,[1] and tetrahydroquinolines bearing simple or complex substituents act as chemotherapeutic and pharmacodynamic agents[2] but are also used as coordinating ligands or dyes.[3] Furthermore, tetrahydroquinoline-containing sulfonamides, acting as carbonic anhydrase selective inhibitors,[4] have recently been shown to be targets of choice in the design of new anticancer agents,[5] which may allow further exploration of the list of tetrahydroquinolines with antitumor activity.[2] Because of the significance of these scaffolds in drug discovery, the development of straightforward synthetic methodologies for the synthesis of tetrahydroquinoline derivatives remains a very attractive field of research.[1] Among the different ways for constructing tetrahydroquinolines, acid-catalyzed intramolecular Friedel−Crafts related reactions of *N*-arylamines is a commonly used strategy.[6] This methodology allows the formation of the C_4−C_{4a} bond of the tetrahydroquinoline ring and has been previously applied to the synthesis of natural products.[7] *N*-Arylated allylamines were found to be the substrate of choice to achieve the synthesis of tetrahydroquinolines through this process.[8] However, the method suffers from a lack of efficiency when applied to electronically deactivated aniline derivatives.[9] In due course of our work on the study of unsaturated nitrogen compounds' behavior in superacid[10] HF/SbF_5,[11] we recently reported the anti-Markovnikov addition to *N*-allylic anilines[12] through an ammonium−carbenium superelectrophilic activation process.[13] Starting from *N*-allylic aniline, after intramolecular reaction, depending on the nature of the aromatic substitution, indolines and tetrahydroquinolines were formed. In addition, fluorinated amines were formed as side products after hydrofluorination reaction.

Fluorinated nitrogen containing compounds are regarded as relevant tools in medicinal chemistry.[14] Due to its unique properties,[15] the insertion of fluorine atom(s) in nitrogen compounds can alter both physical and chemical properties[16] and is now routinely used to modify ADME parameters of a drug.[17] Among fluorinated bioactive compounds, recently, fluorinated arylamines were used in the design of bioactive drugs, going from compounds showing neuroprotective properties,[18] hepatitis C virus entry inhibitors,[19] thrombin inhibitors,[20] selective carbonic anhydrase IX cancer related isoform inhibitors,[21] or potential tools for molecular imaging of apoptosis related caspaces.[22] However, few methodologies focus on their direct preparation and the classically used dehydroxyfluorination method[23] or aziridine ring-opening[24] suffer from rearrangement side product formation.

Taking into account these data, we explored the ability to use HF/SbF_5 superacid chemistry to selectively access either to tetrahydroquinolines or fluorinated arylamines. Then, the use of this divergent method to the synthesis of novel polycyclic and fluorinated heterocycles has been explored.

2. RESULTS AND DISCUSSION

As mentioned above, when studying the anti-Markovnikov-oriented reaction of *N*-arylated allylic amines, *β*- and *γ*-fluorinated amines were found to be side products of the reaction. As a consequence, to evaluate the ability to selectively access to tetrahydroquinolines or to fluorinated aromatic amines, the influence of the reaction conditions (acidity, temperature, ...) on the selectivity of the process were explored (Scheme 1, Table 1).

First, substrate **1a** was submitted to superacid at −20 °C, and a mixture of *β*-fluorinated amine **2a**, tetrahydroquinoline **4a**, and indoline **5a** was formed (Table 1, entry 1). Then the effect of the temperature on the reaction course was evaluated. Increasing temperature led to an increase of cyclic products formation, and working at −50 °C allowed us to selectively

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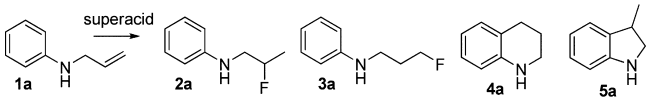
Scheme 1. Reactivity of *N*-Allylaniline 1a in Superacid HF/SbF_5[a]



[a]Reaction conditions: substrate (1 mmol), HF/SbF_5 (4 mL), 10 min. The starting material was observed in all cases (less than 10%).

Table 1. Competition between Intramolecular Friedel–Crafts and Hydrofluorination Reactions of Substrate 1a

			product[b]			
entry	SbF_5[a] (mol %)	*T* (°C)	2a	3a	4a	5a
1	3.8	−20	23	*c*	45	28
2	3.8	0	2	*c*	50	41
3	3.8	−50	86	*c*	3	1
4	0	−20	*d*	*d*	*d*	*d*
5[e]	0	20	*d*	*d*	*d*	*d*
6	12.1	−20	3	*c*	46	43
7[f]	12.1	−20	3	*c*	46	43
8	21.6	−20	3	*c*	51	33
9	21.6	0	*c*	*c*	36	57

[a]HF/SbF_5 media composition defined by SbF_5 molar percentage. [b]Relative abundances determined by analysis of the ^{1}H NMR spectra of the crude reaction. [c]Only traces of the product could be detected by ^{1}H NMR in the crude mixture. [d]No reaction. [e]Concentrated neat H_2SO_4 is used as media for 3 days at room temperature. [f]HF/SbF_5 (6 mL).

access to fluorinated compound **2a** (Table 1, entries 2 and 3). These observations led to the hypothesis that cyclic products could be considered the thermodynamic products of the reaction. To test whether superacid HF/SbF_5 is essential for fluorination and cyclization processes, the reaction was tested in pure HF and in the presence of concentrated sulfuric acid (Table 1, entries 4 and 5). The absence of reaction in these conditions confirmed that the formation of the products is strongly dependent on the acidity of the media, confirming a superlectrophilic activation process through (poly)protonation. However, whatever the tested conditions, only traces of γ-fluorinated product **3a** could be obtained. We next screened various experimental conditions to optimize the formation of the cyclic products. By increasing the acidity of the media, that means increasing SbF_5 concentration, the hydrofluorination process could be decreased in favor of cyclization, with no significant effect of dilution (Table 1, entries 6–8).[10,11] Exclusive formation of the cyclic compounds occurred under optimized conditions (Table 1, entry 9). Thus, starting from *N*-allylic aniline, tetrahydroquinoline and indoline or β-fluorinated aniline could be selectively obtained in optimized conditions: Hydrofluorination SbF_5 (3.8 mol %), −50 °C (conditions A); Friedel–Crafts intramolecular cyclization SbF_5 (21.6 mol %), 0 °C, 10 min (conditions B).

Then, to evaluate the scope of these reactions and the influence of the nucleophilic character of the aromatic ring on the selectivity of the reaction, a variety of differently substituted substrates were submitted to the reaction (Scheme 2, Table 2). As expected, in hydrofluorination conditions, in all cases the β-fluorinated anilines could be formed in good yields. No effect of aromatic ring substitution on this reaction could be observed. Unfortunately, γ-fluorinated products could not be obtained in these conditions, except from substrate **1i** after reaction at 0 °C in more acidic conditions (Table 2, entry 18).

Under cyclization conditions, in all cases the tetrahydroquinoline products were formed.[25] Starting from the activated aniline **1b**, as from the aniline **1a**, tetrahydroquinolines were formed beside the indoline products (Table 2, entries 2 and 4). Increasing the electronic density on the aromatic ring (σ_p Me = −0.15)[26] led to an increase of indoline product formation. However, decreasing the electronic density on the aromatic ring by introducing a trifluoromethyl group (σ_p CF_3 = 0.54) gave the tetrahydroquinoline **4c** as the major product.[27] A similar effect observed after substitution of the aromatic ring with an amido or a methoxy group could be attributed to the protonation of these functions under the superacid conditions. The protonated functions, in equilibrium with their neutral forms, could act in these conditions as strong electron-withdrawing substituents.[28] Increasing the withdrawing effects on the aromatic ring led to the exclusive formation of the tetrahydroquinoline products (Table 2, entries 16, 19, 21, and 23). When the aromatic ring was too deactivated, only deallylation occurred (Table 2, entry 25).

These data allowed us to postulate the following mechanism (Scheme 3).

By conducting mechanistic investigations using in situ NMR experiments, DFT calculations, and labeled substrates reactions, two mechanistic pathways were postulated. Protonation of the *N*-allylated aniline leads to the formation of the ammonium ion **A**. Then, the superacidity of the media allows a second protonation and either the formation of a μ-hydrido-bridged carbocation containing ammonium–carbenium superelectrophile **B** after protonation of the double bond or after protonation of the aromatic ring to the formation of the ammonium–arenium dicationic superelectrophile **C**.[12] With activated substrates, the dicationic ammonium–arenium superelectrophile of type **C** is favored, leading to the formation of a mixture of both cyclic products. With deactivated substrates, the (poly)protonation leads to the superelectrophilic intermediate **B** formation. The aromatic ring, despite its electronic deactivation by the proximal ammonium ion can trap the cation in an intramolecular way to give the dication **E**, precursor of the tetrahydroquinoline products **4**. The formation of a five-membered ring analogue of dication **E** from **B**, precursor of indolines **5** has been shown to be energetically less favorable than the formation of intermediate **E** by more than 4 kcal/mol.[12] It has to be noted that when submitting the cyclic products (for instance for compounds **4a** and **5a**) to cyclization conditions (conditions B), no reaction occurred, confirming the

Scheme 2. Reactivity of Substituted *N*-Allylaniline 1 in Superacid HF/SbF_5

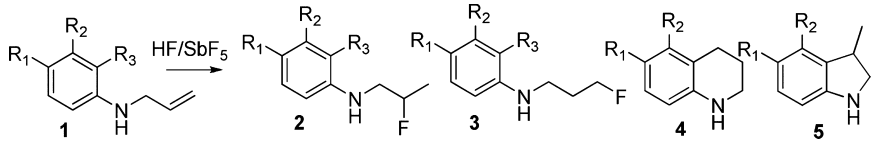


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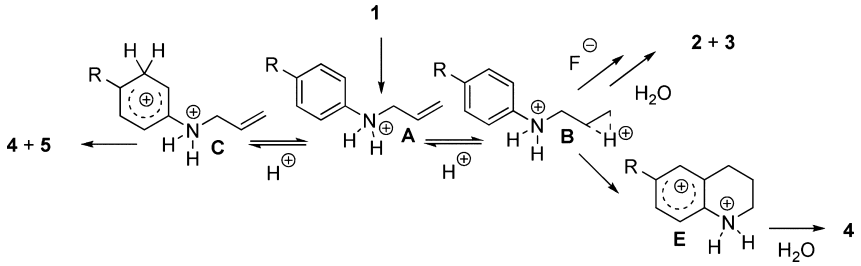
Table 2. Selective Hydrofluorination and Friedel–Crafts Reactions of *N*-Allylic Anilines

