Platinum-Catalyzed Domino Reaction with Benziiodoxole Reagents for Accessing Benzene-Alkynylated Indoles

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Dedication ((optional))

Abstract: Indoles are omnipresent in natural products, bioactive molecules and organic materials. Consequently, their synthesis or functionalization are important fields of research in organic chemistry. Most works focus on installation or modification of the pyrrole ring. To access benzene ring-functionalized indoles with an unsubstituted pyrrole ring remains more challenging. Herein we report a platinum-catalyzed cyclization-alkynylation domino process to obtain selectively C5- or C6- functionalized indoles starting from easily available pyrroles. Our work combines for the first time a platinum catalyst with EthynylBenziiodoxole (EBX) hypervalent iodine reagents in a domino process for the synthesis of polyfunctionalized arene rings and gives access to important building blocks for the synthesis of bioactive compounds and organic materials.

Functionalized indoles occupy a privileged position in organic chemistry, as they can be found in biomolecules, drugs, agrochemicals and materials.^[1] To access these important building blocks, a first approach consists in the introduction of functional groups onto simple, commercially available indoles. In order to have a more efficient alternative to well-established cross-coupling reactions, the transition metal-catalyzed direct functionalization of C-H bond on indoles has been intensively investigated in the last two decades. Nevertheless, this approach is mostly limited to the modification of the more reactive pyrrole ring (innate reactivity, Figure 1, A).^[2] The functionalization of the benzene ring has been only rarely achieved and is limited to C2,C3-disubstituted indoles.^[3] One notable exception is the selective iridium-catalyzed C7-borylation of indoles reported by Hartwig and co-workers.^[4] We were particularly interested by the introduction of an alkyne onto the benzyl ring of indoles, as alkynes are key building blocks in medicinal, synthetic and material chemistry.^[5] Direct alkynylation approaches can be used only to access 2- and 3-substituted indoles.^[6] This is an important limitation, as 5- or 6-alkynylated indoles can be found in bioactive compounds such as 5-LOX (5-lipoxygenase) inhibitor **1**,^[7a] or NMDA (N-Methyl-D-Aspartate Receptor) antagonist **2**.^[7b] Alkynylated carbazoles are especially important for organic materials, such as macrocycle **3**, an organic sensor for the detection of TNT.^[7c] If an efficient method for the synthesis of benzene-alkynylated indoles can be developed, more complex compounds could then be easily obtained by using well-established C-H functionalization at the C2 or C3 positions or transformations of the triple bond.

As C-H metalation of the arene ring of indoles is extremely difficult in presence of the more reactive C2 and C3 C-H bonds, we wondered if the desired reactive intermediate could be generated in situ during a metal-catalyzed cyclization step (Scheme 1). The use of such “domino” or “cascade” processes is one of the most efficient ways to increase molecular complexity in organic synthesis,^[8] but it had not yet been

applied to the synthesis of benzene alkynylated indoles. In fact, reported cascade approaches by the group of Cacchi and Zhu for the synthesis of alkynylated indoles have focused on the construction of the pyrrole ring using palladium catalysis (Scheme 1, A).^[9] To develop a domino process to access indoles functionalized on the benzene ring, another type of cyclization would be needed. In this respect, we were particularly attracted by the works of Alcaide, Hashmi, and Ma among others to form the benzene ring of heterocycles via the cyclization of alkynes^[10] using well-established π -activation catalysts such as gold and platinum.^[11] In fact, one single example of gold-catalyzed indole ring formation starting from easily available pyrrole ethers has been reported.^[10b] This precedence gave solid basis for the cyclization step of the domino process, but the envisaged alkynylation appeared highly challenging, as the generated intermediates are known to broadly favor protodemetalation over further C-C bond formation. The formation of a new C-C bond on a Csp² center of an indole arene ring after cyclization has to the best of our knowledge never been realized.

A. CH functionalization of indoles: breakthroughs and limitations

B. Examples of C5- and C6-alkynylated indoles and carbazoles

Figure 1. 5- and 6-alkynylated indoles: outside the scope of C-H functionalization!

To solve the challenge associated with the low reactivity of gold intermediates in C-C bond forming reactions, our group has turned to the exceptional reactivity of hypervalent iodine alkynylation reagents.^[6b-d,12] We recently reported the first successful domino process in the synthesis of 3-alkynylated furans by the cyclization-alkynylation of allene ketones.^[13] Although this work resulted in the synthesis of regioisomers difficult to access via C-H functionalization, it was still limited to the more reactive heteroarene class of substrates. Herein, we report that the change to a platinum catalyst in combination with ethynylbenziiodoxole reagent **4a**^[14] led to a successful cyclization-alkynylation domino process starting from pyrrole homopropargylic ethers to give either C5 or C6-alkynylated indoles in good yields and high regioselectivity (Scheme 1, B). In addition to giving access to

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important building blocks and scaffolds, this new transformation represents also a breakthrough in the field of catalysis and hypervalent iodine chemistry, as it is the first example of a platinum-catalyzed process with EBX reagents.

A. Previous domino processes: alkynylated pyrrole rings.

B. This work: domino process to access alkynylated benzene rings.

Scheme 1. Domino processes to access alkynylated indoles.

We started our investigation with pyrrole derivatives **5** and hypervalent iodine reagent **4a**. Substrate **5** is easily accessible in two steps from commercially available compounds and the generation of only one molecule of water is required for aromatization. The previous catalytic conditions developed in our group for the domino cyclization-alkynylation of allene ketones^[13] were not suitable for the pyrrole system. After a broad screening of gold catalysts, the desired product could not be obtained. We then turned our attention to platinum catalysts (Table 1).^[10c,11a] Preliminary results with PtCl₂ were promising, as 13% of 5-ethynyl indole **8a** could be isolated with sodium carbonate as base (entry 1). Attempts to modulate the reactivity of the catalyst by formation of a more electrophilic platinum salt (entry 2) or using nitrogen-based ligands (entries 3 and 4) both suppressed the formation of **8a**. In contrast, changing the base to sodium bicarbonate allowed increasing the yield to 40% (entry 5). Investigation of solvents showed that CH₃CN was best (entries 6–8). Neither the use of other hypervalent iodine reagents, such as TIPS-EBX (**4b**) or alkynyliodonium salt **4c** (entries 9–10), nor platinum(IV) or (0) catalysts (entries 11–12) led to improved results. At this point, we decided to investigate the influence of the group eliminated in the aromatization step. Changing the leaving group from hydroxy to methoxy led to a major increase in yield to 91% (entry 13). A silyl ether could also be used,^[10b] but led to a lower yield (80%, entry 14). A bromide counterion led to a slightly higher yield (entry 15) and an iodide completely suppressed the reaction (entry 16). The results obtained with PtCl₂ and PtBr₂ were difficult to reproduce, probably due to the poor solubility of reagent **4a** in CH₃CN. Using a co-solvent led to more reproducible results (entries 17–19). THF was the best, giving the desired product **8a** in 96% yield (entry 18).

With optimized conditions in hand, we then examined the scope of the cyclization-ethynylation domino reaction (Table 2). Indole **8a** was obtained in 84% isolated yield on a 0.3 mmol scale (entry 1). Only C5-ethynylation was observed. Modification of the substituent on the nitrogen was investigated first. A tolyl and a benzyl group were well tolerated (entries 2–3), as well as different substituents on an alkyl chain such as methoxy and trifluoromethyl (entries 4–5). Substitution of the alkyne was examined next. The desired C5-alkynylated product **8f** was obtained in 70% yield with a methyl group (entry 6). With aromatic substituents, formation of the C6-alkynylated product **10** was

observed for the first time. The C5-alkynylated product **8** was still the major product with a phenyl, a tolyl or a *para*-bromophenyl substituent (entries 7–9). The latter case also demonstrated that halogen substituents were tolerated under the reaction conditions, allowing further functionalization of the products via classical cross-coupling chemistry. With a naphthyl group, a 1:1 mixture of regioisomers was obtained (entry 10). With a methyl substituent in propargylic position, the C5-alkynylated product **8k** was obtained in 75% yield (entry 11). In contrast, when tertiary ether **6l** was used, the C6-alkynylated product **10e** was formed (entry 12). Alkynylated carbazole **8m** was obtained in 76% yield (entry 13). The domino process could also be applied to the synthesis of thiophene-fused heterocycle **8n** in 78% yield (entry 14).

Table 1. Optimization of the Domino Cyclization-Alkynylation Reaction

entry	pyrrole	catalyst	reagent	base	solvent	yield ^[a]
1	5	PtCl ₂	4a	Na ₂ CO ₃	CH ₃ CN	13%
2	5	PtCl ₂ /AgOTf	4a	Na ₂ CO ₃	CH ₃ CN	<5%
3	5	PtCl ₂ /bipyridine	4a	Na ₂ CO ₃	CH ₃ CN	<5%
4	5	Pt(NH ₃) ₂ Cl ₂	4a	Na ₂ CO ₃	CH ₃ CN	<5%
5	5	PtCl ₂	4a	NaHCO ₃	CH ₃ CN	40%
6	5	PtCl ₂	4a	NaHCO ₃	toluene	30%
7	5	PtCl ₂	4a	NaHCO ₃	THF	21%
8	5	PtCl ₂	4a	NaHCO ₃	MeOH	14%
9	5	PtCl ₂	4b	NaHCO ₃	CH ₃ CN	27%
10	5	PtCl ₂	4c	NaHCO ₃	CH ₃ CN	<5%
11	5	PtCl ₄	4a	NaHCO ₃	CH ₃ CN	<5%
12	5	Pt(PPh ₃) ₄	4a	NaHCO ₃	CH ₃ CN	<5%
13	6a	PtCl ₂	4a	NaHCO ₃	CH ₃ CN	91%
14	7	PtCl ₂	4a	NaHCO ₃	CH ₃ CN	80%
15	6a	PtBr ₂	4a	NaHCO ₃	CH ₃ CN	98% ^[b]
16	6a	PtI ₂	4a	NaHCO ₃	CH ₃ CN	<5%
17	6a	PtBr ₂	4a	NaHCO ₃	CH ₃ CN/C ₆ H ₅ Cl (v/v = 1/5)	45%
18	6a	PtBr ₂	4a	NaHCO ₃	CH ₃ CN/THF (v/v = 1/5)	96%
19	6a	PtBr ₂	4a	NaHCO ₃	CH ₃ CN/THF (v/v = 1/10)	93%

^[a]Reaction condition: **5–7** (0.10 mmol), catalyst (10 mol %), **4** (0.20 mmol), base (0.20 mmol), 0.1 M, RT, 72 h. Isolated yields after column chromatography. ^[b]Not reproducible.

Having achieved the synthesis of C5-alkynylated indoles starting from C2-substituted pyrroles, we then turned to C3-substituted derivatives to achieve C6 functionalization. (Table 3). Pyrrole **9a** bearing a terminal alkyne gave C6-alkynylated indole **10a** exclusively in 77% yield (entry 1). Substituted alkynes could also be used to access 6,7-disubstituted indoles in 47–53% yield (entries 2–4). Starting from tertiary ethers, 4,6-disubstituted products could be obtained (entries 5 and 6). In this case, the same products were obtained as when starting from C2-substituted pyrroles. We then wondered if more complex trisubstituted indoles could be accessed. In fact, 4,6,7- and 4,5,6-substituted indoles **10g** and **10h** could be obtained in 44% and 34% yield respectively (entries 7 and 8). Although the yields are moderate, the synthesis of these poly-substituted compounds using another method would have been

extremely difficult. Finally, the synthesis of C6-alkynylated carbazoles **10i-j** was also possible (entries 9 and 10).

Table 2. Scope of 5-Alkynylated Indoles.

entry	substrate	product	yield ^[a]
1	R = Me (6a)	8a	84%
2	R = tolyl (6b)	8b	81%
3	R = benzyl (6c)	8c	83%
4	R = 3-methoxy propyl (6d)	8d	80%
5	R = 1,1,1-trifluorobutyl (6e)	8e	82%
6	R = Me (6f)	8f	70%
7	R = phenyl (6g)	8g/10c (4/1)	70% (56%) ^[b]
8	R = tolyl (6h)	8h/10k (3/1)	69% (52%) ^[b]
9	R = <i>p</i> -Br-phenyl (6i)	8i/10l (2.5/1)	62% (44%) ^[b]
10	R = naphthyl (6j)	8j/10d (1/1)	31%/31%
11			75%
12			54%
13			76%
14			78%

^[a]Reaction conditions: Substrate **6** (0.30 mmol), PtBr₂ (10 mol%), EBX reagent **4a** (0.60 mmol), NaHCO₃ (0.60 mmol), THF/CH₃CN (3 mL, v/v=5/1), 72–120 h, isolated yields after column chromatography are given. ^[b]Yield determined by ¹H NMR. The isolated yield of isomer **8** is given in parenthesis.

The developed domino process is highly complex. Consequently, any proposal about the reaction mechanism is highly speculative at this stage of development. Based on the well-established π -acidity of platinum,^[11a] the first step of the catalytic cycle is most probably activation of the alkyne to give complex **I** (Scheme 2). At this point,

cyclization could occur either on the C2 or C3 position of the pyrrole ring to give intermediates **II** and **IV** respectively. Attack on the more nucleophilic C2 position, leading to **II** is more probable. From **II**, two different pathways are possible: 1,2 shift of the Pt-bearing vinyl group via platinum carbene-cyclopropane intermediate **III**^[11a,15] to give carbocation **IV**, or 1,2-shift of the alkoxy substituent to give intermediate **VII**.^[10] C5- or C6- metalated intermediates **V** and **VIII** will then be generated from **IV** and **VII** respectively after deprotonation and aromatization via methanol elimination. Alkynylated products **8** and **10** can be formed by reaction of EBX reagent **4a** with the organoplatinum intermediates. As this point, it is not clear if the alkynylation step proceeds via an oxidative addition/reductive elimination mechanism on platinum^[16] or by direct nucleophilic attack of the organometallic intermediates onto reagent **4a**.

Table 3. Scope of 6-Alkynylated Indoles.

entry	substrate	product	yield ^[a]
1			77%
2	R = Me (9b)	10b	49%
3	R = phenyl (9c)	10c	53%
4	R = naphthyl (9d)	10d	47%
5	R = Me (9e)	10e	54%
6	R = phenyl (9f)	10f	65%
7			44%
8			34%
9	R = H (9i)	10i	58%
10	R = OMe (9j)	10j	64%

^[a]Reaction conditions: Substrate **9** (0.30 mmol), PtBr₂ (10 mol%), EBX reagent **4a** (0.60 mmol), NaHCO₃ (0.60 mmol), THF/CH₃CN (3 mL, v/v=5/1), 72–120 h, isolated yields after column chromatography are given.

If the C3-substituted pyrrole is used as starting material, the mechanism is simpler as C2-attack of the indole leads directly to a 6-membered ring and therefore to exclusive formation of the C6-alkynylated product **10**. The observed regioselectivity for secondary ethers is in accordance with a shift of the vinyl group. In contrast, shift of the alkoxy group had been observed in the cyclization step when using gold catalysts.^[10b] This may be due to an easier formation of platinum carbene intermediate **III** when compared to gold catalysts.^[17] This result further emphasizes an advantage of the platinum catalyst, as with gold both C2- and C3-substituted pyrroles would have given C6-alkynylated products. With pyrroles substituted with tertiary ethers, C6-alkynylated products were observed independent of the structure of the starting material. In this case, the presence of the methyl group may further stabilize transition state **VI** and favor the shift of the alkoxy group.

Scheme 2. Speculative mechanism for the domino cyclization-alkynylation.

The obtained alkynylated indoles are interesting building blocks, as the unsubstituted pyrrole ring can be easily further derivatized using established methods and the terminal alkyne obtained after silyl group removal can serve as platform for further functionalization. For example, deprotection of alkyne **8a** followed by gold-catalyzed selective C3 alkynylation with TIPS-EBX (**4b**)^[6b] gave monoprotected diyne **11**, ready for further selective derivatization (Scheme 3, **A**). Starting from naphthyl derivative **10d**, deprotection followed by platinum-catalyzed cycloisomerization^[18] gave access to helicene **12** (Scheme 3, **B**). Helicenes are important molecules in asymmetric catalysis and material science, but have never been synthesized with a terminal pyrrole ring to the best of our knowledge.^[19]

Scheme 3. Further transformations of the alkynylated indole products.

In conclusion, we have reported a new domino cyclization strategy for the efficient synthesis of C5- or C6-alkynylated indoles starting from easily available C2- or C3-substituted pyrroles. Our strategy is

complementary to C-H functionalization, as the benzene positions on indole are difficult to modify directly, due to the higher reactivity of the pyrrole ring. Key for success was the unprecedented combination of a platinum catalyst with EthynylBenziodoXole (EBX) reagents. The domino process realized in this work represents a new general strategy for the synthesis of alkynylated arenes. Further investigations will focus on the synthesis of other (hetero)arenes and on the introduction of different functional groups in the final bond forming step.^[20]

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Keywords: Domino Reactions, Alkynes, Indoles, Hypervalent Iodine, Platinum Catalysis.

