

Electronic Supplementary Information

Metal catalyst free cyclization of 3-alkynyl substituted 2-(indol-3-yl)quinoxalines in TFA alone: A new synthesis of indolophenazines

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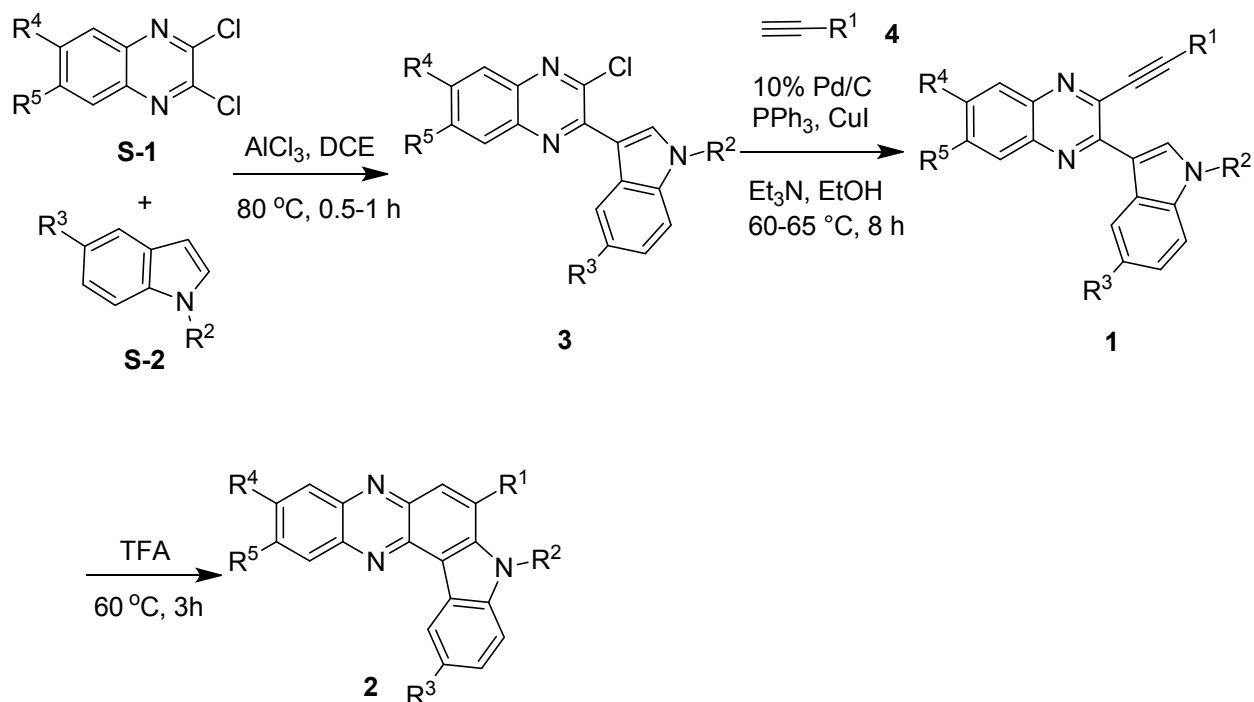
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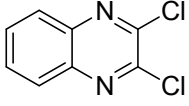
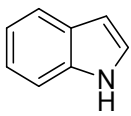
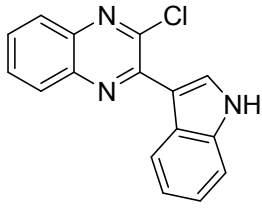
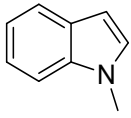
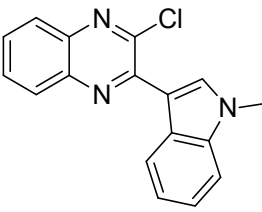
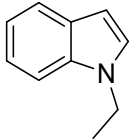
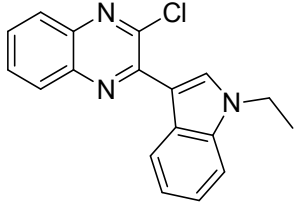
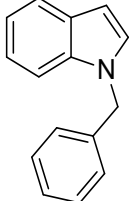
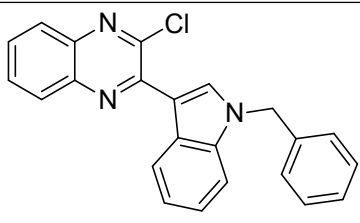
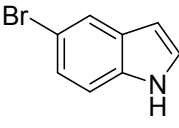
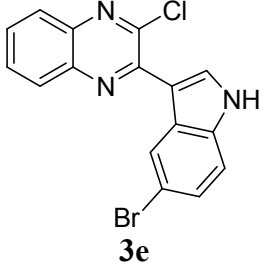
Scheme S-1. The complete scheme for the synthesis of compound 2

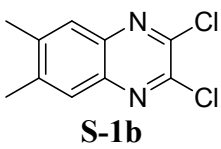
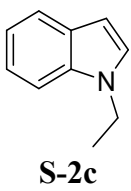
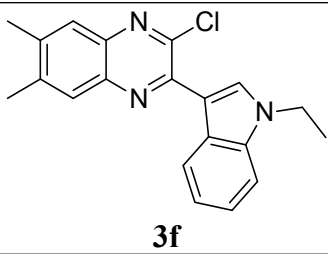


Chemistry

General methods: Unless stated otherwise, solvents and chemicals were obtained from commercial sources and were used without further purification. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254), visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (230–400 mesh) using hexane and ethyl acetate. ^1H and ^{13}C NMR spectra were determined in $\text{DMSO-}d_6$ solutions by using 400 or 100 MHz spectrometers, respectively. Proton chemical shifts (δ) are relative to tetramethylsilane (TMS, $\delta = 0.00$) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants (J) are given in hertz. Infrared spectra were recorded on a FT-IR spectrometer. Melting points were determined using a melting point apparatus and are uncorrected. MS spectra were obtained on a mass spectrometer. Chromatographic purity by HPLC (Agilent 1200) was determined by using area normalization method and the condition specified in each case: column, mobile phase (range used), flow rate, detection wavelength, and retention times.

Table S-1: AlCl₃ mediated synthesis of Compound **3^a** (see ref 1).

Entry	S-1 ;Quinoxaline R ⁴ , R ⁵ =	Indoles S-2 ; R ² , R ³ =	2-Chloro-3-(indol-3-yl)quinoxaline derivatives 3 ; R ² , R ³ , R ⁴ , R ⁵ =	Yield ^b
1	 S-1a	 S-2a	 3a	85
2	S-1a	 S-2b	 3b	87
3	S-1a	 S-2c	 3c	74
4	S-1a	 S-2d	 3d	81
5	S-1a	 S-2e	 3e	81

6	 S-1b	 S-2c	 3f	75
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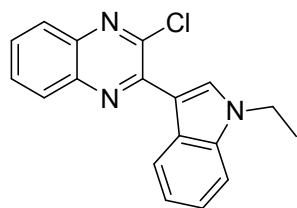
^a All the reactions were carried out using compound **S-1** (1.0 equiv), an indole **S-2** (1.0 equiv) and AlCl₃ (1.1 equiv) in dichloroethane (5 mL) at 80 °C for 0.5h.

^b Isolated yields after column chromatography.

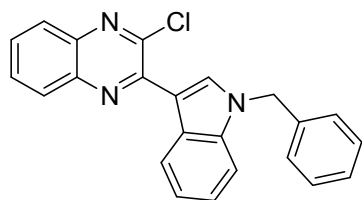
General Procedure for the preparation of 3¹: A mixture of 2,3-dichloroquinoxaline (**S-1**, 1.0 equiv), an appropriate indole (**S-2**, 1.0 equiv) and AlCl₃ (1.1 equiv) in dichloroethane (5 mL) was stirred at 80 °C for 0.5-1 h under a nitrogen atmosphere. After completion of the reaction, the mixture was poured into ice-cold water (15 mL), stirred for 10 min and then extracted with ethylacetate (3 × 20 mL). The organic layers were collected, combined, washed with cold water (2 × 20 mL), dried over anhydrous Na₂SO₄ and concentrated under vacuum. The residue obtained was purified by column chromatography using 5-7% ethylacetate/hexene to give the desired product.

The compound 2-chloro-3-(1*H*-indol-3-yl)quinoxaline (**3a**)¹, 2-chloro-3-(1-methyl-1*H*-indol-3-yl)quinoxaline (**3b**),¹ and 2-(5-bromo-1*H*-indol-3-yl)-3-chloroquinoxaline (**3e**)¹ are known.

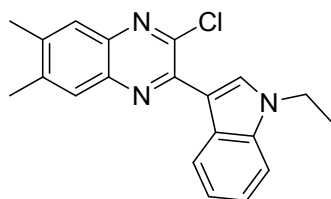
2-Chloro-3-(1-ethyl-1*H*-indol-3-yl)quinoxaline (**3c**)



Yellow solid; Yield: 86%; mp: 105-107 °C; *R_f* = 0.5 (10% EtOAc/ *n*-hexane) ; IR: 1435, 1295, 1201, 755 cm⁻¹cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.69 (d, *J* = 6.8 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.40 Hz, 1H), 7.76-7.68 (m, 2H), 7.45-7.43 (m, 1H), 7.35-7.32 (m, 2H) 4.31 (q, *J* = 7.6 Hz, 2H), 1.57 (t, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 148.6, 145.1, 141.0, 138.9, 136.1, 131.7, 130.0, 129.1, 128.4, 127.8 (2C), 123.0, 122.8, 121.5, 111.0, 109.6, 41.6, 15.3; Mass: *m/z* (CI) 308 (*M* + 1, 100%).