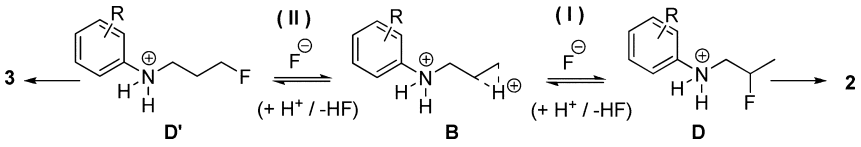
entry	substrates[a]		method[b]	products (yield, %)[c]			
1	**1a**	R_1 = H	A	**2a** (50)	**3a** (*d*)		
2		R_3 = H	B			**4a** (22)	**5a** (39)
3	**1b**	R_1 = Me	A	**2b** (82)	**3b** (*d*)		
4		R_3 = H	B			**4b** (14)	**5b** (46)
5	**1c**	R_1 = CF_3	A	**2c** (92)	**3c** (*d*)		
6		R_3 = H	B			**4c** (39)	**5c** (5)
7	**1d**	R_1 = NHAc	A	**2d** (87)	**3d** (*d*)		
8		R_3 = H	B			**4d** (72)	**5d** (17)
9	**1e**	R_1 = OMe	A	**2e** (85)	**3e** (*d*)		
10		R_3 = H	B			**4e** (32)	**5e**(*d*)
11	**1f**	R_1 = $N(Me)_2$	A	**2f** (52)	**3f** (*d*)		
12		R_3 = H	B		*e*		
13	**1g**	R_1 = COOEt	A	**2g** (87)	**3g** (*d*)		
14		R_3 = H	B		*e*		
15	**1h**	R_1 = SO_2NH_2	A	**2h** (66)	**3h** (*d*)		
16		R_3 = H	B			**4h** (92)	
17	**1i**	R_1 = NO_2	A	**2i** (95)	**3i** (*d*)		
18			A[f]	**2i** (79)	**3i** (6)		
19		R_3 = H	B			**4i** (85)	
20	**1j**	R_1 = H	A[f]	**2j** (97)	**3j** (*d*)		
21		R_3 = H	B			**4j** (66)[g]	
22	**1k**	R_1 = NO_2	A	**2k** (95)	**3k** (*d*)		
23		R_3 = Me	B			**4k** (84)	
24	**1l**	R_1 = NO_2	A	**2l** (48)	**3l** (*d*)		
25		R_3 = NO_2	B		*h*		

[a]For substrate **1j** R_2 = NO_2, and for all substrates R_2 = H. [b]Reaction conditions: method A, substrate (1 mmol), HF/SbF_5 (4 mL), 10 min, SbF_5 (3.8 mol %), −50 °C; method B, substrate (1 mmol), HF/SbF_5 (4 mL), SbF_5 (21.6 mol %), 0 °C. The starting material was observed in all cases (less than 10%). [c]After column chromatography. [d]Only traces were detected in the crude mixture. [e]Complex mixture. [f]SbF_5 12.5 (mol %), 0 °C. [g]5-Nitro-1,2,3,4-tetrahydroquinoline **4j′** was also formed in 10% yield. [h]Only deallylation occured.

Scheme 3. Postulated Mechanism for Hydrofluorination and Cyclization Reactions



Scheme 4. Postulated Reaction Equilibriums in Fluorinated Products Formation



irreversibility of the cyclization reactions. Then, we investigated whether the fluorinated derivative could be considered as an intermediate in the cyclization process. Starting from the fluorinated derivative **2a**, after reaction under cyclization conditions, the tetrahydroquinoline and indoline derivatives **4a** and **5a** were exclusively formed, a result that confirmed the postulated reaction equilibriums (Scheme 4).

However, to discuss the displacement of equilibrium (**I**) toward the formation of the ammonium–carbenium ion **B** in cyclization conditions, the composition of the media has to be analyzed. The following conclusions were proposed and largely accepted from extensive reported studies of ionic composition in HF/SbF_5 solutions.[29] For SbF_5 concentration lower than 10 mol %, SbF_6^- is practically the only anionic species present and $H_3F_2^+$ the predominant cationic species. From 10 to 22 mol % of SbF_5 in HF, the anions are essentially SbF_6^- and $Sb_2F_{11}^-$ in slow equilibrium and only H_2F^+ is observed. Taking into account these conclusions, we can consider that the nucleophilicity of fluoride ion source strongly decreases as the SbF_5 concentration increases, and it has now largely been shown that increasing the amount of SbF_5 increases the acidity strength of the media. In cyclization conditions, the fluorinated

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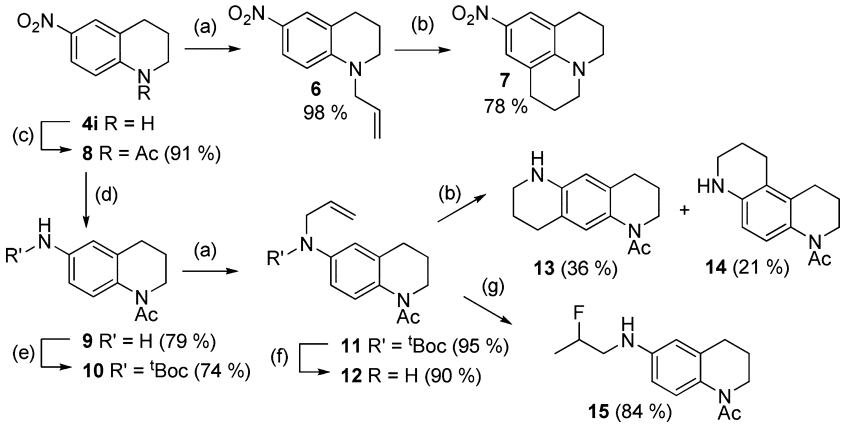
Scheme 5. Synthesis of Nitrogen-Containing Polycyclic (Fluorinated) Compounds[a]



[a]Conditions: (a) NaH, allyl bromide, DMF; (b) HF/SbF_5 (SbF_5, 21.6 mol %); (c) NaH, AcCl, CH_2Cl_2; (d) $SnCl_2$, EtOH; (e) $(Boc)_2O$, THF; (f) TFA, CH_2Cl_2; (g) HF/SbF_5 (SbF_5, 3.8 mol %).

intermediate **D**, after protonation and HF elimination, could give **B**, which could be trapped by the more nucleophilic species (aromatic ring) to give the dication **E**, precursor of the tetrahydroquinoline after hydrolysis. Elimination from the dication **B** could also give the unsaturated ammonium ion **A** under these conditions (Scheme 3).

The formation of the β-fluorinated products was largely favored, and thus despite a possible superelectrophilic charge−charge repulsive effect[30] in the μ-hydrido-bridged carbocation-containing ammonium−carbenium superelectrophile **B** (Scheme 3). In this case, no repulsive effect predominates, as the three-center two-electron bond intermediate has been shown by DFT calculations to correspond to a symmetrically μ-hydrido-bridged species (μ-H---C distances: 1.33 Å, activated C═C bond length: 1.39 Å).[12] However, an equilibrated distribution between the β-fluoro and the γ-fluoro derivatives could have been expected. The favored formation of the β-fluorinated product in this reaction could be attributed to a displacement of the equilibriums **I** and **II** between fluorinated ammonium precursors **D**, **D′**, and ion **B**. After protonation (or activation),[31] HF elimination could be postulated (equilibriums **I** and **II**). When submitting substrate **3i** in superacid, a mixture of β-fluoro product **2i** and γ-fluoro product **3i** were obtained beside unsaturated aniline **1i** (**1i**/**2i**/**3i** ratio = 3/87/7). Analogously, when substrate **2i** was submitted to superacid, a similar mixture of compound was formed (**1i**/**2i**/**3i** ratio = 3/88/6). These results confirm the thermodynamic stability of intermediate **D** under superacid conditions. Through electrostatic interactions between the fluorine atom and the ammonium ion,[32] a stabilization of the intermediate could be postulated. However, the strong electronic withdrawing effect of the fluorine atom should destabilize the ammonium ion (with a stronger effect in intermediate **D**). Another aspect should be appreciated: The elimination of hydrogen fluoride could be more favorable from **D′**, than from **D**. All these parameters must influence the displacement of the equilibrium toward the formation of the precursors of the β-fluorinated products.

Having in hand a straightforward and selective method to synthesize electronically deactivated tetrahydroquinolines and/or β-fluorinated aniline derivatives, we decided to further explore its potential in accessing structurally more complex structures. As previously mentioned, tetrahydroquinolines are widespread molecules in medicinal chemistry research, and among tetrahydroquinolines containing bioactive compounds, two families retain our attention. First, julolidine derivatives have found numerous interests as photoconductive materials, chemoluminescence substances, and dyes intermediates and also in biological systems as fluorescent probes.[33] However, even if elegant methods have been developed to synthesize julolidines,[34] accessing to the electronically deactivated analogues is rather limited, and methods existing to prepare these products suffer from safety concern, poor selectivity, and oxidation.[35] The second family that interested us is the diazaoctahydroanthracene one. In the quest for molecules with helical structure, exhibiting optical and electronic properties,[36] the development of methods to synthesize new constrained functionalized nitrogen-containing polycyclic systems is of great interest.[37] In this context, the previously described method could be applied to the synthesis of novel diazaoctahydroanthracene.