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- [20] The use of arylodonium salts, Togni's reagent and cyano- or azido-benziodoxolones under the optimized reaction conditions did not result in the formation of the domino cyclization-functionalization products. The design of new catalyst systems and reagents will be required in the future.

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1. General method

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et₂O, CH₃CN, toluene, hexane and CH₂Cl₂ were dried by passage over activated alumina under nitrogen atmosphere (H₂O content < 10 ppm, *Karl-Fischer* titration). NEt₃ and pyridine were distilled under nitrogen from KOH. PtBr₂ was purchased from Aldrich, **crushed into fine powder** and kept in desiccator under anhydrous condition (decrease of reactivity has been observed for catalyst if prolonged exposition to air (*ca* 1 month)). The solvents were degassed by Freeze-Pump-Thaw method when mentioned. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F₂₅₄ TLC glass plates or aluminium plates and visualized with UV light, permanganate stain, CAN stain or Anisaldehyde stain. Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries, the data is uncorrected. ¹H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in chloroform-d, DMSO-d₆ or CD₃OD, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm or the internal methanol signal at 3.30 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation). ¹³C-NMR spectra were recorded with ¹H-decoupling on a Bruker DPX-400 100 MHz spectrometer in chloroform-d, DMSO-d₆ or CD₃OD, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm or the internal methanol signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm⁻¹ (w = weak, m = medium, s = strong, br = broad). Gas chromatographic and low resolution mass spectrometric measurements were performed on a Perkin-Elmer Clarus 600 gas chromatographer and mass spectrometer using a Perkin-Elmer Elite fused silica column (length: 30 m, diameter: 0.32 mm) and Helium as carrier gas. High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. HPLC measurement were done on a JASCO HPLC system with an AS2055 Autosampler, a PU 2089 Pump, a UV 2075 detector and a SEDEX 85 (SEDERE) detector using a CHIRALPAK IC column from DAICEL Chemical Industries Ltd. HPLC grade solvents from Sigma-Aldrich were used.

2. Preparation of Reagents

Triisopropylsilyl trimethylsilylacetylene (**14**)

Following a reported procedure,^[1] *n*-butyllithium (2.5 M in hexanes, 12.0 mL, 29.9 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**13**) (3.0 g, 30 mmol, 1.0 equiv) in THF (48 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to -78 °C and chlorotriisopropylsilane (6.4 mL, 30 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (40 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water and brine, then dried over MgSO₄, filtered and concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation (56-57°C/0.25 mmHg) to yield **14** (7.16 g, 28.0 mmol, 92% yield) as a colorless liquid.

¹H NMR (400 MHz, CDCl₃) δ 1.08 (m, 21 H, TIPS), 0.18 (s, 9 H, TMS). IR ν 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m). Characterization data of **14** corresponded to the literature values.^[1]

1-Chloro-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (**17**)

Following a reported procedure,^[2] TMEDA (distilled over KOH) (1.26 mL, 8.20 mmol, 0.2 equiv) was added to a solution of ⁿBuLi (2.5 M in hexanes, 36.6 mL, 91.6 mmol, 2.2 equiv). After 15 min, the cloudy solution was cooled to 0 °C and **15** (7.0 mL, 42 mmol, 1 equiv) in THF (6 mL) was added dropwise. The reaction was stirred 30 min at 0 °C and then at RT overnight. I₂ (11.2 g, 44.0 mmol, 1.06 equiv) was then added portion wise at 0 °C and the mixture stirred at 0 °C for 30 min and 4 h at RT. The reaction was quenched with saturated NH₄Cl. Et₂O (100 mL) was added and the layers were separated. The aqueous layer was then extracted twice with Et₂O (3 x 50 mL). The organic layers were combined, washed twice with saturated Na₂S₂O₃ (2 x 50 mL), dried over MgSO₄, filtered and reduced to afford 15.6 g of **16** as an brown oil which was used without further purification.

[1] C J. Helal, P A. Magriotis, E J. Corey, *J. Am. Chem. Soc.* **1996**, *118*, 10938.

[2]. E. F. Perozzi, R. S. Michalak, G. D. Figuly, W. H. Stevenson, D. B. Dess, M. R. Ross, J. C. Martin, *J. Org. Chem.* **1981**, *46*, 1049.

The crude oil was dissolved in wet CH_2Cl_2 (40 mL) in the dark under air. $t\text{BuOCl}$ (5.2 mL, 44 mmol, 1.05 equiv) was then added dropwise at 0 °C. After 30 min, the resulting suspension was filtered to afford **17** (7.30 g, 18.1 mmol, 43%) as a yellow solid. The mother liquors were carefully reduced to one third and filtered to afford **17** (3.51 g, 8.71 mmol, 21%) as a yellow solid. Combined yield: 64%. Mp 167 – 169°C. ^1H NMR (400 MHz, CDCl_3) δ 8.09 (d, 1 H, J = 8.4 Hz, ArH), 7.85 (m, 1 H, ArH), 7.73 (m, 2 H, ArH). ^{13}C NMR (101 MHz, CDCl_3) δ 133.8, 132.1, 131.6, 129.7, 128.5, 122.8 (q, 289 Hz), 113.4, 84.8. Consistent with reported values.^[2]

1-Hydroxy-3,3-bis(trifluoromethyl)-3-(1*H*)-1,2-benziodoxole (**18**)

Following a preported procedure,^[3] Et_3BnNCl (83 mg, 0.36 mmol, 0.05 equiv) was added to a stirring solution of **17** (10.7 g, 26.5 mmol, 1 equiv) in CH_2Cl_2 (150 mL) and KOH (1.48 g, 26.5 mmol, 1 equiv) in water (28 mL). The reaction was kept under air until TLC indicated that all starting material was consumed. The organic layer was separated and dried over MgSO_4 . The resulting solid was purified over a silica plug eluting with EtOAc, then recrystallized in EtOAc (30 mL) and washed with pentane to afford **18** (7.42 g, 19.2 mmol, 73%) as a white solid. ^1H NMR (400 MHz, DMSO) δ 7.96 (m, 2 H, ArH), 7.73 (m, 2 H, ArH). ^{13}C NMR (101 MHz, DMSO) δ 133.3, 131.0, 130.8, 128.9, 127.9, 123.4 (q, J = 290 Hz), 117.2, 83.7 (m). IR 1464 (w), 1435 (w), 1290 (w), 1263 (m), 1185 (s), 1139 (s), 1103 (m), 1041 (w), 1021 (w), 952 (s), 760 (m), 730 (m), 692 (m).

1-[(Triisopropylsilyl)ethynyl]-3,3-bis(trifluoromethyl)-3(1*H*)-1,2-benziodoxole (**1a**)

TMSOTf (3.80 g, 17.1 mmol, 1.1 equiv) was added to **18** (6.00 g, 15.5 mmol, 1.0 equiv) in CH_2Cl_2 (200 mL) at RT. After 20 min, the solution was concentrated at 0 °C under reduced pressure. After evaporation of the solvent, the reaction flask was directly filled with Ar, to prevent decomposition of the hygroscopic triflate intermediate. Then the resulting yellow solid was dissolved in CH_3CN (200 mL). (Trimethylsilyl)(triisopropylsilyl)acetylene (**14**) (5.14 g, 20.2 mmol, 1.3 equiv) was added and after 20 min several drops of pyridine were added. The reaction was then concentrated under vacuum, dissolved in Et_2O and filtered over

[3]. A. J. Blake, A. Novak, M. Davies, R. I. Robinson, S. Woodward, *Synth. Commun.* **2009**, 39, 1065

Rf (PET/Et₂O 95/5): 0.4. Mp 131 – 132°C. ¹H NMR (400 MHz, CDCl₃) (*ca* 0.10 mmol/mL) δ 8.36 (dd, 1 H, *J* = 7.9, 1.7 Hz, ArH), 7.84 (d, 1 H, *J* = 6.7 Hz, ArH), 7.68 (m, 2H, ArH), 1.15 (m, 21 H, TIPS). ¹³C NMR (101 MHz, CDCl₃) δ 132.7, 131.1, 129.9, 129.9 (m), 128.2, 123.6 (q, 288 Hz), 112.1, 110.8, 81.4 (m), 69.7, 18.5, 11.2. Characterization data of **1a** corresponded to the literature values.^[4]

1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (20)

Following the reported procedure,^[5] NaIO₄ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid (**19**) (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure product **20** (8.3 g, 31 mmol, 98%) as a colorless solid.

¹H NMR (400 MHz, (CD₃)₂SO) δ 8.02 (dd, 1 H, *J* = 7.7, 1.4 Hz, Ar*H*), 7.97 (m, 1 H, Ar*H*), 7.85 (dd, 1 H, *J* = 8.2, 0.7 Hz, Ar*H*), 7.71 (td, 1 H, *J* = 7.6, 1.2 Hz, Ar*H*); ¹³C NMR (100 MHz, (CD₃)₂SO) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4; IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m); the reported values correspond to the ones in literature.^[5]

1-[(Triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX, 1b)

Following a reported procedure,^[6] 2-iodosylbenzoic acid (**20**) (21.7 g, 82.0 mmol, 1.0 equiv) was charged in oven-dried three-neck 1L flask equipped with a magnetic stirrer. After 3 vacuum/nitrogen cycles, anhydrous acetonitrile (500 mL) was added via canula and cooled to 0 °C. Trimethylsilyltriflate (16.4 mL, 90.0 mmol, 1.1 equiv) was added dropwise via a dropping funnel over 30 min (no temperature increase was observed). After 15 min,

[4] Y. LI, J. Brand, J. Waser, *Angew. Chem., Int. Ed.* **2013**, 52, 6743.

[5]. L. Kraszkiewicz, L. Skulski, *Arkivoc.* **2003**, 6, 120.

[6] J. P. Brand, J. Waser, *Angew. Chem., Int. Ed.* **2010**, *49*, 7304.

(trimethylsilyl)(triisopropylsilyl)acetylene (**14**) (23.0 g, 90.0 mmol, 1.1 equiv) was added via canula over 15 min (no temperature increase was observed). After 30 min, the suspension became an orange solution. After 10 min, pyridine (7.0 mL, 90 mmol, 1.1 equiv) was added via syringe. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and reduced under vacuum until a solid was obtained. The solid was dissolved in DCM (200 mL) and transferred in a 1L separatory funnel. The organic layer was added and washed with 1 M HCl (200 mL) and the aqueous layer was extracted with CH₂Cl₂ (200 mL). The organic layers were combined, washed with a saturated solution of NaHCO₃ (2 x 200 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 120 mL) afforded **1b** (30.1 g, 70.2 mmol, 86%) as colorless crystals.

Melting point (Dec.) 170-176°C

¹H NMR (400 MHz, CDCl₃) δ 8.44 (m, 1 H, *ArH*), 8.29 (m, 1 H, *ArH*), 7.77 (m, 2 H, *ArH*), 1.16 (m, 21 H, TIPS). ¹³C NMR (100 MHz, CDCl₃) δ 166.4, 134.6, 132.3, 131.4, 131.4, 126.1, 115.6, 114.1, 64.6, 18.4, 11.1. IR ν 2943 (m), 2865 (m), 1716 (m), 1618 (m), 1604 (s), 1584 (m), 1557 (m), 1465 (m), 1439 (w), 1349 (m), 1291 (m), 1270 (w), 1244 (m), 1140 (m), 1016 (m), 999 (m), 883 (m), 833 (m), 742 (m), 702 (s), 636 (m); Characterization data of **1b** corresponded to the literature values.^[6]

Phenyl(triisopropylsilyl)iodonium triflate (**1c**)

Following a slight modification of the reported procedure,^[7] phenyliodonium diacetate (**21**) (2.53 g, 7.85 mmol, 1.00 equiv) was diluted with DCM (7 mL) and the mixture was stirred for 5 minutes. Tf₂O (0.60 mL, 3.9 mmol, 0.50 equiv.) was added dropwise at 0 °C and the resulting yellow mixture was stirred 30 min. (Trimethylsilyl)(triisopropylsilyl)acetylene (**14**) (2.00 g, 7.86 mmol, 1.00 equiv) was added and the mixture was then stirred 2 h. Water was then added (30 mL) followed by extraction of the aqueous layer with DCM (2 x 30 mL). The combined organic layers were dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. The resulting solid was triturated in hexane (10 mL). Filtration and removal of solvent *in vacuo* afforded phenyl(triisopropylsilyl)iodonium triflate (**1c**) (2.90 g, 11.2 mmol, 70% yield) as a colorless solid.

Melting point: 109 – 114°C. ¹H NMR (400 MHz, CDCl₃) δ 8.09 (m, 2 H, *ArH*), 7.65 (m, 1 H, *ArH*), 7.52 (m, 2 H, *ArH*), 1.15-1.01 (m, 21 H, TIPS); ¹³C NMR (100 MHz, CDCl₃) δ 133.7, 132.5, 132.4, 119.7, 117.6, 117.6, 44.9, 18.3, 11.1; IR ν 3288 (w), 3088 (m), 2949 (m), 2894 (m), 2869 (w), 1563 (m), 1467 (w), 1451 (w), 1388 (w), 1281 (s), 1236 (s), 1221 (s), 1174 (s), 1068 (w), 1028 (s), 988 (m), 916 (m), 884 (m), 736 (s), 679 (m), 639 (s); HRMS (ESI) calcd

[7] T. Kitamura, M. Kotani, Y. Fujiwara, *Synthesis* **1998**, 10, 1416.

for $\text{C}_{17}\text{H}_{26}\text{ISi}^+$ (M-OTf) 385.0843; found 385.0812; the reported values corresponded to the ones in literature.^[5]

3. Synthesis of starting materials:

1-(3-Methoxypropyl)-1H-pyrrole-2-carbaldehyde (**24**)

A solution of **22** (475 mg, 5.00 mmol, 1.0 equiv) in THF (5 mL) was added into a suspension of NaH (126 mg, 5.25 mmol, 1.05 equiv) in THF (5 mL). 15 minutes later, **23** (765 mg, 5.00 mmol, 1.00 equiv) was added into the mixture. The reaction was quenched by sat NH_4Cl after 4 h. The aqueous layer and organic layer were separated and the aqueous layer was extracted with ether (3x10 mL). After drying over MgSO_4 , filtrating and concentrating under vacuum, the crude product was purified by column chromatography (Pentane/EtOAc= 10:1) to afford **24** as brown oil (500 mg, 3.00 mmol, 60 %).

Rf (Pentane / EtOAc= 10:1): 0.4. ^1H NMR (400 MHz, CDCl_3) δ 9.37 (s, 1 H, *CHO*), 6.81 (s, 1 H, *pyrroleH*), 6.78 (dd, 1 H, $J = 4.0, 1.7$ Hz, *pyrroleH*), 6.06 (dd, 1 H, $J = 4.0, 2.5$ Hz, *pyrroleH*), 4.24 (t, 2 H, $J = 6.8$ Hz, *NCH₂*), 3.16 (s, 3 H, *OCH₃*), 3.12 (t, 2 H, $J = 5.8$ Hz, *CH₂OCH₃*), 1.85 (m, 2 H, *CH₂*). ^{13}C NMR (101 MHz, CDCl_3) δ 178.5, 131.4, 130.8, 124.3, 108.9, 68.4, 57.9, 45.5, 30.5. IR 1659 (m), 1482 (w), 1405 (w), 1370 (w), 1322 (w), 1117 (w), 1071 (w), 913 (w), 732 (s). HRMS (ESI) calcd for $\text{C}_9\text{H}_{13}\text{NNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$ 190.0838; found 190.0834.

1-(4,4,4-Trifluorobutyl)-1H-pyrrole-2-carbaldehyde (**26**)

A solution of **22** (475 mg, 5.00 mmol, 1.0 equiv) in THF (5 mL) was added into a solution of NaH (126 mg, 5.25 mmol, 1.05 equiv) in THF (5 mL). 15 minutes later, **25** (955 mg, 5.00 mmol, 1.00 equiv) was added into the mixture. The reaction was quenched with sat NH_4Cl after 4 h. The aqueous and organic layers were separated and the aqueous layer was extracted with ether (3x10 mL). After drying over MgSO_4 , filtrating and concentrating under vacuum, the crude product was purified by column chromatography (Pentane/EtOAc= 20:1) to afford **26** as yellow oil (720 mg, 3.51 mmol, 70 %).