2-(1-Benzyl-1*H*-indol-3-yl)-3-chloroquinoxaline (3d)

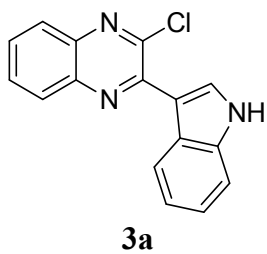
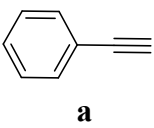
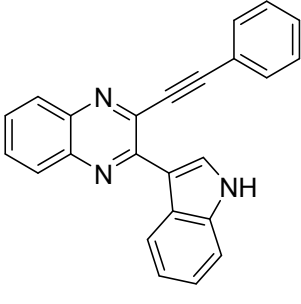
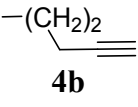
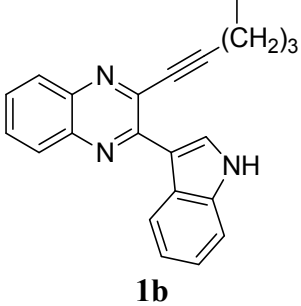
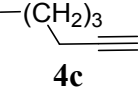
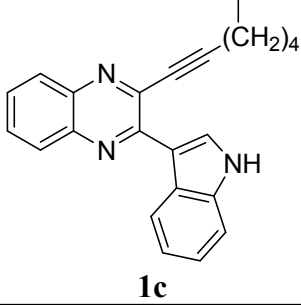
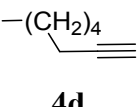
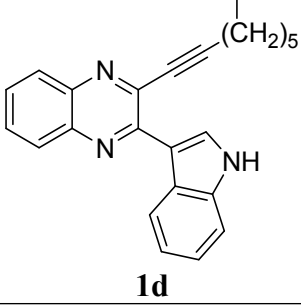
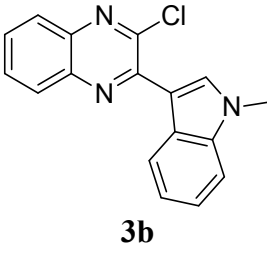
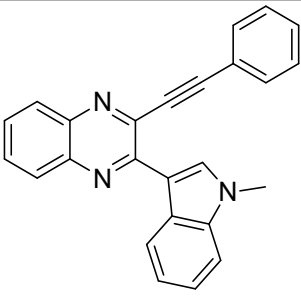
Light brown solid; Yield: 81%; mp: 145-150 °C; R_f = 0.6 (10% EtOAc/ *n*-hexane) ; IR : 1523, 1385, 1176, 734 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 8.71 (d, J = 8 Hz, 1H), 8.34 (s, 1H), 8.17 (d, J = 8.4 Hz, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.76 (t, J =7.6 Hz, 1H), 7.69 (t, J =7.6 Hz, 1H), 7.37-7.28 (m, 6H), 7.20 (d, J = 7.6 Hz, 2H), 5.45 (s, 2H); ^{13}C NMR (100 MHz, CDCl_3): δ 148.4, 145.1, 141.0, 139.0, 136.6, 136.4, 132.8, 130.1, 129.3, 128.9 (2C), 128.4, 127.9(2C), 127.8, 126.8 (2C), 123.3, 122.7, 121.8, 111.5, 110.1, 50.7; Mass: m/z (CI) 370 ($M + 1$, 100%).

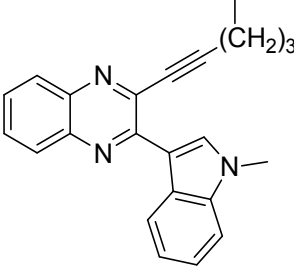
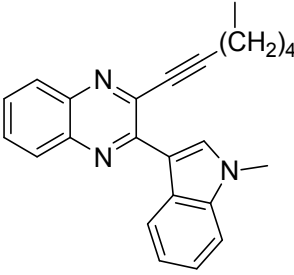
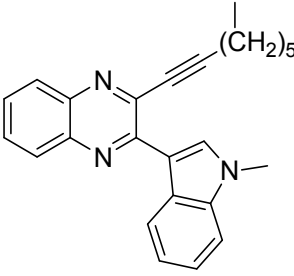
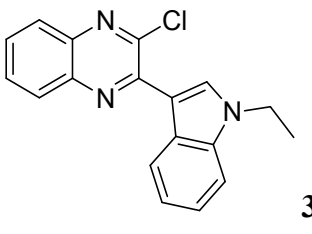
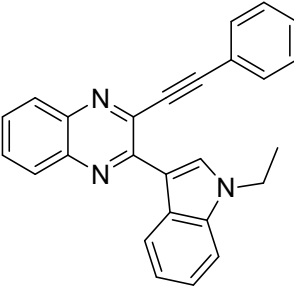
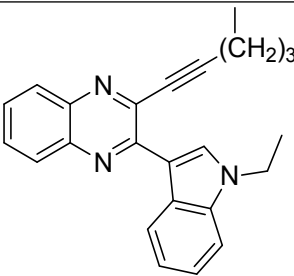
2-Chloro-3-(1-ethyl-1*H*-indol-3-yl)-6,7-dimethylquinoxaline (3f)

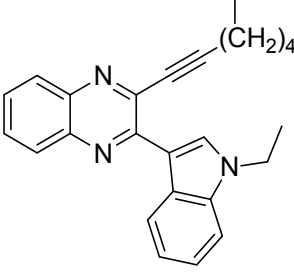
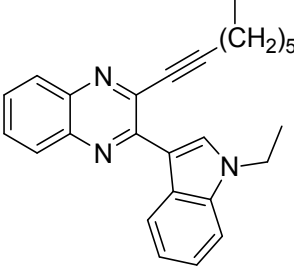
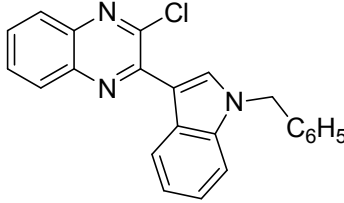
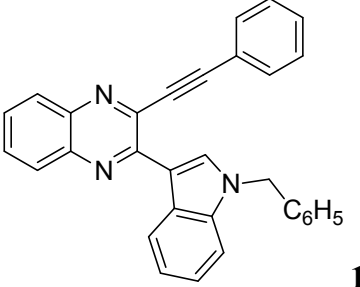
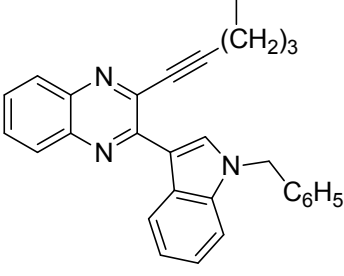
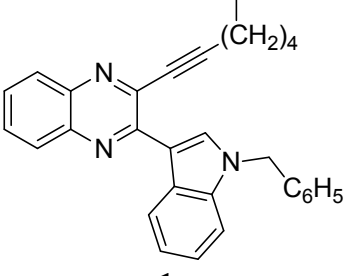
Light yellow solid; Yield: 75%; mp: 155-160 °C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR: 1352, 1456, 1025, 754 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 8.66 (d, J = 6.4 Hz, 1H), 8.25 (s, 1H), 7.90 (s, 1H), 7.71 (s, 1H), 7.42 (d, J =6.8 Hz, 1H), 7.35-7.28 (m, 2H), 4.29 (m, 2H), 2.49 (s, 3H), 2.48 (s, 3H), 1.56 (t, J =7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 147.6, 144.2, 140.5, 140.0, 139.7, 137.9, 136.1, 131.2, 127.8, 127.6, 127.0, 122.8(2C), 121.3, 111.2, 109.5, 41.5, 20.3 (2C), 15.4; Mass: m/z (CI) 336 ($M + 1$, 100%).

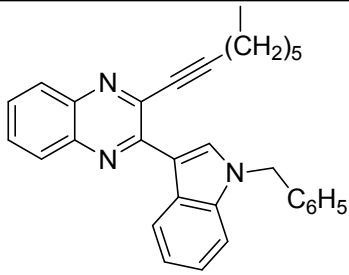
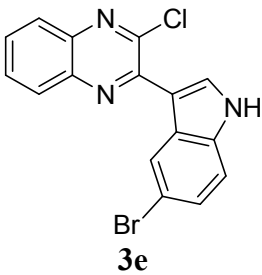
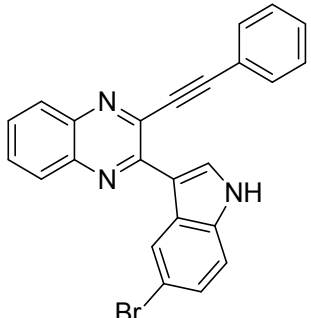
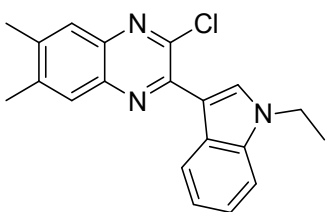
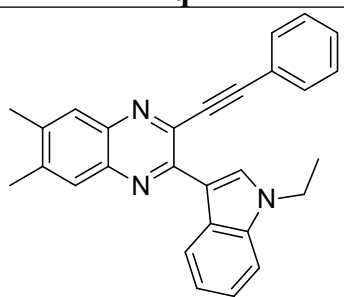
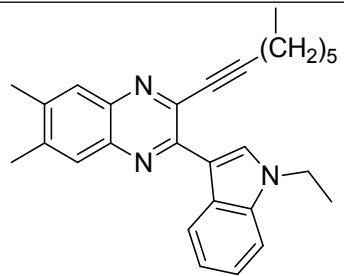
Table S-2: Pd/C mediated synthesis of Compound 1.¹

Entry	3 ; $\text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5 =$	Alkyne 4 ; $\text{R}^1 =$	Product 1 ; $\text{R}^1, \text{R}^2, \text{R}^3, \text{R}^4, \text{R}^5 =$	Yield ^b
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1	 3a	 4 a	 1a	85
2	3a	 4b	 1b	87
3	3a	 4c	 1c	74
4	3a	 4d	 1d	81
5	 3b	4a	 1e	81

6	3b	4b	 1f	87
7	3b	4c	 1g	85
8	3b	4d	 1h	82
9	 c 3	4a	 1i	84
10	3c	4b	 1j	81

11	3c	4c	 1k	82
12	3c	4d	 1l	84
13	 3d	4a	 1m	81
14	3d	4b	 1n	85
15	3d	4c	 1o	82

16	3d	4d	 1p	82
17	 3e	4a	 1q	81
18	 3f	4a	 1r	80
19	3f	4d	 1s	78

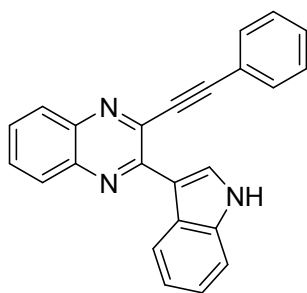
^aAll reactions were carried out by using **3** (1.0 equiv.), **4** (1.5 equiv.), 10% Pd/C (0.035 equiv.), PPh₃ (0.35 equiv.), CuI (0.06 equiv.) and Et₃N (3.0 equiv.) in ethanol (5 mL) at 60-65 °C for 8 h under nitrogen. ^b Isolated yields.

General procedure for the synthesis of **1**¹

A mixture of quinaxoline derivative **3** (1.0 equiv.), Pd/C (0.035 equiv.), PPh₃ (0.35 equiv.), CuI (0.06 equiv.), and TEA (3.0 equiv.) in ethanol (5 mL) was stirred for 30 min at RT under a nitrogen atmosphere. To this was added alkyne **4** (1.5 equiv.). The mixture was stirred initially at

room temperature for 1 h and then at 60–65 °C for 8 h. After completion of the reaction, the mixture was cooled to room temperature, diluted with EtOAc (50 mL), and filtered through celite. The filtrate was collected, washed with water (3 × 30 mL), dried over anhydrous Na₂SO₄, filtered and concentrated. The crude residue was purified by column chromatography on silica gel using 4-7% hexane/ethyl acetate to give the desired product.

