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Synthesis of γ -carboline *N*-oxide under gold(I)-catalysis and C-1 amino and fluoro γ -carboline.

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ABSTRACT

Intramolecular gold (I)-catalyzed cyclization of 2-alkynylindole-3-carbaldehyde oximes enabled direct construction of the unknown γ -carboline *N*-oxide scaffold at ambient temperature. This reaction proceeded through an interesting 6-endo-dig mechanism and afforded the desired products with satisfactory to high yields. The scope and limitations of the methodology were evaluated and the final compounds fully characterized. From the 3-phenyl-*N*-oxide derivative, fluorination assays were achieved in two steps including the design of several C-1 ammonium salts and their nucleophilic displacements by fluorine to yield 1-fluoro- γ -carboline.

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1. Introduction

Indole-containing fused heterocyclic systems, such as indolocarbazoles,¹ carbolines,² and azaindoles³ have demonstrated their potential as bioactive compounds and are used in a number of pharmaceutical reagents.⁴ Therefore, with a view to increasing molecular diversity, the development of efficient methodologies to design and functionalize fused indole heterocycles is crucial.⁵ In this area, transition metal-catalyzed enyne cyclizations have become a powerful strategy to generate functionalized cyclic indole structures.⁶ Our team recently reported a tandem silver-catalyzed cyclization/nucleophilic functionalization of 2-alkynylindole-3-carbaldehyde oximes to provide original 1,3-disubstituted γ -carboline *N*-oxides which were then involved in several reactions such as *in situ* S_NAr reactions after a PyBrop *N*-oxide activation.⁷

Despite our efforts, however, several nucleophilic substitutions such as fluorinations failed. The stability of the O-PyBrop leaving group and the use of a poor nucleophile could explain this result. We therefore envisioned developing a strategy able to furnish the *N*-oxide derivative, which would then be subjected to the nucleophilic fluorinations using ammonium salts as leaving groups. To achieve the first objective, we became interested in the potential of gold(I)-catalyzed reactions as homogenous gold catalysis.⁸

Reactions involving this transition metal have proven to be an efficient synthetic tool to allow the nucleophilic addition of an alkyne bond, affording original cyclization products⁹ with a highly atom-economical strategy and without the need for experimental precautions against moisture or ambient atmosphere.¹⁰

One synthetic pathway to generate *C*-1 substituted γ -carboline heterocycles was described by Verma's group who reported a **Table 1**. Synthesis of *E*-oximes of type **I**^a.

facile access to *N*-methyl pyridoindoles fused with oxazoles using a gold-catalyzed cascade reaction *via* a 6-*endo-dig* cyclization (Figure 1).¹¹

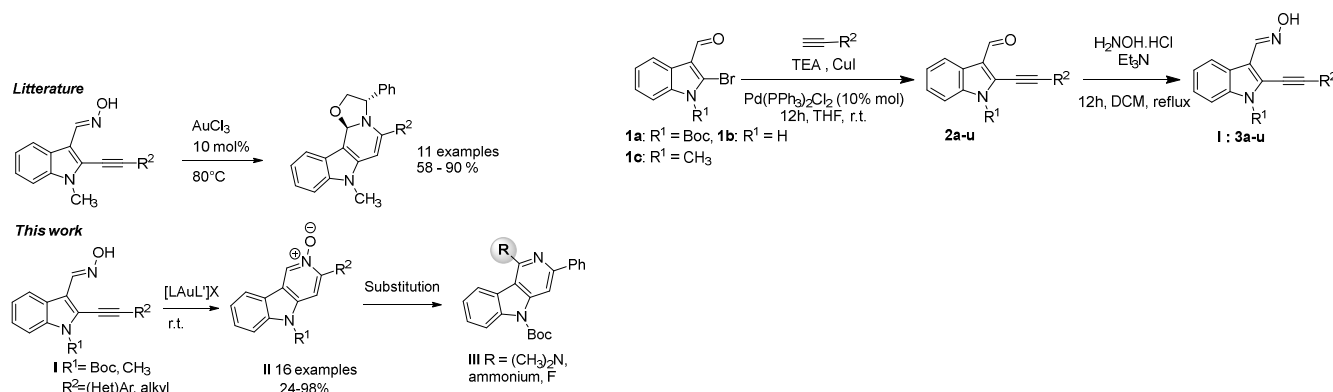
Figure 1. Gold catalyzed annulations leading to the γ -carbolines. and presentation in this work.

This innovative strategy appeared useful to incorporate a 6-membered heteroaromatic ring into the indole nucleus which could be functionalized at a later stage.

In this paper, we report a fast and efficient gold-catalyzed annulation to synthesize new γ -carboline *N*-oxide derivatives **II** from 2-alkynylindole-3-carbaldehyde oximes **I** with perfect control of the regioselectivity of the cyclization. Furthermore, we take advantage of the isolation of the *N*-oxide derivatives to explore the synthesis of *C*-1quaternary ammonium salts which will serve to achieve unprecedented γ -carboline *C*-1 fluorinations under S_NAr .

2. Results and discussion

In order to set up the gold-catalyzed cyclization, we first designed (3*E*)-2-alkyne-3-oximeindoles **3** in a two-step synthesis from 2-bromo-3-formyl-1*H*-indole derivatives **1a-c** (Table 1).¹⁴ Compared to our previous report, changes in Sonogashira cross-coupling conditions (*i.e.* amount of catalyst and use of THF instead of DMF) increased the yield and prevented degradation. 16 examples of 2-alkynyl indoles of type **2** were obtained with yields up to 78%. For the second step, we reduced the amount of reagents without any major impact on yields, which remained up to 75% except with the NH or *N*-Me derivatives **3o** and **3p**.



Entry	R ¹	R ²	2, Yield ^b	3, Yield ^b	Entry	R ¹	R ²	2, Yield ^b	3, Yield ^b
1	Boc		2a , 96%	3a , 74%	9	Boc		2i , 89%	3i , 56%
2	Boc		2b , 95%	3b , 66%	10	Boc		2j , 90%	3j , 65%
3	Boc		2c , 96%	3c , 54%	11	Boc		2k , 92%	3k , 55%
4	Boc		2d , 91%	3d , 55%	12	Boc		2l , 90%	3l , 72%
5	Boc		2e , 78%	3e , 69%	13	Boc		2m , 99%	3m , 63%
6	Boc		2f , 90%	3f , 75%	14	Boc		2n , 99%	3n , 63%
7	Boc		2g , 93%	3g , 67%	15	H		2o , 78%	3o , 24%

8	Boc		2h , 82%	3h , 62%	16	CH ₃		2p , 99%	3p , 38%
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^a Reaction conditions. Step 1: **1a-c** (1.0 equiv.), alkyne (1.5 equiv.), Et₃N (2.0 equiv.), Pd(PPh₃)₂Cl₂ (10.0 mol%), CuI (5.0 mol%), THF, 12 h, r.t.; Step 2: NH₂OH·HCl (1.1 equiv.), Et₃N (2.0 equiv.), CH₂Cl₂, 24 h, reflux. ^b Isolated yield.

The desired *E*-isomers of oximes of type **I** were only isolated, whereas the *Z*-isomers, detected on crude material (¹H NMR, ratio *E/Z* 9/1), were fully removed during the purification.

2.1. γ -Carboline *N*-oxide formation

Having in hand a representative library of **I**, we then focused our efforts on finding an efficient gold catalytic system to achieve the envisioned 6-*endo-dig* cyclization toward γ -carboline *N*-oxide derivatives. Starting from **3a**, AuCl₃ was first used as gold source¹² in CH₂Cl₂ at room temperature but proved unsuccessful as starting material was fully recovered (Table 2, entry 1). The same behavior was observed with the gold(I) complex containing chlorine atom as ligand (entries 2-3). To our delight, with the bis-(trifluoromethanesulfonyl)imide gold ligand the desired product **4a** was regioselectively obtained in a 70% yield. With JohnPhosAu(MeCN)SbF₆, the starting material was totally consumed and the yield increased remarkably to 96%. Next, we switched the phosphine for more substituted *t*-BuXPhos or *t*-BuBrettPhos, but yields decreased significantly indicating that the steric effects on ligands play a primordial role in the approach between the catalyst and **3a**. The *N*-reaction leading to an aromatic pyridinium is preferred to a *O*-reaction and the formation of a seven-membered ring. This full regioselectivity could be explained by the gain induced by Hückel aromaticity for **4a** as a driving force, *versus* the building of a non-aromatic cyclic system with oxygen as nucleophile.¹³

With the optimized conditions (entry 5), the intramolecular reaction was investigated with other compounds of type **I** (Table 3). With electron-donating groups such as methyl, methoxy or *N,N*-dimethylamine groups present in para position of the phenylalkyne moiety, yields remained up to 98% (entries 1, 2, 5, 6). The presence of an NH₂ group led to a small reduction in the efficiency of the reaction and **4g** was isolated in an 82% yield.

Table 2. Gold catalyst optimization.^a



Table 3. Scope of reaction^a

Entry	R ¹	R ²	4 , Yield ^b	5 , Yield ^b	Entry	R ¹	R ²	4 , Yield ^b	5 , Yield ^b
1	Boc		4a , 96%	5a , 86%	9	Boc		4i , 72%	5i , 87%
2	Boc		4b , 96%	5b , 66%	10	Boc		4j , 85%	5j , 65%
3	Boc		4c , 73%	5c , 76%	11	Boc		4k , 72%	5k , 97%
4	Boc		4d , 70%	5d , 95%	12	Boc		4l , 84%	5l , 87%
5	Boc		4e , 95%	5e , 64%	13	Boc		4m , 82%	5m , 99%
6	Boc		4f , 98%	5f , 81%	14	Boc		4n , 45%	5n , 90%

Entry	Catalyst	Yield ^b
1	AuCl ₃	ND
2	(Ph ₃ P)AuCl	ND
3	JohnPhosAuCl	ND
4	JohnPhos AuNTf ₂	70%
5	JohnPhos Au(MeCN)SbF ₆	96%
6	<i>t</i> BuXPhos Au(MeCN)SbF ₆	34%
7	<i>t</i> -BuBrettPhos Au(MeCN)SbF ₆	26%

^a Reaction conditions: **3a** (1.0 equiv.), gold catalyst (5 mol%), CH₂Cl₂, 16 h, r.t. ^b Yield is indicated as isolated compound. ND : Not Detected.

The same behavior was observed with a substituent positioned in meta or ortho positions (entries 3, 4) suggesting that the substituent interfered with the catalyst coordination. This behavior was confirmed with alkyl groups. A linear alkynyl alkane led to a better result than the reaction with a branched alkynyl alkane (entries 13, 14). Finally, on substituting the phenyl ring with thiophene, which is regarded as an *electron-rich* aromatic ring system similar to benzene, the reaction led to the attempted derivative **4l** in a fairly good yield with no poisoning due to the presence of sulfur atom.

With electron-withdrawing substituents on the phenylalkyne moiety, the efficiency of the cyclization decreased slightly as the presence of chlorine atom or trifluoromethyl and cyano groups induced a small decrease in yield. This effect increased with the nitro group as **4h** was obtained in only 62% yield (entries 9-12, 8).

To further extend the scope of this efficient methodology, we changed the indolic nitrogen substitution. While the total absence of a protective group on the indolic nitrogen atom revealed a total absence of reactivity (entry 15), its methylation restored the effectiveness of the reaction. Comparing the reactions of entries 8, 15 and 16, we can therefore conclude that i) gold catalyzed cyclization is favored when the pyrrole ring is deactivated and ii) the reaction does not support the presence of an acidic proton.

7	Boc		4g , 82%	5g , 50%	15	H		4o , ND	---
8	Boc		4h , 62%	5h , 86%	16	CH ₃		4p , 24%	---

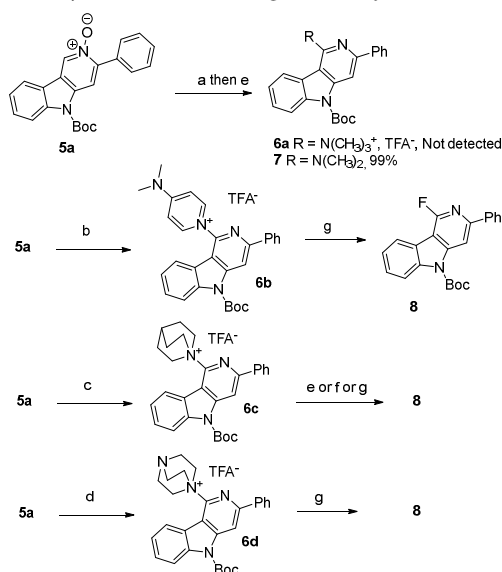
^a Reaction conditions: Step 1 : **3a-p** (1.0 equiv.), JohnPhos Au(MeCN)SbF₆ (5.0 mol%), CH₂Cl₂, 16 h, r.t. ; Step 2 : **4a-n** (1.0 equiv.), TFA/DCM (1:3), 16 h, r.t.. ^b Yield is indicated as isolated compound. ND : Not Detected.

2.2. Synthesis of C-1 substituted γ -carboline

We then turned our attention to the substitution of the C-1 position with the final objective of fluorination. We started with compound **4a** and used a method based on Xiong *et al.* who reported a comprehensive study of the activation of a pyridine *N*-oxide in the presence of a tertiary amine to furnish a trialkylammonium salt.¹⁵

The assay was performed with trimethylamine, TFAA for 2h at room temperature but unfortunately the TBAF treatment at the end of the procedure led to demethylation and derivative **7** was the sole compound isolated in a near quantitative yield (Scheme 1). All attempts to isolate **6a** remained unsuccessful. To circumvent this undesired elimination, we then used successively 4-(dimethylamino)pyridine, quinuclidine and finally DABCO which led to the corresponding ammonium salts **6b-d** with yields between 50 and 62%.

Pyridinium salt **6b** and DABCO salt **6d** appeared as too stable to allow any nucleophilic substitution in the presence of TBAF. Fortunately with **6c**, the substitution occurred and **8** was isolated in a low 25% yield using TBAF in THF at 60°C. To be able to perform the fluorination under microwave irradiation we replaced the solvent with CH₃CN and performed the reaction at 120°C for 30 minutes. In this case, fluorination of **6b** led to the attempted C-1-fluoro- γ -carboline **8** in a higher 35% yield.



Scheme 1 . Synthesis of C-1 substituted γ -carbolines. Reagents and conditions: a) Me₃N (1M in THF, 6.0 equiv.), TFAA (3.0 equiv.), CH₂Cl₂, 0 °C to r.t. 2h ; b) idem a) with 4-DMAP (6.0 equiv.), 1h, 50% c) idem b) with quinuclidine (6.0 equiv.), 62% ; d) idem b) with DABCO (3.0 equiv.) 57% ; e) TBAF (1M in THF, 5.0 equiv.), THF, 60 °C, 1h, from **6c** : **8** 25% ; f) TBAF (1M in THF, 5.0 equiv.), CH₃CN, μ W, 120°C, 30 min, from **6c** : **8** 35% ; g) idem f) with additional treatment Boc₂O (1.5 equiv.), 4-DMAP (0.1 equiv.), Et₃N (2.0 equiv.), r.t., 12 h, from **6b** : **8** 13%, from **6c** : **8** 49%, from **6d** : **8** 43%.

Nevertheless, during LC-MS monitoring a partial Boc deprotection was clearly observed.¹⁵ To be able to quantify the fluorination rate, we first envisaged full Boc removal by adding TFA to the reaction mixture at the end of the reaction. Unfortunately this additional treatment led to a complete

degradation. We therefore added at the end of each reaction a small amount of Boc₂O with 4-DMAP/Et₃N to trap the deprotected derivative. Starting from highly stable **6b**, the C-1 fluoro derivative **8** was isolated in a 13 % yield whereas the alkylammonium salts **6c-d** led to **8** in better 49 and 43 % yields respectively.

3. Conclusion

In this paper we described the first synthesis of γ -carboline-*N*-oxide under gold catalysis from 2-alkynylindole-3-carbaldehyde oximes. We show that the efficiency of the annelation depends on several criteria such as nature of catalyst, steric hindrance induced by gold ligand and alkyne substituent. C-1 aminations were performed by activating the *N*-oxide with TFAA. Several ammonium salts were isolated prior to be used to perform S_NAr fluorinations under microwave irradiation. Even if yields remain moderate, we obtained for the first time 1-fluoro- γ -carbolines after only few minutes. We hope that this method will be useful for designing other bioactive fluorocarboline using ¹⁹F or ¹⁸F to design PET tracers as example.

