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Benzannulation via the Reaction of Ynamides and Vinylketenes. Application to the Synthesis of Highly Substituted Indoles

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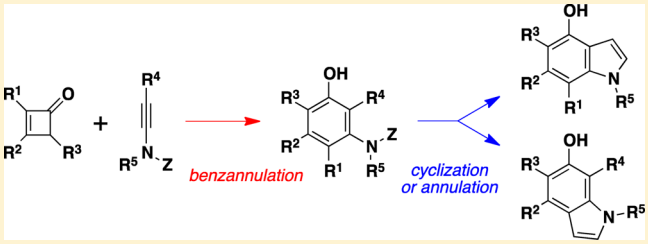
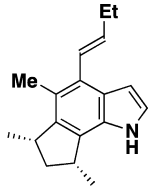
Supporting Information

ABSTRACT: A two-stage "tandem strategy" for the synthesis of indoles with a high level of substitution on the six-membered ring is described. Benzannulation based on the reaction of cyclobutenones with ynamides proceeds via a cascade of four pericyclic reactions to produce multiply substituted aniline derivatives in which the position ortho to the nitrogen can bear a wide range of functionalized substituents. In the second stage of the tandem strategy, highly substituted indoles are generated via acid-, base-, and palladium-catalyzed cyclization and annulation processes.



INTRODUCTION

The indole ring system is a key feature in the structure of numerous natural products, pharmaceutical agents, and commercially significant synthetic compounds.[1] Despite a century and a half of research, the efficient construction of indoles with certain substitution patterns remains a challenging problem.[2,3] While a number of effective strategies are available for the synthesis of indoles substituted on the five-membered ring, few methods provide regiocontrolled access to indoles bearing multiple substituents on the benzenoid ring.[4] Metalation and electrophilic substitution provide reliable vehicles for the introduction of substituents on the five-membered ring, but attempts to install substituents on the six-membered ring of indoles are often frustrated by problems of reactivity and regiochemical ambiguity. The efficient synthesis of multiply substituted indoles such as the natural products shown below thus continues to pose a formidable challenge for organic synthesis.



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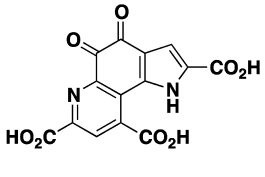
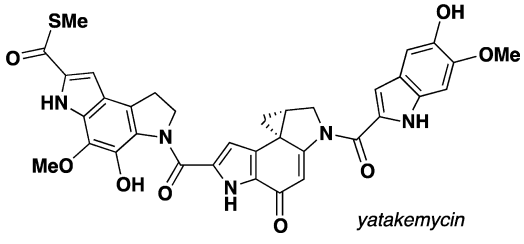


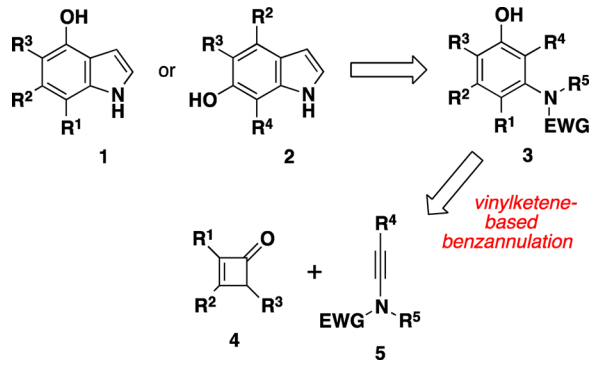
pyrroloquinoline quinone



yatakemycin

The majority of methods for the synthesis of indoles involve the elaboration of the five-membered ring from anilines, *o*-haloanilines, or other 2-substituted aniline derivatives. Recently we reported a versatile approach to the synthesis of highly substituted benzofused nitrogen heterocycles based on a tandem ynamide benzannulation ring-closing metathesis strategy.[5] This two-step sequence provides efficient access to highly substituted dihydroquinolines, benzazepines, and benzazocines, including a key intermediate in a formal total synthesis of (+)-FR900482. In this paper we now report the extension of this general strategy to the preparation of highly substituted indoles. As outlined in Scheme 1, benzannulation of suitably substituted ynamides with cyclobutenones furnishes multiply substituted anilines that are functionally equipped for cyclization and annulation reactions to form indoles in the second stage of this "tandem strategy". Herein we describe a

Scheme 1. Tandem Strategy for the Synthesis of Highly Substituted Indoles



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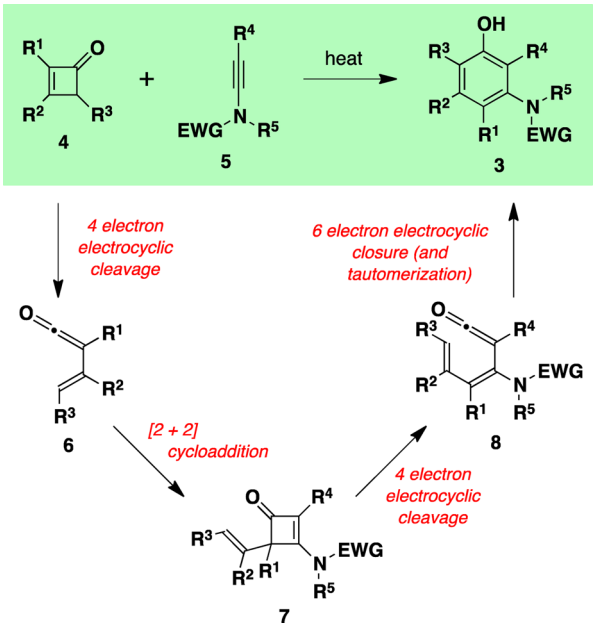
number of complementary tandem benzannulation/cyclization protocols that can be employed in this context for the synthesis of highly substituted indoles.

The vinylketene-based benzannulation strategy developed in our laboratory provides an efficient route to highly substituted benzenoid aromatic compounds[6−8] as demonstrated in its application to the total synthesis of a number of naturally occurring compounds.[9,10] Operationally the benzannulation involves a single synthetic step, but mechanistically it proceeds via a "cascade" of four consecutive pericyclic reactions. As outlined in Scheme 2, electrocyclic ring-opening of the

Scheme 2. Pericyclic Cascade Mechanism of the Vinylketene-Based Benzannulation

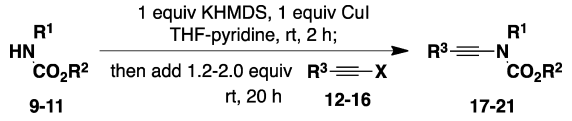


cyclobutenone annulation partner **4** triggers the cascade, generating a vinylketene, **6**, that is intercepted by the alkyne **5** in a [2 + 2] cycloaddition to afford the key 4-vinylcyclobutenone intermediate **7**. Under the reaction conditions, this intermediate then undergoes reversible 4-electron electrocyclic cleavage to generate dienylketene **8**, which rapidly cyclizes via 6−π electrocyclic closure to furnish the final aromatic product **3** following tautomerization. Note that while the two electrocyclic ring-opening events require activation by heat or light, the [2 + 2] cycloaddition and 6−π electrocyclic closure steps proceed at room temperature or below.

RESULTS AND DISCUSSION

Synthesis of Benzannulation Partners. Synthesis of the requisite benzannulation partners for these studies was conveniently accomplished using methods previously developed in our laboratory. Cyclobutenones are available in one to two steps via ketene−alkyne cycloadditions,[11] and the synthesis of ynamides[12] is achieved in good yield via alkynyl bromides[13] by using the copper-promoted *N*-alkynylation reaction pioneered in our laboratory[14] and that of Hsung.[15,16] Table 1 summarizes the application of our *N*-alkynylation protocol to the synthesis of the new carboalkoxy ynamide derivatives employed in the present study.

Table 1. Synthesis of Ynamides from Carbamates

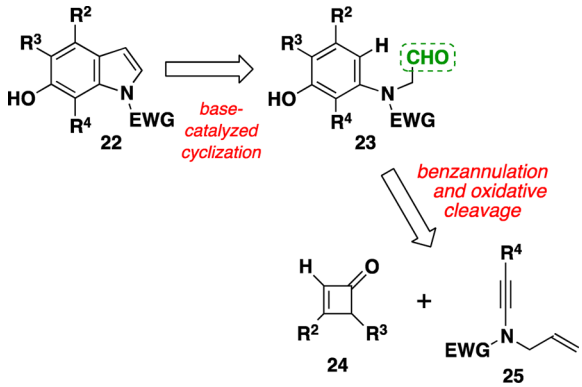


entry	carbamate	haloalkyne	ynamide	yield[a] (%)
1[b]	**9** (R^1 = allyl; R^2 = Me)	**12** (R^3 = Me; X = I)	**17**	55
2	**9**	**13** (R^3 = CH_2OSi-*t*-$BuMe_2$; X = Br)	**18**	55
3	**9**	**14** (R^3 = $(CH_2)_2OSi$-*t*-$BuMe_2$; X = Br)	**19**	66
4	**10** (R^1 = Me; R^2 = *t*-Bu)	**15** (R^3 = allyl; X = Br)	**20**	43
5	**11** (R^1 = Bn; R^2 = $(CH_2)_2SiMe_3$)	**16** (R^3 = $CH_2CH(OMe)_2$; X = Br)	**21**	57−69

[a]Isolated yield of products purified by column chromatography. [b]Reaction performed in pyridine−benzene−THF.

Synthesis of Indoles via *N*-Allyl Ynamides. Anilines substituted on nitrogen with a 2-oxo carbon chain (or its functional equivalent) can be converted to indoles by the action of Brønsted and Lewis acids.[17,18] This transformation proceeds via aromatic substitution followed by elimination and serves as a key step in the classic Bischler indole synthesis and its variants. Our first plan for the application of our tandem strategy to the synthesis of indoles called for a variant of this venerable process in which ring closure would be achieved via the *base-catalyzed* cyclization of an α-anilino aldehyde derivative of type **23** (Scheme 3). Benzannulation employing *N*-allyl

Scheme 3. Strategy for the Synthesis of Indoles via *N*-Allyl Ynamides



ynamides of type **25** followed by oxidative cleavage would provide access to the key cyclization substrates. Of particular interest to us was the possibility of exploiting the presence of the hydroxyl group in **23**, which we hoped would allow us to effect the key cyclization step under mild basic conditions in contrast to the strongly acidic conditions typically employed in the Bischler synthesis. The products of these cyclizations would be 6-hydroxyindoles, with the hydroxyl group serving as a potential handle for further synthetic elaboration via transition-metal-catalyzed coupling reactions of sulfonate derivatives.

The feasibility of this approach was investigated using readily available 3-butylcyclobutenone[11] as the vinylketene precursor. As expected, the optimal conditions for benzannulation with *N*-allyl ynamides involve a staged heating protocol as outlined in Table 2. This procedure minimizes [3,3]-sigmatropic rearrange-

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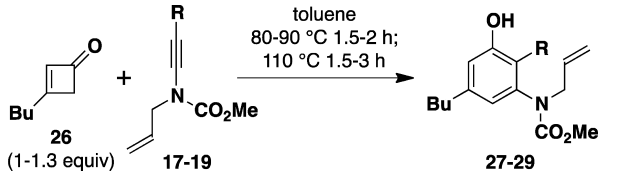
Table 2. Benzannulation with *N*-Allyl Ynamides



entry	R	ynamide	aniline	yield[a] (%)
1	Me	**17**	**27**	78
2	CH_2OSi-*t*-$BuMe_2$	**18**	**28**	85
3	$(CH_2)_2OSi$-*t*-$BuMe_2$	**19**	**29**	94

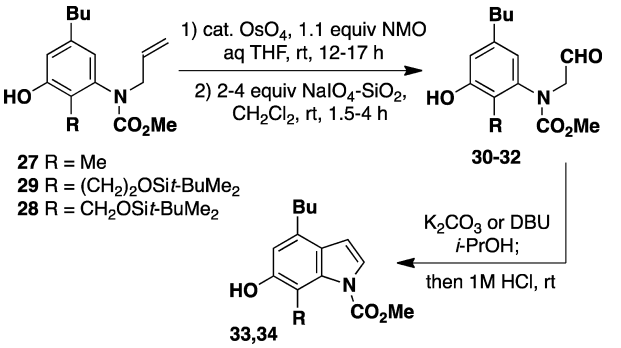
[a]Isolated yield of products purified by column chromatography.

ment of the 1,6-enyne moiety present in these ynamides which occurs at temperatures above 125 °C.[19] In our optimized benzannulation protocol, initial thermolysis is performed at 80−90 °C until all of the ynamide is consumed. This generally leads to a mixture of the desired benzannulation product and intermediate 4-vinylcyclobutenone (i.e., **7** in Scheme 2). Further heating at 110 °C converts the vinylcyclobutenone to the desired phenol product. As predicted, ketene [2 + 2] cycloaddition to these *N*-allyl ynamides occurs chemoselectively at the electron-rich ynamide π bond, and no products resulting from competitive reaction at the alkene double bond were detected in these benzannulations.

With benzannulation products **27**−**29** in hand, we next investigated conditions for the oxidative cleavage of the pendant alkene. Both ozonolysis and one-pot Lemieux−Johnson oxidation[20] afforded the desired aldehydes in modest yield accompanied by side products that were difficult to separate by chromatography. As shown in Table 3, however, dihydroxylation followed by treatment of the resultant crude diol with $NaIO_4$ on silica gel[21] furnished the desired aldehydes in excellent yield.

A systematic investigation of conditions for cyclization of aldehyde **30** revealed that the best results are obtained under the basic conditions described in Table 3. Initial exploratory

Table 3. Synthesis of Indoles 33 and 34



entry	alkene	aldehyde	yield[a] (%)	method[b]	indole	yield[a] (%)
1	**27**	**30**	82−84	A	**33**	71
2				B		74−82
3	**29**	**31**	91−98	A	**34**[c]	74
4				B		65

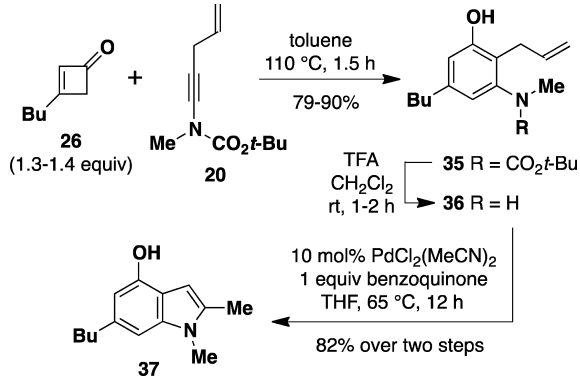
[a]Isolated yield of products purified by column chromatography. [b]Method A: K_2CO_3 (1.0 equiv), *i*-PrOH, 50−70 °C, 2−4 h. Method B: DBU (0.5 equiv), *i*-PrOH, 65−70 °C, 1.5−2 h. [c]R = $(CH_2)_2OH$ (cleavage of the silyl group occurs during the reaction).

experiments employing Lewis acids were not promising. Importantly, we observed that cyclizations are best conducted under relatively dilute conditions (0.1−0.2 M) to minimize side reactions involving condensation of the aldehydes with the electron-rich indole products. 2-Propanol proved superior to methanol as the solvent as some cleavage of the carbamate protecting group was observed in the latter solvent. Reaction with DBU and K_2CO_3 gave similar results; under these conditions a mixture of the desired indole and its secondary alcohol precursor is typically obtained. Complete dehydration to the indole is then achieved by addition of HCl to the reaction mixture after cooling to room temperature.

Although conversion of benzannulation product **29** to indole **34** took place smoothly under these conditions, cyclization of the aldehyde **32** derived from **28** to the desired indole proceeded in low and variable yield (0−30%). In this case we believe that the intermediate phenoxide undergoes facile elimination of silanolate to afford a highly reactive *o*-quinone methide species.

Synthesis of Indoles via *C*-Allyl Ynamides. Hegedus has shown that *o*-allylanilines undergo cyclization to form indoles upon exposure to Pd(II) catalysts in the presence of benzoquinone.[3,22] Scheme 4 illustrates the application of the

Scheme 4. Synthesis of Indole 37 via Benzannulation and Hegedus Cyclization



Hegedus cyclization as the second stage of our tandem benzannulation−cyclization strategy for the synthesis of indoles. Cleavage of the BOC group on nitrogen reveals the nucleophilic amino group, and exposure to the conditions developed by Hegedus results in cyclization via reaction of the Pd(II)-coordinated alkene with the amino rather than hydroxyl group. Note that the products of these cyclizations are 4-hydroxyindoles, in contrast to the 6-hydroxy derivatives generated by the *N*-allyl ynamide approach.

More conveniently, conversion of the BOC derivative **35** to indole **37** can be achieved in a one-pot operation as outlined in Scheme 5. In this case, Hegedus-type cyclization of **35** furnishes benzofuran **38** by cyclization via the phenolic hydroxyl group. Addition of concentrated HCl then leads directly to the desired indole, presumably via BOC cleavage, cleavage of the furan ring, and cyclization as previously described by Guiotto and coworkers.[23]

Synthesis of Indoles via Ynamide 21. The cyclization of amino aldehydes of type **40** (Scheme 6) constitutes a well-established route to indoles. Cyclizations of this type, for example, comprise a key step in the well-known Plieninger indole synthesis.[24] We anticipated that multiply substituted

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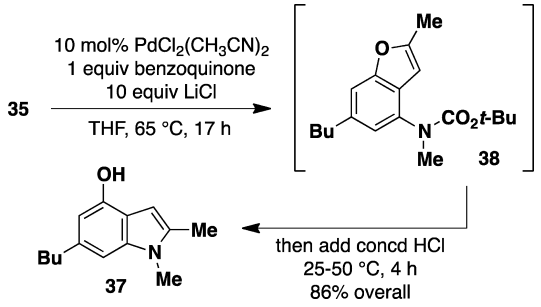
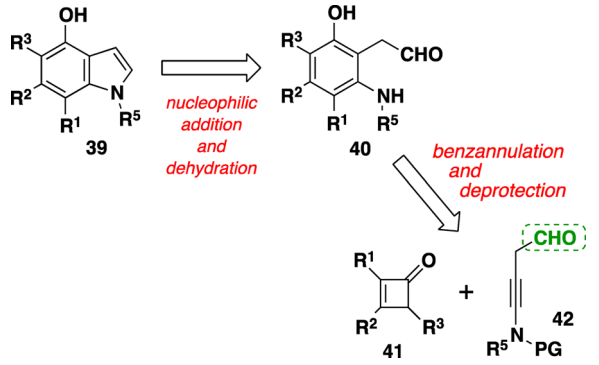
Scheme 5. Indole Synthesis via Hegedus Cyclization: An Alternative Route



Scheme 6. Strategy for the Synthesis of Indoles via Aminobutynal Derivatives

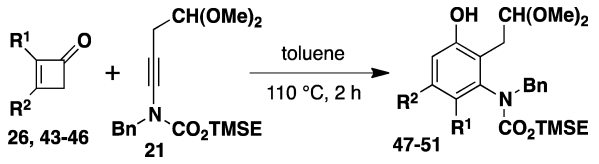


indoles of general structure **39** would be available via benzannulations based on alkynes of type **42** bearing a latent $-CH_2CHO$ substituent attached at C-2 of the ynamide.

