Synthesis of Functionalized Indole- and Benzo-Fused Heterocyclic Derivatives through Anionic Benzyne Cyclization

José Barluenga,*[a] Francisco J. Fañanás,[a] Roberto Sanz,[b] and Yolanda Fernández[b]

Abstract: The development of a new method for the regioselective synthesis of functionalized indoles and six-membered benzo-fused N-, O-, and S-heterocycles is reported. The key step involves the generation of a benzyne-tethered vinyl or aryllithium compound that undergoes a subsequent intramolecular anionic cyclization. Reaction of the organolithium intermediates with selected electrophiles allows the preparation of a wide variety of indole, tetrahydrocarbazole, dihydrofenantridine, dibenzopyran, and dibenzothiopyran derivatives. Finally, the application of this strategy to the appropriate starting materials allows the preparation of some tryptamine and serotonin analogues.

Keywords: benzynes · cyclization · heterocycles · indoles · organolithium

Introduction

The addition of a nucleophile that is part of an aryne side chain to the benzyne intermediate to form a new ring has provided a simple synthetic route to a variety of carbocyclic and heterocyclic systems fused to benzene.[1] This strategy, introduced independently by Huisgen[2] and Bunnet,[3] has been successfully applied to the synthesis of natural products and of a variety of heterocyclic and homocyclic systems. In this context, a series of benzoxazole[4] and benzothiazole[5] derivatives, functionalized at C(7), have been synthesized. Also, 7-substituted indolines have been prepared by the intramolecular cyclization of (2-phenethyl)formamidines[6] and several diversely substituted isoindolin-1-ones have been obtained by base-induced aryne-mediated cyclization.[7] Moreover, a new route to chromanes and chromenes through benzyne cyclization using intramolecular benzyne trapping by alcohols has recently been described.[8] Cyclization of side chain α-lithionitriles or other stabilized carbanions has found extensive use in the synthesis of 1-substituted benzocyclobutenes which are versatile synthons.[3b, c, 9] Although in all the previous examples the side chain nucleophile is a stabilized carbanion or nitrogen, oxygen, or sulfur anion, only two examples of the generation and cyclization of benzyne-tethered alkyllithiums have been reported.[10] Interestingly, with this anionic benzyne cyclization methodology, it could be possible to functionalize the cyclized product by further reaction with electrophiles, which represents an important advantage over the corresponding radical cyclizations. Moreover, cyclizations of vinyllithiums rather than alkyllithiums, would also incorporate an alkene into the product with control of its stereochemistry and also could allow further functionalization.[11]

Among the methods of aryne generation, the aryl halide strong base route is one of the most widely used.[12] Aryl anions with a good leaving group in the *ortho* position readily afford arynes. Since both the deprotonation and the benzyne formation steps can be reversible, many factors such as the nature of the leaving group, the base, and the solvent play an important role in the rate and efficiency of aryne generation.[13] The ease of halide expulsion is I > Br > Cl > F but the rates of initial proton removal are in the reverse order and in the case of aryl fluorides, reprotonation can compete with benzyne formation. However, Schlosser et al. demonstrated that fluorine-substituted anilines could be selectively deprotonated next to the halogen atom, and that while 2-fluorophenyllithiums are stable up to $-50\,^{\circ}C$, 2-fluoro-3-methoxyphenyllithium decomposes with loss of LiF above $-75\,^{\circ}C$ indicating that the elimination of LiF could be assisted by heteroatoms.[14]

On the other hand, the development of new synthetic routes to indolic systems continues to be an active area of interest owing to the fact that the indole nucleus is a common

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moiety in a variety of natural products.[15] Many of these compounds and their analogues possess biological activity and are medicinal agents. Although a large number of methods exist for the synthesis of substituted indoles, the preparation of 3,4-disubstituted indoles still represents a formidable task. The main difficulty is that the 4-position of the indole ring system is much less electron-rich than other positions.[16] For this reason, electrophilic aromatic substitution is not very efficient and special methods that use transition metal complexes and polysubstituted benzenoid starting materials have been developed for the synthesis of these compounds.[17]

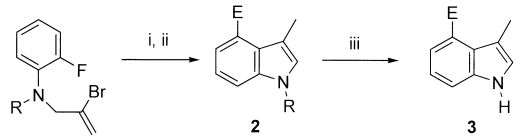
The development of new strategies directed towards the preparation of regioselectively functionalized heterocyclic systems continues to be an important synthetic goal in our research group. Coupled with our interest in the preparation of heterocycles by carbometallation reactions,[18] we have reported the facile intramolecular carbolithiation of *N*-allyl-*N*-(2-lithioallyl)amines that proceeds through 5-*exo* or 6-*endo* modes depending on the electron density at the nitrogen atom.[18c] In this paper we describe the development of a methodology which allows the synthesis of 3,4-disubstituted functionalized indoles and other benzo-fused heterocyclic derivatives based on the cyclization of benzyne-tethered aryl or vinyllithiums.[19]

Results and Discussion

Intramolecular cyclization of *N*-(2-lithioallyl)-2-fluoroanilines: Reaction of *N*-(2-bromoallyl)-*N*-methyl-2-fluoroaniline (**1a**) with 3.5 equiv *tert*-butyllithium in THF at −110 to −40 °C for 3 h, and further treatment with different electrophiles at −78 to 20 °C, gave rise, after workup and purification, to 1,3-dimethyl-4-functionalized indoles **2** in moderate to good yields (Scheme 1 and Table 1).

It is interesting to note that this methodology allows the preparation of 4-functionalized indole derivatives starting from a simple acyclic precursor in a "one-pot" sequence. To prepare N-unsubstituted indoles, we choose the allyl moiety as a result to its stability to strong basic conditions and the variety of methods for its removal.[20] We therefore used an approach based on the isomerization/hydrolysis of the allyl group[21] with diisobutylaluminium hydride (DIBAL-H) and a catalytic amount of dichlorobis(diphenylphosphino)propane nickel [$NiCl_2$(dppp)], which has been recently reported.[22] This simple procedure proved to be very efficient with our compounds and moreover, we found that the removal of the allyl group could be carried out without the isolation of the intermediate *N*-allylindole. Thus, the reaction of *N*-allyl-2-fluoroaniline **1b** with 3.5 equiv *t*BuLi, at −110 to 20 °C, afforded, after the addition of several electrophiles, the corresponding functionalized indoles **2** (R = allyl). These compounds were not isolated and the crude products were treated with 1.5 equiv DIBAL-H and a catalytic amount of [$NiCl_2$(dppp)] in toluene, to afford 4-functionalized-3-methylindoles **3** in moderate yields (Scheme 1 and Table 1). The intermediacy of the corresponding *N*-allylindole **2** is supported by the isolation of *N*-allyl-3-methylindole **2i**.

For the formation of indoles **2** and **3** we assumed that amines **1** first reacted with *t*BuLi at −110 °C to give *N*-(2-lithioallyl)amines **4**, through halogen–metal exchange;[23] this was confirmed by deuteration and isolation of the deuteriated amine **5a** (Scheme 2). Intermediate **4**, which is stable for several hours at −110 °C, probably undergoes proton-abstraction *ortho* to the fluorine atom by the additional equivalents of *t*BuLi when the temperature is raised to −40 °C giving the intermediate **6**. The subsequent elimination of LiF produces a benzyne intermediate **7**, which is efficiently



1 a: R=Me
b: R=allyl
c: R=2-butenyl

Scheme 1. Synthesis of 4-functionalized indole derivatives **2** and **3** from 2-fluoroanilines **1**. i) *t*BuLi (3.5 equiv), THF, −110 → −40 °C (for **1a**, **c**) or to 20 °C (for **1b**); ii) E^+, −78 → 20 °C; iii) for **1b**, DIBAL-H (1.5 equiv), cat. [$NiCl_2$(dppp)], toluene, 20 °C.

Table 1. Preparation of 4-functionalized indole derivatives **2** and **3** from *N*-(2-bromoallyl)-2-fluoroanilines (**1**).

Starting amine	R	E^+	Product	E	Yield [%][a]
1a	Me	H_2O	**2a**	H	75
1a	Me	Bu_3SnCl	**2b**	$SnBu_3$	67
1a	Me	PhCHO	**2c**	PhC(H)OH	69
1a	Me	Me_2CO	**2d**	Me_2COH	73
1a	Me	$ClCO_2Et$	**2e**	CO_2Et	73
1a	Me	PhCH=NPh	**2f**	PhCHNHPh	59
1a	Me	4-ClC_6H_4CN	**2g**	4-ClC_6H_4CO	62
1a	Me	$BrCH_2CH_2Br$	**2h**	Br	61
1b	$CH_2CH=CH_2$	H_2O	**2i**	H	38[b]
1c	$CH_2CH=CHCH_3$	H_2O	**2j**	H	72
1b	$CH_2CH=CH_2$	D_2O	**3a**	D	53
1b	$CH_2CH=CH_2$	Bu_3SnCl	**3b**	$SnBu_3$	52
1b	$CH_2CH=CH_2$	Me_3SiCl	**3c**	$SiMe_3$	48
1b	$CH_2CH=CH_2$	Ph_2S_2	**3d**	SPh	49
1b	$CH_2CH=CH_2$	PhCH=NPh	**3e**	PhCHNHPh	46
1b	$CH_2CH=CH_2$	4-MeC_6H_4CHO	**3f**	4-$MeC_6H_4C(H)OH$	52
1b	$CH_2CH=CH_2$	$BrCH_2CH_2Br$	**3g**	Br	50

[a] Isolated yield based on the starting amine **1**. [b] Yield lowered by the partial decomposition in the silica gel chromatography.

Abstract in Spanish: *Se describe el desarrollo de un nuevo método para la síntesis regioespecífica de indoles funcionalizados y de heterociclos de seis miembros benzofusionados de nitrógeno, oxígeno y azufre. El paso clave implica la generación de un compuesto vinil o arillitio que presenta un bencino en su estructura, el cual experimenta posteriormente una ciclación aniónica intramolecular. La reacción de los organolíticos intermedios con electrófilos permite la preparación de una amplia variedad de derivados de indoles, tetrahidrocarbazoles, dihidrofenantridinas, dibenzopiranos y dibenzotiiranos. Finalmente, la aplicación de esta estrategia a los productos de partida apropiados permite la preparación de algunos análogos de triptamina y serotonina.*

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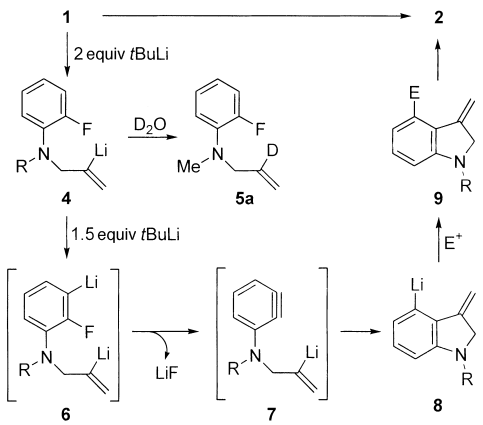
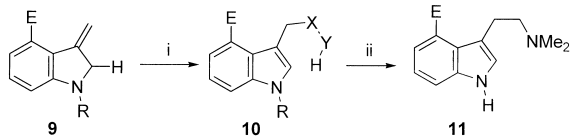
trapped by the 2-lithioallyl moiety, affording a regioselectively C(4)-lithiated 3-methyleneindoline derivative **8**. Quenching of the lithiated species **8** with selected electrophiles allowed the functionalization at this position through products **9** which isomerized on workup or on silica gel chromatography to the corresponding indole derivatives **2** (Scheme 2). If the addition of *t*BuLi is carried out at −78 °C



Scheme 2. Anionic cyclization of *N*-(2-lithioallyl)-*N*-2-fluoroanilines **1** via benzyne intermediates **7**.

and the reaction mixture is allowed to reach room temperature,[19] a competitive reaction involving a β-elimination from **4** affords the corresponding *N*-alkyl-2-fluoroaniline (25–30 %), probably as a result of the lower electron density at the nitrogen atom.[18c] To minimize this undesired by-product, several changes to the reaction conditions were tried and we found that the addition of a slight excess of base (3.5–4.0 equiv) at a constant −40 °C reduced the β-elimination process to below 10–15 %. On the other hand, with *N*-allylamine **1b**, the carbolithiation of the allyl moiety by the 2-lithioallyl group also takes place as we have previously described.[18c] However, we found that when the reaction of **1b** was carried out at −110 to 20 °C the intramolecular carbolithiation was almost avoided. To summarize, the best reaction conditions found to avoid any lateral reaction are 3.5–4.0 equivalents of *t*BuLi in THF at −110 to −40 °C for amines **1a**, **c** and at −110 to 20 °C for **1b**. These results could be explained if we assume that the slow step in our anionic cyclization is the removal of the proton *ortho* to the fluorine atom and this process is favored by an excess of base and by an increase in the temperature. On the other hand, the β-elimination from intermediates **4** is always possible and it is also favored by the increase in the temperature. With *N*-allylamines, the carbolithiation reaction also takes place at −40 °C but at higher temperatures it is slower than the *ortho*-lithiation of the fluoronaniline, so a fast increase in the reaction temperature minimizes this pathway.

Reaction of 3-methyleneindolines with enophiles: We have observed that the isomerization of the methyleneindolines **9** to their aromatic methylindoles **2** isomers, did not take place just after the addition of the electrophiles but on the workup or silica gel chromatography of the reaction. Buchwald et al.[17f,h,i] demonstrated that 3-methylenindolines could undergo Alder-ene reactions with activated enophiles to give indole derivatives.[24] Thus, we added several activated enophiles to the methyleneindolines **9** in THF at reflux and we observed the formation of the corresponding 3,4-functionalized indoles **10** in moderate yields based on the starting amines **1** (Scheme 3 and Table 2). Moreover, when the amine **1b** was used, the corresponding *N*-allylindole **10** (R = $CH_2CH{=}CH_2$; XYH=CH_2NMe_2) was not isolated and the allyl group was removed by treatment with DIBAL-H and catalytic [$NiCl_2$(dppp)] in toluene affording the indole derivatives **11**. It is interesting to note that compounds **11** are *N*,*N*-dimethyltryptamine derivatives. Our methodology therefore allows the synthesis of a wide range of tryptamine analogues from readily available starting products in a "one-pot" procedure; the preparation of these compounds usually involves multi-step syntheses.[25]



Scheme 3. Synthesis of 3,4-functionalized indole derivatives **10** and **11** by Alder-ene reactions. i) X=Y, THF, 67 °C [X=Y: $H_2C{=}N^+Me_2I^-$, $EtO_2CN{=}NCO_2Et$, $EtO_2CC(=O)CO_2Et$]; ii) for R = allyl, DIBAL-H (1.5 equiv), cat. [$NiCl_2$(dppp)], toluene, 20 °C.

Table 2. Preparation of 3,4-functionalized indole derivatives **10** and **11** from *N*-(2-bromoallyl)-2-fluoroanilines (**1**).

Starting amine	R	E^+	X=Y[a]	Product	E	Yield [%][b]
1a	Me	H_2O	A	**10a**	H	64
1a	Me	4-MeC_6H_4CN	A	**10b**	4-MeC_6H_4CO	60
1a	Me	H_2O	B	**10c**	H	58
1a	Me	$ClCO_2Et$	B	**10d**	CO_2Et	53
1a	Me	Bu_3SnCl	B	**10e**	$SnBu_3$	55
1a	Me	H_2O	C	**10f**	H	62
1a	Me	Ph_2S_2	C	**10g**	SPh	50
1a	Me	$ClCO_2Et$	C	**10h**	CO_2Et	61
1c	$CH_2CH{=}CHCH_3$	H_2O	A	**10i**	H	64
1b	$CH_2CH{=}CH_2$	H_2O	A	**11a**	H	51
1b	$CH_2CH{=}CH_2$	$BrCH_2CH_2Br$	A	**11b**	Br	36

[a] Enophiles: A = $H_2C{=}N^+Me_2I^-$; B = $EtO_2CN{=}NCO_2Et$; C = $EtO_2CC(=O)CO_2Et$. [b] Isolated yield based on the starting amine **1**.