Thus, we explored the divergent synthesis of the 9-nitrojulolidine and 1,5-diazaoctahydroanthracene derivatives. To access to both compounds in a divergent way, the employed synthetic strategy was based on the same crucial intermediate 6-nitro-1,2,3,4-tetrahydroquinoline **4i** (Scheme 5), synthesized in 85% yield after anti-Markovnikov Friedel−Crafts superacid-catalyzed reaction (Table 2). After allylation, in the presence of allylbromide, *N*-allylated compound **6** was synthesized in 98% yield. Then, the cyclization in superacid HF/SbF_5 allowed us to access to the 9-nitrojulolidine **7** in good yield. The key intermediate **4i** was also engaged in the multistep synthesis of novel nitrogen-containing heterocycles. After acetylation of the amino function, the reduction of the nitro group to its amino derivative analogue was performed in the presence of $SnCl_2$. A subsequent protection of the formed amine in its carbamate analogue, followed by allylation in the presence of allyl bromide, led to the synthesis of product **11**. When product **11** was submitted to cyclization in superacid, only a complex mixture of compounds could be obtained. Thus, compound **11** was deprotected to give amine **12**. Gratifyingly, the cyclization of compound **12** under superacid conditions led to the synthesis of two tricyclic compounds **13**[38] and **14** in 36 and 21% yields, respectively. At this stage, the selective hydrofluorination of the same substrate could also be achieved in good yield to give the β-fluorinated bicyclic compound **15**.

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Starting from *N*-allylic-4-nitroaniline, these multistep strategies, including two reactions in superacid, allowed the synthesis of the targeted cyclic products **13** and **14** in 22% overall yield, the synthesis of the original fluorinated product **15** in 32% yield, and the synthesis of 9-nitrojulolidine **7** in 65% yield, making these synthetic routes good alternatives to existing methods.

3. CONCLUSION

To conclude, a new selective method to access either β-fluorinated anilines or electronically deactivated tetrahydroquinolines was developed. This original method is based on a superacid HF/SbF_5 activation through the formation of an original μ-hydrido-bridged carbocation containing an ammonium−carbenium superelectrophile. This anti-Markovnikov-oriented reaction was also applied to the straightforward synthesis of highly valued (fluorinated) nitrogen-containing heterocyclic compounds showing the synthetic potential of the developed method.

4. EXPERIMENTAL SECTION

4.1. General Methods. We draw the reader's attention to the dangerous features of superacidic chemistry. Handling of hydrogen fluoride and antimony pentafluoride must be done by experienced chemists with all the necessary safety arrangements in place.

Reactions performed in superacid were carried out in a sealed Teflon flask with a magnetic stirrer. No further precautions have to be taken to prevent mixture from moisture (test reaction worked out in anhydrous conditions leads to the same results as expected). Yields refer to isolated pure products. ^{1}H, ^{13}C, and ^{19}F NMR were recorded on a 400 MHz Bruker Advance DPX spectrometer using $CDCl_3$, CD_3COCD_3, or CD_3OD as solvent. COSY ^{1}H−^{1}H and ^{1}H−^{13}C experiments were used to confirm the NMR peaks assignments. Melting points were determined in a capillary tube with a device melting point appartus and were uncorrected. Mass Spectra (MS) were performed with coupled gas chromatography (electronic impact). All separations were done under flash chromatography conditions on silica gel (15−40 μm). High-resolution mass spectrometry (HRMS) spectra were performed with a quadrupole mass analyzer.

Preparation of HF/SbF_5 Mixture. After liquid condensation of the desired quantity of hydrogen fluoride in a Teflon reactor at −30 °C, antimony pentafluoride was slowly added to the reactor at the same temperature and the reactor was then sealed and maintained at reaction temperature. Under these conditions, the SbF_5 molar percentage was determined accordingly: For example, 1 mL of SbF_5 (13.8×10^{-3} mol) was added to 7 mL of anhydrous liquid HF (0.35 mol) to give a HF/SbF_5 solution with a SbF_5 molar percentage of 3.8 mol %.

4.2. Hydrofluorination Reactions. *Optimized Procedure in Superacidic Media.* To a mixture of HF/SbF_5 (4 mL, SbF_5 3.8 mol %) maintained at −50 °C was added nitrogen derivative. The mixture was magnetically stirred at the same temperature during 10 min. The reaction mixture was then neutralized with water−ice−Na_2CO_3 and extracted with dichloromethane (×3). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Products were isolated by column chromatography over silica gel.

*N-(2-Fluoropropyl)aniline (**2a**).* This compound was obtained from substrate **1a** (133 mg, 1 mmol) following the general procedure. The reaction crude was purified with the eluent petroleum ether/ethyl acetate 99/1, thereby obtaining compound **2a** (76 mg, 50%) as brown oil. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.42 (dd, CH_3, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 3.28 (m, CH_2, $H_{1'}$), 3.98 (broad s, NH, H_1). 4.89 (dm, CH, J = 49.4 Hz, $H_{2'}$), 6.64 (dd, 2CH, J = 8.5 Hz, J = 0.9 Hz, H_2, H_6), 6.74 (t, CH, J = 7.3 Hz, H_4), 7.19 (dd, 2CH, J = 8.4 Hz, J = 7.4 Hz, H_3, H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.8 (d, CH_3, J = 22 Hz, $C_{3'}$), 49.6 (d, CH_2, J = 21 Hz, $C_{1'}$), 89.6 (d, CH, J = 167 Hz, $C_{2'}$), 113.1 (2CH, C_2, C_6), 118.1 (1CH, C_4), 129.4 (2CH, C_5, C_3), 147.9 (C_7). ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz, ppm) δ: −180.0. MS (IES+, ACN): m/z 154 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_9H_{12}FN$ $[M + Na]^+$ 176.08515, found 176.0852.

*N-(2-Fluoropropyl)-4-methylaniline (**2b**).* This compound was obtained from the substrate **1b** (147 mg, 1 mmol) following the general procedure. The reaction crude was purified with the eluent petroleum ether/ethyl acetate 99/1, thereby obtaining compound **2b** (137 mg, 82%) as a brown oil. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.43 (dd, CH_3, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 2.27 (s, CH_3), 3.29 (m, CH_2, $H_{1'}$), 3.68 (broad s, NH), 4.90 (dm, CHF, J = 49.5 Hz, $H_{2'}$), 6.59 (d, 2CH, J = 8.4 Hz, H_2 and H_6), 7.03 (d, 2CH, J = 8.5 Hz, H_3 and H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.8 (d, CH_3, J = 22 Hz, $C_{3'}$), 20.5 (CH_3), 50.0 (d, CH_2, J = 21 Hz, $C_{1'}$), 89.6 (d, CHF, J = 167 Hz, $C_{2'}$), 113.4 (2CH, C_2 and C_6), 127.3 (C_4), 129.9 (2CH, C_3 and C_5), 145.6 (C_1). ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz, ppm) δ: −179.9. MS (IES+, ACN): m/z 168 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{10}H_{14}FN$ $[M + Na]^+$ 190.1008, found 190.1008.

*N-(2-Fluoropropyl)-4-(trifluoromethyl)aniline (**2c**).* This compound was obtained from the substrate **1c** (196 mg, 1 mmol) following the general procedure. The reaction crude was purified with the eluent pentane/ethyl acetate 95/5, thereby obtaining compound **2c** (196 mg, 92%) as a light yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.43 (dd, CH_3, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 3.34 (m, CH_2, $H_{1'}$), 4.31 (broad s, NH), 4.88 (dm, CHF, J = 49.3 Hz, $H_{2'}$), 6.63 (d, 2CH, J = 8.5 Hz, H_2 and H_6), 7.42 (d, 2CH, J = 8.4 Hz, H_3 and H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.7 (d, CH_3, J = 22 Hz, $C_{3'}$), 48.9 (d, CH_2, J = 21 Hz, $C_{1'}$), 89.4 (d, CHF, J = 168 Hz, $C_{2'}$), 112.2 (2CH, C_2 and C_6), 119.5 (q, J = 33 Hz, C_4), 125.1 (q, J = 270 Hz, CF_3), 126.8 (q, 2CH, J = 4 Hz, C_3 and C_5), 150.4 (C_1). ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz, ppm) δ: −179.92 (CF), −61.07 (CF_3). MS (IES+, ACN): m/z 202 $[M - HF + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{10}H_{11}F_4N$ $[M + H]^+$ 222.09059, found 222.0907.

*N-(4-(2-Fluoropropylamino)phenyl)acetamide (**2d**).* This compound was obtained from the substrate **1d** (189 mg, 1 mmol) following the general procedure. The compound **2d** was obtained without purification (183 mg, 87%) as an orange solid. Mp: 90−93 °C. ^{1}H NMR (MeOD, 400 MHz, ppm) δ: 1.34 (dd, CH_3, J = 23.6 Hz, J = 6.3 Hz, $H_{3'}$), 2.06 (s, CH_3), 3.22 (m, CH_2, $H_{1'}$), 4.78 (dm, CHF, J = 49.4 Hz, $H_{2'}$), 6.61 (d, 2CH, J = 8.9 Hz, H_2 and H_6), 7.25 (d, 2CH, J = 8.9 Hz, H_3 and H_5). ^{13}C NMR (MeOD, 100 MHz, ppm) δ: 18.9 (d, CH_3, J = 22 Hz, $C_{3'}$), 23.5 (CH_3), 50.6 (d, CH_2, J = 22 Hz, $C_{1'}$), 90.5 (d, CHF, J = 167 Hz, $C_{2'}$), 114.0 (2CH, C_3 and C_5), 123.3 (2CH, C_2 and C_6), 129.7 (C_1), 147.0 (C_4), 171.2 (CO). ^{19}F{^{1}H} NMR (MeOD, 376 MHz, ppm) δ: −179.52. MS (IES+, ACN): m/z 211 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{11}H_{15}FN_2O$ $[M + Na]^+$ 233.10661, found 233.1065.

