Supporting Information

For

A general synthesis of arylindoles and (1-arylvinyl)carbazoles via a one-pot reaction from $N$-tosylhydrazones and 2-nitro-haloarenes and their potential application to colon cancer

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List of Contents

Table des matières

I. COMPARATIVE SYNTHESIS OF COMPOUND 71 BY: ................................................................. 2
   a) the one-pot approach from $N$-tosylhydrazones and ortho-nitro-haloarenes, followed by reduction. .......... 2
   b) functionalization of carbazole and coupling with $N$-tosylhydrazones. ............................................................ 2

II. GENERAL METHODS ...................................................................................................................... 2

III. GENERAL PROCEDURE FOR ONE-POT SYNTHESIS OF INDOLES AND CARBAZOLES ................................................................................................................................. 3

IV. PRODUCT CHARACTERIZATIONS ................................................................................................. 3

V. GENERAL PROCEDURE FOR THE METHYLATION REACTION .............................................. 22

VI. $N$-METHYLATED PRODUCT CHARACTERIZATIONS ............................................................. 22

VII. BIOLOGY .................................................................................................................................... 24

VIII. $^1$H, $^{13}$C NMR SPECTRA ........................................................................................................... 25
I. Comparative synthesis of compound 7i by:

a) the one-pot approach from \( N \)-tosylhydrazones and ortho-nitro-haloarenes, followed by reduction.

\[
\begin{align*}
\text{R}^1 &= \text{Br} & \text{R}^2 &= \text{NO}_2 \\
1) & \text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3 (2.5 \text{ mol %}) & \text{XPhos (10 mol %)} & \text{LiOtBu (2.2 equiv)} & \text{dioxane, 110°C, 5h} \\
2) & \text{PPH}_3 (4 \text{ equiv}) & 100°C, 24h & \text{Sealed tube}
\end{align*}
\]

- **Overall yield = 61%**
- **Access to the free amine carbazole**

b) functionalization of carbazole and coupling with \( N \)-tosylhydrazones.

For comparison, compound 7i was prepared from commercial carbazole (Scheme 1, SI). After methylation of the free amine, Friedel-Craft acylation which constitutes the limiting step leads to the corresponding (carbazol-3-yl)ethanone. This latter was converted to hydrazone and then, the coupling with 5-iodo-3,4,5-trimethoxybenzene afforded compound 7i in a 14% overall yield.

- **Overall yield = 14%**
- **Difficulty to access to the free amine carbazole**

Scheme 1. a) NaH, CH\(_3\)I, DMF, 0°C to RT (96%); b) AcCl, AlCl\(_3\), DCM, RT to reflux, 2h (50%); c) TsNHNH\(_2\), APTS cat., MeOH, reflux, 4h (52%); 5-iodo-1,2,3-trimethoxybenzene, Pd\(_2\)(dba)\(_3\)·CHCl\(_3\), XPhos, LiOtBu, dioxane, sealed tube, 100°C, 3h (57%).

II. General methods

Melting points (mp) were recorded on a Büchi B-450 apparatus and were uncorrected. NMR spectra were performed on a Bruker AMX 200 (\( ^1\text{H} \), 200 MHz; \( ^{13}\text{C} \), 50 MHz; \( ^{19}\text{F} \), 88 MHz), Bruker AVANCE 300 or Bruker AVANCE 400 (\( ^1\text{H} \), 300 MHz or 400 MHz; \( ^{13}\text{C} \), 75 MHz or 100 MHz). Solvent peaks were used as reference values with CDCl\(_3\) at 7.26 ppm for \( ^1\text{H} \) NMR and 77.16 ppm for \( ^{13}\text{C} \) NMR, with DMSO at 2.50 ppm for \( ^1\text{H} \) NMR and 39.52 ppm for \( ^{13}\text{C} \) NMR.
with CD$_3$CN at 1.94 ppm for $^1$H NMR and 1.32 and 118.26 ppm for $^{13}$C NMR, and with (CD$_3$)$_2$CO at 2.05 ppm for $^1$H NMR and 29.84 and 206.26 ppm for $^{13}$C NMR. Chemical shifts $\delta$ are given in ppm, and the following abbreviations are used: singlet (s), doublet (d), doublet of doublet (dd), triplet (t), quadruplet (q) and multiplet (m). Infrared spectra (IR) were measured on a Bruker Vector 22 spectrophotometer and were recorded in film (film, cm$^{-1}$). High resolution mass spectra were recorded on a MicrotofQ Bruker Daltonics. Reaction courses and product mixtures were routinely monitored by TLC on silica gel (precoated F254 Merck plates), and compounds were visualized under a UVP Mineralight UVGL-58 lamp (254 nm) and with phosphomolybdic acid/Δ, or vanillin/Δ. Flash chromatography was performed using silica gel 60 (40–63 mm, 230–400 mesh) at medium pressure (200 mbar). Dioxane was distilled over CaH$_2$. Others solvents were used as received. N-Tosylhydrazones were prepared according to literature procedure. Pd$_2$(dba)$_3$·CHCl$_3$ was prepared according to literature procedure (Organometal. Chem. 1974, 65, 253). XPhos was purchased from Sigma-Aldrich. Others reagent were purchased from Sigma-Aldrich, Alfa Aesar and Acros. All products reported showed $^1$H and $^{13}$C NMR spectra in agreement with the assigned structures.

III. General procedure for one-pot synthesis of indoles and carbazoles
A 5 mL sealed tube under argon atmosphere was charged with N-tosylhydrazone (0.5 mmol, 1.0eq), 1-bromo-2-nitroarene (0.5 mmol, 1.0eq), Pd$_2$(dba)$_3$·CHCl$_3$ (5 mol %), and XPhos (10 mol %). Then dioxane (2mL) was added via syringe and the mixture was stirred at room temperature for 1 min before the addition of LiO-t-Bu (1.1 mmol, 2.2 eq). Then the flask was put into a preheated oil bath (110 °C) and stirred. After 5h, PPh$_3$ (2 mmol, 4.0eq) was added to the same reaction mixture which was stirred at 160 °C for 24-30 h. The crude reaction mixture was allowed to cool to room temperature. EtOAc was added to the mixture, which was filtered through Celite®. The solvents were evaporated under reduced pressure, and the crude residue was purified by column chromatography on silica gel.

IV. Product characterizations
3-(3,4,5-trimethoxyphenyl)-1H-indole (4a)

Column chromatography on silica gel afforded 123 mg of the desired indole 4a (0.44 mmol, yield 87%), white solid, m.p.: 140-141 °C. TLC: Rf= 0.15 (cyclohexane/EtOAc 8/2). IR (film, cm$^{-1}$):2936, 2834, 2360, 1735, 1585, 1547, 1502, 1459, 1409, 1362, 1335, 1285, 1237, 1222, 1175, 1123, 1098, 1045. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) 8.55(s, 1H), 7.95 (d, $J$=7.8 Hz,
H), 7.45 (d, J = 7.8 Hz, 1H), 7.35 (s, 1H), 7.32-7.19 (m, 2H), 6.92 (s, 2H); 3.96(s, 9H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm) 153.7 (C), 136.8 (C), 131.5 (C), 125.8 (C), 122.6 (CH), 121.8 (CH), 120.5 (CH), 119.8 (CH), 118.6 (C), 111.6 (CH), 105.0 (2CH), 60.8 (CH$_3$), 56.3 (2CH$_3$). HRMS (ESI): for C$_{17}$H$_{17}$NO$_3$Na (M+Na)$^+$: m/z calcd 306.1106, found 306.1105.