Intramolecular cyclization of *N*-(2-lithioallyl)-2-chloroanilines: Given that the β-elimination of organolithium **4** is a possible competitive pathway, we thought that substitution of fluorine by chlorine could solve this problem owing to the less electron-withdrawing nature of chlorine. We therefore chose 2-chloroaniline derivative **12** as a starting material. However, when compound **12** was treated with 3.3 or 3.5 equiv *t*BuLi in THF at −110 to 20 °C, only secondary amine **14** was obtained indicating that complete β-elimination from anion **13** had occurred (Scheme 4). This result indicates that the *ortho*-lithiation of the chloroaniline is slower than the β-elimination process, probably as a result of the lower acidity of this proton relative to the fluorinated case. However, it has been reported that 3-chloroanisole is smoothly lithiated by *s*BuLi at −105 °C.[9d] We therefore examined the lithiation of a

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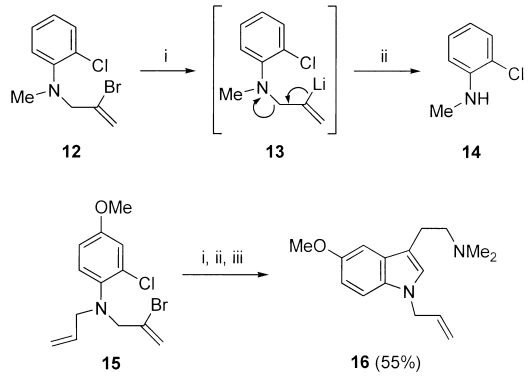
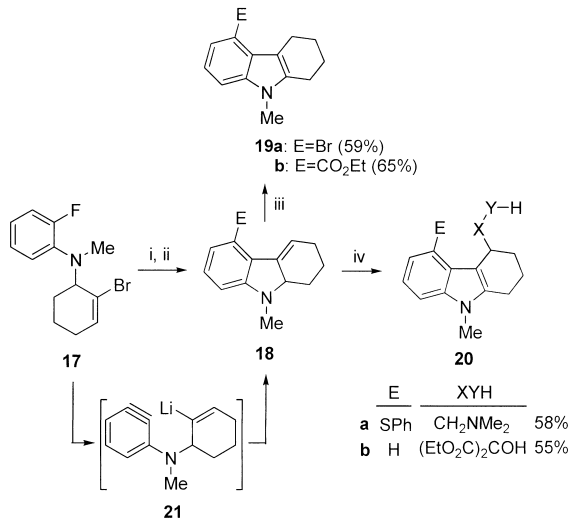
chloroaniline with an oxygen atom at the *para*-position. Moreover, since serotonin derivatives are based on the 5-hydroxytryptamine structure we prepared the analogue **16** in good yield from the readily accessible 2-chloro-4-methoxyaniline derivative **15**, by using *N*,*N*-dimetylmethyleneammonium iodide as the enophile (Scheme 4). As expected, the powerful activating effect of the methoxy group on the *ortho*-lithiation is an important feature for facile benzyne formation, and, therefore, the β-elimination of the vinyllithium intermediate is not a problem and the amount of base is not so critical.



Scheme 4. Anionic cyclization of benzyne-tethered organolithiums from 2-chloroanilines **12** and **15**. Synthesis of the serotonin analogue **16**.i) *t*BuLi (3.3 equiv), THF, $-110 \rightarrow 20\,^{\circ}C$; ii) H_2O, $-78 \rightarrow 20\,^{\circ}C$; iii) $CH_2N^+Me_2I^-$, THF, 67 °C.

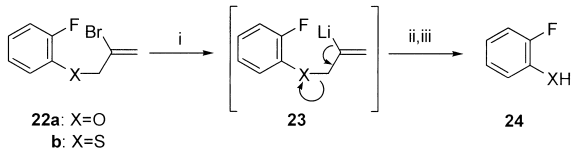
Intramolecular cyclization of *N*-(2-lithio-2-cyclohexenyl)-2-fluoroanilines—Synthesis of tetrahydrocarbazole derivatives: In view of the highly efficient preparation of indole derivatives from 2-bromoallylamines **1** and to extend the synthetic scope of this methodology, we prepared *N*-(2-bromo-2-cyclohexenyl)-2-fluoro-*N*-methylaniline (**17**). Treatment of **17** with 3.5 equiv *t*BuLi in THF at -110 to 20 °C, and subsequent electrophilic trapping, gave compounds **18**. In this case the β-elimination process is disfavored and the temperature could be raised to 20 °C. In contrast to the corresponding 3-methyleneindolines **9**, which were isomerized under the mildly acidic workup conditions to their indole counterparts, compounds **18** were rather stable and more difficult to isomerize. The addition of a catalytic amount of *p*-toluenesulfonic acid and heating at reflux in toluene[26] were required to generate the functionalized tetrahydrocarbazole derivatives **19** (Scheme 5). Again, we postulate that a benzyne-tethered vinyllithium intermediate (**21**) undergoes anionic cyclization onto the benzyne moiety. As for compound **9**, the addition of an enophile led to the formation of the corresponding functionalized carbazole derivatives **20** (Scheme 5).

Intramolecular cyclization of 2-lithiobenzyl-2-halophenyl amines, ethers, and thioethers—Synthesis of phenanthridine, dibenzopyran, and dibenzothiopyran derivatives: Having demonstrated the efficiency of this methodology for the preparation of indole derivatives, we prepared the 2-fluorophenyl ether and thioether **22a**,**b** to study their potential as substrates that could afford oxygen and sulfur heterocycles. However, treatment of **22a**,**b** with *t*BuLi afforded, after



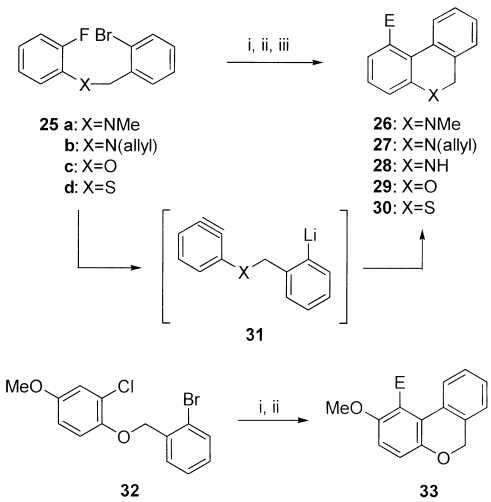
Scheme 5. Intramolecular cyclization of *N*-(2-lithio-2-cyclohexenyl)-2-fluoroaniline (**17**). Preparation of the carbazole derivatives **19** and **20**. i) *t*BuLi (3.5 equiv), THF, $-110 \rightarrow 20\,^{\circ}C$; ii) E^+, $-78 \rightarrow 20\,^{\circ}C$; iii) cat. *p*TsOH, toluene, 110 °C; iv) X=Y, THF, 67 °C, [X=Y: $H_2C{=}N^+Me_2I^-$, $EtO_2CC({=}O)CO_2Et$].

hydrolysis, compounds **24**, derived from a β-elimination reaction of the intermediate organolithium **23**; no cyclization products were observed (Scheme 6).



Scheme 6. Attempted anionic cyclization of 2-bromoallyl ether and thioether **22**. i) *t*BuLi (3.5 equiv), THF, $-110\,^{\circ}C$; ii) $-110 \rightarrow 20\,^{\circ}C$; iii) H_2O, 20 °C.

As a result of the facile breakdown of the β-oxygen and β-sulfur functionalized organolithiums, we prepared starting materials that could afford the much more stable γ-functionalized organolithium compounds. 2-Bromobenzyl 2-fluorophenyl amines, ether, and thioether derivatives **25a**–**d** were synthesized by conventional routes. The reaction of compounds **25a**–**d** with 3.5 equiv *t*BuLi in THF at -110 to 20 °C, and further treatment with different electrophiles, afforded the corresponding six-membered benzofused N-, O-, or S-heterocycles **26**–**30** in moderate to good yields via the benzyne intermediate **31** (Scheme 7 and Table 3).[27] Moreover, the dihydrophenanthridines **27**, derived from amine **25b**, could easily be deprotected by treatment with DIBAL-H and catalytic [$NiCl_2$(dppp)] in toluene after their functionalization with different electrophiles. With the successful result achieved with derivative **15** in mind, we aimed to extend this strategy of using 1,3-chloromethoxy derivatives as precursors of benzynes and we therefore prepared the 2-chloro-4-methoxyphenylether **32**. Treatment of **32** with 3.3 equiv *t*BuLi and quenching with selected electrophiles led to dibenzopyran[28] derivatives **33** in good yields (Scheme 7 and Table 3).



Scheme 7. Preparation of benzo-fused six-membered heterocycles **26**–**30** and **33** from 2-halophenyl 2-bromobenzyl ethers, amines, and thioether **25** and **32**. i) *t*BuLi (3.5 equiv for **25a**,**b**, 3.3 equiv for **25c**,**d**, and **32**), THF, $-110 \rightarrow 20\,^{\circ}C$; ii) E^+, $-78 \rightarrow 20\,^{\circ}C$; iii) for X = N(allyl), DIBAL-H (1.5 equiv), cat. [$NiCl_2$(dppp)], toluene, 20 °C.

Table 3. Preparation of functionalized derivatives of dihydrophenanthridines **26**–**28**, dibenzopyrans **29** and **33**, and dibenzothiopyrans **30**, from 2-bromobenzyl compounds **25** and **32**.

Starting product	X	E^+	Product	E	Yield [%][a]
25a	NMe	H_2O	**26a**	H	81
25a	NMe	$BrCH_2CH_2Br$	**26b**	Br	68
25a	NMe	Ph_2S_2	**26c**	SPh	80
25a	NMe	$ClCO_2Et$	**26d**	CO_2Et	78
25a	NMe	Bu_3SnCl	**26e**	$SnBu_3$	76
25b	$NCH_2CH{=}CH_2$	H_2O	**27a**	H	71
25b	$NCH_2CH{=}CH_2$	$ClCO_2Et$	**27b**	CO_2Et	73
25b	$NCH_2CH{=}CH_2$	H_2O	**28a**	H	70
25b	$NCH_2CH{=}CH_2$	$ClCO_2Et$	**28b**	CH_2OH	69
25b	$NCH_2CH{=}CH_2$	$BrCH_2CH_2Br$	**28c**	Br	73
25b	$NCH_2CH{=}CH_2$	Bu_3SnCl	**28d**	$SnBu_3$	71
25c	O	$BrCH_2CH_2Br$	**29a**	Br	61
25c	O	$ClCO_2Et$	**29b**	CO_2Et	68
25c	O	PhCHO	**29c**	PhCH(OH)	56
25c	O	Bu_3SnCl	**29d**	$SnBu_3$	60
25d	S	H_2O	**30a**	H	59
25d	S	$ClCO_2Et$	**30b**	CO_2Et	50
25d	S	$4\text{-}MeC_6H_4CHO$	**30c**	$4\text{-}MeC_6H_4C(H)OH$	57
32		H_2O	**33a**	H	81
32		$ClCO_2Et$	**33b**	CO_2Et	75
32		$4\text{-}MeC_6H_4CHO$	**33c**	$4\text{-}MeC_6H_4C(H)OH$	79
32		Ph_2S_2	**33d**	SPh	73

[a] Isolated yield based on the starting products **25** and **32**.

Conclusion

In summary, a novel methodology for the regioselective synthesis of functionalized indole and other benzofused heterocyclic derivatives has been developed. The key step of the synthesis involves the generation of a benzyne-tethered organolithium compound, which undergoes an intramolecular anionic cyclization to provide regiospecifically metalated heterocyclic ring. The resulting organolithium reagents react with a range of electrophiles to give new and interesting fused heterocyclic compounds. It is noteworthy that this process represents the first example of the intramolecular trapping of benzyne intermediates by tethered non-stabilized vinyl and aryllithiums. Moreover, this simple and straightforward synthesis of functionalized heterocycles allows access to some compounds that are otherwise more difficult or tedious to prepare. Further studies on the applications of this methodology to organic syntheses are actively underway in our laboratories.

Experimental Section

General methods: All reactions were carried out under a nitrogen atmosphere in oven-dried glassware. Temperatures are reported as bath temperatures. Tetrahydrofuran and toluene were continuously refluxed and freshly distilled from sodium or sodium/benzophenone under nitrogen. Solvents used in extraction and purification were distilled prior to use. TLC was performed on aluminum-backed plates coated with silica gel 60 with F_{254} indicator (Merck) and compounds were visualized by UV light (254 nm) or iodine. Flash column chromatography was carried out on silica gel 60, 230–400 mesh (Merck). Melting points were measured on a Büchi–Tottoli apparatus with open capillary tubes and are uncorrected. ^1H (^{13}C) NMR spectra were recorded at 400, 300 (75.5), 200 (50.5), and 80 (20.2) MHz with tetramethylsilane ($\delta = 0.0$ in ^1H NMR spectra) and $CDCl_3$ ($\delta = 77.0$ in ^{13}C NMR spectra) as internal standards by using the DEPT pulse sequence. Low-resolution electron impact mass spectra (EI-LRMS) were obtained at 70 eV on an HP-5987A instrument and the intensities are reported as percentages relative to the base peak after the corresponding *m*/*z* value. Elemental analyses were performed with a Perkin–Elmer and LECO elemental analyzers. All commercially available reagents were used without further purification unless otherwise indicated and were purchased from Aldrich Chemical Co., Acros Organics, or Fluorochem. *t*BuLi was used as a 1.5 M or 1.7 M solution in pentane. BuLi was used as 1.6 or 2.5 M solutions in hexane. *N*-Benzylideneaniline was prepared by heating a mixture of benzaldehyde and aniline in toluene at reflux, in the presence of a catalytic amount of *p*-toluenesulfonic acid, in a system equipped with a Dean–Stark trap. 2-Chloro-4-methoxyaniline[29] was prepared by reduction of 2-chloro-4-methoxynitrobenzene (which was synthesized by nitration of 3-chlorophenol) with Fe/HCl, separation by steam-distillation of the resulting *o*- and *p*-isomers, and subsequent methylation (MeI/K_2CO_3) of the resulting 3-chloro-4-nitrophenol. 1,6-Dibromocyclohexene was prepared according to a published procedure.[30]

General procedure for the preparation of *N*-alkyl-2-haloanilines: A solution of 2-haloaniline (62.5 mmol) in THF (60 mL) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol) at $-50\,^{\circ}C$. The reaction was stirred for 30 min at this temperature and then allowed to reach 20 °C, and stirring was continued for 45 min. The reaction was re-cooled to $-50\,^{\circ}C$ and the corresponding alkyl halide (25 mmol) was added. After 15 min at this temperature, the reaction was allowed to warm up and stirring was continued for 5 h. The mixture was hydrolyzed with water, extracted with ethyl acetate (3 × 30 mL), and the combined organic layers were washed with saturated aqueous Na_2CO_3 solution, and dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the residue was purified by silica gel column chromatography (hexane/ethyl acetate) to afford *N*-alkyl-2-haloanilines.