We recognized that the realization of this strategy would require carefully planned choreography in the unveiling of the various reactive functional groups to ensure that cyclization via the amino group rather than the hydroxyl group would occur. With this consideration in mind, we focused our attention on benzannulations of ynamide **21** in which the aldehyde is masked as an acetal derivative. As shown in Table 4, we found that benzannulation with this ynamide and most cyclobutenones proceeds in good yield upon heating in toluene at reflux. As expected, benzannulation with the more highly substituted cyclobutenone **46** requires a higher temperature, a consequence of the slower [2 + 2] cycloaddition of the "ketoketene" intermediate involved in this case.[25]

A systematic investigation of conditions for conversion of benzannulation products **47**–**51** to the desired indoles led to the optimized one-pot protocol shown in Table 5. First,

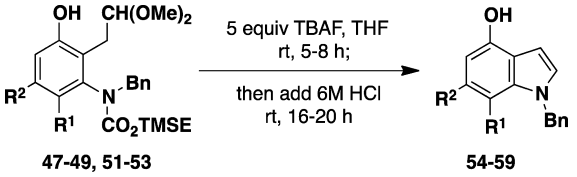
Table 4. Benzannulation with Ynamide 21



entry	R^1	R^2	cyclobutenone (equiv)	aniline	yield[a] (%)
1	H	Bu	**26** (1.0–1.1)	**47**	84
2	H	Ph	**43** (1.0)	**48**	79
3	H	OEt	**44** (1.5)	**49**	53–61
4	H	$SnBu_3$	**45** (1.2)	**50**	87
5[b]	Me	Me	**46** (1.8)	**51**	63

[a]Isolated yield of products purified by column chromatography. [b]Reaction conditions: 145 °C, 49 h; then 5 M KOH, MeOH, 65 °C, 2.5 h (to hydrolyze some phenol ester).

Table 5. Indole Synthesis via Nucleophilic Cyclization

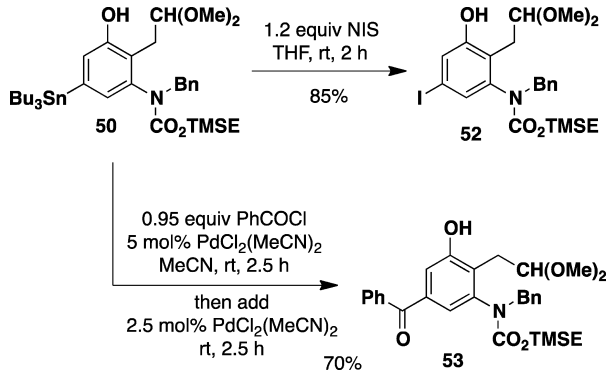


entry	aniline	R^1	R^2	indole	yield[a] (%)
1	**47**	H	Bu	**54**	79–84
2	**48**	H	Ph	**55**	78
3	**49**	H	OEt	**56**	85
4	**52**	H	I	**57**	53
5	**53**	H	COPh	**58**	87
6	**51**	Me	Me	**59**	74–80

[a]Isolated yield of products purified by column chromatography.

cleavage of the (trimethylsilyl)ethyl carbamate group proceeds smoothly on exposure to excess TBAF at room temperature. HCl is added, and the reaction mixture is then stirred overnight to afford the desired indoles in good yield. Although the arylstannane benzannulation product **50** is not itself stable to these acidic cyclization conditions, it does serve as a versatile precursor to derivatives such as the iodide **52** and ketone **53** (Scheme 7) that undergo smooth cyclization to indoles **57** and **58**, respectively, under the standard conditions.

Scheme 7. Elaboration of Arylstannane 50



The 6-iodoindole **57** is itself a particularly versatile intermediate, serving as a precursor to indoles with a variety of substituents at the C-6 position as illustrated in Scheme 8. Finally, if desired, debenzylation of the indole products can be conveniently effected under dissolving metal conditions as shown in Scheme 9.

Synthesis of Indoles via Iodo Ynamides. Recently we reported the first synthesis of 2-iodo ynamides and demonstrated that these compounds participate in [2 + 2] cycloadditions with ketene to furnish 2-iodocyclobutenones in good yield.[26] We recognized that benzannulation with this new class of ynamides could furnish access to 2-iodoanilines whose utility as substrates in a variety of indole-forming annulation processes is well established. We therefore turned our attention

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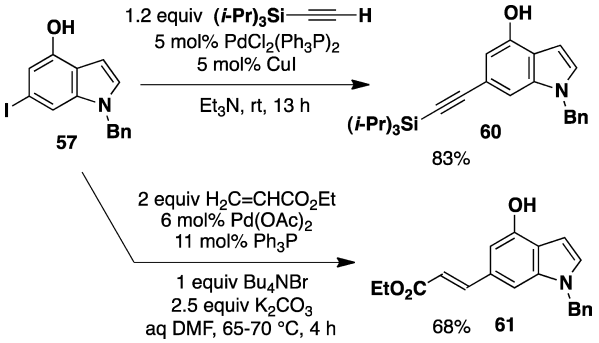
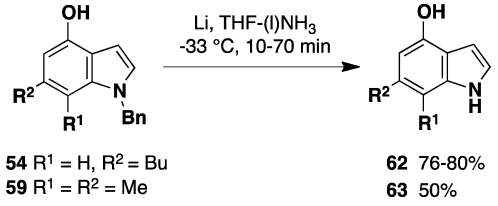
Scheme 8. Cross-Coupling Reactions of 6-Iodoindole 57

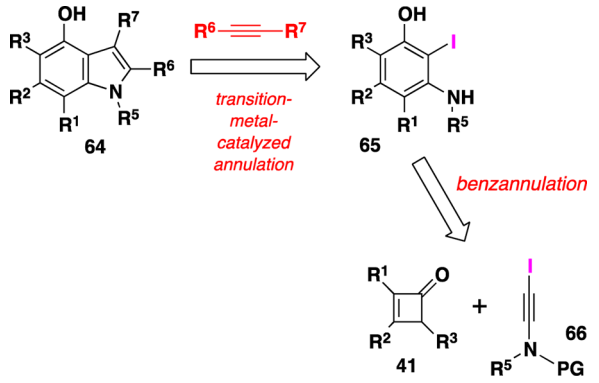


Scheme 9. Debenzylation of Indoles 54 and 59



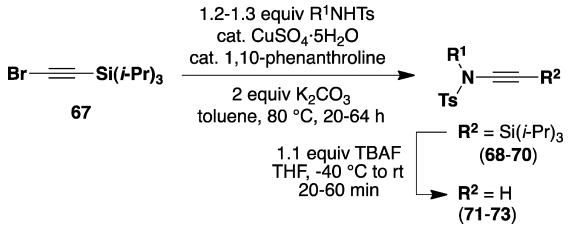
to the investigation of tandem strategies based on the application of iodo ynamides in our vinylketene-based benzannulation in conjunction with various transition-metal-catalyzed annulation processes (Scheme 10).

Scheme 10. Strategy for the Synthesis of Indoles via Iodo Ynamides



The *N*-sulfonyl ynamides employed in this variant of our tandem strategy were best prepared by using the *N*-alkynylation protocol of Hsung (Table 6). Conversion of terminal ynamides **71**–**73** to the corresponding iodo derivatives then proceeded smoothly under our previously reported conditions[26] (Table 7). Attempts to purify the iodo ynamides using column chromatography resulted in significant losses, and these ynamides were therefore employed in benzannulations without purification. Optimization studies indicated that reaction of the iodo ynamides with cyclobutenone **26** were best conducted by heating in toluene at 80 °C for 2 h, at which point TLC analysis indicated that all of the ynamide had been consumed. We believe that the ynamide is reacting primarily by [2 + 2] cycloaddition since we had previously observed in control experiments that pure *N*-sulfonyl iodo ynamides have half-lives on the order of 40 h at 80 °C in toluene and that iodo ynamides are recovered unchanged after being heated for several hours at 80 °C in the presence of phenols such as the

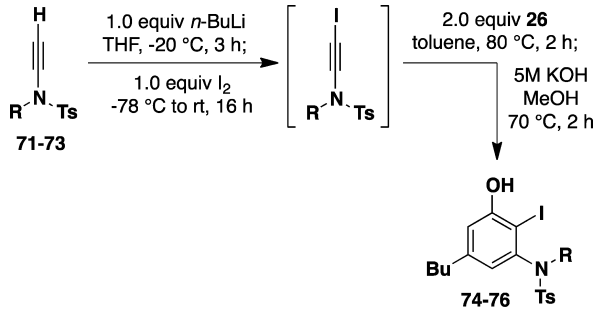
Table 6. Synthesis of Alkynyl Sulfonamides



R^1	silyl ynamide	yield[a] (%)	terminal ynamide	yield[a] (%)
PMB	**68**	88	**71**	94–96
allyl	**69**[b]	90–91	72[c]	87–91
2-furfuryl	**70**	61–64[d]	**73**	94–98

[a]Isolated yield of products purified by column chromatography. [b]Zhang, Y.; DeKorver, K. A.; Lohse, A. G.; Zhang, Y.-S.; Huang, J.; Hsung, R. P. *Org. Lett.* **2009**, *11*, 899–902. [c]Reference 54. [d]Reaction performed in toluene–DMF.

Table 7. Iodination and Benzannulation of Terminal Ynamides 71–73



entry	R	ynamide	aniline	yield[a] (%)
1	PMB	**71**	**74**	59–77
2	allyl	**72**	**75**	41–49
3[b]	2-furfuryl	**73**	**76**	49

[a]Overall two-step isolated yield of products purified by column chromatography. [b]KHMDS is used in place of *n*-BuLi in the first step.

benzannulation products **74**–**76**. Improved yields in these benzannulations were obtained by using an excess of the cyclobutenone and by treating the crude product with KOH in methanol. Base treatment serves to hydrolyze any esters formed by trapping of the phenolic hydroxyl group with ketene intermediates during the reaction.[27]

In recent years, the "Larock indole synthesis" has emerged as one of the most powerful methods for the construction of 2,3-disubstituted indoles.[3,28] This heteroannulation process involves the palladium-catalyzed reaction of 2-iodoanilines with internal alkynes, and its chief limitation in scope is the difficulty associated with the regioselective synthesis of substituted iodoaniline substrates. We recognized that our vinylketene-based benzannulation provides an attractive means of accessing substituted substrates for the Larock heteroannulation, and Scheme 11 illustrates an application of this strategy. To avoid potential complications resulting from competitive reaction of the nucleophilic phenolic oxygen,[29] the hydroxyl group was first protected as a methyl ether. After removal of the PMB group,[30] reaction with 1-(trimethylsilyl)-1-hexyne under standard Larock conditions gave indole **79** in 51% yield after chromatographic purification.

The Castro–Stephens reaction and its variants provide a useful vehicle for elaborating indoles from 2-iodoanilines by

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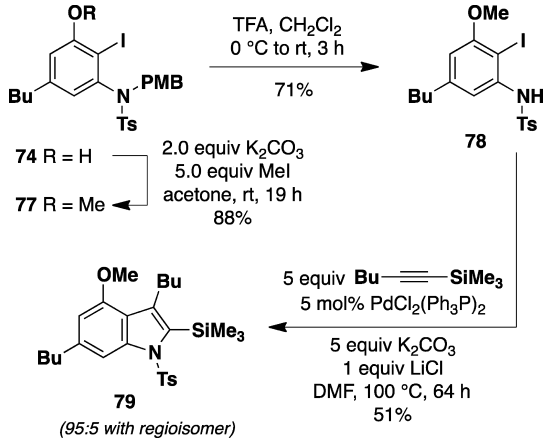
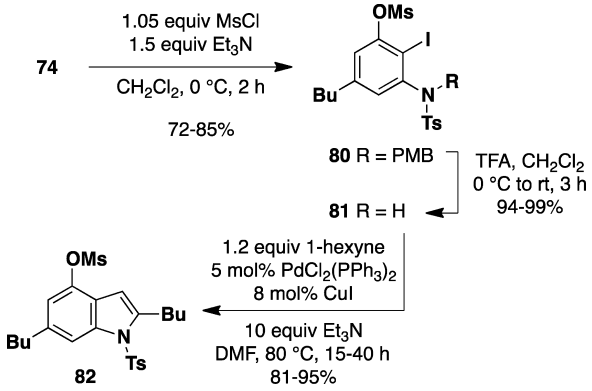
Scheme 11. Synthesis of Indole 79 via Larock Heteroannulation



reaction with terminal alkynes.[3,31] This heteroannulation process involves initial Sonogashira reaction of the aryl iodide with the alkyne to produce a 2-alkynylaniline that cyclizes either in situ or in a separate step to furnish a 2-substituted indole.[32] Scheme 12 illustrates the application of a one-pot variant of the

Scheme 12. Synthesis of Indole 82

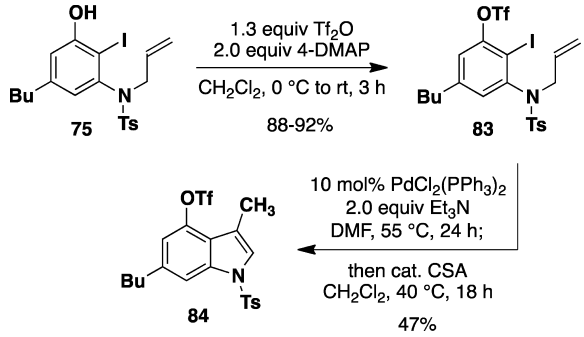


Castro–Stephens reaction to a 2-iodoaniline generated via our ynamide-based benzannulation. In this case the phenolic hydroxyl group was first converted to the corresponding mesylate, providing a potential handle for further elaboration via cross-coupling chemistry. Heteroannulation with 1-hexyne proceeded efficiently under the indicated conditions to afford indole **82** in high yield.

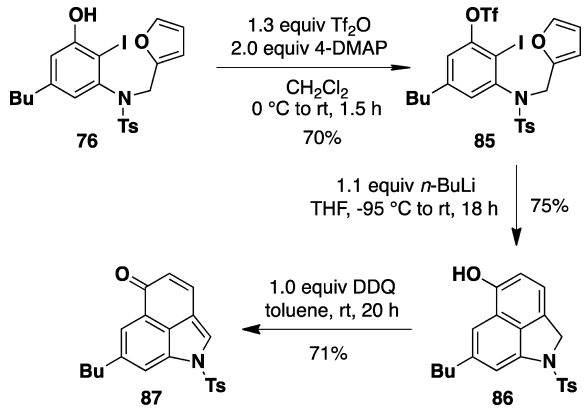
Iodoanilines of type **65** bearing an *N*-allyl moiety are potential substrates for intramolecular Heck reactions leading to indolines and indoles. This approach to the synthesis of indoles was pioneered by Mori and Ban,[3,33] and its application to an iodoaniline prepared by our ynamide-based benzannulation is illustrated in Scheme 13. Since the Mori–Ban cyclization can be performed at low temperatures, in this case we found it possible to employ the triflate derivative of **75** in the cyclization leading to formation of the 3-methylindole **84**, which is equipped with a handle for further elaboration at the C-4 carbon.

Scheme 14 presents a final example of the application of iodo ynamide-derived benzannulation products as intermediates for the synthesis of highly substituted indoles. This approach exploits the *ortho* relationship of the hydroxyl and iodo

Scheme 13. Synthesis of Indole 84 via Mori–Ban Cyclization



Scheme 14. Intramolecular Aryne Cyclization and Oxidation from Aniline 76



substituents on the benzannulation products, which enables these compounds to serve as precursors to arynes via vicinal elimination of their triflate derivatives.[34] Treatment of benzannulation product **76** with Tf_2O furnishes triflate **85**, setting the stage for an intramolecular aryne cycloaddition involving the tethered furan ring. On exposure to *n*-BuLi, tricyclic phenol **86** forms presumably via initial [4 + 2] cycloaddition of an aryne followed by ring-opening isomerization of the resulting highly strained bridged ring species. Finally, oxidation of **86** with DDQ[35] furnishes the benz[*cd*]-indolone **87** in good yield.[36]

CONCLUSION

The combination of the ynamide-based benzannulation with various heterocyclization and annulation processes provides access to indoles bearing multiple substituents on the benzenoid ring. In the present study, cyclobutenones were employed as the vinylketene precursors, and this version of the benzannulation serves as the basis for a versatile synthesis of indoles of type **1** (Scheme 1) with substituents R^2 and R^3 and of indoles of type **2** with substituents R^2 and R^4. Our previous studies have established that substituted cyclobutenones are readily available in one or two steps from alkyne–ketene cycloadditions and that a variety of cyclobutenone vinylketene precursors participate in the benzannulation in good yield. For the synthesis of indoles bearing substituents R^3, or in which the benzenoid ring is fused to another ring system, we anticipate that the "second-generation" version of our benzannulation strategy will be the preferred method, and the application of this photo-Wolff variant of our strategy[6b] to the synthesis of indoles is under active investigation in our laboratory.

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EXPERIMENTAL SECTION

General Procedures. All reactions were performed in flame-dried glassware under a positive pressure of argon and stirred magnetically unless otherwise indicated. Air- and moisture-sensitive liquids and solutions were transferred via gastight syringe or cannula and introduced into reaction vessels through rubber septa. Reaction product solutions and chromatography fractions were concentrated at 20 mmHg and then at 20 °C and 0.05 mmHg overnight unless otherwise indicated. Filtration was conducted through sintered-glass Büchner funnels with vacuum suction (20 mmHg) unless otherwise indicated. Thin-layer chromatography was performed on precoated glass-backed silica gel 60 F-254 250 μm plates. Column chromatography was performed using 230−400 mesh silica gel.

Materials. Commercial-grade reagents and solvents were used without further purification except as indicated below. Dichloromethane, diethyl ether, and tetrahydrofuran were purified by pressure filtration through activated alumina. Toluene was purified by pressure filtration through activated alumina and copper(II) oxide. Pyridine and triethylamine were distilled under argon from calcium hydride. Dimethylformamide and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were distilled under vacuum from calcium hydride. Triflic anhydride was distilled under argon from P_2O_5. Lithium chloride and potassium carbonate were dried at 110−130 °C and 0.1 mmHg for 24 h. *N*-Bromosuccinimide was recrystallized from boiling water.[37] Copper(I) iodide was extracted with THF for 24 h in a Soxhlet extractor and then dried under vacuum (0.05 mmHg) in a vacuum desiccator over P_2O_5 for 24 h. Iodomethane was passed through neutral alumina immediately prior to use. Bis(triphenylphosphine)palladium(II) chloride was prepared according to the method of Heck[38] and recrystallized from chloroform. Sodium periodate supported on silica gel was prepared according to the procedure of Zhong and Shing.[21] *n*-Butyllithium was titrated according to the Watson−Eastham method using menthol in THF with 1,10-phenanthroline as an indicator.[39]

Instrumentation. Melting points were determined with a melting point apparatus and are uncorrected. ^{1}H NMR chemical shifts are expressed in parts per million (δ) downfield relative to tetramethylsilane (with the $CHCl_3$ peak at 7.27 ppm used as a standard). ^{13}C NMR chemical shifts are expressed in parts per million (δ) downfield relative to tetramethylsilane (with the central peak of $CDCl_3$ at 77.23 ppm used as a standard). High-resolution mass spectrometry (HRMS) was performed with a Fourier transform ion cyclotron resonance mass spectrometer.