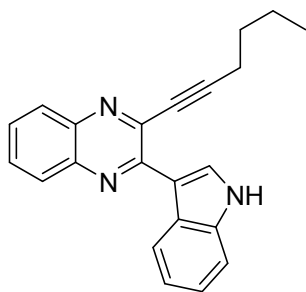
2-(1*H*-Indol-3-yl)-3-(phenylethynyl)quinoxaline (1a)



Chemical Formula: C₂₄H₁₅N₃
Exact Mass: 345.1266

Pale yellow solid; Yield: 81%; mp: 215-220 °C; *R_f* = 0.2 (10% EtOAc/ *n*-hexane); IR : 2924, 2207, 1532, 1125, 770 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆): δ 11.85 (s, 1H), 8.75 (d, *J* = 2.8 Hz, 1H), 8.65 (d, *J* = 7.2 Hz, 1H), 8.2 (d, *J* = 8.8 Hz, 1H), 8.2 (d, *J* = 8.2 Hz, 1H), 7.83 (t, *J* = 8.2 Hz, 1H), 7.76 (t, 8 Hz, 1H), 7.70 (t, *J* = 8 Hz, 2H), 7.50-54 (m, 4H), 7.26-7.19 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆): δ 150.9, 140.7, 139.1, 136.8, 136.6, 132.3, 132.2 (2C), 131.5, 130.6, 130.0, 129.6, 129.5 (2C), 128.7, 126.8, 123.0, 122.6, 121.4, 121.2, 112.4, 112.1, 93.8, 89.8; Mass : *m/z* (CI) 346 (*M* + 1, 100%).

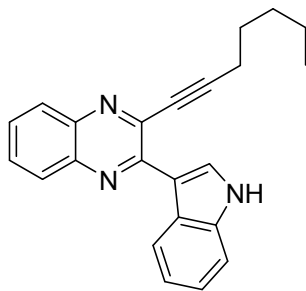
2-(Hex-1-ynyl)-3-(1*H*-indol-3-yl)quinoxaline(1b)



Chemical Formula: $C_{22}H_{19}N_3$
Exact Mass: 325.1579

Yellow solid; Yield: 81%; mp: 185-190 °C; R_f = 0.2 (10% EtOAc/ *n*-hexane); IR : 2955, 2223, 1528, 1436, 1136, 745 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.73 (t, J = 4.8 Hz, 1H), 8.66 (s, 1H), 8.55 (d, J = 2.4 Hz, 1H), 8.12 (d, J = 8 Hz, 1H), 8.02 (d, J = 8 Hz, 1H), 7.73-7.63 (m, 2H), 7.45 (t, J = 5.6 Hz, 1H), 7.33-7.30 (m, 2H), 2.55 (t, J = 8 Hz, 2H), 1.68-1.60 (m, 2H), 1.51-1.43 (m, 2H), 0.92 (t, J = 8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 140.8, 139.3, 137.5, 136.2, 130.0, 128.8, 128.6, 128.4, 127.8, 126.7, 123.2, 122.7, 121.5, 114.0, 111.1, 96.9, 81.0, 30.0, 22.2, 19.5, 13.5; Mass : m/z (CI) 326 ($M + 1$, 100%).

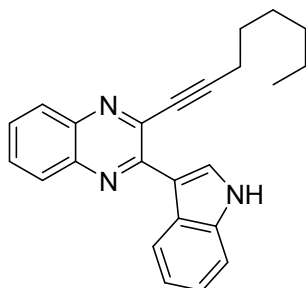
2-(Hept-1-ynyl)-3-(1H-indol-3-yl)quinoxaline(1c)



Chemical Formula: $C_{23}H_{21}N_3$
Exact Mass: 339.1735

Yellow solid; Yield: 76%; mp: 135-140 °C; R_f = 0.3 (10% EtOAc/ *n*-hexane); IR : 2923, 1530, 1437, 1130, 749 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 3.2 Hz, 1H), 8.54-56 (m, 2H), 8.12 (d, J = 8 Hz, 1H), 8.03 (d, J = 8 Hz, 1H), 7.73-7.63 (m, 2H), 7.44 (d, J = 8 Hz, 1H), 7.34-7.30 (m, 2H), 2.55 (t, J = 7.2 Hz, 2H), 1.72-1.64 (m, 2H), 1.46-1.39 (m, 2H), 1.37-1.30 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 140.8, 139.3, 137.5, 136.2, 130.1, 128.8, 128.6, 128.3, 127.8, 126.7, 123.2, 122.7, 121.5, 113.9, 111.2, 97.0, 80.9, 31.2, 27.7, 22.1, 19.8, 13.9; Mass : m/z (CI) 340 ($M + 1$, 100%).

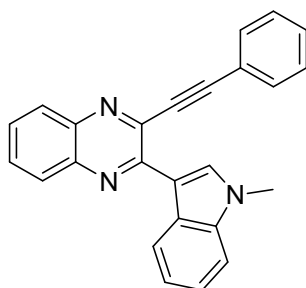
2-(1*H*-indol-3-yl)-3-(oct-1-ynyl)quinoxaline(1d)



Chemical Formula: C₂₄H₂₃N₃
Exact Mass: 353.1892

Light Brown solid; Yield: 81%; mp: 145-150 °C; *R_f* = 0.3 (10% EtOAc/ *n*-hexane) ; IR : 2925, 2225, 1530, 1130, 748 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.73 (t, *J* = 7.5 Hz, 1H), 8.59 (s, 1H), 8.56 (d, *J* = 2.8 Hz, 1H), 8.13 (d, *J* = 8 Hz, 1H), 8.03 (d, *J* = 8 Hz, 1H), 7.74-7.64 (m, 2H), 7.47 (d, *J* = 8.8 Hz, 1H), 7.33-7.31 (m, 2H), 2.56 (t, *J* = 7.2 Hz, 2H), 1.71-1.64 (m, 2H), 1.48-1.40 (m, 2H), 1.31-1.25 (m, 4H), 0.88 (t, *J* = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 150.5, 140.8, 139.4, 137.5, 136.2, 130.1, 128.8, 128.7, 128.4, 127.8, 126.7, 123.2, 122.7, 121.5, 114.0, 111.2, 97.0, 81.0, 31.3, 28.8, 28.0, 22.5, 19.9, 14.0 ; Mass: *m/z* (CI) 354 (*M* + 1, 100%).

2-(1-Methyl-1*H*-indol-3-yl)-3-(phenylethynyl)quinoxaline(1e)

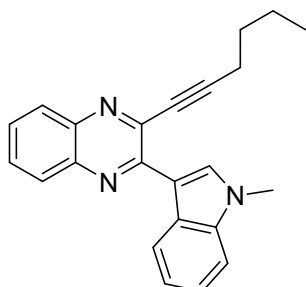


Chemical Formula: C₂₅H₁₇N₃
Exact Mass: 359.1422

Pale yellow solid; Yield: 81%; mp: 140-145 °C; *R_f* = 0.3 (10% EtOAc/ *n*-hexane) ; IR : 2209, 1535, 1214, 1130, 745 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.75 (d, *J* = 8 Hz, 1H), 8.46 (s, 1H), 8.13 (d, *J* = 8 Hz, 1H), 8.06 (d, *J* = 8 Hz, 1H), 7.76-7.65 (m, 2H), 7.61 (d, *J* = 8 Hz, 2H), 7.44-7.40 (m, 4H), 7.39-7.32 (m, 2H), 3.91 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 150.6, 141.0,

139.3, 137.2, 136.9, 132.5, 132.0(2C), 130.4, 129.5, 128.8, 128.6(3C), 128.5, 127.4, 122.9, 122.8, 121.9, 121.4, 112.3, 109.5, 94.1, 89.6, 33.4; Mass: m/z (CI) 360 ($M + 1$, 100%).

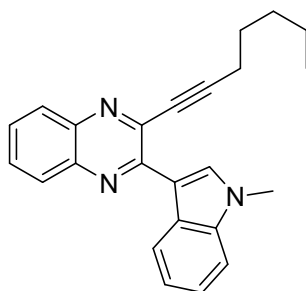
2-(Hex-1-ynyl)-3-(1-methyl-1*H*-indol-3-yl)quinoxaline(1f)



Chemical Formula: $C_{23}H_{21}N_3$
Exact Mass: 339.1735

Yellow solid; Yield: 81%; mp: 125-130 °C; R_f = 0.4 (10% EtOAc/ *n*-hexane) ; IR : 2220, 1525, 1369, 1086, 741 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, J = 8.4 Hz, 1H), 8.46 (s, 1H), 8.10 (d, J = 8.4 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.70-7.68 (m, 1H), 7.65-7.63 (m, 1H), 7.41-7.32 (m, 3H), 3.91 (s, 3H), 2.61 (t, J = 7.2 Hz, 2H), 1.73-1.67 (m, 2H), 1.55-1.50 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.3, 140.9, 139.2, 137.3, 137.2, 132.4, 130.0, 128.6, 128.5, 128.4, 127.5, 122.9, 122.8, 121.3, 112.3, 109.3, 96.5, 81.2, 33.3, 30.0, 22.2, 19.6, 13.6; Mass: m/z (CI) 340 ($M + 1$, 100%).

2-(Hept-1-ynyl)-3-(1-methyl-1*H*-indol-3-yl)quinoxaline(1g)

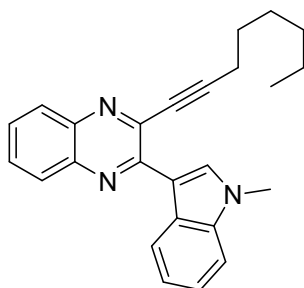


Chemical Formula: $C_{24}H_{23}N_3$
Exact Mass: 353.1892

Light yellow solid; Yield: 81%; mp: 125-130 °C; R_f = 0.5 (10% EtOAc/ *n*-hexane); IR : 2226, 1531, 1370, 1214, 1088, 933, 741 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.76 (d, J = 6.8 Hz, 1H),

8.47 (s, 1H), 8.10 (d, $J = 8.4$ Hz, 1H), 8.01 (d, $J = 8.4$ Hz, 1H), 7.73-7.62 (m, 2H), 7.41 (d, $J = 6.8$ Hz, 1H), 7.37-7.31 (m, 2H), 3.92 (s, 3H), 2.60 (t, $J = 7.2$ Hz, 2H), 1.77-1.69 (m, 2H), 1.51-1.44 (m, 2H), 1.41-1.34 (m, 2H), 0.92 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 150.4, 140.9, 139.2, 137.3, 137.2, 132.4, 130.0, 128.6, 128.5, 128.4, 127.5, 123.0, 122.9, 121.3, 112.4, 109.3, 96.7, 81.2, 33.3, 31.3, 27.7, 22.2, 19.9, 13.9; Mass: m/z (CI) 354 ($M + 1$, 100%).