2-Fluoro-*N*-methylaniline: Prepared from 2-fluoroaniline (6.93 g, 62.5 mmol) and methyl iodide (3.55 g, 25 mmol) in THF (60 mL) according to the general procedure described above to give the title compound (2.50 g, 80%) as a colorless oil. $R_f = 0.40$ (hexane/ethyl acetate 20:1); ^1H NMR ($CDCl_3$, 80 MHz): $\delta = 7.2-6.5$ (m, 4H), 3.7 (br s, 1H), 2.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): $\delta = 151.6$ (d, $J = 238.7$ Hz), 138.0 (d, $J = 16.1$ Hz), 124.4 (d, $J = 3.3$ Hz), 116.5 (d, $J = 7.3$ Hz), 114.0 (d, $J = 20.2$ Hz), 111.4 (d, $J = 3.3$ Hz), 29.8; MS (70 eV, EI): *m*/*z* (%): 125 (85) $[M]^+$, 124 (100); elemental analysis calcd (%) for C_7H_8FN (125.1): C 67.18, H 6.44, N 11.19; found: C 67.22, H 6.29, N 10.98.

***N*-Allyl-2-fluoroaniline**: Prepared from 2-fluoroaniline (6.93 g, 62.5 mmol) and allyl bromide (3.03 g, 25 mmol) in THF (60 mL) according to the general procedure described above to give the title compound (2.83 g, 75%) as an orange oil. $R_f = 0.35$ (hexane/ethyl acetate 30:1); ^1H NMR

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($CDCl_3$, 80 MHz): $\delta = 7.2-6.5$ (m, 4H), 6.2–5.7 (m, 1H), 5.4–5.0 (m, 2H), 4.0 (br s, 1H), 3.8 (d, $J = 4.0$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): $\delta =$ 151.6 (d, $J = 238.2$ Hz), 136.5 (d, $J = 11.2$ Hz), 134.9, 124.4 (d, $J = 3.0$ Hz), 116.6 (d, $J = 6.7$ Hz), 116.0, 114.2 (d, $J = 18.5$ Hz), 112.3 (d, $J = 2.6$ Hz), 45.9; MS (70 eV, EI): m/z (%): 151 (100) $[M]^+$; elemental analysis calcd (%) for $C_9H_{10}FN$ (151.2): C 71.50, H 6.67, N 9.26; found: C 71.35, H 6.73, N 9.19.

***N*-(2-Butenyl)-2-fluoroaniline**: Prepared from 2-fluoroaniline (6.93 g, 62.5 mmol) and crotyl bromide (3.38 g, 25 mmol) in THF (60 mL) according to the general procedure described above to give the title compound (3.50 g, 85%) as an orange oil and as a mixture of diastereoisomers (E/Z). $R_f = 0.4$ (hexane/ethyl acetate 30:1); ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 7.1-6.6$ (m, 4H), 5.9–5.5 (m, 2H), 4.0 (br s, 1H), 3.9–3.8 (m, 2H; minor diast.), 3.8–3.6 (m, 2H; major diast.), 1.8 (dd, $J = 6.0$, 1.2 Hz, 3H; major diast.), 1.7–1.6 (m, 3H; minor diast.); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 151.6$ (d, $J = 238.0$ Hz), 136.6 (d, $J = 11.4$ Hz), 128.0, 127.6, 124.5, 116.4 (d, $J = 6.8$ Hz), 114.2 (d, $J = 18.9$ Hz), 112.2 (d, $J = 3.8$ Hz), 45.5 (NCH_2; E isomer), 40.4 (NCH_2; Z isomer), 17.6 (CH_3; E isomer), 13.0 (CH_3; Z isomer); MS (70 eV, EI): m/z (%): 165 (80) $[M]^+$, 111 (100); elemental analysis calcd (%) for $C_{10}H_{12}FN$ (165.2): C 72.70, H 7.32, N 8.48; found: C 72.61, H 7.35, N 8.34.

2-Chloro-*N*-methylaniline: Prepared from 2-chloroaniline (7.96 g, 62.5 mmol) and methyl iodide (3.55 g, 25 mmol) in THF (60 mL) according to the general procedure described above to give the title compound (2.86 g, 81%) as a colorless oil. $R_f = 0.41$ (hexane/ethyl acetate 10:1); ^1H NMR ($CDCl_3$, 80 MHz): $\delta = 7.3-6.5$ (m, 4H), 4.3 (br s, 1H), 2.8 (s, 3H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): $\delta = 144.8$, 128.7, 127.6, 118.7, 116.7, 110.4, 29.9; MS (70 eV, EI): m/z (%): 143 (24) $[M+2]^+$, 141 (70) $[M]^+$, 140 (100); elemental analysis calcd (%) for C_7H_8ClN (141.6): C 59.38, H 5.69, N 9.89; found: C 59.31, H 5.51, N 9.80.

Preparation of *N*-allyl-2-chloro-4-methoxyaniline: A mixture of 2-chloro-4-methoxyaniline (7.87 g, 50 mmol), K_2CO_3 (3.79 g, 27.5 mmol), and allyl bromide (3.0 g, 25 mmol) in acetonitrile (50 mL) was stirred for 48 hours under reflux. The mixture was extracted with ethyl acetate (3 × 30 mL) and the combined organic layers were washed with saturated aqueous Na_2CO_3 and dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the residue was purified by silica gel column chromatography to afford the title compound (2.85 g, 58%) as a yellow oil. $R_f = 0.30$ (hexane/ethyl acetate 40:1); ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 6.9$ (d, $J =$ 2.9 Hz, 1H), 6.75 (dd, $J = 8.9$, 2.8 Hz, 1H), 6.6 (d, $J = 8.9$ Hz, 1H), 6.1–5.9 (m, 1H), 5.4–5.2 (m, 2H), 4.1 (br s, 1H), 3.8 (d, $J = 6.7$ Hz, 2H), 3.7 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 151.4$, 138.2, 135.1, 119.5, 116.1, 115.1, 113.6, 112.4, 55.8, 46.7; MS (70 eV, EI): m/z (%): 199 (32) $[M+2]^+$, 197 (98) $[M]^+$, 156 (100); elemental analysis calcd (%) for $C_{10}H_{12}ClNO$ (197.7): C 60.76, H 6.12, N 7.09; found: C 60.58, H 6.19, N 6.95.

General procedure for the preparation of 2-haloanilines 1a–c, 12, 17, and 25a–b: A solution of *N*-alkyl-2-haloaniline (25 mmol) in THF (30 mL) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol) at −50 °C. The reaction mixture was stirred for 15 min and was then allowed to warm up to 20 °C, and stirring was continued for 45 min. The reaction mixture was cooled to −50 °C and the corresponding dibromo derivative (25 mmol) was added. After 15 min at this temperature, the reaction was allowed to warm up and stirring was continued for 5 h. The mixture was hydrolyzed with water, extracted with ethyl acetate (3 × 30 mL), and the combined organic layers were washed with saturated aqueous Na_2CO_3 and dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the residue was purified by silica gel column chromatography (hexane/ethyl acetate) to afford the corresponding tertiary amine.

***N*-(2-Bromoallyl)-2-fluoro-*N*-methylaniline (1a)**: 2-Fluoro-*N*-methylaniline (3.1 g, 25 mmol) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol). Addition of 2,3-dibromopropene (5.0 g, 25 mmol) and workup as above yielded **1a** (4.25 g, 70%) as a colorless oil. $R_f = 0.25$ (hexane/ethyl acetate 50:1); ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 7.1-6.8$ (m, 4H), 5.9–5.8 (m, 1H), 5.65–5.6 (m, 1H), 4.1 (s, 2H), 3.0 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 154.3$ (d, $J = 244.5$ Hz), 138.3 (d, $J = 8.3$ Hz), 130.1, 124.2 (d, $J = 2.9$ Hz), 120.8 (d, $J = 7.6$ Hz), 118.8 (d, $J = 2.8$ Hz), 117.3, 116.2 (d, $J = 20.8$ Hz), 62.6 (d, $J = 6.5$ Hz), 39.4 (d, $J = 2.0$ Hz); MS (70 eV, EI): m/z (%): 245 (25) $[M+2]^+$, 243 (25) $[M]^+$, 138 (100); elemental analysis calcd (%) for $C_{10}H_{11}BrFN$ (244.1): C 49.20, H 4.54, N 5.74; found: C 49.01, H 4.61, N 5.59.

***N*-Allyl-*N*-(2-bromoallyl)-2-fluoroaniline (1b)**: 2-Fluoro-*N*-allylaniline (3.8 g, 25 mmol) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol). Addition of 2,3-dibromopropene (5.0 g, 25 mmol) and workup as above yielded **1b** (4.77 g, 71%) as a colorless oil. $R_f = 0.28$ (hexane/ethyl acetate 50:1); ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 7.15-6.8$ (m, 4H), 6.05–5.8 (m, 2H), 5.7–5.6 (m, 1H), 5.35–5.2 (m, 2H), 4.1 (s, 2H), 3.9 (d, $J = 5.6$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 155.6$ (d, $J = 244.0$ Hz), 138.1 (d, $J = 8.5$ Hz), 135.2, 131.2, 125.1 (d, $J = 3.0$ Hz), 122.1 (d, $J = 7.5$ Hz), 121.1 (d, $J = 2.9$ Hz), 118.5, 118.1, 117.4 (d, $J = 21.0$ Hz), 60.1 (d, $J = 4.6$ Hz), 55.5 (d, $J = 4.0$ Hz); MS (70 eV, EI): m/z (%): 271 (33) $[M+2]^+$, 269 (33) $[M]^+$, 164 (100); elemental analysis calcd (%) for $C_{12}H_{13}BrFN$ (270.1): C 53.35, H 4.85, N 5.18; found: C 53.19, H 4.81, N 5.07.

***N*-(2-Bromoallyl)-*N*-(2-butenyl)-2-fluoroaniline (1c)**: *N*-(2-Butenyl)-2-fluoroaniline (4.13 g, 25 mmol) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol). Addition of 2,3-dibromopropene (5.0 g, 25 mmol) and workup as above yielded **1c** (5.0 g, 71%) as a colorless oil and as a mixture of diastereoisomers (E/Z). $R_f = 0.21$ (hexane/ethyl acetate 50:1); ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 7.1-6.7$ (m, 4H), 5.9–5.5 (m, 4H), 4.2 (s, 2H; minor diast.), 4.05 (s, 2H; major diast.), 3.95 (d, $J = 6.2$ Hz, 2H; minor diast.), 3.85 (d, $J = 5.3$ Hz, 2H; major diast.), 1.7 (d, $J = 5.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): $\delta = 154.6$ (d, $J = 244.0$ Hz), 137.3 (d, $J =$ 8.4 Hz), 130.4, 128.9, 126.9, 124.1, 120.9 (d, $J = 7.8$ Hz), 120.1 (d, $J = 3.5$ Hz), 117.0, 116.3 (d, $J = 21.4$ Hz), 59.3 (d, $J = 5.3$ Hz; minor diast.), 58.7 (d, $J =$ 4.5 Hz; major diast.), 53.8 (d, $J = 2.8$ Hz; major diast.), 48.1 (d, $J = 3.1$ Hz; minor diast.), 17.7, 13.0; MS (70 eV, EI): m/z (%): 285 (30) $[M+2]^+$, 283 (30) $[M]^+$, 124 (100); elemental analysis calcd (%) for $C_{13}H_{15}BrFN$ (284.2): C 54.95, H 5.32, N 4.93; found: C 55.02, H 5.26, N 4.81.

***N*-(2-Bromoallyl)-2-chloro-*N*-methylaniline (12)**: 2-Chloro-*N*-methylaniline (3.5 g, 25 mmol) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol). Addition of 2,3-dibromopropene (5.0 g, 25 mmol) and workup as above yielded **12** (4.85 g, 75%) as a colorless oil. $R_f = 0.32$ (hexane/ethyl acetate 40:1); ^1H NMR ($CDCl_3$, 80 MHz): $\delta = 7.4-6.9$ (m, 4H), 6.0–5.9 (m, 1H), 5.65–5.55 (m, 1H), 3.9 (s, 2H), 2.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): $\delta = 148.5$, 130.6, 130.0, 128.3, 127.2, 123.4, 121.6, 117.7, 63.2, 40.1; MS (70 eV, EI): m/z (%): 263 (4) $[M+4]^+$, 261 (14) $[M+2]^+$, 259 (13) $[M]^+$, 154 (100); elemental analysis calcd (%) for $C_{10}H_{11}BrClN$ (260.6): C 46.10, H 4.26, N 5.38; found: C 45.98, H 4.21, N 5.30.

***N*-(2-Bromo-2-cyclohexenyl)-2-fluoro-*N*-methylaniline (17)**: 2-Fluoro-*N*-methylaniline (3.1 g, 25 mmol) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol). Addition of 1,6-dibromocyclohexene (6.0 g, 25 mmol) and workup as above yielded **17a** (5.51 g, 78%) as a colorless oil. $R_f = 0.2$ (hexane/ethyl acetate 50:1); ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 7.1-6.8$ (m, 4H), 6.4–6.3 (m, 1H), 4.45–4.3 (m, 1H), 2.8 (s, 3H), 2.2–1.6 (m, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 145.5$ (d, $J =$ 243.4 Hz), 139.4 (d, $J = 7.6$ Hz), 134.0, 125.6, 124.0 (d, $J = 3.2$ Hz), 120.1 (d, $J = 8.4$ Hz), 119.6 (d, $J = 3.6$ Hz), 116.0 (d, $J = 21.3$ Hz), 62.4 (d, $J = 7.5$ Hz), 32.6, 27.9, 27.5, 21.1; MS (70 eV, EI): m/z (%): 285 (13) $[M+2]^+$, 283 (13) $[M]^+$, 125 (100); elemental analysis calcd (%) for $C_{13}H_{15}BrFN$ (284.2): C 54.95, H 5.32, N 4.93; found: C 55.04, H 5.23, N 4.85.

***N*-(2-Bromobenzyl)-2-fluoro-*N*-methylaniline (25a)**: 2-Fluoro-*N*-methylaniline (3.1 g, 25 mmol) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol). Addition of 2-bromobenzylbromide (6.2 g, 25 mmol) and workup as above yielded **25a** (5.27 g, 72%) as a colorless oil. $R_f = 0.45$ (hexane/ethyl acetate 30:1); ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 7.7-7.6$ (m, 2H), 7.4 (dt, $J = 7.4$, 1.4 Hz, 1H), 7.25–6.9 (m, 5H), 4.5 (s, 2H), 3.0 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 154.7$ (d, $J = 244.1$ Hz), 139.8 (d, $J =$ 8.4 Hz), 137.6, 132.5, 129.1, 128.3, 127.3, 124.2 (d, $J = 2.6$ Hz), 123.3, 120.7 (d, $J = 7.6$ Hz), 118.6 (d, $J = 3.8$ Hz), 116.1 (d, $J = 21.4$ Hz), 58.8 (d, $J = 4.5$ Hz), 39.4 (d, $J = 2.8$ Hz); MS (70 eV, EI): m/z (%): 295 (86) $[M+2]^+$, 293 (86) $[M]^+$, 138 (100); elemental analysis calcd (%) for $C_{14}H_{13}BrFN$ (294.2): C 57.16, H 4.45, N 4.76; found: C 57.07, H 4.51, N 4.75.

***N*-Allyl-*N*-(2-bromobenzyl)-2-fluoroaniline (25b)**: 2-Fluoro-*N*-allylaniline (3.8 g, 25 mmol) was treated with BuLi (10 mL, 2.5 M solution in hexanes, 25 mmol). Addition of 2-bromobenzylbromide (6.2 g, 25 mmol) and workup as above yielded **25b** (5.90 g, 74%) as a colorless oil. $R_f = 0.3$ (hexane/ethyl acetate 60:1); ^1H NMR ($CDCl_3$, 80 MHz): $\delta = 7.6-6.7$ (m, 8H), 6.2–5.7 (m, 1H), 5.4–5.0 (m, 2H), 4.4 (s, 2H), 3.8 (d, $J = 5.6$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 154.8$ (d, $J = 244.2$ Hz), 138.1 (d, $J = 8.5$ Hz), 137.6, 134.3, 132.6, 129.0, 128.2, 127.3, 124.1 (d, $J = 3.5$ Hz), 123.2, 120.8 (d, $J =$ 7.6 Hz), 120.0 (d, $J = 3.8$ Hz), 117.3, 116.3 (d, $J = 21.5$ Hz), 55.4 (d,

$J = 2.7$ Hz), 55.1 (d, $J = 4.8$ Hz); MS (70 eV, EI): m/z (%): 321 (83) $[M+2]^+$, 319 (83) $[M]^+$, 169 (100); elemental analysis calcd (%) for $C_{16}H_{15}BrFN$ (320.2): C 60.02, H 4.72, N 4.37; found: C 59.91, H 4.65, N 4.27.