4. Experimental section

¹H NMR and ¹³C NMR spectra were recorded on a Bruker DPX 250 MHz or 400 MHz instrument using CDCl₃ or DMSO-*d*₆. The chemical shifts are reported in parts per million (δ scale) and all coupling constant (*J*) values are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet doublet) and ddd (doublet doublet doublet). Melting points are uncorrected. IR absorption spectra were obtained on a Perkin Elmer PARAGON 1000 PC and values are reported in cm⁻¹. HRMS were recorded on a Bruker maXis mass spectrometer. Monitoring of the reactions was performed using silica gel TLC plates (silica Merck 60 F254). Spots were visualized by UV light at 254 nm and 356 nm. Chromatography Columns were performed using silica gel 60 (0.063-0.200 mm, Merck). Reactions requiring anhydrous conditions were performed under argon. All solvents were freshly distilled under argon prior to being used. Chemical products were commercially obtained from Aldrich and Alpha Aesar. Microwave irradiation was carried out in sealed 2–5 mL vessels placed in a Biotage Initiator system using a standard absorbance level (300 W maximum power). The temperatures were externally measured by an IR probe that determined the temperature on the surface of the vial and could be read directly from the instrument screen. The reaction time was measured from when the reaction mixture reached the stated temperature for temperature-controlled experiments. Pressure was measured by a non-invasive sensor embedded in the cavity lid.

4.1. *tert*-Butyl 3-formyl-2-(phenylethynyl)-1*H*-indole-1-carboxylate (**2a**)

To the solution of *tert*-butyl 2-bromo-3-formyl-1*H*-indole-1-carboxylate **1a** (0.150 g, 0.7 mmol) in anhydrous THF (3 mL) TEA (0.2 mL, 1.4 mmol, 2.0 equiv.) and phenylacetylene (0.12 mL, 1.1 mmol, 1.5 equiv.) were added. The mixture was flushed by argon for 30 minutes then Pd(PPh₃)₂Cl₂ (0.049 g, 5 %mol) and CuI (0.008 g, 0.04 mmol, 0.05 equiv.) were added. The reaction was stirred under

argon atmosphere for 4 h at r.t. then filtered through a Celite® pad and the filtrate washed with EtOAc. After concentration under reduced pressure, the crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as an orange solid (0.162 g, 96%). *R_f* (9:1 PE/EtOAc) 0.2; mp: 130-132 °C; IR (ATR diamond) ν 2981, 2932, 1750, 1727, 1667, 1613, 1567, 1546, 1506, 1474, 1449, 1381, 1366, 1316, 1292, 1275, 1250, 1227, 1154, 1134, 981, 910, 836 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.48 (s, 1H, H_{Ar}), 8.33 (m, 1H, H_{Ar}), 8.22-8.13 (m, 1H, H_{Ar}), 7.62 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 7.43 (m, 5H, 5 $\times\text{H}_{\text{Ar}}$), 1.68 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 187.6 (C=O), 149.2 (C_q), 136.5 (C_q), 132.2 (CH_{Ar}), 130.7 (C_q), 130.2 (CH_{Ar}), 129.1 (CH_{Ar}), 127.3 (CH_{Ar}), 125.6 (CH_{Ar}), 125.5, (CH_{Ar}) 124.8 (C_q), 122.3 (CH_{Ar}), 122.2 (CH_{Ar}), 115.8 (CH_{Ar}), 102.6 (C_q), 86.4 (C_q), 79.4 (C_q), 28.6 (3 $\times\text{CH}_3$); HRMS (EI-MS): MH^+ , found 346.1437 $\text{C}_{22}\text{H}_{20}\text{NO}_3$ requires 346.1438.

4.2. *tert*-Butyl 3-formyl-2-[2-(*p*-tolyl)ethynyl]indole-1-carboxylate (**2b**)

Compound **2b** was obtained as described for **2a** using **1a** and 4-methylphenylacetylene. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a yellow solid (0.644 g, 95%). *R_f* (9:1PE/EtOAc) 0.24; mp: 145-147 °C; IR (ATR diamond) ν 2976, 2209, 1749, 1661, 1412, 1381, 1346, 1289, 1231, 1114, 812, 741 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.44 (s, 1H, CHO), 8.33 (d, J = 7.4 Hz, 1H, H_{Ar}), 8.17 (d, J = 8.2 Hz, 1H, H_{Ar}), 7.51 (d, J = 8.0 Hz, 2H, 2 $\times\text{H}_{\text{Ar}}$), 7.45-7.35 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 7.22 (d, J = 7.9 Hz, 2H, 2 $\times\text{H}_{\text{Ar}}$), 2.41 (s, 3H, CH_3), 1.73 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 187.3 (CHO), 148.9 (C_q), 140.4 (C_q), 136.0 (C_q), 131.8 (2 $\times\text{CH}_{\text{Ar}}$), 130.7 (C_q), 129.5 (2 $\times\text{CH}_{\text{Ar}}$), 126.9 (CH_{Ar}), 125.3 (C_q), 125.1 (CH_{Ar}), 124.2 (C_q), 121.9 (CH_{Ar}), 118.8 (C_q), 115.4 (CH_{Ar}), 102.7 (C_q), 86.0 (C_q), 78.6 (C_q), 28.3 (3 $\times\text{CH}_3$), 21.8 (CH_3); HRMS (EI-MS): MH^+ , found 360.1594 $\text{C}_{23}\text{H}_{22}\text{NO}_3$ requires 360.1594.

4.3. *tert*-Butyl 3-formyl-2-[2-(*m*-tolyl)ethynyl]indole-1-carboxylate (**2c**)

Compound **2c** was obtained as described for **2a** using **1a** and 2-methylphenylacetylene. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a pale brown solid (0.212 g, 96%). *R_f* (95:5 PE/EtOAc) 0.32; mp: 93-95 °C; IR (ATR diamond) ν 2981, 2929, 2196, 1747, 1666, 1479, 1449, 1379, 1368, 1343, 1315, 1279, 1249, 1225, 1160, 1133, 1115, 1032, 873, 784, 745 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.47 (s, 1H, CHO), 8.35 (d, J = 7.4 Hz, 1H, H_{Ar}), 8.19 (d, J = 8.3 Hz, 1H, H_{Ar}), 7.48-7.38 (m, 4H, 4 $\times\text{H}_{\text{Ar}}$), 7.35-7.27 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 2.42 (s, 3H, CH_3), 1.75 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 187.4 (CHO), 148.9 (C_q), 138.6 (C_q), 136.1 (C_q), 132.4 (CH_{Ar}), 130.8 (CH_{Ar}), 130.5 (C_q), 129.0 (CH_{Ar}), 128.7 (CH_{Ar}), 127.0 (CH_{Ar}), 125.3 (C_q), 125.1 (CH_{Ar}), 124.4 (C_q), 122.0 (CH_{Ar}), 121.7 (C_q), 115.4 (CH_{Ar}), 102.6 (C_q), 86.05 (C_q), 78.7 (C_q), 28.3 (CH_3), 21.4 (3 $\times\text{CH}_3$); HRMS (EI-MS): MH^+ , found 360.1593. $\text{C}_{23}\text{H}_{22}\text{NO}_3$ requires 360.1594.

4.4. *tert*-Butyl 3-formyl-2-[2-(*o*-tolyl)ethynyl]indole-1-carboxylate (**2d**)

Compound **2d** was obtained as described for **2a** using **1a** and 2-methylphenyl acetylene. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a pale brown solid (0.201 g, 91%). *R_f* (95:5 PE/EtOAc) 0.38; mp: 111-113 °C; IR (ATR diamond) ν 2979, 2927, 2201, 1665, 1368, 1345, 1294, 1230, 1136, 1120, 745 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.47 (s, 1H, CHO), 8.35 (d, J = 7.3 Hz, 1H, H_{Ar}), 8.11 (d, J = 8.2 Hz, 1H, H_{Ar}), 7.58 (d, J = 7.5

Hz, 1H, H_{Ar}), 7.45-7.27 (m, 4H, 4 $\times\text{H}_{\text{Ar}}$), 7.23 (t, J = 7.4 Hz, 1H, H_{Ar}), 2.58 (s, 3H, CH_3), 1.72 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 187.1 (CHO), 148.7 (C_q), 141.0 (C_q), 135.8 (C_q), 132.2 (CH_{Ar}), 130.6 (C_q), 129.8 (CH_{Ar}), 129.7 (CH_{Ar}), 126.7 (CH_{Ar}), 125.8 (CH_{Ar}), 125.2 (C_q), 125.0 (CH_{Ar}), 124.0 (C_q), 121.9 (CH_{Ar}), 121.6 (C_q), 115.2 (CH_{Ar}), 101.4 (C_q), 85.9 (C_q), 82.3 (C_q), 28.2 (3 $\times\text{CH}_3$), 20.9 (CH_3); HRMS (EI-MS): MH^+ , found 360.1594. $\text{C}_{23}\text{H}_{22}\text{NO}_3$ requires 360.1594.

4.5. *tert*-Butyl 3-formyl-2-((4-methoxyphenyl)ethynyl)-1H-indole-1-carboxylate (**2e**)

Compound **2e** was obtained as described for **2a** using **1a** and 4-ethynylanisole. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5) to obtain the pure product as a yellow solid (0.179 g, 78%). *R_f* (9:1 PE/EtOAc) 0.2; mp: 146-148 °C; IR (ATR diamond) ν 2981, 2932, 1747, 1726, 1662, 1603, 1567, 1567, 1546, 1506, 1474, 1449, 1381, 1366, 1316, 1292, 1275, 1250, 1227, 1154, 1134, 1026, 981, 910, 836 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.52 (s, 1H, CHO), 8.47-8.25 (m, 1H, H_{Ar}), 8.23-8.06 (m, 1H, H_{Ar}), 7.45-7.28 (m, 3H, 3 $\times\text{H}_{\text{Ar}}$), 6.58 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 3.93 (s, 3H, OCH_3), 1.73 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 189.4 (CHO), 162.4 (C=O), 149.5 (C_q), 136.35 (C_q), 131.9 (2 $\times\text{CH}_{\text{Ar}}$), 131.8 (C_q), 126.9 (2 $\times\text{CH}_{\text{Ar}}$), 125.8 (C_q), 125.3 (CH_{Ar}), 124.5 (CH_{Ar}), 122.2 (CH_{Ar}), 115.6 (CH_{Ar}), 103.9 (C_q), 101.0 (C_q), 97.0 (C_q), 87.5 (C_q), 86.3 (C_q), 56.5 (OCH_3), 28.5 (3 $\times\text{CH}_3$); HRMS (EI-MS): MH^+ , found 376.1476. $\text{C}_{23}\text{H}_{22}\text{NO}_4$ requires 376.1471.

4.6. *tert*-Butyl 2-((4-(dimethylamino)phenyl)ethynyl)-3-formyl-1H-indole-1-carboxylate (**2f**)

Compound **2f** was obtained as described for **2a** using **1a** and 4-ethynyl-*N,N'*-dimethylaniline. The crude product was purified by silica gel chromatography using PE/EtOAc (85:15) to obtain the pure product as a yellow solid (0.213 g, 90%). *R_f* (9:1 PE/EtOAc) 0.28; mp: 111-113 °C; IR (ATR diamond) ν 3278, 2970, 1740, 1490, 1464, 1374, 1369, 1330, 1320, 1275, 1258, 1245, 1200, 1155, 1136, 1117, 1057, 998, 938, 912, 866 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 10.43 (s, 1H, CHO), 8.34-8.27 (m, 1H, H_{Ar}), 8.18-8.11 (m, 1H, H_{Ar}), 7.51-7.44 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 6.74-6.62 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 3.04 (s, 6H, 2 $\times\text{CH}_3$), 1.73 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 187.5 (CHO), 148.9 (C_q), 143.8 (C_q), 136.5 (CH_{Ar}), 134.5 (2 $\times\text{CH}_{\text{Ar}}$), 126.7 (C_q), 126.2 (2 $\times\text{CH}_{\text{Ar}}$), 124.5 (C_q), 123.0 (CH_{Ar}), 122.5 (C_q), 115.3 (CH_{Ar}), 112.7 (CH_{Ar}), 108.0 (C_q), 103.1 (C_q), 100.2 (C_q), 84.9 (C_q), 79.3 (C_q), 20.5 (2 $\times\text{CH}_3$), 28.9 (3 $\times\text{CH}_3$); HRMS (EI-MS): MH^+ , found 389.1785. $\text{C}_{24}\text{H}_{25}\text{N}_2\text{O}_3$ requires 389.1787.

4.7. *tert*-Butyl 2-[2-(4-aminophenyl)ethynyl]-3-formyl-indole-1-carboxylate (**2g**)

Compound **2g** was obtained as described for **2a** using **1a** and 4-ethynylphenylaniline. The crude product was purified by silica gel chromatography using PE/EtOAc (6:4) to obtain the pure product as a yellow solid after an additional precipitation with *n*-pentane (0.175 g, 93%). *R_f* (6:4 PE/EtOAc) 0.41; mp: 191–193 °C; IR (ATR diamond) ν 3452, 3353, 3232, 2182, 1742, 1651, 1603, 1534, 1503, 1384, 1311, 1220, 1156, 1136, 753 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.44 (s, 1H, CHO), 8.34 (d, *J* = 7.2 Hz, 1H, H_{Ar}), 8.17 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.42 (dd, *J* = 17.9, 8.7 Hz, 4H, 4xH_{Ar}), 6.70 (d, *J* = 8.5 Hz, 2H, 2xH_{Ar}), 4.01 (s, 2H, NH₂), 1.75 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, CDCl₃) δ 187.5 (HCO), 149.0 (C_q), 148.2 (C_q), 136.0 (C_q), 133.6 (2xCH_{Ar}), 131.6 (C_q), 126.6 (CH_{Ar}), 125.5 (C_q), 125.0 (CH_{Ar}), 123.6 (C_q), 121.8 (CH_{Ar}), 115.4 (CH_{Ar}), 114.9 (2xCH_{Ar}), 110.8 (C_q), 104.1 (C_q), 85.9 (C_q), 28.4 (3xCH₃); HRMS (EI-MS): MH⁺, found 361.1548. C₂₂H₂₁N₂O₃ requires 361.1547.

4.8. tert-Butyl 3-formyl-2-[2-(4-nitrophenyl)ethynyl]indole-1-carboxylate (2h)

Compound **2h** was obtained as described for **2a** using **1a** and 1-ethynyl-4-nitrobenzene. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a yellow solid (0.137 g, 82%). *R_f* (9:1 PE/EtOAc) 0.39; mp: 171–173 °C; IR (ATR diamond) ν 2979, 1748, 1667, 1591, 1518, 1338, 1231, 1135, 1104, 852, 746 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.44 (s, 1H, CHO), 8.34 (d, *J* = 7.2 Hz, 1H, H_{Ar}), 8.17 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.42 (dd, *J* = 17.9, 8.7 Hz, 4H, 4xH_{Ar}), 6.70 (d, *J* = 8.5 Hz, 2H, 2xH_{Ar}), 4.01 (s, 2H, NH₂), 1.75 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, CDCl₃) δ 186.7 (CHO), 148.7 (C_q), 148.0 (C_q), 136.2 (C_q), 132.7 (2xCH_{Ar}), 128.7 (C_q), 128.6 (C_q), 127.6 (CH_{Ar}), 125.4 (CH_{Ar}), 125.3 (C_q), 125.2 (C_q), 124.0 (2xCH_{Ar}), 122.3 (CH_{Ar}), 115.6 (CH_{Ar}), 99.4 (C_q), 86.4 (C_q), 83.7 (C_q), 28.3 (3xCH₃). HRMS (EI-MS): MH⁺, found 391.1282. C₂₂H₁₉N₂O₅ requires 391.1285.

4.9. tert-Butyl 2-[2-(4-chlorophenyl)ethynyl]-3-formyl-indole-1-carboxylate (2i)

Compound **2i** was obtained as described for **2a** using **1a** and 4-chloro-1-ethynylbenzene. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a yellow solid (0.206 g, 89%). *R_f* (9:1 PE/EtOAc) 0.58; mp: 151–153 °C; IR (ATR diamond) ν 2977, 2823, 2212, 1751, 1666, 1482, 1410, 1345, 1288, 1231, 1135, 1115, 829, 741 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.42 (s, 1H, CHO), 8.38–8.29 (m, 1H, H_{Ar}), 8.20–8.10 (m, 1H, H_{Ar}), 7.59–7.51 (m, 2H, 2xH_{Ar}), 7.48–7.37 (m, 4H, 4xH_{Ar}), 1.72 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, CDCl₃) δ 187.1 (CHO), 148.8 (C_q), 136.1 (C_q), 133.8 (C_q), 133.1 (2xCH_{Ar}), 129.9 (C_q), 129.2 (2xCH_{Ar}), 129.0 (C_q), 127.1 (CH_{Ar}), 125.2 (CH_{Ar}), 124.6 (C_q), 122.0 (CH_{Ar}), 120.4 (C_q), 115.5 (CH_{Ar}), 100.9 (C_q), 86.1 (C_q), 80.0 (C_q), 28.3 (3xCH₃); HRMS (EI-MS): MH⁺, found 380.1046. C₂₂H₁₉ClNO₃ requires 380.1048.