3-(3,5-dimethoxyphenyl)-1H-indole (4b)

![3-(3,5-dimethoxyphenyl)-1H-indole (4b)](image)

Column chromatography on silica gel afforded 117 mg of the desired indole 4b (0.46 mmol, yield 92%). Yellowish-brown oil. TLC: Rf= 0.43 (cyclohexane/EtOAc 8/2). IR (film, cm$^{-1}$):2960, 2926, 2361, 2340, 1605,1590, 1527, 1454, 1424, 1351, 1278, 1205, 1157, 1065, 1049, 909.$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) 8.19 (s, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.33(d, J = 7.5 Hz 1H), 7.26 (d, J = 2.4 Hz, 1H), 7.22 – 7.09 (m, 2H), 6.78 (d, J = 2.1 Hz, 2H), 6.38 (t, J = 2.1 Hz, 1H), 3.82 (s, 6H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm) 161.2 (2C), 137.6 (C), 136.8 (C), 125.8 (C), 122.6 (CH), 122.2 (CH), 120.5 (CH), 120.0 (CH), 118.3 (C), 111.6 (CH), 106.8 (2CH), 98.3 (CH), 55.5 (2CH$_3$). HRMS (ESI): for C$_{16}$H$_{16}$NO$_2$ (M+H)$^+$: m/z calcd 254.1181, found 254.1177.

3-(4-methoxyphenyl)-1H-indole (4c)

![3-(4-methoxyphenyl)-1H-indole (4c)](image)

Column chromatography on silica gel afforded 84 mg of the desired indole 4c (0.38 mmol, yield 75%). Off-white solid, m.p. = 133-135°C. TLC: Rf= 0.43 (cyclohexane/EtOAc 8/2). IR (film, cm$^{-1}$):3403, 2835, 1612, 1549, 1502, 1456, 1408, 1332, 1303, 1281, 1246, 1179, 1110, 1032. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ (ppm) 8.18 (s, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 8.3 Hz, 2H), 7.42 (d, J = 8.1 Hz, 1H), 7.29 (d, J = 2.4 Hz, 1H), 7.3– 7.17 (m, 2H), 7.02 (d, J = 8.3 Hz, 2H), 3.88 (s, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ (ppm) 158.2 (C), 136.7 (C), 128.8 (2CH), 128.3 (C), 126.1 (C), 122.4 (CH), 121.3 (CH), 120.3 (CH), 119.9 (CH), 118.2 (C), 114.4 (2CH), 111.5 (CH), 55.5 (CH$_3$). HRMS (ESI): for C$_{15}$H$_{14}$NO (M+H)$^+$: m/z calcd 224.1075, found 224.1075.
3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1H-indole (4d)

![Chemical structure of 3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1H-indole (4d)](image)

Column chromatography on silica gel afforded 92 mg of the desired indole 4d (0.365 mmol, yield 73%). Light brown solid, m.p. = 101-103°C. TLC: Rf= 0.46 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3407, 2977, 2927, 2874, 2360, 1617, 1586, 1552, 1500, 1456, 1411, 1348, 1330, 1317, 1298, 1281, 1260, 1244, 1189, 1124, 1096, 1067, 1048, 1014. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.10 (s, 1H), 8.07 (d, J = 6.7 Hz, 1H), 7.41 – 7.34 (m, 3H), 7.32 (dd, J = 7.2, 2.0 Hz, 1H), 7.28 (dd, J = 8.3, 2.0 Hz, 1H), 7.23 (d, J = 2.2 Hz, 1H), 7.10 (d, J = 8.3 Hz, 1H), 4.34 (s, 4H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 143.8 (C), 142.1 (C), 136.7 (2C), 129.3 (C), 125.8 (C), 122.4 (CH), 121.5 (CH), 120.8 (CH), 120.2 (CH), 119.8 (CH), 117.6 (CH), 116.2 (CH), 111.5 (CH), 64.6 (CH₂), 64.5 (CH₂). HRMS (ESI): for C₁₆H₁₄NO₂ (M+H)⁺: m/z calcd 252.1025, found 252.1020.

3-(4-fluorophenyl)-1H-indole (4e)

![Chemical structure of 3-(4-fluorophenyl)-1H-indole (4e)](image)

Column chromatography on silica gel afforded 85 mg of the desired indole 4e (0.4 mmol, yield 80%). Off-white solid, m.p. = 102-103°C. TLC: Rf= 0.56 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3407, 3059, 2926, 2360, 1595, 1551, 1500, 1456, 1424, 1403, 1331, 1296. 1258, 1236, 1216, 1157, 1096, 1014. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.21 (s, 1H), 7.90 (d, J = 7.2 Hz, 1H), 7.69-7.59 (m, 2H), 7.45 (d, J = 7.6 Hz, 1H), 7.32 (s, 1H), 7.30-7.20 (m, 2H), 7.20-7.12 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 161.6 (d, J = 244.7 Hz, CF), 136.7 (C), 131.7 (d, J = 3.0 Hz, C), 129.1 (d, J = 7.7 Hz, 2CH) 125.9 (C), 122.7 (CH), 121.7 (CH), 120.5 (CH), 119.7 (CH), 117.6 (C), 115.7 (d, J = 21.3 Hz, 2CH), 111.6 (CH). ¹⁹F NMR (188 MHz, CDCl₃) δ (ppm) -115.1 (s). HRMS (ESI): for C₁₄H₁₁NF (M+H)⁺: m/z calcd 212.0876, found 212.0872.
4-(1H-indol-3-yl)benzonitrile (4f)

Column chromatography on silica gel afforded 87 mg of the desired indole 4f (0.4 mmol, yield 80%). White-yellowish solid, m.p.= 168-169°C. TLC: Rf= 0.38 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3357, 2963, 2954, 2362, 2224, 1604, 1554, 1540, 1491, 1430, 1407, 1335, 1261, 1239, 1179, 1114, 1016, 961. 1H NMR (300 MHz, CDCl₃) δ (ppm) 8.46 (s, 1H), 7.91 (d, J = 7.7 Hz, 1H), 7.76 (d, J = 8.2 Hz, 2H), 7.69 (d, J = 8.5 Hz, 2H), 7.47-7.44 (m, 2H), 7.31 – 7.21 (m, 2H). 13C NMR (75 MHz, CDCl₃) δ (ppm) 140.8 (C), 136.9 (C), 132.7 (2CH), 127.5 (2CH), 125.2 (C), 123.3 (CH), 123.1 (CH), 121.2 (CH), 119.6 (CH), 116.8 (C), 111.9 (CH), 108.9 (C). HRMS (ESI): for C₁₅H₁₁N₂ (M+H)⁺: m/z calcld 219.0922, found 219.0915.

3-([1,1'-biphenyl]-4-yl)-1H-indole (4g)

Column chromatography on silica gel afforded 123 mg of the desired indole 4g (0.455 mmol, yield 91%). Off-white solid, m.p.= 181-183°C. TLC: Rf= 0.6 (cyclohexane/ Ethyl acetate 8/2). IR (film, cm⁻¹): 3429, 3057, 3029, 1485, 1456, 1425, 1403, 1256, 1236, 1119. 1H NMR (300 MHz, CDCl₃) δ (ppm) 8.15 (s, 1H), 7.93 (d, J = 7.5 Hz, 1H), 7.69 (d, J= 8.3 Hz, 2H), 7.64-7.58 (m, 4H), 7.42-7.32 (m, 4H), 7.30 (d, J = 7.2 Hz, 1H), 7.24 – 7.11 (m, 2H). 13C NMR (75 MHz, CDCl₃) δ (ppm) 141.2 (C), 138.9 (C), 136.9 (C), 134.8 (C), 128.9 (2CH), 127.9 (2CH), 127.6 (2CH), 127.2 (CH), 127.1 (2CH), 125.9 (C), 122.6 (CH), 122.0 (CH), 120.5 (CH), 120.0 (CH), 118.0 (C), 111.6 (CH). HRMS (ESI): for C₂₀H₁₆N (M+H)⁺: m/z calcld 270.1283, found 270.1275.
3-(naphthalen-2-yl)-1H-indole (4h)

Column chromatography on silica gel afforded 103 mg of the desired indole 4h (0.425 mmol, yield 85%). Light brown solid, m.p. = 139-140°C. TLC: Rf = 0.41 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3423, 3393, 3056, 1626, 1596, 1541, 1455, 1416, 1336, 1264, 1238, 1199, 1130, 1112, 1015. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.26 (s, 1H), 8.16 (s, 1H), 8.09 (d, J = 7.3 Hz, 1H), 7.95 - 7.81 (m, 4H), 7.52 - 7.45 (m, 4H), 7.34 – 7.23 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 136.9 (C), 134.1 (C), 133.2 (C), 132.2 (C), 128.4 (CH), 127.9 (CH), 127.8 (CH), 126.6 (CH), 126.3 (CH), 126.0 (C), 125.4 (2CH), 122.7 (CH), 122.3 (CH), 120.6 (CH), 120.1 (CH), 118.4 (C), 111.6 (CH). HRMS (ESI): for C₁₈H₁₄N (M+H)⁺: m/z calcd 244.1126, found 244.1121.