***N*-Allyl-*N*-(2-bromoallyl)-2-chloro-4-methoxyaniline (15)**: Solid K_2CO_3 (3.8 g, 27.5 mmol) and 2,3-dibromopropene (5.0 g, 25 mmol) were added to a solution of *N*-allyl-2-chloro-4-methoxyaniline (4.9 g, 25 mmol) in acetonitrile (40 mL) at 20 °C. The resulting mixture was heated at reflux for 48 h and was then allowed to warm up to 20 °C. The crude mixture was treated with water, extracted with ethyl acetate (3 × 30 mL), and the combined organic layers were washed with saturated aqueous Na_2CO_3 solution and dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the residue was purified by silica gel column chromatography (hexane/ethyl acetate) to afford **15** (6.0 g, 76%) as a colorless oil. $R_f = 0.40$ (hexane/ethyl acetate 40:1); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.05$ (d, $J = 8.8$ Hz, 1H), 6.95 (d, $J = 2.9$ Hz, 1H), 6.75 (dd, $J = 8.8$, 2.9 Hz, 1H), 5.9 (m, 1H), 5.9–5.7 (m, 1H), 5.5 (d, $J = 1.2$ Hz, 1H), 5.3–5.1 (m, 2H), 3.9 (s, 2H), 3.75 (s, 3H), 3.7 (d, $J = 6.2$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 156.0$, 139.7, 134.3, 131.2, 130.5, 125.1, 117.9, 117.8, 115.6, 112.6, 60.0, 56.0, 55.5; MS (70 eV, EI): m/z (%): 319 (64) $[M+4]^+$, 317 (82) $[M+2]^+$, 315 (23) $[M]^+$, 210 (100); elemental analysis calcd (%) for $C_{13}H_{15}BrClNO$ (316.6): C 49.31, H 4.78, N 4.42; found: C 49.52, H 4.65, N 4.35.

General procedure for the preparation of 2-halophenyl ethers 22a, 25c, 32, and 2-fluorophenyl thioethers 22b, 25d: Solid K_2CO_3 (1.1 equiv) and the dibromo derivative (1.0 equiv) were added to a solution of the corresponding phenol (1.0 equiv) in acetone (40 mL) at 20 °C. The resulting mixture was heated at reflux, overnight for ethers and 48 h for thioethers, and then allowed to warm up to 20 °C. The crude mixture was treated with water, extracted with ethyl acetate (3 × 30 mL), and the combined organic layers were washed with an aqueous K_2CO_3 solution and dried over anhydrous Na_2SO_4. The solvents were removed under vacuum and the residue was purified by silica gel column chromatography (hexane/ethyl acetate) to afford the corresponding ether or thioether.

2-Bromoallyl 2-fluorophenyl ether (22a): 2-Fluorophenol (2.2 g, 20 mmol) was treated with K_2CO_3 (3.0 g, 22 mmol). 2,3-Dibromopropene (4.0 g, 20 mmol) was added and the mixture was heated at reflux overnight. Workup according to the general procedure above gave **22a** (3.68 g, 80%) as a brown oil. $R_f = 0.50$ (hexane/ethyl acetate 25:1); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.2$–6.9 (m, 4H), 6.1–6.0 (m, 1H), 5.75–5.65 (m, 1H), 4.7 (s, 2H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 152.7$ (d, $J = 247.3$ Hz), 145.5 (d, $J = 10.7$ Hz), 126.5, 124.2 (d, $J = 3.9$ Hz), 122.2 (d, $J = 6.9$ Hz), 118.0, 116.5, 116.1 (d, $J = 6.0$ Hz), 72.8; MS (70 eV, EI): m/z (%): 232 (8) $[M+2]^+$, 230 (8) $[M]^+$, 112 (100); elemental analysis calcd (%) for C_9H_8BrFO (231.1): C 46.78, H 3.49; found: C 46.62, H 3.51.

2-Bromobenzyl 2-fluorophenyl ether (25c): 2-Fluorophenol (2.2 g, 20 mmol) was treated with K_2CO_3 (3.0 g, 22 mmol). 2-Bromobenzyl bromide (5.0 g, 20 mmol) was added and the mixture was heated at reflux overnight. Workup according to the general procedure above yielded **25c** (4.8 g, 85%) as a white solid. M.p. 35–37 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.7$–6.9 (m, 8H), 5.2 (s, 2H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 152.7$ (d, $J = 245.6$ Hz), 146.3 (d, $J = 10.7$ Hz), 135.8, 132.4, 129.2, 128.7, 127.5, 124.2 (d, $J = 3.8$ Hz), 122.0, 121.6 (d, $J = 6.9$ Hz), 116.2 (d, $J = 17.5$ Hz), 115.4, 70.3; MS (70 eV, EI): m/z (%): 282 (28) $[M+2]^+$, 280 (28) $[M]^+$, 171 (100); elemental analysis calcd (%) for $C_{13}H_{10}BrFO$ (281.1): C 55.54, H 3.59; found: C 55.62, H 3.51.

2-Bromobenzyl 2-chloro-4-methoxyphenyl ether (32): 2-Chloro-4-methoxyphenol (3.2 g, 20 mmol) was treated with K_2CO_3 (3.0 g, 22 mmol). 2-Bromobenzylbromide (5.0 g, 20 mmol) was added and the mixture was heated at reflux overnight. Workup according to the general procedure above yielded **32** (5.5 g, 85%) as a white-pink solid. M.p. 31–33 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.7$ (d, $J = 7.6$ Hz, 1H), 7.6 (d, $J = 7.8$ Hz, 1H), 7.4 (t, $J = 7.6$ Hz, 1H), 7.2 (t, $J = 7.6$ Hz, 1H), 7.0 (d, $J = 3.0$ Hz, 1H), 6.9 (d, $J = 9.0$ Hz, 1H), 6.7 (dd, $J = 9.0$, 3.0 Hz, 1H), 5.1 (s, 2H), 3.7 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 154.1$, 147.9, 135.9, 132.2, 128.9, 128.5, 127.4, 123.7, 121.7, 115.9, 115.1, 112.6, 70.6, 55.5; MS (70 eV, EI): m/z (%): 330 (15) $[M+4]^+$, 328 (54) $[M+2]^+$, 326 (41) $[M]^+$, 171 (100); elemental analysis calcd (%) for $C_{14}H_{12}BrClO_2$ (327.6): C 51.33, H 3.69; found: C 51.21, H 3.71.

2-Bromoallyl 2-fluorophenyl thioether (22b): 2-Fluorothiophenol (1.3 g, 10 mmol) was treated with K_2CO_3 (1.5 g, 11 mmol). 2,3-Dibromopropene (2.0 g, 10 mmol) was added and the mixture was heated at reflux for 24 h. Workup according to the general procedure above yielded **22b** (1.5 g, 60%) as a colorless oil. $R_f = 0.25$ (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.5$–7.0 (m, 4H), 5.65–5.6 (m, 1H), 5.4–5.35 (m, 1H), 3.8 (s, 2H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 161.8$ (d, $J = 246.4$ Hz), 134.0, 129.6 (d, $J = 7.9$ Hz), 128.3, 124.4 (d, $J = 3.7$ Hz), 119.3, 115.7 (d, $J = 23.2$ Hz), 43.9; MS (70 eV, EI): m/z (%): 248 (38) $[M+2]^+$, 246 (38) $[M]^+$, 167 (100); elemental analysis calcd (%) for C_9H_8BrFS (247.1): C 43.74, H 3.26; found: C 43.59, H 3.22.

2-Bromobenzyl 2-fluorophenyl thioether (25d): 2-Fluorothiophenol (1.3 g, 10 mmol) was treated with K_2CO_3 (1.5 g, 11 mmol). 2-Bromobenzyl bromide (2.5 g, 10 mmol) was added and the mixture was heated at reflux for 48 h. Workup according to the general procedure above yielded **25d** (2.5 g, 85%) as a colorless oil. $R_f = 0.28$ (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.55$ (d, $J = 8.3$ Hz, 1H), 7.3–7.0 (m, 7H), 4.2 (s, 2H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 162.0$ (d, $J = 245.5$ Hz), 136.6, 133.8, 132.9, 130.6, 129.2 (d, $J = 7.3$ Hz), 128.8, 127.3, 124.4, 124.3 (d, $J = 4.5$ Hz), 122.0 (d, $J = 17.5$ Hz), 115.5 (d, $J = 22.7$ Hz), 38.9; MS (70 eV, EI): m/z (%): 298 (88) $[M+2]^+$, 296 (88) $[M]^+$, 171 (100); elemental analysis calcd (%) for $C_{13}H_{10}BrFS$ (297.2): C 52.54, H 3.39; found: C 52.31, H 3.41.

General procedure for the preparation of 4-functionalized-1-alkyl-3-methylindoles (2): A solution of the starting amine **1** (2 mmol) in THF (15 mL) was treated with *t*BuLi (7 mmol, 3.5 equiv) at −110 °C. The reaction mixture was stirred at this temperature for 15 min and then at −40 °C for 3 h. The reaction mixture was re-cooled to −78 °C and the electrophile (3 mmol) was added. The reaction mixture was stirred overnight at room temperature, then hydrolyzed with water, and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash column chromatography (hexane/ethyl acetate) and/or by recrystallization to afford products **2**.

1,3-Dimethyl-1*H*-indole (2a): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M in pentane, 7 mmol). Addition of water (excess) and workup according to the general procedure above yielded **2a** (0.22 g, 75%) as a brown oil. $R_f = 0.50$ (hexane/ethyl acetate 50:1); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 7.7$ (d, $J = 7.6$ Hz, 1H), 7.4–7.1 (m, 3H), 6.9 (s, 1H), 3.8 (s, 3H), 2.4 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta = 136.9$, 128.5, 126.4, 121.3, 118.8, 118.4, 109.9, 108.9, 32.4, 9.5; MS (70 eV, EI): m/z (%): 145 (64) $[M]^+$, 144 (100); elemental analysis calcd (%) for $C_{10}H_{11}N$ (145.2): C 82.72, H 7.64, N 9.65; found: C 82.61, H 7.69, N 9.51.

1,3-Dimethyl-4-tributylstannyl-1*H*-indole (2b): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M pentane, 7 mmol). Addition of tributyltin chloride (0.98 g, 3 mmol) and workup according to the general procedure above yielded **2b** (0.58 g, 67%) as a yellow oil. $R_f = 0.44$ (hexane/ethyl acetate 15:1); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.2$–7.0 (m, 3H), 6.8 (s, 1H), 3.6 (s, 3H), 2.3 (s, 3H), 1.6–0.7 (m, 27H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): $\delta = 136.2$, 133.9, 131.8, 127.6, 127.0, 120.6, 111.5, 109.4, 32.3, 29.6, 27.4, 13.6, 11.3; MS (70 eV, EI): m/z (%): 435 (7) $[M]^+$, 264 (100); elemental analysis calcd (%) for $C_{22}H_{37}NSn$ (434.3): C 60.85, H 8.59, N 3.23; found: C 60.67, H 8.68, N 3.16.

4-(1-Hydroxy-1-phenylmethyl)-1,3-dimethyl-1*H*-indole (2c): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M in pentane, 7 mmol). Addition of benzaldehyde (0.31 g, 3 mmol) and workup according to the general procedure above yielded **2c** (0.35 g, 69%) as a colorless oil. $R_f = 0.36$ (hexane/ethyl acetate 3:1); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.3$–6.8 (m, 8H), 6.6 (s, 1H), 6.4 (s, 1H), 3.5 (s, 3H), 2.4 (brs, 1H), 2.2 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): $\delta = 143.7$, 137.7, 136.3, 128.0, 127.8, 126.9, 126.8, 125.4, 121.2, 117.5, 109.6, 108.8, 72.5, 32.3, 12.8; MS (70 eV, EI): m/z (%): 271 (10) $[M]^+$, 126 (100); elemental analysis calcd (%) for $C_{17}H_{17}NO$ (251.3): C 81.24, H 6.82, N 5.57; found: C 81.32, H 6.93, N 5.49.

4-(1-Hydroxy-1-methylethyl)-1,3-dimethyl-1*H*-indole (2d): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M in pentane, 7 mmol). Addition of acetone (0.18 g, 3 mmol) and workup according to the general procedure above yielded **2d** (0.30 g, 73%) as a white solid. M.p. 130–132 °C (hexane); ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 7.35$–7.15 (m, 3H), 6.95 (q, $J = 0.8$ Hz, 1H), 3.8 (s, 3H), 2.6 (d, $J = 0.8$ Hz, 3H), 2.0 (brs, 1H), 1.8 (s, 6H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): $\delta = 141.2$, 138.8, 128.9, 124.5, 120.4, 115.4, 110.1, 109.1, 72.9, 32.5, 31.9, 15.7; MS (70 eV, EI): m/z (%): 203 (66) $[M]^+$, 146 (100); elemental analysis calcd (%) for $C_{13}H_{17}NO$ (203.3): C 76.81, H 8.43, N 6.89; found: C 76.75, H 8.52, N 6.78.

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Ethyl 1,3-dimethyl-1*H*-indole-4-carboxylate (2e): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M in pentane, 7 mmol). Addition of ethyl chloroformate (0.33 g, 3 mmol) and workup according to the general procedure above yielded **2e** (0.32 g, 73 %) as a green oil. R_f = 0.33 (hexane/ethyl acetate 10:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.65 (d, J = 6.8 Hz, 1 H), 7.4 (d, J = 7.6 Hz, 1 H), 7.2 (t, J = 7.6 Hz, 1 H), 6.9 (s, 1 H), 4.5 (q, J = 7.2 Hz, 2 H), 3.7 (s, 3 H), 2.4 (s, 3 H), 1.4 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 168.5, 138.1, 129.8, 125.3, 124.4, 121.5, 120.1, 112.8, 110.4, 60.6, 32.4, 14.3, 13.1; MS (70 eV, EI): m/z (%): 217 (91) $[M]^+$, 188 (100); elemental analysis calcd (%) for $C_{13}H_{15}NO_2$ (217.3): C 71.87, H 6.96, N 6.45; found: C 71.75, H 6.82, N 6.29.

1,3-Dimethyl-4-(1-phenyl-1-phenylaminomethyl)-1*H*-indole (2f): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of *N*-benzylideneaniline (0.55 g, 3 mmol) and workup according to the general procedure above yielded **2f** (0.39 g, 59 %) as a white solid. M.p. 154–156 °C (hexane); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.3–6.4 (m, 14 H), 6.26 (s, 1 H), 4.2 (br s, 1 H), 3.6 (s, 3 H), 2.3 (s, 3 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 147.1, 142.7, 137.9, 135.3, 129.0, 128.4, 127.9, 127.8, 127.0, 125.8, 121.5, 118.5, 117.0, 113.0, 110.0, 108.6, 58.5, 32.5, 12.8; MS (70 eV, EI): m/z (%): 326 (10) $[M]^+$, 234 (100); elemental analysis calcd (%) for $C_{23}H_{22}N_2$ (326.4): C 84.63, H 6.79, N 8.58; found: C 84.71, H 6.73, N 8.39.