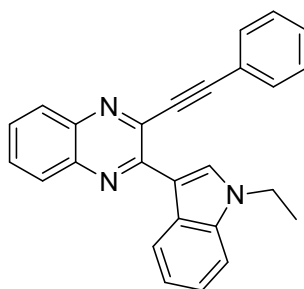
2-(1-Methyl-1*H*-indol-3-yl)-3-(oct-1-ynyl)quinoxaline(1h)



Chemical Formula: $\text{C}_{25}\text{H}_{25}\text{N}_3$
Exact Mass: 367.2048

Brown solid; Yield: 76%; mp: 105-110 °C; $R_f = 0.5$ (10% EtOAc/ *n*-hexane); IR : 2225, 1533, 1454, 1213, 1086, 739 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.76 (d, $J = 8$ Hz, 1H), 8.45 (s, 1H), 8.10 (d, $J = 8$ Hz, 1H), 8.00 (d, $J = 8$ Hz, 1H), 7.71-7.61 (m, 2H), 7.39 (d, $J = 7.2$, 1H), 7.36-7.30 (m, 2H), 3.90 (s, 3H) 2.59 (t, $J = 7.2$ Hz, 2H), 1.75-1.68 (m, 2H), 1.52-1.44 (m, 2H), 1.34-1.29 (m, 4H), 0.88 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (400 MHz, CDCl_3): δ 150.3, 140. 8, 139.1, 137.3, 137.2, 132.4, 130.0, 128.5 (2C), 128.4, 127.4, 123.0, 122.8, 121.3, 112.3, 109.3, 96.7, 81.2, 33.3, 31.4, 28.9, 28.0, 22.5, 20.0, 14.0; Mass: m/z (CI) 368 ($M + 1$, 100%).

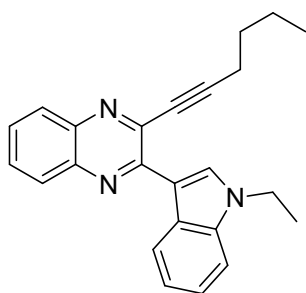
2-(1-Ethyl-1*H*-indol-3-yl)-3-(phenylethynyl)quinoxaline(1i)



Chemical Formula: $\text{C}_{26}\text{H}_{19}\text{N}_3$
Exact Mass: 373.1579

Yellow solid; Yield: 81%; mp: 120-125 °C; R_f = 0.4 (10% EtOAc/ *n*-hexane); IR : 2208, 1533, 1393, 1205, 1130, 750 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 8.74 (d, J = 8.4 Hz, 1H), 8.51 (s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8 Hz, 1H), 7.74 (t, J = 8 Hz, 1H), 7.68 (t, J = 8.4 Hz, 1H), 7.62 (d, J = 7.2 Hz, 2H), 7.46-7.41 (m, 4H), 7.37-7.31 (m, 2H), 4.31-4.26 (m, 2H), 1.54 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 150.7, 141.1, 139.3, 137.0, 136.3, 132.0 (2C), 130.8, 130.4, 129.5, 128.8, 128.7, 128.6 (3C), 127.7, 122.9, 122.8, 121.9, 121.4, 112.4, 109.5, 93.9, 89.6, 41.6, 15.3; Mass: m/z (CI) 374 ($M + 1$, 100%).

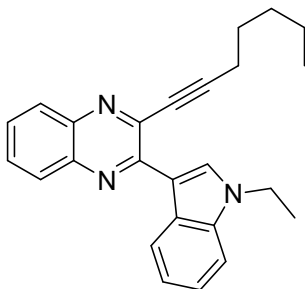
2-(1-Ethyl-1*H*-indol-3-yl)-3-(hex-1-ynyl)quinoxaline(1j)



Chemical Formula: $\text{C}_{24}\text{H}_{23}\text{N}_3$
Exact Mass: 353.1892

Pale yellow solid; Yield: 81%; mp: 105-110 °C; R_f = 0.4 (10% EtOAc/ *n*-hexane); IR : 2224, 1530, 1397, 1200, 742 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 8.76 (t, J = 6.4 Hz, 1H), 8.52 (s, 1H), 8.10 (d, J = 8 Hz, 1H), 8.00 (d, J = 8 Hz, 1H), 7.69-7.61 (m, 2H), 7.42 (d, J = 6 Hz, 1H), 7.35-7.29 (m, 2H), 4.30-4.25 (m, 2H), 2.60 (t, J = 7.2 Hz, 2H), 1.74-1.66 (m, 2H), 1.57-1.47 (m, 5H), 0.96 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 150.4, 140.9, 139.2, 137.3, 136.3, 130.7, 130.0, 128.6, 128.5, 128.4, 127.7, 123.0, 122.7, 121.3, 112.4, 109.4, 96.5, 81.2, 41.5, 30.1, 22.2, 19.6, 15.3, 13.6; Mass: m/z (CI) 354 ($M + 1$, 100%).

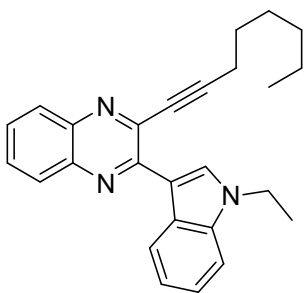
2-(1-Ethyl-1*H*-indol-3-yl)-3-(hept-1-ynyl)quinoxaline(1k)



Chemical Formula: $C_{25}H_{25}N_3$
Exact Mass: 367.2048

Yellow solid; Yield: 81%; mp: 95-100 °C; R_f = 0.4 (10% EtOAc/ *n*-hexane); IR : 2226, 1532, 1393, 1201, 1098, 770 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.75 (d, J = 8.8 Hz, 1H), 8.53 (s, 1H), 8.10 (d, J = 8 Hz, 1H), 8.01 (d, J = 8 Hz, 1H), 7.70 (t, J = 8.2 Hz, 1H), 7.64 (t, J = 8.2 Hz, 1H), 7.41-7.44 (m, 1H), 7.36-7.30 (m, 2H), 4.31-4.26 (m, 2H), 2.60 (t, J = 7.6 Hz, 2H), 1.76-1.69 (m, 2H), 1.57 (t, J = 7.2, 3H), 1.50-1.43 (m, 2H), 1.39-1.33 (m, 2H), 0.91 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 140.9, 139.2, 137.4, 136.3, 130.7, 130.0, 128.6, 128.5, 128.4, 127.7, 123.0, 122.7, 121.3, 112.4, 109.4, 96.6, 81.2, 41.5, 31.3, 27.8, 22.2, 20.0, 15.4, 13.9; Mass: m/z (CI) 368 ($M + 1$, 100%).

2-(1-Ethyl-1H-indol-3-yl)-3-(oct-1-ynyl)quinoxaline(1I)

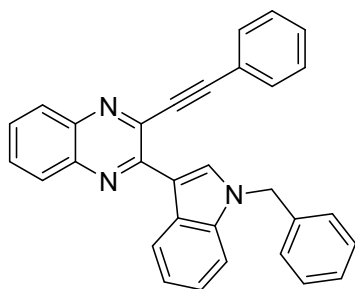


Chemical Formula: $C_{26}H_{27}N_3$
Exact Mass: 381.2205

Light brown solid; Yield: 76%; mp: 105-110 °C; R_f = 0.4 (10% EtOAc/ *n*-hexane); IR : 1533, 1394, 1217, 1089, 771 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 8.4 Hz, 1H), 8.52 (s, 1H), 8.10 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.70 (t, J = 8 Hz, 1H), 7.64 (t, J = 8 Hz, 1H), 7.41-7.44 (m, 1H), 7.36-7.29 (m, 2H), 4.31-4.26 (m, 2H), 2.59 (t, J = 7.2 Hz, 2H), 1.75-1.68 (m, 2H), 1.57 (t, J = 7.2 Hz, 3H), 1.52-1.44 (m, 2H), 1.34-1.29 (m, 4H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 140.9, 139.2, 137.4, 136.3, 130.7, 130.0, 128.6, 128.5,

128.4, 127.7, 123.0, 122.7, 121.3, 112.4, 109.4, 96.6, 81.2, 41.5, 31.4, 28.9, 28.1, 22.5, 20.0, 15.4, 14.0; Mass: m/z (CI) 382 ($M + 1$, 100%).

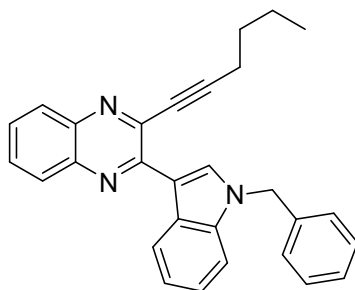
2-(1-Benzyl-1*H*-indol-3-yl)-3-(phenylethynyl)quinoxaline(1m)



Chemical Formula: $C_{31}H_{21}N_3$
Exact Mass: 435.1735

Brown solid; Yield: 81%; mp: 195-200 °C; R_f = 0.3 (10% EtOAc/ *n*-hexane); IR : 2208, 1533, 1388, 1178, 937, 744 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.78 (d, J = 6.4 Hz, 1H), 8.53 (s, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8 Hz, 1H), 7.75 (t, J = 6.8 & 8.4 Hz, 1H), 7.68 (t, J = 8.4 & 6.8 Hz, 1H), 7.43-7.38 (m, 4H), 7.36-7.29 (m, 4H), 7.27-7.25 (m, 3H), 7.19-7.15 (m, 2H), 5.43 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.5, 141.0, 139.3, 137.0, 136.5, 132.0 (2C), 131.9, 130.5, 129.4, 128.9 (3C), 128.8, 128.7, 128.5 (3C), 127.9, 127.6, 126.8 (2C), 123.2, 122.8, 121.7(2C), 112.9, 109.9, 94.2, 89.3, 50.5; Mass: m/z (CI) 436 ($M + 1$, 100%).

2-(1-Benzyl-1*H*-indol-3-yl)-3-(hex-1-ynyl)quinoxaline(1n)

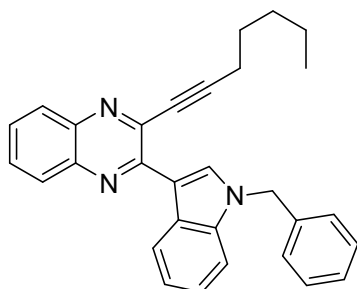


Chemical Formula: $C_{29}H_{25}N_3$
Exact Mass: 415.2048

Brown solid; Yield: 81%; mp: 100-105 °C; R_f = 0.4 (10% EtOAc/ *n*-hexane); IR : 2223, 1536, 1453, 1389, 1182, 758 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.79 (d, J = 7.6 Hz, 1H), 8.51 (s, 1H), 8.11 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.72-7.62 (m, 2H), 7.38-7.25 (m, 6H),

7.21 (d, $J = 6.8$ Hz, 2H), 5.41 (s, 2H), 2.41 (t, $J = 7.6$ Hz, 2H), 1.59-1.48 (m, 2H), 1.46-1.34 (m, 2H), 0.90 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 150.3, 140.8, 139.2, 137.4, 136.9, 136.6, 131.8, 130.0, 128.9 (2C), 128.6 (2C), 128.4, 127.9, 127.7, 126.9 (2C), 123.0 (2C), 121.5, 112.9, 109.8, 96.7, 81.0, 50.4, 30.0, 22.2, 19.4, 13.5; Mass: m/z (CI) 416 ($M + 1$, 100%).