2-(Trimethylsilyl)ethyl *N*-Benzylcarbamate (11). A 250 mL, three-necked, round-bottomed flask equipped with a rubber septum fitted with a thermocouple temperature probe, glass stopper, and reflux condenser fitted with an argon inlet adapter was charged with phenylacetic acid (7.085 g, 52.0 mmol, 1.0 equiv), 70 mL of toluene, and Et_3N (8.0 mL, 5.8 g, 58 mmol, 1.1 equiv). Diphenylphosphoryl azide (11.7 mL, 15.0 g, 54 mmol, 1.0 equiv) was added via syringe over 20 min (exothermic) at a rate to maintain the internal temperature below 36 °C. The rubber septum was replaced by a glass stopper, and the reaction mixture was heated at 85 °C for 2 h, during which time the evolution of N_2 was observed. The reaction mixture was allowed to cool to room temperature, and 2-(trimethylsilyl)ethanol (9.0 mL, 7.4 g, 63 mmol, 1.2 equiv) was rapidly added via syringe over ca. 2 min. The reaction mixture was then heated at 85−90 °C for 16 h. After being cooled to room temperature, the reaction mixture was transferred to a 300 mL, one-necked, round-bottomed flask and concentrated to a volume of ca. 10 mL. This residue was dissolved in 150 mL of Et_2O, washed with two 100 mL portions of 10% NaOH solution and 100 mL of H_2O, dried over $MgSO_4$, filtered, and concentrated to a volume of ca. 20 mL, at which point a white precipitate appeared. This residue was filtered, washing with ca. 50 mL of Et_2O, and the filtrate was concentrated to afford 12.8 g of a pale yellow gel. This material was triturated with 80 mL of hexanes and cooled at −18 °C for 1 h. The white crystalline solid formed was filtered, washing with ca. 30 mL of hexanes, and then the filtrate was concentrated to provide ca. 12 g of a yellow oil containing a small amount of white solid. Column chromatography on 150 g of silica gel (elution with 10% EtOAc−hexanes) provided 9.474 g (72%) of carbamate **11** as a pale yellow oil: IR (film) 3334, 3065, 3032, 2953, 1697, 1530, 1454, 1250, 1179, 1135, 1060, and 1043 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.39 (m, 5H), 4.95 (br s, 1H), 4.38 (d, J = 5.9 Hz, 2H), 4.20 (t, J = 8.5 Hz, 2H), 1.00 (t, J = 8.5 Hz, 2 H), 0.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 138.8, 128.6, 127.5, 127.4, 63.2, 44.9, 17.8, and −1.3; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{13}H_{21}NO_2Si$ 274.1234, found 274.1242.

4,4-Dimethoxybut-1-yne.[40] A 250 mL, three-necked, round-bottomed flask equipped with a rubber septum fitted with a thermocouple temperature probe, coldfinger reflux condenser, and addition funnel fitted with an argon inlet adapter was charged with aluminum powder (2.7 g, 100 mmol, 1.5 equiv) and 20 mL of Et_2O. To this stirred suspension was added $HgCl_2$ (0.100 g, 0.37 mmol, 1.0 equiv), and the reaction mixture was heated at 33 °C (bath temperature 50 °C) for 30 min. The oil bath was removed, and propargyl bromide solution (90 wt % in toluene, ca. 0.2 mL) was rapidly added dropwise over ca. 1 min via syringe. As soon as the reaction of aluminum and propargyl bromide began (indicated by an increase in internal temperature), a solution of propargyl bromide (90 wt % in toluene, 13.3 g, 101 mmol, 1.5 equiv) diluted with 40 mL of Et_2O was added dropwise via the addition funnel over 30 min. During this addition, the internal temperature increased to 38 °C. The black suspension was kept at reflux for 1 h and then allowed to cool to room temperature. After the solid settled, the supernatant solution was transferred via cannula (rinse with 250 mL of Et_2O) to a 1 L, three-necked, round-bottomed flask equipped with a rubber septum fitted with a thermocouple temperature probe, glass stopper, and argon inlet adapter. The solution was cooled at −78 °C while a solution of trimethyl orthoformate (7.1 mL, 6.9 g, 65 mmol, 1.0 equiv) in 15 mL of Et_2O was added via syringe over 20 min. The milky-white mixture was stirred at −78 °C for 15 min and then cooled at −90 °C while 90 mL of H_2O was added in 10 portions over 45 min, while the internal temperature was kept below −65 °C. The cold bath was removed, and the reaction mixture was allowed to warm to room temperature over 2 h. The organic layer was separated, and the aqueous layer was extracted with three 40 mL portions of Et_2O. The combined organic layers were washed with 80 mL of ice-cold aq 5 M NaOH solution and two 80 mL portions of H_2O, dried over $MgSO_4$, and filtered into a 1 L, one-necked, round-bottomed flask. Most of the Et_2O was removed via short-path distillation at 35 °C (760 mmHg). The residue was next distilled through a 75 mm, vacuum-jacketed Vigreux column topped with a Perkin triangle. Initially, additional Et_2O was distilled at 35 °C (760 mmHg), after which the residue was transferred to a 50 mL, one-necked, round-bottomed flask. Distillation was then continued to afford a forerun of 2.830 g of a colorless oil (bp 30−66 °C, 75 mmHg) which was a mixture of the desired product, toluene, and Et_2O. The desired acetal was distilled at 66−68 °C (75 mmHg), yielding 4.656 g (63%) of a colorless oil: IR (film) 3291, 2940, 2834, 2124, 1448, 1423, 1364, 1241, 1194, 1123, and 1068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56 (t, J = 5.6 Hz, 1H), 3.39 (s, 6H), 2.54 (dd, J = 5.6, 2.6 Hz, 2H), and 2.05 (t, J = 2.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.4, 79.5, 70.3, 53.7, and 23.9; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_6H_{10}O_2$: 137.0573, found 137.0576.

General Procedure for the Bromination of Terminal Acetylenes. 1-Bromo-3-(*tert*-butyldimethylsiloxy)prop-1-yne (13). A 250 mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with *tert*-butyldimethyl(2-propynyloxy)silane (1.954 g, 11.5 mmol, 1.0 equiv) and 60 mL of acetone. NBS (2.250 g, 12.6 mmol, 1.1 equiv) and silver(I) nitrate (0.098 g, 0.58 mmol, 0.05 equiv) were added. The flask was wrapped in aluminum foil, and the resulting mixture was stirred at room temperature for 1 h. The resulting cloudy mixture was diluted with 200 mL of 1:1 Et_2O−pentane, extracted with 50 and 30 mL portions of 10% $Na_2S_2O_3$ solution, 50 mL of H_2O, and 50 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated at 30 mmHg to yield 2.741 g (96%) of alkyne **13** as a colorless oil: IR (film) 2930, 2886, 2858, 2220, 1472, 1463, 1364, 1255, and 1100 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.35 (s, 2H), 0.92 (s, 9H), and 0.13 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 78.7, 52.6, 44.8, 25.9,

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18.4, and −5.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_9H_{17}BrOSi$ 249.0305, found 249.0316.

1-Bromo-4,4-dimethoxybut-1-yne (16). Reaction of 4,4-dimethoxybut-1-yne (4.699 g, 41.2 mmol, 1.0 equiv), NBS (8.092 g, 45.5 mmol, 1.1 equiv), and silver(I) nitrate (0.077 g, 0.45 mmol, 0.01 equiv) in 200 mL of acetone for 1 h according to the general procedure gave 7.652 g (96%) of alkyne **16** as a colorless oil: IR (film) 2993, 2939, 2833, 2224, 1446, 1421, 1362, 1238, 1193, 1121, 1071, 1037, and 1009 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.54 (t, J = 5.4 Hz, 1H), 3.38 (s, 6H), 2.55 (d, J = 5.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.2, 75.3, 53.7, 40.2, and 25.0; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_6H_9BrO_2$ 214.9678, found 214.9686.

***N*-(Methoxycarbonyl)-*N*-prop-2-enylprop-1-ynylamine (17).** A 250 mL, three-necked, round-bottomed flask equipped with a rubber septum, glass stopper, and addition funnel fitted with a rubber septum and argon inlet needle was charged with carbamate **9**[41] (0.860 g, 7.47 mmol, 1.0 equiv) and 30 mL of pyridine. The solution was cooled at 0 °C while 8.2 mL of KHMDS solution (0.91 M in THF, 7.5 mmol, 1.0 equiv) was added via syringe over 5 min. The resulting yellow slurry was stirred at 0 °C for 10 min, and then a solution of CuI (1.42 g, 7.47 mmol, 1.0 equiv) in 15 mL of pyridine was added via cannula in one portion (5 mL pyridine rinse). The ice bath was removed, and the dark green reaction mixture was stirred at room temperature for 2 h. A solution of iodoalkyne **12**[42] (25 mL, 0.60 M in benzene, 15 mmol, 2.0 equiv) was then added via the addition funnel over 1 h, and the resulting dark brown mixture was stirred at room temperature for 22 h. The reaction mixture was diluted with 500 mL of Et_2O and washed with three 200 mL portions of a 2:1 mixture of saturated NaCl solution and concentrated NH_4OH solution. The combined aqueous layers were extracted with three 75 mL portions of Et_2O, and the combined organic layers were washed with 150 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to provide 2.81 g of a dark brown oil. Column chromatography on 90 g of silica gel (elution with 10% EtOAc−hexanes) afforded 0.689 g of a yellow oil, which was purified on 35 g of silica gel (elution with 10% EtOAc−hexanes) to give 0.629 g (55%) of ynamide **17** as a pale yellow oil: IR (film) 3085, 2956, 2920, 2858, 2271, 1726, 1646, 1446, 1396, 1370, 1343, 1299, 1281, 1236, 1192, and 1152 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (ddt, J = 17.0, 10.5, 5.5 Hz, 1H), 5.27 (dd, J = 17.0, 1.0 Hz, 1H), 5.23 (dd, J = 10.5, 1.0 Hz, 1H), 4.04 (d, J = 5.5 Hz, 2H), 3.81 (s, 3H), and 1.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.0, 131.9, 118.1, 72.4, 65.4, 53.9, 52.5, and 3.2; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_8H_{11}NO_2$ 176.0682, found 176.0683.

General Procedure for the Synthesis of Ynamides via *N*-Alkynylation of Carbamates. *N*-(Methoxycarbonyl)-*N*-prop-2-enyl[3-(*tert*-butyldimethylsiloxy)prop-1-ynyl]amine (18). A 100 mL, three-necked, round-bottomed flask equipped with a rubber septum, glass stopper, and addition funnel fitted with a rubber septum and argon inlet needle was charged with carbamate **9**[41] (0.584 g, 5.07 mmol, 1.0 equiv) and 20 mL of THF. The pale yellow solution was cooled at 0 °C while KHMDS solution (5.6 mL, 0.91 M in THF, 5.1 mmol, 1.0 equiv) was added via syringe over 3 min. The resulting yellow solution was stirred at 0 °C for 10 min, and then pyridine (10 mL, 9.8 g, 123 mmol, 24 equiv) and CuI (0.966 g, 5.07 mmol, 1.0 equiv) were added. The ice bath was removed, and the dull green reaction mixture was stirred at room temperature for 2 h, during which time the reaction mixture turned brown. A solution of bromoalkyne **13** (2.53 g, 10.2 mmol, 2.0 equiv) in 10 mL of THF was added via the addition funnel over 1 h, and the resulting dark brown mixture was stirred at room temperature for 22 h. The reaction mixture was diluted with 120 mL of Et_2O and washed with three 60 mL portions of a 2:1 mixture of saturated NaCl solution and concentrated NH_4OH solution. The combined aqueous layers were extracted with two 40 mL portions of Et_2O, and the combined organic layers were washed with two 40 mL portions of ice-cold 1 M HCl solution and 80 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to provide 2.905 g of a brown oil. This material was dissolved in ca. 20 mL of CH_2Cl_2 and concentrated onto 12 g of silica gel. The free-flowing powder was added to the top of a column of 120 g of silica gel and eluted with 0−5% EtOAc−hexanes to provide 1.4 g of a mixture of ynamide **18** and the diyne byproduct as a brown oil. This material was purified by column chromatography on 70 g of silica gel (elution with 0−2.5% EtOAc−hexanes) to afford 0.334 g of ynamide **18** as a yellow oil and 0.755 g of a mixture of ynamide **18** and the diyne byproduct as a yellow oil. The mixed sample was purified by column chromatography on 30 g of silica gel (elution with 0−2.5% EtOAc−hexanes) to give 0.199 g of ynamide **18** as a yellow oil and 0.361 g of a mixture of ynamide **18** and the diyne byproduct as a yellow oil. This mixture was purified on 10 g of silica gel (elution with 1−2.5% EtOAc−hexanes) to provide 0.253 g of ynamide **18** as a yellow oil. The total yield was 0.786 g (55%) of ynamide **18** as a yellow oil: IR (film) 3086, 2956, 2930, 2858, 2255, 1736, 1646, 1444, 1392, 1361, 1297, 1280, 1253, 1237, and 1079 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (ddt, J = 17.1, 10.2, 6.0 Hz, 1H), 5.28 (dd, J = 17.7, 1.3 Hz, 1H), 5.24 (dd, J = 10.3, 1.2 Hz, 1H), 4.46 (s, 2H), 4.07 (d, J = 6.0 Hz, 2H), 3.81 (s, 3H), 0.92 (s, 9H), and 0.13 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8, 131.6, 118.6, 78.6, 69.5, 54.1, 52.6, 51.9, 25.9, 18.4, and −4.9; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{14}H_{25}NO_3Si$ 306.1496, found 306.1496.

***N*-(Methoxycarbonyl)-*N*-prop-2-enyl[4-(*tert*-butyldimethylsiloxy)but-1-ynyl]amine (19).** Reaction of a solution of carbamate **9**[41] (0.519 g, 4.50 mmol, 1.0 equiv) in 18 mL of THF with KHMDS (5.0 mL, 0.91 M in THF, 4.55 mmol, 1.0 equiv), pyridine (9.0 mL, 8.8 g, 111 mmol, 25 equiv), CuI (0.857 g, 4.50 mmol, 1.0 equiv), and bromoalkyne **14**[43] (2.373 g, 9.01 mmol, 2.0 equiv) in 9.0 mL of THF for 21 h according to the general procedure gave 2.578 g of a brown oil. This material was dissolved in ca. 20 mL of CH_2Cl_2 and concentrated onto 13.5 g of silica gel. The free-flowing powder was added to the top of a column of 135 g of silica gel and eluted with 0−5% EtOAc−hexanes to provide 0.886 g (66%) of ynamide **19** as a yellow oil: IR (film) 3085, 2955, 2930, 2857, 2262, 1732, 1646, 1445, 1391, 1330, 1298, 1233, and 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (ddt, J = 17.0, 10.3, 6.0 Hz, 1H), 5.25 (d, J = 18.4 Hz, 1H), 5.23 (d, J = 10.4 Hz, 1H), 4.04 (d, J = 5.9 Hz, 2H), 3.80 (s, 3H), 3.71 (t, J = 7.1 Hz, 2H), 2.51 (t, J = 7.1 Hz, 2H), 0.90 (s, 9H), and 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 131.8, 118.3, 74.4, 67.0, 62.3, 53.9, 52.7, 25.9, 22.9, 18.4, and −5.1; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{15}H_{27}NO_3Si$ 320.1652, found 320.1650.

***N*-(*tert*-Butoxycarbonyl)-*N*-methylpent-4-en-1-ynylamine (20).** Reaction of a solution of carbamate **10**[44] (0.683 g, 5.21 mmol, 1.0 equiv) in 21 mL of THF with KHMDS (5.8 mL, 0.91 M in THF, 5.3 mmol, 1.0 equiv), pyridine (10.0 mL, 9.78 g, 124 mmol, 23.8 equiv), CuI (0.992 g, 5.21 mmol, 1.0 equiv), and bromoalkyne **15**[5] (13 mL, 0.60 M in benzene, 7.8 mmol, 1.5 equiv) according to the general procedure afforded 2.235 g of a brown oil. Column chromatography on 110 g of silica gel (gradient elution 0−5% EtOAc−hexanes) gave 0.517 g of a yellow oil. This material was further purified by column chromatography on 50 g of silica gel (elution with 3% EtOAc−hexanes) to afford 0.436 g (43%) of ynamide **20** as a pale yellow oil: IR (film) 2980, 2934, 2267, 1720, 1642, 1478, 1457, 1421, 1369, 1318, 1254, and 1155 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (ddt, J = 16.8, 10.0, 4.8 Hz, 1H), 5.35 (br d, J = 16.8 Hz, 1H), 5.09 (dd, J = 10.0, 1.6 Hz, 1H), 3.07 (s, 3H), 3.04−3.06 (m, 2H), and 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 133.2, 115.8, 82.1, 78.3, 64.8, 37.3, 28.2, and 22.9; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{11}H_{17}NO_2$ 218.1151, found 218.1156.

***N*-Benzyl-*N*-[[2-(trimethylsilyl)ethoxy]carbonyl][4,4-dimethoxybut-1-ynyl]amine (21).** Reaction of a solution of carbamate **11** (1.355 g, 5.39 mmol, 1.0 equiv) in 22 mL of THF with KHMDS (5.9 mL, 0.91 M in THF, 5.4 mmol, 1.0 equiv), pyridine (11.0 mL, 10.8 g, 136 mmol, 25 equiv), CuI (1.03 g, 5.41 mmol, 1.0 equiv), and bromoalkyne **16** (2.14 g, 11.1 mmol, 2.1 equiv) in 10 mL of THF for 18 h according to the general procedure[45] gave 2.905 g of a brown oil. This material was dissolved in ca. 50 mL of CH_2Cl_2 and concentrated onto 12 g of silica gel. The free-flowing powder was added to the top of a column of 150 g of silica gel and eluted with 10% EtOAc−hexanes to afford 1.623 g of a mixture of ynamide **21** and unreacted carbamate **11** as a yellow oil. This material was dissolved in ca. 25 mL of CH_2Cl_2 and concentrated onto 8 g of activated basic aluminum oxide. The free-flowing powder was added to the top of a column of 90 g of

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activated basic aluminum oxide and eluted with 10% EtOAc–hexanes to give 1.123 g (57%) of ynamide **21** as a pale yellow oil (another run of the reaction on a larger scale provided the product in 69% yield): IR (film) 2953, 2831, 2267, 1721, 1455, 1400, 1275, 1250, 1218, 1121, and 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28–7.41 (m, 5H), 4.60 (s, 2H), 4.46 (t, J = 5.7 Hz, 1H), 4.28 (t, J = 8.5 Hz, 2H), 3.33 (s, 6H), 2.59 (d, J = 5.7 Hz, 2H), 1.06 (t, J = 8.4 Hz, 2H), and 0.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 136.5, 128.5, 128.5, 127.9, 102.8, 75.5, 65.6, 53.7, 53.4, 53.4, 23.9, 17.6, and −1.3; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{19}H_{29}NO_4Si$ 386.1758, found 386.1765.

General Procedure for the Synthesis of Highly Substituted Aniline Derivatives: Method A, via the Benzannulation of Cyclobutenones and Ynamides with Two Stages of Heating. *N*-(Methoxycarbonyl)-*N*-prop-2-enyl(5-butyl-3-hydroxy-2-methylphenyl)amine (27). A 10 mL, one-necked, round-bottomed flask equipped with a reflux condenser fitted with an argon inlet adapter was charged with ynamide **17** (0.262 g, 1.71 mmol, 1.0 equiv), cyclobutenone **26**[11] (0.219 g, 1.76 mmol, 1.0 equiv), and 2.1 mL of toluene. The yellow solution was heated at 75–90 °C for 2 h and at reflux for 3 h and then allowed to cool to room temperature. Concentration provided 0.475 g of an orange solid, which was dissolved in 10 mL of CH_2Cl_2 and concentrated onto 2 g of silica gel. The free-flowing powder was added to the top of a column of 48 g of silica gel and eluted with 30% EtOAc–hexanes to afford 0.370 g (78%) of **27** as a pale yellow solid: mp 94–95 °C; IR (film) 3344, 2956, 2929, 2858, 1675, 1619, 1586, 1515, 1456, 1391, 1318, and 1272 cm^{-1}; ^1H NMR (500 MHz, toluene-d_8, 90 °C) δ 6.51 (s, 1H), 6.32 (s, 1H), 5.84–5.92 (m, 1H), 5.12 (br s, 1H), 4.97 (dd, J = 17.3, 1.0 Hz, 1H), 4.93 (dd, J = 10.5, 1.0 Hz, 1H), 4.27 (br s, 1H), 3.91 (br s, 1H), 3.45 (s, 3H), 2.40 (t, J = 7.8 Hz, 2H), 2.05 (s, 3H), 1.50 (app quintet, J = 7.5 Hz, 2H), 1.28 (app sextet, J = 7.3 Hz, 2H), and 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, 20 °C, mixture of two rotamers) (major rotamer) δ 156.5, 154.6, 141.6, 141.0, 133.3, 120.4, 119.7, 118.3, 114.5, 53.6, 53.2, 35.2, 33.4, 22.4, 14.1, and 10.6; additional resonances appeared for the minor rotamer at δ 155.0, 133.6, 120.3, 117.8, and 114.9; HRMS m/z $[M + Na]^+$ calcd for $C_{16}H_{23}NO_3$ 300.1570, found 300.1567. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.21; H, 8.36; N, 4.98.