4-(4-Chlorobenzoyl)-1,3-dimethyl-1*H*-indole (2g): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of 4-chlorobenzonitrile (0.41 g, 3 mmol) and workup according to the general procedure above yielded **2g** (0.35 g, 62 %) as a yellow oil. R_f = 0.3 (hexane/ethyl acetate 5:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.7 (d, J = 8.4 Hz, 2 H), 7.4 (d, J = 8.0 Hz, 1 H), 7.33 (d, J = 8.4 Hz, 2 H), 7.25 (t, J = 7.6 Hz, 1 H), 7.0 (d, J = 7.0 Hz, 1 H), 6.85 (s, 1 H), 3.8 (s, 3 H), 1.9 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 177.3, 137.7, 137.4, 136.8, 133.1, 129.9, 128.4, 124.4, 121.1, 118.4, 110.0, 109.7, 32.6, 11.5; MS (70 eV, EI): m/z (%): 285 (33) $[M+2]^+$, 283 (100) $[M]^+$; elemental analysis calcd (%) for $C_{17}H_{14}ClNO$ (283.8): C 71.96, H 4.97, N 4.94; found: C 71.81, H 4.93, N 4.83.

4-Bromo-1,3-dimethyl-1*H*-indole (2h): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of 1,2-dibromoethane (0.56 g, 3 mmol) and workup according to the general procedure above yielded **2h** (0.27 g, 61 %) as a white solid. M.p. 68–70 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.25 (d, J = 8.4 Hz, 1 H), 7.2 (d, J = 8.0 Hz, 1 H), 7.0 (t, J = 8.0 Hz, 1 H), 6.8 (s, 1 H), 3.7 (s, 3 H), 2.6 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 138.2, 128.3, 126.3, 122.8, 122.1, 114.8, 111.2, 108.4, 32.6, 12.3; MS (70 eV, EI): m/z (%): 225 (50) $[M+2]^+$, 224 (100), 223 (50) $[M]^+$, 222 (100); elemental analysis calcd (%) for $C_{10}H_{10}BrN$ (224.1): C 53.60, H 4.50, N 6.25; found: C 53.48, H 4.62, N 6.31.

1-Allyl-3-methyl-1*H*-indole (2i): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol), and the cooling bath was removed to allow the reaction to warm up to room temperature. Addition of H_2O (excess) and workup according to the general procedure above yielded **2i** (0.13 g, 38 %) as a colorless oil. R_f = 0.39 (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.65 (d, J = 7.0 Hz, 1 H), 7.4–7.1 (m, 3 H), 6.9 (s, 1 H), 6.15–5.9 (m, 1 H), 5.3–5.1 (m, 2 H), 4.7 (dt, J = 5.4, 1.6 Hz, 2 H), 2.4 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 136.3, 133.7, 128.8, 125.4, 121.4, 118.9, 118.6, 116.9, 110.5, 109.3, 48.5, 9.6; MS (70 eV, EI): m/z (%): 171 (100) $[M]^+$, 170 (100); elemental analysis calcd (%) for $C_{12}H_{13}N$ (171.2): C 84.17, H 7.65, N 8.18; found: C 84.25, H 7.62, N 8.03.

1-(2-Butenyl)-3-methyl-1*H*-indole (2j): Amine **1c** (0.57 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of H_2O (excess) and workup according to the general procedure above yielded **2j** (0.27 g, 72 %) as a colorless oil. R_f = 0.25 (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.75 (d, J = 7.6 Hz, 1 H), 7.5–7.2 (m, 3 H), 7.0 (s, 1 H), 5.9–5.6 (m, 2 H), 4.8 (d, J = 8.4 Hz, 2 H; minor diast.), 4.75–4.65 (m, 2 H; major diast.), 2.5 (s, 3 H), 1.95 (d, J = 8.0 Hz, 3 H; minor diast.), 1.9–1.8 (m, 3 H; major diast.); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 136.2, 128.8, 128.4, 127.3, 126.6, 126.0, 125.2, 125.0, 121.2, 118.9, 118.5, 110.2, 109.3, 109.2, 47.8 (major diast.), 42.6 (minor diast.), 17.5 (major diast.), 13.0 (minor diast.), 9.5; MS (70 eV, EI): m/z (%): 185 (78) $[M]^+$, 130 (100); elemental analysis calcd (%) for $C_{13}H_{15}N$ (185.3): C 84.28, H 8.16, N 7.56; found: C 84.11, H 8.02, N 7.58.

General procedure for the preparation of 4-functionalized 3-methylindoles (3): A solution of the starting amine **1b** (2 mmol) in THF (15 mL) was treated with *t*BuLi (7 mmol, 3.5 equiv) at −110 °C. The reaction mixture was stirred for 15 min at this temperature, and the cooling bath was then removed to allow the reaction to warm up to room temperature. The mixture was re-cooled to −78 °C, and the corresponding electrophile (3 mmol) was added. Workup according to the general procedure above yielded a residue. The residue and [$NiCl_2$(dppp)] (0.03 g, 0.08 mmol) were dissolved in toluene (6 mL). DIBAL-H (1.5 equiv, 2 mL, 1.5 M solution in toluene, 3.0 mmol) was added at 0 °C and the temperature was increased to room temperature. After stirring at the same temperature for 2 h, the mixture was treated with 0.5 M NaOH (2 mL) and Et_2O (9 mL) for 1 h and it was then dried directly over $MgSO_4$. After evaporation of the solvent, the residue was purified by flash column chromatography (hexane/ethyl acetate) to afford products **3**.

4-Deuterio-3-methyl-1*H*-indole (3a): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Deuterium oxide (excess) was added and the mixture was treated according to the general procedure above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the residue and [$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL). Workup as described above yielded **3a** (0.14 g, 53 %) as a white solid. M.p. 96–98 °C (methanol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.9 (br s, 1 H), 7.35 (d, J = 8.4 Hz, 1 H), 7.2 (dd, J = 8.4, 6.0 Hz, 1 H), 7.15 (d, J = 6.0 Hz, 1 H), 7.0 (s, 1 H), 2.4 (s, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 136.2, 128.1, 121.8, 121.5, 118.9, 111.6, 110.9, 9.7; MS (70 eV, EI): m/z (%): 132 (60) $[M]^+$, 131 (100); elemental analysis calcd (%) for C_9H_8DN (132.2): C 81.78, H/D 7.62, N 10.60; found: C 81.88, H/D 7.47, N 10.59.

3-Methyl-4-tributylstannyl-1*H*-indole (3b): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Tributyltin chloride (0.98 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the residue and [$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL). Workup according to the general procedure above yielded **3b** (0.44 g, 52 %) as a colorless oil. R_f = 0.20 (hexane/ethyl acetate 20:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.9 (br s, 1 H), 7.3 (d, J = 8.0 Hz, 1 H), 7.25 (d, J = 8.8 Hz, 1 H), 7.15 (dd, J = 8.8, 8.0 Hz, 1 H), 7.0 (s, 1 H), 2.4 (s, 3 H), 1.6–1.5 (m, 6 H), 1.4–1.3 (m, 6 H), 1.2–1.1 (m, 6 H), 0.9 (t, J = 7.6 Hz, 9 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 135.7, 133.5, 131.7, 128.3, 122.1, 121.1, 113.3, 111.4, 29.1, 27.4, 13.6, 11.4; MS (70 eV, EI): m/z (%): 421 (5) $[M]^+$, 130 (100); elemental analysis calcd (%) for $C_{21}H_{35}NSn$ (420.2): C 60.02, H 8.40, N 3.33; found: C 60.21, H 8.32, N 3.31.

3-Methyl-4-trimethylsilyl-1*H*-indole (3c): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Chlorotrimethylsilane (0.3 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the resultant residue and [$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL). Workup according to the general procedure above yielded **3c** (0.20 g, 48 %) as a yellow solid. M.p. 53–55 °C (methanol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.95 (br s, 1 H), 7.4–7.35 (m, 2 H), 7.2 (dd, J = 8.4, 7.2 Hz, 1 H), 7.0 (s, 1 H), 2.5 (s, 3 H), 0.5 (s, 9 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 136.1, 131.4, 131.2, 126.8, 123.1, 120.9, 112.7, 13.5, 1.6; MS (70 eV, EI): m/z (%): 203 (50) $[M]^+$, 188 (100); elemental analysis calcd (%) for $C_{12}H_{17}NSi$ (203.4): C 70.88, H 8.43, N 6.89; found: C 70.76, H 8.37, N 6.77.

3-Methyl-4-phenylthio-1*H*-indole (3d): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Diphenyl disulfide (0.6 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the resultant residue and [$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL). Workup according to the general procedure above yielded **3d** (0.23 g, 49 %) as a yellow solid. M.p. 68–70 °C (methanol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.0 (br s, 1 H), 7.35 (d, J = 7.6 Hz, 1 H), 7.25–7.1 (m, 7 H), 6.95 (s, 1 H), 2.5 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 139.1, 137.2, 129.3, 128.9, 128.4, 127.8, 126.8, 125.3, 124.8, 123.3, 122.2, 113.1, 12.4; MS (70 eV, EI): m/z (%): 239 (100) $[M]^+$; elemental analysis calcd (%) for $C_{15}H_{13}NS$ (239.3): C 75.27, H 5.47, N 5.85; found: C 75.19, H 5.49, N 5.73.

3-Methyl-4-(1-phenyl-1-phenylaminomethyl)-1*H*-indole (3e): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). *N*-Benzylideneaniline (0.54 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution

in toluene, 3 mmol) was added to a solution of the resultant residue and [$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL). Workup according to the general procedure above yielded **3e** (0.29 g, 46%) as a yellow solid. M.p. 92–94 °C (methanol); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.9 (br s, 1H), 7.5–6.5 (m, 14H), 6.4 (s, 1H), 4.45 (br s, 1H), 2.4 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 147.1, 142.7, 137.3, 135.3, 129.1, 128.4, 128.0, 127.0, 125.5, 122.9, 122.0, 119.1, 117.1, 113.1, 111.7, 110.7, 58.5, 13.0; MS (70 eV, EI): *m/z* (%): 312 (11) [*M*]$^+$, 220 (100); elemental analysis calcd (%) for $C_{22}H_{20}N_2$ (312.4): C 84.58, H 6.45, N 8.97; found: C 84.43, H 6.41, N 8.91.

4-[1-Hydroxy-1-(4-methylphenyl)methyl]-3-methyl-1*H*-indole (3f): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). 4-Methylbenzaldehyde (0.36 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the resultant residue and [$NiCl_2$(dppp)] (0.043 g, 0.08 mmol) in toluene (6 mL). Workup according to the general procedure above yielded **3f** (0.26 g, 52%) as a brown solid. M.p. 98–100 °C (methanol); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.1 (br s, 1H), 7.4–7.0 (m, 7H), 6.9 (s, 1H), 6.6 (s, 1H), 2.4 (s, 3H), 2.4–2.3 (br s, 1H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 140.9, 137.3, 136.8, 136.5, 128.9, 127.0, 125.2, 123.0, 121.8, 118.0, 111.4, 110.9, 72.7, 21.1, 13.1; MS (70 eV, EI): *m/z* (%): 251 (100) [*M*]$^+$; elemental analysis calcd (%) for $C_{17}H_{17}NO$ (251.3): C 81.24, H 6.82, N 5.57; found: C 81.11, H 6.79, N 5.50.

4-Bromo-3-methyl-1*H*-indole (3g): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). 1,2-Dibromoethane (0.56 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the resultant residue and [$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL). Workup according to the general procedure above yielded **3g** (0.21 g, 50%) as a brown solid. M.p. 80–82 °C (methanol); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.95 (br s, 1H), 7.3–7.25 (m, 2H), 7.0–6.95 (m, 2H), 2.6 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 137.5, 126.1, 123.4, 122.6, 114.7, 112.9, 110.4, 12.5; MS (70 eV, EI): *m/z* (%): 211 (93) [*M*+2]$^+$, 210 (100), 209 (93) [*M*]$^+$, 208 (100); elemental analysis calcd (%) for C_9H_8BrN (210.1): C 51.46, H 3.84, N 6.67; found: C 51.53, H 3.77, N 6.71.

***N*-(2-Deuterioallyl)-2-fluoro-*N*-methylaniline (5a)**: A solution of amine **1a** (0.49 g, 2 mmol) in THF (15 mL) was treated with 2.2 equiv *t*BuLi (2.9 mL, 4.4 mmol) at −110 °C. The reaction mixture was stirred for 30 min at this temperature and then quenched with deuterium oxide (excess), and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash column chromatography to afford product **5a** (0.30 g, 91%) as a colorless oil. R_f = 0.4 (hexane/ethyl acetate 30:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.1–6.8 (m, 4H), 5.2–5.1 (m, 2H), 3.7 (s, 2H), 2.8 (s, 3H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): δ = 155.0 (d, *J* = 244.6 Hz), 139.8 (d, *J* = 8.6 Hz), 134.3(t, *J* = 23.7 Hz), 124.1 (d, *J* = 3.2 Hz), 120.7 (d, *J* = 7.9 Hz), 118.7 (d, *J* = 3.3 Hz), 116.8, 116.0 (d, *J* = 21.4 Hz), 57.8 (d, *J* = 5.3 Hz), 38.9; MS (70 eV, EI): *m/z* (%): 166 (65) [*M*]$^+$, 138 (100); elemental analysis calcd (%) for $C_{10}H_{11}DFN$ (166.2): C 72.26, H/D 7.88, N 8.43; found: C 72.34, H/D 7.71, N 8.37.

General procedure for the preparation of 3,4-functionalized indoles 10, 11, and 16: The procedure for the preparation of indoles **2** and **3** was repeated until the addition of the electrophile. Then, different enophiles [*N*,*N*-dimethylmethyleneammonium iodide, diethylazodicarboxylate (DEAD), or diethyl ketomalonate, 2.2 mmol] were added and the reaction mixture was heated at reflux for 3 h (monitored by TLC). The mixture was hydrolyzed with water and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. For the preparation of **11**, the same procedure described for compounds **3** was followed. The solvent was removed under vacuum and the residue was purified by flash column chromatography (hexane/ethyl acetate/diethylamine) and/or recrystallization to afford products **10**, **11**, and **16**.

3-(2-Dimethylaminoethyl)-1-methyl-1*H*-indole (10a): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of water (0.05 mL, 3 mmol) and then *N*,*N*-dimetylmethyleneammonium iodide(0.41 g, 2.2 mmol) and workup as described above yielded **10a** (0.26 g, 64%) as a colorless oil. R_f = 0.2 (ethyl acetate/triethylamine 25:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.7 (d, *J* = 8.0 Hz, 1H), 7.35–7.25 (m, 2H), 7.2 (t, *J* = 8.0 Hz, 1H), 6.9 (s, 1H), 3.75 (s, 3H), 3.05–2.95 (m, 2H), 2.75–2.65 (m, 2H), 2.4 (s, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 136.8, 127.7, 126.1, 121.3, 118.7, 118.4, 112.7, 109.0, 60.5, 45.4, 32.3, 23.5; MS (70 eV, EI): *m/z* (%): 202 (12) [*M*]$^+$, 58 (100); elemental analysis calcd (%) for $C_{13}H_{18}N_2$ (202.3): C 77.18, H 8.97, N 13.85; found: C 77.12, H 8.92, N 13.74.