*N-(2-Fluoropropyl)-4-methoxyaniline (**2e**).* This compound was obtained from the substrate **1e** (165 mg, 1 mmol) following the general procedure. The reaction crude was purified with the eluent pentane/ethyl acetate 99/1 to 96/4, thereby obtaining compound **2e** (158 mg, 85%) as a brown solid. Mp: 34−35 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.42 (dd, CH_3, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 3.75 (m, NH), 3.25 (m, CH_2, $H_{1'}$), 4.89 (dm, 1H, J = 49.5 Hz, $H_{2'}$), 3.77 (s, CH_3, OMe), 6.63 (d, 2CH, J = 9.0 Hz, H_2 and H_6), 6.82 (d, 2CH, J = 9.0 Hz, H_3 and H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.7 (d, CH_3, J = 22 Hz, $C_{3'}$), 50.6 (d, CH_2, J = 21 Hz, $C_{1'}$), 55.8 (CH_3, OMe), 89.6 (d, CHF, J = 166 Hz, $C_{2'}$), 114.6 (2CH, C_2 and C_6), 115.0 (2CH, C_3 and C_5), 142.0 (C_1), 152.5 (C_4). ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz, ppm) δ: −179.9. MS (IES+, ACN): m/z 184 $[M + H]^+$. HRMS (ESI, solvent): calcd for $C_{10}H_{14}FNO$ $[M + Na]^+$ 206.09571, found 206.0957.

*N^1-(2-Fluoropropyl)-N^4,N^4-dimethylbenzene-1,4-diamine (**2f**).* This compound was obtained from the substrate **1f** (140 mg, 0.66 mmol) following the general procedure (with 2.7 mL of the mixture HF/SbF_5). The reaction crude was purified with the eluent petroleum ether/ethyl acetate 85/15, thereby obtaining compound **2f** (79 mg, 52%) as a black oil. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.41 (dd, CH_3, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 2.85 (m, $2CH_3$, $N(CH_3)_2$), 3.23 (m, CH_2, $H_{1'}$), 3.56 (broad s, NH), 4.89 (dm, CHF, J = 49.5 Hz, $H_{2'}$), 6.65 (m, $2CH_{ar}$), 6.76 (m, $2CH_{ar}$). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.8 (d, CH_3, J = 22 Hz, $C_{3'}$), 42.3 (broad s, $2CH_3$,

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$N(CH_3)_2$), 50.8 (broad s, CH_2, $C_{1'}$), 89.7 (broad d, CH, J = 161 Hz, $C_{2'}$), 114.9 ($2CH_{ar}$), 116.0 ($2CH_{ar}$), 140.4 (broad s, C^{IV}_{ar}), 144.2 (C^{IV}_{ar}). $^{19}F\{^1H\}$ NMR ($CDCl_3$, 376 MHz, ppm) δ: −179.75. MS (IES+, ACN): m/z 197 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{11}H_{17}FN_2$ $[M + H]^+$ 197.1454, found 197.1452.

*Ethyl 4-(2-Fluoropropylamino)benzoate (**2g**).* This compound was obtained from the substrate **1g** (205 mg, 1 mmol) following the general procedure. The reaction crude was purified with the eluent petroleum ether/ethyl acetate 95/5, thereby obtaining compound **2g** (194 mg, 87%) as a light pink solid. Mp: 76−77 °C. ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.22 (t, CH_3, J = 7.1 Hz, $H_{2''}$), 1.23 (dd, CH_3, J = 23.7 Hz, J = 6.3 Hz, $H_{3'}$), 3.28 (m, CH_2, $H_{1'}$), 4.29 (q, CH_2, J = 7.1 Hz, $H_{1''}$), 4.65 (broad s, NH), 4.81 (dm, CHF, J = 49.3 Hz, $H_{2'}$), 6.55 (d, 2CH, J = 8.8 Hz, H_3 and H_5), 7.86 (d, 2CH, J = 8.8 Hz, H_2 and H_6). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 14.3 (CH_3, $C_{2''}$), 18.4 (d, CH_3, J = 22 Hz, $C_{3'}$), 48.4 (d, CH_2, J = 22 Hz, $C_{1'}$), 60.1 (CH_2, $C_{1''}$), 89.1 (d, CHF, J = 168 Hz, $C_{2'}$), 111.5 (2CH, C_3 and C_5), 118.8 (C_1), 131.4 (2CH, C_2 and C_6), 151.6 (C_4), 166.8 (CO). $^{19}F\{^1H\}$ NMR ($CDCl_3$, 376 MHz, ppm) δ: −179.9. MS (IES+, ACN): m/z 227 $[M + H + 1]^+$. HRMS (ESI, CH_3OH): calcd for $C_{12}H_{16}FNO_2$ $[M + Na]^+$ 248.10628, found 248.1064.

*4-(2-Fluoropropylamino)benzenesulfonamide (**2h**).* This compound was obtained from the substrate **1h** (296 mg, 1.39 mmol) following the general procedure (extracted with ethylacetate). The reaction crude was purified with a combi-flash with the eluent pentane/ethyl acetate 60/40, thereby obtaining compound **2h** (216 mg, 66%) as a white solid. Mp: 110 °C. ^1H NMR (MeOD, 400 MHz, ppm) δ: 1.40 (dd, CH_3, J = 23.6 Hz, J = 6.3 Hz, $H_{3'}$), 3.37 (m, CH_2, $H_{1'}$), 4.85 (dm, CHF, J = 49.1 Hz, $H_{2'}$), 6.73 (d, 2CH, J = 8.9 Hz, H_3 and H_5), 7.67 (d, 2CH, J = 8.9 Hz, H_2 and H_6). ^{13}C NMR (MeOD, 100 MHz, ppm) δ: 18.8 (d, CH_3, J = 22 Hz, $C_{3'}$), 49.2 (d, CH_2, J = 22 Hz, $C_{1'}$), 90.4 (d, CHF, J = 168 Hz, $C_{2'}$), 112.4 (s, 2CH, C_3 and C_5), 128.9 (s, 2CH, C_2 and C_6), 130.8 (C_1), 153.3 (C_4). $^{19}F\{^1H\}$ NMR (MeOD, 376 MHz, ppm) δ: −179.18. MS (IES+, ACN): m/z 255 $[M + Na]^+$. HRMS (ESI, CH_3OH): calcd for $C_9H_{13}FN_2O_2S$ $[M + Na]^+$ 255.05795, found 255.0578.

*N-(2-Fluoropropyl)-4-nitroaniline (**2i**).* This compound was obtained from the substrate **1i** (178 mg, 1 mmol) following the general procedure. The reaction crude was purified with the eluent petroleum ether/ethyl acetate 95/5 up to 80/20, thereby obtaining compound **2i** (188 mg, 95%) as a yellow solid. Mp: 62−63 °C. ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.40 (dd, CH_3, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 3.38 (m, CH_2, $H_{1'}$), 4.86 (dm, CHF, J = 49.2 Hz, $H_{2'}$), 5.06 (broad s, NH), 6.55 (d, 2CH, J = 9.2 Hz, H_2 and H_6), 8.03 (d, 2CH, J = 9.2 Hz, H_3 and H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.4 (d, CH_3, J = 22 Hz, $C_{3'}$), 48.4 (d, CH_2, J = 21 Hz, $C_{1'}$), 89.2 (d, CHF, J = 168 Hz, $C_{2'}$), 111.3 (2CH, C_2 and C_6), 126.4 (2CH, C_3 and C_5), 138.0 (C_4), 153.4 (C_1). $^{19}F\{^1H\}$ NMR ($CDCl_3$, 376 MHz, ppm) δ: −179.2. MS (IES+, ACN): m/z 199 $[M + H]^+$. HRMS (ESI, CH_3OH/CH_2Cl_2: 90/10): calcd for $C_9H_{11}FN_2O_2$ $[M + Na]^+$ 221.07023, found 221.0704.

*N-(3-Fluoropropyl)-4-nitroaniline (**3i**).* To a mixture of HF/SbF_5 (3 mL, SbF_5 12.5 mol %) maintained at 0 °C was added 173 mg of *N*-allylaniline **1i** (0.97 mmol). The mixture was magnetically stirred at the same temperature during 10 min. The reaction mixture was then neutralized with water−ice−Na_2CO_3 and extracted with ethyl acetate (×3). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The reaction crude was purified with the eluent pentane/ethyl acetate 75/25, thereby obtaining compound **2i** (151 mg, 79%) and **3i** as a yellow solid (11 mg, 6%) as a yellow solid. Mp: 42−43 °C. ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 2.05 (dm, CH_2, J = 28.3 Hz, $H_{2'}$), 3.42 (dt, CH_2, J = 6.6 Hz, J = 5.8 Hz, $H_{1'}$), 4.61 (dt, CH_2, J = 41.7 Hz, J = 5.4 Hz, $H_{3'}$), 4.65 (broad s, NH), 6.55 (d, 2CH, J = 9.2 Hz, H_2 and H_6), 8.09 (d, 2CH, J = 9.2 Hz, H_3 and H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 30.0 (d, CH_2, J = 20 Hz, $C_{2'}$), 40.4 (d, CH_2, J = 4 Hz, $C_{1'}$), 82.2 (d, CH_2F, J = 173 Hz, $C_{3'}$), 111.2 (2CH, C_2 and C_6), 126.6 (2CH, C_3 and C_5), 138.4 (C_4), 153.2 (C_1). $^{19}F\{^1H\}$ NMR (MeOD, 376 MHz, ppm) δ: −219.9. MS (IES+, ACN): m/z 199 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_9H_{11}FN_2O_2$ $[M + Na]^+$ 221.07023, found 221.0703.