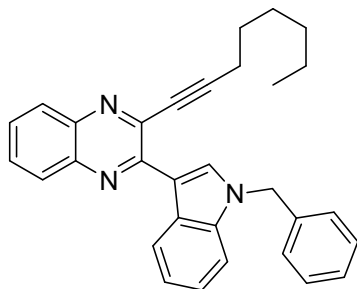
2-(1-Benzyl-1*H*-indol-3-yl)-3-(hept-1-ynyl)quinoxaline (1o)



Chemical Formula: $\text{C}_{30}\text{H}_{27}\text{N}_3$
Exact Mass: 429.2205

Light Yellow solid; Yield: 81%; mp: 90-95 °C; $R_f = 0.4$ (10% EtOAc/ *n*-hexane); IR : 2226, 1533, 1390, 1179, 935, 769 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 8.79 (d, $J = 8$ Hz, 1H), 8.51 (s, 1H), 8.11 (d, $J = 8.4$ Hz, 1H), 8.01 (d, $J = 8$ Hz, 1H), 7.70 (t, $J = 8.4$ Hz, 1H), 7.64 (t, $J = 8.4$ Hz, 1H), 7.38-7.25 (m, 6H), 7.21 (d, $J = 6.8$ Hz, 2H), 5.42 (s, 2H), 2.40 (t, $J = 7.6$ Hz, 2H), 1.60-1.54 (m, 2H), 1.39-1.25 (m, 4H), 0.87 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 150.3, 140.8, 139.2, 137.4, 136.9, 136.6, 131.8, 130.0, 128.9(2C), 128.6(2C), 128.4, 127.9, 127.7, 126.9(2C), 123.0(2C), 121.6, 112.9, 109.8, 96.8, 81.0, 50.5, 31.3, 27.7, 22.1, 19.7, 13.9; Mass: m/z (CI) 430 ($M + 1$, 100%).

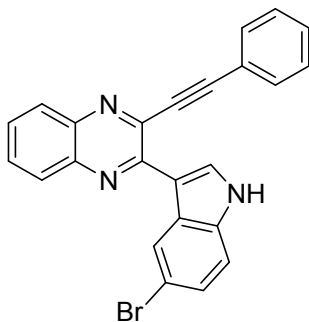
2-(1-Benzyl-1*H*-indol-3-yl)-3-(oct-1-ynyl)quinoxaline(1p)



Chemical Formula: $C_{31}H_{29}N_3$
Exact Mass: 443.2361

Yellow solid; Yield: 76%; mp: 75-80 °C; R_f = 0.4 (10% EtOAc/ *n*-hexane); IR : 2226, 1533, 1390, 1179, 935, 769 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, J = 8.4 Hz, 1H), 8.51 (s, 1H), 8.11 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.4 Hz, 1H), 7.71 (t, J = 8.4 Hz, 1H), 7.64 (t, J = 8.4 Hz, 1H), 7.38-7.27 (m, 6H), 7.21 (d, J = 8 Hz, 2H), 5.43 (s, 2H), 2.40 (t, J = 7.6 Hz, 2H), 1.61-1.54 (m, 2H), 1.42-1.36 (m, 2H), 1.29-1.22 (m, 4H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.3, 140.8, 139.2, 137.4, 136.9, 136.6, 131.8, 130.0, 128.9 (2C), 128.7, 128.6, 128.4, 128.0, 127.7, 126.9 (2C), 123.1, 123.0, 121.6, 112.9, 109.8, 96.8, 81.0, 50.5, 31.3, 28.9, 28.0, 22.5, 19.8, 14.0; Mass: m/z (CI) 444 ($M + 1$, 100%).

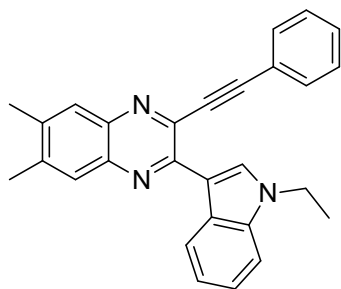
2-(5-Bromo-1H-indol-3-yl)-3-(phenylethynyl)quinoxaline (1q)



Chemical Formula: $C_{24}H_{14}BrN_3$
Exact Mass: 423.04

Yellow solid; Yield: 81%; mp: 230-235°C; R_f = 0.4 (10% EtOAc/ *n*-hexane); IR : 2925, 2203, 1530, 1431, 1131, 749 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 8.91 (s, 1H), 8.86 (s, 1H), 8.59 (d, J = 2.8 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.80-7.71 (m, 2H), 7.60 (d, J = 8 Hz, 2H), 7.43-7.34 (m, 5H); ^{13}C NMR (100 MHz, $DMSO-d_6$): δ 150.3, 140.6, 139.3, 136.5, 135.6, 132.3 (2C), 131.6, 131.3, 130.6, 129.8, 129.5 (2C), 128.7, 128.6, 128.0, 125.6, 124.8, 121.3, 114.5, 114.0, 111.8, 94.0, 89.6; Mass : m/z (CI) 424 ($M + 1$, 100%).

2-(1-Ethyl-1*H*-indol-3-yl)-6,7-dimethyl-3-(phenylethynyl)quinoxaline (1r)

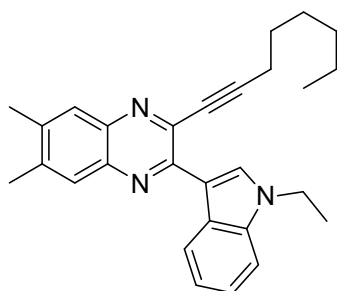


Chemical Formula: C₂₈H₂₃N₃

Exact Mass: 401.1892

Brown solid; Yield: 80%; mp: 195-200 °C; *R_f* = 0.4 (10% EtOAc/ *n*-hexane); IR : 3012, 2198, 1458, 1456, 762 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 8.71 (d, *J* = 8.8 Hz, 1H), 8.45 (s, 1H), 7.89 (s, 1H), 7.80 (s, 1H), 7.60-7.58 (m, 2H), 7.42-7.39 (m, 3H), 7.35-7.28 (m, 3H), 4.30-4.24 (m, 2H), 2.51 (s, 3H), 2.49 (s, 3H), 1.53 (t, *J* = 8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 150.0, 141.1, 140.0, 139.2, 138.4, 136.3, 135.9, 131.9(2C), 130.4, 129.3, 128.5(2C), 127.9, 127.7(2C), 122.9, 122.6, 122.2, 121.2, 112.6, 109.4, 93.4, 89.8, 41.5, 20.4, 20.3, 15.3; Mass: *m/z* (CI) 402 (*M* + 1, 100%).

2-(1-Ethyl-1*H*-indol-3-yl)-6,7-dimethyl-3-(oct-1-yn-1-yl)quinoxaline (1s)



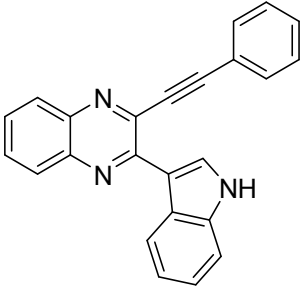
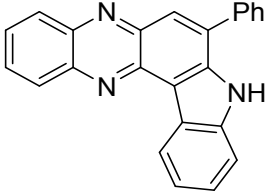
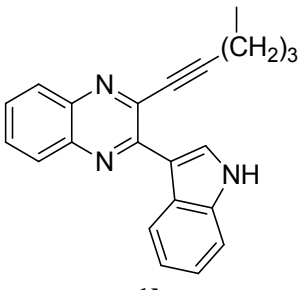
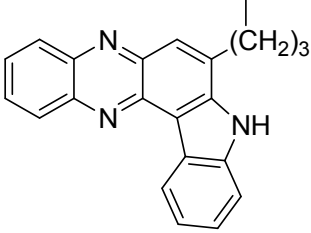
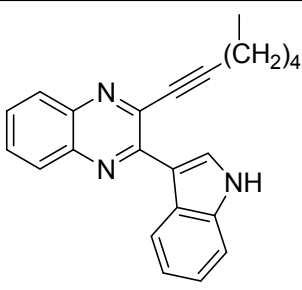
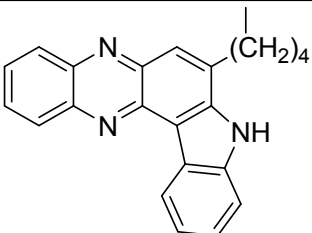
Chemical Formula: C₂₈H₃₁N₃

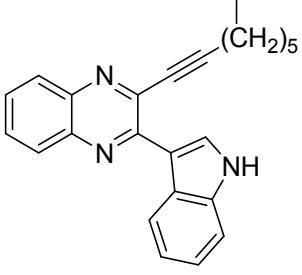
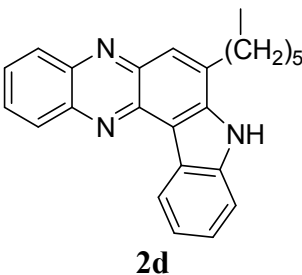
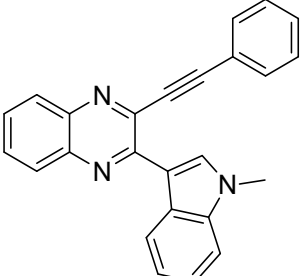
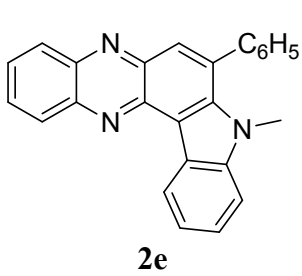
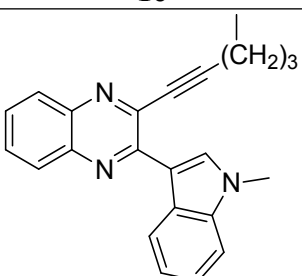
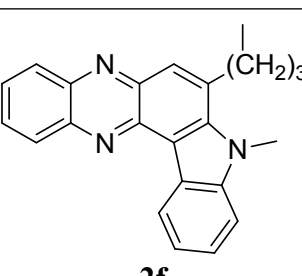
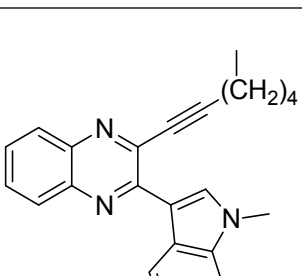
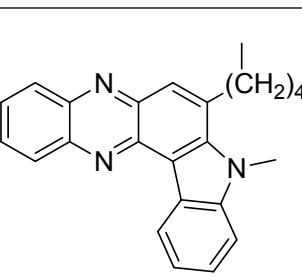
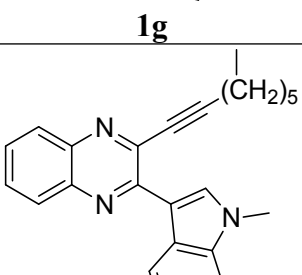
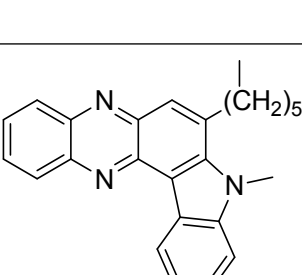
Exact Mass: 409.2518