***N*-(Methoxycarbonyl)-*N*-prop-2-enyl[5-butyl-2-[(*tert*-butyldimethylsiloxy)methyl]-3-hydroxyphenyl]amine (28).** Reaction of a solution of ynamide **18** (0.354 g, 1.25 mmol, 1.0 equiv) and cyclobutenone **26** (0.160 g, 1.29 mmol, 1.0 equiv) in 1.6 mL of toluene at 80 °C for 90 min and then at reflux for 2 h according to general procedure A gave 0.508 g of an orange oil. Column chromatography on 20 g of silica gel (elution with 10% EtOAc–hexanes) afforded 0.433 g (85%) of **28** as a pale yellow solid: mp 60–62 °C; IR (film) 3339, 3081, 2955, 2858, 1711, 1680, 1628, 1579, 1461, 1388, 1313, 1254, 1194, 1148, and 1054 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 6.67 (d, J = 1.6 Hz, 1H), 6.46 (s, 1H), 5.86–5.94 (m, 1H), 5.14 (d, J = 10.1 Hz, 1H), 5.13 (d, J = 17.1 Hz, 1H), 4.76–4.83 (m, 2H), 4.22 (dd, J = 14.5, 6.2 Hz, 1H), 4.00 (dd, J = 14.7, 6.7 Hz, 1H), 3.64 (s, 3H), 2.53 (t, J = 7.7 Hz, 2H), 1.57 (app quintet, J = 7.6 Hz, 2H), 1.34 (app sextet, J = 7.4 Hz, 2H), 0.93 (s, 9H), 0.92 (t, J = 7.6 Hz, 3H), 0.14 (s, 3H), and 0.13 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 156.0, 144.1, 138.4, 133.0, 119.5, 118.8, 118.7, 116.3, 61.8, 53.8, 53.1, 35.2, 33.2, 25.8, 22.4, 18.2, 14.0, −5.4, and −5.5. Anal. Calcd for $C_{22}H_{37}NO_4Si$: C, 64.82; H, 9.15; N, 3.44. Found: C, 64.78; H, 9.18; N, 3.48.

***N*-(Methoxycarbonyl)-*N*-prop-2-enyl[5-butyl-2-[(*tert*-butyldimethylsiloxy)ethyl]-3-hydroxyphenyl]amine (29).** Reaction of a solution of ynamide **19** (0.379 g, 1.27 mmol, 1.0 equiv) and cyclobutenone **26** (0.212 g, 1.71 mmol, 1.3 equiv) in 1.6 mL of toluene at 90 °C for 2 h and then at reflux for 90 min according to general procedure A gave 0.607 g of a light brown solid. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 3 g of silica gel. The free-flowing powder was added to the top of a column of 50 g of silica gel and eluted with 20% EtOAc–hexanes to provide 0.501 g (94%) of **29** as a light yellow solid: mp 95.5–95.7 °C; IR (KBr pellet) 3320, 2956, 2930, 2858, 1710, 1680, 1619, 1584, 1460, 1387, 1256, and 1083 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 6.75 (s, 1H), 6.50 (s, 1H), 5.84–5.94 (m, 1H), 5.12 (d, J = 9.6 Hz, 1H), 5.10 (d, J = 17.4 Hz, 1H), 4.28 (dd, J = 14.4, 5.8 Hz, 1H), 3.92 (dd, J = 14.7, 6.8 Hz, 1H), 3.75–3.91 (m, 2H), 3.62 (s, 3H), 2.70–2.86 (m, 2H), 2.53 (t, J = 7.7 Hz, 2H), 1.57 (app quintet, J = 7.6 Hz, 2H), 1.33 (app sextet, J = 7.4 Hz, 2H), 0.92 (s, 9H), 0.89–0.92 (m, 3H), 0.10 (s, 3H), and 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 156.4, 143.1, 140.5, 133.2, 122.4, 120.3, 118.5, 116.9, 65.0, 54.1, 52.9, 35.2, 33.2, 29.2, 25.9, 22.4, 18.4, 14.1, and −5.5. Anal. Calcd for $C_{23}H_{39}NO_4Si$: C, 65.52; H, 9.32; N, 3.32. Found: C, 65.49; H, 9.29; N, 3.35.

General Procedure for the Synthesis of Amino Aldehyde Precursors to Indoles via the Oxidative Cleavage of *N*-Allylaniline Derivatives. *N*-(Methoxycarbonyl)-*N*-(2-oxoethyl)-(5-butyl-3-hydroxy-2-methylphenyl)amine (30). A 25 mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with carbamate **27** (0.335 g, 1.21 mmol, 1.0 equiv), 9 mL of THF, 3 mL of H_2O, OsO_4 (4 wt % in H_2O, 0.160 mL, 0.154 g, 0.024 mmol, 0.02 equiv), and NMO (0.156 g, 1.33 mmol, 1.1 equiv). The rubber septum and argon inlet needle were replaced by an argon inlet adapter, and the light brown solution was stirred at room temperature for 12 h (TLC with 60% EtOAc–hexanes; R_f of carbamate **27**, 0.65; R_f of diol, 0.2). A solution of $NaHSO_3$ (1.3 g, 13 mmol, 11 equiv) in 12 mL of water was added, and the resulting mixture was stirred at room temperature for 10 min. The mixture was diluted with 20 mL of saturated NaCl solution and extracted with three 30 mL portions of EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to give 0.382 g of the diol as a white foam used in the next step without purification: IR (film) 3354, 2956, 2930, 2872, 1679, 1619, 1585, 1459, 1393, 1337, 1280, 1196, 1142, 1126, and 1035 cm^{-1}.

A 25 mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with $NaIO_4$ supported on silica gel (2.0 g, 2.4 mmol, 2.0 equiv) and 6 mL of CH_2Cl_2. To this stirred suspension was added a solution of the diol (0.382 g, 1.0 equiv) prepared in the previous reaction in 6 mL of CH_2Cl_2. The yellow suspension was stirred at room temperature for 40 min. The reaction mixture was filtered through a sintered glass funnel, and the residue was washed with three 10 mL portions of CH_2Cl_2. The filtrate was concentrated to provide 0.347 g of a yellow oil, which was purified by column chromatography on 25 g of silica gel (elution with 30% EtOAc–hexanes) to give 0.277 g (82%) of aldehyde **30** as a white solid: mp 88–90 °C; IR (film) 3373, 2957, 2929, 2859, 1731, 1680, 1619, 1585, 1458, 1376, 1279, 1198, 1144, 1126, 1053, and 1024 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ca. 76:24 mixture of rotamers) (major rotamer) δ 9.74 (s, 1H), 6.66 (s, 1H), 6.61 (s, 1H), 4.78 (s, 1H), 4.53 (d, J = 18.4 Hz, 1H), 4.03 (d, J = 18.4 Hz, 1H), 3.71 (s, 3H), 2.52 (t, J = 7.8 Hz, 2H), 2.10 (s, 3H), 1.55 (app quintet, J = 7.6 Hz, 2H), 1.34 (app sextet, J = 7.4 Hz, 2H), and 0.92 (t, J = 7.4 Hz, 3H); additional resonances appeared for the minor rotamer at δ 6.58 (s, 1H), 4.88 (s, 1H), 4.44 (d, J = 18.4 Hz, 1H), 3.79 (s, 3H), and 2.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) (major rotamer) δ 197.8, 156.9, 154.7, 142.4, 141.2, 120.0, 119.5, 114.9, 60.3, 53.8, 35.2, 33.4, 22.5, 14.1, and 10.5; additional resonances appeared for the minor rotamer at δ 119.7, 115.3, 60.4, 53.7, and 22.6. Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.55; H, 7.53; N, 4.97.

***N*-(Methoxycarbonyl)-*N*-(2-oxoethyl)[5-butyl-2-[(*tert*-butyldimethylsiloxy)ethyl]-3-hydroxyphenyl]amine (31).** Reaction of alkene **29** (0.498 g, 1.18 mmol, 1.0 equiv) with OsO_4 (4 wt % in H_2O, 0.375 mL, 0.390 g, 0.036 mmol, 0.05 equiv) and NMO (0.166 g, 1.42 mmol, 1.2 equiv) in 8 mL of THF and 4 mL of H_2O for 14 h according to the general procedure gave 0.550 g of a pale yellow oil. This material was transferred to a 50 mL, one-necked, recovery flask equipped with an argon inlet adapter, and 12 mL of CH_2Cl_2 and $NaIO_4$ supported on silica gel (2.95 g, 3.54 mmol, 3.0 equiv) were added. The yellow suspension was stirred at room temperature for 2 h. The reaction mixture was filtered through a sintered glass funnel, and the residue was washed with three 15 mL portions of CH_2Cl_2. The filtrate was concentrated to provide 0.473 g (95%) of aldehyde **31** as a

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pale yellow solid: mp 92−93.5 °C; IR (KBr pellet) 3291, 2957, 2930, 2858, 2711, 1753, 1734, 1678, 1615, 1582, 1509, 1461, 1432, 1402, 1379, 1342, 1292, 1254, 1194, 1131, and 1077 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ca. 78:22 mixture of rotamers) (major rotamer) δ 9.70 (s, 1H), 8.62 (s, 1H), 6.77 (s, 1H), 6.60 (s, 1H), 4.44 (d, J = 18.3 Hz, 1H), 4.08 (d, J = 18.3 Hz, 1H), 3.87 (t, J = 4.8 Hz, 2H), 3.67 (s, 3H), 2.88 (t, J = 5.0 Hz, 2H), 2.52 (t, J = 7.8 Hz, 2H), 1.56 (app quintet, J = 7.6 Hz, 2H), 1.34 (app sextet, J = 7.4 Hz, 2H), 0.92 (s, 9H), 0.88−0.95 (m, 3H), 0.10 (s, 3H), and 0.09 (s, 3H); additional resonances appeared for the minor rotamer at δ 8.72 (s, 1H), 4.36 (d, J = 18.8 Hz, 1H), 4.14 (d, J = 18.8 Hz, 1H), and 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 157.0, 156.8, 143.9, 140.8, 122.3, 119.6, 117.4, 65.0, 61.0, 53.5, 35.2, 33.2, 29.2, 25.9, 22.5, 18.4, 14.1, and −5.4. Anal. Calcd for $C_{22}H_{37}NO_5Si$: C, 62.38; H, 8.80; N, 3.31. Found: C, 62.38; H, 8.67; N, 3.36.

4-Butyl-6-hydroxy-1-(methoxycarbonyl)-7-methylindole (33). A 100 mL, one-necked, recovery flask equipped with a rubber septum and argon inlet needle was charged with aldehyde **30** (0.186 g, 0.67 mmol, 1.0 equiv), 44 mL of 2-propanol, and DBU (0.050 mL, 0.051 g, 0.34 mmol, 0.5 equiv). The colorless solution was heated at 65 °C for 100 min, during which time the color changed to pale yellow. The reaction mixture was allowed to cool to room temperature and then treated with 5 mL of aq 1 M HCl solution to adjust the pH to 7. The resulting mixture was concentrated to a volume of ca. 5 mL and then diluted with 50 mL of Et_2O, washed with 15 mL of H_2O and 15 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to afford 0.175 g of a pale orange solid. This material was dissolved in 5 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The free-flowing powder was added to the top of a column of 11 g of silica gel and eluted with 20% EtOAc−hexanes to give 0.129 g (74%) of indole **33** as a white solid: mp 75−77 °C; IR (film) 3411, 2956, 2923, 2857, 1708, 1602, 1451, 1382, 1343, 1278, 1075, 1028, and 1018 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 4.0 Hz, 1H), 6.67 (s, 1H), 6.56 (d, J = 4.0 Hz, 1H), 4.94 (s, 1H), 3.99 (s, 3H), 2.75 (t, J = 7.6 Hz, 2H), 2.42 (s, 3H), 1.64 (app quintet, J = 7.7 Hz, 2H), 1.39 (app sextet, J = 7.4 Hz, 2H), and 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 152.1, 136.3, 133.6, 126.5, 125.2, 112.5, 109.0, 106.7, 54.1, 33.1, 32.5, 22.7, 14.2, and 13.6. Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.78; H, 7.32; N, 5.31.

4-Butyl-6-hydroxy-7-(2-hydroxyethyl)-1-(methoxycarbonyl)-indole (34). A 100 mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with aldehyde **31** (0.250 g, 0.59 mmol, 1.0 equiv), 30 mL of 2-propanol, and K_2CO_3 (0.082 g, 0.59 mmol, 1.0 equiv). The septum was replaced by a coldfinger condenser fitted with an argon inlet, and the colorless mixture was heated at 75−80 °C for 2 h, during which time the color changed to yellow. The reaction mixture was allowed to cool to room temperature and then diluted with 15 mL of H_2O and treated with 5 mL of 1 M HCl solution to adjust the pH to 1. The resulting mixture was concentrated to a volume of ca. 10 mL and diluted with 70 mL of Et_2O, washed with two 30 mL portions of H_2O and 30 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to afford 0.177 g of a brown oil. This material was dissolved in 5 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The free-flowing powder was added to the top of a column of 14 g of silica gel and eluted with 10% EtOAc−benzene to give 0.128 g (74%) of indole **34** as a white solid: mp 129−130.5 °C; IR (KBr pellet) 3409, 3184, 2953, 2840, 1754, 1723, 1597, 1440, 1392, 1342, 1271, 1208, and 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.45 (d, J = 4.0 Hz, 1H), 6.82 (s, 1H), 6.56 (d, J = 4.0 Hz, 1H), 4.34−4.37 (m, 2H), 3.94 (s, 3H), 3.12 (t, J = 4.8 Hz, 2H), 2.77 (t, J = 7.7 Hz, 2H), 2.36 (t, J = 3.5 Hz, 1H), 1.66 (app quintet, J = 7.6 Hz, 2H), 1.40 (app sextet, J = 7.4 Hz, 2H), and 0.94 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 152.3, 136.0, 135.0, 125.9, 125.0, 114.3, 112.1, 107.0, 66.1, 54.1, 33.0, 32.5, 30.8, 22.7, and 14.2. Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.94; H, 7.41; N, 4.85.

General Procedure for the Synthesis of Highly Substituted Aniline Derivatives: Method B, via Benzannulation of Cyclobutenones and Ynamides in Toluene at Reflux. *N*-(*tert*-Butoxycarbonyl)-*N*-methyl(5-butyl-3-hydroxy-2-prop-2-enylphenyl)amine (35). A 25 mL, one-necked, round-bottomed flask equipped with a reflux condenser fitted with an argon inlet adapter was charged with ynamide **20** (0.430 g, 2.20 mmol, 1.0 equiv), cyclobutenone **26** (0.362 g, 2.90 mmol, 1.3 equiv), and 2.8 mL of toluene. The light brown solution was heated at reflux for 80 min, allowed to cool to room temperature, and then concentrated to give 0.830 g of a brown oil. Column chromatography on 90 g of silica gel (elution with 10% EtOAc−hexanes) provided 0.635 g (90%) of **35** as a light yellow solid: mp 82−85 °C; IR (film) 3323, 3077, 2958, 2931, 2859, 1668, 1616, 1584, 1435, 1385, 1367, 1340, 1253, and 1156 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, mixture of two rotamers) (major rotamer) δ 6.62 (s, 1H), 6.54 (s, 1H), 5.92−6.00 (m, 1H), 5.11−5.18 (m, 2H), 5.07 (s, 1H), 3.24−3.36 (m, 2H), 3.10 (s, 3H), 2.53 (t, J = 7.5 Hz, 2H), 1.49−1.60 (m, 4H), 1.33 (s, 9H), and 0.91 (t, J = 7.3 Hz, 3H); for the minor rotamer the resonance of the *tert*-butyl group appears at δ 1.52 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, mixture of two rotamers) (major rotamer) δ 155.7, 155.2, 143.1, 142.7, 136.1, 120.3, 120.1, 116.1, 115.0, 80.4, 37.7, 35.1, 33.4, 29.9, 28.4, 22.2, and 14.1; (minor rotamer) δ 155.7, 155.2, 143.1, 142.7, 137.0, 121.4, 119.5, 115.5, 115.2, 79.9, 38.6, 35.3, 33.2, 30.2, 28.6, 22.6, and 14.1; HRMS m/z $[M + Na]^+$ calcd for $C_{19}H_{29}NO_3$ 342.2040, found 342.2039. Anal. Calcd for $C_{19}H_{29}NO_3$: C, 71.44; H, 9.15; N, 4.38. Found: C, 71.49; H, 9.15; N, 4.38.

5-Butyl-3-(methylamino)-2-prop-2-enylphenol (36). A 25 mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with carbamate **35** (0.217 g, 0.679 mmol, 1.0 equiv), 7 mL of CH_2Cl_2, and trifluoroacetic acid (0.78 mL, 1.2 g, 10 mmol, 15 equiv). The brown solution was stirred at room temperature for 1 h and then diluted with 5 mL of CH_2Cl_2 and washed with 5 mL of saturated $NaHCO_3$ solution. The aqueous layer was neutralized to pH 7 by dropwise addition of aq 1 M HCl solution and then extracted with three 5 mL portions of CH_2Cl_2. The combined organic layers were washed with 20 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to give 0.149 g (100%) of phenol **36** as a brown oil which darkened upon storage: IR (film) 3433, 3361, 3076, 2956, 2929, 2857, 2815, 1633, 1618, 1589, 1529, 1454, 1419, 1313, 1204, and 1123 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.12 (s, 1H), 6.10 (s, 1H), 5.92 (ddt, J = 16.8, 10.4, 5.6 Hz, 1H), 5.05−5.11 (m, 2H), 4.54 (s, 1H), 3.74 (br s, 1H), 3.33 (dt, J = 5.6, 2.0 Hz, 2H), 2.84 (s, 3H), 2.52 (t, J = 7.8 Hz, 2H), 1.55−1.63 (m, 2H), 1.37 (app sextet, J = 7.4 Hz, 2H), and 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 148.8, 143.2, 136.0, 115.3, 107.0, 105.5, 103.9, 36.0, 33.6, 31.3, 28.1, 22.7, and 14.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{14}H_{21}NO$ 220.1696, found 220.1700.