*N-(2-fluoropropyl)-3-nitroaniline (**2j**).* This compound was obtained from the substrate **1j** (178 mg, 1 mmol) following the general procedure. The compound **2j** was obtained without purification (192 mg, 97%) as an orange solid. Mp: 59−61 °C. ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.44 (dd, CH_3, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 3.36 (m, CH_2, $H_{1'}$), 4.42 (broad s, NH), 4.90 (dd, CHF, J = 49.4 Hz, J = 1.7 Hz, $H_{2'}$), 6.91 (ddd, CH, J = 8.2 Hz, J = 2.4 Hz, J = 0.7 Hz, H_6), 7.28 (t, CH, J = 8.1 Hz, H_5), 7.40 (t, CH, J = 2.3 Hz, H_2), 7.53 (ddd, CH, J = 8.1 Hz, J = 2.1 Hz, J = 0.8 Hz, H_4). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.6 (d, CH_3, J = 22 Hz, $C_{3'}$), 49.0 (d, CH_2, J = 21 Hz, $C_{1'}$), 89.3 (d, CHF, J = 168 Hz, $C_{2'}$), 106.4 (C_2), 112.4 (CH, C_4), 119.3 (CH, C_6), 129.9 (CH, C_5), 148.7 (C_1), 149.4 (C_3). $^{19}F\{^1H\}$ NMR (MeOD, 376 MHz, ppm) δ: −179.24. MS (IES+, ACN): m/z 199 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_9H_{11}FN_2O_2$ $[M + Na]^+$ 221.07023, found 221.0701.

*N-(2-Fluoropropyl)-2-methyl-4-nitroaniline (**2k**).* This compound was obtained from the substrate **1k** (96 mg, 0.5 mmol) following the general procedure (with 2 mL of the mixture HF/SbF_5). The compound **2k** was obtained without purification (183 mg, 95%) as an orange solid. Mp: 75−76 °C. ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.43 (dd, CH_3, J = 23.8 Hz, J = 6.3 Hz, $H_{3'}$), 2.17 (s, CH_3), 3.43 (m, CH_2, $H_{1'}$), 4.64 (broad s, NH), 4.91 (dm, CHF, J = 49.4 Hz, $H_{2'}$), 6.52 (d, CH, J = 9.0 Hz, H_6), 7.93 (dd, CH, J = 2.6 Hz, J = 0.7 Hz, H_3), 8.00 (dd, CH, J = 9.0 Hz, J = 2.7 Hz, H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 17.2 (CH_3), 18.6 (d, CH_3, J = 22 Hz, $C_{3'}$), 48.7(d, CH_2, J = 21 Hz, $C_{1'}$), 89.1 (d, CHF, J = 168 Hz, $C_{2'}$), 107.9 (CH, C_6), 121.62 (C_2), 124.5 (CH, C_3 or C_5), 126.10 (CH, C_3 or C_5), 137.8 (C_4), 151.4 (C_1). $^{19}F\{^1H\}$ NMR ($CDCl_3$, 376 MHz, ppm) δ: −179.75. MS (IES+, ACN): m/z 213.17 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{10}H_{13}FN_2O_2$ $[M + Na]^+$ 235.08588, found 235.0858.

4.3. Cyclization Reactions. *Optimized Procedure in Superacidic Media.* To a mixture of HF/SbF_5 (4 mL, SbF_5 21.6 mol %) maintained at 0 °C was added nitrogen derivative. The mixture was magnetically stirred at the same temperature for the entire reaction time. The reaction mixture was then neutralized with water−ice−Na_2CO_3 and extracted with ethyl acetate (×3). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Products were isolated by column chromatography over silica gel.

*Formation of Compounds **4a** and **5a**.* These compounds were obtained from substrate **1a** (126 mg, 0.95 mmol) following the general procedure (reaction time: 10 min). The reaction crude was purified with the eluent pentane/ethyl acetate 99/1, compound **5a** (49 mg, 39%, brown oil) first eluted followed by compound **4a** (28 mg, 22%, brown oil).

*1,2,3,4-Tetrahydroquinoline (**4a**).* ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.96 (m, CH_2, H_3), 2.78 (t, CH_2, J = 6.4 Hz, H_4), 3.31 (t, CH_2, J = 5.4 Hz, H_2), 3.56 (broad s, NH, H_1), 6.49 (d, CH, J = 7.9 Hz, H_8), 6.63, (dt, CH, J = 7.4 Hz, J = 1.1 Hz, H_6), 6.98 (m, 2CH, H_5, H_7). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 22.3 (CH_2, C_3), 27.1 (CH_2, C_4), 42.1 (CH_2, C_2), 114.4 (CH, C_8), 117.1 (CH, C_6), 121.6 (C_{10}), 126.8 (CH, C_7), 129.6 (CH, C_5), 144.8 (C_9). MS (IES+, ACN): m/z 134 $[M + H]^+$. Already described in ref 39.

*3-Methylindoline (**5a**).* ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.34 (d, CH_3, J = 6.8 Hz), 3.12 (t, 1H, J = 8.6 Hz, H_2), 3.38 (m, CH, H_3), 3.51 (broad s, NH, H_1), 3.71 (t, 1H, J = 8.6 Hz, H_2), 6.66 (d, CH, J = 7.8 Hz, H_7), 6.75 (td, CH, J = 7.4 Hz, J = 1.0 Hz, H_5), 7.04 (tm, CH, J = 7.7 Hz, H_6), 7.10 (d, CH, J = 7.3 Hz, H_4). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.7 (CH_3), 36.8 (CH, C_3), 55.6 (CH_2, C_2), 109.6 (CH, C_7), 118.8 (CH, C_5), 123.5 (CH, C_4), 128.2 (CH, C_6), 134.5 (C_9), 151.3 (C_8). MS (IES+, ACN): m/z 134 $[M + Na]^+$. Already described in ref 39.

*Formation of Compounds **4b** and **5b**.* These compounds were obtained from substrate **1b** (137 mg, 0.93 mmol) following the general procedure (reaction time 10 min). The reaction crude was purified with the eluent petroleum ether/ethyl acetate 98/2, compound **5b** (63 mg, 46%, brown oil) first eluted followed by compound **4b** (19 mg, 14%, brown oil).

*6-Methyl-1,2,3,4-tetrahydroquinoline (**4b**).* ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.97 (m, CH_2, H_3), 2.25 (s, CH_3, $H_{1'}$), 2.78 (t, CH_2, J = 6.3 Hz, H_4), 3.31 (m, CH_2, H_2), 3.59 (m, NH, H_1), 6.45 (d, CH, J =

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8.6 Hz, H_8), 6.83 (m, 2CH, H_5, H_7). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 20.5 (CH_3, $C_{1'}$), 22.5 (CH_2, C_3), 27.0 (CH_2, C_4), 42.3 (CH_2, C_2), 114.6 (CH, C_8), 121.7 (C_{10}), 126.3 (C_6), 127.3 (CH, C_7), 130.2 (CH, C_5), 142.5 (C_9). MS (IES+, ACN): m/z 148 $[M + H]^+$. Already described in ref 40.

*3,5-Dimethylindoline (**5b**).* ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.36 (d, CH_3, J = 6.8 Hz, $H_{1'}$), 2.33 (s, CH_3, $H_{1''}$), 3.13 (t, CH, J = 8.6 Hz, H_3), 3.38 (m, 1H, H_2), 3.55 (s, NH, H_1), 3.72 (t, 1H, J = 8.6 Hz, H_2), 6.61 (d, CH, J = 7.8 Hz, H_7), 6.89 (d, CH, J = 7.8 Hz, H_6), 6.97 (s, CH, H_4). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.6 (CH_3, $C_{1'}$), 20.9 (CH_3, $C_{1''}$), 36.8 (CH, C_3), 55.8 (CH_2, C_2), 109.6 (CH, C_7), 124.2 (CH, C_6), 127.7 (CH, C_4), 128.2 (C_5), 134.8 (C_9), 148.9 (C_8). MS (IES+, ACN): m/z 148 $[M + H]^+$, m/z 189 $[M + Na]^+$. HRMS (ESI, CH_3OH): calcd for $C_{10}H_{13}N$ $[M + H]^+$ 148.11262, found 148.1126.

*Formation of Compounds **4c** and **5c**.* These compounds were obtained from substrate **1c** (212 mg, 1.05 mmol) following the general procedure (reaction time 30 min). The reaction crude was purified with the eluent pentane/dichloromethane 92/8, compound **5c** (11 mg, 5%, brown oil) first eluted followed by compound **4c** (82 mg, 39%, brown oil).

*6-(Trifluoromethyl)-1,2,3,4-tetrahydroquinoline (**4c**).* ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.94 (m, CH_2, H_3), 2.78 (t, CH_2, J = 6.3 Hz, H_4), 3.34 (t, CH_2, J = 5.4 Hz, H_2), 4.15 (broad s, NH, H_1), 6.44 (d, CH, J = 9.0 Hz, H_8), 7.19 (m, 2CH, H_7, H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 21.5 (CH_2, C_3), 27.1 (CH_2, C_4), 41.8 (CH_2, C_2), 113.1 (CH, C_8), 118.1 (q, J = 32 Hz, C_6), 120.7 (C_{10}), 124.1 (q, CH, J = 4 Hz, C_7), 125.3 (q, J = 270 Hz, CF_3), 126.6 (q, CH, J = 4 Hz, C_5), 147.5 (C_9). $^{19}F\{^1H\}$ NMR ($CDCl_3$, 376 MHz, ppm) δ: −60.80 (CF_3). MS (IES+, ACN): m/z 202 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{10}H_{10}NF_3$ $[M + H]^+$ 202.08436, found 202.0846.