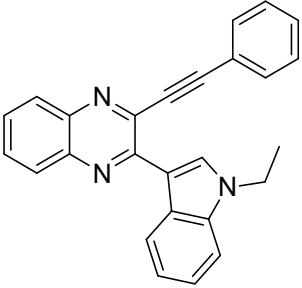
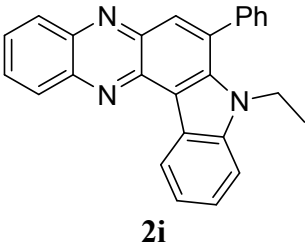
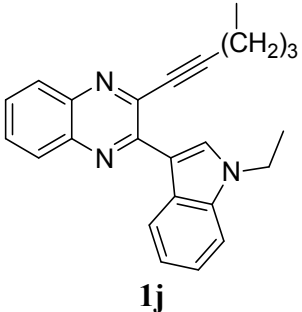
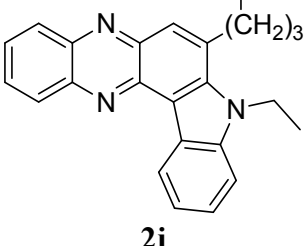
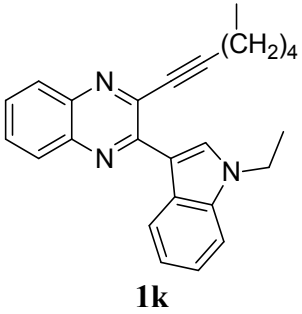
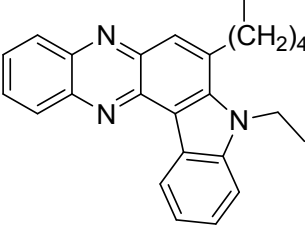
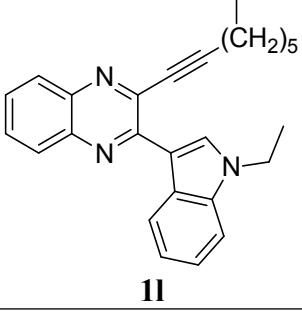
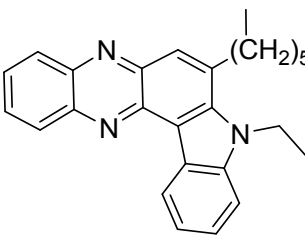
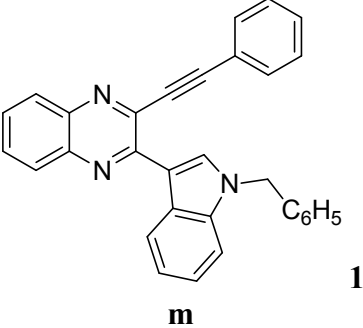
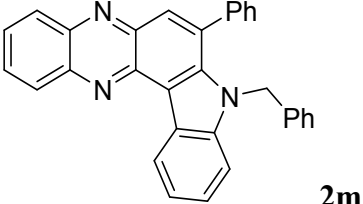
Yellow solid; Yield: 78%; mp: 130-135 °C; *R_f* = 0.4 (10% EtOAc/ *n*-hexane); ¹H NMR (400 MHz, CDCl₃) δ 8.72 (d, *J* = 8.8 Hz, 1H), 8.46 (s, 1H), 7.85 (s, 1H), 7.74 (s, 1H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.33-7.26 (m, 2H), 4.30-4.24 (m, 2H), 2.57 (t, *J* = 7.2 Hz, 2H), 2.49 (s, 3H), 2.47 (s, 3H), 1.74-1.66 (m, 2H), 1.56 (t, *J* = 7.2 Hz, 3H), 1.50-1.43 (m, 2H), 1.33-1.29 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 149.7, 140.5, 139.8, 138.9, 138.2, 136.3, 136.2,

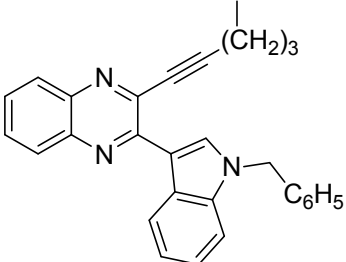
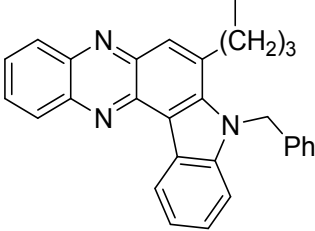
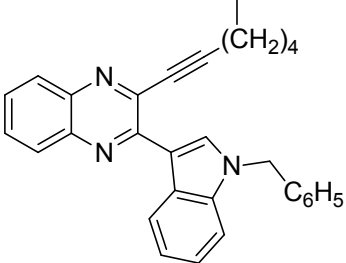
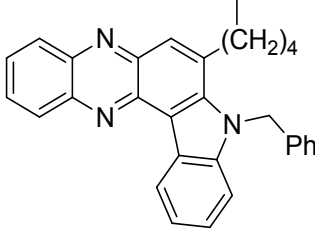
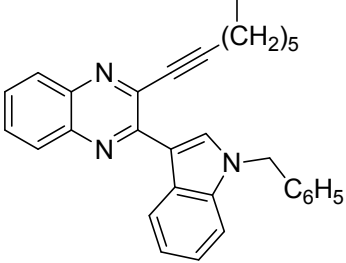
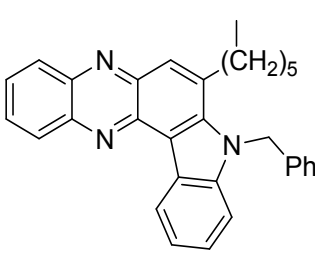
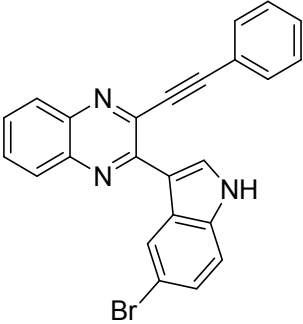
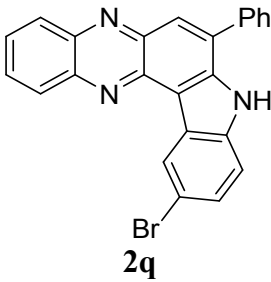
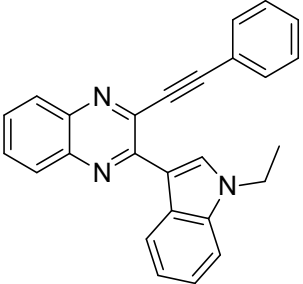
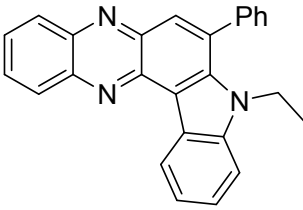
130.3, 127.8, 127.7, 127.5, 123.0, 122.5, 121.0, 112.6, 109.3, 95.9, 81.3, 41.1, 31.4, 28.9, 28.2, 22.5, 20.4, 20.3, 20.0, 15.4, 14.0; Mass: m/z (CI) 410 (M + 1, 100%).

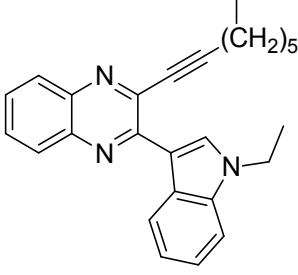
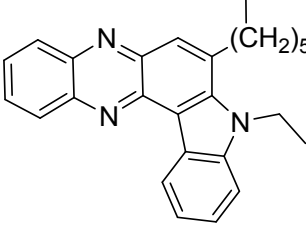
Table S-3; TFA mediated synthesis of indolophenazine (2)^a

Entry	1; R, R ₁ , R ₂ =	2; R, R ₁ , R ₂ =	% Yield ^b
1	 1a	 2a	86
2	 1b	 2b	85
3	 1c	 2c	81

4	 1d	 2d	81
5	 1e	 2e	85
6	 1f	 2f	78
7	 1g	 2g	81
8	 1h	 2h	83

9	 1i	 2i	80
10	 1j	 2j	82
11	 1k	 2k	84
12	 1l	 2l	80
13	 1m	 2m	81

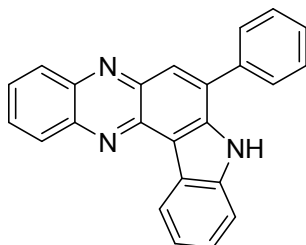
14	 1n	 2n	82
15	 1o	 2o	80
16	 1p	 2p	81
17	 1q	 2q	81
18	 1r	 2r	80

19	 1s	 2s	75
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^aA solution of **1** (0.034 mmol) in TFA (2 mL) was stirred at 60 °C for 3h under open air. ^bYields reported are isolated yield

General procedure for the synthesis of Indolophenazine 2: A solution of 2-(indol-3-yl)-3-(substitutedethynyl)quinoxaline **1** (0.50 mmol) in TFA (2 mL) was stirred at 60 °C for 3 h under open air. After completion of the reaction the mixture was cooled to room temperature and concentrated under vacuum. The residue obtained was purified by column chromatograph using 4-8% ethylacetate / hexene to give the desired product.