4.10. tert-Butyl-3-formyl-2-[2-[4-(trifluoromethyl)phenyl]ethynyl]-1Hindole-1-carboxylate (2j)

Compound **2j** was obtained as described for **2a** using **1a** and 4-(trifluoromethyl)phenylacetylene. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a yellow solid (0.210 g, 90%). *R_f* (9:1 PE/EtOAc) 0.20; mp: 120–122 °C; IR (ATR diamond) ν 2979, 2937, 2847, 2825, 2793, 1749, 1608, 1532, 1504, 1482, 1395, 1367, 1233, 1166, 1149, 1120, 1065, 1045, 1012, 990, 884, 804 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.47 (s, 1H, CHO), 8.40–8.33 (m, 1H, H_{Ar}), 8.18–8.09 (m, 1H, H_{Ar}), 7.73 (s, 4H, 4xH_{Ar}), 7.53–7.37 (m, 2H, 2xH_{Ar}), 1.75 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, CDCl₃) δ 186.8 (CHO), 148.7 (C_q), 136.1 (C_q), 132.0 (2xCH_{Ar}), 132.0 (2xCH_{Ar}), 131.1 (C_q), 129.2 (CH_{Ar}), 127.2 (C_q), 125.7 (CH_{Ar}), 125.6 (q, *J* = 4Hz, C_q-F), 124.8 (C_q), 122.3 (CH_{Ar}), 122.0

(C_q), 115.4 (CH_{Ar}), 100.1 (C_q), 86.2 (C_q), 81.0 (C_q), 28.2 (3xCH₃); HRMS (EI-MS): MH⁺, found 414.1311. C₂₃H₁₈F₃NO₃ requires 414.1311.

4.11. tert-Butyl 2-[2-(4-cyanophenyl)ethynyl]-3-formyl-indole-1-carboxylate (2k)

Compound **2k** was obtained as described for **2a** using **1a** and 4-ethynylbenzonitrile. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a yellow solid (0.208 g, 92%). *R_f* (9:1 PE/EtOAc) 0.22; mp: 173–175 °C; IR (ATR diamond) ν 2991, 2226, 1741, 1668, 1602, 1480, 1448, 1381, 1348, 1316, 1229, 1153, 1136, 1115, 836, 742 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.43 (s, 1H, CHO), 8.38–8.28 (m, 1H, H_{Ar}), 8.18–8.09 (m, 1H, H_{Ar}), 7.71 (s, 4H, 4xH_{Ar}), 7.49–7.36 (m, 2H, 2xH_{Ar}), 1.73 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, CDCl₃) δ 186.7 (CHO), 148.7 (C_q), 136.2 (C_q), 132.5 (2xCH_{Ar}), 132.3 (2xCH_{Ar}), 128.8 (C_q), 127.5 (CH_{Ar}), 126.7 (C_q), 125.4 (CH_{Ar}), 125.2 (C_q), 125.1 (C_q), 122.2 (CH_{Ar}), 118.3 (C_q), 115.6 (CH_{Ar}), 113.1 (C_q), 99.7 (C_q), 86.4 (C_q), 83.0 (C_q), 28.3 (3xCH₃); HRMS (EI-MS): MH⁺, found 371.1387. C₂₃H₁₉N₂O₃ requires 371.1390.

4.12. tert-Butyl 3-formyl-2-[2-(2-thienyl)ethynyl]indole-1-carboxylate (2l)

Compound **2l** was obtained as described for **2a** using **1a** and 2-ethynylthiophene. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a yellow solid (0.193 g, 90%). *R_f* (9:1 PE/EtOAc) 0.46; mp: 107–109 °C; IR (ATR diamond) ν 2926, 2189, 1748, 1655, 1479, 1381, 1359, 1313, 1224, 1132, 1045, 742 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.38 (s, 1H, CHO), 8.35–8.27 (m, 1H, H_{Ar}), 8.21–8.14 (m, 1H, H_{Ar}), 7.45–7.32 (m, 4H, 4xH_{Ar}), 7.10–7.04 (m, 1H, H_{Ar}), 1.71 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, CDCl₃) δ 187.2 (CHO), 148.9 (C_q), 136.2 (C_q), 133.9 (CH_{Ar}), 129.8 (C_q), 129.6 (CH_{Ar}), 127.7 (CH_{Ar}), 127.1 (CH_{Ar}), 125.3 (C_q), 125.3 (CH_{Ar}), 124.4 (C_q), 122.0 (CH_{Ar}), 121.7 (C_q), 115.5 (CH_{Ar}), 95.6 (C_q), 86.2 (C_q), 83.0 (C_q), 28.3 (3xCH₃); HRMS (EI-MS): MH⁺, found 352.1003. C₂₀H₁₈NO₃S requires 352.1002.

4.13. tert-Butyl 3-formyl-2-hex-1-ynyl-indole-1-carboxylate (2m)

Compound **2m** was obtained as described for **2a** using **1a** and *n*-hex-1-yne. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5) to obtain the pure product as a yellow solid (0.198 g, 99%). *R_f* (9:1 PE/EtOAc) 0.67; mp: 107–109 °C; IR (ATR diamond) ν 3435, 2931, 1741, 1656, 1530, 1453, 1369, 1313, 1227, 1139, 1059, 839, 748 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.28 (s, 1H, H_{Ar}), 8.31–8.23 (m, 1H, H_{Ar}), 8.13–8.06 (m, 1H, H_{Ar}), 7.41–7.28 (m, 2H, 2xH_{Ar}), 2.56 (t, *J* = 7.0 Hz, 2H, -CH₂CH₂CH₂CH₃), 1.68 (s, 9H, 3xCH₃), 1.66–1.41 (m, 4H CH₂CH₂CH₂CH₃), 0.95 (t, *J* = 7.2 Hz, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 187.6 (C_q), 148.9 (C_q), 135.7 (C_q), 131.5 (C_q), 126.6 (CH_{Ar}), 125.2 (C_q), 125.0 (CH_{Ar}), 124.2 (C_q), 121.7 (CH_{Ar}), 115.3 (CH_{Ar}), 105.0 (C_q), 85.6 (C_q), 70.5 (C_q), 30.4 (CH₂), 28.2 (3xCH₃), 22.3 (CH₂), 20.0 (CH₂), 13.7 (CH₃); HRMS (EI-MS): MH⁺, found 326.1752. C₂₀H₂₄NO₃ requires 326.1751.

4.14. tert-Butyl 3-formyl-2-(3-methylbut-1-ynyl)indole-1-carboxylate (2n)

Compound **2n** was obtained as described for **2a** using **1a** and 3-methyl-1-butyne. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1) to obtain the pure product as a yellow solid (0.189 g, 99%). *R_f* (9:1 PE/EtOAc) 0.67; mp: 107–109 °C; IR (ATR diamond) ν 2973, 2221, 1742, 1668, 1527, 1451, 1360, 1336, 1313, 1226, 1139, 1098, 1043, 836, 751 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.30 (s, 1H, CHO), 8.28 (d, *J* =

8.3 Hz, 1H, H_{Ar}), 8.11 (d, *J* = 8.0 Hz, 1H, H_{Ar}), 7.42-7.32 (m, 2H, H_{Ar}), 2.99-2.89 (m, 1H, CH), 1.72 (s, 9H, 3xCH₃), 1.35 (d, *J* = 6.9 Hz, 6H, 2xCH₃). ; ¹³C NMR (101 MHz, CDCl₃) δ 187.7 (CHO), 148.9 (C_q), 135.7 (C_q), 131.4 (C_q), 126.6 (CH_{Ar}), 125.2 (C_q), 125.0 (CH_{Ar}), 124.1 (C_q), 121.7 (CH_{Ar}), 115.3 (CH_{Ar}), 109.9 (C_q), 85.8 (C_q), 69.9 (C_q), 28.3 (3xCH₃), 22.5 (2xCH₃), 22.0 (CH); HRMS (EI-MS): MH⁺, found 312.1594. C₁₉H₂₂NO₃ requires 312.1594.

4.15. 2-((4-Nitrophenyl)ethynyl)-1H-indole-3-carbaldehyde (**2o**)

Compound **2o** was obtained as described for **2a** using **1b** and 1-ethynyl-4-nitrobenzene. The crude product was purified by silica gel chromatography using PE/EtOAc (1:1) to obtain the pure product as a yellow solid (0.568 g, 78%). R_f (1:1 PE/EtOAc) 0.34; mp: 221-223 °C; IR (ATR diamond) ν 3082, 1598, 1525, 1493, 1427, 1394, 1368, 1225, 1109, 1000, 928, 894, 802 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.90 (s, 1H, NH), 10.93 (s, 1H, CHO), 8.44-8.53 (m, 3H, H_{Ar}), 7.99-7.85 (m, 2H, 2xH_{Ar}), 7.57-7.43 (m, 3H, H_{Ar}); ¹³C NMR (101 MHz, CDCl₃) δ 184.8 (CHO), 148.7 (C_q), 137.1 (C_q), 132.3 (2xCH_{Ar}), 132.2 (C_q), 128.7 (C_q), 126.2 (CH_{Ar}), 124.2 (C_q), 121.5 (2xCH_{Ar}), 121.1 (CH_{Ar}), 122.5 (CH_{Ar}), 121.4 (C_q), 109.8 (CH_{Ar}), 100.8 (C_q), 85.6 (C_q); HRMS (EI-MS): MH⁺, found 291.0688. C₁₇H₁₁N₂O₃ requires 291.0691.

4.16. 1-Methyl-2-[2-(4-nitrophenyl)ethynyl]indole-3-carbaldehyde (**2p**)

Compound **2p** was obtained as described for **2a** using **1c** and 1-ethynyl-4-nitrobenzene. The crude product was purified by silica gel chromatography using PE/CH₂Cl₂ (6:4) to obtain the pure product as a yellow solid (0.555 g, 99%). R_f (8:2 PE/EtOAc) 0.30; mp: 151-153 °C; IR (ATR diamond) ν 1650, 1592, 1510, 1465, 1381, 1338, 1105, 1042, 854, 744 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 10.30 (s, 1H, CHO), 8.39-8.23 (m, 3H, H_{Ar}), 7.78 (d, *J* = 8.7 Hz, 2H, H_{Ar}), 7.46-7.32 (m, 3H, H_{Ar}), 3.96 (s, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 184.9 (CHO), 148.0 (C_q), 138.0 (C_q), 132.7 (2xCH_{Ar}), 130.1 (C_q), 128.1 (C_q), 125.8 (CH_{Ar}), 124.6 (C_q), 124.2 (2xCH_{Ar}), 124.0 (CH_{Ar}), 122.5 (CH_{Ar}), 121.0 (C_q), 110.0 (CH_{Ar}), 98.7 (C_q), 82.4 (C_q), 31.5 (CH₃); HRMS (EI-MS): MH⁺, found 305.0918. C₁₈H₁₃N₂O₃ requires 305.0921.

4.17. *tert*-Butyl 3-[(*E*)-hydroxyiminomethyl]-2-[2-(*p*-tolyl)ethynyl]indole-1-carboxylate (**3a**)

The compound **3a** (0.196 g, 0.56 mmol) was dissolved in CH₂Cl₂ (5 mL) than Et₃N (0.15 mL, 1.08 mmol, 2.0 equiv.) and H₂NOH-HCl (0.041 g, 0.59 mmol, 1.1 equiv.) were added. The reaction mixture was refluxed for 24 h. The solvent was evaporated and the crude product was purified by silica gel chromatography using PE/EtOAc (9:1). The pure product was obtained as a yellow solid (0.151 g, 74%). R_f (9:1 PE/EtOAc) 0.45; mp: 171-173 °C; IR (ATR diamond) ν 3288, 2992, 2195, 1735, 1449, 1342, 1320, 1227, 1152, 1136, 1114, 976, 942, 808, 767, 746 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.61 (s, 1H, -CH), 8.21 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 8.16 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.64 (s, 1H, OH), 7.49 (d, *J* = 8.0 Hz, 2H, 2xH_{Ar}), 7.41 (t, *J* = 8.3 Hz, 1H, H_{Ar}), 7.32 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 7.20 (d, *J* = 7.9 Hz, 2H, 2xH_{Ar}), 2.40 (s, 3H, CH₃), 1.70 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 149.3 (C_q), 146.2 (CH), 139.5 (C_q), 136.4 (C_q), 131.6 (2xCH_{Ar}), 129.4 (2xCH_{Ar}), 126.5 (CH_{Ar}), 125.7 (C_q), 124.1 (CH_{Ar}), 122.9 (C_q), 122.5 (CH_{Ar}), 120.0 (C_q), 119.5 (C_q), 115.5 (CH_{Ar}), 101.2 (C_q), 85.0 (C_q), 79.4 (C_q), 28.4 (3xCH₃), 21.8 (CH₃); HRMS (EI-MS): MH⁺, found 375.1703. C₂₃H₂₃N₂O₃ requires 375.1703.

4.18. *tert*-Butyl 3-[(*E*)-hydroxyiminomethyl]-2-[2-(*p*-tolyl)ethynyl]indole-1-carboxylate (**3b**)

The compound **3b** was obtained as described for **3a** using **2b** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1). The pure product was obtained as a yellow solid (0.137 g, 66%). R_f (9:1 PE/EtOAc) 0.45; mp: 171-173 °C; IR (ATR diamond) ν 3288, 2992, 2195, 1735, 1449, 1342, 1320, 1227, 1152, 1136, 1114, 976, 942, 808, 767, 746 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.61 (s, 1H, CH), 8.21 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 8.16 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.64 (s, 1H, =N-OH), 7.49 (d, *J* = 8.0 Hz, 2H, 2xH_{Ar}), 7.41 (t, *J* = 8.3 Hz, 1H, H_{Ar}), 7.32 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 7.20 (d, *J* = 7.9 Hz, 2H, 2xH_{Ar}), 2.40 (s, 3H, CH₃), 1.70 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 149.3 (C_q), 146.2 (CH), 139.5 (C_q), 136.4 (C_q), 131.6 (CH_{Ar} x2), 129.4 (CH_{Ar} x2), 126.5 (CH_{Ar}), 125.7 (C_q), 124.1 (CH_{Ar}), 122.9 (C_q), 122.5 (CH_{Ar}), 120.0 (C_q), 119.5 (C_q), 115.5 (CH_{Ar}), 101.2 (C_q), 85.0 (C_q), 79.4 (C_q), 28.4 (3xCH₃), 21.8 (CH₃); HRMS (EI-MS): MH⁺, found 375.1702. C₂₃H₂₃N₂O₃ requires 375.1703.

4.19. *tert*-Butyl 3-[(*E*)-hydroxyiminomethyl]-2-[2-(*m*-tolyl)ethynyl]indole-1-carboxylate (**3c**)

The compound **3c** was obtained as described for **3a** using **2c** as starting material. The crude product was purified by silica gel chromatography PE/EtOAc (9:1). The pure product was obtained as a yellow solid (0.130 g, 54%). R_f (8:2 PE/EtOAc) 0.5; mp: 171-173 °C; IR (ATR diamond) ν 3275, 2917, 2194, 1731, 1450, 1344, 1225, 1154, 1134, 1116, 949, 766, 73 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.61 (s, 1H, CH), 8.22-8.14 (m, 2H, 2xH_{Ar}), 7.46 (s, 1H, OH), 7.43-7.38 (m, 3H, 3xH_{Ar}), 7.35-7.28 (m, 2H, 2xH_{Ar}), 7.21 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 2.39 (s, 3H, CH₃), 1.70 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 149.3 (C_q), 146.2 (-CH=NOH), 138.4 (C_q), 136.4 (C_q), 132.2 (CH_{Ar}), 130.1 (CH_{Ar}), 128.8 (CH_{Ar}), 128.5 (CH_{Ar}), 126.6 (CH_{Ar}), 125.7 (C_q), 124.1 (CH_{Ar}), 122.7 (C_q), 122.6 (CH_{Ar}), 122.4 (C_q), 120.2 (C_q), 115.5 (CH_{Ar}), 101.1 (C_q), 85.0 (C_q), 79.7 (C_q), 28.4 (3xCH₃), 21.4 (CH₃); HRMS (EI-MS): MH⁺, found 375.1701. C₂₃H₂₃N₂O₃ requires 375.1703.

4.20. *tert*-Butyl 3-[(*E*)-hydroxyiminomethyl]-2-[2-(*o*-tolyl)ethynyl]indole-1-carboxylate (**3d**)

The compound **3d** was obtained as described for **3a** using **2d** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1). The pure product was obtained as a yellow solid (0.116 g, 55%). R_f (8:2 PE/EtOAc) 0.42; mp: 119-121 °C; IR (ATR diamond) ν 3270, 2970, 1732, 1451, 1321, 1232, 1138, 1120, 1106, 941, 738 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.63 (s, 1H, CH), 8.20-8.14 (m, 2H, 2xH_{Ar}), 7.56 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 7.46 (s, 1H, OH), 7.43-7.38 (m, 1H, H_{Ar}), 7.35-7.27 (m, 3H, 3xH_{Ar}), 7.21 (t, *J* = 8.1 Hz, 1H, H_{Ar}), 2.58 (s, 3H, CH₃), 1.69 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 160.3 (C=O), 146.1 (CH), 140.8 (C_q), 136.3 (C_q), 132.1 (CH_{Ar}), 129.8 (CH_{Ar}), 129.2 (CH_{Ar}), 126.5 (CH_{Ar}), 125.8 (CH_{Ar}), 124.8 (C_q), 124.1 (CH_{Ar}), 123.0 (C_q), 122.6 (CH_{Ar}), 122.4 (C_q), 119.9 (C_q), 115.5 (CH_{Ar}), 100.1 (C_q), 85.0 (C_q), 83.5 (C_q), 28.4 (3xCH₃), 21.1 (CH₃); HRMS (EI-MS): MH⁺, found 375.1705. C₂₃H₂₃N₂O₃ requires 375.1703.