*3-Methyl-5-(trifluoromethyl)indoline (**5c**).* ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.34 (d, CH_3, J = 6.8 Hz), 3.20 (t, 1H, J = 8.5 Hz, H_2), 3.39 (m, CH, H_3), 3.78 (t, 1H, J = 8.8 Hz, H_2), 3.95 (broad s, NH, H_1), 6.60 (d, CH, J = 8.7 Hz, H_7), 7.27 (m, 2CH, J = 6.1 Hz, H_4, H_6). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.9 (CH_3), 36.3 (CH, C_3), 55.5 (CH_2, C_2), 108.1 (CH, C_7), 120.3 (q, J = 32 Hz, C_5), 120.6 (q, 2CH, J = 4 Hz, C_4 or C_6), 125.3 (q, J = 271 Hz, CF_3), 125.4 (q, 2CH, J = 4 Hz, C_4 or C_6), 134.5 (C_9), 154.2 (C_8). $^{19}F\{^1H\}$ NMR ($CDCl_3$, 376 MHz, ppm) δ: −60.67 (CF_3). MS (IES+, ACN): m/z 202 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{10}H_{10}NF_3$ $[M + H]^+$ 202.08436, found 202.0846.

*Formation of Compounds **4d** and **5d**.* These compounds were obtained from substrate **1d** (189 mg, 1 mmol) following the general procedure (reaction time 10 min). The reaction crude was purified with the eluent petroleum ether/ethyl acetate: 50/50, compound **5d** (33 mg, 17%) first eluted followed by compound **4d** (135 mg, 72%).

*N-(1,2,3,4-Tetrahydroquinolin-6-yl)acetamide (**4d**).* ^1H NMR (CD_3OD, 400 MHz, ppm) δ: 1.84 (m, CH_2, $H_{3'}$), 2.04 (s, CH_3, H_2), 2.66 (t, CH_2, J = 6.4 Hz, $H_{4'}$), 3.16 (m, CH_2, $H_{2'}$), 6.43 (d, CH, J = 8.4 Hz, $H_{8'}$), 7.01 (dd, CH, J = 8.5 Hz, J = 2.2 Hz, $H_{7'}$), 7.03 (m, CH, $H_{5'}$). ^{13}C NMR (CD_3OD, 100 MHz, ppm) δ: 23.2 (CH_2, C_3), 23.5 (CH_3, $C_{3'}$), 28.0 (CH_2, C_4), 42.8 (CH_2, C_2), 115.7 (CH, C_8), 121.0 (CH, C_7), 122.9 (C_{10}), 123.3 (CH, C_5), 129.4 (C_6), 143.5 (C_9), 171.1 ($C_{2'}$). MS (IES+, ACN): m/z 191 $[M + H]^+$, 213 $[M + Na]^+$. Already described in ref 41.

*N-(3-Methylindolin-5-yl)acetamide (**5d**).* ^1H NMR (CD_3OD, 400 MHz, ppm) δ: 1.29 (d, CH_3, J = 6.8 Hz, $H_{1''}$), 2.08 (s, CH_3, H_2), 3.02 (t, 1H, J = 8.7 Hz, $H_{2'}$), 3.30 (m, CH, $H_{3'}$), 3.61 (t, 1H, J = 8.7 Hz, $H_{2'}$), 6.62 (d, CH, J = 8.3 Hz, $H_{7'}$), 7.08 (ddd, CH, J = 8.3 Hz, J = 2.1 Hz, J = 0.7 Hz, $H_{6'}$), 7.27 (dd, CH, J = 1.7 Hz, J = 1.1 Hz, $H_{4'}$). ^{13}C NMR (CD_3OD, 100 MHz, ppm) δ: 18.9 (CH_3, $C_{1''}$), 23.5 (CH_3, C_2), 38.2 (CH, $C_{3'}$), 56.4 (CH_2, $C_{2'}$), 111.3 (CH, $C_{7'}$), 118.0 (CH, $C_{4'}$), 121.4 (CH, $C_{6'}$), 131.9 ($C_{5'}$), 136.8 ($C_{9'}$), 149.4 ($C_{8'}$), 171.3 (C_1). MS (IES+, ACN): m/z 191 $[M + H]^+$, 213 $[M + Na]^+$. HRMS (ESI, CH_3OH): calcd for $C_{11}H_{14}N_2O$ $[M + H]^+$ 191.11844, found 191.1183.

*6-Methoxy-1,2,3,4-tetrahydroquinoline (**4e**).* This compound was obtained from substrate **1e** (165 mg, 1 mmol) following the general procedure (reaction time 30 min). The reaction crude was purified with the eluent pentane/ethyl acetate 98/1, thereby obtaining compound **4e** (52 mg, 32%) as a brown solid. Mp: 35−38 °C. ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.94 (m, CH_2, H_3), 2.77 (t, CH_2, J = 6.5 Hz, H_4), 3.26 (t, CH_2, J = 5.4 Hz, H_2), 3.56 (broad s, NH, H_1), 3.74 (s, CH_3, $H_{1'}$), 6.46 (d, CH, J = 8.5 Hz, H_8), 6.58 (d, CH, J = 2.7 Hz, H_5), 6.62 (dd, CH, J = 8.5 Hz, J = 2.9 Hz, H_7). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 22.5 (CH_2, C_3), 27.2 (CH_2, C_4), 42.4 (CH_2, C_2), 55.9 (CH_3, $C_{1'}$), 112.9 (CH, C_7), 114.9 (CH, C_5), 115.6 (CH, C_8), 122.9 (C_{10}), 138.9 (C_9), 151.9 (C_6). MS (IES+, ACN): m/z 164 $[M + H]^+$. Already described in ref 42.

*1,2,3,4-Tetrahydroquinoline-6-sulfonamide (**4h**).* This compound was obtained from substrate **1h** (107 mg, 0.5 mmol) following the general procedure (2 mL of HF/SbF_5 mixture, reaction time 60 min). The reaction crude was purified with the eluent petroleum ether/ethyl acetate 25/75, thereby obtaining compound **4h** (98 mg, 92%) as a white solid. Mp: 141−143 °C. ^1H NMR (CD_3OD, 400 MHz, ppm) δ: 1.88 (m, CH_2, H_3), 2.74 (t, CH_2, J = 6.3 Hz, H_4), 3.30 (m, CH_2, H_2), 6.47 (d, CH, J = 9.1 Hz, H_8), 7.39 (m, 2CH, H_5, H_7). ^{13}C NMR (CD_3OD, 100 MHz, ppm) δ: 22.3 (CH_2, C_3), 28.2 (CH_2, C_4), 42.2 (CH_2, C_2), 113.4 (CH, C_8), 121.0 (C_{10}), 126.5 (CH, C_7), 128.5 (CH, C_5), 129.5 (C_6), 150.2 (C_9). MS (IES+, ACN): m/z 235 $[M + Na]^+$, 235 $[M + Na]^+$. HRMS (ESI, CH_3OH): calcd for $C_9H_{12}N_2SO_2$ $[M + Na]^+$ 235.05172, found 235.0516.

*6-Nitro-1,2,3,4-tetrahydroquinoline (**4i**).* This compound was obtained from substrate **1i** (155 mg, 0.87 mmol) following the general procedure (reaction time 24 h). The reaction crude was purified with the eluent pentane/ethyl acetate: 85/15, thereby obtaining compound **4i** (139 mg, 85%) as a yellow solid. Mp: 160−162 °C. ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.95 (m, CH_2, H_3), 2.79 (t, CH_2, J = 6.3 Hz, H_4), 3.41 (m, CH_2, H_2), 4.72 (broad s, NH, H_1), 6.36 (d, CH, J = 9.5 Hz, H_8), 7.88 (m, 2CH, H_7, H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 20.9 (CH_2, C_3), 27.0 (CH_2, C_4), 41.9 (CH_2, C_2), 112.3 (CH, C_8), 120.0 (C_{10}), 124.4 (CH, C_7), 126.1 (CH, C_5), 137.4 (C_6), 150.5 (C_9). MS (IES+, ACN): m/z 179 $[M + H]^+$, 201 $[M + Na]^+$. Already described in ref 35b.

*Formation of Compounds **4j** and **4j′**.* These compounds were obtained from substrate **1i** (178 mg, 1 mmol) following the general procedure (reaction time 24 h). The reaction crude was purified with the eluent pentane/CH_2Cl_2 70/30 up to 60/40, thereby obtaining compound **4j** (116 mg, 66%, orange solid, mp 62−64 °C) followed by **4j′** (20 mg, 10%, orange solid, mp 80−82 °C).

*7-Nitro-1,2,3,4-tetrahydroquinoline (**4j**).* ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.93 (td, CH_2, J = 6.4 Hz, J = 11.6 Hz, H_3), 2.79 (t, CH_2, J = 6.4 Hz, H_4), 3.33 (t, CH_2, J = 5.6 Hz, H_2), 4.21 (broad s, NH, 1), 7.00 (d, CH, J = 8.2 Hz, H_5), 7.25 (d, CH, J = 2.3 Hz, H_8), 7.37 (dd, CH, J = 2.3 Hz, J = 8.2 Hz, H_6).^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 21.1 (CH_2, C_3), 27.3 (CH_2, C_4), 41.6 (CH_2, C_2), 107.8 (CH, C_8), 111.3 (CH, C_6), 128.4 (C_{10}), 129.8 (CH, C_5), 145.3 (C_9), 147.3 (C_7). MS (IES+, ACN): m/z 179.08 $[M + H]^+$. Already described in ref 35b.

*5-Nitro-1,2,3,4-tetrahydroquinoline (**4j**).* ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.92 (m, CH_2, H_3), 2.93 (t, CH_2, J = 6.5 Hz, H_4), 3.32 (t, CH_2, J = 5.6 Hz, H_2), 6.66 (dd, CH, J = 1.1 Hz, J = 8.0 Hz, H_8), 7.03 (t, CH, J = 8.0 Hz, H_7), 7.13 (dd, CH, J = 1.2 Hz, J = 8.0 Hz, H_6). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 21.2 (CH_2, C_3), 24.1 (CH_2, C_4), 41.2 (CH_2, C_2), 112.7 (CH, C_6), 115.5 (C_6), 118.3 (CH, C_8), 126.8 (CH, C_7), 146.0 (C_9), 150.7 (C_5). MS (IES+, ACN): m/z 179.24 $[M + H]^+$. Already described in ref 35b.