Rf (Pentane / EtOAc= 20:1): 0.5. ^1H NMR (400 MHz, CDCl_3) δ 9.44 (d, 1 H, $J = 1.0$ Hz, *CHO*), 6.87 (m, 2 H, *pyrroleH*), 6.16 (dd, 1 H, $J = 4.0, 2.5$ Hz, *pyrroleH*), 4.30 (t, 2 H, $J = 6.8$ Hz, *NCH₂*), 1.97 (m, 4 H, *CH₂CH₂*). ^{13}C NMR (101 MHz, CDCl_3) δ 179.0, 131.0, 126.7 (q, J

= 276.6 Hz), 124.9, 109.6 (two peaks overlap), 47.1, 30.3 (q, $J = 29.3$ Hz), 23.7 (q, $J = 2.9$ Hz). IR 1660 (m), 1482 (w), 1409 (w), 1394 (w), 1370 (w), 1338 (w), 1327 (w), 1316 (w), 1297 (w), 1280 (w), 1255 (m), 1240 (w), 1221 (w), 1184 (w), 1136 (m), 1079 (w), 1065 (w), 1033 (m), 1018 (w), 910 (m), 766 (m), 729 (s). HRMS (ESI) calcd for $C_9F_3H_{11}NO^+$ $[M+H]^+$ 206.0787; found 206.0786.

1-Methyl-1H-pyrrole-3-carbaldehyde (**29**)

Following a reported procedure^[8], dry DMF (1.88 mL, 24.3 mmol, 1.2 equiv) was added into a solution of oxalyl dichloride (1.82 mL, 22.3 mmol, 1.1 equiv) in DCM (50 mL) slowly at 0 °C. After 15 minutes, the solution turned cloudy. **27** (4.50 g, 20.2 mmol, 1.0 equiv) was added into the mixture slowly at 0 °C, following by heating the solution at reflux during 1 h. The solution was cooled down and filtrated. The filtrating cake was dissolved into 5 % NaOH solution (200 mL). The solution was kept stirring during 4 hours, and extracted by ether (3 x 50 mL). After drying over $MgSO_4$, filtrating and concentrating under vacuum, yellow oil **28** was obtained as a yellow oil (735 mg, 7.73 mmol, <38%). The crude product was used without further purification.

A solution of **28** (735 mg, 7.73 mmol, 1.0 equiv) in THF (8 mL) was added into a suspension of NaH (291 mg, 8.50 mmol, 1.1 equiv) in THF (8 mL). After 15 minutes, CH_3I (0.53 mL, 8.5 mmol, 1.1 equiv) was added into the solution. The reaction was quenched with sat NH_4Cl after 4 h. The aqueous and organic layers were separated and the aqueous layer was extracted with ether (3x10 mL). After drying over $MgSO_4$, filtrating and concentrating under vacuum, the crude product was purified by column chromatography (Pentane/EtOAc= 10:1) to afford **29** as brown oil (610 mg, 5.59 mmol, 72 %).

1H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1 H, CHO), 7.20 (t, 1 H, $J = 1.8$ Hz, *pyrroleH*), 6.59 (m, 1 H, *pyrroleH*), 6.55 (dd, 1 H, $J = 2.9, 1.8$ Hz, *pyrroleH*), 3.66 (s, 3 H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.0, 129.9, 126.5, 124.3, 108.1, 36.5. Characterization data corresponded to the literature values^[9].

2-(1-Methoxybut-3-yn-1-yl)-1-methyl-1H-pyrrole (**6a**)

[8] B L. Bray, J M. Muchowaski, *J. Org. Chem.* **1988**, 53, 6115.

[9] T Purkarthofer, K. Gruber, M. Fechter, H. Griengl, *Tetrahedron*. **2005**, 61, 7661.

A 50 mL two-necked flask was charged with Mg (321 mg, 13.2 mmol, 1.32 equiv), HgCl₂ (2.7 mg, 0.10 mmol, 0.01 equiv) and dry diethyl ether (30 mL), then propargyl bromide was added dropwise (2.86 g, 12.0 mmol, 1.20 equiv). When the solution became homogeneous, **30** (1.09 g, 10.0 mmol, 1.00 equiv) was added dropwise. The reaction was quenched with sat NH₄Cl solution (30 mL) when TLC (Pentane/EtOAc: 5/1) indicated that the aldehyde was completely consumed after 4 hours. The aqueous and organic layers were separated; the aqueous layer was extracted with diethyl ether (3×20 mL). The combined organic layers were dried over MgSO₄ and concentrated under vacuum to obtain 1.34 g crude product as brown oil. The crude product was used for the next step directly without further purification. Crude propargylic alcohol (1.34 g, 8.98 mmol, 0.89 equiv) in THF (18 mL) was added into a suspension of NaH (237 mg, 9.88 mmol, 0.98 equiv) in THF (18 mL). 15 minutes later, MeI (1.40 g, 9.88 mmol, 1.10 equiv) was added into the mixture. The reaction was quenched with sat NH₄Cl after 4 h. The aqueous and organic layers were separated and the aqueous layer was extracted with ether (3×10 mL). After drying over MgSO₄, filtrating and concentrating under vacuum, the crude product was purified by column chromatography (Pentane/EtOAc= 15:1, 1 % Et₃N) to afford **6a** as brown oil (1.00 g, 6.13 mmol, 61 % over two steps).

Rf (Pentane:EtOAc = 25 / 1): 0.6. ¹H NMR (400 MHz, CDCl₃) δ 6.62 (m, 1 H, *pyrroleH*), 6.18 (dd, 1 H, *J* = 3.6, 1.8 Hz, *pyrroleH*), 6.10 (dd, 1 H, *J* = 3.6, 2.7 Hz, *pyrroleH*), 4.58 (t, 1 H, *J* = 6.9 Hz, *CHO*), 3.68 (s, 3 H, *NCH₃*), 3.27 (s, 3 H, *OCH₃*), 2.79 (ddd, 2 H, *J* = 16.8, 6.5, 2.7 Hz, *CH₂*), 2.05 (t, 1 H, *J* = 2.7 Hz, alkyne *CH*). ¹³C NMR (101 MHz, CDCl₃) δ 129.9, 123.3, 108.5, 106.4, 80.7, 73.9, 69.8, 54.7, 34.0, 24.0. IR 2946 (m), 2866 (m), 2088 (w), 1707 (s), 1502 (w), 1366 (w), 1274 (w), 1273 (w), 1272 (w), 1253 (w), 1205 (m), 1175 (w), 998 (w), 886 (m). HRMS (ESI) calcd for C₁₀H₁₃NNaO⁺ [M+Na]⁺ 186.0889; found 186.0895.

The protocol for the synthesis of **6a** represents the typical procedure for the preparation of **6b**, **6c**, **6d**, **6e**, **6f**, **6j**, **6k**, **6l**, **6m**, **9a**, **9e**, **9f**, **9h**, **9i**, **9j**.

2-(1-Methoxybut-3-yn-1-yl)-1-(p-tolyl)-1H-pyrrole (**6b**)

1.0 g (5.4 mmol) of the corresponding aldehyde was used to obtain the crude propargylic alcohol (880 mg, 3.91 mmol, 72%). 440 mg (1.95 mmol) of crude propargylic alcohol was used for methylation. 2-(1-Methoxybut-3-yn-1-yl)-1-(p-tolyl)-1H-pyrrole (**6b**) was obtained as a colorless oil (398 mg, 1.66 mmol, 62% over two steps).

Rf (Pentane / EtOAc = 15 / 1): 0.6. ¹H NMR (400 MHz, CDCl₃) δ 7.31 (m, 4 H, *benzene*), 6.82 (dd, 1 H, *J* = 2.7, 1.8 Hz, *pyrroleH*), 6.43 (dd, 1 H, *J* = 3.6, 1.8 Hz, *pyrroleH*), 6.32 (m, 1 H, *pyrroleH*), 4.44 (t, 1 H, *J* = 6.9 Hz, *CHOCH₃*), 3.20 (s, 3 H, *OCH₃*), 2.71 (ddd, 2 H, *J* = 15.2, 7.0, 2.7 Hz, *CH₂*), 2.47 (s, 3 H, *tolyl CH₃*), 2.01 (t, 1 H, *J* = 2.7 Hz, alkyne *CH*). ¹³C NMR (101 MHz, CDCl₃) δ 137.4, 137.2, 131.7, 129.5, 126.5, 123.4, 108.5, 108.0, 80.9, 73.0, 69.8, 55.3, 24.7, 21.0. IR 3303 (w), 2986 (w), 2928 (w), 2902 (w), 2821 (w), 2246 (w), 2122 (w), 1518 (s), 1468 (m), 1432 (w), 1329 (m), 1241 (w),

1183 (w), 1150 (w), 1095 (s), 1046 (w), 1034 (w), 974 (w), 941 (w), 912 (m), 894 (w), 825 (s), 797 (w), 716 (s), 687 (w), 672 (w), 645 (s), 636 (s), 625 (m), 613 (m). HRMS (ESI) calcd for $C_{16}H_{17}NaO^+$ $[M+Na]^+$ 262.1202; found 262.1198.

1-Benzyl-2-(1-methoxybut-3-yn-1-yl)-1H-pyrrole (6c)

690 mg (3.73 mmol) of the corresponding aldehyde was used to obtain the crude propargylic alcohol (880 mg, 2.83 mmol, <76%), which was used directly in the methylation step. **6c** was obtained as a yellow oil (678 mg, 2.83 mmol, 76% over two steps).

Rf (Pentane / EtOAc = 25 / 1): 0.5. 1H NMR (400 MHz, $CDCl_3$) δ 7.32 (m, 3 H, *benzene*), 7.09 (d, 2 H, $J = 7.0$ Hz, *benzene*), 6.72 (dd, 1 H, $J = 2.6$, 1.7 Hz, *pyrroleH*), 6.29 (dd, 1 H, $J = 3.6$, 1.7 Hz, *pyrroleH*), 6.21 (m, 1 H, *pyrroleH*), 5.23 (s, 2 H, NCH_2), 4.51 (t, 1 H, $J = 6.8$ Hz, $CHOCH_3$), 3.17 (s, 3 H, OCH_3), 2.69 (ddd, 2 H, $J = 16.5$, 7.2, 2.7 Hz, CH_2), 2.02 (t, 1 H, $J = 2.7$ Hz, alkyne CH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.0, 130.1, 128.3, 127.0, 126.2, 122.8, 108.5, 107.0, 80.6, 73.5, 69.9, 54.5, 50.2, 24.1. IR 2247 (w), 2123 (w), 1735 (w), 1497 (w), 1482 (w), 1455 (w), 1357 (w), 1299 (w), 1096 (m), 1078 (m), 909 (s), 728 (s). HRMS (ESI) calcd for $C_{16}H_{17}NNaO^+$ $[M+Na]^+$ 262.1202; found 262.1207.

2-(1-Methoxybut-3-yn-1-yl)-1-(3-methoxypropyl)-1H-pyrrole (6d)

573 mg of **24** (3.73 mmol) was used to obtain the crude propargylic alcohol (490 mg, 2.21 mmol, <74%), which was used directly in the methylation step. **6d** was obtained as yellow oil (248 mg, 1.12 mmol, 40% over two steps).

Rf (Pentane / EtOAc = 25 / 1): 0.6. 1H NMR (400 MHz, $CDCl_3$) δ 6.66 (dd, 1 H, $J = 2.8$, 1.8 Hz, *pyrroleH*), 6.15 (m, 1 H, *pyrroleH*), 6.09 (dd, 1 H, $J = 3.5$, 2.8 Hz, *pyrroleH*), 4.58 (t, 1 H, $J = 6.9$ Hz, $CHOCH_3$), 4.03 (m, 2 H, NCH_2), 3.33 (s, 3H, $CHOCH_3$), 3.32 (m, 2 H, CH_2OCH_3), 3.23 (s, 3H, CH_2OCH_3), 2.77 (ddd, 2 H, $J = 16.2$, 6.7, 2.7 Hz, CH_2), 1.99 (m, 3 H, alkyne $CH + NCH_2CH_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 129.8, 122.0, 107.8, 106.8, 80.8, 73.1, 69.9, 68.9, 58.3, 54.4, 43.3, 31.3, 23.9. IR 1664 (w), 1483 (w), 1458 (w), 1348 (w), 1297 (w), 1190 (w), 1116 (s), 1075 (s), 1029 (w), 914 (w), 833 (w), 717 (s). HRMS (ESI) calcd for $C_{13}H_{19}NaO_2^+$ $[M+Na]^+$ 244.1308; found 244.1306.

2-(1-Methoxybut-3-yn-1-yl)-1-(4,4,4-trifluorobutyl)-1H-pyrrole (6e)

720 mg of **27** (3.51 mmol) was used to obtain the crude propargylic alcohol (850 mg, 3.47 mmol, <99%), which was used directly in the methylation step. **6e** was obtained as yellow oil (548 mg, 2.11 mmol, 60 % over two steps).

Rf (Pentane / EtOAc = 25 / 1): 0.4. 1H NMR (400 MHz, $CDCl_3$) δ 6.67 (dd, 1 H, $J = 2.7$, 1.8 Hz, *pyrroleH*), 6.21 (dd, 1 H, $J = 3.6$, 1.8 Hz, *pyrroleH*), 6.15 (m, 1 H, *pyrroleH*), 4.58 (t, 1 H, $J = 7.0$ Hz, $CHOCH_3$), 4.03 (m, 2 H, NCH_2), 3.25 (s, 3 OCH_3), 2.81 (ddd, 2 H, $J = 16.8$ Hz, 6.9 Hz, 2.7 Hz, CH_2), 2.08 (m, 4 H, $CH_2CH_2CF_3$), 2.03 (t, 1 H, $J = 2.7$ Hz, alkyne CH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 129.8, 126.8 (q, $J = 276.6$ Hz), 121.8, 108.7, 107.4, 80.5, 73.3, 70.1, 54.2, 45.3, 30.9 (q, $J = 29.3$ Hz), 23.9 (q, $J = 2.9$ Hz). 23.6. IR 3310 (w), 2945 (w), 2338 (w), 1485 (w), 1455 (w), 1393 (w), 1374 (w), 1318 (w), 1295 (m), 1255 (s), 1212 (w), 1135 (s), 1119 (m), 1095 (m), 1080 (m), 1027 (m), 1009 (w), 913 (w), 833 (w), 795 (w), 720 (s). HRMS (ESI) calcd for $C_{13}H_{16}F_3NNaO^+$ $[M+Na]^+$ 282.1076; found 282.1078.

2-(1-Methoxypent-3-yn-1-yl)-1-methyl-1H-pyrrole (**6f**)

1.0 g of **30** (5.4 mmol) was used to obtain crude propargylic alcohol (880 mg, 3.91 mmol, <72%). 448 mg of crude propargylic alcohol (3.00 mmol), NaH (144 mg, 6.00 mmol, 2 equiv) and CH₃I (1.06 g, 7.50 mmol, 2.5 equiv) were used for the methylation. **6f** was obtained as yellow oil (384 mg, 1.83 mmol, 48% over two steps).

Rf (Pentane / EtOAc = 15 / 1): 0.5. ¹H NMR (400 MHz, CDCl₃) δ 6.59 (m, 1 H, *pyrroleH*), 6.15 (dd, 1 H, *J* = 3.6, 1.8 Hz, *pyrroleH*), 6.08 (dd, 1 H, *J* = 3.6, 2.7 Hz, *pyrroleH*), 4.50 (m, 1 H, *CHOCH*₃), 3.66 (s, 3 H, *NCH*₃), 3.25 (s, 3 H, *OCH*₃), 2.72 (m, 2 H, *CH*₂), 1.79 (t, 3 H, *J* = 2.6 Hz, *CH*₃). ¹³C NMR (101 MHz, CDCl₃) δ 130.4, 123.1, 108.2, 106.4, 76.9, 75.4, 74.4, 54.6, 33.9, 24.3, 3.3. IR 2978 (w), 2937 (w), 2921 (w), 2869 (w), 2821 (w), 1706 (w), 1494 (w), 1466 (w), 1465 (w), 1438 (w), 1421 (w), 1345 (w), 1302 (m), 1095 (s), 1059 (w), 1003 (w), 955 (w). HRMS (ESI) calcd for C₁₁H₁₅NNaO⁺ [M+Na]⁺ 200.1046; found 200.1047.

2-(1-Methoxy-4-phenylbut-3-yn-1-yl)-1-methyl-1H-pyrrole (**6g**)

Iodobenzene (**31**) (179 mg, 0.880 mmol, 1.1 equiv) was added into a solution of **6a** (130 mg, 0.800 mmol, 1.0 equiv), Pd(PPh₃)Cl₂ (6.3 mg, 0.033 mmol, 0.03 equiv) and CuI (39 mg, 0.055 mmol, 0.05 equiv) in degassed THF (2 mL) and Et₃N (2 mL). The mixture was kept overnight at 60 °C. The reaction was filtered through a plug of celite and the crude was purified by column chromatography (Pentane/EtOAc= 50:1, 1 % Et₃N) to afford **6g** as brown oil (236 mg, 0.986 mmol, 90 %).