6-Butyl-4-hydroxy-1,2-dimethylindole (37). A 25 mL, one-necked, round-bottomed flask equipped with a coldfinger condenser with argon inlet side arm was charged with $PdCl_2(CH_3CN)_2$ (0.018 g, 0.069 mmol, 0.1 equiv), benzoquinone (0.072 g, 0.67 mmol, 1.0 equiv), and 6.5 mL of THF. The orange solution was stirred for 5 min, and a solution of aniline **36** (0.146 g, 0.67 mmol, 1.0 equiv) in 7 mL of THF was added via syringe. The resulting dark orange solution was heated at reflux for 12 h and then allowed to cool to room temperature. The reaction mixture was filtered through a 1.5 cm pad of silica gel in a 30 mL sintered glass funnel with the aid of three 20 mL portions of Et_2O. The orange filtrate was concentrated to give 0.264 g of a dark brown oil, which was dissolved in 5 mL of CH_2Cl_2 and concentrated onto 1.5 g of silica gel. The free-flowing powder was added to the top of a column of 23 g of silica gel and eluted with 5−10% EtOAc−hexanes to give 0.120 g (82%) of indole **37** as a pale yellow solid: mp 95−96 °C; IR (KBr pellet) 3461, 3404, 2954, 2924, 2854, 1624, 1583, 1552, 1473, 1445, 1425, 1350, 1222, and 1019 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.69 (s, 1H), 6.37 (s, 1H), 6.21 (s, 1H), 4.77 (s, 1H), 3.62 (s, 3H), 2.68 (t, J = 7.5 Hz, 2H), 2.41 (s, 3H), 1.65 (app quintet, J = 7.6 Hz, 2H), 1.39 (app sextet, J = 7.4 Hz, 2H), and 0.94 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 139.6, 137.1, 135.3, 115.2, 105.3, 101.8, 95.3, 36.3, 34.5, 29.9, 22.6, 14.3, and 13.0. Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.41; H, 8.82; N, 6.53.

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***N*-Benzyl-*N*-[[2-(trimethylsilyl)ethoxy]carbonyl][5-butyl-3-hydroxy-2-(2,2-dimethoxyethyl)phenyl]amine (47).** Reaction of a solution of ynamide **21** (0.657 g, 1.81 mmol, 1.0 equiv) and cyclobutenone **26** (0.256 g, 2.06 mmol, 1.1 equiv) in 2.0 mL of toluene at reflux for 100 min according to general procedure B provided 0.864 g of a yellow oil, which was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 5 g of silica gel. The free-flowing powder was added to the top of a column of 85 g of silica gel and eluted with 15% EtOAc–hexanes to afford 0.748 g (85%) of acetal **47** as a viscous yellow oil: IR (film) 3321, 2954, 2932, 1700, 1670, 1624, 1572, 1437, 1408, 1361, 1315, 1296, 1251, and 1115 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, ca. 72:28 mixture of rotamers) (major rotamer) δ 8.03 (s, 1H), 7.15–7.30 (m, 5H), 6.70 (d, J = 1.5 Hz, 1H), 6.30 (s, 1H), 4.81 (d, J = 14.0 Hz, 1H), 4.61 (d, J = 14.0 Hz, 1H), 4.10–4.50 (m, 3H), 3.39 (br s, 3H), 3.32 (br s, 3H), 2.62 (d, J = 5.3 Hz, 2H), 2.48 (t, J = 7.6 Hz, 2H), 1.51 (app quintet, J = 7.6 Hz, 2H), 1.30 (app sextet, J = 7.4 Hz, 2H), 0.92 (t, J = 7.4 Hz, 3H), 0.89 (br s, 2H), and −0.05 (s, 9H); additional resonances appeared for the minor rotamer at δ 6.40 (s, 1H), 1.17 (br s, 2H), and 0.11 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 156.5, 143.4, 141.0, 137.6, 129.6, 128.5, 127.8, 121.2, 118.9, 117.1, 105.6, 64.2, 54.8, 53.6, 35.2, 33.2, 30.5, 22.3, 17.9, 14.1, and −1.5 (one additional resonance at 129.1 for the minor rotamer); HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{27}H_{41}NO_5Si$ 510.2646, found 510.2635.

***N*-Benzyl-*N*-[[2-(trimethylsilyl)ethoxy]carbonyl][3-hydroxy-2-(2,2-dimethoxyethyl)-5-phenylphenyl]amine (48).** Reaction of a solution of ynamide **21** (0.350 g, 0.96 mmol, 1.0 equiv) and cyclobutenone **43**[11] (0.138 g, 0.96 mmol, 1.0 equiv) in 1.2 mL of toluene at reflux for 90 min according to general procedure B gave 0.501 g of a viscous yellow oil. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 2.5 g of silica gel. The free-flowing powder was added to the top of a column of 45 g of silica gel and eluted with 0–20% EtOAc–hexanes to provide 0.383 g (79%) of acetal **48** as a viscous yellow oil: IR (film) 3305, 3032, 2952, 2833, 1699, 1668, 1621, 1563, 1454, 1409, 1322, 1250, 1115, and 1069 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ca. 73:27 mixture of rotamers) (major rotamer) δ 8.21 (s, 1H), 7.17–7.49 (m, 10H), 7.14 (d, J = 1.8 Hz, 1H), 6.75 (s, 1H), 4.86 (d, J = 14.1 Hz, 1H), 4.72 (d, J = 14.3 Hz, 1H), 4.07–4.50 (m, 3H), 3.40 (s, 3H), 3.32 (s, 3H), 2.65 (d, J = 4.4 Hz, 2H), 0.81–0.94 (m, 2H), and −0.08 (s, 9H); additional resonances appeared for the minor rotamer at δ 8.26 (s, 1H), 6.86 (s, 1H), 1.08–1.21 (m, 2H), and 0.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 156.4, 141.7, 141.4, 140.0, 137.5, 129.7, 128.8, 128.6, 127.9, 127.6, 126.9, 120.9, 119.8, 115.6, 105.5, 64.4, 54.9, 53.7, 30.6, 17.9, and −1.4; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{29}H_{37}NO_5Si$ 530.2333, found 530.2316.

***N*-Benzyl-*N*-[[2-(trimethylsilyl)ethoxy]carbonyl][5-ethoxy-3-hydroxy-2-(2,2-dimethoxyethyl)phenyl]amine (49).** Reaction of a solution of ynamide **21** (0.360 g, 0.99 mmol, 1.0 equiv) and cyclobutenone **44**[46] (0.168 g, 1.50 mmol, 1.5 equiv) in 1.2 mL of toluene at reflux for 90 min according to general procedure B gave 0.539 g of a dark brown oil. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 3 g of silica gel. The free-flowing powder was added to the top of a column of 51 g of silica gel and eluted with 20% EtOAc–hexanes to provide 0.289 g (61%) of **49** as a yellow solid: mp 103–105 °C; IR (KBr pellet) 3333, 2985, 2961, 1659, 1617, 1589, 1512, 1438, 1375, 1324, 1283, 1173, 1125, and 1042 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ca. 75:25 mixture of rotamers) (major rotamer) δ 8.17 (s, 1H), 7.13–7.34 (m, 5H), 6.44 (d, J = 2.6 Hz, 1H), 6.12 (s, 1H), 4.73 (s, 2H), 3.96–4.43 (m, 3H), 3.79–3.95 (m, 2H), 3.35 (s, 3H), 3.27 (s, 3H), 2.51 (d, J = 5.1 Hz, 2H), 1.34 (t, J = 6.9 Hz, 3H), 0.82–0.96 (m, 2H), and −0.06 (s, 9H); additional resonances appeared for the minor rotamer at δ 6.20 (s, 1H), 1.04–1.22 (m, 2H), and 0.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 157.6, 156.2, 141.9, 137.4, 129.5, 128.5, 127.7, 114.1, 107.5, 105.6, 103.3, 64.3, 63.4, 54.7, 53.6, 30.2, 17.9, 14.8, and −1.5. Anal. Calcd for $C_{25}H_{37}NO_6Si$: C, 63.13; H, 7.84; N, 2.94. Found: C, 63.09; H, 7.85; N, 2.89.

***N*-Benzyl-*N*-[[2-(trimethylsilyl)ethoxy]carbonyl][3-hydroxy-2-(2,2-dimethoxyethyl)-5-(tributylstannyl)phenyl]amine (50).** Reaction of a solution of ynamide **21** (0.587 g, 1.61 mmol, 1.0 equiv) and cyclobutenone **45**[47] (0.688 g, 1.93 mmol, 1.2 equiv) in 2.0 mL of toluene at reflux for 2 h according to general procedure B gave 1.301 g of a brown oil. Column chromatography on 60 g of silica gel (elution with 15% EtOAc–hexanes) afforded 1.011 g (87%) of **50** as a golden brown oil: IR (film) 3324, 2955, 2927, 2852, 1700, 1669, 1550, 1456, 1410, 1359, 1289, 1249, 1116, and 1040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ca. 74:26 mixture of rotamers) (major rotamer) δ 8.02 (s, 1H), 7.13–7.32 (m, 5H), 6.97 (s, 1H), 6.51 (s, 1H), 4.87 (d, J = 14.1 Hz, 1H), 4.57 (d, J = 14.1 Hz, 1H), 4.08–4.53 (m, 3H), 3.38 (br s, 3H), 3.31 (br s, 3H), 2.64 (d, J = 4.7 Hz, 2H), 1.37–1.58 (m, 6H), 1.30 (app sextet, J = 7.3 Hz, 6H), 0.99–1.20 (m, 2H), 0.96 (t, J = 8.1 Hz, 6H), 0.88 (t, J = 7.3 Hz, 9H), and −0.09 (s, 9H); additional resonances appeared for the minor rotamer at δ 8.08 (s, 1H) and 0.09 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 156.0, 142.3, 140.6, 137.5, 129.5, 128.8, 128.5, 127.7, 124.6, 121.3, 105.5, 64.2, 54.9, 53.5, 30.7, 29.1, 27.4, 17.8, 13.8, 9.6, and −1.4 (one additional resonance at 54.8 for the minor rotamer); HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{35}H_{59}NO_5SiSn$ 744.3094, found 744.3063.

***N*-Benzyl-*N*-[[2-(trimethylsilyl)ethoxy]carbonyl][3-hydroxy-2-(2,2-dimethoxyethyl)-5,6-dimethylphenyl]amine (51).** A threaded Pyrex tube (13 mm o.d., 10.2 cm length) equipped with a rubber septum and argon inlet needle was charged with ynamide **21** (0.172 g, 0.47 mmol, 1.0 equiv), cyclobutenone **46**[48] (0.083 g, 0.86 mmol, 1.8 equiv), and 1.0 mL of toluene. The yellow solution was degassed (three freeze–pump–thaw cycles at −196 °C, 0.05 mmHg), and then the tube was sealed with a threaded Teflon cap. The reaction mixture was heated at 145 °C for 49 h, allowed to cool to room temperature, and then concentrated to give 0.252 g of a yellow oil. Filtration through a column of silica gel (3 cm wide, 1 cm high) with the aid of 50 mL of 20% EtOAc–hexanes and concentration gave 0.237 g of an ester derivative of the desired product. This material was transferred to a 25 mL, one-necked, round-bottomed flask equipped with a coldfinger condenser with an argon inlet side arm, and 2 mL of MeOH and 2 mL of 5 M KOH solution were added. The reaction mixture was heated at 65–70 °C for 2.5 h and then allowed to cool to room temperature. The resulting brown mixture was diluted with 30 mL of Et_2O and washed with 15 mL of 1 M HCl solution. The pH of the aqueous layer was adjusted to 7 using ca. 2 mL of 10% NaOH solution and then extracted with two 15 mL portions of Et_2O. The combined organic layers were washed with 30 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to provide 0.213 g of a yellow oil. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The free-flowing powder was added to the top of a column of 11 g of silica gel and eluted with 15% EtOAc–hexanes to afford 0.182 g of a yellow oil. This material was further purified by column chromatography on 15 g of silica gel (elution with 15% EtOAc–hexanes) to give 0.144 g of a pale yellow oil. This material was taken up in 25 mL of Et_2O, washed with three 10 mL portions of saturated $NaHCO_3$ solution and 15 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to provide 0.137 g (63%) of acetal **51** as a pale yellow oil: IR (film) 3328, 3031, 2951, 2834, 1698, 1619, 1575, 1495, 1456, 1408, 1361, 1312, 1251, and 1116 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ca. 80:20 mixture of rotamers) (major rotamer) δ 7.81 (s, 1H), 7.06–7.28 (m, 5H), 6.72 (s, 1H), 4.91 (d, J = 14.0 Hz, 1H), 4.25 (d, J = 13.9 Hz, 1H), 3.99–4.35 (m, 3H), 3.28 (s, 3H), 3.14 (s, 3H), 2.35 (d, J = 5.3 Hz, 2H), 2.17 (s, 3H), 1.79 (s, 3H), 0.76–0.92 (m, 2H), and −0.12 (s, 9H); additional resonances appeared for the minor rotamer at δ 7.79 (s, 1H), 4.87 (d, J = 14.0 Hz, 1H), 3.30 (s, 3H), 3.16 (s, 3H), 1.88 (s, 3H), 1.12–1.17 (m, 2H), and 0.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, mixture of two rotamers) (major rotamer) δ 156.6, 154.0, 139.7, 137.6, 137.1, 130.1, 128.5, 127.9, 126.3, 119.2, 118.7, 105.6, 64.2, 55.1, 54.5, 52.8, 31.1, 20.6, 18.0, 14.3, and −1.5; (minor rotamer) δ 155.7, 154.1, 140.1, 137.7, 136.9, 129.8, 128.5, 128.0, 126.2, 119.7, 118.9, 105.8, 64.3, 55.6, 54.3, 52.8, 31.1, 20.6, 18.2, 14.4, and −1.2; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{25}H_{37}NO_5Si$ 482.2333, found 482.2334.

***N*-Benzyl-*N*-[[2-(trimethylsilyl)ethoxy]carbonyl][3-hydroxy-5-iodo-2-(2,2-dimethoxyethyl)phenyl]amine (52).** A 25 mL, one-

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necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with arylstannane **50** (0.398 g, 0.55 mmol, 1.0 equiv), 11 mL of THF, and *N*-iodosuccinimide (0.149 g, 0.66 mmol, 1.2 equiv). The flask was wrapped in aluminum foil, and the reaction mixture was stirred at room temperature for 2 h and then concentrated to a volume of ca. 0.5 mL. CH_2Cl_2 (ca. 20 mL) was added to give a pink solution, which was divided equally into two 50 mL, one-necked, round-bottomed flasks equipped with argon inlet adapters. A 1 M NaOH solution (10 mL) was added to each flask.[49] The resulting mixtures were stirred vigorously for 2 h and then combined. The aqueous layer was separated, and the organic layer was washed with 20 mL of 1 M NaOH solution. The combined aqueous phases were adjusted to pH 7 with ca. 14 mL of 10% HCl solution and then extracted with two 15 mL portions of CH_2Cl_2. The combined organic layers were washed with 40 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to give 0.467 g of a yellow oil. Column chromatography on 45 g of silica gel (elution with 20% EtOAc–hexanes) afforded 0.303 g of a pale yellow oil. This was further purified by column chromatography on 30 g of silica gel (elution with 20% EtOAc–hexanes) to provide 0.260 g (85%) of aryl iodide **52** as a yellow oil: IR (film) 3266, 3031, 2952, 2833, 1700, 1667, 1593, 1574, 1495, 1454, 1408, 1360, 1285, 1249, 1178, 1115, and 1069 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ca. 68:32 mixture of rotamers) (major rotamer) δ 8.26 (s, 1H), 7.27–7.33 (m, 3H), 7.23 (app d, J = 2.0 Hz, 2H), 7.20 (s, 1H), 6.90 (s, 1H), 4.77 (d, J = 14.4 Hz, 1H), 4.63 (d, J = 14.1 Hz, 1H), 3.89–4.46 (m, 3H), 3.34 (s, 3H), 3.25 (s, 3H), 2.42–2.61 (m, 2H), 0.88 (br s, 2H), and −0.06 (s, 9H); additional resonances appeared for the minor rotamer at δ 9.23 (s, 1H), 4.79 (d, J = 14.4 Hz, 1H), 1.13 (br s, 2H), and 0.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) (major rotamer) δ 157.5, 155.9, 142.2, 136.9, 129.5, 128.6, 128.0, 126.3, 122.4, 105.0, 100.4, 91.8, 64.5, 54.8, 53.6, 30.6, 17.9, and −1.4; additional resonances appeared for the minor rotamer at δ 136.8, 129.8, 128.7, 128.1, 104.7, 64.7, and 54.7; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{23}H_{32}INO_5Si$ 580.0987, found 580.0973.

***N*-Benzyl-*N*-[[2-(trimethylsilyl)ethoxy]carbonyl][5-benzoyl-3-hydroxy-2-(2,2-dimethoxyethyl)phenyl]amine (53).** A 25 mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with $PdCl_2(MeCN)_2$ (0.007 g, 0.026 mmol, 0.05 equiv), and then the flask was evacuated and filled with argon (three cycles). Arylstannane **50** (0.374 g, 0.52 mmol, 1.0 equiv), 5.2 mL of acetonitrile, and benzoyl chloride (0.069 mg, 0.057 mL, 0.49 mmol, 0.95 equiv) were then added. The resulting brown solution was stirred at room temperature for 2.5 h, and then $PdCl_2(MeCN)_2$ (0.0035 g, 0.013 mmol, 0.025 equiv) was added in one portion. The reaction mixture was stirred for 2.5 h and then diluted with 50 mL of acetonitrile and washed with four 50 mL portions of hexanes to remove tin byproducts. The acetonitrile layer was concentrated to provide 0.272 g of a brown oil, which was purified by column chromatography on 15 g of silica gel (elution with 30% EtOAc–hexanes) to afford 0.222 g of a light tan oil consisting of a mixture of the desired ketone and tin byproducts. This material was dissolved in ca. 5 mL of CH_2Cl_2 and concentrated onto 1.2 g of silica gel. The free-flowing powder was added to the top of a column of 20 g of silica gel and eluted with 25% EtOAc–hexanes to give 0.195 g (70%) of ketone **53** as a colorless paste: IR (film) 3289, 2953, 2834, 1699, 1660, 1598, 1576, 1495, 1422, 1366, 1323, 1249, 1178, 1116, and 1069 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, ca. 70:30 mixture of rotamers) (major rotamer) δ 8.40 (s, 1H), 7.68 (app d, J = 7.1 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.43 (app t, J = 7.7 Hz, 2H), 7.37 (s, 1H), 7.16–7.34 (m, 5H), 6.98 (s, 1H), 4.67–4.97 (m, 2H), 4.10–4.58 (m, 3H), 3.42 (s, 3H), 3.34 (s, 3H), 2.75 (br s, 2H), 0.81–0.99 (m, 2H), and −0.05 (s, 9H); additional resonances appeared for the minor rotamer at δ 7.14 (s, 1H), 1.07–1.26 (m, 2H), and 0.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 156.9, 156.1, 141.2, 137.5, 137.1, 137.0, 132.4, 129.9, 129.4, 128.6, 128.3, 127.9, 127.1, 122.9, 118.4, 104.9, 64.5, 54.8, 54.6, 53.7, 31.0, 17.8, and −1.5; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{30}H_{37}NO_6Si$ 558.2282, found 558.2261.