3-(benzofuran-2-yl)-1H-indole (4i)

Column chromatography on silica gel afforded 64 mg of the desired indole 4i (0.275 mmol, yield 55%). White solid, m.p. = 165-166 °C. TLC: Rf = 0.34 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3405, 3056, 2923, 2853, 2360, 2341, 1626, 1611, 1453, 1426, 1360, 1334, 1308, 1251, 1172, 1102, 1011. ¹H NMR (300 MHz, CD₃CN) δ (ppm) 9.55 (s, 1H), 7.90 (dd, J = 6.1, 2.3 Hz, 1H), 7.67 (d, J = 2.7 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.41 – 7.36 (m, 2H), 7.14 – 7.07 (m, 4H), 6.86 (d, J = 0.7 Hz, 1H). ¹³C NMR (75 MHz, CD₃CN) δ (ppm) 154.7 (C), 154.4 (C), 137.8 (C), 130.8 (C), 125.2 (C), 125.0 (CH), 124.2 (CH), 123.8 (CH), 123.6 (CH), 121.6 (CH), 121.1 (CH), 120.8 (CH), 113.0 (CH), 111.4 (CH), 108.1 (C), 99.9 (CH). HRMS (ESI): for C₁₆H₁₂NO (M+H)⁺: m/z calcd 234.0919, found 234.0912.
6,11-dihydrochromeno[4,3-b]indole (4j)

Column chromatography on silica gel afforded 47 mg of the desired indole 4j (0.21 mmol, yield 42%). Yellowish oil. TLC: Rf = 0.16 (cyclohexane/EtOAc 9/1). IR (film, cm⁻¹): 3399, 3071, 2930, 1504, 1455, 1391, 1365, 1334, 1277, 1254, 1223, 1195, 1150, 1104, 1034, 1012, 928. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.05 (s, 1H), 8.03 – 7.96 (m, 1H), 7.82 – 7.77 (m, 1H), 7.45 – 7.39 (m, 1H), 7.29 – 7.25 (m, 2H), 7.11 – 7.08 (m, 2H), 7.02 – 6.98 (m, 1H), 5.48 (s, 2H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 151.4 (C), 136.8 (C), 130.1 (C), 126.1 (CH), 124.7 (C), 124.1 (C), 122.8 (CH), 122.5 (CH), 122.3 (CH), 121.2 (CH), 119.8 (CH), 116.4 (CH), 111.7 (CH), 107.2 (C), 63.9(CH₂). HRMS (ESI): for C₁₅H₁₂NO (M+H)⁺: m/z calcd 222.0919, found 222.0921.

2,3,4,9-tetrahydro-1H-carbazole (4k)

Column chromatography on silica gel afforded 46 mg of the desired indole 4k (0.27 mmol, yield 54%). Yellowish solid, m.p. = 108-110 °C. TLC: Rf = 0.44 (cyclohexane/EtOAc 9/1). IR (film, cm⁻¹): 3399, 3051, 2929, 2852, 2360, 1621, 1589, 1469, 1440, 1364, 1326, 1304, 1235, 1010.¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.64 (s, 1H), 7.47 (d, J = 6.9 Hz, 1H), 7.30 – 7.24 (m, 1H), 7.16 – 7.05 (m, 2H), 2.75 – 2.71 (m, 4H), 1.94 – 1.87 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 135.8 (C), 134.2 (C), 127.9 (C), 121.1 (CH), 119.2 (CH), 117.8 (CH), 110.5 (CH), 110.3 (C), 23.4 (2CH₂), 23.3 (CH₂), 21.0 (CH₂). HRMS (ESI): for C₁₂H₁₄N (M+H)⁺: m/z calcd 172.1126, found 172.1123.
6-methoxy-3-(3,4,5-trimethoxyphenyl)-1H-indole (4l)

Column chromatography on silica gel afforded 102 mg of the desired indole 4l (0.325 mmol, yield 65%). White solid, m.p.: 111-113 °C. TLC: Rf = 0.11 (cyclohexane/EtOAc 8/2). IR (film, cm\(^{-1}\)) :2833, 1629, 1586, 1547, 1395, 1363, 1337, 1251, 1234, 1199, 1161, 1124, 1029. 1H NMR (300 MHz, CDCl\(_3\)) \(\delta\) (ppm) 8.36 (s, 1H), 7.78 (d, \(J = 8.5\) Hz, 1H), 7.22 (d, \(J = 2.3\) Hz, 1H), 6.90 (s, 2H), 6.87 (s, 2H), 3.93 (s, 6H), 3.92 (s, 3H), 3.86 (s, 3H). 13C NMR (75 MHz, CDCl\(_3\)) \(\delta\) (ppm) 156.9 (C), 153.7 (C), 137.6 (C), 131.5 (C), 120.5 (CH), 120.4 (CH), 120.3 (C), 118.6 (C), 110.5 (CH), 104.8 (2CH), 95.0 (CH), 61.1 (CH\(_3\)), 56.3 (2CH\(_3\)), 55.8 (CH\(_3\)). HRMS (ESI): for C\(_{18}\)H\(_{19}\)NO\(_4\)Na (M+Na)*: \(m/z\) calcd 336.1212, found 336.1205.

3-(3,5-dimethoxyphenyl)-6-methoxy-1H-indole (4m)

Column chromatography on silica gel afforded 130 mg of the desired indole 4m (0.46 mmol, yield 92%). White solid, m.p.: 105-107°C. TLC: Rf = 0.23 (cyclohexane/EtOAc 8/2). IR (film, cm\(^{-1}\)) : 3407, 2998, 2835, 1631, 1605, 1590, 1572, 1546, 1502, 1454, 1425, 1394, 1394, 1360, 1338, 1300, 1252, 1201, 1151, 1113, 1065, 1057, 1029, 1007. 1H NMR (300 MHz, CDCl\(_3\)) \(\delta\) (ppm) 8.52 (s, 1H), 8.23 (d, \(J = 8.6\) Hz, 1H), 7.67 (d, \(J = 2.1\) Hz, 1H), 7.30-7.25 (m, 2H), 7.23 (d, \(J = 2.2\) Hz, 2H), 6.84 (t, \(J = 2.1\) Hz, 1H), 4.27 (s, 9H). 13C NMR (75 MHz, CDCl\(_3\)) \(\delta\) (ppm) 161.2 (3C), 156.8 (C), 137.6 (C), 120.9 (CH), 120.7 (CH), 120.1 (C), 118.5 (C), 110.5 (CH), 106.6 (2CH), 98.3 (CH), 94.9 (CH), 55.8 (CH\(_3\)), 55.5 (2CH\(_3\)). HRMS (ESI): for C\(_{17}\)H\(_{18}\)NO\(_3\) (M+H)*: \(m/z\) calcd 284.1287, found 284.1283.
3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-6-methoxy-1H-indole (4n)

Column chromatography on silica gel afforded 110 mg of the desired indole 4n (0.4 mmol, yield 78%). White solid, m.p. = 146-147°C. TLC: Rf= 0.19 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3362, 3347, 2990, 2928, 2883, 2363, 1623, 1552, 1495, 1453, 1435, 1388, 1358, 1324, 1296, 1280, 1260, 1243, 1230, 1201, 1163, 1126, 1105, 1064, 1028. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.04 (s, 1H), 7.78 (d, J = 8.6 Hz, 1H), 7.17 (s, 2H), 7.14 (dd, J = 8.4, 1.3 Hz, 1H), 6.95 (d, J = 8.3 Hz, 1H), 6.89 (s, 1H), 6.85 (d, J = 8.6 Hz, 1H), 4.31 (s, 4H), 3.86 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 156.8 (C), 143.8 (C), 142.1 (C), 137.5 (C), 129.3 (C), 120.7 (CH), 120.6 (CH), 120.3 (C), 120.1 (CH), 117.9 (C), 117.6 (CH), 116.1 (CH), 110.3 (CH), 94.9 (CH), 64.6 (2CH₂), 55.8 (CH₃). HRMS (ESI): for C₁₇H₁₆NO₃ (M+H)⁺: m/z calcd 282.1130, found 282.1127.