3-(2-Dimethylaminoethyl)-1-methyl-4-(4-methylphenylcarbonyl)-1*H*-indole (10b): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of 4-methylbenzonitrile (0.35 g, 3 mmol) and then *N*,*N*-dimetylmethyleneammonium iodide(0.41 g, 2.2 mmol) and workup as described above yielded **10b** (0.38 g, 60%) as a yellow oil. R_f = 0.3 (ethyl acetate/triethylamine 10:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.65 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.2 (dd, *J* = 8.4, 8.0 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.9 (s, 1H), 3.75 (s, 3H), 2.55–2.5 (m, 2H), 2.35 (s, 3H), 2.35–2.25 (m, 2H), 2.1 (s, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 178.0, 140.9, 137.3, 136.1, 133.7, 128.8, 128.4, 127.8, 123.9, 120.8, 118.6, 112.6, 109.7, 60.2, 44.9, 32.6, 23.8, 21.3; MS (70 eV, EI): *m/z* (%): 320 (7) [*M*]$^+$, 44 (100); elemental analysis calcd (%) for $C_{21}H_{24}N_2O$ (320.4): C 78.71, H 7.55, N 8.74; found: C 78.76, H 7.38, N 8.66.

Diethyl 1-(1-methyl-1*H*-indol-3-ylmethyl)-1,2-hydrazinedicarboxylate (10c): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of water (0.05 mL, 3 mmol), followed by DEAD (0.38 g, 2.2 mmol) and workup as described above yielded **10c** (0.37 g, 58%) as a yellow solid. M.p. 106–108 °C (hexane); ^{1}H NMR ($CDCl_3$, 80 MHz): δ = 7.6–6.9 (m, 4H), 6.9 (s, 1H), 6.4 (br s, 1H), 4.8 (s, 2H), 4.1 (m, 4H), 3.6 (s, 3H), 1.3–0.9 (m, 6H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): δ = 155.9, 155.6, 136.9, 128.7, 127.2, 121.6, 119.1, 118.9, 109.1, 108.9, 62.0, 61.4, 44.3, 32.2, 14.2, 14.0; MS (70 eV, EI): *m/z* (%): 319 (3) [*M*]$^+$, 144 (100); elemental analysis calcd (%) for $C_{16}H_{21}N_3O_4$ (319.4): C 60.17, H 6.63, N 13.16; found: C 59.98, H 6.71, N 13.24.

Diethyl 1-(4-ethoxycarbonyl-1-methyl-1*H*-indol-3-ylmethyl)-1,2-hydrazinedicarboxylate (10d): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of ethyl chloroformate (0.32 g, 3 mmol), followed by DEAD (0.38 g, 2.2 mmol) and workup as described above yielded **10d** (0.415 g, 53%) as a yellow solid. M.p. 117–119 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.7 (d, *J* = 7.6 Hz, 1H), 7.4 (d, *J* = 8.3 Hz, 1H), 7.25–7.15 (m, 2H), 6.8 (br s, 1H), 5.0 (s, 2H), 4.4 (q, *J* = 7.1 Hz, 2H), 4.2 (q, *J* = 7.0 Hz, 2H), 4.1 (q, *J* = 7.3 Hz, 2H), 3.7 (s, 3H), 1.4 (t, *J* = 7.1 Hz, 3H), 1.3–1.0 (m, 6H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): δ = 168.1, 156.4, 155.9, 138.3, 131.9, 124.6, 124.1, 122.6, 120.4, 113.2, 109.8, 62.0, 61.4, 60.8, 47.2, 32.7, 14.4, 14.1; MS (70 eV, EI): *m/z* (%): 345 (8) [*M* − C_2H_6O]$^+$, 216 (100); elemental analysis calcd (%) for $C_{19}H_{25}N_3O_6$ (391.4): C 58.30, H 6.44, N 10.74; found: C 58.42, H 6.51, N 10.53.

Diethyl 1-(1-methyl-4-tributylstannyl-1*H*-indol-3-ylmethyl)-1,2-hydrazinedicarboxylate (10e): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of tributyltin chloride (0.96 g, 3 mmol), followed by DEAD (0.38 g, 2.2 mmol) and workup as described above yielded **10e** (0.67 g, 55%) as a yellow oil. R_f = 0.32 (hexane/ethyl acetate 2:1); ^{1}H NMR ($CDCl_3$, 80 MHz): δ = 7.3–7.0 (m, 3H), 6.9 (s, 1H), 6.6 (br s, 1H), 4.9 (s, 2H), 4.3–3.9 (m, 4H), 3.6 (s, 3H), 1.7–0.6 (m, 33H); ^{13}C NMR ($CDCl_3$, 20.2 MHz): δ = 156.7, 155.8, 136.5, 132.6, 131.4, 128.6, 127.2, 121.1, 111.5, 109.5, 62.5, 61.7, 47.0, 32.5, 29.0, 27.2, 14.4, 13.5, 11.0; elemental analysis calcd (%) for $C_{28}H_{47}N_3O_4Sn$ (608.4): C 55.28, H 7.79, N 6.91; found: C 55.12, H 7.72, N 6.72.

Diethyl 2-hydroxy-2-(1-methyl-1*H*-indol-3-ylmethyl)propanedioate (10f): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of water (0.05 mL, 3 mmol), followed by diethyl ketomalonate (0.38 g, 2.2 mmol) and workup as described above yielded **10f** (0.40 g, 62%) as a yellow solid. M.p. 69–71 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.7 (d, *J* = 7.0 Hz, 1H), 7.35–7.05 (m, 3H), 7.0 (s, 1H), 4.4–4.1 (m, 4H), 3.85 (br s, 1H), 3.75 (s, 3H), 3.5 (s, 2H), 1.25 (t, *J* = 7.1, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 170.2, 136.4, 128.6, 128.4, 121.3, 119.1, 118.7, 109.0, 106.8, 79.3, 62.3, 32.6, 30.4, 13.9; MS (70 eV, EI): *m/z* (%): 319 (7) [*M*]$^+$, 144 (100); elemental analysis calcd (%) for $C_{17}H_{21}NO_5$ (319.4): C 63.94, H 6.63, N 4.39; found: C 63.82, H 6.75, N 4.21.

Diethyl 2-hydroxy-2-(1-methyl-4-phenylthio-1*H*-indol-3-ylmethyl)propanedioate (10g): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of diphenyl disulfide (0.65 g, 3 mmol), followed by diethyl ketomalonate (0.38 g, 2.2 mmol) and workup as described above yielded **10g** (0.43 g, 50%) as a yellow solid. M.p. 67–69 °C (hexane); ^{1}H NMR ($CDCl_3$, 80 MHz): δ = 7.4–6.9 (m, 9H),

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4.2 (q, $J=7.1$ Hz, 4H), 4.1 (brs, 1H), 3.9 (s, 2H), 3.7 (s, 3H), 1.2 (t, $J=7.1$ Hz, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=170.3$, 138.4, 137.2, 129.9, 128.8, 128.5, 128.0, 127.4, 125.5, 124.0, 121.5, 110.1, 108.2, 79.7, 62.2, 32.8, 30.6, 13.8; MS (70 eV, EI): m/z (%): 427 (7) $[M]^+$, 207 (100); elemental analysis calcd (%) for $C_{23}H_{25}NO_5S$ (427.5): C 64.62, H 5.89, N 3.28; found: C 64.52, H 5.94, N 3.19.

Diethyl 2-(4-ethoxycarbonyl-1-methyl-1*H*-indol-3-ylmethyl)-2-hydroxypropanedioate (10h): Amine **1a** (0.49 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of ethyl chloroformate (0.32 g, 3 mmol), followed by diethyl ketomalonate (0.38 g, 2.2 mmol) and workup as described above yielded **10h** (0.48 g, 61%) as a yellow solid. M.p. 98–100 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta=7.6$ (d, $J=7.6$ Hz, 1H), 7.4 (d, $J=8.4$ Hz, 1H), 7.3–71 (m, 2H), 4.85 (brs, 1H), 4.4 (q, $J=7.2$ Hz, 2H), 4.2 (q, $J=7.0$ Hz, 4H), 3.75 (s, 2H), 3.7 (s, 3H), 1.4 (t, $J=7.2$ Hz, 3H), 1.2 (t, $J=7.0$, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=170.3$, 169.6, 137.7, 131.4, 125.8, 124.3, 122.5, 120.1, 113.2, 107.5, 80.1, 61.9, 61.2, 32.7, 31.1, 14.1, 13.8; MS (70 eV, EI): m/z (%): 391 (5) $[M]^+$, 216 (100); elemental analysis calcd (%) for $C_{20}H_{25}NO_7$ (391.4): C 61.37, H 6.44, N 3.58; found: C 61.12, H 6.51, N 3.42.

1-(2-Butenyl)-3-(2-dimethylaminoethyl)-1*H*-indole (10i): Amine **1c** (0.57 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of water (0.05 mL, 3 mmol), followed by *N*,*N*-dimetylmethyleneammonium iodide(0.41 g, 2.2 mmol) and workup as above yielded **10i** (0.31 g, 64%) as a yellow oil. $R_f=0.25$ (ethyl acetate/triethylamine 20:1) for the major diastereoisomer: ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta=7.7$ (d, $J=7.0$ Hz, 1H), 7.4–7.1 (m, 3H), 7.0 (s, 1H), 5.7–5.6 (m, 2H), 4.7–4.6 (m, 2H), 3.1–3.0 (m, 2H), 2.75–2.65 (m, 2H), 2.4 (s, 6H), 1.8–1.7 (m, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=136.2$, 128.4, 128.0, 126.4, 124.8, 121.2, 118.8, 118.5, 112.9, 109.4, 60.4, 47.8, 45.3, 23.6, 17.4; MS (70 eV, EI): m/z (%): 242 (3) $[M]^+$, 58 (100); elemental analysis calcd (%) for $C_{16}H_{22}N_2$ (242.4): C 79.29, H 9.15, N 11.56; found: C 79.46, H 9.01, N 11.34.

3-(2-Dimethylaminoethyl)-1*H*-indole (11a): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of water (0.05 mL, 3 mmol), followed by *N*,*N*-dimetylmethyleneammonium iodide(0.41 g, 2.2 mmol) and workup as described above yielded a residue. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the residue and [$NiCl_2$(dppp)] (0.004 g, 0.08 mmol) in toluene (6 mL). Workup as described above yielded **11** (0.19 g, 51%) as a yellow oil.[31] ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.2$ (brs, 1H), 7.6 (d, $J=7.6$ Hz, 1H), 7.35 (d, $J=7.6$ Hz, 1H), 7.2 (t, $J=7.6$ Hz, 1H), 7.1 (t, $J=7.6$ Hz, 1H), 7.0 (s, 1H), 3.0–2.9 (m, 2H), 2.7–2.62 (m, 2H), 2.3 (s, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=136.3$, 127.4, 121.8, 121.4, 119.1, 118.7, 114.3, 111.1, 60.3, 45.4, 23.7; MS (70 eV, EI): m/z (%): 188 (6) $[M]^+$, 58 (100); elemental analysis calcd (%) for $C_{12}H_{16}N_2$ (188.3): C 76.55, H 8.57, N 14.88; found: C 76.43, H 8.55, N 14.81.

4-Bromo-3-(2-dimethylaminoethyl)-1*H*-indole (11b): Amine **1b** (0.54 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of 1,2-dibromoethane (0.47 g, 2.4 mmol), followed by *N*,*N*-dimetylmethyleneammonium iodide(0.41 g, 2.2 mmol) and workup as described above yielded a residue. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the residue and [$NiCl_2$(dppp)] (0.004 g, 0.08 mmol) in toluene (6 mL). Workup as described above yielded **11b** (0.19 g, 36%) as a white solid. M.p. 114–116 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=8.8$ (brs, 1H), 7.3–7.2 (m, 2H), 7.0 (s, 1H), 6.95 (t, $J=8.0$Hz, 1H), 3.2–3.15 (m, 2H), 2.75–2.65 (m, 2H), 2.4 (s, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=137.6$, 125.4, 123.8, 123.6, 122.5, 114.8, 114.1, 110.5, 61.7, 45.3, 24.3; MS (70 eV, EI): m/z (%): 187 (9) $[M-Br]^+$, 58 (100); elemental analysis calcd (%) for $C_{12}H_{15}BrN_2$ (267.2): C 53.95, H 5.66, N 10.49; found: C 54.06, H 5.51, N 10.38.

1-Allyl-3-(2-dimethylaminoethyl)-5-methoxy-1*H*-indole (16): Amine **15** (0.63 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of water (0.05 mL, 3 mmol), followed by *N*,*N*-dimetylmethyleneammonium iodide(0.41 g, 2.2 mmol) and workup as above yielded **16** (0.28 g, 55%) as a brown oil. $R_f=0.2$ (ethyl acetate/diethylamine 50:1); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta=7.2$ (d, $J=8.6$ Hz, 1H), 7.05 (d, $J=2.1$ Hz, 1H), 6.9 (s, 1H), 6.85 (dd, $J=8.6$, 2.1 Hz, 1H), 6.1–5.9 (m, 1H), 5.25–5.0 (m, 2H), 4.6 (d, $J=5.4$ Hz, 2H), 3.9 (s, 3H), 3.0–2.85 (m, 2H), 2.65–2.55 (m, 2H), 2.35 (s, 6H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=153.6$, 133.7, 131.7, 128.3, 125.8, 117.0, 112.7, 111.6, 110.3, 100.8, 60.4, 55.9, 48.8, 45.5, 23.8; MS (70 eV, EI): m/z (%): 258 (20) $[M]^+$, 58 (100); elemental analysis calcd (%) for $C_{16}H_{22}N_2O$ (258.4): C 74.38, H 8.58, N 10.84; found: C 74.19, H 8.42, N 10.68.

General procedure for the preparation of carbazoles 19a–b: A solution of the starting amine **17** (0.57 g, 2 mmol) in THF (15 mL) was treated with 3.5 equiv *t*BuLi (7 mmol) at −110 °C. The reaction mixture was stirred for 15 min at this temperature and the cooling bath was then removed to allow the reaction to warm up to room temperature. The reaction mixture was recooled to −78 °C, 1,2-dibromoethane or ethyl chloroformate (3 mmol) was added, and the mixture was stirred for 3 h at room temperature. The mixture was hydrolyzed with water and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. A solution of the residue and *p*-toluenesulfonic acid (0.27 g, 1.6 mmol) in dry toluene (25 mL) was heated at reflux for 2 h, then cooled, washed successively with 1 M NaOH, water, and brine. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexane/ethyl acetate) to afford products **19a–b**.

5-Bromo-1,2,3,4-tetrahydro-9-methyl-9*H*-carbazole (19a): Amine **17** (0.57 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). 1,2-Dibromoethane (0.56 g, 3 mmol) was added and the mixture was treated as described above. *p*-Toluenesulfonic acid (0.25 g, 1.6 mmol) was added to a solution of the resultant residue in dry toluene (25 mL), heated at reflux for 2 h. Workup as described above gave **19a** (0.31 g, 59%) as a white solid. M.p. 91–93 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.2$ (d, $J=7.0$ Hz, 1H), 7.15 (d, $J=8.0$ Hz, 1H), 7.0 (dd, $J=8.0$, 7.0 Hz, 1H), 3.55 (s, 3H), 3.2 (t, $J=6.0$ Hz, 2H), 2.7 (t, $J=6.0$ Hz, 2H), 2.0–1.8 (m, 4H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=137.6$, 136.8, 125.7, 122.4, 120.9, 113.5, 109.8, 107.5, 28.9, 23.3, 23.0, 22.6, 22.2; MS (70 eV, EI): m/z(%): 265 (85) $[M+2]^+$, 263 (77) $[M]^+$, 237 (100), 235 (80); elemental analysis calcd (%) for $C_{13}H_{14}BrN$ (264.2): C 59.11, H 5.34, N 5.30; found: C 58.93, H 5.42, N 5.21.