*8-Methyl-6-nitro-1,2,3,4-tetrahydroquinoline (**4k**).* This compound was obtained from substrate **1k** (96 mg, 0.5 mmol) following the general procedure (2 mL of HF/SbF_5 mixture, reaction time 8 h). The reaction crude was purified with the eluent petroleum ether/ethyl acetate 83/17, thereby obtaining compound **4k** (81 mg, 84%) as an orange solid. Mp: 143−145 °C. ^1H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.95 (m, CH_2, H_3), 2.11 (s, CH_3, $H_{1'}$), 2.81 (t, CH_2, J = 6.3 Hz, H_4), 3.48 (m, CH_2, H_2), 4.53 (broad s, NH, H_1), 7.78 (d, CH, J = 2.1 Hz, H_5), 7.81 (d, CH, J = 2.1 Hz, H_7). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 17.1 (CH_3, $C_{1'}$), 21.0 (CH_2, C_3), 27.3 (CH_2, C_4), 42.2 (CH_2, C_2), 119.4 (C_{10} or C_8), 119.6 (C_{10} or C_8), 124.1 (CH, C_5), 124.6 (CH, C_7), 136.6 (C_6), 148.7 (C_9). MS (IES+, ACN): m/z 193 $[M + H]^+$. HRMS

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(ESI, CH_3OH): calcd for $C_{10}H_{12}N_2O_2$ $[M + Na]^+$ 215.07965, found 215.0799.

4.4. Nitrojulolidine Synthesis. *1-Allyl-1,2,3,4-tetrahydro-6-nitroquinoline (**6**).* Twelve mg of sodium hydride were introduced into a mixture of 59 mg of the compound **4i** dissolved with 3 mL of DMF at 0 °C. After 15 min, 70 μL of the allyl bromide was added. After 3 days, 20 mL of ethanol was introduced. The solvent was then evaporated under reduced pressure. The residue was taken up in water, and the solution was extracted three times with ethyl acetate. The organic layers were combined and dried with anhydrous magnesium sulfate, and the solvent was evaporated. The reaction crude was purified by flash chromatography using the eluent petroleum ether/ethyl acetate 92/8, obtaining the compound **6** (73 mg, 98%) as an orange solid. Mp: 47−48 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.97 (m, CH_2, H_3), 2.78 (t, CH_2, J = 6.0 Hz, H_4), 3.40 (m, CH_2, H_2), 3.96 (m, CH_2, J = 1.7 Hz, J = 4.5 Hz, $H_{1'}$), 5.13 (d, 1H, J = 17.1 Hz, $H_{3'}$), 5.20 (d, 1H, J = 10.4 Hz, $H_{3'}$), 5.80 (m, CH, $H_{2'}$), 6.42 (dm, CH, J = 9.2 Hz, H_8), 7.83 (s, CH, H_5), 7.91 (dm, 1H, J = 9.2 Hz, H_7). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 21.5 (CH_2, C_3), 28.0 (CH_2, C_4), 49.6 (CH_2, C_2), 53.7 (CH_2, $C_{1'}$), 109.3 (CH, C_8), 116.7 (CH_2, $C_{3'}$), 121.5 (C_{10}), 124.7, 125.0 (2CH, C_5 and C_7), 131.3 (CH, $C_{2'}$), 136.5 (C_6), 150.6 (C_9). MS (IES+, ACN): m/z 219 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{12}H_{14}N_2O_2$ $[M + H]^+$ 219.1134, found 219.1131.

*9-Nitrojulolidine (**7**).* To a mixture of HF/SbF_5 (1 mL, SbF_5 21.6 mol %) maintained at 0 °C was added 60 mg of compound **6** (0.275 mmol). The solution was then kept at 0 °C for 24 h. The reaction mixture was then neutralized with water−ice−Na_2CO_3 and extracted with ethyl acetate (×3). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The reaction crude was purified by flash chromatography using the eluent dichloromethane/methanol: 90/10, obtaining the compound **7** (47 mg, 78%) as an orange solid. Mp: 141−143 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.95 (tt, $2CH_2$, J = 6.1 Hz, J = 6.1 Hz, H_2 and H_6), 2.74 (t, $2CH_2$, J = 6.3 Hz, H_1 and H_7), 3.31 (t, $2CH_2$, J = 6.0 Hz, H_3 and H_5), 7.69 (s, 2CH, H_8 and H_{10}). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 21.1 ($2CH_2$, C_2 and C_6), 27.8 ($2CH_2$, C_1 and C_7), 50.2 ($2CH_2$, C_3 and C_5), 120.0 (C_{11} and C_{13}), 123.7 (2CH, C_8 and C_{10}), 135.3 (C_9), 148.1 (C_{12}). MS (IES+, ACN): m/z 219 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{12}H_{14}N_2O_2$ $[M + H]^+$ 219.1134, found 219.1132.

4.5. *N*-Acetyl-1,5-diazaoctahydroanthracene and *N*-Acetyl-4,5-diazaoctahydroanthracene. *1-(1,2,3,4-Tetrahydro-6-nitroquinolinyl)ethanone (**8**).* Sodium hydride (60% in oil, 175 mg, 3.38 mmol) was added slowly into a solution of 600 mg of the compound **4i** (3.38 mmol) dissolved in 70 mL of dichloromethane under nitrogen atmosphere. After 30 min under magnetic stirring, 310 μL of acetyl chloride (1.3 equiv, 4.38 mmol) was added. The reaction mixture was then heated to 30 °C. After 2 days at the same temperature, the reaction mixture was hydrolyzed with a saturated solution of ammonium chloride. The solution was extracted three times with dichloromethane. The organic phases were combined and dried with anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The reaction crude was purified by flash chromatography using petroleum ether/ethyl acetate 70/30 as eluent, obtaining the compound **8** (678 mg, 91%) as a yellow solid. Mp: 66−68 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 2.02 (m, CH_2, H_3), 2.31 (s, CH_3), 2.85 (dd, CH_2, J = 6.6 Hz, J = 6.6 Hz, H_4), 3.80 (t, CH_2, J = 6.3 Hz, H_2), 7.64 (d, CH, J = 6.9 Hz, H_8), 8.04 (m, 2CH, H_5 and H_7). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 23.5 (CH_2, H_3), 23.9 (CH_3), 27.5 (CH_2, H_4), 45.1 (CH_2, H_2), 121.8 (CH, C_7), 124.1 (CH, C_5), 124.8 (CH, C_8), 132.5 (C_{10}), 143.9 (C_6 or C_9), 144.6 (C_6 or C_9), 170.4 (CO). MS (IES+, ACN): m/z 221 $[M + H]^+$. Already described in ref 35b.

*1-(6-Amino-1,2,3,4-tetrahydroquinolin)ethanone (**9**).* Compound **8** (656 mg, 2.98 mmol) followed by 3.36 g of stannyl chloride (5 equiv, 14.9 mmol) were dissolved in 86 mL of ethanol. After being stirred and heated (70 °C) for 22 h, the crude mixture was cooled to room temperature. Then, 170 mL of aqueous $NaHCO_3$ (5 mol %) was added, and the solution was extracted three times with ethyl acetate. The organic phases were combined and dried with anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The reaction crude was purified by using automatic flash chromatography with dichloromethane/methanol 97/3 as eluant to afford compound **9** (450 mg, 79%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.88 (m, CH_2, H_3), 2.14 (broad s, CH_3), 2.56 (broad s, CH_2, H_4), 3.64 (broad s, NH_2), 3.74 (broad s, CH_2, H_2), 6.48 (m, 2CH, H_5 and H_7), 6.83 (d, CH, J = 7.1 Hz, 85% H_8), 7.59 (broad s, CH, 15% H_8). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 22.9 (CH_3), 24.1 (CH_2, C_3), 26.9 (CH_2, C_4), 42.5 (CH_2, C_2), 112.7 (CH, C_7), 114.4 (CH, C_5), 125.5 (CH, C_8), 130.8 (C_8 ou C_{10}), 135.2 (C_8 ou C_{10}), 144.2 (C_6), 170.2 (CO). MS (IES+, ACN): m/z 191 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{11}H_{14}N_2O$ $M + Na]^+$ 213.10038, found 213.1004.

*tert-Butyl 1-Acetyl-1,2,3,4-tetrahydroquinolin-6-ylcarbamate (**10**).* Compound **9** (250 mg, 1.32 mmol), 288 mg of *tert*-butyl dicarbonate, and 16 mg of DMAP were dissolved with 6 mL of THF. After 3 days at room temperature, the solvent was evaporated under reduced pressure. The reaction crude was purified with the eluent dichloromethane/MeOH/NH_3 98.5/1.5, thereby obtaining compound **10** (283 mg, 74%) as a solid. Mp: 126−129 °C. There was a splitting of the signals for carbons number 5 and 7 and the carbonyl carbon of the *tert*-butylcarbamate and acetyl group in ^{13}C NMR spectrum, characteristic of the presence of two conformers. In addition, some signals were output as broad singlet. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.49 (s, $3CH_3$, Boc), 1.90 (m, CH_2, H_3), 2.18 (s, CH_3, Ac), 2.66 (m, CH_2, H_4), 3.74 (m, CH_2, H_2), 6.79 (broad s, CH and NH), 6.97 (broad s, CH, H_8), 7.08 (broad s, CH, H_7), 7.31 (broad s, CH, H_5). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 23.1 (CH_3, Ac), 24.0 (CH_2, C_3), 27.1 (CH_2, C_4), 28.4 ($3CH_3$, Boc), 42.7 (CH_2, C_2), 80.6 (C^{IV}, Boc), 116.3, 116.4 (CH, C_7), 118.3, 118.4 (CH, C_5), 125.0, (CH, C_8), 134.5 (broad s, C^{IV}), 135.8 (broad s, C^{IV}), 152.9, 153.0 (CO, Boc), 170.2 (CO, Ac). MS (IES+, ACN): m/z 313 $[M + Na]^+$. HRMS (ESI, CH_3OH): calcd for $C_{16}H_{22}N_2O_3$ $[M + Na]^+$ 313.15281, found 313.1528.