4.21. *tert*-Butyl 3-[(*E*)-hydroxyiminomethyl]-2-[2-(4-methoxyphenyl)ethynyl]indole-1-carboxylate (**3e**)

The compound **3d** was obtained as described for **3a** using **2e** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (8:2). The pure product was obtained as a yellow solid (0.120 g, 69%). R_f (8:2 PE/EtOAc)

0.31; mp: 174-176 °C; IR (ATR diamond) ν 3278, 2970, 1740, 1490, 1464, 1369, 1338, 1330, 1295, 1268, 1245, 1200, 1155, 1136, 1127, 1067, 998, 912, 866 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 11.43 (s, 1H, CH), 8.60 (s, 1H, OH), 8.29-7.99 (m, 2H, 2xH_{Ar}), 7.53 (d, J = 8.8 Hz, 2H, H_{Ar}) 7.46-7.27 (m, 3H, 3xH_{Ar}), 6.96-6.86 (d, J = 8.8 Hz, 2H, 2xH_{Ar}), 3.58 (s, 3H, OCH₃), 1.69 (s, 9H, 3xCH₃); ^{13}C NMR (101 MHz, DMSO- d_6) δ 160.3 (C=O), 146.1 (CH), 140.8 (C_q), 136.3 (C_q), 132.1 (CH_{Ar}), 129.8 (CH_{Ar}), 129.2 (CH_{Ar}), 126.5 (CH_{Ar}), 125.8 (CH_{Ar}), 124.8 (C_q), 124.1 (CH_{Ar}), 123.0 (C_q), 122.6 (CH_{Ar}), 122.4 (C_q), 119.9 (C_q), 115.5 (CH_{Ar}), 100.1 (C_q), 85.0 (C_q), 83.5 (C_q), 28.4 (3xCH₃), 21.1 (CH₃); HRMS (EI-MS): MH⁺, found 391.1652. C₂₃H₂₃N₂O₄ requires 391.1655.

4.22. *tert*-Butyl 2-[2-[4-(dimethylamino)phenyl]ethynyl]-3-[(1*E*)-(hydroxyimino)methyl]-1*H*-indole-1-carboxylate (**3f**)

The compound **3f** was obtained as described for **3a** using **2f** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (8:2). The pure product was obtained as a yellow solid (0.141 g, 75%). R_f (8:2 PE/EtOAc) 0.28; mp: 116-118 °C; IR (ATR diamond) ν 3278, 2970, 1740, 1490, 1464, 1374, 1369, 1330, 1320, 1275, 1258, 1245, 1200, 1155, 1136, 1117, 1057, 998, 938, 912, 866 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 11.39 (s, 1H, -CH=NOH), 8.39 (s, 1H, OH), 8.19-8.00 (m, 2H, 2xH_{Ar}), 7.52-7.25 (m, 4H, 4xH_{Ar}), 6.86-6.67 (m, 2H, 2xH_{Ar}), 2.99 (s, 6H, 2xCH₃), 1.66 (s, 9H, 3xCH₃).; ^{13}C NMR (101 MHz, DMSO- d_6) δ 151.1 (CH), 149.1 (C_q), 143.6 (C_q), 136.0 (CH_{Ar}), 133.9 (2xCH_{Ar}), 126.7 (C_q), 125.7 (CH_{Ar}), 124.4 (C_q), 122.4 (CH_{Ar}), 122.1 (C_q) 119.6 (C_q), 115.5 (CH_{Ar}), 112.4 (2xCH_{Ar}), 107.8 (C_q), 103.0 (C_q), 100.0 (C_q), 85.3 (C_q), 78.3 (C_q), 20.1 (2xCH₃), 28.2 (3xCH₃); HRMS (EI-MS): MH⁺, found 404.1968. C₂₄H₂₆N₃O₃ requires 404.1967.

4.23. *tert*-Butyl 2-[2-(4-aminophenyl)ethynyl]-3-[(1*E*)-hydroxyiminomethyl]indole-1-carboxylate (**3g**)

The compound **3g** was obtained as described for **3a** using **2g** as starting material. The crude product was purified by silica gel chromatography using CH₂Cl₂/MeOH (99:1). The pure product was obtained as a yellow solid (0.076 g, 67%). R_f (7:3 PE/EtOAc) 0.39; mp: 193-195 °C; IR (ATR diamond) ν 3431, 3353, 2973, 2185, 1724, 1454, 1340, 1323, 1240, 1174, 1149, 1135, 751. cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 11.43 (s, 1H, CH), 8.37 (s, 1H, OH), 8.16-8.06 (m, 2H, 2xH_{Ar}), 7.46-7.25 (m, 4H, 4xH_{Ar}), 6.61 (d, J = 8.5 Hz, 2H, 2xH_{Ar}), 5.73 (s, 2H, NH₂), 1.65 (s, 9H, 3xCH₃); ^{13}C NMR (101 MHz, DMSO- d_6) δ 150.3 (CH), 148.6 (C_q), 143.1 (C_q), 135.4 (CH_{Ar}), 132.6 (2xCH_{Ar}), 126.1 (C_q), 125.2 (CH_{Ar}), 123.9 (C_q), 121.8 (CH_{Ar}), 118.9 (CH_{Ar}), 115.0 (C_q), 113.7 (2xCH_{Ar}), 107.1 (C_q), 102.9 (C_q), 84.8 (CH_{Ar}), 77.1 (C_q), 27.7 (3xCH₃); HRMS (EI-MS): MH⁺, found 376.1654. C₂₂H₂₂N₃O₃ requires 376.1656.

4.24. *tert*-Butyl 3-[(1*E*)-hydroxyiminomethyl]-2-[2-(4-nitrophenyl)ethynyl]indole-1-carboxylate (**3h**)

The compound **3h** was obtained as described for **3a** using **2h** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (8:2). The pure product was obtained as a yellow solid (0.088 g, 62%). R_f (9:1 PE/EtOAc) 0.19; mp: 191-193 °C; IR (ATR diamond) ν 2189, 1741, 1593, 1515, 1337, 1136, 1117, 947, 763, 743 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 8.58 (s, 1H, CH), 8.27 (d, J = 8.8 Hz, 2H, 2xH_{Ar}), 8.19 (t, J = 8.9 Hz, 2H, 2xH_{Ar}), 7.74 (d, J = 8.8 Hz, 2H, 2xH_{Ar}), 7.50-7.42 (m, 2H, OH and H_{Ar}), 7.34 (t, J = 7.6 Hz, 1H, H_{Ar}), 1.71 (s, 9H, 3xCH₃); ^{13}C NMR (101 MHz, DMSO- d_6) δ 148.4 (C_q), 147.2 (CH), 142.7 (C_q), 135.9 (C_q), 132.4 (2xCH_{Ar}), 128.2 (C_q), 127.2 (CH_{Ar}), 124.9 (CH_{Ar}), 124.2 (CH_{Ar}), 124.1 (2xCH_{Ar}),

122.4 (C_q), 122.0 (CH_{Ar}), 119.2 (C_q), 115.3 (C_q), 98.4 (C_q), 85.4 (C_q), 84.5 (C_q), 27.7 (3xCH₃); HRMS (EI-MS): MH⁺, found 406.1399. C₂₂H₂₀N₃O₅ requires 406.1398.

4.25. *tert*-Butyl 2-[2-(4-chlorophenyl)ethynyl]-3-[(1*E*)-hydroxyiminomethyl]indole-1-carboxylate (**3i**)

The compound **3i** was obtained as described for **3a** using **2i** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1). The pure product was obtained as a yellow solid (0.120 g, 56%). R_f (9:1 PE/EtOAc) 0.22; mp: 163-165 °C; IR (ATR diamond) ν 3281, 2978, 1724, 1455, 1416, 1354, 1307, 1213, 1144, 1118, 744 cm^{-1} ; ^1H NMR (400 MHz, CDCl₃) δ 8.58 (s, 1H, CH), 8.25-8.13 (m, 2H, 2xH_{Ar}), 7.56-7.50 (m, 2H, 2xH_{Ar}), 7.45-7.28 (m, 4H, 4xH_{Ar}), 1.69 (s, 9H, 3xCH₃); ^{13}C NMR (101 MHz, CDCl₃) δ 149.3 (C_q), 146.0 (CH), 136.5 (C_q), 135.3 (C_q), 132.9 (2xCH_{Ar}), 129.0 (2xCH_{Ar}), 126.8 (CH_{Ar}), 125.7 (C_q), 124.2 (CH_{Ar}), 122.7 (CH_{Ar}), 122.2 (C_q), 121.1 (C_q), 120.6 (C_q), 115.6 (CH_{Ar}), 99.7 (C_q), 85.1 (C_q), 81.0 (C_q), 28.4 (3xCH₃); HRMS (EI-MS): MH⁺, found 395.1157. C₂₂H₂₀ClN₂O₃ requires 395.1157.

4.26. *tert*-Butyl 3-[(1*E*)-hydroxyiminomethyl]-2-[2-[4-(trifluoromethyl)phenyl]ethynyl]indole-1-carboxylate (**3j**)

The compound **3j** was obtained as described for **3a** using **2j** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1). The pure product was obtained as a yellow solid (0.153 g, 65%). R_f (9:1 PE/EtOAc) 0.24; mp: 153-155 °C; IR (ATR diamond) ν 3453, 2985, 1829, 1711, 1614, 1558, 1514, 1406, 1395, 1371, 1275, 1240, 1216, 1154, 1137, 1115, 1105, 1066, 1033, 1015, 979 cm^{-1} ; ^1H NMR (400 MHz, CDCl₃) δ 8.61 (s, 1H, CH), 8.21-8.13 (m, 2H, 2xH_{Ar}), 7.76-7.64 (m, 4H, 4xH_{Ar}), 7.59 (s, 1H, H_{Ar}), 7.46-7.36 (m, 2H, 2xH_{Ar}), 1.71 (s, 9H, 3xCH₃); ^{13}C NMR (101 MHz, CDCl₃) δ 149.1 (C_q), 145.6 (CH), 139.4 (C_q), 131.8 (2xCH_{Ar}), 130.8 (C_q), 130.5 (C_q), 126.8 (2xCH_{Ar}), 126.2 (CH_{Ar}), 125.9 (C_q), 125.6 (q, J = 4 Hz, C_q), 124.6 (C_q), 122.7 (CH_{Ar}), 121.6 (C_q), 120.9 (C_q), 115.5 (CH_{Ar}), 99.0 (C_q), 85.1 (C_q), 82.2 (C_q), 28.3 (3xCH₃); ^{19}F NMR (376 MHz, CDCl₃) δ -62.61 (CF₃); HRMS (EI-MS): MH⁺, found 391. 1652. C₂₃H₂₀F₃N₂O₃ requires 391.1649.

4.27. *tert*-Butyl 2-[2-(4-cyanophenyl)ethynyl]-3-[(1*E*)-hydroxyiminomethyl]indole-1-carboxylate (**3k**)

The compound **3k** was obtained as described for **3a** using **2k** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (5:1). The pure product was obtained as a yellow solid (0.119 g, 55%). R_f (7:3 PE/EtOAc) 0.27; mp: 203-205 °C; IR (ATR diamond) ν 3396, 2980, 2233, 1732, 1599, 1394, 1339, 1233, 1153, 1137, 1115, 977, 946, 831, 761, 750 cm^{-1} ; ^1H NMR (400 MHz, CDCl₃) δ 8.57 (s, 1H, CH), 8.28-8.12 (m, 2H, 2xH_{Ar}), 7.68 (s, 4H, 4xH_{Ar}), 7.59 (s, 1H, OH), 7.48-7.30 (m, 2H, 2xH_{Ar}), 1.70 (s, 9H, 3xCH₃); ^{13}C NMR (101 MHz, CDCl₃) δ 149.1 (C_q), 145.6 (CH), 136.6 (C_q), 132.4 (2xCH_{Ar}), 132.1 (2xCH_{Ar}), 127.5 (C_q), 127.2 (CH_{Ar}), 125.6 (C_q), 124.4 (CH_{Ar}), 122.9 (CH_{Ar}), 121.4 (C_q), 121.3 (C_q), 118.5 (C_q), 115.6 (CH_{Ar}), 112.4 (C_q), 98.8 (C_q), 85.4 (C_q), 84.3 (C_q), 28.4 (3xCH₃); HRMS (EI-MS): MH⁺, found 386.1499. C₂₃H₂₀N₃O₃ requires 386.1499.

4.28. *tert*-Butyl 3-[(1*E*)-hydroxyiminomethyl]-2-[2-(2-thienyl)ethynyl]indole-1-carboxylate (**3l**)

The compound **3l** was obtained as described for **3a** using **2l** as starting material. The crude product was purified by silica gel chromatography using CH₂Cl₂. The pure product was obtained as a yellow solid (0.146 g, 72%). R_f (9:1 PE/EtOAc) 0.29; mp: 181-

183 °C; IR (ATR diamond) ν 3446, 1457, 1360, 1323, 1237, 1135, 1109, 970, 936, 761, 700 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.59 (s, 1H, CH), 8.26 (d, J = 8.4 Hz, 1H, H_{Ar}), 8.19 (d, J = 7.9 Hz, 1H, H_{Ar}), 7.57 (s, 1H, OH), 7.47-7.38 (m, 3H, $3\times\text{H}_{\text{Ar}}$), 7.34 (t, J = 7.5 Hz, 1H, H_{Ar}), 7.11-7.06 (m, 1H, H_{Ar}), 1.73 (s, 9H, $3\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 149.3 (C_q), 146.0 (CH), 136.6 (C_q), 133.0 (CH_{Ar}), 128.6 (CH_{Ar}), 127.5 (CH_{Ar}), 126.8 (CH_{Ar}), 125.7 (C_q), 124.2 (CH_{Ar}), 122.7 (C_q), 122.5 (CH_{Ar}), 122.1 (C_q), 120.5 (C_q), 115.6 (CH_{Ar}), 94.0 (C_q), 85.2 (C_q), 83.7 (C_q), 28.4 ($3\times\text{CH}_3$); HRMS (EI-MS): MH^+ , found 367.1110. $\text{C}_{20}\text{H}_{19}\text{N}_2\text{O}_3\text{S}$ requires 367.1111.

4.29. *tert*-Butyl 2-hex-1-ynyl-3-[(*E*)-hydroxyiminomethyl]indole-1-carboxylate (**3m**)

The compound **3m** was obtained as described for **3a** using **2m** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (9:1). The pure product was obtained as a yellow solid (0.130 g, 63%). R_f (9:1 PE/EtOAc) 0.29; mp: 117-119 °C; IR (ATR diamond) ν 3483, 3423, 2952, 2216, 1711, 1454, 1352, 1321, 1144, 1068, 963, 828, 759, 739 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.51 (s, 1H, CH), 8.13 (dd, J = 17.2, 8.0 Hz, 2H, $2\times\text{H}_{\text{Ar}}$), 7.77 (s, 1H, OH), 7.40-7.27 (m, 2H, $2\times\text{H}_{\text{Ar}}$), 2.56 (t, J = 7.2 Hz, 2H, CH_2), 1.73-1.63 (m, 11H, CH_2 and $3\times\text{CH}_3$ [Boc]), 1.57-1.47 (m, 2H, CH_2), 0.98 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, CDCl_3) δ 149.4 (C_q), 146.4 (CH_{Ar}), 136.0 (C_q), 126.1 (CH_{Ar}), 125.6 (C_q), 124.0 (CH_{Ar}), 123.5 (C_q), 122.2 (CH_{Ar}), 119.4 (C_q), 115.4 (C_q), 103.1 (C_q), 84.7 (C_q), 71.3 (C_q), 30.7 (CH_2), 28.3 ($3\times\text{CH}_3$), 22.3 (CH_2), 20.0 (CH_2), 13.7 (CH_3); HRMS (EI-MS): MH^+ , found 341.1858. $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_3$ requires 341.1860.