Rf (Pentane / EtOAc = 50 / 1): 0.3. ¹H NMR (400 MHz, CDCl₃) δ 7.41 (m, 2 H, *benzeneH*), 7.29 (m, 3 H, *benzeneH*), 6.63 (dd, 1 H, *J* = 2.5, 2.0 Hz, *pyrroleH*), 6.24 (m, 1 H, *pyrroleH*), 6.12 (dd, 1 H, *J* = 3.5, 2.7 Hz, *pyrroleH*), 4.64 (t, 1 H, *J* = 6.9 Hz, *CHOCH*₃), 3.70 (s, 3 H, *NCH*₃), 3.33 (s, 3 H, *OCH*₃), 3.01 (dd, 2 H, *J* = 16.8, 6.6 Hz, *CH*₂). ¹³C NMR (101 MHz, CDCl₃) δ 131.6, 130.5, 128.1, 127.7, 123.6, 123.4, 108.6, 106.6, 86.5, 82.1, 74.6, 55.3, 34.2, 25.5. IR 2361 (w), 1491 (m), 1465 (w), 1443 (w), 1417 (w), 1344 (w), 1300 (w), 1091 (s), 1061 (w), 950 (w), 910 (s), 758 (m), 729 (s). HRMS (ESI) calcd for C₁₆H₁₈NO⁺ [M+H]⁺ 240.1383; found 240.1388.

The protocol for **6g** represents the typical procedure for the synthesis of **6h**, **6i**, **9c** and **9d**.

2-(1-Methoxy-4-(p-tolyl)but-3-yn-1-yl)-1-methyl-1H-pyrrole (**6h**)

Following the conditions described for **6g**, **6a** (194 mg, 1.19 mmol) was used. The crude product was purified by flash column chromatography (Pentane/EtOAc= 50:1, 1 % Et₃N) to afford **6h** as yellow oil (267 mg, 1.05 mmol, 88%)

Rf (Pentane / EtOAc = 50 / 1): 0.5. ¹H NMR (400 MHz, CDCl₃) δ 7.32 (d, 2 H, *J* = 8.1 Hz, *benzeneH*), 7.12 (m, 2 H, *benzeneH*), 6.64 (t, 1 H, *J* = 2.0 Hz, *pyrroleH*), 6.25 (dd, 1 H, *J* = 3.6, 1.8 Hz, *pyrroleH*), 6.14 (m, 1 H, *pyrroleH*), 4.65 (t, 1 H, *J* = 6.9 Hz, *CHOCH*₃), 3.71 (s, 3 H, *NCH*₃), 3.34 (s, 3 H, *OCH*₃), 3.02 (dd, 2 H, *J* = 16.8, 6.6 Hz, *CH*₂), 2.37 (s, 3 H, *CH*₃). ¹³C NMR (101 MHz, CDCl₃) δ 137.6, 131.4, 130.6, 128.8, 123.3, 120.5, 108.5, 106.6, 85.6, 82.1, 74.6, 55.2, 34.1, 25.5, 21.3. IR 2981 (w), 2927 (m), 2362 (w), 1712 (w), 1508 (m), 1496 (w), 1445 (w), 1444 (w), 1345 (w), 1301 (w), 1267 (w), 1186 (w), 1093 (s), 950 (w), 820 (s), 786 (w), 717 (s). HRMS (ESI) calcd for C₁₇H₂₀NO⁺ [M+H]⁺ 254.1539; found 254.1542.

2-(4-(4-Bromophenyl)-1-methoxybut-3-yn-1-yl)-1-methyl-1H-pyrrole (**6i**)

Following the conditions described for **6g**, **6a** (163 mg, 1.00 mmol) was used. The crude product was purified by flash column chromatography (Pentane/EtOAc= 20:1, 1 % Et₃N) to afford **6i** as yellow oil (260 mg, 0.817 mmol, 82 %)

Rf (Pentane / EtOAc = 20 / 1): 0.2

¹H NMR (400 MHz, CDCl₃) δ 7.31 (d, 2 H, *J* = 8.5 Hz, *benzeneH*), 7.15 (d, 2 H, *J* = 8.5 Hz, *benzeneH*), 6.52 (t, 1 H, *J* = 2.1 Hz, *pyrroleH*), 6.12 (dd, 1 H, *J* = 3.5, 1.7 Hz, *pyrroleH*), 6.01 (m, 1 H, *pyrroleH*), 4.53 (t, 1 H, *J* = 6.9 Hz, *CHOCH*₃), 3.59 (s, 3 H, *NCH*₃), 3.21 (s, 3 H, *OCH*₃), 2.89 (ddd, 2 H, *J* = 16.9, 7.2, 2.6 Hz, *CH*₂). ¹³C NMR (101 MHz, CDCl₃) δ 133.0, 131.3, 130.3, 123.4, 122.5, 121.7, 108.6, 106.6, 87.8, 81.0, 74.3, 55.2, 34.2, 25.4. IR 2981 (m), 2930 (m), 2907 (m), 2819 (w), 1488 (m), 1344 (w), 1300 (w), 1076 (s), 1008 (w), 990 (w),

826 (s), 787 (w), 716 (s). HRMS (ESI) calcd for $C_{16}H_{17}BrNO^+$ $[M+H]^+$ 318.0488; found 318.0484.

2-(1-Methoxy-4-(naphthalen-1-yl)but-3-yn-1-yl)-1-methyl-1H-pyrrole (6j)

Following the conditions described for **6g**, **6a** (163 mg, 1.00 mmol) was used. The crude product was purified by flash column chromatography (Pentane/EtOAc = 50:1, 1 % Et_3N) to afford **6j** as yellow oil (269 mg, 0.930 mmol, 93%)

Rf (Pentane / EtOAc = 50 / 1): 0.3. 1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, 1 H, J = 8.0 Hz, *benzeneH*), 7.84 (m, 2 H, *benzeneH*), 7.67 (d, 1 H, J = 6.8 Hz, *benzeneH*), 7.56 (m, 2 H, *benzeneH*), 7.43 (m, 1 H, *benzeneH*), 6.69 (m, 1 H, *pyrroleH*), 6.37 (dd, 1 H, J = 3.5, 1.7 Hz, *pyrroleH*), 6.22 (m, 1 H, *pyrroleH*), 4.76 (t, 1 H, J = 7.1 Hz, $CHOCH_3$), 3.74 (m, 3 H, NCH_3), 3.39 (s, 3 H, OCH_3), 3.21 (dd, 2 H, J = 16.8, 6.6 Hz, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.4, 133.0, 130.4, 129.9, 128.0, 128.0, 126.5, 126.3, 126.1, 125.0, 123.4, 121.2, 108.9, 106.7, 91.4, 80.2, 74.6, 55.3, 34.2, 25.8. IR 3053 (w), 2979 (w), 2931 (m), 1738 (w), 1664 (w), 1582 (w), 1497 (m), 1466 (w), 1427 (w), 1405 (w), 1343 (w), 1300 (w), 1198 (w), 1187 (w), 1168 (w), 1162 (w), 1092 (s), 969 (w), 802 (s), 778 (s), 718 (s). HRMS (ESI) calcd for $C_{20}H_{20}NO^+$ $[M+H]^+$ 290.1539; found 290.1541.

2-(1-Methoxy-2-methylbut-3-yn-1-yl)-1-methyl-1H-pyrrole (6k)

218 mg of **30** (2.00 mmol, 1.0 equiv) and 3-bromobut-1-yne (319 mg, 2.40 mmol) were used to obtain the crude propargylic alcohol (300 mg, 1.84 mmol, <92%), which was used directly in the methylation step. **6k** was obtained as transparent oil (260 mg, 1.47 mmol, 74% over two steps as a mixture of diastereoisomers, the major one was characterized).

Rf (Pentane / EtOAc = 15 / 1): 0.5. 1H NMR (400 MHz, $CDCl_3$) δ 6.58 (m, 1 H, *pyrroleH*), 6.11 (m, 1 H, *pyrroleH*), 6.07 (m, 1 H, *pyrroleH*), 4.22 (d, 1 H, J = 8.9 Hz, $CHOCH_3$), 3.66 (s, 3 H, NCH_3), 3.24 (s, 3 H, OCH_3), 2.93 (m, 1 H, $CHCH_3$), 2.15 (d, 1 H, J = 2.4 Hz, alkyne CH), 1.05 (d, 3 H, J = 7.1 Hz, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 128.8, 123.6, 110.3, 106.7, 86.7, 80.2, 69.2, 56.1, 34.5, 31.4, 17.7. IR 3291 (w), 3282 (w), 2979 (w), 2935 (w), 2901 (w), 2821 (w), 1493 (w), 1451 (w), 1417 (w), 1376 (w), 1298 (m), 1204 (w), 1132 (w), 1092 (s), 960 (w), 924 (w), 805 (w), 783 (w), 715 (s), 688 (m), 678 (m), 651 (s), 632 (m), 615 (m). HRMS (ESI) calcd for $C_{11}H_{16}NO^+$ $[M+H]^+$ 178.1226; found 178.1235.

2-(2-Methoxypent-4-yn-2-yl)-1-methyl-1H-pyrrole (6l)

246 mg of the corresponding ketone (2.00 mmol) was used to obtain the crude propargylic alcohol (300 mg, 1.84 mmol, <92%), which was used directly in

the methylation step. **6l** was obtained as yellow oil (230 mg, 1.30 mmol, 65 % over two steps).

Rf (Pentane / EtOAc = 15 / 1): 0.6. ^1H NMR (400 MHz, CDCl_3) δ 6.59 (m, 1 H, *pyrroleH*), 6.07 (dd, 1 H, $J = 3.7, 1.9$ Hz, *pyrroleH*), 6.03 (dd, 1 H, $J = 3.7, 2.7$ Hz, *pyrroleH*), 3.76 (s, 3 H, NCH_3), 3.07 (s, 3 H, OCH_3), 2.82 (dd, 2 H, $J = 16.0$ Hz, 2.7 Hz, CH_2), 2.05 (t, 1 H, $J = 2.7$ Hz, alkyne CH), 1.70 (s, 3 H, CH_3). ^{13}C NMR (101 MHz, CDCl_3) δ 132.3, 124.6, 109.5, 106.0, 80.2, 75.6, 70.7, 50.4, 35.3, 29.9, 23.8. IR 3304 (w), 3292 (w), 2983 (m), 2942 (m), 2867 (w), 2824 (w), 2146 (w), 1653 (w), 1532 (w), 1512 (w), 1486 (m), 1430 (w), 1411 (w), 1372 (w), 1353 (w), 1311 (m), 1294 (m), 1262 (w), 1239 (w), 1203 (w), 1154 (w), 1099 (s), 1062 (s), 896 (w), 885 (w), 859 (w), 844 (m), 822 (w). HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{15}\text{NNaO}^+$ $[\text{M}+\text{Na}]^+$ 200.1046; found 200.1046.

2-(1-Methoxybut-3-yn-1-yl)-1-methyl-1H-indole (**6m**)

478 mg of the corresponding aldehyde (3.00 mmol) was used to obtain the crude propargylic alcohol (500 mg, 2.51 mmol, <84%), which was used directly in the methylation step. **6m** was obtained as a yellow oil (450 mg, 2.11 mmol, 70 % over two steps).

Rf (Pentane / EtOAc = 25 / 1): 0.5. ^1H NMR (400 MHz, CDCl_3) δ 7.84 (d, 1 H, $J = 7.8$ Hz, *benzeneH*), 7.50-7.43 (m, 2 H, *benzeneH*), 7.35 (m, 1 H, *benzeneH*), 6.73 (s, 1 H, *pyrroleH*), 4.89 (t, 1 H, $J = 6.9$ Hz, CHOCH_3), 3.91 (s, 3 H, NCH_3), 3.47 (s, 3 H, OCH_3), 3.04 (ddd, 2 H, $J = 16.4, 7.3, 2.7$ Hz, CH_2), 2.29 (t, 1 H, $J = 2.7$ Hz, alkyne CH). ^{13}C NMR (101 MHz, CDCl_3) δ 137.9, 137.0, 126.9, 121.5, 120.4, 119.3, 108.8, 101.6, 80.2, 74.7, 70.3, 55.2, 29.9, 24.4. IR 3667 (w), 3479 (w), 2992 (s), 2961 (m), 2906 (m), 1402 (w), 1248 (w), 1236 (w), 1072 (s), 1034 (m), 901 (w), 866 (w). HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{15}\text{NO}$ $[\text{M}]^+$ 214.1226; found 214.1228.

5-(1-Methoxybut-3-yn-1-yl)-4-methyl-4H-thieno[3,2-b]pyrrole (**6n**)

250 mg of the corresponding aldehyde (1.51 mmol) was used to obtain the crude propargylic alcohol (250 mg, 1.22 mmol, <81%). 123 mg of crude propargylic alcohol (0.599 mmol) was used for methylation. **6n** was obtained as a yellow oil (93 mg, 0.42 mmol, 57% over two steps).

Rf (Pentane / EtOAc = 15 / 1): 0.5. ^1H NMR (400 MHz, CDCl_3) δ 7.10 (d, 1 H, $J = 5.3$ Hz, *thiopheneH*), 6.94 (d, 1 H, $J = 5.3$, *thiopheneH*), 6.44 (s, 1 H, *pyrroleH*), 4.64 (t, 1 H, $J = 7.1$ Hz, CHOCH_3), 3.81 (s, 3 H, NCH_3), 3.32 (s, 3 H, OCH_3), 2.84 (ddd, 2 H, $J = 15.2, 7.3, 2.7$ Hz, CH_2), 2.06 (t, 1 H, $J = 2.7$ Hz, alkyne CH). ^{13}C NMR (101 MHz, CDCl_3) δ 142.0, 135.3, 123.3, 121.4, 109.8, 100.9, 80.5, 75.1, 70.2, 55.4, 32.6, 24.7. IR 3285 (w), 2934 (w), 2821 (w), 1530 (w), 1399 (w), 1354 (w), 1319 (w), 1187 (w), 1135 (w), 1095 (m), 1085 (m), 1006 (w), 840 (w), 769 (w), 714 (s), 687 (m), 677 (s), 663 (s), 655 (s), 613 (w). HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{14}\text{NOS}^+$ $[\text{M}+\text{H}]^+$ 220.0791; found 220.0786.

3-(1-Methoxybut-3-yn-1-yl)-1-methyl-1H-pyrrole (**9a**)

610 mg of **29** (5.59 mmol) was used to obtain the crude propargylic alcohol (600 mg, 4.02 mmol, <72%), which was used directly in the methylation step. **9a** was obtained as yellow oil (480 mg, 2.94 mmol, 53% over two steps).

Rf (Pentane / EtOAc = 15 / 1): 0.6. ^1H NMR (400 MHz, CDCl_3) δ 6.60 (s, 1 H, *pyrroleH*), 6.54 (t, 1 H, $J = 2.5$ Hz, *pyrroleH*), 6.11 (m, 1 H, *pyrroleH*), 4.28 (t, 1 H, $J = 6.5$ Hz, CHOCH_3), 3.59 (s, 3 H, NCH_3), 3.27 (s, 3 H, OCH_3), 2.64 (ddd, 2 H, $J = 16.4, 6.2, 2.7$ Hz, CH_2), 1.97 (t, 1 H, $J = 2.6$ Hz, alkyne CH). ^{13}C NMR (101 MHz, CDCl_3) δ 122.8, 121.4, 119.6, 106.3, 81.4, 75.5, 69.0, 55.5, 35.5, 26.6. IR 3303 (w), 2939 (m),

2868 (w), 2820 (w), 1558 (w), 1509 (w), 1466 (w), 1424 (w), 1319 (w), 1270 (w), 1165 (w), 1164 (w), 1099 (s), 1005 (w), 822 (w), 787 (w), 740 (m), 706 (w). HRMS (ESI) calcd for $C_{10}H_{13}NNaO^+$ $[M+Na]^+$ 186.0889; found 186.0895.