3-(4-fluorophenyl)-6-methoxy-1H-indole (4o)

Column chromatography on silica gel afforded 98 mg of the desired indole 4o (0.41 mmol, yield 82%). Light brown solid, m.p. = 100-101°C. TLC: Rf= 0.3 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3414, 3383, 2927, 1625, 1546, 1499, 1455, 1390, 1355, 1329, 1306, 1281, 1265, 1247, 1221, 1198, 1164, 1111, 1024. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.08 (s, 1H), 7.78 (d, J = 8.6 Hz, 1H), 7.68 – 7.56 (m, 2H), 7.24 – 7.10 (m, 3H), 6.97 – 6.83 (m, 2H), 3.87 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 161.6 (d, J = 244.5 Hz, CF), 156.8 (C), 152.6 (C), 137.5 (C), 131.7 (C), 128.8 (d, J = 7.7 Hz, 2CH), 120.5 (CH), 120.3 (CH), 117.4 (C), 115.7 (d, J = 21.3 Hz, 2CH), 110.5 (CH), 94.9 (CH), 55.8 (CH₃). ¹⁹F NMR (188 MHz, CDCl₃) δ (ppm) -115.2 (s). HRMS (ESI): for C₁₅H₁₃NOF (M+H)⁺: m/z calcd 242.0981, found 242.0975.
3-(3,5-dimethoxyphenyl)-1H-indole-6-carbonitrile (4p)

Column chromatography on silica gel afforded 75mg of the desired indole 4p (0.27 mmol, yield 54%). Off-white solid, m.p. = 172-173 °C. TLC: Rf= 0.28 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 2959, 2926, 2854, 2219, 1725, 1606, 1593, 1459, 1361, 1340, 1287, 1205, 1156, 1121, 1070, 1012. ¹H NMR (300 MHz, CD₃CN) δ (ppm) 9.76 (s, 1H), 7.85 (d, J = 8.3 Hz, 1H), 7.74 (s, 1H), 7.60 (s, 1H), 7.24 (d, J = 9.1 Hz, 1H), 6.65 (s, 2H), 6.30 (s, 1H), 3.69 (s, 6H).¹³C NMR (75 MHz, CD₃CN) δ (ppm) 162.3 (2C), 137.5 (C), 136.6 (C), 129.3 (C), 128.2 (CH), 123.6 (CH), 121.4 (CH), 121.2 (C), 118.6 (C), 117.8 (CH), 106.3 (2CH), 106.0 (C), 99.3 (CH), 56.0 (2CH₃). HRMS (ESI): for C₁₇H₁₅N₂O₂ (M+H)⁺: m/z calcld 279.1134, found 279.1141.

3-(3,5-dimethoxyphenyl)-6-(trifluoromethyl)-1H-indole (4q)

Column chromatography on silica gel afforded 112 mg of the desired indole 4q (0.35 mmol, yield 70%). Off-white solid, m.p. = 151-153°C. TLC: Rf= 0.33 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3344, 2925, 1724, 1609, 1593, 1512, 1457, 1430, 1333, 1302, 1266, 1223, 1204, 1154, 1145, 1113, 1084, 1053, 1007. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.45 (s, 1H), 8.02 (d, J = 8.2 Hz, 1H), 7.71 (s, 1H), 7.51 (s, 1H), 7.43 (d, J = 8.6 Hz, 1H), 6.80 (s, 2H), 6.47 (s, 1H), 3.87 (s, 6H).¹³C NMR (75 MHz, CDCl₃) δ (ppm) 161.3 (2C), 136.7 (C), 135.6 (C), 128.1 (C), 124.6 (CH), 124.0 (q, J = 153.8 Hz, C), 120.4 (CH), 119.8 (C), 118.9 (C), 117.6 (d, J = 3.0 Hz, CH), 109.14 (d, J = 3.8 Hz, CH), 106.9 (2CH), 98.6 (CH), 55.6 (2CH₃). ¹⁹F NMR (188 MHz, CDCl₃) δ (ppm) -58.7 (s). HRMS (ESI): for C₁₇H₁₅NO₂F₃ (M+H)⁺: m/z calcld 322.1055, found 322.1058.
3-(3,5-dimethoxyphenyl)-1H-pyrrolo[2,3-b]pyridine (4r)

Column chromatography on silica gel afforded 64 mg of the desired indole 4r (0.25 mmol, yield 50%). Light brown solid, m.p. = 156-158°C. TLC: Rf = 0.42 (cyclohexane/EtOAc 5/5). IR (film, cm⁻¹): 2959, 2925, 2854, 2359, 1729, 1596, 1538, 1461, 1356, 1283, 1204, 1155, 1110, 1068, 1012. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 11.29 (s, 1H), 8.41 (s, 1H), 8.30 (d, J = 7.4 Hz, 1H), 7.59 (s, 1H), 7.19 (s, 1H), 6.82 (d, J = 2.2 Hz, 2H), 6.45 (t, J = 2.2 Hz, 1H), 3.87 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 161.4 (2C), 149.3 (C), 142.9 (CH), 137.1 (C), 128.7 (CH), 122.8 (CH), 119.0 (C), 116.4 (CH), 113.0 (C), 106.5 (2CH), 98.4 (CH), 55.5 (2CH₃). HRMS (ESI): for C₁₅H₁₅N₂O₂ (M+H)⁺: m/z calcd 255.1134, found 255.1128.

3-phenyl-1H-pyrrolo[2,3-b]pyridine (4s)

Column chromatography on silica gel afforded 53 mg of the desired indole 4s (0.275 mmol, yield 55%). White solid, m.p. = 194-196°C. TLC: Rf = 0.23 (cyclohexane/EtOAc 7/3). IR (film, cm⁻¹): 2961, 2923, 2852, 2360, 1736, 1601, 1536, 1495, 1463, 1437, 1417, 1260, 1202, 1161, 1075, 1029, 1015. ¹H NMR (300 MHz, DMSO) δ (ppm) 11.88 (s, 1H), 8.25 (d, J = 6.3 Hz, 2H), 7.83 (d, J = 1.8 Hz, 1H), 7.69 (d, J = 7.8 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.22 (t, J = 7.3 Hz, 1H), 7.15 – 7.09 (m, 1H). ¹³C NMR (75 MHz, DMSO) δ (ppm) 149.1 (C), 142.9 (CH), 135.1 (C), 128.9 (2CH), 127.4 (CH), 126.2 (2CH), 12.6 (CH), 123.7 (CH), 117.3 (C), 116.0 (CH), 114.3(C). HRMS (ESI): for C₁₃H₁₁N₂ (M+H)⁺: m/z calcd 195.0922, found 195.0918.
3-(3,5-dimethoxyphenyl)-1H-pyrrolo[3,2-b]pyridine (4t)

Column chromatography on silica gel afforded 58 mg of the desired indole 4t (0.23 mmol, yield 46%). White solid, m.p.= 218-220°C. TLC: Rf= 0.5 (cyclohexane/EtOAc 5/5). IR (film, cm⁻¹): 3114, 2942, 2814, 2360, 1606, 1587, 1451, 1409, 1354, 1333, 1282, 1246, 1204, 1154, 1124, 1106, 1062, 1020.¹H NMR (300 MHz, DMSO-d₆) δ (ppm) 11.57 (s, 1H), 8.44 (d, J = 4.0 Hz, 1H), 8.20 (d, J = 2.5 Hz, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.53 (s, 2H), 6.35 (s, 1H), 3.80 (s, 6H).¹³C NMR (300 MHz, DMSO-d₆) δ (ppm) 160.5 (2C), 143.5 (C), 142.7 (CH), 136.5 (C), 129.5 (C), 127.1 (CH), 118.9 (CH), 116.5 (CH), 114.0 (C), 104.1 (2CH), 97.2 (CH), 55.1 (2CH₃). HRMS (ESI): for C₁₅H₁₅N₂O₂ (M+H)⁺: m/z calcd 255.1134, found 255.1128.