General Procedure for the Synthesis of Indoles from Benzannulation Products Derived from Ynamide 21. 1-Benzyl-6-butyl-4-hydroxyindole (54). A 25 mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with carbamate **47** (0.302 g, 0.62 mmol, 1.0 equiv) and 3.1 mL of THF, and the resulting solution was cooled at 0 °C while TBAF solution (1 M in THF, 3.1 mL, 3.1 mmol, 5.0 equiv) was added dropwise over 3 min. The brown reaction mixture was stirred at room temperature for 8 h and then cooled to 0 °C and treated with 6 M aq HCl (3.1 mL, 18.6 mmol, 30 equiv) dropwise over 3 min. The rubber septum was replaced by an argon inlet adapter, and the pale yellow solution was stirred at room temperature for 20 h. During this time the reaction mixture turned green and then dark blue. The reaction mixture was diluted with 50 mL of Et_2O and washed with two 25 mL portions of saturated $NaHCO_3$ solution. The combined aqueous layers were extracted with two 20 mL portions of Et_2O, and the combined organic phases were washed with 40 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to provide 0.204 g of a brown oil. This material was dissolved in ca. 5 mL of CH_2Cl_2 and concentrated onto 0.9 g of silica gel. The free-flowing powder was added to the top of a column of 12 g of silica gel and eluted with 15% EtOAc–hexanes to give 0.146 g (84%) of indole **54** as a pale brown solid: mp 81.5–83 °C; IR (film) 3398, 2955, 2927, 2856, 1629, 1576, 1508, 1495, 1465, 1453, 1373, and 1242 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27–7.35 (m, 3H), 7.12 (app d, J = 6.9 Hz, 2H), 6.99 (d, J = 3.2 Hz, 1H), 6.81 (s, 1H), 6.53 (d, J = 3.2 Hz, 1H), 6.40 (s, 1H), 5.28 (s, 2H), 4.85 (s, 1H), 2.63 J = 7.7 Hz, 2H), 1.60 (app quintet, J = 7.6 Hz, 2H), 1.34 (app sextet, J = 7.4 Hz, 2H), and 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7, 138.7, 138.5, 137.8, 128.9, 127.7, 127.0, 126.8, 116.3, 105.4, 102.5, 97.8, 50.3, 36.6, 34.3, 22.6, and 14.2. Anal. Calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.47; H, 7.59; N, 4.93.

1-Benzyl-4-hydroxy-6-phenylindole (55). Reaction of carbamate **48** (0.294 g, 0.58 mmol, 1.0 equiv) with TBAF (1 M in THF, 2.9 mL, 2.9 mmol, 5.0 equiv) in 2.9 mL of THF for 5 h and then with 6 M aq HCl (2.9 mL, 17.4 mmol, 30 equiv) for 16 h according to the general procedure provided 0.222 g of a brown oil. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 1.5 g of silica gel. The free-flowing powder was added to the top of a column of 12 g of silica gel and eluted with 20% EtOAc–hexanes to give 0.136 g (78%) of indole **55** as a pale yellow solid: mp 117–119 °C; IR (KBr pellet) 3434, 3098, 3058, 3025, 2929, 1624, 1571, 1502, 1465, 1433, 1373, 1246, and 1182 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (app dd, J = 8.3, 1.2 Hz, 2H), 7.42 (app t, J = 7.6 Hz, 2H), 7.31 (app d, J = 7.3 Hz, 1H), 7.28–7.35 (m, 3H), 7.15 (app d, J = 6.6 Hz, 2H), 7.11 (s, 1H), 7.10 (d, J = 3.2 Hz, 1H), 6.81 (d, J = 1.2 Hz, 1H), 6.61 (dd, J = 3.2, 0.8 Hz, 1H), 5.36 (s, 2H), and 5.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.2, 142.2, 138.9, 137.4, 136.8, 128.9, 128.8, 127.9, 127.8, 127.5, 126.9, 126.9, 117.6, 104.3, 101.8, 98.1, and 50.4. Anal. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68. Found: C, 84.10; H, 5.64; N, 4.51.

1-Benzyl-6-ethoxy-4-hydroxyindole (56). Reaction of carbamate **49** (0.205 g, 0.43 mmol, 1.0 equiv) with TBAF (1 M in THF, 2.2 mL, 2.2 mmol, 5.1 equiv) in 2.2 mL of THF for 7 h and then with 6 M aq HCl (2.2 mL, 13.2 mmol, 31 equiv) for 19 h according to the general procedure provided 0.138 g of a brown oil. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 0.5 g of silica gel. The free-flowing powder was added to the top of a column of 6 g of silica gel and eluted with 20% EtOAc–hexanes to give 0.098 g (85%) of indole **56** as a pale yellow solid: mp 122.5–124.5 °C; IR (KBr pellet) 3381, 3029, 2979, 2900, 1630, 1596, 1506, 1476, 1452, 1436, 1400, 1252, 1166, 1129, and 1050 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23–7.35 (m, 3H), 7.11 (app d, J = 6.8 Hz, 2H), 6.95 (d, J = 3.3 Hz, 1H), 6.50 (d, J = 3.2 Hz, 1H), 6.37 (d, J = 1.3 Hz, 1H), 6.25 (d, J = 1.9 Hz, 1H), 5.23 (s, 2H), 4.96 (s, 1H), 3.99 (q, J = 7.0 Hz, 2H), and 1.39 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 149.5, 138.5, 137.6, 128.9, 127.7, 126.9, 126.1, 112.8, 98.0, 95.3, 87.6, 64.1, 50.3, and 15.0. Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.46; H, 6.30; N, 5.09.

1-Benzyl-4-hydroxy-6-iodoindole (57). Reaction of carbamate **52** (0.237 g, 0.43 mmol, 1.0 equiv) with TBAF (1 M in THF, 2.2 mL, 2.2 mmol, 5.1 equiv) in 2.2 mL of THF for 7 h and then with 6 M aq

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HCl (2.2 mL, 13.2 mmol, 31 equiv) for 20 h according to the general procedure provided 0.152 g of a red-brown oil.[50] This crude material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 0.7 g of silica gel. The free-flowing powder was added to the top of a column of 15 g of silica gel and eluted with 20% EtOAc–hexanes to give 0.078 g (53%) of indole **57** as a pink solid: mp 141–143 °C; IR (KBr pellet) 3328, 2921, 1617, 1567, 1496, 1462, 1435, 1351, 1297, 1239, and 1201 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.26–7.34 (m, 3H), 7.27 (s, 1H), 7.07–7.11 (m, 2H), 7.04 (d, J = 3.2 Hz, 1H), 6.82 (d, J = 1.2 Hz, 1H), 6.55 (dd, J = 3.2, 0.8 Hz, 1H), 5.25 (s, 2H), and 5.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.5, 139.3, 137.0, 129.0, 128.0, 127.5, 126.8, 118.0, 113.4, 112.4, 98.5, 85.5, and 50.4. Anal. Calcd for $C_{15}H_{12}INO$: C, 51.60; H, 3.46; N, 4.01. Found: C, 51.48; H, 3.31; N, 4.29.

6-Benzoyl-1-benzyl-4-hydroxyindole (58). Reaction of carbamate **53** (0.277 g, 0.52 mmol, 1.0 equiv) with TBAF (1 M in THF, 2.6 mL, 2.6 mmol, 5.0 equiv) in 2.6 mL of THF for 7 h and then with 6 M aq HCl (2.6 mL, 15.6 mmol, 30 equiv) for 20 h according to the general procedure provided 0.197 g of a dark yellow solid. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 1.2 g of silica gel. The free-flowing powder was added to the top of a column of 10 g of silica gel and eluted with 30% EtOAc–hexanes to give 0.164 g of a yellow solid. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The free-flowing powder was added to the top of a column of 8 g of silica gel and eluted with 25% EtOAc–hexanes to give 0.147 g (87%) of indole **58** as a yellow solid with low solubility in CH_2Cl_2 and $CDCl_3$: mp 160–162 °C; IR (KBr pellet) 3390, 1625, 1570, 1497, 1472, 1384, and 1248 cm^{-1}; ^1H NMR (500 MHz, $(CD_3)_2O$) δ 8.84 (s, 1H), 7.66 (app d, J = 7.9 Hz, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.54 (d, J = 3.1 Hz, 1H), 7.47 (app t, J = 7.6 Hz, 2H), 7.39 (s, 1H), 7.24–7.35 (m, 3H), 7.17 (app d, J = 7.2 Hz, 2H), 7.05 (s, 1H), 6.75 (d, J = 3.1 Hz, 1H), and 5.44 (s, 2H); ^{13}C NMR (100 MHz, $(CD_3)_2O$) δ 196.6, 151.4, 139.8, 138.7, 137.8, 132.8, 132.4, 131.7, 130.5, 129.5, 128.9, 128.4, 127.9, 123.4, 107.6, 105.5, 99.9, and 50.9. Anal. Calcd for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.60; H, 5.31; N, 4.12.

1-Benzyl-4-hydroxy-6,7-dimethylindole (59). Reaction of carbamate **51** (0.263 g, 0.57 mmol, 1.0 equiv) with TBAF (1 M in THF, 3.0 mL, 3.0 mmol, 5.3 equiv) in 3.0 mL of THF for 8 h and then with 6 M aq HCl (3.0 mL, 18.0 mmol, 32 equiv) for 18 h according to the general procedure provided 0.173 g of a brown foam. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The free-flowing powder was added to the top of a column of 18 g of silica gel and eluted with 20% EtOAc–hexanes to give 0.107 g (74%) of indole **59** as a pale yellow solid: mp 115.5–117.5 °C; IR (KBr pellet) 3327, 2981, 2901, 1625, 1585, 1502, 1450, 1423, 1385, 1350, 1228, 1211, and 1097 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.21–7.35 (m, 3H), 6.96 (d, J = 3.2 Hz, 2H), 6.95 (app d, J = 7.4 Hz, 2H), 6.57 (d, J = 3.2 Hz, 1H), 6.41 (s, 1H), 5.59 (s, 2H), 4.85 (s, 1H), 2.34 (s, 3H), and 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 139.8, 137.3, 131.0, 129.6, 129.0, 127.4, 125.6, 118.0, 112.1, 107.5, 97.7, 52.7, 20.6, and 13.9. Anal. Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.19; H, 6.85; N, 5.64.

1-Benzyl-4-hydroxy-6-[(triisopropylsilyl)ethynyl]indole (60). A 25 mL, one-necked, recovery flask equipped with a rubber septum and argon inlet needle was charged with iodide **57** (0.046 g, 0.13 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (0.005 g, 0.007 mmol, 0.05 equiv), and CuI (0.001 g, 0.005 mmol, 0.04 equiv). The flask was evacuated and filled with argon (three cycles), and then 1.8 mL of Et_3N and (triisopropylsilyl)acetylene (0.029 g, 0.035 mL, 0.16 mmol, 1.2 equiv) were added. The resulting pale brown mixture was stirred at room temperature for 13 h and then filtered through a 4 cm column of silica gel in a 1 cm wide column with the aid of 20 mL of EtOAc. The filtrate was concentrated to a thick paste and then dissolved in 20 mL of EtOAc, washed with 15 mL of H_2O and 15 mL of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to give 0.074 g of a brown solid. This material was dissolved in ca. 5 mL of CH_2Cl_2 and concentrated onto 0.3 g of silica gel. The free-flowing powder was added to the top of a column of 2 g of silica gel and eluted with 10% EtOAc–hexanes to give 0.044 g (83%) of indole **60** as a brown solid: mp 102–106 °C; IR (KBr pellet) 3467, 2941, 2864, 2152, 1619, 1571, 1499, 1465, 1405, 1382, 1351, 1232, 1202, and 1121 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28–7.37 (m, 3H), 7.09–7.14 (m. 3H), 7.08 (d, J = 3.2 Hz, 1H), 6.68 (d, J = 1.0 Hz, 1H), 6.60 (dd, J = 3.2, 0.8 Hz, 1H), 5.29 (s, 2H), 5.11 (br s, 1H), and 1.15 (s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 137.9, 137.3, 129.0, 128.6, 127.9, 126.9, 118.8, 117.3, 108.6, 108.1, 107.3, 98.7, 88.6, 50.2, 18.9, and 11.5. Anal. Calcd for $C_{26}H_{33}NOSi$: C, 77.37; H, 8.24; N, 3.47. Found: C, 77.29; H, 8.38; N, 3.41.

Ethyl 3-(1-Benzyl-4-hydroxyindol-6-yl)acrylate (61). A 10 mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with iodide **57** (0.048 g, 0.14 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.002 g, 0.009 mmol, 0.06 equiv), PPh_3 (0.004 g, 0.015 mmol, 0.11 equiv), Bu_4NBr (0.044 g, 0.14 mmol, 1.0 equiv), and K_2CO_3 (0.048 g, 0.35 mmol, 2.5 equiv). The flask was evacuated and filled with argon (three cycles), and then 1.3 mL of DMF, 0.13 mL of H_2O, and ethyl acrylate (0.028 g, 0.030 mL, 0.28 mmol, 2.0 equiv) were added. The rubber septum was replaced by a coldfinger condenser with an argon inlet side arm, and the dark green mixture was stirred at 65–70 °C for 4 h. The resulting dark brown mixture was allowed to cool to room temperature and then filtered through a 4 cm column of silica gel in a 1 cm wide column with the aid of 20 mL of EtOAc. The filtrate was washed with three 12 mL portions of saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to give 0.070 g of a dark brown oil. This material was dissolved in ca. 5 mL of CH_2Cl_2 and concentrated onto 0.5 g of silica gel. The free-flowing powder was added to the top of a column of 7 g of silica gel and eluted with 25% EtOAc–hexanes to give 0.030 g (68%) of indole **61** as a yellow solid: mp 143.5–145.5 °C; IR (KBr pellet) 3359, 2979, 1691, 1637, 1610, 1581, 1497, 1467, 1438, 1368, 1307, 1280, 1254, and 1188 cm^{-1}; ^1H NMR (400 MHz, $(CD_3)_2O$) δ 8.68 (s, 1H), 7.67 (d, J = 15.9 Hz, 1H), 7.37 (d, J = 3.2 Hz, 1H), 7.21–7.35 (m, 6H), 6.81 (d, J = 1.1 Hz, 1H), 6.67 (dd, J = 3.2, 0.8 Hz, 1H), 6.37 (d, J = 15.9 Hz, 1H), 5.47 (s, 2H), 4.18 (q, J = 7.1 Hz, 2H), and 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $(CD_3)_2O$) δ 167.8, 152.2, 147.5, 139.5, 139.4, 130.5, 130.4, 129.8, 128.7, 128.3, 122.3, 116.6, 105.7, 103.4, 100.4, 60.9, 50.9, and 15.2. Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.61; H, 6.09; N, 4.24.

General Procedure for the Debenzylation of *N*-Benzylindoles. 6-Butyl-4-hydroxyindole (62). A 25 mL, two-necked, round-bottomed flask was equipped with a rubber septum with an argon inlet needle and a Dewar condenser fitted with an inlet adapter connected to an oil bubbler by Tygon tubing. The flask and condenser were cooled at −78 °C while 3 mL of NH_3 was condensed in the flask. Li wire (0.016 g, 2.3 mmol, 21 equiv) cut into small pieces (3.2 mm diameter, ca. 3 mm in length) was added to give a dark blue solution which was stirred for 5 min at −78 °C. A solution of indole **54** (0.030 g, 0.11 mmol, 1 equiv) in 1.5 mL of THF was added dropwise over 5 min, and the syringe was rinsed with 0.5 mL of THF, which was then added to the reaction mixture in one portion. The cooling bath was removed to allow the reaction mixture to warm to reflux. After 10 min at reflux, 2 mL of H_2O was added at a rate such that NH_3 did not boil too vigorously (ca. 2–3 min). The color of the reaction mixture changed from dark blue to pale yellow. The Dewar condenser and rubber septum were removed, and the reaction flask was placed in a water bath (ca. 20 °C) to promote the evaporation of the NH_3. The reaction mixture turned blue during the evaporation of NH_3, and the color darkened gradually. The resulting dark blue cloudy mixture was diluted with 15 mL of EtOAc and extracted with 10 mL of H_2O. The aqueous layer was acidified with 10% HCl solution to pH 7 and then extracted with two 15 mL portions of EtOAc. The combined organic layers were washed with 25 mL of saturated NaCl solution, dried over Na_2SO_4, filtered, and concentrated to provide 0.022 g of a dark purple paste. This material was dissolved in ca. 2 mL of CH_2Cl_2 and concentrated onto 0.3 g of silica gel. The free-flowing powder was added to the top of a column of 2 g of silica gel and eluted with 20% EtOAc–hexanes to afford 0.016 g (80%) of indole **62** as a pale brown paste: IR (film) 3413, 3127, 2954, 2924, 2853, 1630, 1580, 1515, 1454, 1368, 1319, 1258, 1220, 1077, and 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (br s, 1H), 7.08 (dd, J = 3.2, 2.5 Hz, 1H), 6.83 (s, 1H),

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6.54−6.57 (m, 1H), 6.41 (d, J = 0.8 Hz, 1H), 4.95 (s, 1H), 2.67 (t, J = 7.7 Hz, 2H), 1.64 (app quintet, J = 7.6 Hz, 2H), 1.38 (app sextet, J = 7.4 Hz, 2H), and 0.95 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 138.6, 138.1, 122.7, 115.6, 105.5, 103.8, 98.7, 36.0, 34.2, 22.5, and 14.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{12}H_{15}NO$ 190.1226, found 190.1226.

4-Hydroxy-6,7-dimethylindole (63). Reaction of indole **59** (0.187 g, 0.74 mmol, 1.0 equiv) with Li wire (0.102 g, 14.7 mmol, 20 equiv) in 8 mL of NH_3 and 4.5 mL of THF at −33 °C for 70 min according to the general procedure provided 0.126 g of a black waxy solid. This material was dissolved in ca. 10 mL of EtOAc and concentrated onto 1 g of silica gel. The free-flowing powder was deposited on the top of a column of 13 g of silica gel and eluted with 20% EtOAc−hexanes to give 0.060 g (50%) of indole **63** as a light pink solid with low solubility in CH_2Cl_2 and $CDCl_3$: mp 169.5−171.5 °C dec; IR (KBr pellet) 3383, 3107, 2922, 2861, 1631, 1589, 1519, 1504, 1449, 1376, 1349, 1323, 1255, 1186, and 1118 cm^{-1}; ^{1}H NMR (500 MHz, $(CD_3)_2CO$) δ 9.90 (br s, 1H), 7.94 (s, 1H), 7.09 (t, J = 2.8 Hz, 1H), 6.53 (dd, J = 3.3, 2.3 Hz, 1H), 6.32 (s, 1H), 2.30 (s, 3H), and 2.26 (s, 3H); ^{13}C NMR (125 MHz, $(CD_3)_2CO$) δ 149.1, 139.3, 130.0, 123.2, 117.4, 110.5, 107.3, 100.2, 19.7, and 13.0. Anal. Calcd for $C_{10}H_{11}NO$: C, 74.51; H, 6.88; N, 8.69. Found: C, 74.41; H, 6.68; N, 8.54.

General Procedure for the Synthesis of Ynamides via *N*-Alkynylation of Sulfonamides. *N*-(4-Methoxybenzyl)-*N*-(*p*-tolylsulfonyl)[2-(triisopropylsilyl)ethynyl]amine (68). A 50 mL, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with *N*-(4-methoxybenzyl)-*p*-toluenesulfonamide[51] (3.26 g, 11.2 mmol, 1.3 equiv), bromoalkyne **67**[52] (2.25 g, 8.60 mmol, 1.0 equiv), $CuSO_4 \cdot 5H_2O$ (0.429 g, 1.72 mmol, 0.2 equiv), 1,10-phenanthroline (0.620 g, 3.44 mmol, 0.4 equiv), K_2CO_3 (2.38 g, 17.2 mmol, 2.0 equiv), and 12 mL of toluene. The pale green suspension was heated at 80 °C with vigorous stirring for 64 h and then allowed to cool to rt. The resulting dark green reaction mixture was filtered through a pad of Celite with the aid of ca. 50 mL of ethyl acetate. The filtrate was concentrated to afford 6.17 g of a viscous green oil. This material was added to the top of a column of 75 g of silica gel with the aid of hexane and eluted with a gradient of 0−20% EtOAc−hexane to afford 3.56 g (88%) of ynamide **68** as a viscous colorless oil: IR (film) 2942, 2865, 2165, 1613, 1515, 1464, 1370, 1251, 1169, 1035, 738, and 665 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (app d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.6 Hz, 2H), 7.21 (app d, J = 8.7 Hz, 2H), 6.80 (app d, J = 8.8 Hz, 2H), 4.44 (s, 2H), 3.79 (s, 3H), 2.44 (s, 3H), and 0.96 (s, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 144.6, 134.9, 130.7, 129.7, 128.0, 126.6, 114.0, 96.6, 70.4, 55.5, 55.2, 21.8, 18.7, and 11.5; HRMS (DART) m/z $[M - H]^-$ calcd for $C_{26}H_{37}NO_3SSi$ 470.2191, found 470.2208.