3-(1-Methoxy-3-yn-1-yl)-1-methyl-1H-pyrrole (9b)

BuLi (0.386 mL, 0.965 mmol, 1.05 equiv) was added to a solution of **9a** (150 mg, 0.919 mmol, 1.0 equiv) in dry THF (3 mL) at -78°C . The solution was kept during 30 minutes at -78°C and 15 minutes at room temperature. Then the solution was re-cooled down to -78°C , MeI (272 mg, 1.92 mmol, 1.0 equiv) was added dropwise. The reaction was quenched with a sat NH_4Cl solution (30 mL) 2 hours later. The aqueous and organic layers were separated and the aqueous layer was extracted with ether (3x10 mL). After drying over MgSO_4 and concentrating under vacuum, the crude product was purified by column chromatography (Pentane/EtOAc= 25:1, 1 % Et_3N) to afford **9b** as brown oil (89 mg, 0.50 mmol, 55 %)

Rf (Pentane/EtOAc= 25:1): 0.3. ^1H NMR (400 MHz, CDCl_3) δ 6.58 (t, 1 H, $J = 1.9$ Hz, *pyrroleH*), 6.54 (t, 1 H, $J = 2.5$ Hz, *pyrroleH*), 6.11 (m, 1 H, *pyrroleH*), 4.22 (t, 1 H, $J = 6.3$ Hz, CHOCH_3), 3.62 (s, 3 H, NCH_3), 3.28 (s, 3 H, OCH_3), 2.67-2.50 (m, 2 H, CH_2), 1.78 (t, 3 H, $J = 2.5$ Hz, alkyne CH_3). ^{13}C NMR (101 MHz, CDCl_3) δ 123.6, 121.6, 119.8, 106.6, 76.4, 76.4, 76.3, 56.0, 35.9, 27.3, 3.5. IR 3667 (w), 3522 (w), 3512 (w), 3489 (w), 3479 (w), 2992 (s), 2961 (m), 2960 (m), 2906 (m), 1402 (w), 1248 (w), 1072 (s), 1034 (m), 900 (w), 865 (w), 746 (w). HRMS (ESI) calcd for $C_{11}H_{15}NNaO^+$ $[M+Na]^+$ 200.1046; found 200.1047.

3-(1-Methoxy-4-phenylbut-3-yn-1-yl)-1-methyl-1H-pyrrole (9c)

Following the conditions described for **6g**, **9a** (289 mg, 1.77 mmol) was used. The crude product was purified by flash column chromatography (Pentane/EtOAc= 50:1, 1 % Et_3N) to afford **9c** as yellow oil (334 mg, 1.40 mmol, 79%).

Rf (Pentane / EtOAc = 50 / 1): 0.4. ^1H NMR (400 MHz, CDCl_3) δ 7.50-7.47 (m, 2 H, *benzeneH*), 7.34-7.31 (m, 3 H, *benzeneH*), 6.69 (t, 1 H, $J = 1.8$ Hz, *pyrroleH*), 6.62 (t, 1 H, $J = 2.4$ Hz, *pyrroleH*), 6.26 (m, 1 H, *pyrroleH*), 4.45 (t, 1 H, $J = 6.4$ Hz, CHOCH_3), 3.63 (s, 3 H, NCH_3), 3.41 (s, 3 H, OCH_3), 2.96 (dd, 2 H, $J = 16.2, 6.7$ Hz, CH_2). ^{13}C NMR (101 MHz, CDCl_3) δ 131.3, 127.8, 127.2, 123.8, 123.4, 121.6, 119.7, 106.6, 87.5, 81.4, 76.2, 56.0, 35.7, 28.1. IR 2936 (w), 2935 (w), 2243 (w), 1508 (w), 1495 (w), 1163 (w), 1096 (m), 909 (s), 785 (w), 729 (s). HRMS (ESI) calcd for $C_{16}H_{17}NO^+$ $[M+]$ 262.1202; found 262.1207.

3-(1-Methoxy-4-(naphthalen-1-yl)but-3-yn-1-yl)-1-methyl-1H-pyrrole (9d)

Following the conditions described for **6g**, **9a** (163 mg, 1.00 mmol) was used. The crude product was purified by flash column chromatography (Pentane/EtOAc = 50:1, 1 % Et₃N) to afford **9d** as yellow oil (210 mg, 0.730 mmol, 73 %).

R_f (Pentane / EtOAc = 50 / 1): 0.4. ¹H NMR (400 MHz, CDCl₃) δ 8.11-8.08 (m, 1 H, *benzeneH*), 7.71-7.69 (m, 1 H, *benzeneH*), 7.65 (d, 1 H, *J* = 8.3 Hz, *benzeneH*), 7.51 (d, 1 H, *J* = 7.1 Hz, *benzeneH*), 7.41-7.37 (m, 2 H, *benzeneH*), 7.27 (m, 1 H, *benzeneH*), 6.58 (s, 1 H, *pyrroleH*), 6.50 (t, 1 H, *J* = 2.3 Hz, *pyrroleH*), 6.14 (m, 1 H, *pyrroleH*), 4.36 (t, 1 H, *J* = 6.6 Hz, *CHOCH*₃), 3.52 (s, 3 H, *NCH*₃), 3.28 (s, 3 H, *OCH*₃), 2.94 (dd, 2 H, *J* = 16.6, 6.8 Hz, *CH*₂). ¹³C NMR (101 MHz, CDCl₃) δ 133.6, 133.1, 129.8, 128.0, 127.9, 126.5, 126.2, 126.1, 125.1, 123.6, 121.9, 121.6, 120.2, 106.9, 92.6, 79.7, 76.5, 56.3, 36.1, 28.4. IR 3052 (w), 2975 (w), 1735 (w), 1583 (w), 1555 (w), 1507 (w), 1218 (w), 1163 (m), 1094 (s), 1006 (w), 962 (w), 914 (w), 799 (s), 776 (s), 703 (w). HRMS (ESI) calcd for C₂₀H₂₀NO⁺ [M⁺] 312.1359; found 312.1356.

3-(2-Methoxypent-4-yn-2-yl)-1-methyl-1H-pyrrole (9e)

616 mg of the corresponding ketone (5.00 mmol) was used to obtain the crude propargylic alcohol (555 mg, 3.40 mmol, <68%). 326 mg of crude propargylic alcohol (2.00 mmol) was used for methylation. **9e** was obtained as a transparent oil (297 mg, 1.68 mmol, 57% over two steps).

R_f (Pentane / EtOAc = 15 / 1): 0.6. ¹H NMR (400 MHz, CDCl₃) δ 6.55 (d, 2 H, *J* = 2.3 Hz, *pyrroleH*), 6.10 (t, 1 H, *J* = 2.3 Hz, *pyrroleH*), 3.62 (s, 3 H, *NCH*₃), 3.09 (s, 3 H, *OCH*₃), 2.68 (dd, 2 H, *J* = 16.0 Hz, 2.7 Hz, *CH*₂), 2.00 (t, 1 H, *J* = 2.7 Hz, *alkyne CH*), 1.60 (s, 3 H, *CH*₃). ¹³C NMR (101 MHz, CDCl₃) δ 126.3, 121.6, 119.5, 106.8, 81.3, 74.6, 70.0, 50.1, 35.9, 31.8, 23.5. IR 3686 (w), 3674 (w), 3296 (w), 3285 (w), 2987 (s), 2941 (m), 2940 (m), 2910 (m), 2902 (s), 2822 (w), 1556 (w), 1509 (w), 1473 (w), 1456 (w), 1420 (w), 1407 (w), 1394 (w), 1378 (w), 1258 (w), 1251 (w), 1243 (w), 1233 (w), 1210 (w), 1191 (w), 1098 (s), 1092 (s), 1067 (s), 1059 (s), 1017 (w), 787 (w), 744 (m), 699 (w), 682 (w), 660 (s), 652 (m), 644 (s), 633 (m), 622 (w), 606 (w). HRMS (ESI) calcd for C₁₁H₁₅NNaO⁺ [M+Na]⁺ 200.1046; found 200.1039.

3-(1-Methoxy-1-phenylbut-3-yn-1-yl)-1-methyl-1H-pyrrole (9f)

460 mg of the corresponding ketone (2.48 mmol) was used to obtain the crude propargylic alcohol (500 mg, 2.20 mmol, <89%). 250 mg of crude propargylic alcohol (1.11 mmol) was used for methylation. **9f** was obtained as yellow oil (106 mg, 0.443 mmol, 36 % over two steps).

R_f (Pentane / EtOAc = 25 / 1): 0.8. ¹H NMR (400 MHz, CDCl₃) δ 7.51 (m, 2 H, *benzeneH*), 7.33 (m, 2 H, *benzeneH*), 7.26 (m, 1 H, *benzeneH*), 6.56 (m, 2 H, *pyrroleH*), 6.04 (dd, 1 H, *J* = 2.6, 2.0 Hz, *pyrroleH*), 3.63 (s, 3 H, *NCH*₃), 3.18 (s, 3 H, *OCH*₃), 3.08 (dd, 2 H, *J* = 16.0 Hz, 2.7 Hz, *CH*₂), 1.93 (t, 1 H, *J* = 2.7 Hz, *alkyne CH*). ¹³C NMR (101 MHz, CDCl₃) δ 144.0, 127.5, 127.1, 126.8,

125.5, 121.6, 121.3, 108.6, 80.8, 79.5, 70.8, 51.0, 36.2, 30.8. IR 3288 (w), 3287 (w), 3057 (w), 2938 (w), 2918 (w), 2823 (w), 1544 (w), 1509 (w), 1492 (w), 1472 (w), 1447 (w), 1422 (w), 1263 (w), 1200 (w), 1166 (m), 1089 (s), 1033 (w), 1015 (w), 864 (w), 785 (m), 765 (m), 707 (s). HRMS (ESI) calcd for $C_{16}H_{18}NO^+$ $[M+H]^+$ 240.1383; found 240.1378.

3-(2-Methoxyhex-4-yn-2-yl)-1-methyl-1H-pyrrole (9g)

Starting from **9e** (340 mg, 1.92 mmol, 1.0 equiv) and following the conditions described for **9b**, the crude product was purified by flash column chromatography (Pentane/EtOAc= 25:1, 1 % Et₃N) to afford **9g** as yellow oil (192 mg, 1.00 mmol, 52 %)

Rf (Pentane/EtOAc= 25:1): 0.5. ¹H NMR (400 MHz, CDCl₃) δ 6.54 (m, 2 H, *pyrroleH*), 6.10 (m, 1 H, *pyrroleH*), 3.63 (s, 3 H, *NCH*₃), 3.09 (s, 3 H, *OCH*₃), 2.64 (m, 2 H, *CH*₂), 1.80 (t, 3 H, *J* = 2.6 Hz, alkyne *CH*₃), 1.56 (s, 3 H, *CH*₃COCH₃). ¹³C NMR (101 MHz, CDCl₃) δ 127.1, 121.6, 119.7, 107.1, 77.4, 76.0, 75.1, 50.4, 36.2, 32.1, 23.9, 3.8. IR 2979 (m), 2933 (w), 2910 (w), 2820 (w), 1552 (w), 1509 (m), 1484 (w), 1423 (m), 1371 (m), 1307 (w), 1262 (m), 1237 (w), 1208 (m), 1191 (m), 1152 (w), 1093 (s), 1069 (m), 965 (w), 914 (m), 832 (w), 814 (w), 783 (s), 755 (w), 737 (m), 705 (w). HRMS (ESI) calcd for $C_{12}H_{17}NNaO^+$ $[M+Na]^+$ 214.1202; found 214.1200.

Methylpent-4-yn-2-yl)-1-methyl-1H-pyrrole (9h)

616 mg of the corresponding ketone (5.00 mmol) and 3-bromobut-1-yne (864 mg, 6.50 mmol) were used to obtain the crude propargylic alcohol (777 mg, 4.76 mmol, <95%), which was used directly in the methylation step. **9h** was obtained as yellow oil (551 mg, 2.88 mmol, 58% over two steps, dr=2:1, obtained by integration of the ¹H NMR peaks at 6.11 and 6.04).

Rf (Pentane / EtOAc = 25 / 1): 0.5. ¹H NMR (400 MHz, CDCl₃) δ 6.57 (t, 1 H, *J* = 2.1 Hz, *pyrroleH* major diastereoisomer), 6.54 (t, 1.5 H, *J* = 2.1 Hz, *pyrroleH* major and minor diastereoisomer), 6.48 (t, 0.5 H, *J* = 2.1 Hz, *pyrroleH* minor diastereoisomer), 6.11 (dd, 1 H, *J* = 2.7, 1.8 Hz, *pyrroleH* major diastereoisomer), 6.04 (dd, 0.5 H, *J* = 2.7, 1.8 Hz, *pyrroleH* minor diastereoisomer), 3.62 (s, 3 H, *NCH*₃ major diastereoisomer), 3.60 (s, 1 H, *NCH*₃ minor diastereoisomer), 3.12 (s, 1 H, *OCH*₃ minor diastereoisomer), 3.08 (s, 3 H, *OCH*₃ major diastereoisomer), 2.89 (m, 1.5 H, *CH*₃*CH* major and minor diastereoisomer), 2.11 (d, 0.5 H, *J* = 2.5 Hz, alkyne *CH* minor diastereoisomer), 2.01 (d, 1 H, *J* = 2.5 Hz, alkyne *CH* major diastereoisomer), 1.53 (two s, 4.5 H, *CH*₃*OMe* major and minor diastereoisomer), 1.23 (d, 3 H, *J* = 7.0 Hz, *CH*₃*CH* major diastereoisomer), 1.03 (d, 1.5 H, *J* = 7.0 Hz, *CH*₃*CH* minor diastereoisomer). ¹³C NMR (101 MHz, CDCl₃) δ 126.0, 124.9, 121.4, 121.1, 120.4, 120.3, 107.5, 107.4, 87.2, 86.9, 77.9, 77.2, 69.6, 69.5, 50.1, 50.0, 37.5, 36.8, 36.0, 35.9, 19.6, 18.2, 16.6, 15.6. IR 3308 (w), 2983 (w), 2982 (w), 2940 (w), 1508 (w), 1374 (w), 1219 (w), 1196 (w), 1089 (w), 1074 (w), 909 (s), 780 (w), 729 (s), 706 (w). HRMS (ESI) calcd for $C_{12}H_{17}NNaO^+$ $[M+Na]^+$ 214.1202; found 214.1204.

3-(1-Methoxybut-3-yn-1-yl)-1-methyl-1H-indole (9i)

970 mg of the corresponding aldehyde (6.09 mmol) was used to obtain the crude propargylic alcohol (1.03 g, 5.14 mmol, <84%). 398 mg of crude propargylic alcohol (2.00 mmol) was used for methylation. **9i** was obtained as a yellow oil (372 mg, 1.74 mmol, 73% over two steps).

Rf (Pentane / EtOAc = 15 / 1): 0.2. ^1H NMR (400 MHz, CDCl_3) δ 7.85 (m, 1 H, *benzeneH*), 7.40-7.32 (m, 2 H, *benzeneH*), 7.23 (m, 1 H, *benzeneH*), 7.14 (s, 1 H, *pyrroleH*), 4.79 (t, 1 H, $J = 6.5$ Hz, CHOCH_3), 3.80 (s, 3 H, NCH_3), 3.42 (s, 3 H, OCH_3), 2.95 (ddd, 2 H, $J = 16.8, 6.3, 2.7$ Hz, CH_2), 2.11 (t, 1 H, $J = 2.6$ Hz, alkyne CH). ^{13}C NMR (101 MHz, CDCl_3) δ 137.0, 127.2, 126.2, 121.6, 119.5, 119.1, 113.5, 109.2, 81.6, 75.7, 69.6, 56.2, 32.5, 26.7. IR 3308 (w), 2341 (w), 1473 (w), 1378 (w), 1331 (w), 1243 (w), 1096 (m), 1068 (w), 907 (s), 726 (s), 685 (w), 672 (w), 660 (m), 634 (m). HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{15}\text{NNaO}^+$ $[\text{M}+\text{Na}]^+$ 236.1046; found 236.1048.

5-methoxy-3-(1-methoxybut-3-yn-1-yl)-1-methyl-1H-indole (**9j**)

250 mg of the corresponding aldehyde (1.32 mmol) was used to obtain the crude propargylic alcohol (280 mg, 1.22 mmol, <92%), which was used directly in the methylation step. **9j** was obtained as a yellow oil (264 mg, 1.09 mmol, 83 % over two step).

Rf (Pentane / EtOAc = 25 / 1): 0.3. ^1H NMR (400 MHz, CDCl_3) δ 7.21-7.18 (m, 2H, *benzeneH*), 7.04 (s, 1 H, *pyrroleH*), 6.91 (dd, 1 H, $J = 8.8, 2.5$ Hz, *benzeneH*), 4.65 (t, 1 H, $J = 6.6$ Hz, CHOCH_3), 3.86 (s, 3 H, NCH_3), 3.75 (s, 3 H, OCH_3), 3.33 (s, 3 H, CHOCH_3), 2.84 (ddd, 2 H, $J = 16.4, 6.1, 2.7$ Hz, CH_2), 2.02 (t, 1 H, $J = 2.6$ Hz, alkyne CH). ^{13}C NMR (101 MHz, CDCl_3) δ 153.9, 132.6, 127.9, 126.6, 113.1, 112.1, 110.1, 101.5, 81.8, 75.9, 69.6, 56.3, 55.9, 32.9, 26.7. IR 3291 (w), 3284 (w), 2989 (w), 2975 (w), 2935 (w), 2852 (w), 1623 (w), 1578 (w), 1548 (w), 1491 (s), 1456 (m), 1425 (m), 1325 (w), 1267 (w), 1224 (s), 1174 (w), 1138 (w), 1123 (w), 1096 (s), 1065 (m), 1035 (w), 912 (w), 875 (w), 819 (w), 797 (m), 734 (m). HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{17}\text{NNaO}_2^+$ $[\text{M}+\text{Na}]^+$ 266.1151; found 266.1162.