3-(2,4-dimethoxyphenyl)-2-methyl-1H-indole (4u)

Column chromatography on silica gel afforded 87 mg of the desired indole 4u (0.325 mmol, yield 65%). Off-white solid, m.p.= 198-200°C. TLC: Rf= 0.42 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3385, 2958, 2958, 1611, 1563, 1502, 1461, 1437, 1414, 1332, 1302, 1278, 1258, 1209, 1186, 1157, 1136, 1049, 1032.¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.87 (s, 1H), 7.35 (d, J = 7.6 Hz, 1H), 7.24 (d, J = 2.8 Hz, 1H), 7.21 (d, J = 2.3 Hz, 1H), 7.08 (t, J = 7.2 Hz, 1H), 7.01 (t, J = 7.4 Hz, 1H), 6.59 – 6.53 (m, 2H), 3.84 (s, 3H), 3.73 (s, 3H), 2.31 (s, 3H).¹³C NMR (75 MHz, CDCl₃) δ (ppm) 159.9 (C), 158.4 (C), 153.5 (C), 132.6 (CH), 132.5 (C), 128.8 (C), 128.0 (C), 121.1 (CH), 119.6 (CH), 119.4 (CH), 116.6 (C), 110.3 (CH), 104.4 (CH), 99.1 (CH), 55.5 (2CH₃), 12.9 (CH₃). HRMS (ESI): for C₁₇H₁₈NO₂ (M+H)⁺: m/z calcd 268.1338, found 268.1330.
6-methoxy-2,3-diphenyl-1H-indole (4v)

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  +---+      +---+
 |    |      |    |
 | NH |      |    |
 |    |      +---+
 | OMe|      |    |
 +---+      +---+
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Column chromatography on silica gel afforded 116 mg of the desired indole 4v (0.385 mmol, yield 77%). White solid, m.p. = 207-208°C. TLC: Rf= 0.45 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3336, 2959, 2923, 2853, 1736, 1622, 1603, 1556, 1499, 1459, 1436, 1378, 1327, 1260, 1195, 1157, 1120, 1094, 1071, 1017. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.13 (s, 1H), 7.56 (d, J = 8.7 Hz, 1H), 7.47 – 7.37 (m, 5H), 7.37-7.27 (m, 5H), 6.93 (s, 1H), 6.83 (d, J = 8.7 Hz, 1H), 3.88 (s, 3H). ¹³C NMR (75 MHz, (CD₃)₂CO) δ (ppm) 158.0 (C), 138.4 (C), 136.9 (C), 134.2 (C), 133.9 (C), 131.0 (2CH), 129.5 (2CH), 129.4 (2CH), 129.0 (2CH), 128.1 (CH), 127.1 (CH), 124.2 (C), 120.7 (CH), 115.2 (C), 111.1 (CH), 95.4 (CH), 55.9 (CH₃). HRMS (ESI): for C₂₁H₁₈NO (M+H)⁺: m/z calcd 300.1388, found 300.1393.