7-Phenyl-8*H*-indolo[3,2-*a*]phenazine (**2a**)

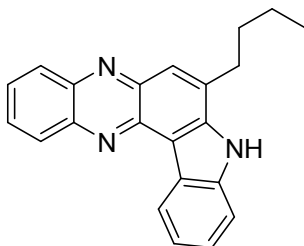


Chemical Formula: C₂₄H₁₅N₃
Exact Mass: 345.1266

Brown solid; Yield: 87%; mp: 235-240 °C; *R_f* = 0.4 (10% EtOAc/ *n*-hexane); IR : 3020, 1528, 1214, 747 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.00 (s, 1H), 9.08 (d, *J*= 7.2 Hz, 1H), 8.40 (d, *J*= 7.2 Hz, 1H), 8.28 (d, *J*= 8 Hz, 1H), 8.04 (s, 1H), 7.99-7.87 (m, 4H), 7.76 (d, *J*= 7.2 Hz, 1H), 7.69 (t, *J*= 7.2 Hz, 2H), 7.61 (t, *J*= 7.2 Hz, 1H), 7.50-7.42 (m, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆): δ 142.3, 141.6, 141.3, 141.2, 139.3, 137.7, 137.1, 135.1, 130.7, 129.7(3C), 129.3(3C), 129.2, 129.1, 126.1, 125.2, 124.2, 123.1, 121.5, 114.2, 113.2; HPLC:92.3%, Column: X-Bridge C18 (4.6X100mm) 3.5μm, mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN, Gradient Time%B: 0/5, 6/98, 11.5/98 & 12/5.

Column Temp : 30°C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80 : 20) V/V; UV 215 nm, retention time 7.9 min ; Mass : m/z (CI) 346 (M + 1, 100%).

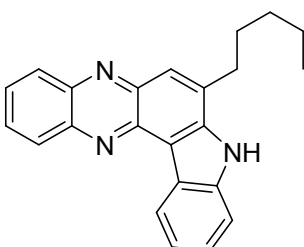
7-Butyl-8*H*-indolo[3,2-*a*]phenazine(2b)



Chemical Formula: C₂₂H₁₉N₃
Exact Mass: 325.1579

Light yellow solid; Yield: 76%; mp: 120-125 °C; R_f = 0.4 (10% EtOAc/ *n*-hexane); IR: 2924, 1529, 1447, 1135, 750 cm⁻¹; ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.26 (s, 1H), 9.00 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 8.4 Hz, 1H), 7.94-7.83 (m, 3H), 7.74 (d, J = 8.2 Hz, 1H), 7.49-7.39 (m, 2H), 3.16 (t, J = 7.6 Hz, 2H), 1.85 (t, J =7.6 Hz, 2H), 1.52-1.46 (m, 2H), 0.97 (t, J = 7.6 Hz, 3H) ; ¹³C NMR (100 MHz, DMSO-*d*₆): δ 142.0, 141.9, 141.0, 140.8, 139.5, 138.8, 136.3, 130.2, 129.6, 129.2, 128.8, 125.0(2C), 124.3, 123.0, 121.3, 113.1, 112.7, 31.3 (2C), 22.4, 14.3; HPLC: 84.1 %, Column: X-SELECT CSH C18 (4.6X150mm) 5 μ m, mobile phase A: 0.05% Formic acid in MliQwater, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/5, 1.5/5, 4/50, 10/80, 15/98, 18/98, 20/5. Column Temp : 35°C, flow rate: 1 ml/min, Diluent : (ACN : WATER); UV 215 nm, retention time 14.3 min ; Mass : m/z (CI) 326 ((M + 1, 100%).

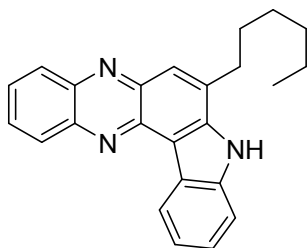
7-Pentyl-8*H*-indolo[3,2-*a*]phenazine (2c)



Chemical Formula: C₂₃H₂₁N₃
Exact Mass: 339.1735

Yellow solid; Yield: 81%; mp: 230-235 °C; R_f = 0.5 (10% EtOAc/ *n*-hexane); IR : 2927, 1529, 1447, 1330, 1133, 747 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 12.25 (s, 1H), 9.00 (d, J = 7.6 Hz, 1H), 8.34 (d, J = 8 Hz, 1H), 8.23 (d, J = 8.0 Hz, 1H), 7.92-7.86 (m, 3H), 7.74 (d, J = 8 Hz, 1H), 7.47-7.41 (m, 2H), 3.15 (s, 2H), 1.87 (s, 2H), 1.45-1.37 (m, 4H), 0.89 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ 142.0, 141.9, 141.0, 140.8, 139.5, 138.8, 136.3, 130.2, 129.6, 129.2, 128.8, 125.0 (2C), 124.3, 123.0, 121.3, 113.1, 112.7, 31.5 (2C), 28.8, 22.5, 14.4; HPLC: 99.3 %, Column: X-Bridge C18 (4.6X100mm) 3.5 μm , mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/5, 1.5/5, 4/50, 10/80, 15/98, 18/98, 20/5. Column Temp : 35°C, flow rate: 1 ml/min, Diluent : (ACN : WATER); UV 215 nm, retention time 12.9 min ; Mass : m/z (CI) 340 ($M + 1$, 100%).

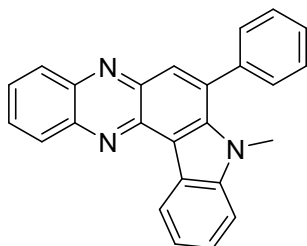
7-Hexyl-8*H*-indolo[3,2-*a*]phenazine(2d)



Chemical Formula: $\text{C}_{24}\text{H}_{23}\text{N}_3$
Exact Mass: 353.1892

Brown color solid; Yield: 81%; mp: 180-185 °C; R_f = 0.5 (10% EtOAc/ *n*-hexane) ; IR : 2922, 1670, 1184, 770 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 10.86 (s, 1H), 8.69 (d, J = 8.0 Hz, 1H), 8.29 (d, J = 8 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.94-7.85 (m, 2H), 7.70 (s, 1H), 7.20 (t, J = 7.6 Hz, 1H), 7.01 (d, J = 8.0 Hz, 1H), 6.84 (t, J =7.6 Hz, 1H), 3.09 (t, J =7.6 Hz, 2H), 1.82-1.75 (m, 2H), 1.50-1.44 (m, 2H), 1.37-1.33 (m, 4H), 0.90 (t, J = 7.2 Hz, 3H) ; ^{13}C NMR (100 MHz, CDCl_3): δ 141.9, 141.9, 140.5, 137.3 (2C), 131.4 (2C), 129.9 (2C), 129.8, 126.0, 123.1 (2C), 122.8, 122.7, 121.5, 113.2, 111.2, 31.5, 29.6, 29.1, 28.6, 22.5, 14.0; HPLC: 97.8 %, Column: X-Bridge C18 (4.6X100mm) 3.5 μm , mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/5, 6/98, 11.5/98 & 12/5. Column Temp : 30°C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80 : 20) V/V ; UV 215 nm, retention time 8.7 min ; Mass : m/z (CI) 354 ($M + 1$, 100%).

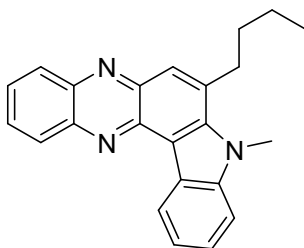
8-Methyl-7-phenyl-8*H*-indolo[3,2-*a*]phenazine(2e)



Chemical Formula: C₂₅H₁₇N₃
Exact Mass: 359.1422

Yellow solid; Yield: 81%; mp: 235-240 °C; *R_f* = 0.5 (10% EtOAc/ *n*-hexane) ; IR : 1516, 1379, 1085, 771 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 9.37 (d, *J* = 8 Hz, 1H), 8.45 (d, *J* = 8 Hz, 1H), 8.32 (s, 1H), 8.04 (s, 1H), 7.89-7.82 (m, 2H), 7.64 (d, *J* = 6.4 Hz, 2H), 7.58-7.55 (m, 6H), 3.54 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 143.0 (2C), 141.4, 140.7(2C), 138.9, 138.0 (2C), 129.7 (3C), 129.4, 129.3, 128.5 (2C), 128.4 (2C), 125.0 (2C), 124.0, 123.8, 121.5 (2C), 109.6, 33.2; HPLC: 99.1 %, Column: X-Bridge C18 (4.6X100mm) 3.5μm, mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/5, 6/98, 11.5/98 & 12/5. Column Temp : 30°C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80:20) V/V ; UV 215 nm, retention time 8.6 min; Mass: *m/z* (CI) 360 (*M* + 1, 100%).

7-Butyl-8-methyl-8*H*-indolo[3,2-*a*]phenazine(2f)

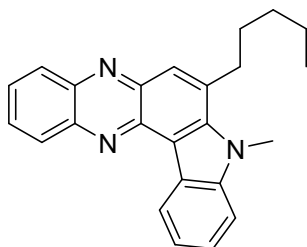


Chemical Formula: C₂₃H₂₁N₃
Exact Mass: 339.1735

Yellow solid; Yield: 76%; mp: 140-145 °C; *R_f* = 0.6 (10% EtOAc/ *n*-hexane) ; IR : 2927, 1510, 1437, 1082, 741 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.18 (d, *J* = 7.2 Hz, 1H), 8.34 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 8.4 Hz, 1H), 7.85-7.76 (m, 3H), 7.50-7.43 (m, 3H), 4.12 (s, 3H), 3.19 (t, *J* = & 8 Hz, 2H), 1.84-1.77 (m, 2H), 1.55-1.50 (m, 2H), 1.01 (t, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆): δ 142.7, 141.3, 140.2, 139.1 (2C), 138.6, 136.7, 129.4 (2C), 129.0, 128.0, 125.2,

124.9, 123.7, 123.6, 121.5, 114.9, 109.3, 33.6, 32.6, 32.4, 22.5, 13.9; HPLC: 99.2%, Column: X-Bridge C18 (4.6X150mm) 3.5 μ m, mobile phase A : 10mM AmmoniumAcetate in Mli-Q-water, mobile phase B: 100%ACN; Gradient Time%B: 0/5,1.5/5,4/50, 10/80, 15/98, 18/95, 20/5. Column Temp : 30 $^{\circ}$ C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80:20) V/V; UV 190-800 nm, retention time 16.9 min ; Mass: m/z (CI) 340 (M + 1, 100%).

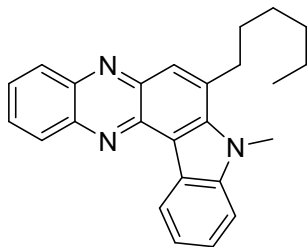
8-Methyl-7-pentyl-8*H*-indolo[3,2-*a*]phenazine(2g)



Chemical Formula: C₂₄H₂₃N₃
Exact Mass: 353.1892

Pale yellow solid; Yield: 76%; mp: 160-165 $^{\circ}$ C; R_f = 0.7 (10% EtOAc/ *n*-hexane); IR : 1511, 1219, 1080, 949, 772 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.36 (d, J = 7.2 Hz, 1H), 8.41 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.89 (s, 1H), 7.86-7.76 (m, 2H), 7.60-7.56 (m, 2H), 7.54-7.49 (m, 1H), 4.28 (s, 3H), 3.36 (t, J = 8 Hz, 2H), 1.96-1.89 (m, 2H), 1.56-1.50 (m, 2H), 1.46-1.41 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 142.7, 141.2 (2C), 141.1, 140.3, 138.8, 135.4, 129.4, 129.3, 129.2, 128.2, 126.9, 124.7, 124.0, 123.7, 121.3, 115.0, 109.3, 33.9, 32.6, 31.6, 30.2, 22.6, 14.0; HPLC:95.4%, Column: X-Bridge C18 (4.6X150mm) 3.5 μ m, Buffer : 0.01M AmmoniumAcetate in Mli-Q-water, mobile phase B: ACN; Gradient Time%B: 0/5,1.5/5,6/80,10/98,15/98& 15.10/55. Column Temp : 35 $^{\circ}$ C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80:20) V/V; UV 215 nm, retention time 12.5 min ; Mass: m/z (CI) 354 (M + 1, 100%).