***N*-(Furan-2-ylmethyl)-*N*-(*p*-tolylsulfonyl)[2-(triisopropylsilyl)-ethynyl]amine (70).** Reaction of *N*-(furan-2-ylmethyl)-*p*-toluenesulfonamide[53] (0.500 g, 1.99 mmol, 1.2 equiv), bromoalkyne **67**[52] (0.433 g, 1.66 mmol, 1.0 equiv), $CuSO_4 \cdot 5H_2O$ (0.041 g, 0.17 mmol, 0.1 equiv), 1,10-phenanthroline (0.060 g, 0.33 mmol, 0.2 equiv), and K_2CO_3 (0.458 g, 3.32 mmol, 2.0 equiv) in 3.3 mL of toluene and 0.6 mL of DMF for 20 h according to the general procedure afforded 1.05 g of a wet green crystalline solid. This material was dissolved in ca. 5 mL of CH_2Cl_2 and concentrated onto 2.5 g of silica gel. The resulting free-flowing powder was added to the top of a column of 40 g of silica gel and eluted with 5% EtOAc−hexane to afford 0.459 g (64%) of ynamide **70** as colorless crystals: mp 47−48 °C; IR (film) 2942, 2865, 2165, 1598, 1502, 1462, 1452, 1370, 1169, 1091, 1008, 883, and 665 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (app d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 7.27 (dd, J = 2.7, 1.4 Hz, 1H), 6.25 (m, 2H), 4.57 (s, 2H), 2.43 (s, 3H), and 0.99 (s, 21H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 144.7, 143.1, 134.7, 129.6, 128.1, 110.7, 110.5, 96.0, 70.4, 48.2, 21.8, 18.7, and 11.5; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{23}H_{33}NO_3SSi$ 454.1843, found 454.1853.

General Procedure for the Desilylation of Triisopropylsilyl Ynamides. *N*-(4-Methoxybenzyl)-*N*-(*p*-tolylsulfonyl)-ethynylamine (71). A 50 mL, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with ynamide **68** (1.00 g, 2.12 mmol, 1.0 equiv) and 21 mL of THF. The colorless solution was cooled at −40 °C, and a solution of TBAF (1.0 M in THF, 2.33 mL, 2.33 mmol, 1.1 equiv) was added dropwise via syringe over 4 min. The resulting orange suspension was allowed to warm to rt over 20 min and diluted with 20 mL of satd aq NH_4Cl solution and 20 mL of Et_2O. The aqueous phase was separated and extracted with two 15 mL portions of Et_2O, and the combined organic phases were washed with 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 1.23 g of a wet off-white solid. This material was transferred to a 25 mL, round-bottomed flask and dissolved in 2 mL of hot benzene (70 °C), and 2 mL of hot hexane (70 °C) was added. The solution was allowed to slowly cool to rt and then −20 °C overnight. The resulting crystals were collected by removal of the mother liquor via cannula under argon, washed with two 2.5 mL portions of ice-cold hexane, and dried to afford 0.643 g (96%) of ynamide **71** as colorless crystals: mp 123−125 °C; IR (film) 3286, 2972, 2937, 2839, 2133, 1612, 1594, 1514, 1358, 1304, 1255, 1189, 1169, 1030, and 706 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (app d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 7.22 (app d, J = 8.8 Hz, 2H), 6.83 (app d, J = 8.8 Hz, 2H), 4.44 (s, 2H), 3.80 (s, 3H), 2.68 (s, 1H), and 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 144.9, 134.9, 130.4, 129.9, 127.9, 126.4, 114.0, 76.4, 60.0, 55.4, 55.0, and 21.8; HRMS (DART) m/z $[M + H]^+$ calcd for $C_{17}H_{17}NO_3S$ 316.1002, found 316.1004.

***N*-(Furan-2-ylmethyl)-*N*-(*p*-tolylsulfonyl)ethynylamine (73).** Reaction of ynamide **70** (0.458 g, 1.06 mmol, 1.0 equiv) and TBAF solution (1.0 M in THF, 1.17 mL, 1.17 mmol, 1.1 equiv) in 10 mL of THF for 1 h according to the general procedure afforded 0.542 g of a pale yellow solid. This material was transferred to a 25 mL, round-bottomed flask and dissolved in 0.5 mL of hot benzene (70 °C), and 1.5 mL of hot hexane (70 °C) was added. The solution was allowed to slowly cool to rt and then −20 °C overnight. The resulting crystals were collected by removal of the mother liquor via cannula under argon, washed with two 2 mL portions of ice-cold hexanes, and dried to afford 0.287 g (98%) of ynamide **73** as pale yellow crystals: mp 103−104 °C; IR (film) 3279, 3113, 2136, 1597, 1503, 1359, 1307, 1289, 1171, 1152, 1089, 1008, 932, 750, 706, and 576 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (app d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 7.30 (dd, J = 1.8, 0.9 Hz, 1H), 6.27−6.30 (m, 2H), 4.58 (s, 2H), 2.73 (s, 1H), and 2.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.8, 144.9, 143.2, 134.7, 129.8, 127.9, 110.7, 110.6, 75.9, 59.9, 48.0, and 21.8; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{14}H_{13}NO_3S$ 298.0508, found 298.0513.

General Procedure for the Synthesis of Highly Substituted *o*-Iodoaniline Derivatives. *N*-(4-Methoxybenzyl)-*N*-(*p*-tolylsulfonyl)(5-butyl-3-hydroxy-2-iodophenyl)amine (74). A 250 mL, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with ynamide **71** (2.18 g, 6.92 mmol, 1.0 equiv) and 70 mL of THF. The solution was cooled at −15 °C, and a solution of *n*-BuLi (2.26 M in hexane, 3.06 mL, 6.92 mmol, 1.0 equiv) was added dropwise via syringe over 7 min. The resulting brown solution was stirred at −15 °C for 3 h and then cooled to −78 °C. Powdered iodine (1.76 g, 6.92 mmol, 1.0 equiv) was added in one portion, and the reaction mixture was allowed to slowly warm to rt and stirred for a total of 17 h. The resulting red-brown mixture was diluted with 150 mL of Et_2O and washed with 150 mL of a 1:1 mixture of satd aq $Na_2S_2O_3$ and $NaHCO_3$ solutions. The organic phase was separated and washed with 150 mL of water, and the combined aqueous phases were extracted with two 75 mL portions of Et_2O. The combined organic phases were washed with 150 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 3.01 g of a brown solid. This material was found to contain ca. 95% iodo ynamide, and no purification was attempted at this stage.

The iodo ynamide was transferred to a 100 mL pear flask equipped with a rubber septum and argon inlet needle, and cyclobutenone **26** (1.71 g, 13.8 mmol, 2.0 equiv) and 20 mL of toluene were added. The brown reaction mixture was heated at 80 °C for 2 h, allowed to cool to rt, and concentrated to afford 5.45 g of a dark brown oil. This material was diluted with 20 mL of MeOH and 20 mL of 5 M aqueous KOH solution, the same flask was equipped with a rubber septum and argon inlet needle, and the reaction mixture was heated at 70 °C for 2 h. The

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resulting brown suspension was cooled to rt and diluted with 125 mL of 1 M aqueous HCl solution and 125 mL of CH_2Cl_2. The aqueous phase was separated and extracted with two 60 mL portions of CH_2Cl_2, and the combined organic phases were washed with two 100 mL portions of water and 100 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 5.28 g of a dark red oil. This material was dissolved in ca. 30 mL of CH_2Cl_2 and concentrated onto 10 g of silica gel. The resulting free-flowing powder was added to the top of a column of 200 g of silica gel and eluted with 50:40:10 benzene−hexane−EtOAc to afford 2.72 g (69%) of phenol **74** as a pale yellow solid: mp 150−153 °C; IR (film) 3415, 2955, 2930, 2860, 1612, 1586, 1514, 1423, 1347, 1304, 1249, 1159, 1090, 1035, and 815 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.04 (app d, J = 8.7 Hz, 2H), 6.72 (d, J = 1.8 Hz, 1H), 6.71 (app d, J = 8.7 Hz, 2H), 6.08 (d, J = 1.9 Hz, 1H), 4.80 (d, J = 13.6 Hz, 1H), 4.40 (d, J = 13.6 Hz, 1H), 3.75 (s, 3H), 2.46 (s, 3H), 2.38 (t, J = 7.6 Hz, 2H), 1.38 (app quintet, J = 7.6 Hz, 2H), 1.21 (sextet, J = 7.4 Hz, 2H), and 0.89 (t, J = 7.3 Hz, 3H), phenolic proton not observed; ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 156.2, 144.8, 143.9, 141.4, 136.3, 131.5, 129.6, 128.5, 127.0, 123.2, 115.2, 113.7, 92.2, 55.4, 55.3, 35.0, 33.2, 22.2, 21.8, and 14.1; HRMS (DART) m/z $[M + H]^+$ calcd for $C_{25}H_{28}INO_4S$ 566.0856, found 566.0864.

***N*-Allyl-*N*-(*p*-tolylsulfonyl)(5-butyl-3-hydroxy-2-iodophenyl)amine (75).** Reaction of ynamide **72**[54] (0.466 g, 1.98 mmol, 1.0 equiv), *n*-BuLi (2.34 M in hexane, 0.85 mL, 1.99 mmol, 1.0 equiv), and iodine (0.503 g, 1.98 mmol, 1.0 equiv) in 20 mL of THF followed by reaction with cyclobutenone **26** (0.492 g, 3.96 mmol, 2.0 equiv) in 10 mL of toluene and then with 5 mL of MeOH and 5 mL of 5 M aqueous KOH solution according to the general procedure gave 1.05 g of a red oil. This material was dissolved in ca. 15 mL of CH_2Cl_2 and concentrated onto 5 g of silica gel. The resulting free-flowing powder was added to the top of a column of 100 g of silica gel and eluted with 50:42.5:7.5 benzene−hexane−EtOAc to afford 0.392 g (41%) of phenol **75** as a viscous yellow oil: IR (film) 3416, 2955, 2929, 2860, 1597, 1581, 1423, 1345, 1305, 1161, 1089, 929, 813, 722, and 663 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (app d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 1.9 Hz, 1H), 6.13 (d, J = 1.8 Hz, 1H), 5.78−5.87 (m, 1H), 5.73 (br s, 1H), 5.01 (dd, J = 10.1, 1.0 Hz, 1H), 4.97 (dq, J = 17.0, 1.2 Hz, 1H), 4.26 (ddt, J = 14.3, 6.2, 1.3 Hz, 1H), 3.96 (dd, J = 14.3, 7.5 Hz, 1H), 2.45 (s, 3H), 2.42 (td, J = 7.6, 2.4 Hz, 2H), 1.44 (quintet, J = 7.6 Hz, 2H), 1.26 (sextet, J = 7.4 Hz, 2H), and 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 144.9, 143.9, 141.5, 136.0, 132.2, 129.6, 128.4, 122.5, 119.9, 115.4, 92.1, 55.0, 34.9, 33.1, 22.2, 21.7, and 14.1; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{20}H_{24}INO_3S$ 508.0414, found 508.0418.

***N*-(Furan-2-ylmethyl)-*N*-(*p*-tolylsulfonyl)(5-butyl-3-hydroxy-2-iodophenyl)amine (76).** Reaction of ynamide **73** (0.140 g, 0.508 mmol, 1.0 equiv), KHMDS (0.91 M in THF, 0.56 mL, 0.51 mmol, 1.0 equiv), and iodine (0.129 g, 0.508 mmol, 1.0 equiv) in 5 mL of THF followed by reaction with cyclobutenone **26** (0.097 g, 0.78 mmol, 1.5 equiv) in 2 mL of toluene and then with 1 mL of MeOH and 1 mL of 5 M aqueous KOH solution according to the general procedure gave 0.289 g of a brown oil. This material was dissolved in ca. 3 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The resulting free-flowing powder was added to the top of a column of 20 g of silica gel and eluted with 50:40:10 hexane−benzene−EtOAc. The mixed fractions were concentrated onto 1 g of silica gel, and the resulting free-flowing powder was added to the top of a column of 20 g of silica gel and eluted again with 50:40:10 hexane−benzene−EtOAc. The fractions containing pure **76** from the two columns were combined, concentrated, and dried to afford 0.129 g (49%) of phenol **76** as a viscous pale yellow oil: IR (film) 3419, 2955, 2929, 2859, 1597, 1581, 1423, 1348, 1289, 1159, 1091, 1010, 814, and 719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.3 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 7.23−7.24 (m, 1H), 6.76 (d, J = 1.8 Hz, 1H), 6.20 (dd, J = 3.1, 1.9 Hz, 1H), 6.03−6.04 (m, 2H), 5.59 (br s, 1H), 4.80 (d, J = 15.3 Hz, 1H), 4.66 (d, J = 15.4 Hz, 1H), 2.45 (s, 3H), 2.37 (t, J = 7.6 Hz, 2H), 1.37 (app quintet, J = 7.5 Hz, 2H), 1.22 (sextet, J = 7.4 Hz, 2H), and 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.3, 149.2, 145.0, 143.8, 142.7, 141.3, 136.7, 129.5, 128.4, 123.3, 115.5, 110.58, 110.55, 91.3, 47.9, 34.9, 33.0, 22.2, 21.8, and 14.1; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{22}H_{24}INO_4S$ 548.0363, found 548.0375.

***N*-(4-Methoxybenzyl)-*N*-(*p*-tolylsulfonyl)(5-butyl-2-iodo-3-methoxyphenyl)amine (77).** A 25 mL pear flask equipped with a rubber septum and argon inlet needle was charged with phenol **74** (0.200 g, 0.354 mmol, 1.0 equiv), K_2CO_3 (0.098 g, 0.71 mmol, 2.0 equiv), 3.5 mL of acetone, and iodomethane (0.11 mL, 1.77 mmol, 5.0 equiv). The pale yellow reaction mixture was stirred at rt for 19 h and diluted with 10 mL of Et_2O and 10 mL of satd aq NH_4Cl solution. The aqueous phase was separated and extracted with two 5 mL portions of Et_2O, and the combined organic phases were washed with 10 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.232 g of a yellow oil. This material was dissolved in ca. 3 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The resulting free-flowing powder was added to the top of a column of 10 g of silica gel and eluted with 15% EtOAc−hexane to afford 0.180 g (88%) of aniline **77** as a viscous pale yellow oil: IR (film) 2956, 2932, 2860, 1612, 1568, 1514, 1415, 1351, 1248, 1161, 1117, 1091, 1034, 816, and 724 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.06 (app d, J = 8.7 Hz, 2H), 6.70 (app d, J = 8.7 Hz, 2H), 6.51 (d, J = 1.7 Hz, 1H), 6.23 (d, J = 1.8 Hz, 1H), 4.69 (d, J = 14.0 Hz, 1H), 4.65 (d, J = 14.1 Hz, 1H), 3.82 (s, 3H), 3.73 (s, 3H), 2.44 (s, 3H), 2.42 (t, J = 7.7 Hz, 2H), 1.38 (app quintet, J = 7.6 Hz, 2H), 1.20 (sextet, J = 7.6 Hz, 2H), and 0.88 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.32, 159.26, 144.3, 143.6, 141.9, 137.0, 131.3, 129.5, 128.4, 127.4, 124.4, 113.5, 111.2, 91.2, 56.6, 55.3, 54.7, 35.3, 33.3, 22.2, 21.7, and 14.0; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{26}H_{30}INO_4S$ 602.0832, found 602.0828.

General Procedure for the Removal of the *p*-Methoxybenzyl Group from *N*-(*p*-Methoxybenzyl)anilines. *N*-(*p*-Tolylsulfonyl)-(5-butyl-2-iodo-3-methoxyphenyl)amine (78). A 25 mL pear flask equipped with a rubber septum and argon inlet needle was charged with aniline **77** (0.180 g, 0.310 mmol, 1.0 equiv) and 3 mL of CH_2Cl_2. The pale yellow reaction mixture was cooled at 0 °C, and TFA (0.36 mL, 4.6 mmol, 15 equiv) was added dropwise via syringe over 2 min. The resulting purple solution was allowed to warm to rt and stirred for a total of 3 h. The reaction mixture was then diluted with 10 mL of CH_2Cl_2, and 15 mL of satd aq $NaHCO_3$ solution was carefully added. The aqueous phase was separated and extracted with three 5 mL portions of CH_2Cl_2. The combined organic phases were washed with 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.216 g of an orange oil. This material was dissolved in ca. 3 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The resulting free-flowing powder was added to the top of a column of 20 g of silica gel and eluted with 10% EtOAc−hexane to afford 0.101 g (71%) of aniline **78** as a colorless oil: IR (film) 3303, 2955, 2930, 2859, 1577, 1452, 1420, 1388, 1328, 1242, 1165, 1082, 813, and 666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 1.7 Hz, 1H), 7.03 (s, 1H), 6.37 (d, J = 1.7 Hz, 1H), 3.80 (s, 3H), 2.57 (t, J = 7.7 Hz, 2H), 2.36 (s, 3H), 1.56 (app quintet, J = 7.7 Hz, 2H), 1.30 (sextet, J = 7.6 Hz, 2H), and 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 145.6, 144.2, 138.5, 135.9, 129.7, 127.6, 114.1, 107.9, 80.4, 56.6, 35.8, 33.4, 22.3, 21.7, and 14.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{18}H_{22}INO_3S$ 460.0438, found 460.0427.

3,6-Dibutyl-4-methoxy-1-(*p*-tolylsulfonyl)-2-(trimethylsilyl)-indole (79). A 25 mL pear flask equipped with a rubber septum and argon inlet needle was charged with aniline **78** (0.101 g, 0.220 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (0.008 g, 0.01 mmol, 0.05 equiv), K_2CO_3 (0.152 g, 1.10 mmol, 5.0 equiv), LiCl (0.009 g, 0.2 mmol, 1.0 equiv), 1-(trimethylsilyl)-1-hexyne (0.088 mL, 0.44 mmol, 2.0 equiv), and 4.4 mL of DMF. The yellow suspension was heated at 100 °C for 40 h and cooled to rt, and additional 1-(trimethylsilyl)-1-hexyne (0.132 mL, 0.66 mmol, 3.0 equiv) was added. The reaction mixture was heated at 100 °C for an additional 24 h and allowed to cool to rt. The resulting brown suspension was diluted with 40 mL of Et_2O and 40 mL of satd aq NH_4Cl solution. The aqueous phase was separated and extracted with two 20 mL portions of Et_2O, and the combined organic phases were washed with 40 mL of water and 40 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.139 g of a brown oil.