2,3-bis(4-methoxyphenyl)-1H-indole (4w)

```
  +---+      +---+
 |    |      +---+
 | MeO|      |    |
 |    |      +---+
 |    |      |    |
 | NH |      +---+
 |    |      |    |
 | MeO|      +---+
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Column chromatography on silica gel afforded 135 mg of the desired indole 4w (0.41 mmol, yield 82%). White solid, m.p. = 92-93°C. TLC: Rf= 0.38 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3405, 2835, 1611, 1556, 1519, 1496, 1455, 1438, 1369, 1330, 1304, 1283, 1242, 1175, 1109, 1031. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.15 (s, 1H), 7.66 (d, J = 7.8 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.36 (d, J = 8.6 Hz, 4H), 7.25 – 7.11 (m, 2H), 6.96 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 3.86 (s, 3H), 3.82 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 159.3 (C), 158.2 (C), 135.9 (C), 133.9 (C), 131.3 (2CH), 130.1 (C), 129.5 (2CH), 129.18 (C), 127.7 (C), 125.5 (C), 122.4 (CH), 120.4 (CH), 119.6 (CH), 114.3 (2CH), 114.2 (2CH), 110.8 (CH), 55.4 (2CH₃). HRMS (ESI): for C₂₂H₂₀NO₂ (M+H)⁺: m/z calcd 330.1494, found 330.1496.
6,7-diphenyl-5H-[1,3]dioxolo[4,5-f]indole (4x)

Column chromatography on silica gel afforded 118 mg of the desired indole 4x (0.375 mmol, yield 75%). White solid, m.p.= 188-189°C. TLC: Rf= 0.49 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3400, 3043, 1601, 1537, 1357, 1336, 1245, 1200, 1163, 1119, 1072, 1039.¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.10 (s, 1H), 7.41–7.37 (m, 6H), 7.35–7.27 (m, 4H), 7.06 (s, 1H), 6.90 (s, 1H), 5.96 (s, 2H).¹³C NMR (75 MHz, CDCl₃) δ (ppm) 145.5 (C), 143.7 (C), 135.2 (C), 132.9 (C), 131.0 (C), 130.1 (2CH), 128.8 (CH), 128.7 (2CH), 127.8 (2CH), 127.3 (CH), 126.4 (2CH), 124.5 (C), 123.0 (C), 115.5 (C), 100.8 (CH₂), 98.4 (CH), 91.9 (CH). HRMS (ESI): for C₂₁H₁₆NO₂ (M+H)⁺: m/z calcd 314.1181, found 314.1180.

5-fluoro-6-methoxy-3-(3,4,5-trimethoxyphenyl)-1H-indole (4y)

Column chromatography on silica gel afforded 99 mg of the desired indole 4y (0.3 mmol, yield 60%). White solid, m.p.= 126-127°C. TLC: Rf= 0.15 (cyclohexane/EtOAc 7/3). IR (film, cm⁻¹): 3328, 2926, 2360, 1588, 1552, 1505, 1481, 1462, 1402, 1368, 1324, 1255, 1223, 1199, 1162, 1126, 1027, 1000.¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.27 (s, 1H), 7.54 (d, J = 11.9 Hz, 1H), 7.25 (s, 1H), 6.97 (d, J = 7.2 Hz, 1H), 6.79 (s, 2H), 3.92 (s, 9H), 3.90 (s, 3H).¹³C NMR (75 MHz, CDCl₃) δ (ppm) 153.7 (2C), 149.6 (d, J = 234.8 Hz, CF), 145.5 (d, J = 14.0 Hz, C), 136.8 (C), 132.7 (C), 131.2 (C), 121.3 (CH), 118.7 (d, J = 7.7 Hz, C), 118.6 (d, J = 8.8 Hz, C). ¹⁹F NMR (188 MHz, CDCl₃) δ (ppm) -143.2 (s). (HRMS (ESI): for C₁₈H₁₉NO₄F (M+H)⁺: m/z calcd 332.1298, found 332.1294.
From 6-(benzyloxy)-5-methoxy-3-(3,4,5-trimethoxyphenyl)-1H-indole
to 5-methoxy-3-(3,4,5-trimethoxyphenyl)-1H-indol-6-ol (4z)

Column chromatography on silica gel afforded 130 mg of 6-(benzyloxy)-5-methoxy-3-(3,4,5-
trimethoxyphenyl)-1H-indole (0.31 mmol, yield 62%). TLC: Rf= 0.25 (cyclohexane/EtOAc 7/3).

Then a stirred solution of 6-(benzyloxy)-5-methoxy-3-(3,4,5-trimethoxyphenyl)-1H-indole (0.19
mmol, 80 mg) and ammonium formate (0.95 mmol) in a anhydrous MeOH was degassed and
then 10% Pd/C (50% wt) was added under argon. The mixture was stirred at r.t. overnight. The
catalyst was filtered through celite® and the filtrate was concentrated under vacuum. The crude
residue was purified by column chromatography on silica gel to afford 51
mg of the title
compound 4z as dark red oil (yield 81%). TLC: Rf= 0.28 (cyclohexane/EtOAc 5/5). IR (film,
cm⁻¹): 3329, 2960, 2854, 2360, 2341, 1580, 1546, 1505, 1481, 1463, 1411, 1341, 1238, 1159, 1126, 1001. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.17 (s, 1H), 7.30 (t, $J = 5.7$ Hz,
1H), 7.18 (d, $J = 2.3$ Hz, 1H), 6.99 (t, $J = 5.9$ Hz, 1H), 6.83 (t, $J = 5.9$ Hz, 2H), 3.94 (s, 3H), 3.93
(s, 6H), 3.92 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 153.7 (3C), 143.7 (C), 143.3 (C),
131.8 (C), 131.5 (C), 120.3 (CH), 118.6 (C), 118.4 (C), 104.9 (2CH), 100.5 (CH), 96.9 (CH),
61.1 (CH₃), 56.6 (CH₃), 56.3 (2CH₃). HRMS (ESI): for C₁₈H₂₀NO₅ (M + H)⁺: m/z calcd
330.1341, found 330.1341.
From 6-(benzyloxy)-5-fluoro-3-(3,4,5-trimethoxyphenyl)-1H-indole to 5-fluoro-3-(3,4,5-trimethoxyphenyl)-1H-indol-6-ol (4aa)

Column chromatography on silica gel afforded 126 mg of 6-(benzyloxy)-5-fluoro-3-(3,4,5-trimethoxyphenyl)-1H-indole (0.31 mmol, yield 62%). TLC: Rf= 0.22 (cyclohexane/EtOAc 7/3).

Then a stirred solution of 6-(benzyloxy)-5-fluoro-3-(3,4,5-trimethoxyphenyl)-1H-indole (0.23 mmol, 100 mg) and ammonium formate (1.16 mmol) in anhydrous MeOH was degassed and then 10% Pd/C (50% wt) was added under argon. The mixture was stirred at r.t. overnight. The catalyst was filtered through celite® and the filtrate was concentrated under vacuum. The crude residue was purified by column chromatography on silica gel to afford 66mg of the title compound 4aa as dark red oil (yield 89%), TLC: Rf= 0.37 (cyclohexane/EtOAc 5/5).IR (film, cm⁻¹): 2961, 2924, 2853, 2360, 1738, 1554, 1506, 1469, 1412, 1332, 1261, 1235, 1160, 1126, 1102, 1010.¹H NMR (400 MHz, CDCl₃) δ 8.44 (s, 1H), 7.54 (d, J = 11.1 Hz, 1H), 7.25 (s, 1H), 7.03 (d, J = 5.6 Hz, 1H), 5.63(s, 1H), 6.80 (s, 2H), 3.92 (s, 9H).¹³C NMR (101 MHz, CDCl₃) δ (ppm) 153.7 (2C), 148.5 (d, J = 229.4 Hz, CF), 141.10 (d, J = 17.6 Hz, C), 136.8 (C), 133.2 (C), 131.19 (C), 121.6 (CH), 118.8 (d, J = 8.3 Hz, C), 118.4 (d, J = 3.0 Hz, C), 104.9 (d, J = 26.1 Hz, CH), 104.7 (2CH), 98.8 (CH), 61.1 (CH₃), 56.3 (2CH₃).¹⁹F NMR (188 MHz, CDCl₃) δ (ppm) -146.8 (s).HRMS (ESI): for C₁₇H₁₇NO₄F (M+H)⁺: m/z calcd 318.1142, found 318.1140.
2-(1-(3,4,5-trimethoxyphenyl)vinyl)-9H-carbazole (5a)

![Image of compound 5a]

Column chromatography on silica gel afforded 108 mg of the desired carbazole 5a (0.3 mmol, yield 60%). Brownish solid, m.p.=167-168 °C. TLC: Rf= 0.47 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3409, 2936, 1610, 1580, 1503, 1461, 1440, 1412, 1347, 1327, 1238, 1175, 1125, 1001. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.08 (d, J = 7.2 Hz, 2H), 8.03 (d, J = 8.1 Hz, 1H), 7.42 (d, J = 3.4 Hz, 2H), 7.39 (s, 1H), 7.31 – 7.24 (m, 2H), 6.62 (s, 2H), 5.55 (s, 1H), 5.47 (s, 1H), 3.90 (s, 3H), 3.80 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 160.6, 150.7, 144.4, 140.1, 139.6, 139.2, 126.0, 123.3, 123.1, 120.5, 120.2, 120.0, 119.7, 114.5, 110.7, 110.6, 106.9, 100.1, 55.5. HRMS (ESI): for C_{22}H_{20}NO₂ (M+H)^+: m/z calcd 360.1600, found 360.1599.

2-(1-(3,5-dimethoxyphenyl)vinyl)-9H-carbazole (5b)

![Image of compound 5b]