4. Cyclization-alkynylation domino process.

Optimization of the reaction:

A solution of **6a** (0.1 mmol, 1.0 equiv) in solvent (0.5 mL) was added into a solution of catalyst (0.03 mmol, 0.1 equiv), base (0.060 mmol, 2.0 equiv) and hypervalent iodine reagent (0.600 mmol, 2 equiv) in solvent (0.5 mL). The reaction was stopped after 72 h. The solvent was removed under vacuum, and the crude product was purified by column chromatography (Pentane/DCM= 15:1) directly without any further work-up.

Entry	Pyrrole	Cat	Reagent	Base	Solvent	Yield*
1	5	PPh ₃ AuCl/AgOTf	1a	Na ₂ CO ₃	CH ₃ CN	<5%
2	5	AuCl ₃ /AgOTf	1a	Na ₂ CO ₃	CH ₃ CN	<5%
3	5	AuCl ₃	1a	Na ₂ CO ₃	CH ₃ CN	<5%
4	5	AuCl ₃ [†]	1a	Na ₂ CO ₃	CH ₃ CN	<5%
5	5	Au(OAc) ₃ [†]	1a	Na ₂ CO ₃	CH ₃ CN	<5%
6	5	35 [†]	1a	Na ₂ CO ₃	CH ₃ CN	<5%
7	5	36 [†]	1a	Na ₂ CO ₃	CH ₃ CN	<5%
8	5	PtCl ₂	1a	Na ₂ CO ₃	CH ₃ CN	13%
9	5	PtCl ₂ / AgOTf	1a	Na ₂ CO ₃	CH ₃ CN	<5%

10	5	PtCl ₂ /bipyridine	1a	Na ₂ CO ₃	CH ₃ CN	<5%
11	5	Pt(NH ₃) ₂ Cl ₂	1a	Na ₂ CO ₃	CH ₃ CN	<5%
12	5	PtCl ₂ (COD)	1a	Na ₂ CO ₃	CH ₃ CN	<5%
13	5	PtCl ₂	1a	2,6-lutidine	CH ₃ CN	13%
14	5	PtCl ₂	1a	Na ₃ PO ₄	CH ₃ CN	15%
15	5	PtCl ₂	1a	KHCO ₃	CH ₃ CN	<5%
16	5	PtCl ₂	1a	NaOAc	CH ₃ CN	<5%
17	5	PtCl ₂	1a	NaHCO ₃	CH ₃ CN	40%
18	5	PtCl ₂	1a	NaHCO ₃	Toluene	30%
19	5	PtCl ₂	1a	NaHCO ₃	THF	21%
20	5	PtCl ₂	1a	NaHCO ₃	MeOH	14%
21	5	PtCl ₂	1b	NaHCO ₃	CH ₃ CN	27%
22	5	PtCl ₂	1c	NaHCO ₃	CH ₃ CN	<5%
23	5	PtCl ₄	1a	NaHCO ₃	CH ₃ CN	<5%
24	5	Pt(PPh ₃) ₄	1a	NaHCO ₃	CH ₃ CN	<5%
25	6a	PtCl ₂	1a	NaHCO ₃	CH ₃ CN	91% [‡]
26	7	PtCl ₂	1a	NaHCO ₃	CH ₃ CN	80%
27	7	(IPr)AuCl/AgNTf ₂	1a	NaHCO ₃	CH ₃ CN	<5%
28	6a	PtBr ₂	1a	NaHCO ₃	CH ₃ CN	98% [‡]
29	6a	PtI ₂	1a	NaHCO ₃	CH ₃ CN	<5%
30	6a	PtBr ₂	1a	NaHCO ₃	CH ₃ CN/C ₆ H ₅ Cl (v/v = 1/5)	45%
31	6a	PtBr ₂	1a	NaHCO ₃	CH ₃ CN/THF (v/v = 1/5)	96%
32	6a	PtBr ₂	1a	NaHCO ₃	CH ₃ CN/THF (v/v = 1/10)	93%

*Isolated yields were given. [†] The reaction was performed at 80 °C. [‡]Not reproducible.

General procedure for cyclization-alkynylation domino process.

A solution of **6** or **9** (0.30 mmol, 1.0 equiv) in THF (1.5 mL) was added into a solution of PtBr_2 (11 mg, 0.030 mmol, 0.1 equiv), NaHCO_3 (50 mg, 0.600 mmol, 2.0 equiv) and 1-[(triisopropylsilyl)ethynyl]-3,3-bis(trifluoromethyl)-3(*1H*)-1,2-benziodoxole (**1a**) (330 mg, 0.600 mmol, 2 equiv) in THF (1.0 mL) and CH_3CN (0.5 mL). The reaction was stopped after 72h- 120h. The solution was removed under vacuum, and the crude product was purified by column chromatography (Pentane/DCM) directly without any further work-up.

1-Methyl-5-((triisopropylsilyl)ethynyl)-1H-indole (8a**)**

Starting from **6a** (49 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 15:1) to afford **8a** as yellow oil (79 mg, 0.25 mmol, 84%)

Rf (Pentane / DCM= 15 / 1): 0.5. ^1H NMR (400 MHz, CDCl_3) δ 7.79 (d, 1 H, J = 0.7 Hz, *benzeneH*), 7.34 (dd, 1 H, J = 8.5, 1.4 Hz, *benzeneH*), 7.23 (d, 1 H, J = 8.5 Hz, *benzeneH*), 7.05 (d, 1 H, J = 3.1 Hz, *pyrroleH*), 6.45 (dd, 1 H, J = 3.1, 0.7 Hz, *pyrroleH*), 3.78 (s, 3 H, CH_3), 1.23 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, CDCl_3) δ 136.3, 129.7, 128.1, 125.5, 125.2, 114.1, 109.1, 109.0, 101.2, 87.0, 32.8, 18.7, 11.4. IR 2941 (m), 2863 (m), 2145 (m), 1616 (w), 1514 (w), 1487 (m), 1464 (m), 1423 (w), 1381 (w), 1333 (w), 1283 (w), 1147 (w), 1078 (w), 1014 (w), 996 (w), 945 (w), 919 (w), 884 (s), 820 (s), 802 (m), 717 (s), 710 (s). HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{30}\text{NSi}^+ [\text{M}+\text{H}]^+$ 312.2142; found 312.2145.

Confirmation of the structure of 1-methyl-5-((triisopropylsilyl)ethynyl)-1H-indole (**8a**) by Sonogashira coupling

37 (219 mg, 1.20 mmol, 1.2 equiv) was added into a solution of **36** (242 mg, 1.00 mmol, 1.1 equiv), $\text{Pd(PPh}_3\text{)Cl}_2$ (35 mg, 0.050 mmol, 0.05 equiv) and CuI (38 mg, 0.20 mmol, 0.2 equiv) in degazed dioxane (2 mL). The mixture was kept overnight at 80 °C. The reaction was filtered through a plug of celite and the crude was purified by column chromatography (Pentane/DCM= 15:1) to afford **8a** as yellow oil (290 mg, 0.930 mmol, 90%).

Rf (Pentane / DCM= 15 / 1): 0.5. ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, 1 H, J = 0.7 Hz, *benzeneH*), 7.39 (dd, 1 H, J = 8.5, 1.4 Hz, *benzeneH*), 7.24 (d, 1 H, J = 8.5 Hz, *benzeneH*), 7.06 (d, 1 H, J = 3.1 Hz, *pyrroleH*), 6.49 (dd, 1 H, J = 3.1, 0.7 Hz, *pyrroleH*), 3.77 (s, 3 H,

*CH*₃), 1.23 (m, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 136.3, 129.7, 128.1, 125.5, 125.2, 114.1, 109.1, 109.0, 101.2, 87.0, 32.8, 18.7, 11.4. IR 2941 (m), 2863 (m), 2145 (m), 1616 (w), 1514 (w), 1487 (m), 1464 (m), 1423 (w), 1381 (w), 1333 (w), 1283 (w), 1147 (w), 1078 (w), 1014 (w), 996 (w), 945 (w), 919 (w), 884 (s), 820 (s), 802 (m), 717 (s), 710 (s). HRMS (ESI) calcd for C₂₀H₃₀NSi⁺ [M+H]⁺ 312.2142; found 312.2150.

1-(p-Tolyl)-5-((triisopropylsilyl)ethynyl)-1H-indole (8b)

Starting from **6b** (72 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 15:1) to afford **8b** was obtained as yellow oil (94 mg, 0.24 mmol, 81%).

Rf (Pentane / DCM= 15 / 1): 0.5. ¹H NMR (400 MHz, CDCl₃) δ 7.85 (d, 1 H, *J* = 0.8 Hz, *benzeneH*), 7.42 (m, 1 H, *benzeneH*), 7.35 (m, 4 H, *benzeneH*), 7.31 (d, 2 H, *J* = 3.0 Hz, *benzene* + *pyrroleH*), 6.63 (d, 1 H, *J* = 3.0 Hz, *pyrroleH*), 2.44 (s, 3 H, *CH*₃), 1.15 (m, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 136.9, 136.6, 135.6, 130.2, 129.0, 128.9, 126.2, 125.4, 124.3, 115.1, 110.3, 108.7, 103.3, 87.5, 21.1, 18.7, 11.4. IR 2944 (w), 2865 (w), 2149 (w), 1611 (w), 1520 (m), 1471 (m), 1336 (w), 1222 (w), 884 (w), 806 (w), 762 (w), 743 (w), 721 (w), 680 (m), 660 (w), 647 (w), 631 (w), 618 (w). HRMS (ESI) calcd for C₂₆H₃₄NSi⁺ [M+H]⁺ 388.2455; found 388.2460.

1-Benzyl-5-((triisopropylsilyl)ethynyl)-1H-indole (8c)

Starting from **6c** (76 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 30:1) to afford **8c** as yellow oil (96 mg, 0.25 mmol, 83%).

Rf (Pentane / DCM= 30 / 1): 0.4. ¹H NMR (400 MHz, CDCl₃) δ 7.84 (dd, 1 H, *J* = 1.4, 0.6 Hz, *benzeneH*), 7.30 (m, 4 H, *benzeneH*), 7.19 (d, 1 H, *J* = 8.5 Hz, *benzeneH*), 7.14 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 7.07 (m, 2 H, *benzeneH*), 6.53 (dd, 1 H, *J* = 3.1, 0.6 Hz, *pyrroleH*), 5.31 (s, 2 H, *CH*₂), 1.17 (m, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 137.2, 135.9, 129.2, 128.8, 128.5, 127.7, 126.6, 125.8, 125.3, 114.5, 109.6, 108.9, 102.0, 87.2, 50.2, 18.7, 11.4. IR 2958

(m), 2942 (s), 2928 (m), 2892 (m), 2865 (s), 2148 (m), 1667 (w), 1512 (w), 1496 (w), 1480 (m), 1464 (m), 1457 (m), 1391 (w), 1356 (w), 1331 (w), 1265 (m), 1234 (w), 1215 (w), 1077 (w), 1016 (w), 998 (w), 946 (w), 884 (m), 824 (m), 803 (w), 777 (w), 761 (m), 741 (s), 731 (s). HRMS (ESI) calcd for $C_{26}H_{34}NSi^+$ $[M+H]^+$ 388.2455; found 388.2460.

1-(3-Methoxypropyl)-5-((triisopropylsilyl)ethynyl)-1H-indole (**8d**)

Starting from **6d** (66 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 10:1) to afford **8d** as yellow oil (89 mg, 0.24 mmol, 80%).

R_f (Pentane / DCM= 10 / 1): 0.1. ¹H NMR (400 MHz, CDCl₃) δ 7.81 (d, 1 H, *J* = 0.6 Hz, *benzeneH*), 7.34 (dd, 1 H, *J* = 8.5 Hz, 1.5 Hz, *benzeneH*), 7.28 (d, 1 H, *J* = 8.5 Hz, *benzeneH*), 7.10 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 6.47 (dd, 1 H, *J* = 3.1 Hz, 0.7 Hz, *pyrroleH*), 4.25 (t, 1 H, *J* = 6.7 Hz, *NCH₂*), 3.32 (s, 3 H, *OCH₃*), 3.24 (t, 2 H, *J* = 5.8 Hz, *CH₂OCH₃*), 2.04 (m, 2 H, *CH₂*), 1.17 (m, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 135.7, 128.9, 128.2, 125.5, 125.3, 114.1, 109.2, 109.0, 101.4, 87.0, 68.8, 58.6, 42.9, 30.3, 18.7, 11.4. IR 2942 (s), 2890 (m), 2865 (s), 2812 (w), 2147 (s), 1513 (w), 1482 (s), 1463 (m), 1392 (w), 1352 (w), 1332 (w), 1254 (w), 1237 (w), 1207 (w), 1121 (s), 1076 (w), 1015 (w), 996 (w), 946 (w), 915 (w), 884 (s), 821 (s), 804 (m), 763 (w), 722 (m). HRMS (ESI) calcd for $C_{23}H_{36}NOSi^+$ $[M+H]^+$ 370.2561; found 370.2552.

1-(4,4,4-Trifluorobutyl)-5-((triisopropylsilyl)ethynyl)-1H-indole (**8e**)

Starting from **6e** (83 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 30:1) to afford **8e** as yellow oil (100 mg, 0.250 mmol, 82%).

R_f (Pentane / DCM= 30 / 1): 0.2. ¹H NMR (400 MHz, CDCl₃) δ 7.82 (m, 1 H, *benzeneH*), 7.36 (dd, 1 H, *J* = 8.5, 1.4 Hz, *benzeneH*), 7.22 (d, 1 H, *J* = 8.5 Hz, *benzeneH*), 7.08 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 6.50 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 4.20 (t, 3 H, *J* = 6.5 Hz, *NCH₂*), 2.07 (m, 4 H, *CH₂CH₂CF₃*), 1.15 (m, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 135.5, 128.4, 128.3, 126.8 (q, *J* = 275.8 Hz), 125.8, 125.5, 114.6, 108.9, 108.7, 102.1, 87.4, 44.9, 31.0 (q, *J* = 29.3 Hz), 22.9 (q, *J* = 2.9 Hz), 18.7, 11.4. IR 2943 (m), 2869 (m), 2235 (w), 1687 (w), 1675

(w), 1674 (w), 1617 (w), 1466 (w), 1466 (w), 1325 (s), 1168 (m), 1101 (s), 1067 (s), 1012 (m), 927 (w), 883 (m), 840 (m), 809 (w), 735 (s). HRMS (ESI) calcd for $C_{23}F_3H_{33}NSi^+$ $[M+H]^+$ 408.2329; found 408.2338.

1,4-Dimethyl-5-((triisopropylsilyl)ethynyl)-1H-indole (8f)

Starting from **6f** (53 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **8f** as yellow oil (68 mg, 0.21 mmol, 70%).

Rf (Pentane / DCM= 20 / 1): 0.4. 1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 1 H, $J = 8.5$ Hz, *benzeneH*), 7.10 (d, 1 H, $J = 8.5$ Hz, *benzeneH*), 7.05 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 6.52 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 3.77 (s, 3 H, NCH_3), 2.71 (s, 3 H, CH_3), 1.19 (s, 21 H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.0, 133.9, 128.9, 128.3, 126.2, 113.5, 107.6, 106.7, 100.2, 91.2, 32.9, 18.8, 17.2, 11.5. IR 2941 (s), 2925 (m), 2891 (m), 2863 (s), 2144 (s), 1517 (w), 1483 (m), 1463 (m), 1421 (w), 1379 (w), 1366 (w), 1335 (w), 1283 (m), 1236 (w), 1152 (w), 1090 (w), 1071 (w), 1014 (w), 996 (w), 911 (m), 882 (s), 816 (s). HRMS (ESI) calcd for $C_{21}H_{32}NSi^+$ $[M+H]^+$ 326.2299; found 326.2301.