Ethyl 1,2,3,4-tetrahydro-9-methyl-9*H*-carbazole-5-carboxylate (19b): Amine **17** (0.57 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Ethyl chloroformate (0.32 g, 3 mmol) was added and the mixture was treated as described above. *p*-Toluenesulfonic acid (0.25 g, 1.6 mmol) was added to a solution of the resultant residue in dry toluene (25 mL) and then heated at reflux for 2 h. Workup as described above gave **19b** (0.33 g, 65%) as a white solid. M.p. 116–118 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.6$ (d, $J=6.6$ Hz, 1H), 7.4 (d, $J=7.4$ Hz, 1H), 7.1 (dd, $J=7.4$, 6.6 Hz, 1H), 4.4 (q, $J=7.2$ Hz, 2H), 3.6 (s, 3H), 2.9 (t, $J=6.0$ Hz, 2H), 2.75 (t, $J=6.0$ Hz, 2H), 2.0–1.9 (m, 2H), 1.85–1.75 (m, 2H), 1.4 (t, $J=7.2$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=168.5$, 138.3, 137.6, 125.0, 122.8, 121.7, 119.1, 112.2, 109.4, 60.5, 28.9, 24.3, 23.7, 22.6, 22.5, 14.3; MS (70 eV, EI): m/z(%): 257 (98) $[M]^+$, 228 (100); elemental analysis calcd (%) for $C_{16}H_{19}NO_2$ (257.3): C 74.68, H 7.44, N 5.44; found: C 74.72, H 7.29, N 5.32.

General procedure for the preparation of carbazoles 20a–b: A solution of the starting amine **17** (2 mmol) in THF (15 mL) was treated with 3.5 equiv *t*BuLi (7 mmol) at −110 °C. The reaction was stirred for 15 min at this temperature and the cooling bath was then removed to allow the reaction mixture to warm up to room temperature. The reaction mixture was cooled to −78 °C and diphenyl disulfide or water (3 mmol) was added, and the reaction mixture was stirred for 3 h at room temperature. *N*,*N*-Dimetylmethyleneammonium iodide or diethyl ketomalonate (2.2 mmol) was then added and the reaction mixture was heated at reflux for 3 h (monitored by TLC). The mixture was hydrolyzed with water and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum and the residue was purified by flash column chromatography using hexane/ethyl acetate or ethyl acetate/diethylamine, and subsequently recrystallized to afford products **20a–b**.

4-(*N*,*N*-Dimethylaminomethyl)-1,2,3,4-tetrahydro-9-methyl-5-phenylthio-9*H*-carbazole (20a): Amine **17** (0.57 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of diphenyl disulfide (0.65 g, 3 mmol), followed by *N*,*N*-dimetylmethyleneammonium iodide(0.41 g, 2.2 mmol) and workup as described above yielded **20a** (0.41 g, 58%) as a yellow solid. M.p. 87–89 °C (hexane/$CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta=7.3$–7.0 (m, 8H), 3.65–3.55 (m, 2H), 3.6 (s, 3H), 2.85–2.4 (m, 4H), 2.3 (s, 6H), 2.0–1.9 (m, 2H), 1.55–1.45 (m, 1H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=139.3$, 137.4, 137.3, 128.8, 127.6, 127.3, 126.7, 125.1,

122.3, 120.8, 112.3, 109.0, 62.9, 45.4, 29.6, 29.1, 24.0, 22.2, 16.9; MS (70 eV, EI): m/z(%): 351 (2) $[M]^+$, 292 (100); elemental analysis calcd (%) for $C_{22}H_{26}N_2S$ (350.5): C 75.38, H 7.48, N 7.99; found: C 75.13, H 7.55, N 8.05.

Diethyl 2-hydroxy-2-(1,2,3,4-tetrahydro-9-methyl-9*H*-carbazol-4-yl)propanedioate (20b): Amine **17** (0.57 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of water (0.05 mL, 3 mmol), followed by diethyl ketomalonate (0.38 g, 2.2 mmol) and workup as described above yielded **20b** (0.40 g, 55%) as a white solid. M.p. 149–151 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.5 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 7.4 Hz, 1H), 7.1 (dd, J = 8.0, 7.4 Hz, 1H), 7.0 (t, J = 8.0 Hz, 1H), 4.4 (q, J = 7.0 Hz, 2H), 4.30–4.15 (m, 3H), 3.6 (s, 3H), 3.45 (s, 1H), 2.9–2.8 (m, 1H), 2.7–2.6 (m, 1H), 2.55–2.4 (m, 1H), 2.05–1.95 (m, 1H), 1.9–1.75 (m, 2H), 1.4 (t, J = 7.0 Hz, 3H), 1.2 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 170.5, 170.1, 139.0, 136.7, 126.3, 120.5, 118.6, 118.5, 108.5, 105.1, 83.1, 62.6, 62.4, 37.7, 29.0, 26.4, 21.4, 19.0, 14.0, 13.7; MS (70 eV, EI): m/z(%): 359 (1) $[M]^+$, 184 (100); elemental analysis calcd (%) for $C_{20}H_{25}NO_5$ (359.4): C 66.83, H 7.01, N 3.90; found: C 66.69, H 6.87, N 3.94.

General procedure for the preparation of 5-alkyl-1-functionalized-5,6-dihydrophenanthridines (26 and 27): A solution of the starting amine **25a** or **25b** (2 mmol) in THF (15 mL) was treated with 3.5 equiv *t*BuLi (7 mmol) at −110 °C. The reaction mixture was stirred for 15 min at this temperature. The cooling bath was then removed allowing the reaction to warm up to room temperature. The reaction mixture was then re-cooled to −78 °C, the electrophile (3 mmol) was added, and the mixture was stirred for 3 h at room temperature. The mixture was hydrolyzed with water and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by flash column chromatography (hexane/ethyl acetate) to afford products **26**–**27**.

5,6-Dihydro-5-methylphenanthridine (26a): Amine **25a** (0.59 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of H_2O (excess) and workup as described above yielded **26a** (0.32 g, 81%) as a yellow solid. M.p. 80–82 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.8 (d, J = 6.2 Hz, 1H), 7.45–7.15 (m, 5H), 6.95 (t, J = 7.6 Hz, 1H), 6.8 (d, J = 7.9 Hz, 1H), 4.2 (s, 2H), 3.0 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 147.2, 133.1, 132.1, 129.0, 127.6, 126.9, 125.6, 123.5, 123.3, 122.4, 118.5, 112.3, 55.0, 38.5; MS (70 eV, EI): m/z(%): 195 (62) $[M]^+$, 194 (100); elemental analysis calcd (%) for $C_{14}H_{13}N$ (195.3): C 86.12, H 6.71, N 7.17; found: C 86.01, H 6.90, N 7.03.

1-Bromo-5,6-dihydro-5-methylphenanthridine (26b): Amine **25a** (0.59 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of 1,2-dibromoethane (0.56 g, 3 mmol) and workup as described above yielded **26b** (0.37 g, 68%) as a yellow solid. M.p. 82–84 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.6 (d, J = 8.4 Hz, 1H), 7.4 (t, J = 7.6 Hz, 1H), 7.3 (t, J = 7.6 Hz, 1H), 7.3–7.2 (m, 2H), 7.1 (t, J = 8.2 Hz, 1H), 6.8 (d, J = 8.0 Hz, 1H), 4.0 (s, 2H), 3.0 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 150.4, 135.5, 130.9, 128.9, 127.2, 126.3, 125.0, 123.5, 120.3, 111.7, 55.3, 39.0; MS (70 eV, EI): m/z(%): 275 (50) $[M+2]^+$, 274 (100), 273 (50) $[M]^+$, 272 (100); elemental analysis calcd (%) for $C_{14}H_{12}BrN$ (274.2): C 61.33, H 4.41, N 5.11; found: C 61.50, H 4.29, N 5.14.

5,6-Dihydro-5-methyl-1-phenylthiophenanthridine (26c): Amine **25a** (0.59 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of diphenyl disulfide (0.66 g, 3 mmol) and workup as described above yielded **26c** (0.485 g, 80%) as a yellow solid. M.p. 145–147 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.3 (d, J = 8.0 Hz, 1H), 7.4–7.2 (m, 8H), 7.1 (t, J = 8.2 Hz, 1H), 6.8 (d, J = 8.0 Hz, 1H), 6.7 (d, J = 8.4 Hz, 1H), 4.0 (s, 2H), 3.0 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 149.5, 136.6, 135.5, 133.0, 130.8, 128.9, 128.2, 127.5, 126.9, 126.6, 126.4, 125.2, 124.9, 123.9, 111.2, 55.3, 39.0; MS (70 eV, EI): m/z(%): 303 (66) $[M]^+$, 302 (100); elemental analysis calcd (%) for $C_{20}H_{17}NS$ (303.4): C 79.17, H 5.65, N 4.62; found: C 78.98, H 5.71, N 4.51.

Ethyl 5,6-dihydro-5-methyl-1-phenanthridinecarboxylate (26d): Amine **25a** (0.59 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of ethyl chloroformate (0.32 g, 3 mmol) and workup as described above yielded **26d** (0.42 g, 78%) as a green oil. R_f = 0.2 (hexane/ethyl acetate 20:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.4–7.2 (m, 5H), 7.1 (d, J = 7.2 Hz, 1H), 6.8 (d, J = 8.4 Hz, 1H), 4.3 (q, J = 7.2 Hz, 2H), 4.1 (s, 2H), 2.9 (s, 3H), 1.2 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 170.8, 148.4, 134.3, 130.5, 128.1, 127.0, 126.6, 126.3, 125.1, 122.4, 119.5, 114.6, 61.1, 54.8, 38.6, 13.7; MS (70 eV, EI): m/z(%): 267 (67) $[M]^+$, 266 (100); elemental analysis calcd (%) for $C_{17}H_{17}NO_2$ (267.3): C 76.38, H 6.41, N 5.24; found: C 76.51, H 6.25, N 5.21.

5,6-Dihydro-5-methyl-1-tributylstannylphenanthridine (26e): Amine **25a** (0.59 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of tributyltin chloride (0.96 g, 3 mmol) and workup as above yielded **26e** (0.74 g, 76%) as a yellow oil. R_f = 0.35 (hexane/ethyl acetate 25:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.6 (d, J = 7.7 Hz, 1H), 7.5–7.2 (m, 5H), 6.9 (d, J = 8.0 Hz, 1H), 4.1 (s, 2H), 3.0 (s, 3H), 1.7–1.5 (m, 6H), 1.4–1.3 (m, 6H), 1.1–1.0 (m, 6H), 0.9 (t, J = 7.3 Hz, 9H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 148.5, 139.1, 135.3, 135.0, 131.7, 128.6, 128.0, 127.0, 126.6, 125.0, 124.8, 112.5, 55.4, 38.8, 28.9, 27.3, 13.6, 12.1; MS (70 eV, EI): m/z(%): 485 (4) $[M]^+$, 312 (100); elemental analysis calcd (%) for $C_{26}H_{39}NSn$ (484.3): C 64.48, H 8.12, N 2.89; found: C 64.27, H 8.17, N 2.77.

5-Allyl-5,6-dihydrophenanthridine (27a): Amine **25b** (0.64 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of H_2O (excess) and workup as described above yielded **27a** (0.31 g, 71%) as a colorless oil. R_f = 0.6 (hexane/ethyl acetate 25:1); ^{1}H NMR ($CDCl_3$, 80 MHz): δ = 7.8–6.8 (m, 8H), 6.3–5.8 (m, 1H), 5.5–5.2 (m, 2H), 4.3 (s, 2H), 3.9 (dt, J = 5.4, 1.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 20 MHz): δ = 145.9, 133.2, 132.9, 132.1, 128.9, 127.5, 126.9, 125.5, 123.6, 123.2, 122.3, 118.2, 117.7, 112.9, 53.3, 52.0; MS (70 eV, EI): m/z(%): 221 (77) $[M]^+$, 220 (100); elemental analysis calcd (%) for $C_{16}H_{15}N$ (221.3): C 86.84, H 6.83, N 6.33; found: C 86.62, H 6.85, N 6.19.

Ethyl 5-allyl-5,6-dihydro-1-phenanthridinecarboxylate (27b): Amine **25b** (0.64 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Addition of ethyl chloroformate (0.27 g, 2.5 mmol) and workup as described above yielded **27b** (0.43 g, 73%) as a yellow oil. R_f = 0.35 (hexane/ethyl acetate 20:1); ^{1}H NMR ($CDCl_3$, 80 MHz): δ = 7.3–6.6 (m, 7H), 6.0–5.5 (m, 1H), 5.4–5.0 (m, 2H), 4.2 (q, J = 7.0 Hz, 2H), 4.05 (s, 2H), 3.85 (dt, J = 5.3, 1.3 Hz, 2H), 1.1 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 20 MHz): δ = 170.8, 147.3, 134.2, 132.9, 130.9, 128.0, 127.0, 126.6, 125.0, 122.7, 119.6, 117.7, 115.5, 61.0, 53.8, 52.2, 13.7; MS (70 eV, EI): m/z(%): 293 (63) $[M]^+$, 292 (100); elemental analysis calcd (%) for $C_{19}H_{19}NO_2$ (293.4): C 77.79, H 6.53, N 4.77; found: C 77.82, H 6.45, N 4.58.

General procedure for the preparation of 1-functionalized-5,6-dihydrophenanthridines (28): A solution of the starting amine **25b** (0.64 g, 2 mmol) in THF (15 mL) was treated with 3.5 equiv *t*BuLi (7 mmol) at −110 °C. The reaction was stirred for 15 min at this temperature. The cooling bath was then removed and the reaction mixture was allowed to warm up to room temperature. The reaction mixture was re-cooled to −78 °C, the electrophile (3 mmol) was added, and the mixture was stirred for 3 h at room temperature. The mixture was hydrolyzed with water and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The residue and $[NiCl_2(dppp)]$ (0.04 g, 0.08 mmol) were dissolved in toluene (6 mL). DIBAL-H (3 mmol, 1.5 equiv) was added to the reaction mixture at 0 °C and the temperature was then raised to 20 °C. After stirring at the same temperature for 2 h, the mixture was treated with 0.5 M NaOH (2 mL) and Et_2O (9 mL) for 1 h and then dried directly over $MgSO_4$. After evaporation of the solvent, the residue was purified by flash column chromatography to afford products **28**.

5,6-Dihydrophenanthridine (28a): Amine **25b** (0.64 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Water (excess) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the resultant residue and $[NiCl_2(dppp)]$ (0.04 g, 0.08 mmol) in toluene (6 mL). The subsequent treatment with NaOH (2 mL, 0.5 M solution in water, 1 mmol), Et_2O (9 mL), and workup as described above yielded **28a** (0.25 g, 70%) as a white solid. M.p. 102–104 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.8–7.7 (m, 2H), 7.35 (t, J = 6.4 Hz, 1H), 7.25 (t, J = 6.7 Hz, 1H), 7.2–7.1 (m, 2H), 6.9 (t, J = 7.4 Hz, 1H), 6.7 (d, J = 8.1 Hz, 1H), 4.4 (s, 2H), 3.9 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 145.6, 132.6, 131.9, 128.7, 127.5, 127.0, 125.9, 123.4, 122.3, 121.8, 119.1, 115.0, 46.2; MS (70 eV, EI): m/z(%): 181 (38) $[M]^+$, 180 (100); elemental analysis calcd (%) for $C_{13}H_{11}N$ (181.3): C 86.15, H 6.12, N 7.73; found: C 85.98, H 6.10, N 7.59.

5,6-Dihydro-1-hydroxymethylphenanthridine (28b): Amine **25b** (0.64 g, 2 mmol) was treated with *t*BuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Ethyl chloroformate (0.32 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the resultant residue and

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[$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL) and subsequent treatment with NaOH (2 mL, 0.5 M solution in water, 1 mmol), Et_2O (9 mL), and workup as described above yielded **28b** (0.29 g, 69 %) as a white solid. M.p. 108–110 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.98 (d, J = 7.6 Hz, 1 H), 7.35 (dt, J = 7.6, 1.6 Hz, 1 H), 7.25 (dt, J = 7.2, 1.6 Hz, 1 H), 7.2 (d, J = 7.6 Hz, 1 H), 7.15 (t, J = 7.6 Hz, 1 H), 7.0 (dd, J = 7.6, 1.2 Hz, 1 H), 6.7 (dd, J = 7.6, 1.2 Hz, 1 H), 4.9 (s, 2 H), 4.15 (s, 2 H), 3.3 (br s, 2 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 147.4, 137.6, 135.4, 131.3, 127.9, 127.2, 126.7, 125.5, 122.7, 121.5, 115.0, 63.6, 46.5; MS (70 eV, EI): m/z (%): 211 (48) $[M]^+$, 210 (100); elemental analysis calcd (%) for $C_{14}H_{13}NO$ (211.3): C 79.59, H 6.20, N 6.63; found: C 79.65, H 6.17, N 6.61.