Column chromatography on silica gel afforded 115 mg of the desired carbazole 5b (0.35 mmol, yield 70%). White solid, m.p.=127-128 °C. TLC: Rf= 0.67 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3406, 3000, 2837, 2359, 1604, 1583, 1458, 1439, 1421, 1351, 1328, 1283, 1239, 1204, 1154, 1064, 1048. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.07 (d, J = 7.8 Hz, 2H), 7.98 (s, 1H), 7.41 (d, J = 3.7 Hz, 2H), 7.37 (s, 1H), 7.30 – 7.23 (m, 2H), 6.56 (d, J = 2.0 Hz, 2H), 6.48 (t, J = 2.3 Hz, 1H), 5.56 (s, 1H), 5.50 (s, 1H), 3.77 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 160.6, 150.7, 144.4, 140.1, 139.6, 139.2, 126.0, 123.3, 123.1, 120.5, 120.2, 120.0, 119.7, 114.5, 110.7, 110.6, 106.9, 100.1, 55.5. HRMS (ESI): for C_{22}H_{20}NO₂ (M+H)^+: m/z calcd 330.1494, found 330.1497.
4-(1-(9H-carbazol-2-yl)vinyl)benzonitrile (5c)

Column chromatography on silica gel afforded 70 mg of the desired carbazole 5c (0.235 mmol, yield 47%). Off-white solid, m.p. = 202-203°C. TLC: Rf = 0.39 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3407, 2361, 2341, 2227, 1605, 1563, 1492, 1460, 1441, 1399, 1327, 1241, 1205, 1066, 1017, 1000.¹H NMR (300 MHz, CDCl₃) δ (ppm): 8.09-8.02 (m, 3H), 7.64 (d, J = 8.2 Hz, 2H), 7.50 (d, J = 8.2 Hz, 2H), 7.32 (s, 1H), 7.26 (s, 1H), 7.18 (d, J = 8.1 Hz, 1H), 5.68 (s, 1H), 5.58 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 149.5 (C), 146.8 (C), 140.1 (C), 139.6 (C), 138.2 (C), 132.2 (2CH), 129.2 (2CH), 126.3 (CH), 123.5 (C), 123.1 (C), 120.6 (CH), 120.3 (CH), 120.1 (CH), 119.9 (CH), 119.1 (C), 116.7 (CH₂), 111.4 (C), 110.8 (CH), 110.5 (CH). HRMS (ESI): for C₂₁H₁₅N₂ (M+H)⁺: m/z calcd 295.1235, found 295.1245.

2-(1-(4-fluorophenyl)vinyl)-9H-carbazole (5d)

Column chromatography on silica gel afforded 108 mg of the desired carbazole 5d (0.375 mmol, yield 75%). Off-white solid, m.p. = 212-213°C. TLC: Rf = 0.48 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3412, 2363, 1600, 1504, 1460, 1440, 1370, 1328, 1243, 1217, 1156, 1014. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 10.32 (s, 1H), 8.12 (t, J = 8.0 Hz, 2H), 7.52 (d, J = 7.9 Hz, 1H), 7.47 - 7.38 (m, 4H), 7.23 - 7.13 (m, 4H), 5.57 (s, 1H), 5.49 (s, 1H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm): 162.5 (d, J = 244.6 Hz, CF), 150.0 (C), 145.9 (C), 140.6 (C), 140.1 (C), 138.9 (C), 138.4 (C), 130.2 (2CH, d, J = 8.5 Hz), 125.7 (CH), 122.9 (C), 120.1 (CH), 119.8 (CH), 119.3 (CH), 119.0 (CH), 114.8 (2CH, d, J = 21.8 Hz), 113.5 (CH₂), 110.9 (CH), 110.5 (CH). ¹⁹F NMR (188 MHz, CDCl₃) δ (ppm): -114.5 (s). HRMS (ESI): for C₂₀H₁₅NF (M+H)⁺: m/z calcd 288.1189, found 288.1183.
2-(1-(3,5-dimethoxyphenyl)vinyl)-6-methoxy-9H-carbazole (5e)

Column chromatography on silica gel afforded 144 mg of the desired carbazole 5e (0.4 mmol, yield 80%). White solid, m.p.=170-171 °C. TLC: Rf= 0.41 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3413, 3006, 2361, 1630, 1606, 1582, 1503, 1462, 1441, 1425, 1339, 1325, 1284, 1268, 1239, 1200, 1161, 1109, 1062, 1050, 1032. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.92 (d, J = 4.6 Hz, 1H), 7.90 (d, J = 4.3 Hz, 1H), 7.88 (s, 1H), 7.31 (s, 1H), 7.25 (d, J= 6.2 Hz, 1H), 6.89 – 6.83 (m, 2H), 6.56 (d, J = 2.1 Hz, 2H), 6.48 (t, J = 2.1 Hz, 1H), 5.54 (s, 1H), 5.47 (s, 1H), 3.90 (s, 3H), 3.77 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 160.6 (2C), 159.2 (C), 150.8 (C), 144.5 (C), 141.5 (C), 139.6 (C), 137.9 (C), 123.4 (C), 121.2 (CH), 120.3 (CH), 119.1 (CH), 117.2 (C), 114.2 (CH₂), 110.4 (CH), 108.5 (CH), 106.5 (2CH), 100.1 (CH), 94.8 (CH), 55.8 (CH₃), 55.5 (2CH₃). HRMS (ESI): for C₂₃H₂₂NO₃ (M+H)⁺: m/z calcd 360.1600, found 360.1602

4-(1-(6-methoxy-9H-carbazol-2-yl)vinyl)benzonitrile (5f)

Column chromatography on silica gel afforded 114 mg of the desired carbazole 5f (0.35 mmol, yield 70%). White solid, m.p.=230-231 °C. TLC: Rf= 0.40 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3426, 2963, 2924, 2361, 2224, 1613, 1503, 1463, 1431, 1397, 1334, 1306, 1224, 1030. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.87 (s, 1H), 7.86 (d, J = 8.6 Hz, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.19 (s, 2H), 7.07 (d, J = 7.2 Hz, 1H), 6.84 (s, 1H), 6.80 (d, J = 8.1 Hz, 1H), 5.59 (s, 1H), 5.48 (s, 1H), 3.84 (s, 3H). ¹³C NMR (75 MHz, DMSO-d₆) δ (ppm) 158.7 (C), 148.8 (C), 146.3 (C), 141.7 (C), 139.7 (C), 135.7 (C), 132.3 (2CH), 129.0 (2CH), 122.7 (C), 121.1 (CH), 119.2 (CH), 118.8 (C), 118.7 (CH), 116.4 (CH₂), 115.9 (C), 110.3 (C), 110.1 (CH), 108.1 (CH), 94.5 (CH), 55.3 (CH₃). HRMS (ESI): for C₂₂H₁₇N₂O (M+H)⁺: m/z calcd 325.1341, found 325.1343.
2-((1-(3,5-dimethoxyphenyl)vinyl)-6-fluoro-9H-carbazole (5g)

![Chemical Structure Image]

Column chromatography on silica gel afforded 127 mg of the desired carbazole 5g (0.365 mmol, yield 73%). White solid, m.p.=132-133 °C. TLC: Rf= 0.44 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3410, 2837, 1635, 1582, 1500, 1454, 1421, 1357, 1317, 1282, 1266, 1230, 1203, 1155, 1130, 1105, 1063, 1045.¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.02 – 7.91 (m, 3H), 7.33 (s, 1H), 7.29 (d, J = 8.1 Hz, 1H), 7.06 (dd, J = 9.5, 2.1 Hz, 1H), 6.97 (td, J = 9.1, 2.2 Hz, 1H), 6.57 (d, J = 2.2 Hz, 2H), 6.49 (t, J = 2.2 Hz, 1H), 5.55 (s, 1H), 5.51 (s, 1H), 3.77 (s, 6H).

¹³C NMR (75 MHz, CDCl₃) δ (ppm) 162.1 (d, J = 240 Hz, C), 160.7 (2C), 150.6 (C), 144.3 (C), 140.6 (d, J = 12.8 Hz, C), 140.0 (C), 138.9 (C), 122.7 (C), 121.3 (d, J = 10.5 Hz, CH), 120.6 (CH), 119.7 (C), 119.6 (CH), 114.6 (CH₂), 110.6 (CH), 107.9 (d, J = 24 Hz, CH), 106.9 (2CH), 100.1 (CH), 97.6 (d, J = 26 Hz, CH), 55.5 (2CH₃).

¹⁹F NMR (188 MHz, CDCl₃) δ (ppm) -113.4 (s). HRMS (ESI): for C₂₂H₁₉NO₂F (M+H)⁺: m/z calc 348.1400, found 348.1404.

4-((1-(6-fluoro-9H-carbazol-2-yl)vinyl)benzonitrile (5h)

![Chemical Structure Image]

Column chromatography on silica gel afforded 81 mg of the desired carbazole 5h (0.26 mmol, yield 52%). White solid, m.p.=214-215 °C. TLC: Rf= 0.52 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3406, 2358, 2228, 1613, 1564, 1503, 1458, 1433, 1359, 1319, 1271, 1222, 1144, 1105, 1069.¹H NMR (300 MHz, DMSO-d₆) δ (ppm) 11.36 (s, 1H), 8.16 – 8.06 (m, 2H), 7.86 (d, J = 7.9 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.33 (s, 1H), 7.27 (dd, J = 10.1, 1.8 Hz, 1H), 7.11 (d, J = 8.1 Hz, 1H), 7.04 – 6.95 (m, 1H), 5.72 (s, 1H), 5.65 (s, 1H).¹³C NMR (75 MHz, DMSO-d₆) δ (ppm) 161.3 (d, J = 239.1 Hz, C), 148.6 (C), 146.1 (C), 140.9 (d, J = 13.0 Hz, C), 140.3 (C), 136.9 (C), 132.3 (2CH), 128.9 (2CH₂), 122.0 (C), 121.6 (d, J = 9.8 Hz, CH), 120.0 (CH), 119.2 (CH), 118.9 (C), 118.8 (C), 117.0 (CH₂), 110.4 (CH), 106.8 (d, J = 24.8 Hz, CH), 97.4 (d, J = 26.2 Hz, CH).¹⁹F NMR (188 MHz, CDCl₃) δ (ppm) -115.1 (s). HRMS (ESI): for C₂₁H₁₄N₂F (M+H)⁺: m/z calc 313.1140, found 313.1144.