4.30. *tert*-Butyl 3-[(*E*)-hydroxyiminomethyl]-2-(3-methylbut-1-ynyl)indole-1-carboxylate (**3n**)

The compound **3n** was obtained as described for **3a** using **2m** as starting material. The crude product was purified by silica gel using PE/EtOAc (9:1). The pure product was obtained as a colourless oil (0.115 g, 63%). R_f (9:1 PE/EtOAc) 0.27; mp: 117-119 °C; IR (ATR diamond) ν 2972, 1733, 1453, 1350, 1318, 1258, 1230, 1139, 1097, 959, 747 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.48 (s, 1H, CH), 8.40 (s, 1H, OH), 8.19-8.10 (m, 2H, H_{Ar}), 7.39-7.26 (m, 2H, H_{Ar}), 3.00-2.86 (m, 1H, CH), 1.70 (s, 2H, $3\times\text{CH}_3$), 1.34 (d, J = 6.9 Hz, 6H, $2\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 149.4 (C_q), 146.4 (CH), 136.1 (C_q), 126.1 (CH_{Ar}), 125.7 (C_q), 124.0 (CH_{Ar}), 123.4 (C_q), 122.3 (CH_{Ar}), 119.4 (C_q), 115.4 (CH_{Ar}), 108.1 (C_q), 84.8 (C_q), 70.7 (C_q), 28.4 ($3\times\text{CH}_3$), 22.8 ($2\times\text{CH}_3$), 22.0 (CH); HRMS (EI-MS): MH^+ , found 372.1701. $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_3$ requires 327.1703.

4.31. (*E*)-2-((4-Nitrophenyl)ethynyl)-1H-indole-3-carbaldehyde oxime (**3o**)

The compound **3o** was obtained as described for **3a** using **2o** as starting material. The crude product was purified by silica gel using PE/EtOAc (4:6). The pure product was obtained as a yellow solid (0.190 g, 38%). R_f (4:6 PE/EtOAc) 0.3; mp: >250 °C; IR (ATR diamond) ν 3079, 2176, 1582, 1556, 1501, 1422, 1385, 1236, 1190, 1117, 1001, 952, 838, 782, 750 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 12.86 (s, 1H, NH), 10.95 (s, 1H, CH), 8.88 (bs, 1H, OH), 8.41-8.32 (m, 2H, $2\times\text{H}_{\text{Ar}}$), 8.19-7.99 (m, 2H, $2\times\text{H}_{\text{Ar}}$), 7.68-7.51 (m, 2H, $2\times\text{H}_{\text{Ar}}$), 7.22-7.01 (m, 1H, $2\times\text{H}_{\text{Ar}}$); ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 146.8 (C_q), 142.7 (CH), 137.2 (C_q), 133.5 ($2\times\text{CH}_{\text{Ar}}$), 126.9 (C_q), 125.3 (CH_{Ar}), 124.9 ($2\times\text{CH}_{\text{Ar}}$), 121.0 (C_q), 122.6 (CH_{Ar}), 120.3 (CH_{Ar}), 120.0 (C_q), 115.3 (C_q), 112.3 (CH_{Ar}), 99.2 (C_q), 84.1 (C_q); HRMS (EI-MS): MH^+ , found 306.0799. $\text{C}_{17}\text{H}_{12}\text{N}_3\text{O}_3$ requires 306.0800.

4.32. (*3E*)-1-Methyl-2-[2-(4-nitrophenyl)ethynyl]indole-3-carbaldehyde oxime (**3p**)

The compound **3p** was obtained as described for **3a** using **2p** as starting material. The crude product was purified by silica gel using PE/EtOAc (8:2). The pure product was obtained as a red solid (0.189 g, 24%). R_f (8:2 PE/EtOAc) 0.37; mp: 175-177 °C; IR (ATR diamond) ν 3299, 3103, 2194, 1592, 1515, 1466, 1334, 1104, 982, 853 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 11.11 (s, 1H, CH), 8.46 (s, 1H, OH), 8.35-8.28 (m, 2H, H_{Ar}), 8.08-7.91 (m, 3H, H_{Ar}), 7.59 (s, 1H, H_{Ar}), 7.42-7.33 (m, 1H, H_{Ar}), 7.26-7.17 (m, 1H, H_{Ar}), 3.92 (s, 3H, CH_3); ^{13}C NMR (101 MHz, CDCl_3) δ 147.0 (C_q), 143.1 (CH), 137.8 (C_q), 132.4 ($2\times\text{CH}_{\text{Ar}}$), 128.0 (C_q), 124.8 (CH_{Ar}), 123.9 ($2\times\text{CH}_{\text{Ar}}$), 123.2 (C_q), 122.0 (CH_{Ar}), 121.6 (CH_{Ar}), 121.4 (C_q), 114.9 (C_q), 110.5 (CH_{Ar}), 98.2 (C_q), 83.5 (C_q), 31.0 (CH_3); HRMS (EI-MS): MH^+ , found 320.1029. $\text{C}_{18}\text{H}_{14}\text{N}_3\text{O}_3$ requires 320.1030.

4.33. 5-(*tert*-Butoxycarbonyl)-3-phenyl-5H-pyrido[4,3-*b*]indole 2-oxide (**4a**)

To the solution of compound **3a** (0.109 g, 0.3 mmol) in CH_2Cl_2 (6 mL) $\text{Au}(\text{CH}_3\text{CN})\text{SbF}_6$ (0.015 g, 5 %mol) was added. The reaction mixture was stirred at r.t. for 16 h. The solvent was evaporated and the crude product was purified by silica gel chromatography using $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (9:1) as an eluent. The product was recrystallized with *n*-pentane to obtain the pure product as a pale yellow powder (0.101 g, 96%).

R_f (95:5 $\text{CH}_2\text{Cl}_2/\text{MeOH}$) 0.13; mp: 207-209 °C; IR (ATR diamond) ν 3035, 2981, 2929, 1720, 1488, 1454, 1417, 1359, 1306, 1244, 1209, 1178, 1147, 1116, 840, 751 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.01 (s, 1H, H_{Ar}), 8.36 (s, 1H, H_{Ar}), 8.26 (d, J = 8.4 Hz, 1H, H_{Ar}), 7.92 (t, J = 8.1 Hz, 3H, $3\times\text{H}_{\text{Ar}}$), 7.62-7.40 (m, 5H, $5\times\text{H}_{\text{Ar}}$), 1.75 (s, 9H, $3\times\text{CH}_3$); ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 150.2 (C_q), 147.6 (C_q), 139.7 (C_q), 135.8 (C_q), 133.8 (C_q), 132.3 (CH_{Ar}), 129.8 ($2\times\text{CH}_{\text{Ar}}$), 129.5 (CH_{Ar}), 129.5 (CH_{Ar}), 128.4 ($2\times\text{CH}_{\text{Ar}}$), 124.4 (CH_{Ar}), 123.2 (C_q), 121.9 (C_q), 120.7 (CH_{Ar}), 116.7 (CH_{Ar}), 114.3 (CH_{Ar}), 85.7 (C_q), 28.4 ($3\times\text{CH}_3$); HRMS (EI-MS): MH^+ , found 361.1546. $\text{C}_{22}\text{H}_{21}\text{N}_2\text{O}_3$ requires 361.1547.

4.34. 5-(*tert*-Butoxycarbonyl)-3-(*p*-tolyl)-5H-pyrido[4,3-*b*]indole 2-oxide (**4b**)

The compound **4b** was obtained as described for **4a** using **3b** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5). The pure product was obtained as a yellow solid (0.127 g, 96%). R_f (95:5 $\text{CH}_2\text{Cl}_2/\text{MeOH}$) 0.25; mp: 208-210 °C; IR (ATR diamond) ν 2981, 2834, 1759, 1735, 1661, 1424, 1370, 1306, 1247, 1150, 822, 748 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.99 (s, 1H, H_{Ar}), 8.33 (s, 1H, H_{Ar}), 8.26 (d, J = 8.4 Hz, 1H, H_{Ar}), 7.92 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.81 (d, J = 8.1 Hz, 2H, $2\times\text{H}_{\text{Ar}}$), 7.57 (t, J = 7.9 Hz, 1H, H_{Ar}), 7.42 (t, J = 7.5 Hz, 1H, H_{Ar}), 7.31 (d, J = 8.0 Hz, 2H, $2\times\text{H}_{\text{Ar}}$), 2.42 (s, 3H, CH_3), 1.75 (s, 9H, $3\times\text{CH}_3$); ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ 150.1 (C_q), 147.7 (C_q), 139.7 (C_q), 139.6 (C_q), 135.7 (C_q), 132.2 (CH_{Ar}), 130.9 (C_q), 129.6 ($2\times\text{CH}_{\text{Ar}}$), 129.4 (C_q), 129.0 ($2\times\text{CH}_{\text{Ar}}$), 124.3 (CH_{Ar}), 123.0 (C_q), 121.9 (C_q), 120.6 (CH_{Ar}), 116.6 (CH_{Ar}), 114.0 (CH_{Ar}), 85.6 (C_q), 28.4 ($3\times\text{CH}_3$), 21.6 (CH_3); HRMS (EI-MS): MH^+ , found 375.1702. $\text{C}_{23}\text{H}_{23}\text{N}_2\text{O}_3$ requires 375.1703.

4.35. 5-(*tert*-Butoxycarbonyl)-3-(*m*-tolyl)-5H-pyrido[4,3-*b*]indole 2-oxide (**4c**)

The compound **4c** was obtained as described for **4a** using **3c** as starting material. The crude product was purified by silica gel

chromatography using PE/EtOAc (95:5). The pure product was obtained as an orange solid (0.087 g, 73%). R_f (95:5 CH₂Cl₂/MeOH) 0.29; mp: 153–155 °C; IR (ATR diamond) ν 3337, 3203, 3058, 2974, 2929, 1728, 1605, 1454, 1369, 1349, 1307, 1247, 1212, 1145, 1115, 916, 836, 747 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.98 (s, 1H, H_{Ar}), 8.39–8.17 (m, 2H, 2xH_{Ar}), 7.90 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.74–7.49 (m, 3H, 3xH_{Ar}), 7.45–7.33 (m, 2H, 2xH_{Ar}), 7.23 (s, 1H, H_{Ar}), 2.42 (d, J = 1.9 Hz, 3H, CH₃), 1.73 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.1 (C_q), 147.8 (C_q), 139.7 (C_q), 137.7 (C_q), 135.8 (C_q), 133.7 (C_q), 132.2 (CH_{Ar}), 130.3 (2xCH_{Ar}), 129.4 (CH_{Ar}), 128.3 (CH_{Ar}), 126.8 (CH_{Ar}), 124.4 (CH_{Ar}), 123.1 (C_q), 121.9 (C_q), 120.7 (CH_{Ar}), 116.6 (CH_{Ar}), 114.3 (CH_{Ar}), 85.8 (C_q), 28.4 (3xCH₃), 21.6 (CH₃); HRMS (EI-MS): MH⁺, found 375.1702. C₂₃H₂₃N₂O₃ requires 375.1703.

4.36. 5-(*tert*-Butoxycarbonyl)-3-(*o*-tolyl)-5H-pyrido[4,3-*b*]indole 2-oxide (**4d**)

The compound **4d** was obtained as described for **4a** using **3c** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5). The pure product was obtained as a pale yellow solid (0.080 g, 70%). R_f (95:5 CH₂Cl₂/MeOH) 0.32; mp: 139–141 °C; IR (ATR diamond) ν 3445, 2987, 2359, 1724, 1455, 1416, 1354, 1337, 1176, 1144, 1118, 744 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.03 (s, 1H, H_{Ar}), 8.31–8.20 (m, 2H, 2xH_{Ar}), 7.94 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.63–7.54 (m, 1H, H_{Ar}), 7.46–7.28 (m, 5H, 5xH_{Ar}), 2.30 (s, 3H, CH₃), 1.73 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.1 (C_q), 148.9 (C_q), 139.6 (C_q), 138.0 (C_q), 135.4 (C_q), 134.0 (C_q), 131.8 (CH_{Ar}), 130.1 (CH_{Ar}), 129.7 (CH_{Ar}), 129.5 (2xCH_{Ar}), 126.0 (CH_{Ar}), 124.3 (CH_{Ar}), 123.5 (C_q), 121.9 (C_q), 120.7 (CH_{Ar}), 116.6 (CH_{Ar}), 114.7 (CH_{Ar}), 85.7 (C_q), 31.0, 28.3 (3xCH₃), 19.8 (CH₃); HRMS (EI-MS): MH⁺, found 375.1698. C₂₃H₂₃N₂O₃ requires 375.1703.

4.37. 5-(*tert*-Butoxycarbonyl)-3-(4-methoxyphenyl)-5H-pyrido[4,3-*b*]indole 2-oxide (**4e**)

The compound **4e** was obtained as described for **4a** using **3e** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5). The pure product was obtained as a pale yellow solid (0.114 g, 95%). R_f (95:5 CH₂Cl₂/MeOH) 0.32; mp: 157–159 °C; IR (ATR diamond) ν 3284, 1732, 1449, 1320, 1275, 1122, 1022, 943, 739 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.83 (s, 1H, H_{Ar}), 8.22 (d, J = 8.4 Hz, 1H, H_{Ar}), 8.16 (d, J = 7.8 Hz, 1H, H_{Ar}), 7.50 (d, J = 6.5 Hz, 1H, H_{Ar}), 7.42–7.28 (m, 4H, 4xH_{Ar}), 7.00–6.92 (m, 2H, 2xH_{Ar}), 4.00 (s, 3H, O-CH₃), 1.72 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 160.7 (C_q), 149.4 (C_q), 147.2 (CH_{Ar}), 136.5 (C_q), 132.5 (2xCH_{Ar}), 130.6 (CH_{Ar}), 126.4 (2xCH_{Ar}), 125.9 (C_q), 124.1 (CH_{Ar}), 123.2 (C_q), 122.5 (CH_{Ar}), 120.6 (CH_{Ar}), 120.5 (C_q), 115.5 (CH_{Ar}), 112.0 (C_q), 110.8 (CH_{Ar}), 98.0 (C_q), 85.0 (CH_{Ar}), 84.5 (C_q), 55.7 (OCH₃), 28.4 (3xCH₃); HRMS (EI-MS): MH⁺, found 391.1652. C₂₃H₂₃N₂O₄ requires 391.1652.

4.38. 5-(*tert*-Butoxycarbonyl)-3-(4-(dimethylamino)phenyl)-5H-pyrido[4,3-*b*]indole 2-oxide (**4f**)

The compound **4f** was obtained as described for **4a** using **3f** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5). The pure product was obtained as a pale yellow solid (0.620 g, 98%). R_f (95:5 CH₂Cl₂/MeOH) 0.2; mp: 189–191 °C; IR (ATR diamond) ν 3253, 2927, 1727, 1603, 1496, 1455, 1416, 1349, 1324, 1201, 1147, 1114, 812, 760 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.97 (s, 1H, H_{Ar}), 8.32 (s, 1H, H_{Ar}), 8.26 (d, J = 8.4 Hz, 1H, H_{Ar}), 7.91 (t, J = 8.2 Hz, 3H, 3xH_{Ar}), 7.55 (t, J = 8.4 Hz, 1H, H_{Ar}), 7.41 (t, J = 7.5

Hz, 1H, H_{Ar}), 6.81 (d, J = 9.0 Hz, 2H, 2xH_{Ar}), 3.04 (s, 6H, 2xCH₃), 1.76 (s, 9H, 3xCH₃[Boc]); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 151.2 (C_q), 150.2 (C_q), 148.0 (C_q), 139.7 (C_q), 136.0 (C_q), 132.3 (CH_{Ar}), 130.8 (2xCH_{Ar}), 129.0 (CH_{Ar}), 124.3 (CH_{Ar}), 122.1 (C_q), 122.0 (C_q), 121.1 (C_q), 120.5 (CH_{Ar}), 116.6 (CH_{Ar}), 113.1 (CH_{Ar}), 111.6 (2xCH_{Ar}), 85.4 (C_q), 40.4 (2xCH₃), 28.4 (3xCH₃); HRMS (EI-MS): MH⁺, found 404.1968. C₂₄H₂₆N₃O₃ requires 404.1969.

4.39. 3-(4-Aminophenyl)-5-(*tert*-butoxycarbonyl)-5H-pyrido[4,3-*b*]indole 2-oxide (**4g**)

The compound **4g** was obtained as described for **4a** using **3g** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5). The pure product was obtained as a pale yellow solid (0.091 g, 82%). R_f (95:5 CH₂Cl₂/MeOH) 0.24; mp: 199–201 °C; IR (ATR diamond) ν 3326, 3207, 2975, 1727, 1607, 1495, 1455, 1414, 1368, 1349, 1321, 1245, 1215, 1148, 1113, 914, 834, 757 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.96 (s, 1H, H_{Ar}), 8.31 (s, 1H, H_{Ar}), 8.25 (d, J = 8.4 Hz, 1H, H_{Ar}), 7.90 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.81 (d, J = 8.5 Hz, 2H, 2xH_{Ar}), 7.55 (t, J = 7.9 Hz, 1H, H_{Ar}), 7.41 (t, J = 7.5 Hz, 1H, H_{Ar}), 6.77 (d, J = 8.5 Hz, 2H, 2xH_{Ar}), 3.92 (s, 2H, NH₂), 1.75 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.2 (C_q), 147.9 (C_q), 147.8 (C_q), 139.69 (C_q), 136.0 (C_q), 132.2 (CH_{Ar}), 131.1 (2xCH_{Ar}), 129.2 (CH_{Ar}), 124.3 (CH_{Ar}), 123.5 (C_q), 122.3 (C_q), 122.0 (C_q), 120.6 (CH_{Ar}), 116.6 (CH_{Ar}), 114.5 (2xCH_{Ar}), 113.4 (CH_{Ar}), 85.5 (C_q), 28.4 (3xCH₃); HRMS (EI-MS): MH⁺, found 376.1655. C₂₂H₂₂N₃O₃ requires 376.1656.