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This material was dissolved in ca. 3 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The resulting free-flowing powder was added to the top of a column of 20 g of silica gel and eluted with 3.5% EtOAc–hexane to afford 0.055 g (51%) of a 95:5 mixture of indole **79** and its 2,3-regioisomer as a pale yellow oil: IR (film) 2956, 2930, 2859, 1587, 1465, 1411, 1362, 1248, 1176, 1117, 1088, 843, and 593 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) (major regioisomer **79**) δ 7.41 (app d, J = 8.4 Hz, 2H), 7.41 (s, 1H), 7.04 (d, J = 8.4 Hz, 2H), 6.38 (s, 1H), 3.80 (s, 3H), 2.85–2.88 (m, 2H), 2.63 (t, J = 7.6 Hz, 2H), 2.27 (s, 3H), 1.57 (app quintet, J = 7.6 Hz, 2H), 1.49 (app quintet, J = 7.6 Hz, 2H), 1.24–1.35 (m, 4H), 0.93 (t, J = 7.4 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H), and 0.52 (s, 9H); (minor regioisomer) δ 7.64 (s, 1H), 7.60 (d, J = 8.5 Hz, 2H), 7.18 (d, J = 7.9 Hz, 2H), 6.48 (s, 1H), 3.85 (s, 3H), 2.70 (t, J = 7.6 Hz, 2H), 2.35 (s, 3H), and 0.31 (s, 9H) (all other aliphatic signals overlap with peaks from **79**); ^{13}C NMR (125 MHz, $CDCl_3$) (major regioisomer **79**) δ 153.8, 143.9, 142.3, 141.9, 140.6, 135.8, 134.8, 129.1, 126.8, 120.3, 108.7, 105.7, 55.2, 36.5, 34.3, 34.2, 27.2, 22.8, 22.4, 21.7, 14.23, 14.22, and 2.9; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{27}H_{39}NO_3SSi$ 508.2312, found 508.2345.

5-Butyl-2-iodo-3-[*N*-(4-methoxybenzyl)-*N*-(*p*-tolylsulfonyl)-amino]phenyl Methanesulfonate (80). A 50 mL, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with phenol **74** (0.794 g, 1.40 mmol, 1.0 equiv), Et_3N (0.29 mL, 2.1 mmol, 1.5 equiv), and 14 mL of CH_2Cl_2. The yellow solution was cooled at 0 °C, and MsCl (0.114 mL, 1.47 mmol, 1.05 equiv) was added dropwise via syringe over 1 min. The reaction mixture was stirred at 0 °C for 2 h and diluted with 15 mL of water. The aqueous phase was separated and extracted with two 7.5 mL portions of CH_2Cl_2, and the combined organic phases were washed with 15 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 1.73 g of an orange oil. This material was dissolved in ca. 10 mL of CH_2Cl_2 and concentrated onto 3 g of silica gel. The resulting free-flowing powder was added to the top of a column of 60 g of silica gel and eluted with 30% EtOAc–hexane to afford 0.772 g (85%) of aniline **80** as a yellow semisolid: IR (film) 2956, 2933, 2871, 1612, 1597, 1514, 1413, 1354, 1249, 1181, 1161, 1091, 1034, 962, 815, 800, 789, and 714 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (app d, J = 8.3 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 7.16 (d, J = 1.9 Hz, 1H), 7.00 (app d, J = 8.7 Hz, 2H), 6.69 (app d, J = 8.7 Hz, 2H), 6.50 (d, J = 1.9 Hz, 1H), 4.73 (d, J = 13.7 Hz, 1H), 4.54 (d, J = 13.8 Hz, 1H), 3.72 (s, 3H), 3.14 (s, 3H), 2.45 (s, 3H), 2.44 (t, J = 7.6 Hz, 2H), 1.38 (app quintet, J = 7.6 Hz, 2H), 1.20 (sextet, J = 7.4 Hz, 2H), and 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 150.5, 145.1, 144.0, 142.7, 136.3, 131.4, 130.2, 129.7, 128.3, 126.6, 123.1, 113.6, 96.2, 55.3, 54.9, 39.2, 34.7, 32.9, 22.1, 21.7, and 14.0; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{26}H_{30}INO_6S_2$ 666.0451, found 666.0437.

5-Butyl-2-iodo-3-[*N*-(*p*-tolylsulfonyl)amino]phenyl Methanesulfonate (81). Reaction of aniline **80** (0.772 g, 1.20 mmol, 1.0 equiv) and TFA (2.75 mL, 36.0 mmol, 30 equiv) in 12 mL of CH_2Cl_2 for 3 h according to the general deprotection procedure provided 1.25 g of an orange oil. This material was dissolved in ca. 15 mL of CH_2Cl_2 and concentrated onto 5 g of silica gel. The resulting free-flowing powder was added to the top of a column of 70 g of silica gel and eluted with 25% EtOAc–hexane to afford 0.619 g (99%) of aniline **81** as a pale yellow solid: mp 118–119 °C; IR (film) 3294, 2956, 2931, 2860, 1597, 1566, 1421, 1373, 1331, 1181, 1167, 1091, 1022, 966, 803, and 666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (app d, J = 8.3 Hz, 2H), 7.42 (d, J = 1.8 Hz, 1H), 7.22 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 1.9 Hz, 1H), 6.96 (s, 1H), 3.19 (s, 3H), 2.60 (t, J = 7.7 Hz, 2H), 2.38 (s, 3H), 1.57 (app quintet, J = 7.7 Hz, 2H), 1.30 (sextet, J = 7.4 Hz, 2H), and 0.92 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.6, 146.4, 144.7, 139.4, 135.6, 129.9, 127.6, 120.5, 119.5, 85.0, 39.3, 35.3, 33.1, 22.2, 21.7, and 14.0; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{18}H_{22}INO_5S_2$ 545.9879, found 545.9876.

2,6-Dibutyl-1-(*p*-tolylsulfonyl)indol-4-yl Methanesulfonate (82). A 15 mL threaded Pyrex tube (20 mm o.d.) equipped with a rubber septum and argon inlet needle was charged with aryl iodide **81** (0.134 g, 0.256 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (0.009 g, 0.013 mmol, 0.05 equiv), CuI (0.004 g, 0.020 mmol, 0.08 equiv), Et_3N (0.36 mL, 2.6 mmol, 10 equiv), 2.6 mL of DMF, and 1-hexyne (0.035 mL, 0.31 mmol, 1.2 equiv). The yellow reaction mixture was purged with argon for ca. 5 min, and the reaction tube was sealed with a threaded Teflon cap. The reaction mixture was heated at 80 °C for 17 h. The resulting orange solution was allowed to cool to rt and diluted with 25 mL of satd aq NH_4Cl solution and 25 mL of Et_2O. The aqueous phase was separated and extracted with two 12.5 mL portions of Et_2O, and the combined organic phases were washed with 50 mL of water and 50 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.183 g of a brown oil. This material was dissolved in ca. 3 mL of CH_2Cl_2 and concentrated onto 1.5 g of silica gel. The resulting free-flowing powder was added to the top of a column of 20 g of silica gel and eluted with 13% EtOAc–hexane to afford 0.116 g (95%) of indole **82** as a pale yellow oil: IR (film) 2957, 2932, 2872, 1621, 1596, 1563, 1423, 1371, 1173, 1155, 1141, 1095, 1071, 968, 812, 666, and 592 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.64 (app d, J = 8.5 Hz, 2H), 7.22 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 1.1 Hz, 1H), 6.46 (d, J = 0.8 Hz, 1H), 3.14 (s, 3H), 2.97 (app t, J = 7.7 Hz, 2H), 2.74 (t, J = 7.8 Hz, 2H), 2.36 (s, 3H), 1.73 (app quintet, J = 7.7 Hz, 2H), 1.64 (app quintet, J = 7.6 Hz, 2H), 1.44 (sextet, J = 7.4 Hz, 2H), 1.36 (sextet, J = 7.4 Hz, 2H), 0.96 (t, J = 7.4 Hz, 3H), and 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 143.4, 140.7, 140.2, 139.1, 136.1, 130.1, 126.5, 121.7, 117.1, 113.8, 104.6, 37.8, 36.1, 34.1, 31.0, 28.9, 22.6, 22.4, 21.8, 14.12, and 14.08; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{31}NO_5S_2$ 478.1716, found 478.1738.

General Procedure for the Triflation of Phenols. 3-[*N*-Allyl-*N*-(*p*-tolylsulfonyl)amino]-5-butyl-2-iodophenyl Trifluoromethanesulfonate (83). A 50 mL, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with phenol **75** (0.392 g, 0.808 mmol, 1.0 equiv), DMAP (0.197 g, 1.62 mmol, 2.0 equiv), and 8 mL of CH_2Cl_2. The yellow solution was cooled at 0 °C, and Tf_2O (0.177 mL, 1.05 mmol, 1.3 equiv) was added dropwise via syringe over 2 min. The reaction mixture was allowed to warm to rt and stirred for a total of 3 h. The resulting orange suspension was diluted with 20 mL of CH_2Cl_2 and 20 mL of 1 M aqueous HCl solution. The aqueous phase was separated and extracted with two 15 mL portions of CH_2Cl_2, and the combined organic phases were washed with 30 mL of satd aq $NaHCO_3$ solution and 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.618 g of an orange oil. This material was dissolved in ca. 6 mL of CH_2Cl_2 and concentrated onto 2.5 g of silica gel. The resulting free-flowing powder was added to the top of a column of 50 g of silica gel and eluted with 10% EtOAc–hexane to afford 0.460 g (92%) of aniline **83** as a pale yellow oil: IR (film) 2959, 2931, 2864, 1646, 1598, 1559, 1427, 1358, 1217, 1166, 1139, 1091, 802, 720, and 664 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.66 (app d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.6 Hz, 2H), 7.09 (d, J = 1.9 Hz, 1H), 6.81 (d, J = 1.8 Hz, 1H), 5.87 (ddt, J = 17.0, 10.1, 6.9 Hz, 1H), 5.07 (dq, J = 10.1, 1.0 Hz, 1H), 4.98 (dq, J = 17.0, 1.3 Hz, 1H), 4.15 (d, J = 6.9 Hz, 2H), 2.56 (t, J = 7.7 Hz, 2H), 2.46 (s, 3H), 1.52 (app quintet, J = 7.7 Hz, 2H), 1.32 (sextet, J = 7.3 Hz, 2H), and 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.2, 145.7, 144.3, 143.7, 136.1, 132.0, 130.9, 129.8, 128.3, 122.1, 120.4, 118.9 (q, $^1J_{C-F}$ = 320.7 Hz), 96.0, 54.7, 34.9, 32.9, 22.2, 21.7, and 14.0; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{21}H_{23}F_3INO_5S_2$ 639.9907, found 639.9912.

6-Butyl-3-methyl-1-(*p*-tolylsulfonyl)indol-4-yl Trifluoromethanesulfonate (84). A 25 mL pear flask equipped with a rubber septum and argon inlet needle was charged with aryl iodide **83** (0.173 g, 0.280 mmol, 1.0 equiv), $PdCl_2(PPh_3)_2$ (0.020 g, 0.028 mmol, 0.1 equiv), Et_3N (0.078 mL, 0.56 mmol, 2.0 equiv), and 2.8 mL of DMF. The yellow reaction mixture was heated at 55 °C for 24 h and allowed to cool to rt. The resulting orange-brown solution was diluted with 30 mL of Et_2O and 30 mL of satd aq NH_4Cl solution. The aqueous phase was separated and extracted with two 15 mL portions of Et_2O, and the combined organic phases were washed with 30 mL of water and 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.214 g of an orange oil. This material was dissolved in ca. 5 mL of CH_2Cl_2 and concentrated onto 2 g of silica gel. The resulting free-flowing powder was added to the top of a column of 35 g of silica gel and eluted with 5% EtOAc–hexane. The fractions with R_f = 0.21 in 5% EtOAc–hexane were found to contain indole **84**, while those with R_f =

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0.16 in 5% EtOAc–hexane were found to contain the exocyclic double bond (3-methylene) isomer. The solution of the latter compound was concentrated, and the residue was dissolved in 5 mL of CH_2Cl_2 in a 25 mL pear flask equipped with a reflux condenser, rubber septum, and argon inlet needle. Camphorsulfonic acid (0.050 g, 0.215 mmol) was added, and the reaction mixture was heated at 40 °C for 18 h and then allowed to cool to rt. The resulting pale yellow solution was diluted with 10 mL of CH_2Cl_2 and washed with 20 mL of satd aq $NaHCO_3$ solution. The aqueous phase was separated and extracted with two 10 mL portions of CH_2Cl_2, and the combined organic phases were washed with 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.042 g of a pale yellow oil. This material was dissolved in ca. 3 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The resulting free-flowing powder was added to the top of a column of 15 g of silica gel and eluted with 5% EtOAc–hexane. The pure fractions were combined with the fractions containing **84** from the first column and concentrated to afford 0.065 g (47%) of indole **84** as a viscous orange oil: IR (film) 2957, 2932, 2872, 1630, 1597, 1423, 1377, 1221, 1178, 1141, 1115, 1034, 824, 671, and 583 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 1.0 Hz, 1H), 7.76 (app d, J = 8.4 Hz, 2H), 7.30 (d, J = 1.3 Hz, 1H), 7.26 (d, J = 8.7 Hz, 2H), 6.98 (s, 1H), 2.75 (t, J = 7.7 Hz, 2H), 2.38 (s, 3H), 2.37 (s, 3H), 1.63 (app quintet, J = 7.6 Hz, 2H), 1.35 (sextet, J = 7.5 Hz, 2H), and 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.5, 142.4, 141.2, 137.7, 135.1, 130.2, 127.0, 124.7, 122.0, 118.8 (q, $^1J_{C-F}$ = 320.4 Hz), 116.3, 116.1, 113.5, 35.9, 33.9, 22.3, 21.8, 14.1, and 11.7; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{21}H_{22}F_3NO_5S_2$ 512.0784, found 512.0775.

5-Butyl-3-[*N*-(furan-2-ylmethyl)-*p*-toluenesulfonamido]-2-iodophenyl Trifluoromethanesulfonate (85). Reaction of phenol **76** (0.234 g, 0.445 mmol, 1.0 equiv), DMAP (0.109 g, 0.890 mmol, 2.0 equiv), and Tf_2O (0.097 mL, 0.58 mmol, 1.3 equiv) in 4.5 mL of CH_2Cl_2 at rt for 1.5 h according to the general triflation procedure afforded 0.293 g of a dark yellow oil. This material was dissolved in ca. 3 mL of CH_2Cl_2 and concentrated onto 1.5 g of silica gel. The resulting free-flowing powder was added to the top of a column of 30 g of silica gel and eluted with 9% EtOAc–hexane to afford 0.205 g (70%) of triflate **85** as a viscous pale yellow oil: IR (film) 2958, 2931, 2872, 1598, 1558, 1427, 1357, 1220, 1164, 1139, 1092, 1010, 815, and 719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 (app d, J = 8.2 Hz, 2H), 7.28 (app d, J = 8.6 Hz, 2H), 7.25 (dd, J = 1.9, 0.8 Hz, 1H), 7.05 (d, J = 1.9 Hz, 1H), 6.62 (d, J = 1.9 Hz, 1H), 6.21 (dd, J = 3.2, 1.9 Hz, 1H), 6.08 (dd, J = 3.2, 0.7 Hz, 1H), 4.95 (d, J = 15.4 Hz, 1H), 4.62 (d, J = 15.5 Hz, 1H), 2.48 (t, J = 7.6 Hz, 2H), 2.45 (s, 3H), 1.43 (app quintet, J = 7.6 Hz, 2H), 1.25 (sextet, J = 7.4 Hz, 2H), and 0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.1, 148.9, 145.7, 144.2, 143.5, 142.9, 136.7, 131.6, 129.7, 128.3, 122.2, 118.9 (q, $^1J_{C-F}$ = 320.8 Hz), 110.8, 110.7, 95.3, 47.6, 34.8, 32.9, 22.1, 21.8, and 14.0; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{23}H_{23}F_3INO_6S_2$ 679.9856, found 679.9865.

7-Butyl-1-(*p*-tolylsulfonyl)-1,2-dihydrobenz[*cd*]indol-5-ol (86). A 50 mL, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with aryl triflate **85** (0.570 g, 0.867 mmol, 1.0 equiv) and 17 mL of THF. The slightly yellow solution was cooled to −95 °C in an acetone–liquid nitrogen bath, and *n*-BuLi solution (2.48 M in hexane, 0.384 mL, 0.954 mmol, 1.1 equiv) was added dropwise over 4 min. The resulting bright yellow solution was allowed to slowly warm to rt over 1 h and stirred for an additional 17 h. The resulting orange-yellow reaction mixture was diluted with 20 mL of Et_2O and 20 mL of satd aq NH_4Cl solution. The aqueous phase was separated and extracted with two 20 mL portions of Et_2O, and the combined organic phases were washed with 40 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.445 g of an orange oil. This material was dissolved in ca. 5 mL of CH_2Cl_2 and concentrated onto 2.5 g of silica gel. The resulting free-flowing powder was added to the top of a column of 100 g of silica gel and eluted with 25% EtOAc–hexanes to afford 0.247 g (75%) of cycloadduct **86** as a viscous dark yellow oil: IR (neat) 3444, 2956, 2929, 1601, 1507, 1384, 1349, 1164, 1123, 1090, 1040, 668, and 601 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.78 (app d, J = 8.3 Hz, 2H), 7.35 (s, 1H), 7.26 (s, 1H), 7.21 (d, J = 8.0 Hz, 2H), 6.89 (dt, J = 7.5, 1.5 Hz, 1H), 6.78 (d, J = 7.5 Hz, 1H), 5.72 (br s, 1H), 5.09 (d, J = 1.1 Hz, 2H), 2.77 (t, J = 7.6 Hz, 2H), 2.33 (s, 3H), 1.69 (app quintet, J = 7.6 Hz, 2H), 1.37 (sextet, J = 7.4 Hz, 2H), and 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.4, 144.5, 144.0, 142.8, 134.5, 130.8, 130.0, 127.3, 126.5, 122.5, 116.4, 112.4, 111.7, 109.0, 56.3, 37.1, 34.1, 22.5, 21.7, and 14.2; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{22}H_{23}NO_3S$ 404.1291, found 404.1304.

7-Butyl-1-(*p*-tolylsulfonyl)-1*H*-benz[*cd*]indol-5-one (87). A 50 mL, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with naphthol **86** (0.106 g, 0.279 mmol, 1.0 equiv) and 5.6 mL of toluene. DDQ (0.063 g, 0.28 mmol, 1.0 equiv) was added in one portion, and the resulting orange suspension was stirred at rt for 20 h. The reaction mixture was filtered with the aid of ca. 20 mL of CH_2Cl_2, and the filtrate was concentrated to afford 0.117 g of a brown slurry. This material was dissolved in ca. 3 mL of CH_2Cl_2 and concentrated onto 1 g of silica gel. The resulting free-flowing powder was added to the top of a column of 20 g of silica gel and eluted with 25% EtOAc–hexane to afford 0.075 g (71%) of ketone **87** as a viscous bright yellow oil: IR (film) 3122, 2956, 2929, 2860, 1738, 1643, 1608, 1568, 1370, 1189, 1177, 1149, 1107, 1089, 1033, 837, 669, and 591 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 0.8 Hz, 1H), 7.90 (d, J = 0.8 Hz, 1H), 7.84 (app d, J = 8.7 Hz, 2H), 7.83 (s, 1H), 7.58 (d, J = 9.6 Hz, 1H), 7.29 (d, J = 8.6 Hz, 2H), 6.57 (d, J = 9.6 Hz, 1H), 2.86 (t, J = 7.7 Hz, 2H), 2.37 (s, 3H), 1.68 (app quintet, J = 7.6 Hz, 2H), 1.37 (sextet, J = 7.4 Hz, 2H), and 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.3, 146.1, 143.3, 135.1, 134.3, 131.84, 131.81, 130.4, 128.8, 127.4, 127.2, 126.9, 123.2, 118.7, 116.0, 36.7, 34.4, 22.4, 21.8, and 14.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{22}H_{21}NO_3S$ 380.1315, found 380.1303.

■ ASSOCIATED CONTENT

Supporting Information

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

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Notes

The authors declare no competing financial interest.

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