1-Bromo-5,6-dihydrophenanthridine (28c): Amine **25b** (0.64 g, 2 mmol) was treated with tBuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). 1,2-Dibromoethane (0.56 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the resultant residue and [$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL). Subsequent treatment with NaOH (2 mL, 0.5 M solution in water, 1 mmol) and Et_2O (9 mL), and workup as described above yielded **28c** (0.38 g, 73 %) as a yellow solid. M.p. 83–85 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.55 (d, J = 6.8 Hz, 1 H), 7.4 (dt, J = 8.0, 1.6 Hz, 1 H), 7.3 (dt, J = 7.6, 1.2 Hz, 1 H), 7.2 (d, J = 7.6 Hz, 2 H), 6.9 (t, J = 8.0 Hz, 1 H), 6.65 (d, J = 8.0 Hz, 1 H), 4.1 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 149.2, 135.0, 130.8, 128.6, 127.2, 126.7, 126.3, 125.5, 125.3, 122.2, 120.2, 114.5, 46.3; MS (70 eV, EI): m/z(%): 261 (50) $[M+2]^+$, 259 (50) $[M]^+$, 260 (100), 258 (100); elemental analysis calcd (%) for $C_{13}H_{10}BrN$ (260.1): C 60.02, H 3.87, N 5.38; found: C 60.18, H 3.70, N 5.39.

5,6-Dihydro-1-tributylstannylphenanthridine (28d): Amine **25b** (0.64 g, 2 mmol) was treated with tBuLi (4.7 mL, 1.5 M solution in pentane, 7 mmol). Tributyltin chloride (0.96 g, 3 mmol) was added and the mixture was treated as described above. DIBAL-H (2.0 mL, 1.5 M solution in toluene, 3 mmol) was added to a solution of the resultant residue and [$NiCl_2$(dppp)] (0.04 g, 0.08 mmol) in toluene (6 mL), and the subsequent treatment with NaOH (2 mL, 0.5 M solution in water, 1 mmol), Et_2O (9 mL), and workup as described above yielded **28d** (0.67 g, 71 %) as a colorless oil. R_f = 0.18 (ethyl acetate/hexane 20:1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.55 (d, J = 7.2 Hz, 1 H), 7.3 (dt, J = 7.6, 1.6 Hz, 1 H), 7.25 (dt, J = 7.6, 1.6 Hz, 1 H), 7.2 (d, J = 7.6 Hz, 1 H), 7.15 (t, J = 7.4 Hz, 1 H), 7.05 (dd, J = 7.2, 1.6 Hz, 1 H), 6.7 (dd, J = 7.6, 1.6 Hz, 1 H), 4.2 (s, 2 H), 4.0 (br s, 1 H), 1.5–1.4 (m, 6 H), 1.35–1.25 (m, 6 H), 1.1–1.0 (m, 6 H), 0.85 (t, J = 7.1 Hz, 9 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 147.0, 139.0, 135.0, 134.9, 130.1, 129.3, 127.8, 126.9, 126.6, 125.2, 124.6, 115.3, 46.5, 28.9, 27.2, 13.6, 11.9; MS (70 eV, EI): m/z(%): 471 (2) $[M]^+$, 298 (100); elemental analysis calcd (%) for $C_{25}H_{37}NSn$ (470.3): C 63.85, H 7.93, N 2.98; found: C 63.78, H 8.02, N 2.90.

General procedure for the preparation of 6*H*-dibenzo[*b*,*d*]pyrans 29, 33, and 6*H*-dibenzo[*b*,*d*]thiopyrans (30): A solution of the starting ether **25c** or **32**, or thioether **25d** (2 mmol) in THF (15 mL) was treated with tBuLi (6.6 mmol, 3.3 equiv) at −110 °C. The reaction mixture was stirred for 15 min at this temperature. The cooling bath was then removed to allow the reaction to warm up to room temperature. The reaction mixture was re-cooled to −78 °C, the electrophile (2.5 mmol) was added, and the mixture was allowed to stir for 3 h at room temperature. The mixture was hydrolyzed with water and extracted with ethyl acetate (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was purified by flash column chromatography to afford products **29**, **30**, and **33**.

1-Bromo-6*H*-dibenzo[*b*,*d*]pyran (29a): Ether **25c** (0.56 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of 1,2-dibromoethane (0.47 g, 2.5 mmol) and workup as described above yielded **29a** (0.32 g, 61 %) as a white solid. M.p. 54–56 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.55 (d, J = 7.6 Hz, 1 H), 7.4 (t, J = 7.6 Hz, 1 H), 7.4–7.3 (m, 2 H), 7.2 (d, J = 6.8 Hz, 1 H), 7.1–7.0 (m, 2 H), 4.95 (s, 2 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 157.3, 133.2, 129.3, 129.1, 128.6, 127.9, 127.6, 126.3, 124.7, 123.7, 119.7, 116.8, 69.2; MS (70 eV, EI): m/z(%): 262 (71) $[M+2]^+$, 261 (100), 260 (67) $[M]^+$, 259 (87); elemental analysis calcd (%) for $C_{13}H_9BrO$ (261.1): C 59.80, H 3.47; found: C 60.02, H 3.41.

Ethyl 6*H*-dibenzo[*b*,*d*]pyran-1-carboxylate (29b): Ether **25c** (0.56 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of ethyl chloroformate (0.27 g, 2.5 mmol) and workup as described above yielded **29b** (0.35 g, 68 %) as a yellow solid. M.p. 63–65 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.4–7.2 (m, 6 H), 7.1 (d, J = 7.8 Hz, 1 H), 5.1 (s, 2 H), 4.3 (q, J = 7.2 Hz, 2 H), 1.3 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 169.8, 156.1, 132.3, 130.4, 128.8, 127.8, 126.2, 124.8, 123.6, 122.5, 120.0, 69.0, 61.5, 14.0; MS (70 eV, EI): m/z(%): 254 (100) $[M]^+$; elemental analysis calcd (%) for $C_{16}H_{14}O_3$ (254.3): C 75.57, H 5.55; found: C 75.64, H 5.61.

1-(1-Hydroxy-1-phenylmethyl)-6*H*-dibenzo[*b*,*d*]pyran (29c): Ether **25c** (0.56 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of benzaldehyde (0.26 g, 2.5 mmol) and workup as described above yielded **29c** (0.32 g, 56 %) as a yellow solid. M.p. 47–49 °C (hexane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.85–7.75 (m, 1 H), 7.4–7.0 (m, 11 H), 6.4 (s, 1 H), 5.0 (s, 2 H), 2.8 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 155.9, 143.6, 140.5, 134.0, 129.3, 128.9, 128.2, 127.3, 127.2, 127.1, 126.8, 124.9, 123.7, 123.3, 116.4, 72.2, 68.9; MS (70 eV, EI): m/z(%): 288 (100) $[M]^+$; elemental analysis calcd (%) for $C_{20}H_{16}O_2$ (288.3): C 83.31, H 5.59; found: C 83.18, H 5.64.

1-Tributylstannyl-6*H*-dibenzo[*b*,*d*]pyran (29d): Ether **25c** (0.56 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of tributyltin chloride (0.83 g, 3 mmol) and workup as described above yielded **29d** (0.565 g, 60 %) as a colorless oil. R_f = 0.15 (hexane/ethyl acetate 60:1); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.7–7.0 (m, 7 H), 5.0 (s, 2 H), 1.7–0.9 (m, 27 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 155.9, 139.1, 133.2, 132.9, 131.8, 130.7, 128.7, 127.8, 127.1, 124.5, 124.1, 117.1, 68.8, 28.9, 27.2, 13.6, 11.9; MS (70 eV, EI): m/z(%): 415 $[M-C_4H_9]^+$ (84), 301 (100); elemental analysis calcd (%) for $C_{25}H_{36}OSn$ (471.3): C 63.72, H 7.70; found: C 63.58, H 7.57.

6*H*-Dibenzo[*b*,*d*]thiopyran (30a): Thioether **25d** (0.59 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of water (excess) and workup as described above yielded **30a** (0.23 g, 59 %) as a white solid. M.p. 70–72 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.8 (dd, J = 7.0, 2.2 Hz, 1 H), 7.7 (d, J = 7.2 Hz, 1 H), 7.5–7.2 (m, 6 H), 3.85 (s, 2 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 134.6, 134.4, 134.3, 133.6, 128.4, 127.8, 127.6, 126.9, 126.4, 125.9, 125.7, 31.7; MS (70 eV, EI): m/z(%): 198 (65) $[M]^+$, 197 (100); elemental analysis calcd (%) for $C_{13}H_{10}S$ (198.3): C 78.74, H 5.08; found: C 78.89, H 4.97.

Ethyl 6*H*-dibenzo[*b*,*d*]thiopyran-1-carboxylate (30b): Thioether **25d** (0.59 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of ethyl chloroformate (0.27 g, 2.5 mmol) and workup as described above yielded **30b** (0.27 g, 50 %) as a yellow oil. R_f = 0.18 (ethyl acetate/diethylamine 50:1); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.6 (d, J = 7.8 Hz, 1 H), 7.3–7.2 (m, 6 H), 4.2 (q, J = 7.2 Hz, 2 H), 3.8 (s, 2 H), 1.1 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 170.0, 138.0, 134.7, 134.2, 133.5, 132.1, 130.4, 129.1, 128.1, 127.9, 127.0, 126.8, 126.3, 61.3, 32.3, 13.7; MS (70 eV, EI): m/z(%): 270 (100) $[M]^+$; elemental analysis calcd (%) for $C_{16}H_{14}O_2S$ (270.4): C 71.08, H 5.22; found: C 70.92, H 5.16.

1-[1-Hydroxy-1-(4-methylphenyl)methyl]-6*H*-dibenzo[*b*,*d*]thiopyran (30c): Thioether **25d** (0.59 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of 4-methylbenzaldehyde (0.3 g, 2.5 mmol) and workup as described above yielded **30c** (0.36 g, 57 %) as a white solid. M.p. 84–86 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.6–7.1 (m, 11 H), 6.3 (s, 1 H), 3.7 (s, 2 H), 2.55 (br s, 1 H), 2.4 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 141.5, 141.2, 137.1, 136.9, 136.7, 134.6, 133.1, 129.8, 129.0, 127.8, 127.6, 127.2, 127.0, 126.6, 126.2, 72.9, 32.9, 21.0; MS (70 eV, EI): m/z(%): 318 (6) $[M]^+$, 316 (100); elemental analysis calcd (%) for $C_{21}H_{18}OS$ (318.4): C 79.21, H 5.70; found: C 79.33, H 5.84.

2-Methoxy-6*H*-dibenzo[*b*,*d*]pyran (33a): Ether **32** (0.65 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of water (excess) and workup as described above yielded **33a** (0.34 g, 81 %) as a colorless oil. R_f = 0.2 (ethyl acetate/diethylamine 40:1); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.7 (d, J = 7.2 Hz, 1 H), 7.5–7.1 (m, 4 H), 6.95 (d, J = 8.8 Hz, 1 H), 6.8 (dd, J = 8.8, 2.8 Hz, 1 H), 5.05 (s, 2 H), 3.85 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): δ = 154.8, 148.8, 131.8, 130.2, 128.3, 127.8, 124.7, 123.6, 122.0, 117.9, 115.0, 108.3, 68.6, 55.8; MS (70 eV, EI): m/z (%): 212 (100) $[M]^+$; elemental analysis calcd (%) for $C_{14}H_{12}O_2$ (212.2): C 79.22, H 5.70; found: C 78.99, H 5.73.

Ethyl 2-methoxy-6*H*-dibenzo[*b*,*d*]pyran-1-carboxylate (33b): Ether **32** (0.65 g, 2 mmol) was treated with tBuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of ethyl chloroformate (0.27 g, 2.5 mmol) and workup as described above yielded **33b** (0.43 g, 75 %) as a white solid. M.p. 71–73 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.65–7.55 (m, 1 H),

7.4–7.1 (m, 3H), 7.05 (d, $J=8.8$ Hz, 1H), 6.85 (d, $J=8.8$ Hz, 1H), 5.0 (s, 2H), 4.4 (q, $J=7.0$ Hz, 2H), 3.8 (s, 3H), 1.3 (t, $J=7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=168.3$, 151.8, 149.4, 133.2, 128.7, 128.1, 127.9, 124.8, 124.3, 121.6, 120.4, 118.8, 112.5, 68.8, 61.4, 56.5, 13.8; MS (70 eV, EI): m/z (%): 284 (100) $[M]^+$; elemental analysis calcd (%) for $C_{17}H_{16}O_4$ (284.3): C 71.82, H 5.67; found: C 71.85, H 5.58.

1-[1-Hydroxy-1-(4-methylphenyl)methyl]-2-methoxy-6*H*-dibenzo[*b*,*d*]pyran (33c): Ether **32** (0.65 g, 2 mmol) was treated with *t*BuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of 4-methylbenzaldehyde (0.3 g, 2.5 mmol) and workup as described above yielded **33c** (0.525 g, 79%) as a white solid. M.p. 98–100 °C (hexane); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta=$ 7.40–7.15 (m, 6H), 7.1 (d, $J=8.8$ Hz, 2H), 6.9 (d, $J=8.8$ Hz, 2H), 6.4 (d, $J=11.6$ Hz, 1H), 5.05 (d, $J=12.4$ Hz, 1H), 4.95 (d, $J=12.4$ Hz, 1H), 4.4 (d, $J=11.6$ Hz, 1H), 3.65 (s, 3H), 2.4 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=153.4$, 150.4, 141.1, 136.4, 134.3, 129.6, 128.8, 128.0, 127.4, 126.9, 126.4, 124.9, 124.6, 116.3, 112.7, 72.3, 69.2, 55.9, 21.0; MS (70 eV, EI): m/z(%): 332 (100) $[M]^+$; elemental analysis calcd (%) for $C_{22}H_{20}O_3$ (332.4): C 79.50, H 6.06; found: C 79.52, H 5.97.

2-Methoxy-1-phenylthio-6*H*-dibenzo[*b*,*d*]pyran (33d): Ether **32** (0.65 g, 2 mmol) was treated with *t*BuLi (4.4 mL, 1.5 M solution in pentane, 6.6 mmol). Addition of diphenyl disulfide (0.54 g, 2.5 mmol) and workup as above yielded **33d** (0.47 g, 73%) as a colorless oil. $R_f=0.18$ (ethyl acetate/diethylamine 20:1); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta=8.4-8.3$ (m, 1H), 7.4–7.1 (m, 9H), 6.9 (d, $J=8.8$ Hz, 1H), 5.0 (s, 2H), 3.75 (s, 3H); ^{13}C NMR ($CDCl_3$, 50.5 MHz): $\delta=156.2$, 150.7, 138.2, 133.7, 129.7, 128.6, 127.7, 127.6, 127.4, 126.0, 124.8, 124.4, 118.9, 116.8, 112.2, 69.2, 56.6; MS (70 eV, EI): m/z (%): 320 (100) $[M]^+$; elemental analysis calcd (%) for $C_{20}H_{16}O_2S$ (320.4): C 74.97, H 5.03; found: C 75.08, H 5.11.

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