4.40. 5-(*tert*-Butoxycarbonyl)-3-(4-nitrophenyl)-5H-pyrido[4,3-*b*]indole 2-oxide (**4h**)

The compound **4h** was obtained as described for **4a** using **3h** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5). The pure product was obtained as an orange solid (0.048 g, 62%). R_f (95:5 CH₂Cl₂/MeOH) 0.26; mp: 137–139 °C; IR (ATR diamond) ν 2927, 1732, 1598, 1518, 1455, 1427, 1341, 1146, 1116, 853, 748, 699 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.03 (s, 1H, H_{Ar}), 8.44 (s, 1H, H_{Ar}), 8.36 (d, J = 8.9 Hz, 2H, 2xH_{Ar}), 8.26 (d, J = 8.4 Hz, 1H, H_{Ar}), 8.13 (d, J = 8.9 Hz, 2H, 2xH_{Ar}), 7.97 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.63 (t, J = 7.9 Hz, 1H, H_{Ar}), 7.47 (t, J = 7.5 Hz, 1H, H_{Ar}), 1.76 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.0 (C_q), 148.1 (C_q), 145.0 (C_q), 140.0 (C_q), 139.8 (C_q), 135.8 (C_q), 132.4 (CH_{Ar}), 130.9 (2xCH_{Ar}), 130.0 (CH_{Ar}), 124.6 (CH_{Ar}), 124.2 (C_q), 123.5 (2xCH_{Ar}), 121.5 (C_q), 121.0 (CH_{Ar}), 116.7 (CH_{Ar}), 114.4 (CH_{Ar}), 86.2 (C_q), 28.3 (3xCH₃); HRMS (EI-MS): MH⁺, found 406.1399. C₂₂H₂₀N₃O₅ requires 406.1398.

4.41. 5-(*tert*-Butoxycarbonyl)-3-(4-chlorophenyl)-5H-pyrido[4,3-*b*]indole 2-oxide (**4i**)

The compound **4i** was obtained as described for **4a** using **3i** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5). The pure product was obtained as a yellow solid (0.086 g, 72%). R_f (95:5 CH₂Cl₂/MeOH) 0.42; mp: 103–105 °C; IR (ATR diamond) ν 2978, 1731, 1454, 1422, 1350, 1146, 1012, 830, 763 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.01 (s, 1H, H_{Ar}), 8.36 (s, 1H, H_{Ar}), 8.25 (d, J = 8.4 Hz, 1H, H_{Ar}), 7.94 (d, J = 7.7 Hz, 1H, H_{Ar}), 7.87 (d, J = 8.4 Hz, 2H, 2xH_{Ar}), 7.60 (t, J = 7.9 Hz, 1H, H_{Ar}), 7.51–7.40 (m, 3H, 3xH_{Ar}), 1.75 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.1 (C_q), 146.4 (C_q), 139.8 (C_q), 136.1 (C_q), 135.7 (C_q), 132.4 (C_q), 132.1 (CH_{Ar}), 131.2 (2xCH_{Ar}), 129.7 (CH_{Ar}), 128.7 (2xCH_{Ar}), 124.5 (CH_{Ar}), 121.7 (C_q), 120.9 (CH_{Ar}), 116.7 (CH_{Ar}), 114.1 (CH_{Ar}), 86.0 (C_q), 28.4 (3xCH₃); HRMS (EI-MS): MH⁺, found 395.1157. C₂₂H₂₀ClN₂O₃ requires 395.1157.

4.42. 5-(tert-Butoxycarbonyl)-3-(4-(trifluoromethyl)phenyl)-5H-pyrido[4,3-b]indole 2-oxide (4j)

The compound **4j** was obtained as described for **4a** using **3j** as starting material. The crude product was purified by silica gel chromatography using PE/EtOAc (95:5). The pure product was obtained as a yellow solid (0.116 g, 85%). *R_f* (95:5 CH₂Cl₂/MeOH) 0.28; mp: 141-143 °C; IR (ATR diamond) ν 2979, 1728, 1455, 1427, 1398, 1354, 1321, 1146, 1116, 1069, 1015, 840, 753 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.02 (s, 1H, H_{Ar}), 8.39 (s, 1H, H_{Ar}), 8.25 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 8.04 (d, *J* = 8.1 Hz, 2H, 2xH_{Ar}), 7.95 (d, *J* = 7.5 Hz, 1H, H_{Ar}), 7.76 (d, *J* = 8.2 Hz, 2H, 2xH_{Ar}), 7.66-7.56 (m, 1H, H_{Ar}), 7.45 (t, *J* = 7.9 Hz, 1H, H_{Ar}), 1.75 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 149.9 (C_q), 145.9 (C_q), 139.6 (C_q), 137.1 (C_q), 135.6 (C_q), 132.2 (CH_{Ar}), 131.4 (C_q), 130.9 (C_q), 130.1 (2xCH_{Ar}), 129.7 (CH_{Ar}), 125.2 (q, *J* = 3.7 Hz, 2xCH_{Ar}-CF₃), 124.4 (CH_{Ar}), 123.7 (C_q), 121.5 (C_q), 120.7 (CH_{Ar}), 116.6 (CH_{Ar}), 114.2 (CH_{Ar}), 85.9 (C_q), 28.2 (3xCH₃); ¹⁹F NMR (376 MHz, CDCl₃) δ -62.83; HRMS (EI-MS): MH⁺, found 429.1420. C₂₃H₂₀FN₂O₃ requires 429.1421.

4.43. 5-(tert-Butoxycarbonyl)-3-(4-cyanophenyl)-5H-pyrido[4,3-b]indole 2-oxide (4k)

The compound **4i** was obtained as described for **4a** using **3i** as starting material. The crude product was purified by silica gel chromatography using CH₂Cl₂/MeOH (98:2). The pure product was obtained as a yellow solid (0.057 g, 72%). *R_f* (95:5 CH₂Cl₂/MeOH) 0.27; mp: 157-159 °C; IR (ATR diamond) ν 2978, 2227, 1732, 1454, 1423, 1351, 1212, 1147, 1117, 836, 750 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.01 (s, 1H, H_{Ar}), 8.41 (s, 1H, H_{Ar}), 8.25 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 8.06 (d, *J* = 8.3 Hz, 2H, 2xH_{Ar}), 7.95 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.79 (d, *J* = 8.3 Hz, 2H, 2xH_{Ar}), 7.62 (t, *J* = 7.8 Hz, 1H, H_{Ar}), 7.46 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 1.76 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.1 (C_q), 145.4 (C_q), 139.8 (C_q), 138.2 (C_q), 135.6 (C_q), 132.5 (C_q), 132.1 (2xCH_{Ar}), 130.5 (2xCH_{Ar}), 130.0 (CH_{Ar}), 124.6 (CH_{Ar}), 124.1 (C_q), 121.6 (C_q), 121.0 (CH_{Ar}), 118.6 (C_q), 116.7 (CH_{Ar}), 114.3 (CH_{Ar}), 113.1 (CH_{Ar}), 86.1 (C_q), 28.4 (3xCH₃); HRMS (EI-MS): MH⁺, found 386.1496. C₂₃H₂₀N₃O₃ requires 386.1499.

4.44. 5-(tert-Butoxycarbonyl)-3-(thiophen-2-yl)-5H-pyrido[4,3-b]indole 2-oxide (4l)

The compound **4i** was obtained as described for **4a** using **3i** as starting material. The crude product was purified by silica gel chromatography using CH₂Cl₂/MeOH (95:5). The pure product was obtained as a yellow solid (0.111 g, 84%). *R_f* (95:5 CH₂Cl₂/MeOH) 0.41; mp: >250 °C; IR (ATR diamond) ν 3352, 2975, 2929, 2168, 1735, 1455, 1409, 1345, 1348, 1152, 944, 842, 756 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.96 (s, 1H, H_{Ar}), 8.87 (s, 1H, H_{Ar}), 8.27 (d, *J* = 8.3 Hz, 1H, H_{Ar}), 7.93 (dd, *J* = 9.5, 5.7 Hz, 2H, 2xH_{Ar}), 7.62-7.54 (m, 2H, 2xH_{Ar}), 7.42 (t, *J* = 7.3 Hz, 1H, H_{Ar}), 7.25-7.19 (m, 1H, H_{Ar}), 1.81 (s, 9H, 3xCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.2 (C_q), 141.5 (C_q), 140.1 (C_q), 136.0 (C_q), 132.9 (C_q), 131.2 (CH_{Ar}), 131.2 (CH_{Ar}), 129.5 (CH_{Ar}), 127.1 (CH_{Ar}), 126.1 (CH_{Ar}), 124.4 (CH_{Ar}), 121.9 (C_q), 121.8 (C_q), 120.71 (CH_{Ar}), 116.7 (CH_{Ar}), 108.6 (CH_{Ar}), 85.7 (C_q), 28.5 (3xCH₃); HRMS (EI-MS): MH⁺, found 367.1110. C₂₀H₁₉N₂O₃S requires 367.1111.

4.45. 5-(tert-Butoxycarbonyl)-3-butyl-5H-pyrido[4,3-b]indole 2-oxide (4m)

The compound **4m** was obtained as described for **4a** using **3k** as starting material. The crude product was purified by silica gel chromatography using CH₂Cl₂/MeOH (95:5). The pure product

was obtained as a white solid (0.082 g, 82%). *R_f* (95:5 CH₂Cl₂/MeOH) 0.2; mp: 149-151 °C; IR (ATR diamond) ν 3436, 2921, 2864, 1723, 1460, 1425, 1353, 1321, 1251, 1220, 1142, 1115, 1050, 918, 764 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.93 (s, 1H, H_{Ar}), 8.25 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 8.16 (s, 1H, H_{Ar}), 7.89 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.55 (t, *J* = 7.9 Hz, 1H, H_{Ar}), 7.40 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 3.13-3.05 (m, 2H, CH₂), 1.86-1.80 (m, 2H, -CH₂), 1.77 (s, 9H, 3xCH₃), 1.57-1.46 (m, 2H, CH₂), 1.01 (t, *J* = 7.3 Hz, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 151.0 (C_q), 150.2 (C_q), 139.4 (C_q), 135.8 (C_q), 131.5 (CH_{Ar}), 129.1 (CH_{Ar}), 124.2 (CH_{Ar}), 122.1 (C_q), 122.0 (C_q), 120.4 (CH_{Ar}), 116.6 (CH_{Ar}), 112.0 (CH_{Ar}), 85.5 (C_q), 31.3 (CH₂), 28.9 (CH₂), 28.4 (3xCH₃), 22.7 (-CH₂), 14.0 (CH₃); HRMS (EI-MS): MH⁺, found 341.1860. C₂₀H₂₄N₂O₃ requires 341.1860.

4.46. 5-(tert-Butoxycarbonyl)-3-isopropyl-5H-pyrido[4,3-b]indole 2-oxide (4n)

The compound **4n** was obtained as described for **4a** using **3n** as starting material. The crude product was purified by silica gel chromatography using CH₂Cl₂/MeOH (95:5). The pure product was obtained as a white solid (0.045 g, 45%). *R_f* (95:5 CH₂Cl₂/MeOH) 0.2; mp: 91-93 °C; IR (ATR diamond) ν 3391, 2923, 1732, 1457, 1421, 1347, 1317, 1145, 1111, 916, 839, 759 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.92 (s, 1H, H_{Ar}), 8.25 (d, *J* = 8.4 Hz, 1H, H_{Ar}), 8.15 (s, 1H, H_{Ar}), 7.87 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.58-7.47 (m, 1H, H_{Ar}), 7.42-7.33 (m, 1H, H_{Ar}), 4.06-3.86 (m, 1H, CH), 1.76 (s, 9H, 3xCH₃), 1.38 (d, *J* = 6.9 Hz, 6H, 2xCH₃); ¹³C NMR (101 MHz, CDCl₃) δ 156.1 (C_q), 150.1 (C_q), 139.5 (C_q), 136.0 (C_q), 131.6 (CH_{Ar}), 129.0 (CH_{Ar}), 124.1 (CH_{Ar}), 121.9 (C_q), 121.9 (C_q), 120.4 (CH_{Ar}), 116.6 (CH_{Ar}), 109.7 (CH_{Ar}), 85.4 (C_q), 28.5 (CH), 28.4 (3xCH₃), 21.0 (2xCH₃); HRMS (EI-MS): MH⁺, found 372.1699. C₁₉H₂₃N₂O₃ requires 372.1703.

4.47. 5-Methyl-3-(4-nitrophenyl)-5H-pyrido[4,3-b]indole 2-oxide (4p)

The compound **4p** was obtained as described for **4a** using **3p** as starting material. The crude product was purified by silica gel chromatography using CH₂Cl₂/MeOH (95:5). The pure product was obtained as a white solid (0.042 g, 24%). *R_f* (95:5 CH₂Cl₂/MeOH) 0.2; mp: 125-127 °C; IR (ATR diamond) ν 1593, 1500, 1470, 1454, 1423, 1339, 1171, 1157, 852, 843, 752 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.08 (s, 1H, H_{Ar}), 8.37-8.28 (m, 2H, H_{Ar}), 8.14-7.99 (m, 3H, H_{Ar}), 7.68-7.56 (m, 1H, H_{Ar}), 7.48-7.31 (m, 3H, H_{Ar}), 3.89 (s, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 148.0 (C_q), 144.0 (C_q), 142.9 (C_q), 140.3 (C_q), 138.4 (C_q), 133.1 (C_q), 131.0 (CH_{Ar}), 129.0 (2xCH_{Ar}), 123.4 (CH_{Ar}), 121.7 (2xCH_{Ar}), 121.6 (CH_{Ar}), 120.9 (CH_{Ar}), 119.6 (C_q), 109.9 (CH_{Ar}), 106.7 (CH_{Ar}), 29.9 (CH₃); HRMS (EI-MS): MH⁺, found 406.1399. C₁₈H₁₄N₃O₃ requires 406.1398.

4.48. 3-Phenyl-5H-pyrido[4,3-b]indole 2-oxide (5a)

The compound **4a** (0.089 g, 0.25 mmol) was dissolved in the mixture of DCM/TFA 3:1 (2 mL) then stirred at r.t. for 16 h. The solvent was evaporated, the residue was dissolved in CH₂Cl₂ and the suspension was filtered. The filtrate crystallization led to **5a** as pale yellow crystals (0.047 g, 86%). *R_f* (95:5 CH₂Cl₂/MeOH) 0.25; mp: >250 °C; IR (ATR diamond) ν 3062, 1673, 1611, 1497, 1458, 1197, 1129 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.54 (s, 1H, NH), 9.66 (s, 1H, H_{Ar}), 8.32 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.80 (s, 1H, H_{Ar}), 7.77-7.72 (m, 2H, 2xH_{Ar}), 7.70 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.65-7.60 (m, 1H, H_{Ar}), 7.47-7.37 (m, 4H, 4xH_{Ar}); ¹³C NMR (101 MHz, CDCl₃) δ 148.2 (C_q), 145.0 (C_q), 143.7 (C_q), 136.1 (CH_{Ar}), 132.8 (C_q), 131.4 (CH_{Ar}), 131.1 (2xCH_{Ar}), 130.9 (CH_{Ar}), 129.6 (2xCH_{Ar}), 123.7 (CH_{Ar}), 122.9 (CH_{Ar}), 121.6

(C_q), 121.4 (C_q), 113.7 (CH_{Ar}), 110.2 (CH_{Ar}); HRMS (EI-MS): MH⁺, found 261.1022. C₁₇H₁₃N₂O requires 261.1022.

4.49. 3-(*p*-Tolyl)-5*H*-pyrido[4,3-*b*]indole 2-oxide (**5b**)

The compound **5b** was obtained as described for **5a** using **4b** as starting material. At the end of the reaction, volatiles were evaporated and the residue was dissolved in CH₂Cl₂ then precipitated with *n*-pentane to obtain the pure product as a grey solid (0.073 g, 66%). R_f (95:5 CH₂Cl₂/MeOH) 0.1; mp: >250 °C; IR (ATR diamond) ν 3067, 2233, 1675, 1613, 1502, 1457, 1348, 1185, 1133, 852, 719 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.96 (s, 1H, NH), 9.98 (s, 1H, H_{Ar}), 8.42 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.95 (s, 1H, H_{Ar}), 7.78 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.73-7.63 (m, 3H, 3xH_{Ar}), 7.48 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 7.35 (d, *J* = 7.2 Hz, 2H, 2xH_{Ar}), 2.35 (s, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 146.0 (C_q), 143.5 (C_q), 142.0 (C_q), 140.1 (C_q), 135.8 (C_q), 130.0 (2xCH_{Ar}), 129.5 (C_q), 128.9 (2xCH_{Ar}), 128.3 (C_q), 122.3 (CH_{Ar}), 122.2 (CH_{Ar}), 120.0 (C_q), 119.4 (C_q), 112.9 (CH_{Ar}), 109.2 (CH_{Ar}), 20.8 (CH₃); HRMS (EI-MS): MH⁺, found 275.1178. C₁₈H₁₅N₂O requires 275.1179.