3-(1-(3,4,5-trimethoxyphenyl)vinyl)-9H-carbazole (5i)

Column chromatography on silica gel afforded 113 mg of the desired carbazole (5i) (0.315 mmol, yield 63%). Yellowish oil. TLC: Rf= 0.39 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 3410, 2936, 1607, 1580, 1504, 1462, 1411, 1345, 1237, 1176, 1125, 1005. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 8.26 (s, 1H), 8.12 – 8.04 (m, 2H), 7.47 – 7.41 (m, 3H), 7.36 (d, J = 8.4 Hz, 1H), 7.27 – 7.21 (m, 1H), 6.67 (s, 2H), 5.53 (s, 1H), 5.45 (s, 1H), 3.94 (s, 3H), 3.81 (s, 6H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 153.0 (2C), 150.9 (C), 140.1 (C), 139.4 (C), 138.3 (C), 137.8 (C), 132.9 (C), 126.7 (CH), 126.1 (CH), 123.4 (C), 123.3 (C), 120.5 (CH), 120.2 (CH), 119.7 (CH), 112.9 (CH₂), 110.9 (CH), 110.3 (CH), 106.9 (2CH), 61.1 (CH₃), 56.2 (2CH₃). HRMS (ESI): for C₂₃H₂₃NO₃ (M+H)⁺: m/z calcld 360.1600, found 360.1599.

V. General procedure for the methylation reaction
The carbazole or indole (0.3 mmol, 1equiv) was dissolved in freshly distilled THF, and at 0°C NaH (60 % dispersion in oil, 0.75 mmol, 2.5 eq) was added. After 15 min, MeI (0.4 mmol, 1.34 eq) was added slowly and the reaction mixture was allowed to stir at room temperature for 60 min, then it was cooled to 0°C and ammonium chloride solution was added. The mixture was extracted with Et₂O. The combined organic layers were washed with saturated aqueous NaHCO₃ and brine. The organic phase was dried on MgSO₄, evaporated to dryness and the crude product was purified by column chromatography on silica gel.

VI. N-methylated product characterizations
1-methyl-3-(3,4,5-trimethoxyphenyl)-1H-indole (6a)

Column chromatography on silica gel and afforded 82 mg of the desired methylated indole (6a) (0.28 mmol, yield 92%). White solid, m.p.: 117-118 °C. TLC: Rf= 0.27 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹):2936, 2360, 1582, 1547, 1503, 1449, 1415, 1384, 1332, 1305, 1234, 1158, 1123, 1055, 1006. ¹H NMR (300 MHz, CDCl₃) δ (ppm) 7.93 (d, J=7.9 Hz, 1H), 7.38 (d, J = 8.1 Hz, 1H), 7.32 (t, J = 7.4 Hz, 1H), 7.26 – 7.18 (m, 2H), 6.87 (s, 2H), 3.94 (s, 6H), 3.93 (s, 3H), 3.84 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ (ppm) 153.7 (3C), 137.6 (C), 131.5 (C), 126.5
(CH), 126.3 (C), 122.2 (CH), 120.1 (CH), 119.8 (CH), 117.0 (C), 109.8 (CH), 104.8 (2CH), 61.1 (CH₃), 56.3 (2CH₃), 32.9 (CH₃). HRMS (ESI): for C₁₈H₁₉NO₃Na (M+Na)⁺: m/z calcd 320.1263, found 320.1264.

6-methoxy-1-methyl-3-(3,4,5-trimethoxyphenyl)-1H-indole (6l)

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\text{Column chromatography on silica gel and afforded 89 mg of the desired methylated indole 6l (0.27 mmol, yield 91%). White solid, m.p.: 135-136 °C. TLC: Rf= 0.18 (cyclohexane/EtOAc 8/2). IR (film, cm}^{-1}\): 2936, 2828, 2360, 1623, 1602, 1583, 1552, 1505, 1463, 1416, 1391, 1336, 1241, 1199, 1172, 1126, 1091, 1031, 1008. \text{^1H NMR (300 MHz, CDCl}_3\delta (ppm): 7.92 (dd, J = 8.7, 0.8 Hz, 1H), 7.25 (d, J = 1.2 Hz, 1H), 7.04 – 7.00 (m, 1H), 6.99 (d, J = 1.3 Hz, 2H), 6.97 – 6.94 (m, 1H), 4.08 (s, 3H), 4.07 (s, 3H), 4.06 (s, 6H), 3.91 (d, J = 1.2 Hz, 3H). \text{^13C NMR (75 MHz, CDCl}_3\delta (ppm): 156.7 (C), 153.5 (3C), 138.3 (C), 136.5 (C), 131.5 (C), 125.3 (CH), 120.5 (CH), 116.9 (C), 109.9 (CH), 104.5 (2CH), 93.1 (CH), 61.0 (CH₃), 56.2 (2CH₃), 55.8 (CH₃), 32.9 (CH₃). HRMS (ESI): for C₁₉H₂₁NO₄Na (M+Na)⁺: m/z calcd 350.1368, found 350.1375.}

9-methyl-2-(1-(3,4,5-trimethoxyphenyl)vinyl)-9H-carbazole (7a)

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\text{Column chromatography on silica gel afforded 109 mg of the desired methylated carbazole 7a (0.29 mmol, yield 98%). Yellowish oil. TLC: Rf= 0.61 (cyclohexane/EtOAc 8/2). IR (film, cm}^{-1}\): 2936, 2834, 1601, 1578, 1503, 1450, 1411, 1362, 1338, 1322, 1246, 1232, 1180, 1124, 1001. \text{^1H NMR (300 MHz, CDCl}_3\delta (ppm): 8.13 (d, J = 7.7 Hz, 1H), 8.09 (d, J = 8.1 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.44 (s, 1H), 7.42 (d, J = 8.6 Hz, 1H), 7.33 – 7.28 (m, 2H), 6.70 (s, 2H), 5.62 (s, 1H), 5.56 (s, 1H), 3.96 (s, 3H), 3.85 (s, 9H). \text{^13C NMR (75 MHz, CDCl}_3\delta (ppm): 153.0 (3C), 151.1 (C), 141.6 (C), 141.1 (C), 139.2 (C), 137.9 (C), 125.9 (CH), 122.6 (2C), 120.4 (CH), 119.9}
(2CH), 119.1 (CH), 114.0 (CH2), 108.6 (CH), 108.5 (CH), 106.9 (2CH), 61.0 (CH3), 56.2 (2CH3), 29.2 (CH3). HRMS (ESI): for C24H24NO3 (M+H)+: m/z calcd 374.1756, found 374.1760.

9-methyl-3-(1-(3,4,5-trimethoxyphenyl)vinyl)-9H-carbazole (7i)

Column chromatography on silica gel afforded 108 mg of the desired methylated carbazole 7i (0.29 mmol, yield 97%). Yellowish oil. TLC: Rf = 0.36 (cyclohexane/EtOAc 8/2). IR (film, cm⁻¹): 2936, 2833, 2360, 1600, 1579, 1503, 1450, 1411, 1362, 1343, 1247, 1234, 1180, 1126, 1007. 1H NMR (300 MHz, CDCl3) δ (ppm) 8.14 (s, 1H), 8.11 (d, J = 7.8 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.43 (d, J = 7.9 Hz, 1H), 7.37 (d, J = 8.5 Hz, 1H), 7.28-7.23 (m, 1H), 6.68 (s, 2H), 5.54 (s, 1H), 5.47 (s, 1H), 3.94 (s, 3H), 3.87 (s, 3H), 3.83 (s, 6H). 13C NMR (75 MHz, CDCl3) δ (ppm) 153.0 (2C), 150.9 (C), 141.5 (C), 140.9 (C), 138.3 (C), 137.9 (C), 132.4 (C), 126.5 (CH), 126.0 (CH), 122.9 (C), 122.7 (C), 120.5 (CH), 120.3 (CH), 119.2 (CH), 112.7 (CH2), 108.7 (CH), 108.1 (CH), 106.9 (2CH), 61.0 (CH3), 56.2 (2CH3), 29.3 (CH3). HRMS (ESI): for C24H24NO3 (M+H)+: m/z calcd 374.1756, found 374.1752.

VII. Biology

Cancer cell lines were obtained from the American type Culture Collection (Rockville, MD) and were cultured according to the supplier’s instructions. HCT116 colorectal carcinoma cells were grown in RPMI 1640 containing 10% FCS and 1% glutamine. All cell lines were maintained at 37°C in a humidified atmosphere containing 5% CO2. Cell viability was assessed using Promega CellTiter-Blue TM reagent according to the manufacturer’s instructions. Cells were seeded in 96-well plates (5 x 103 cells/well) containing 50 μL growth medium. After 24 h of culture, the cells were supplemented with 50 μL of the tested compound dissolved in DMSO (less than 0.1% in each preparation). After 72 h of incubation, 20 μL of resazurin was added for 2 h before recording fluorescence (λex = 560 nm, λem = 590 nm) using a Victor microtiter plate fluorimeter (Perkin-Elmer, USA). The GI50 corresponds to the concentration of the tested compound that caused a decrease of 50% in fluorescence of drug treated cells compared with untreated cells. Experiments were performed in triplicate. The GI50 values for all compounds were compared to the GI50 of isoCA-4 and measured the same day under the same conditions.
VIII. $^1$H, $^{13}$C NMR Spectra
5c
108