1-Methyl-4-phenyl-5-((triisopropylsilyl)ethynyl)-1H-indole (8g)

Starting from **6g** (72 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 50:1) to afford **8g** as yellow oil (65 mg, 0.17 mmol, 56%). The ratio of regioisomers (**8g**:**10c** = 4:1) was determined on the 1H NMR spectrum of the crude reaction mixture (Comparing two peaks at δ 6.51 and δ 6.39).

Rf (Pentane / DCM= 50 / 1): 0.5. 1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, 1 H, $J = 8.2$ Hz, *benzeneH*), 7.38 (m, 5 H, *benzeneH*), 7.30 (d, 1 H, $J = 8.2$ Hz, *benzeneH*), 6.97 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 6.49 (d, 1 H, $J = 3.1$ Hz, *benzeneH*), 3.16 (s, 3 H, NCH_3), 0.92 (m, 21 H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 133.8, 132.2, 130.7, 129.7, 129.5, 127.5, 127.4, 123.9, 119.8, 117.0, 107.5, 101.1, 92.0, 36.6, 18.6, 11.2. IR 2942 (m), 2891 (w), 2864 (m), 2145 (w), 1519 (w), 1464 (w), 1314 (w), 1095 (w), 1017 (w), 997 (w), 962 (w), 884 (w), 814 (w), 761 (w), 712 (m). HRMS (ESI) calcd for $C_{26}H_{33}NSi$ $[M]^+$ 387.2382; found 387.2376.

1-Methyl-4-(p-tolyl)-5-((triisopropylsilyl)ethynyl)-1H-indole (**8h**)

Starting from **6h** (76 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 15:1) to afford **8h** as yellow oil (63 mg, 0.16 mmol, 52%). The ratio of regioisomers (**8h:10k** = 3:1) were determined by the spectra of crude product. The ratio of regioisomers was determined on the ^1H NMR spectrum of the crude reaction mixture (Comparing two peaks at δ 6.42 and δ 6.30)..

Rf (Pentane / DCM= 15 / 1): 0.4. ^1H NMR (400 MHz, CDCl_3) δ 7.47 (d, 1 H, J = 8.2 Hz, *benzeneH*), 7.24 (m, 3 H, *benzeneH*), 7.14 (m, 2 H, *benzeneH*), 6.93 (d, 1 H, J = 3.1 Hz, *pyrroleH*), 6.44 (d, 1 H, J = 3.1 Hz, *pyrroleH*), 3.16 (s, 3 H, NCH_3), 2.36 (s, 3 H, CH_3), 0.89 (m, 21 H, *TIPS*). ^{13}C NMR (101 MHz, CDCl_3) δ 136.9, 135.4, 133.9, 132.1, 130.5, 129.8, 129.5, 128.2, 123.8, 119.6, 117.2, 107.6, 101.1, 91.7, 36.6, 21.2, 18.5, 11.3. IR 3298 (w), 2984 (w), 2938 (m), 2868 (w), 2826 (w), 1713 (w), 1459 (w), 1105 (s), 1009 (w), 760 (m). HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{36}\text{NSi}^+$ $[\text{M}+\text{H}]^+$ 402.2612; found 402.2605.

4-(4-Bromophenyl)-1-methyl-5-((triisopropylsilyl)ethynyl)-1H-indole (**8i**)

Starting from **6i** (95 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 30:1) to afford **8i** as yellow oil (62 mg, 0.14 mmol, 44%). The ratio of regioisomers (**8i:10l** = 2.5:1) was determined on the ^1H NMR spectrum of the crude reaction mixture (Comparing the two peaks at δ 6.49 and δ 6.30).

Rf (Pentane / DCM= 30 / 1): 0.3. ^1H NMR (400 MHz, CDCl_3) δ 7.53 (d, 3 H, J = 8.2 Hz, Ar H), 7.29 (dd, 3 H, J = 8.4, 1.5 Hz, Ar H), 6.98 (d, 1 H, J = 3.1 Hz, Ar H), 6.49 (d, 1 H, J = 3.1 Hz, Ar H), 3.21 (s, 3 H, NCH_3), 0.95 (m, 21 H, *TIPS*). ^{13}C NMR (101 MHz, CDCl_3) δ 137.6,

133.6, 132.4, 132.3, 130.8, 129.7, 128.1, 123.9, 121.8, 120.2, 117.1, 107.1, 101.3, 92.6, 36.8, 18.5, 11.2. IR 2945 (s), 2891 (w), 2864 (s), 2390 (w), 2358 (w), 2342 (w), 2297 (w), 2143 (w), 1516 (w), 1464 (m), 1316 (w), 1097 (w), 1072 (w), 1016 (w), 963 (w), 915 (w), 885 (w), 819 (s), 730 (s), 717 (m). HRMS (ESI) calcd for $C_{26}H_{33}BrNSi^+$ $[M+H]^+$ 466.1560; found 466.1556.

1-Methyl-4-(naphthalen-1-yl)-5-((triisopropylsilyl)ethynyl)-1H-indole (8j)

Starting from **6i** (87 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 10:1) to afford **8j** as yellow oil (41 mg, 0.094 mmol, 31%) and **10d** as yellow oil (41mg, 0.094 mmol, 31%).

8j

Rf (Pentane / DCM= 15 / 1): 0.6. ^1H NMR (400 MHz, CDCl_3) δ 7.78-7.74 (m, 2 H, *benzeneH*), 7.44-7.38 (m, 4 H, *benzeneH*), 7.31 (m, 1 H, *benzeneH*), 7.24-7.18 (m, 2H, *benzeneH*), 6.88 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 5.88 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 3.74 (s, 3 H, NCH_3), 0.65-0.60 (m, 21 H, *TIPS*). ^{13}C NMR (101 MHz, CDCl_3) δ 137.4, 136.8, 136.1, 133.7, 132.2, 129.5, 129.1, 127.9, 127.5, 127.4, 126.6, 126.3, 125.5, 125.3, 125.2, 114.6, 108.4, 107.3, 101.5, 90.9, 33.0, 18.3, 11.0. IR 2944 (m), 2892 (w), 2891 (w), 2865 (w), 2864 (w), 2362 (s), 2361 (s), 2148 (w), 1465 (w), 911 (w), 887 (w), 886 (w), 820 (w), 800 (w), 777 (w), 734 (m). HRMS (ESI) calcd for $C_{30}H_{35}NSi^+$ $[M]^+$ 438.2612; found 438.2605.

10d

Rf (Pentane / DCM= 15 / 1): 0.5. ^1H NMR (400 MHz, CDCl_3) δ 7.89-7.86 (m, 2 H, *benzeneH*), 7.62 (d, 1 H, $J = 8.2$ Hz, *benzeneH*), 7.53-7.49 (m, 2 H, *benzeneH*), 7.45-7.30 (m, 4 H, *benzeneH*), 6.93 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 6.53 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 2.88 (s, 3 H, NCH_3), 0.70 (m, 21 H, *TIPS*). ^{13}C NMR (101 MHz, CDCl_3) δ 136.1, 134.6, 133.6, 133.4, 132.0, 129.5, 128.4, 128.0, 127.9, 127.5, 126.6, 126.1, 125.7, 124.9, 123.9, 120.1, 117.8, 107.2, 101.1, 91.8, 35.6, 18.3, 11.0. IR 3055 (w), 2942 (s), 2892 (m), 2863 (s), 2145 (m), 1514 (w), 1464 (m), 1410 (w), 1409 (w), 1387 (w), 1314 (w), 1234 (w), 1082 (w), 1016 (w), 996 (w), 956 (m), 911 (m), 884 (m), 804 (s), 778 (m), 732 (s), 716 (s). HRMS (ESI) calcd for $C_{30}H_{35}NSi^+$ $[M]^+$ 438.2612; found 438.2608.

1,6-Dimethyl-5-((triisopropylsilyl)ethynyl)-1H-indole (8k)

Starting from **6k** (52 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 15:1) to afford **8k** as yellow oil (73 mg, 0.22 mmol, 75%).^[10]

Rf (Pentane / DCM= 15 / 1): 0.4. ¹H NMR (400 MHz, CDCl₃) δ 7.79 (s, 1 H, *benzeneH*), 7.13 (s, 1 H, *benzeneH*), 6.98 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 6.40 (dd, 1 H, *J* = 3.1, 0.7 Hz, *pyrroleH*), 3.74 (s, 3 H, *NCH*₃), 2.60 (s, 3 H, *CH*₃), 1.16 (m, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 136.8, 133.7, 129.1, 126.3, 125.5, 114.9, 109.5, 107.6, 100.9, 91.0, 32.8, 21.6, 18.8, 11.5. IR 2943 (s), 2893 (m), 2865 (s), 2143 (s), 1622 (w), 1514 (w), 1477 (m), 1425 (w), 1377 (w), 1326 (w), 1271 (w), 1238 (w), 1076 (w), 1013 (w), 997 (w), 913 (w), 885 (m), 845 (m), 818 (w), 741 (w), 720 (m). HRMS (ESI) calcd for C₂₁H₃₂NSi⁺ [M+H]⁺ 326.2299; found 326.2303.

1,4-Dimethyl-6-((triisopropylsilyl)ethynyl)-1H-indole (**10e**)

Starting from **6l** (52 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **10e** as yellow oil (53 mg, 0.16 mmol, 54%).

Rf (Pentane / DCM= 20 / 1): 0.5. ¹H NMR (400 MHz, CDCl₃) δ 7.33 (s, 1 H, *benzeneH*), 7.08 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 7.04 (s, 1 H, *benzeneH*), 6.46 (dd, 1 H, *J* = 3.1, 0.8 Hz, *pyrroleH*), 3.78 (s, 3 H, *NCH*₃), 2.51 (s, 3 H, *CH*₃), 1.16 (s, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 135.9, 130.1, 129.6, 128.7, 123.4, 116.2, 110.9, 109.2, 99.8, 87.8, 33.0, 18.8, 18.5, 11.5. IR 2957 (w), 2942 (m), 2927 (w), 2889 (w), 2865 (m), 2144 (w), 1510 (w), 1463 (w), 1299 (w), 884 (w), 767 (w), 740 (w), 710 (m), 682 (m), 671 (m), 659 (w), 648 (w), 637 (s), 617 (w). HRMS (ESI) calcd for C₂₁H₃₂NSi⁺ [M+H]⁺ 326.2299; found 326.2302.

9-Methyl-3-((triisopropylsilyl)ethynyl)-9H-carbazole (**8m**)

[10] The product contains about 5 % impurity.

Starting from **6m** (64 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 50:1) to afford **8m** as yellow oil (82 mg, 0.23 mmol, 76%).

Rf (Pentane / DCM= 50 / 1): 0.3. ¹H NMR (400 MHz, CDCl₃) δ 8.25 (m, 1 H, *benzeneH*), 8.10 (d, 1 H, *J* = 7.8 Hz, *benzeneH*), 7.62 (dd, 1 H, *J* = 1.5, 8.4 Hz, *benzeneH*), 7.51 (m, 1 H, *benzeneH*), 7.40 (m, 1 H, *benzeneH*), 7.31-7.28 (m, 2 H, *benzeneH*), 3.83 (s, 3 H, *NCH*₃), 1.22 (s, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 141.3, 140.5, 129.8, 126.1, 124.4, 122.6, 122.3, 120.5, 119.3, 113.6, 108.7, 108.6, 108.2, 87.7, 29.1, 18.8, 11.5. IR 2944 (w), 2891 (w), 2890 (w), 2866 (w), 2865 (w), 2148 (w), 2147 (w), 1474 (w), 1249 (w), 907 (s), 730 (s). HRMS (ESI) calcd for C₂₄H₃₂NSi⁺ [M]⁺ 362.2299; found 362.2291.

4-Methyl-7-((triisopropylsilyl)ethynyl)-4H-thieno[3,2-b]indole (**8n**)

Starting from **6n** (66 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **8n** as yellow oil (86 mg, 0.23 mmol, 78%).

Rf (Pentane / DCM= 20 / 1): 0.4. ¹H NMR (400 MHz, CDCl₃) δ 7.92 (dd, 1 H, *J* = 1.4, 0.4 Hz, *benzeneH*), 7.43 (dd, 1 H, *J* = 8.5, 1.5 Hz, *benzeneH*), 7.40 (d, 1 H, *J* = 5.2 Hz, *thiophenH*), 7.28 (dd, 1 H, *J* = 8.5, 0.4 Hz, *benzeneH*), 7.06 (d, 1 H, *J* = 5.2 Hz, *thiophenH*), 3.87 (s, 3 H, *NCH*₃), 1.17 (s, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 146.5, 141.5, 127.4, 126.5, 123.0, 121.4, 115.8, 113.9, 110.0, 109.4, 108.6, 87.7, 31.3, 18.8, 11.5. IR 3298 (w), 2979 (w), 2934 (w), 2914 (w), 1509 (w), 1422 (w), 1374 (w), 1256 (w), 1177 (w), 936 (w), 786 (m), 738 (w), 706 (m), 695 (m), 681 (m), 653 (m), 646 (s), 623 (m), 607 (m). HRMS (ESI) calcd for C₂₂H₃₀NSSi⁺ [M+H]⁺ 368.1863; found 368.1861.

1-Methyl-6-((triisopropylsilyl)ethynyl)-1H-indole (**10a**)

Starting from **9a** (49 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **10a** as yellow oil (72 mg, 0.23 mmol, 77%).

Rf (Pentane / DCM= 20 / 1): 0.4. ¹H NMR (400 MHz, CDCl₃) δ 7.56 (d, 1 H, *J* = 8.2, *benzeneH*), 7.49 (s, 1 H, *benzeneH*), 7.26 (dd, 2 H, *J* = 8.2, 1.2 Hz, *benzeneH*), 7.09 (d, 1 H, *J* = 3.0 Hz, *pyrroleH*), 6.50 (d, 1 H, *J* = 3.0 Hz, *pyrroleH*), 3.79 (s, 3 H, *NCH*₃), 1.17 (m, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 136.1, 130.2, 128.6, 123.5, 120.6, 116.1, 113.1, 109.0, 101.2, 88.2, 32.9, 18.7, 11.4. IR 2943 (s), 2893 (m), 2865 (s), 2151 (m), 1511 (w), 1466 (s),

1421 (w), 1344 (w), 1245 (w), 1076 (w), 1012 (w), 944 (m), 885 (m), 857 (w), 816 (m), 763 (w), 714 (s). HRMS (ESI) calcd for $C_{20}H_{30}NSi^+ [M+H]^+$ 312.2142; found 312.2141.

1,7-Dimethyl-6-((triisopropylsilyl)ethynyl)-1H-indole (10b)

Starting from **9b** (52 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **10b** as yellow oil (48 mg, 0.15 mmol, 49%).

Rf (Pentane / DCM= 50 / 1): 0.3. 1H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, 1 H, $J = 8.2$ Hz, *benzeneH*), 7.20 (d, 1 H, $J = 8.2$ Hz, *benzeneH*), 6.97 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 6.39 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 4.06 (s, 3 H, NCH_3), 2.95 (s, 3 H, CH_3), 1.16 (s, 21 H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.1, 132.1, 129.8, 124.5, 124.4, 118.5, 117.2, 107.8, 101.2, 92.5, 37.4, 18.8, 16.9, 11.5. IR 2942 (s), 2892 (m), 2865 (s), 2147 (m), 1515 (w), 1464 (m), 1313 (w), 1312 (w), 1001 (w), 911 (m), 887 (m), 886 (m), 813 (m), 730 (s). HRMS (ESI) calcd for $C_{21}H_{32}NSi^+ [M]^+$ 326.2299; found 326.2295.

1-Methyl-7-phenyl-6-((triisopropylsilyl)ethynyl)-1H-indole (10c)

Starting from **9c** (72 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **10c** as yellow oil (62 mg, 0.16 mmol, 53%).

1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, 1 H, $J = 8.2$ Hz, *benzeneH*), 7.42-7.35 (m, 5 H, *benzeneH*), 7.31 (d, 1 H, $J = 8.2$ Hz, *benzeneH*), 6.97 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 6.49 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 3.16 (s, 3 H, NCH_3), 0.93 (m, 21 H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 133.8, 132.2, 130.7, 129.7, 129.5, 127.5, 127.4, 123.9, 119.8, 117.0, 107.5, 101.1, 92.0, 36.6, 18.6, 11.2. IR 2946 (w), 2866 (w), 2146 (w), 1465 (w), 1295 (w), 1273 (w), 1203 (m), 965 (m), 906 (w), 883 (w), 814 (w), 763 (w), 712 (w). HRMS (ESI) calcd for $C_{26}H_{33}NSi^+ [M]^+$ 388.2455; found 388.2457.

1-Methyl-7-(naphthalen-1-yl)-6-((triisopropylsilyl)ethynyl)-1H-indole (10d)

Starting from **9d** (87 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **10d** as yellow oil (62 mg, 0.14 mmol, 47%).

Characterization data corresponds to the one obtained starting from **6i**.