4.50. 3-(*m*-Tolyl)-5*H*-pyrido[4,3-*b*]indole 2-oxide (**5c**)

The compound **5c** was obtained as described for **5a** using **4c** as starting material. At the end of the reaction, volatiles were evaporated and the residue was dissolved in CH₂Cl₂ then precipitated with *n*-pentane to obtain the pure product as a yellow solid (0.050 g, 76%). R_f (95:5 CH₂Cl₂/MeOH) 0.24; mp: 231-233 °C; IR (ATR diamond) ν 3055, 1669, 1612, 1500, 1457, 1325, 1128, 860, 751, 716 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.58 (s, 1H, H_{Ar}), 9.63 (s, 1H, H_{Ar}), 8.31 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.77 (s, 1H, H_{Ar}), 7.71 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.67-7.61 (m, 1H, H_{Ar}), 7.49 (d, *J* = 7.7 Hz, 1H, H_{Ar}), 7.44-7.37 (m, 2H, 2xH_{Ar}), 7.26 (t, *J* = 7.7 Hz, 1H, H_{Ar}), 7.10 (d, *J* = 7.6 Hz, 1H, H_{Ar}), 2.21 (s, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 145.6 (C_q), 141.8 (C_q), 140.9 (C_q), 137.2 (C_q), 134.5 (CH_{Ar}), 132.0 (C_q), 130.0 (CH_{Ar}), 130.0 (CH_{Ar}), 128.8 (CH_{Ar}), 127.8 (CH_{Ar}), 126.9 (CH_{Ar}), 122.0 (CH_{Ar}), 121.4 (CH_{Ar}), 119.8 (C_q), 119.6 (C_q), 112.5 (CH_{Ar}), 109.0 (CH_{Ar}), 20.7 (CH₃); HRMS (EI-MS): MH⁺, found 275.1177. C₁₈H₁₅N₂O requires 275.1179.

4.51. 3-(*o*-Tolyl)-5*H*-pyrido[4,3-*b*]indole 2-oxide (**5d**)

The compound **5d** was obtained as described for **5a** using **4d** as starting material. At the end of the reaction, volatiles were evaporated and the residue was dissolved in CH₂Cl₂ then precipitated with *n*-pentane to obtain the pure product as a dark green solid (0.048 g, 95%). R_f (95:5 CH₂Cl₂/MeOH) 0.22; mp: >250 °C; IR (ATR diamond) ν 3062, 2922, 2851, 1673, 1613, 1500, 1456, 1183, 1132, 796, 718 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 12.97 (s, 1H, NH), 10.02 (s, 1H, H_{Ar}), 8.44 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.92 (s, 1H, H_{Ar}), 7.78 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.70 (t, *J* = 7.2 Hz, 1H, H_{Ar}), 7.52-7.34 (m, 6H, 6xH_{Ar}), 2.18 (s, 3H, CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 146.7 (C_q), 142.2 (C_q), 140.7 (C_q), 137.8 (C_q), 134.4 (CH_{Ar}), 133.4 (C_q), 130.2 (CH_{Ar}), 130.0 (CH_{Ar}), 129.8 (CH_{Ar}), 129.1 (CH_{Ar}), 125.9 (CH_{Ar}), 122.4 (CH_{Ar}), 121.8 (CH_{Ar}), 120.4 (C_q), 120.2 (C_q), 113.0 (CH_{Ar}), 109.9 (CH_{Ar}), 19.7 (CH₃); HRMS (EI-MS): MH⁺, found 275.1179. C₁₈H₁₅N₂O requires 275.1179.

4.52. 3-(4-Methoxyphenyl)-5*H*-pyrido[4,3-*b*]indole 2-oxide (**5e**)

The compound **5d** was obtained as described for **5a** using **4d** as starting material. At the end of the reaction, volatiles were evaporated and residue was suspended in EtOAc and the solution filtered. The precipitate was dissolved in MeOH and the solution

filtered once again. The filtrate was concentrated under reduced pressure to obtain the pure product as a white powder (0.056 g, 64%). R_f (95:5 CH₂Cl₂/MeOH) 0.22; mp: 163-165 °C; IR (ATR diamond) ν 3065, 1675, 1607, 1497, 1457, 1255, 1177, 1124, 831, 719 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.75 (s, 1H, NH), 9.76 (s, 1H, H_{Ar}), 8.35 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.83 (s, 1H, H_{Ar}), 7.76-7.62 (m, 4H, 4xH_{Ar}), 7.43 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 6.96 (d, *J* = 8.5 Hz, 2H, 2xH_{Ar}), 3.68 (s, 3H, OCH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 160.4 (CH_{Ar}), 145.5 (C_q), 142.5 (C_q), 141.9 (C_q), 135.2 (CH_{Ar}), 131.5 (2xCH_{Ar}), 129.1 (CH_{Ar}), 123.5 (CH_{Ar}), 122.1 (CH_{Ar}), 121.8 (C_q), 119.9 (C_q), 119.3 (C_q), 113.5 (2xCH_{Ar}), 112.7 (C_q), 108.7 (CH_{Ar}), 55.1 (OCH₃); HRMS (EI-MS): MH⁺, found 291.1128. C₁₈H₁₅N₂O₂ requires 291.1128.

4.53. 3-(4-(Dimethylamino)phenyl)-5*H*-pyrido[4,3-*b*]indole 2-oxide (**5f**)

The compound **5f** was obtained as described for **5a** using **4f** as starting material. At the end of the reaction, volatiles were evaporated and the residue was dissolved in CH₂Cl₂ then precipitated with *n*-pentane to obtain the pure product as a dark green solid (0.041 g, 81%). R_f (95:5 CH₂Cl₂/MeOH) 0.1; mp: >250 °C; IR (ATR diamond) ν 3070, 1732, 1644, 1613, 1500, 1457, 1182, 1135, 787, 718, 703 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.88 (s, 1H, NH), 9.96 (s, 1H, H_{Ar}), 8.40 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.89 (s, 1H, H_{Ar}), 7.78-7.64 (m, 4H, 4xH_{Ar}), 7.46 (t, *J* = 7.2 Hz, 1H, H_{Ar}), 6.86 (d, *J* = 8.9 Hz, 2H, 2xH_{Ar}), 3.01 (s, 6H, 2xCH₃); ¹³C NMR (101 MHz, CD₃OD) δ 152.2 (C_q), 148.2 (C_q), 145.4 (C_q), 143.0 (C_q), 135.4 (CH_{Ar}), 131.5 (2xCH_{Ar}), 130.0 (C_q), 122.9 (CH_{Ar}), 122.0 (CH_{Ar}), 120.8 (C_q), 119.9 (C_q), 117.7 (C_q), 112.8 (CH_{Ar}), 111.7 (2xCH_{Ar}), 107.8 (CH_{Ar}), 39.3 (2xCH₃); HRMS (EI-MS): MH⁺, found 304.1443. C₁₉H₁₇N₃O requires 304.1444.

4.54. 3-(4-Aminophenyl)-5*H*-pyrido[4,3-*b*]indole 2-oxide (**5g**)

The compound **5g** was obtained as described for **5a** using **4g** as starting material. At the end of the reaction, the precipitate was washed with EtOAc, dried on air to obtain a pure product as a brown solid (0.039 g, 50%). R_f (95:5 CH₂Cl₂/MeOH) 0.11; mp: 151-153 °C; IR (ATR diamond) ν 3082, 1674, 1620, 1498, 1457, 1417, 1180, 1131, 826, 793, 751, 723 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.88 (s, 1H, NH), 9.95 (s, 1H, H_{Ar}), 8.39 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.86 (s, 1H, H_{Ar}), 7.74 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.67 (t, *J* = 7.6 Hz, 1H, H_{Ar}), 7.56 (d, *J* = 8.5 Hz, 2H, 2xH_{Ar}), 7.45 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 6.75 (d, *J* = 8.5 Hz, 2H, H_{Ar}); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.6 (C_q), 147.1 (C_q), 144.2 (C_q), 142.1 (C_q), 135.8 (CH_{Ar}), 131.5 (2xCH_{Ar}), 129.3 (CH_{Ar}), 122.2 (CH_{Ar}), 122.2 (CH_{Ar}), 120.0 (C_q), 118.7 (C_q), 117.4 (C_q), 113.4 (2xCH_{Ar}), 112.8 (CH_{Ar}), 107.8 (CH_{Ar}); HRMS (EI-MS): MH⁺, found 276.1131. C₁₇H₁₄N₃O requires C₁₇H₁₄N₃O.

4.55. 3-(4-Nitrophenyl)-5*H*-pyrido[4,3-*b*]indole 2-oxide (**5h**)

The compound **5h** was obtained as described for **5a** using **4h** as starting material. At the end of the reaction, the solvent was evaporated and the residue dissolved in CH₂Cl₂. Precipitation with *n*-pentane afforded the pure product as a yellow solid (0.026 g, 86%). R_f (95:5 CH₂Cl₂/MeOH) 0.11; mp: 155-157 °C; IR (ATR diamond) ν 3067, 2233, 1675, 1613, 1502, 1457, 1348, 1185, 1133, 852, 719 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.90 (s, 1H, NH), 9.90 (s, 1H, H_{Ar}), 8.42-8.29 (m, 3H, 3xH_{Ar}), 8.17-7.97 (m, 3H, 3xH_{Ar}), 7.79-7.65 (m, 2H, 2xH_{Ar}), 7.45 (t, *J* = 7.3 Hz, 1H, H_{Ar}); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 147.9 (C_q), 143.4 (C_q), 142.0 (C_q), 141.6 (C_q), 138.0 (C_q), 135.2 (CH_{Ar}), 131.6 (2xCH_{Ar}), 129.4 (CH_{Ar}), 123.1 (2xCH_{Ar}), 122.2 (CH_{Ar}),

122.0 (CH_{Ar}), 120.0 (C_q), 119.8 (C_q), 112.8 (CH_{Ar}), 109.9 (CH_{Ar}); HRMS (EI-MS): MH⁺, found 306.0869. C₁₇H₁₂N₃O₃ requires 306.0873.

4.56. 3-(4-Chlorophenyl)-5H-pyrido[4,3-b]indole 2-oxide (**5i**)

The compound **5i** was obtained as described for **5a** using **4i** as starting material. At the end of the reaction, the solvent was evaporated and the residue was dissolved in a small amount of CH₂Cl₂. Precipitation with *n*-pentane led to the pure product as a white solid (0.056 g, 87%). R_f (95:5 CH₂Cl₂/MeOH) 0.24; mp: >250 °C; IR (ATR diamond) ν 3064, 1669, 1611, 1485, 1456, 1177, 1130, 1011, 825, 715 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.60 (s, 1H, NH), 9.71 (s, 1H, H_{Ar}), 8.34 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 7.86 (s, 1H, H_{Ar}), 7.80 (d, *J* = 8.2 Hz, 2H, 2xH_{Ar}), 7.71 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.64 (t, *J* = 7.7 Hz, 1H, H_{Ar}), 7.52 (d, *J* = 6.9 Hz, 2H, 2xH_{Ar}), 7.40 (t, *J* = 7.5 Hz, 1H, H_{Ar}); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 144.2 (C_q), 141.8 (C_q), 140.7 (C_q), 134.5 (C_q), 134.5 (CH_{Ar}), 131.7 (2xCH_{Ar}), 131.0 (CH_{Ar}), 128.9 (CH_{Ar}), 128.1 (2xCH_{Ar}), 122.1 (CH_{Ar}), 121.5 (C_q), 119.8 (C_q), 119.7 (C_q), 112.5 (CH_{Ar}), 109.2 (CH_{Ar}); HRMS (EI-MS): MH⁺, found 295.0615. C₁₇H₁₂ClN₂O requires 295.0633.

4.57. 3-(4-(Trifluoromethyl)phenyl)-5H-pyrido[4,3-b]indole 2-oxide (**5j**)

The compound **5j** was obtained as described for **5a** using **4j** as starting material. The solvent was evaporated then the residue was dissolved in CH₂Cl₂ and precipitation with *n*-pentane afforded the pure product as a beige solid (0.049 g, 65%). R_f (95:5 CH₂Cl₂/MeOH) 0.24; mp: >250 °C; IR (ATR diamond) ν 3062, 1670, 1611, 1500, 1456, 1324, 1126, 1070, 839, 754, 718 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.67 (s, 1H, NH), 9.79 (s, 1H, H_{Ar}), 8.36 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 8.02 (d, *J* = 8.1 Hz, 2H, 2xH_{Ar}), 7.94 (s, 1H, H_{Ar}), 7.87 (d, *J* = 8.2 Hz, 2H, 2xH_{Ar}), 7.72 (d, *J* = 8.2 Hz, 1H, H_{Ar}), 7.67-7.61 (m, 1H, H_{Ar}), 7.45-7.39 (m, 1H, H_{Ar}); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 158.6 (q, *J* = 34.7 Hz, C_q), 144.5 (C_q), 143.1 (C_q), 142.1 (C_q), 136.0 (CH_{Ar}), 135.5 (C_q), 131.1 (2xCH_{Ar}), 130.2 (q, *J* = 32.0 Hz, C_q), 129.6 (CH_{Ar}), 125.2 (q, *J* = 3.7 Hz, CH_{Ar}), 122.6 (C_q), 122.4 (d, *J* = 4.9 Hz, 2xCH_{Ar}), 120.0 (C_q), 119.8 (C_q), 113.0 (CH_{Ar}), 109.9 (CH_{Ar}); HRMS (EI-MS): MH⁺, found 329.0896. C₁₈H₁₂F₃N₂O requires 329.0896.

4.58. 3-(4-Cyanophenyl)-5H-pyrido[4,3-b]indole 2-oxide (**5k**)

The compound **5k** was obtained as described for **5a** using **4k** as starting material. The solvent was evaporated then the residue was dissolved in CH₂Cl₂ and precipitation with *n*-pentane led to the pure product as a beige solid (0.041 g, 97%). R_f (95:5 CH₂Cl₂/MeOH) 0.22; mp: 169-171 °C; IR (ATR diamond) ν 3100, 2235, 1675, 1613, 1502, 1457, 1196, 1131, 835, 798, 722 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.61 (s, 1H, NH), 9.72 (s, 1H, H_{Ar}), 8.34 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 8.06-7.88 (m, 5H, 5xH_{Ar}), 7.75-7.60 (m, 2H, 2xH_{Ar}), 7.40 (t, *J* = 7.1 Hz, 1H, H_{Ar}); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 143.6 (C_q), 141.9 (C_q), 140.0 (C_q), 137.0 (C_q), 134.3 (CH_{Ar}), 131.9 (2xCH_{Ar}), 130.9 (2xCH_{Ar}), 129.0 (CH_{Ar}), 122.0 (CH_{Ar}), 121.5 (CH_{Ar}), 120.1 (C_q), 119.7 (C_q), 118.4 (CN), 112.6 (CH_{Ar}), 111.9 (C_q), 109.6 (CH_{Ar}); HRMS (EI-MS): MH⁺, found 286.0973. C₁₈H₁₂N₃O requires 286.0975.

4.59. 3-(Thiophen-2-yl)-5H-pyrido[4,3-b]indole 2-oxide (**5l**)

The compound **5l** was obtained as described for **5a** using **4l** as starting material. At the end of the reaction, the precipitate was dissolved in MeOH and the mixture filtered once again. The filtrate was concentrated under reduced pressure. The residue was dissolved in a small amount of CH₂Cl₂ and precipitation with *n*-

pentane led to the pure product as a white powder (0.053 g, 87%). R_f (95:5 CH₂Cl₂/MeOH) 0.13; mp: >250 °C; IR (ATR diamond) ν 3372, 3081, 1612, 1498, 1457, 1417, 1340, 1241, 849, 763, 749, 703 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.30 (s, 1H, NH), 9.64 (s, 1H, H_{Ar}), 8.34 (s, 1H, H_{Ar}), 8.31 (d, *J* = 7.8 Hz, 1H, H_{Ar}), 8.22-8.18 (m, 1H, H_{Ar}), 7.87-7.81 (m, 1H, H_{Ar}), 7.65 (d, *J* = 8.1 Hz, 1H, H_{Ar}), 7.62-7.56 (m, 1H, H_{Ar}), 7.37-7.32 (m, 1H, H_{Ar}), 7.31-7.27 (m, 1H, H_{Ar}); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 142.2 (C_q), 139.4 (C_q), 133.2 (CH_{Ar}), 131.7 (CH_{Ar}), 131.5 (C_q), 129.1 (CH_{Ar}), 128.7 (CH_{Ar}), 126.7 (CH_{Ar}), 122.0 (CH_{Ar}), 121.1 (CH_{Ar}), 119.7 (C_q), 119.0 (C_q), 112.2 (CH_{Ar}), 104.1 (CH_{Ar}), 87.2 (C_q); HRMS (EI-MS): MH⁺, found 267.0586. C₁₅H₁₁N₂OS requires 267.0587.