*tert-Butyl 1-Acetyl-1,2,3,4-tetrahydroquinolin-6-ylallylcarbamate (**11**).* 15 mg of sodium hydride (60% in oil, 0.368 mmol) was introduced slowly into a solution of 89 mg of compound **10** (1.2 equiv, 0.307 mmol) dissolved in 4 mL of THF. Then, 40 μL of allyl bromide (1.5 equiv, 0.461 mmol) was added. The reaction mixture with magnetic stirring was then heated to 40 °C for 24 h. This was hydrolyzed with a saturated aqueous solution of ammonium chloride. The solution was extracted three times with ethyl acetate. The organic phases were combined and dried with anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The reaction crude was purified with the eluent petroleum ether/ethyl acetate 60/40, thereby obtaining compound **11** (96 mg, 95%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.44 ($3CH_3$, Boc), 1.92 (m, CH_2, H_3), 2.20 (s, CH_3, Ac), 2.68 (t, CH_2, J = 5.7 Hz, H_4), 3.75 (t, CH_2, J = 5.7 Hz, H_2), 4.17 (d, CH_2, J = 5.1 Hz, $H_{1'}$), 5.13 (s, 1H, J = 9.3 Hz, $H_{3'}$), 5.14 (d, 1H, J = 18.1 Hz, $H_{3'}$), 5.89 (ddt, CH, J = 15.9 Hz, J = 10.6 Hz, J = 5.4 Hz, $H_{2'}$), 7.03 (broad s, 3CH, H_5, H_7 and H_8). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 23.3 (CH_3, Ac), 23.9 (CH_2, H_3), 27.1 (CH_2, H_4), 28.4 ($3CH_3$, Boc), 42.9 (broad s, CH_2, H_2), 53.0 (CH_2, $H_{1'}$), 80.6 (C^{IV}, Boc), 116.4 (CH_2, $H_{3'}$), 123.9 (CH_{ar}), 124.7 (CH_{ar}), 126.1 (s CH_{ar}), 133.7 (broad s, C_{ar}), 134.4 (CH_2, H_2), 136.8 (broad s, C_{ar}), 139.8 (broad s, C_{ar}), 154.6 (CO, Boc), 170.1 (CO, Ac). MS (IES+, ACN): m/z 353 $[M + Na]^+$. HRMS (ESI, CH_3OH): calcd for $C_{19}H_{26}N_2O_3$ $[M + Na]^+$ 353.18411, found 353.1841.

*1-(6-(Allylamino)-1,2,3,4-tetrahydroquinolin-yl)ethanone (**12**).* 4 mL of trifluoroacetic acid was introduced into a solution of 184 mg of compound **11** (0.558 mmol) dissolved with 4 mL of dichloromethane. After 1 h under magnetic stirring at room temperature, the reaction mixture was hydrolyzed with a mixture of water and sodium carbonate. The solution was extracted three times with ethyl acetate. The organic phases were combined and dried with anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure. The reaction crude was purified with the eluent pentane/dichloromethane 98.5/1.5, thereby obtaining compound **12** (115 mg, 90%) as an orange oil. There were two signals for hydrogen number 8 in the ^{1}H NMR spectrum, characteristic of the presence of two conformers. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.88 (m, CH_2, H_3), 2.15 (s, CH_3, Ac),

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2.58 (m, CH_2, H_4), 3.74 (d, CH_2, J = 5.1 Hz, $H_{1'}$ and CH_2, H_2), 3.86 (broad s, NH), 5.15 (d, 1H, J = 10.2 Hz, $H_{3'}$), 5.26 (d, 1H, J = 17.2 Hz, $H_{3'}$), 5.93 (ddt, 1H, J = 16.7 Hz, J = 10.4 Hz, J = 5.3 Hz, $H_{2'}$), 6.40 (s, CH, H_5), 6.43 (dd, CH, J = 8.5 Hz, J = 2.6 Hz, H_7), 6.86 (d, CH, J = 7.5 Hz, 0.89 H, H_8), 7.63 (s, CH, 0.11 H, H_8). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 23.0 (CH_3, Ac), 24.2 (CH_2, C_3), 27.2 (CH_2, C_4), 42.5 (CH_2, C_2), 46.9 (CH_2, $C_{1'}$), 110.8 (CH, C_7), 112.3 (CH, C_5), 116.6 (CH_2, $C_{3'}$), 125.5 (CH, C_8), 130.2 (C_{10}), 135.3 (CH, $C_{2'}$), 145.8 (C_6), 170.2 (CO). MS (IES+, ACN): m/z 231 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{14}H_{18}N_2O$ $[M + Na]^+$ 253.13168, found 253.1316.

*Formation of Compounds **13** and **14**.* To a mixture of HF/SbF_5 (4 mL, SbF_5 21.6 mol %) maintained at −50 °C was added 59 mg of compound **12** (0.256 mmol). The solution was then kept at 0 °C for 10 min. The reaction mixture was then neutralized with water−ice−Na_2CO_3 and extracted with ethyl acetate (×3). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The reaction crude was purified with the eluent pentane/dichloromethane: 99/1, compound **13** (21 mg, 36%, light oil) first eluted followed by compound **14** (12 mg, 21%, light oil).

*N-Acetyl-1.5-diazaoctahydroanthracene (**13**).* ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.89 (m, CH_2, H_3), 1.95 (m, CH_2, $H_{3'}$), 2.19 (s, CH_3, Ac), 2.55 (broad s, CH_2, H_4), 2.74 (t, CH_2, J = 6.3 Hz, $H_{4'}$), 3.30 (t, CH_2, J = 5.4 Hz, $H_{2'}$), 3.73 (broad s, CH_2, H_2), 6.33 (s, CH, H_5), 6.67 (broad s, CH_2, H_8). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 22.3 (CH_2, $C_{3'}$), 23.0 (CH_3, Ac), 24.2 (CH_2, C_3), 26.7 (CH_2, C_4), 26.9 (CH_2, $C_{4'}$), 42.1 (CH_2, $C_{2'}$), 42.6 (CH_2, C_2), 113.4 (CH, C_5), 119.5 (C_7), 125.6 (CH, C_8), 129.9 (C_9), 132.9 (C_{10}), 142.4 (C_6), 170.2 (CO). MS (IES+, ACN): m/z 231 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{14}H_{18}N_2O$ $[M + Na]^+$ 253.13168, found 253.1315.

*N-Acetyl-4.5-diazaoctahydrophenanthrene (**14**).* ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.93 (m, CH_2, H_9), 2.00 (m, CH_2, H_2), 2.17 (s, CH_3, Ac), 2.56 (t, CH_2, J = 6.7 Hz, H_{10}), 2.62 (t, CH_2, J = 6.1 Hz, H_1), 3.27 (t, CH_2, J = 4.6 Hz, H_3), 3.76 (broad s, CH_2, H_8), 6.43 (d, CH, J = 7.7 Hz, H_5), 6.74 (s, CH, H_6). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 22.1 (CH_2, C_2), 23.1 (CH_3, Ac), 23.6 (CH_2, C_{10}), 23.7 (CH_2, C_1), 23.9 (CH_2, C_9), 41.6 (CH_2, C_3), 42.1 (CH_2, C_8), 113.1 (CH, C_5), 120.6 (C_{11}), 123.4 (CH, C_6), 127.5 (CH, C_6), 131.3 (C_{14}), 142.5 (C_{12}), 170.2 (CO). MS (IES+, ACN): m/z 231 $[M + H]^+$. HRMS (ESI, CH_3OH): calcd for $C_{14}H_{18}N_2O$ $[M + Na]^+$ 253.13168, found 253.1318.

*1-(6-(2-Fluoropropylamino)-1,2,3,4-tetrahydroquinolin-yl)-ethanone (**15**).* To a mixture of HF/SbF_5 (4 mL, SbF_5 3.8 mol %) maintained at −50 °C, was added 58 mg of compound **12** (0.252 mmol). The mixture was magnetically stirred at the same temperature for 10 min. The reaction mixture was then neutralized with water−ice−Na_2CO_3, extracted with ethyl acetate (×3). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Products were isolated by column chromatography over silica gel. The reaction crude was purified with the eluent pentane/dichloromethane 98.5/1.5, thereby obtaining compound **15** (53 mg, 84%) as an orange oil. There were two signals for hydrogen number 8 in the ^{1}H NMR spectrum, characteristic of the presence of two conformers. ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ: 1.39 (dd, CH_3, J = 23.8 Hz, J = 6.2 Hz, $H_{3'}$), 1.89 (m, CH_2, H_3), 2.15 (s, CH_3, Ac), 2.59 (m, CH_2, H_4), 3.25 (m, CH_2, $H_{2'}$), 3.74 (m, CH_2, H_2), 4.02 (broad s, NH), 4.86 (dm, CH, J = 49.4 Hz, $H_{2'}$), 6.41 (broad s, CH, H_5), 6.44 (dd, CH, J = 8.6 Hz, J = 2.5 Hz, H_7), 6.87 (d, CH, J = 5.9 Hz, 0.85 H, H_8), 7.66 (s, CH, 0.15 H, H_8). ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ: 18.7 (d, CH_3, J = 22 Hz, $C_{3'}$), 22.9 (CH_3, Ac), 24.1 (CH_2, C_3), 27.1 (CH_2, C_4), 42.5 (CH_2, C_2), 49.6 (d, CH_2, J = 21 Hz, $C_{1'}$), 89.4 (d, CHF, J = 167 Hz, $C_{1'}$), 110.7 (CH, C_7), 112.2 (CH, C_5), 125.5 (CH, C_8), 130.4 (C_9), 135.2 (C_{10}), 145.6 (C_6), 170.1 (CO, Ac). ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz, ppm) δ: −179.79. MS (IES+, ACN): m/z 251 $[M + H]^+$, 273 $[M + Na]^+$. HRMS (ESI, CH_3OH): calcd for $C_{14}H_{19}FN_2O$ $[M + H]^+$ 251.15597, found 251.1562.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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