1,4-Dimethyl-6-((triisopropylsilyl)ethynyl)-1H-indole (**10e**)

Starting from **9e** (52 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **10e** as yellow oil (53 mg, 0.16 mmol, 54%).

Characterization data corresponds to the one obtained starting from **6k**.

1-Methyl-4-phenyl-6-((triisopropylsilyl)ethynyl)-1H-indole (**10f**)

Starting from **9f** (72 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 15:1) to afford **10f** as yellow oil (75 mg, 0.19 mmol, 65%).

R_f (Pentane / DCM= 15 / 1): 0.4. ¹H NMR (400 MHz, CDCl₃) δ 7.70 (dd, 2 H, *J* = 8.4, 1.2 Hz, *benzeneH*), 7.49 (m, 3 H, *benzeneH*), 7.39 (m, 1 H, *benzeneH*), 7.33 (d, 1 H, *J* = 1.2 Hz, *benzeneH*), 7.14 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 6.62 (dd, 1 H, *J* = 3.1, 0.8 Hz, *pyrroleH*), 3.83 (s, 3 H, *NCH₃*), 1.18 (s, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 140.5, 136.7, 134.4, 130.5, 128.7, 128.5, 127.2, 127.0, 123.3, 116.5, 112.2, 108.8, 100.9, 88.4, 33.1, 18.8, 11.5. IR 2942 (s), 2891 (w), 2864 (s), 2148 (m), 1511 (m), 1499 (w), 1462 (m), 1431 (w), 1327 (w), 1295 (w), 1264 (w), 1212 (w), 1091 (w), 1030 (w), 1017 (w), 971 (m), 920 (w), 883 (m), 850 (w), 781 (m), 761 (w), 729 (w), 711 (m). HRMS (ESI) calcd for C₂₆H₃₄NSi⁺ [M+H]⁺ 388.2455; found 388.2466.

1,4,7-Trimethyl-6-((triisopropylsilyl)ethynyl)-1H-indole (10g)

Starting from **9g** (57 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 20:1) to afford **10g** as yellow oil (45 mg, 0.13 mmol, 44%).

Rf (Pentane / DCM= 20 / 1): 0.2. ¹H NMR (400 MHz, CDCl₃) δ 7.03 (s, 1 H, *benzeneH*), 6.97 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 6.41 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 4.05 (s, 3 H, *NCH*₃), 2.92 (s, 3 H, *CH*₃), 2.46 (s, 3 H, *CH*₃), 1.17 (s, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 134.8, 131.5, 129.9, 127.6, 124.1, 122.0, 117.0, 108.0, 99.6, 92.1, 37.3, 18.8, 18.1, 16.6, 11.5. IR 2958 (s), 2943 (s), 2926 (s), 2892 (m), 2865 (s), 2142 (s), 1517 (w), 1496 (w), 1463 (m), 1384 (w), 1346 (w), 1303 (w), 1091 (w), 1065 (w), 1008 (w), 921 (w), 885 (s), 864 (w), 772 (w), 744 (w), 709 (s). HRMS (ESI) calcd for C₂₂H₃₄NSi⁺ [M+H]⁺ 340.2455; found 340.2460.

1,4,5-Trimethyl-6-((triisopropylsilyl)ethynyl)-1H-indole (10h)

Starting from **9h** (57 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 30:1) to afford **10h** as yellow oil (35 mg, 0.10 mmol, 34%).

Rf (Pentane / DCM= 30 / 1): 0.2. ¹H NMR (400 MHz, CDCl₃) δ 7.36 (s, 1 H, *benzeneH*), 7.04 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 6.42 (dd, 1 H, *J* = 3.1, 0.8 Hz, *pyrroleH*), 3.75 (s, 3 H, *NCH*₃), 2.52 (s, 3 H, *CH*₃), 2.45 (s, 3 H, *CH*₃), 1.16 (s, 21 H, *TIPS*). ¹³C NMR (201 MHz, CDCl₃) δ 134.2, 129.6, 129.5, 128.2, 127.8, 117.2, 111.3, 108.5, 99.5, 91.5, 32.9, 18.8, 17.0, 15.9, 11.5. HRMS IR 2942 (m), 2899 (w), 2140 (w), 1510 (w), 1283 (w), 1085 (w), 997 (w), 912 (w), 885 (w), 849 (w), 714 (w). (ESI) calcd for C₂₂H₃₄NSi⁺ [M+H]⁺ 340.2455; found 340.2462.

9-Methyl-2-((triisopropylsilyl)ethynyl)-9H-carbazole (10i)

Starting from **9i** (64 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 30:1) to afford **10i** as yellow oil (63 mg, 0.17 mmol, 58%).

Rf (Pentane / DCM= 30 / 1): 0.4. ^1H NMR (400 MHz, CDCl_3) δ 8.08 (d, 1 H, $J = 7.8$ Hz, *benzeneH*), 8.00 (d, 1 H, $J = 8.0$ Hz, *benzeneH*), 7.53 (s, 1 H, *benzeneH*), 7.50 (m, 1 H, *benzeneH*), 7.39 (m, 2 H, *benzeneH*), 7.25 (m, 1 H, *benzeneH*), 3.84 (s, 3 H, NCH_3), 1.20 (s, 21 H, *TIPS*). ^{13}C NMR (101 MHz, CDCl_3) δ 141.6, 140.5, 126.1, 123.1, 122.8, 122.4, 120.5, 120.3, 120.0, 119.1, 112.1, 108.5, 108.4, 89.7, 29.1, 18.8, 11.4. IR 2957 (w), 2891 (w), 2865 (w), 2150 (w), 1601 (w), 1498 (w), 1324 (m), 1248 (w), 1119 (w), 1018 (w), 940 (w), 909 (m), 885 (w), 851 (w), 816 (w), 766 (w), 741 (s), 725 (m). HRMS (ESI) calcd for $\text{C}_{24}\text{H}_{32}\text{NSi}^+$ $[\text{M}+\text{H}]^+$ 362.2299; found 362.2307.

6-Methoxy-9-methyl-2-((triisopropylsilyl)ethynyl)-9H-carbazole (**10j**)

Starting from **9j** (73 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/DCM= 30:1) to afford **10j** was obtained as yellow oil (75 mg, 0.19 mmol, 64%).

Rf (Pentane / ether= 30 / 1): 0.5. ^1H NMR (400 MHz, CDCl_3) δ 7.95 (dd, 1 H, $J = 8.0, 0.6$ Hz, *benzeneH*), 7.55 (d, 1 H, $J = 2.4$ Hz, *benzeneH*), 7.49 (d, 1 H, $J = 0.4$ Hz, *benzeneH*), 7.31 (m, 2 H, *benzeneH*), 7.13 (dd, 1 H, $J = 8.8, 2.5$ Hz, *benzeneH*), 3.93 (s, 3 H, NCH_3), 3.82 (s, 3 H, OCH_3), 1.18 (m, 21 H, *TIPS*). ^{13}C NMR (101 MHz, CDCl_3) δ 153.8, 140.9, 136.8, 122.7, 122.6, 120.2, 119.9, 115.5, 112.2, 109.3, 108.5, 103.3, 89.7, 77.2, 56.1, 29.7, 18.8, 11.4. IR 2960 (w), 2186 (w), 1607 (w), 1509 (s), 1463 (w), 1438 (w), 1295 (m), 1250 (s), 1176 (m), 1034 (m), 833 (s), 709 (w). HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{34}\text{NOSi}^+$ $[\text{M}+\text{H}]^+$ 392.2404; found 392.2400.

5. Further functionalization:

5-Ethynyl-1-methyl-1H-indole (39)

TBAF (0.424 mL, 0.424 mmol, 1.2 equiv) was added slowly into a solution of **8a** (110 mg, 0.353 mmol, 1.0 equiv) in THF (4 mL) at 0 °C. The reaction was quenched with sat NH₄Cl solution (20 mL) after 30 min. The aqueous and organic layers were separated and the aqueous layer was extracted with ether (3x10 mL). After drying over MgSO₄ and concentrating under vacuum, the crude product was purified by column chromatography (Pentane/DCM= 10:1) to afford **39** as yellow oil (43 mg, 0.28 mmol, 78%).

R_f (Pentane / DCM= 10 / 1): 0.4. ¹H NMR (400 MHz, CDCl₃) δ 7.85 (s, 1 H, *benzeneH*), 7.38 (dd, 1 H, *J* = 1.3, 8.4 Hz, *benzeneH*), 7.26 (d, 1 H, *J* = 8.4 Hz, *benzeneH*), 7.07 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 6.50 (d, 1 H, *J* = 3.1 Hz, *pyrroleH*), 3.77 (s, 3 H, *NCH₃*), 3.04 (s, 1 H, *Alkyne H*). ¹³C NMR (101 MHz, CDCl₃) δ 136.5, 129.8, 128.1, 125.4, 113.6, 112.5, 109.2, 101.2, 85.4, 74.6, 32.8. IR 1484 (w), 1334 (w), 1245 (w), 886 (w), 805 (w), 728 (w). HRMS (ESI) calcd for C₁₁H₉N [M⁺] 156.0808; found 156.0809.

5-Ethynyl-1-methyl-3-((triisopropylsilyl)ethynyl)-1H-indole (11)

Gold(I) chloride (3.7 mg, 0.016 mmol, 0.050 equiv) was added into a solution of **39** (0.050 g, 0.32 mmol, 1.0 equiv), **1b** (0.166 g, 0.387 mmol, 1.2 equiv), sodium bicarbonate (0.032 g, 0.39 mmol, 1.2 equiv) in Et₂O (8 mL). The solvent was removed under vacuum, and the crude product was purified by column chromatography (Pentane/EtOAc= 15:1) directly without any further work-up. **11** was obtained as yellow oil (68 mg, 0.20 mmol, 63%, 90% based on the unconsumed starting material determined from the ¹H NMR spectra of crude product)

R_f (Pentane/EtOAc= 15:1): 0.3. ¹H NMR (400 MHz, CDCl₃) δ 7.87 (s, 1 H, *benzeneH*), 7.38 (dd, 1 H, *J* = 1.5, 8.5 Hz, *benzeneH*), 7.29 (s, 1 H, *pyrroleH*), 7.23 (d, 1 H, *J* = 8.5 Hz, *benzeneH*), 3.75 (s, 3 H, *NCH₃*), 3.05 (s, 1 H, *Alkyne H*), 1.17 (s, 21 H, *TIPS*). ¹³C NMR (101 MHz, CDCl₃) δ 135.8, 133.7, 129.2, 126.6, 124.7, 113.7, 109.6, 99.5, 98.0, 92.2, 85.0, 75.3, 33.1, 18.8, 11.4. IR 3311 (w), 3296 (w), 2945 (s), 2893 (w), 2865 (s), 2148 (s), 1479 (m),

1468 (m), 1374 (m), 1249 (w), 1017 (w), 997 (w), 910 (w), 888 (s), 804 (m), 731 (s). HRMS (ESI) calcd for $C_{22}H_{29}NSi^+ [M]^+$ 336.2142; found 336.2147.

6-Ethynyl-1-methyl-7-(naphthalen-1-yl)-1H-indole (40)

TBAF (0.18 mL, 0.18 mmol, 1.2 equiv) was added slowly into a solution of **10d** (65 mg, 0.15 mmol, 1.0 equiv) in THF (3 mL) at 0 °C. The reaction was quenched with a sat NH_4Cl solution (20 mL) after 30 min. The aqueous and organic layers were separated and the aqueous layer was extracted with ether (3x10 mL). After drying over $MgSO_4$ and concentrating under vacuum, the crude product was purified by column chromatography (Pentane/DCM= 10:1) to afford **40** as a yellow oil (35 mg, 0.12 mmol, 84%).

Rf (Pentane / DCM= 10 / 1): 0.4. 1H NMR (400 MHz, $CDCl_3$) δ 7.97-7.93 (m, 2 H, *benzeneH*), 7.66 (d, 1 H, $J = 8.2$ Hz, *benzeneH*), 7.60-7.54 (m, 2 H, *benzeneH*), 7.49 (m, 1 H, *benzeneH*), 7.42-7.34 (m, 3 H, *benzeneH*), 6.95 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 6.56 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 2.85 (s, 3 H, NCH_3), 2.65 (s, 1 H, *Alkyne H*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 134.5, 133.4, 133.1, 132.3, 129.8, 128.4, 128.2, 128.1, 127.6, 126.3, 125.9, 124.9, 124.0, 120.3, 116.1, 101.1, 83.9, 78.6, 35.5 (one carbon signal not resolved). IR 3305 (w), 1325 (w), 1324 (w), 1315 (w), 907 (s), 815 (w), 806 (w), 779 (w), 728 (s). HRMS (ESI) calcd for $C_{21}H_{15}N^+ [M]^+$ 282.1277; found 282.1284.

1-Methyl-1H-phenanthro[3,4-g]indole (12)

$PtCl_2$ (3.3 mg, 0.012 mmol, 0.1 equiv) was added into a solution of **40** (35 mg, 0.12 mmol, 1.0 equiv) in toluene (4.8 mL). The mixture was kept at 100 °C overnight. The crude product was purified by column chromatography (Pentane/DCM= 10:1) directly to afford **12** as a yellow oil (26 mg, 0.092 mmol, 74 %).

Rf (Pentane / DCM= 10 / 1): 0.4. 1H NMR (400 MHz, $CDCl_3$) δ 8.31-8.29 (m, 1 H, *benzeneH*), 7.99-7.97 (m, 2 H, *benzeneH*), 7.92-7.90 (m, 3 H, *benzeneH*), 7.76 (d, 1 H, $J = 8.3$ Hz, *benzeneH*), 7.68 (d, 1 H, $J = 8.3$ Hz, *benzeneH*), 7.52 (m, 1 H, *benzeneH*), 7.40 (m, 1 H, *benzeneH*), 7.07 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 6.81 (d, 1 H, $J = 3.1$ Hz, *pyrroleH*), 2.96 (s, 3 H, NCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.5, 131.6, 131.4, 131.0, 131.0, 130.3, 128.3, 128.0, 127.9, 126.7, 126.2, 125.9, 125.6, 125.2, 124.8, 124.2, 121.2, 120.6, 116.6, 103.3, 37.2. IR 3052 (w), 1344 (w), 1265 (m), 840 (w), 819 (w), 790 (w), 773 (w), 734 (s), 705 (m). HRMS (ESI) calcd for $C_{21}H_{15}N^+ [M]^+$ 282.1277; found 282.1280.

6. Spectra for new compounds

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6a

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6a

solvent: <CDCl3>
Frequency: 400.13MHz

6b

solvent: <CDCl3>
Frequency: 100.612769MHz

6b

solvent: <CDCl₃>
Frequency: 400.13 MHz

6c

solvent: <CDCl₃>
Frequency: 100.612769MHz

6c

6c

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6d

solvent: <CDCl3>
Frequency: 100.612769MHz

6d

6d

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6e

solvent: <CDCl3>

Frequency: 100.612769MHz

6e

solvent: <CDCl3>
Frequency: 400.13MHz

6f

solvent: <CDCl3>
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6f

6f

solvent: <CDCl₃>
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solvent: <CDCl3>
Frequency: 400.13MHz

6h

solvent: <CDCl3>
Frequency: 100.612769MHz

6h

solvent: <CDCl₃>
Frequency: 400.13MHz

6i

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Frequency: 100.612769MHz

solvent: <CDCl3>
Frequency: 400.13MHz

6j

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6k

6k

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6l

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6m

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6n

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9a

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9b

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Frequency: 100.612769MHz

9b

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9c

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9c

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9e

solvent: <CDCl₃>
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9e

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9f

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9f

9f

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9g

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9g

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9h

9h

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S103

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S104

9i

S105

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8b

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8f

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8f

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8g

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8h

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8h

S131

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8i

S135

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Frequency: 400.13 MHz

8j

S136

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8j

S137

[illegible][illegible][illegible]

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S143

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8n

S145

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8n

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10a

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solvent: <CDCl₃>
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10b

S153

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10c

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Frequency: 100.612769MHz

10c

S155

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10d

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Frequency: 100.612769MHz

10d

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Frequency: 100.612769MHz

solvent: <CDCl₃>
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solvent: <CDCl3>
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solvent: <CDCl₃>

Frequency: 400.13MHz

S166

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10h

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solvent: <CDCl3>

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solvent: <CDCl3>

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solvent: <CDCl3>
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39

S178

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39

S179

39

S180

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solvent: <CDCl3>
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solvent: <CDCl₃>
Frequency: 400.13MHz

40

solvent: <CDCl₃>
Frequency: 100.612769MHz

40

S185

solvent: <CDCl3>
Frequency: 400.13MHz

12

S187

solvent: <CDCl3>

Frequency: 100.612769MHz