4.60. 3-Butyl-5H-pyrido[4,3-b]indole 2-oxide (**5m**)

The compound **5m** was obtained as described for **5a** using **4m** as starting material. At the end of the reaction, the solvent was evaporated and the residue was dissolved in CH₂Cl₂. Precipitation with *n*-pentane led to the pure product as a grey solid (0.045 g, 99%). R_f (95:5 CH₂Cl₂/MeOH) 0.13; mp: 159-161 °C; IR (ATR diamond) ν 3233, 2966, 1610, 1455, 1399, 1167, 1127, 717 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.71 (s, 1H, NH), 9.85 (s, 1H, H_{Ar}), 8.35 (d, *J* = 7.9 Hz, 1H, H_{Ar}), 7.83 (s, 1H, H_{Ar}), 7.75-7.61 (m, 2H, 2xH_{Ar}), 7.42 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 3.14-3.04 (m, 2H, CH₂), 1.74 (p, *J* = 7.6 Hz, 2H, CH₂), 1.41 (h, *J* = 7.4 Hz, 2H, CH₂), 0.94 (t, *J* = 7.3 Hz, 3H, CH₃); ¹³C NMR (101 MHz, DMSO-*d*₆) δ 149.5 (C_q), 142.1 (C_q), 135.5 (CH_{Ar}), 129.5 (CH_{Ar}), 122.5 (CH_{Ar}), 122.3 (CH_{Ar}), 120.4 (C_q), 119.4 (C_q), 113.1 (CH_{Ar}), 108.1 (CH_{Ar}), 30.7 (CH₂), 29.9 (CH₂), 22.2 (CH₂), 14.1 (CH₃); HRMS (EI-MS): MH⁺, found 241.1335. C₁₅H₁₇N₂O requires 241.1335.

4.61. 3-Isopropyl-5H-pyrido[4,3-b]indole 2-oxide (**5n**)

The compound **5n** was obtained as described for **5a** using **4n** as starting material. At the end of the reaction, the solvent was evaporated then the residue was dissolved in CH₂Cl₂. Precipitation with *n*-pentane afforded the pure product as a grey solid (0.015 g, 90%). R_f (95:5 CH₂Cl₂/MeOH) 0.1; mp: 111-113 °C; IR (ATR diamond) ν 3062, 2979, 1646, 1609, 1499, 1455, 1205, 1129, 751, 721 cm⁻¹; ¹H NMR (250 MHz, Chloroform-*d*) δ 11.51 (s, 1H, NH), 8.85 (s, 1H, H_{Ar}), 7.57 (d, *J* = 7.3 Hz, 1H, H_{Ar}), 7.47-7.28 (m, 2H, 2 H_{Ar}), 7.16-6.99 (m, 2H, H_{Ar}), 3.90-3.56 (m, 1H, CH), 1.28 (s, 6H, 2 CH₃); ¹³C NMR (101 MHz, CDCl₃) δ 155.1 (C_q), 144.2 (C_q), 141.6 (C_q), 133.9 (CH_{Ar}), 129.6 (CH_{Ar}), 122.7 (C_q), 120.8 (C_q), 119.2 (CH_{Ar}), 112.7 (CH_{Ar}), 103.7 (CH_{Ar}), 100.1 (CH_{Ar}), 29.1 (CH), 21.4 (2xCH₃); HRMS (EI-MS): MH⁺, found 227.1179. C₁₄H₁₅N₂O requires 227.1178.

4.62. *tert*-Butyl 1-(dimethylamino)-3-phenyl-5H-pyrido[4,3-b]indole-5-carboxylate (**7**)

Under argon atmosphere, the solution of compound **5a** (0.05 g, 0.14 mmol) and (CH₃)₃N (1M in THF) (0.84 mL, 0.84 mmol, 6.0 equiv.) in anhydrous CH₂Cl₂ (2 mL) was cooled down to 0 °C then TFAA (0.06 mL, 0.42 mmol, 3.0 equiv.) was added. The reaction was allowed to warm up to r.t. and stirring was continued for 2h. The mixture was concentrated under reduced pressure and the residue was dissolved in CH₂Cl₂ and precipitation was realized by adding Et₂O. The precipitate was filtered, washed with Et₂O and dried under reduced pressure. The solid was then dissolved in CH₃CN (2 mL) and TBAF (1M in THF) (0.42 mL, 0.42 mmol, 3.0 equiv.) was added. The mixture was heated up to 90 °C for 2h. The reaction was diluted with EtOAc (5 mL) and washed successively with H₂O (10 mL) and brine (10 mL). The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was

purified by chromatography on silica gel using PE/EtOAc (8:2) to afford the pure product as a yellow solid (0.053 g, 99%). R_f (8:2 PE/EtOAc) 0.39; mp: 209–211 °C; IR (ATR diamond) ν 3205, 1610, 1592, 1552, 1527, 1496, 1455, 1395, 1302, 1278, 1253, 1192, 1067, 1057, 961 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.38 (s, 1H, H_{Ar}), 8.35 (s, 1H, H_{Ar}), 8.22–8.17 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 8.09–8.05 (m, 1H, H_{Ar}), 7.51–7.37 (m, 5H, 5 $\times\text{H}_{\text{Ar}}$), 3.14 (s, 6H, 2 $\times\text{CH}_3$), 1.81 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 158.4 (C_q), 152.7 (C_q), 150.8 (C_q), 147.0 (C_q), 140.4 (C_q), 138.4 (C_q), 128.7 (2 $\times\text{CH}_{\text{Ar}}$), 128.6 (C_q), 127.1 (2 $\times\text{CH}_{\text{Ar}}$), 126.3 (CH_{Ar}), 124.0 (C_q), 123.7 (CH_{Ar}), 122.6 (CH_{Ar}), 115.8 (CH_{Ar}), 110.4 (C_q), 102.2 (CH_{Ar}), 84.7 (C_q), 42.1 (2 $\times\text{CH}_3$), 28.5 (3 $\times\text{CH}_3$); HRMS (EI-MS): MH^+ , found 388.1945. $\text{C}_{24}\text{H}_{26}\text{N}_3\text{O}_2$ requires 388.1947.

4.63. 1-(5-(*tert*-Butoxycarbonyl)-3-phenyl-5H-pyrido[4,3-*b*]indol-1-yl)-4-(dimethylamino)pyridin-1-ium (**6b**)

A solution of compound **5a** (100 mg, 0.28 mmol, 1.0 equiv.) and 4-DMAP (772 mg, 6.32 mmol, 6.0 equiv.) in CH_2Cl_2 (3 mL) was cooled to 0 °C then TFAA (445 μL , 3.16 mmol, 3.0 equiv.) was added. The reaction mixture was left under stirring at r.t. for 1h. After completion of the reaction, volatiles were removed under reduced pressure and the crude material was triturated in CH_3CN , washed with *n*-pentane and dried under reduced pressure to afford the desired product **6b** as a white solid (302 mg, 50%). R_f (9:1 DCM/MeOH) 0.51; mp: 170–172 °C; IR (ATR diamond) ν 3073, 2981, 2933, 1728, 1688, 1647, 1598, 1551, 1396, 1322, 1197, 1158, 1129, 838, cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.93 (s, 1H, H_{Ar}), 8.50–8.44 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 8.38–8.31 (m, 1H, H_{Ar}), 8.12–8.03 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 7.60 (ddd, J = 8.5, 6.2, 2.4 Hz, 1H, H_{Ar}), 7.54–7.36 (m, 7H, 7 $\times\text{H}_{\text{Ar}}$), 3.52 (s, 6H, 2 $\times\text{CH}_3$), 1.84 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 157.7 (C_q), 154.8 (C_q), 150.1 (C_q), 148.1 (C_q), 145.5 (C_q), 141.0 (2CH), 139.5 (C_q), 137.7 (C_q), 130.1 (CH), 129.8 (CH), 129.2 (2CH), 127.3 (2CH), 125.2 (CH), 121.5 (CH), 119.9 (C_q), 116.9 (CH), 113.7 (C_q), 109.0 (3CH), 86.5 (C_q), 41.2 (2 $\times\text{CH}_3$), 28.5 (3 $\times\text{CH}_3$); ^{19}F NMR (376 MHz, CDCl_3) δ -74.76; HRMS (EI-MS): MH^+ , found 465.2262. $\text{C}_{29}\text{H}_{29}\text{N}_4\text{O}_2$ requires 465.2285.

4.64. 1-(5-(*tert*-Butoxycarbonyl)-3-phenyl-5H-pyrido[4,3-*b*]indol-1-yl)quinuclidin-1-ium (**6c**)

Compound **6c** was obtained as described for **6b** using quinuclidine. At the end of the reaction, volatiles were removed under reduced pressure and the crude material was purified by flash chromatography using $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (100/0 to 95/5) as eluent to afford the desired product as a white solid (96 mg, 62%).

R_f (9:1 DCM/MeOH) 0.62; mp: 218–219 °C; IR (ATR diamond) ν 2974, 2936, 2884, 1736, 1681, 1596, 1537, 1371, 1353, 1325, 1252, 1198, 1122, 996, cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.10 (s, 1H, H_{Ar}), 8.57–8.42 (m, 1H, H_{Ar}), 8.12–8.01 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 7.92 (dt, J = 7.6, 1.1 Hz, 1H, H_{Ar}), 7.75–7.58 (m, 2H, 2 $\times\text{H}_{\text{Ar}}$), 7.55–7.40 (m, 3H, 3 $\times\text{H}_{\text{Ar}}$), 4.40–4.23 (m, 6H, 3 $\times\text{CH}_2$), 2.54 (quint, J = 3.3 Hz, 1H, CH), 2.47–2.25 (m, 6H, 2 $\times\text{CH}_2$), 1.77 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 152.6 (C_q), 149.5 (C_q), 149.1 (C_q), 148.8 (C_q), 139.4 (C_q), 136.8 (C_q), 130.4 (CH), 129.7 (CH), 129.2 (2 $\times\text{CH}$), 127.0 (2 $\times\text{CH}$), 125.4 (CH), 123.1 (CH), 119.4 (C_q), 117.4 (CH), 111.4 (C_q), 109.5 (CH), 87.2 (C_q), 56.3 (3 $\times\text{CH}_2$), 28.2 (3 $\times\text{CH}_3$), 24.4 (3 $\times\text{CH}_2$), 19.9 (CH); ^{19}F NMR (235 MHz, CDCl_3) δ -75.67; HRMS (EI-MS): MH^+ , found 454.2490. $\text{C}_{29}\text{H}_{32}\text{N}_3\text{O}_2$ requires 454.2489.

4.65. 1-(5-(*tert*-Butoxycarbonyl)-3-phenyl-5H-pyrido[4,3-*b*]indol-1-yl)-1,4-diazabicyclo[2.2.2]octan-1-ium (**6d**)

Compound **6d** was obtained as described for **6b** using DABCO (3.0 equiv.). At the end of the reaction, volatiles were removed under reduced pressure and the crude material washed with *n*-pentane to afford the desired product as a white solid (318 mg, 57%). R_f (9:1 DCM/MeOH) 0.50; mp: 186–187 °C; IR (ATR diamond) ν 3605, 3430, 3343, 3004, 2991, 1725, 1693, 1663, 1597, 1406, , 1360, 1197, 1154, 1136, 1119, 962, cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 9.14 (s, 1H, H_{Ar}), 8.54 (dd, J = 7.9, 1.6 Hz, 1H, H_{Ar}), 8.16–8.04 (m, 3H,), 7.78–7.63 (m, J = 7.6, 1.4 Hz, 2H, 2 $\times\text{H}_{\text{Ar}}$), 7.58–7.45 (m, 3H, 3 $\times\text{H}_{\text{Ar}}$), 4.39 (dd, J = 8.7, 6.2 Hz, 6H, 3 $\times\text{CH}_2$), 3.69 (dd, J = 8.7, 6.4 Hz, 6H, 3 $\times\text{CH}_2$), 1.84 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 153.1 (C_q), 149.7 (C_q), 149.3 (C_q), 148.2 (C_q), 139.6 (C_q), 137.0 (C_q), 130.5 (CH), 129.9 (CH), 129.3 (2 $\times\text{CH}$), 127.3 (2 $\times\text{CH}$), 125.7 (CH), 123.7 (CH), 119.3 (C_q), 117.5 (CH), 111.8 (C_q), 109.8 (CH), 87.3 (C_q), 53.9 (3 $\times\text{CH}_2$), 46.1 (3 $\times\text{CH}_2$), 28.4 (3 $\times\text{CH}_3$); ^{19}F NMR (376 MHz, CDCl_3) δ -75.26; HRMS (EI-MS): MH^+ , found 455.2437. $\text{C}_{28}\text{H}_{31}\text{N}_4\text{O}_2$ requires 455.2442.

4.66. *tert*-Butyl 1-fluoro-3-phenyl-5H-pyrido[4,3-*b*]indole-5-carboxylate (**8**)

In a microwave tube a suspension of **6c** (80 mg, 0.14 mmol, 1.0 equiv.) in ACN (1 mL) was stirred and TBAF in THF 1M (704 μL , 0.70 mmol, 5.0 equiv.) was added. The tube was sealed and heated up to 120 °C under microwave irradiation for 30 min. After cooling, the solvent was removed under reduced pressure then the crude material was solubilized in THF (1 mL). Boc_2O (46 mg, 0.21 mmol, 1.55 equiv.), DMAP (2 mg, 0.01 mmol, 0.1 equiv.) and Et_3N (39 μL , 0.28 mmol, 2.0 equiv.) were added. The reaction mixture was left under stirring at r.t. for 12h. Volatiles were removed under reduced pressure and the resulting crude was purified by flash chromatography using PE/EtOAc (95/5) to afford the desired product as a white solid (25.2 mg, 49%). R_f (8:2 PE/EtOAc) 0.53; mp: 162–163 °C; IR (ATR diamond) ν 2977, 2928, 2847, 1731, 1604, 1474, 1407, 1319, 1308, 1274, 1256, 1223, 1149, 1127, 926 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.59 (d, J = 2.5 Hz, 1H, H_{Ar}), 8.30 (d, J = 8.4 Hz, 1H, H_{Ar}), 8.16–8.07 (m, 3H, 3 $\times\text{H}_{\text{Ar}}$), 7.59–7.38 (m, 5H, 5 $\times\text{H}_{\text{Ar}}$), 1.81 (s, 9H, 3 $\times\text{CH}_3$); ^{13}C NMR (101 MHz, CDCl_3) δ 159.0 (C_q), 154.9 (d, J = 348.5 Hz, C_q), 153.0 (C_q), 150.4 (C_q), 148.6 (d, J = 11.1 Hz, C_q), 138.7 (d, J = 5.0 Hz, C_q), 129.4 (CH), 129.0 (2CH), 128.0 (CH), 127.3 (2CH), 124.5 (CH), 122.6 (d, J = 3.9 Hz, CH), 121.9 (d, J = 5.9 Hz, C_q), 116.2 (CH), 107.0 (d, J = 38.8 Hz, C_q), 106.1 (d, J = 5.1 Hz, CH), 85.6 (C_q), 28.5 (3 $\times\text{CH}_3$); ^{19}F NMR (376 MHz, CDCl_3) δ -70.06 (d, J = 2.6 Hz); HRMS (EI-MS): MH^+ , found 363.1502. $\text{C}_{22}\text{H}_{20}\text{FN}_2\text{O}_2$ requires 363.1503.

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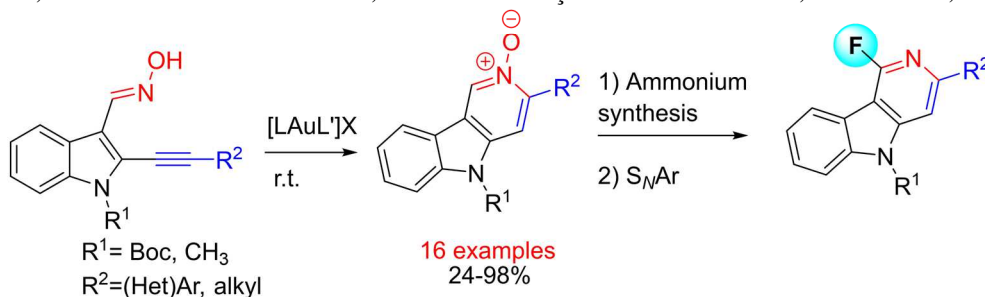
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Synthesis of γ -carboline *N*-oxide under Gold(I)-catalysis and C-1 amino and fluoro γ -carboline.

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