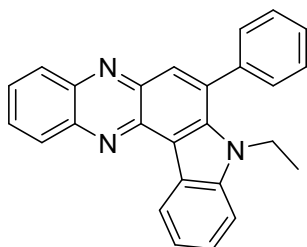
7-Hexyl-8-methyl-8*H*-indolo[3,2-*a*]phenazine(2h)



Chemical Formula: C₂₅H₂₅N₃
Exact Mass: 367.2048

Light brown solid; Yield: 81%; mp: 165-170 °C; *R_f* = 0.7 (10% EtOAc/ *n*-hexane); IR : 2925, 1456, 1323, 1082, 743 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 9.33 (d, *J*= 6.8 Hz, 1H), 8.39 (d, *J*=8.8 Hz, 1H), 8.24 (d, *J*= 8.4 Hz, 1H), 7.85-7.75 (m, 3H), 7.55-7.48 (m, 3H), 4.22 (s, 3H), 3.29 (t, *J*=7.6 Hz, 2H), 1.91-1.84 (m, 2H), 1.56-1.49 (m, 2H), 1.39-1.34 (m, 4H), 0.91 (t, *J*= 6.8 & 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 142.7, 141.3, 140.3, 138.7, 129.4 (3C), 128.7 (2C), 128.6 (3C), 124.8, 123.9, 123.7, 121.5, 115.0, 109.4, 34.0, 31.7, 30.6, 29.7 (2C), 22.6, 14.1; Mass: *m/z* (CI) 368 (*M* + 1, 100%).

8-Ethyl-7-phenyl-8*H*-indolo[3,2-*a*]phenazine(2i)

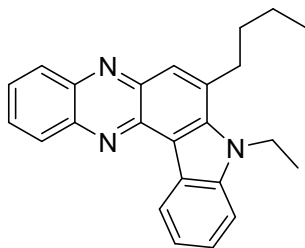


Chemical Formula: C₂₆H₁₉N₃
Exact Mass: 373.1579

Yellow solid; Yield: 81%; mp: 175-180 °C; *R_f* = 0.6 (10% EtOAc/ *n*-hexane); IR : 1514, 1344, 1225, 1089, 754 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 9.38 (d, *J*= 6.4 Hz, 1H), 8.46 (d, *J*= 8.4 Hz, 1H), 8.33 (d, *J*= 8.4 Hz, 1H), 8.00 (s, 1H), 7.89-7.82 (m, 2H), 7.64 (d, *J*= 6.4 Hz, 2H), 7.56-7.52 (m, 6H), 4.07-4.02 (m, 2H), 1.09 (t, *J*= 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 143.1, 141.5, 140.6, 139.9, 139.7, 139.0, 137.1, 135.7, 129.8, 129.5, 128.9 (3C), 128.8, 128.5(3C), 128.1, 125.1, 124.4, 124.0, 121.6, 115.6, 109.9, 39.4, 14.7; HPLC: 90 %, Column: X-Bridge C18 (4.6X100mm) 3.5μm, mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/5, 6/98, 11.5/98 & 12/5. Column Temp :

30°C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80 : 20) V/V ; UV 215 nm, retention time 8.8 min; Mass: m/z (CI) 374 (M + 1, 100%).

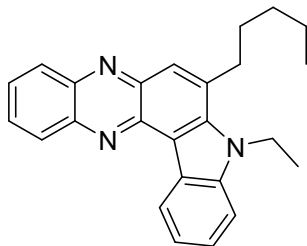
7-Butyl-8-ethyl-8*H*-indolo[3,2-*a*]phenazine(2j)



Chemical Formula: C₂₄H₂₃N₃
Exact Mass: 353.1892

Yellow solid; Yield: 76%; mp: 125-130 °C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR : 2927, 1817, 1330, 1089, 741 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.37 (d, J = 7.2 Hz, 1H), 8.40 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.91 (s, 1H), 7.85-7.75 (m, 2H), 7.60-7.49 (m, 3H), 4.74-4.69 (m, 2H), 3.28 (t, J = 8 Hz, 2H), 1.95-1.87 (m, 2H), 1.61-1.52 (m, 5H), 1.04 (t, J = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 142.7, 141.3, 141.1, 141.0, 139.3, 137.9, 135.2, 129.4, 129.3, 129.2, 128.3, 127.0, 124.7, 124.5, 123.9, 121.4, 115.4, 109.4, 39.9, 33.3, 32.5, 22.5, 15.8, 13.9; HPLC: 94.8 %, Column: X-SELECT CSH C18 (4.6X150mm) 5 μ m, mobile phase A: 0.05% Formic acid in MliQwater, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/5, 1.5/5, 4/50, 10/80, 15/98, 18/98, 20/5. Column Temp : 35°C, flow rate: 1 ml/min, Diluent: (ACN: WATER); UV 215 nm, retention time 16.7 min; Mass: m/z (CI) 354 (M + 1, 100%).

8-Ethyl-7-pentyl-8*H*-indolo[3,2-*a*]phenazine(2k)

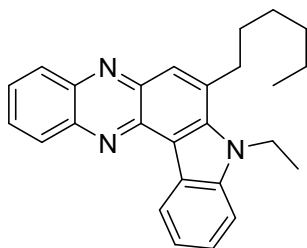


Chemical Formula: C₂₅H₂₅N₃
Exact Mass: 367.2048

Yellow solid; Yield: 76%; mp: 125-130 °C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR : 1511, 1339, 1224, 1090, 771 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.37 (d, J = 8.4 Hz, 1H), 8.41 (d, J = 8.4 Hz,

1H), 8.25 (d, $J=8.4$ Hz, 1H), 7.91 (s, 1H), 7.84 (t, $J=8.4$ Hz, 1H), 7.78 (t, $J=8.4$ Hz, 1H), 7.60 (d, $J=7.6$ Hz, 1H), 7.57-7.49 (m, 2H), 4.75-4.70 (m, 2H), 3.28 (t, $J=8$ Hz, 2H), 1.97-1.89 (m, 2H), 1.54 (t, $J=7.2$ Hz, 3H), 1.48-1.41 (m, 2H), 1.33-1.28 (m, 2H), 0.95 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 142.8, 141.3, 141.2, 141.1, 139.3, 137.9, 135.2, 129.5, 129.3(2C), 128.3, 127.1, 124.8, 124.5, 123.9, 121.4, 115.4, 109.4, 39.9, 33.6, 31.7, 30.1, 22.6, 15.9, 14.0; HPLC: 99.2 %, Column: X-Bridge C18 (4.6X100mm) 3.5 μm , mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/10, 3/90, 11.5/98&12/10. Column Temp : 30°C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80:20) V/V ; UV 215 nm, retention time 8.4 min ; Mass: m/z (CI) 368 ($M+1$, 100%).

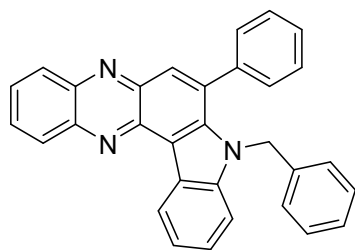
8-Ethyl-7-hexyl-8H-indolo[3,2-a]phenazine(2l)



Chemical Formula: $\text{C}_{26}\text{H}_{27}\text{N}_3$
Exact Mass: 381.2205

Pale yellow solid; Yield: 81%; mp: 150-155 °C; $R_f = 0.6$ (10% EtOAc/ *n*-hexane); IR : 1511, 1431, 1338, 1222, 1090, 771 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 9.37 (d, $J=6.8$ Hz, 1H), 8.41 (d, $J=8.8$ Hz, 1H), 8.26 (d, $J=8.4$ Hz, 1H), 7.92 (s, 1H), 7.85-7.76 (m, 2H), 7.60-7.49 (m, 3H), 4.74-4.69 (m, 2H), 3.28 (t, $J=8$ Hz, 2H), 1.96-1.88 (m, 2H), 1.59-1.54 (m, 5H), 1.43-1.33 (m, 4H), 0.92 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 142.7, 141.3, 140.9, 140.8, 139.3, 137.8, 135.3, 129.4, 129.2, 129.1, 128.3, 126.7, 124.7, 124.4, 123.9, 121.4, 115.3, 109.4, 39.9, 33.6, 31.7, 30.3, 29.2, 22.6, 15.9, 14.1. HPLC: 99.0 %, Column: X-Bridge C18 (4.6X100mm) 3.5 μm , mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/10, 3/90, 11.5/98&12/10. Column Temp : 30°C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80:20) V/V ; UV 215 nm, retention time 9.3 min ; Mass: m/z (CI) 382 ($M+1$, 100%).

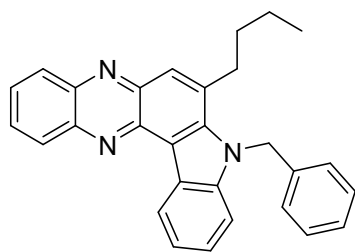
8-Benzyl-7-phenyl-8H-indolo[3,2-a]phenazine(2m)



Chemical Formula: $C_{31}H_{21}N_3$
Exact Mass: 435.1735

Yellow solid; Yield: 81%; mp: 210-215 °C; R_f = 0.5 (10% EtOAc/ *n*-hexane); IR: 1514, 1451, 1217, 1088, 771 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 9.45 (d, J = 7.6 Hz, 1H), 8.47 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.7 Hz, 1H), 7.94 (s, 1H), 7.91-7.87 (m, 1H), 7.83-7.79 (m, 1H), 7.55 (t, J = 8 Hz, 1H), 7.50-7.46 (m, 1H), 7.44-7.39 (m, 2H), 7.35-7.28 (m, 4H), 7.14-7.07 (m, 3H), 6.54 (d, J = 6.8 Hz, 2H), 5.29 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 140.7, 139.2, 137.6, 137.1, 129.8, 129.5, 129.0 (3C), 128.8, 128.3 (2C), 128.2(5C), 127.0, 125.4 (3C), 125.3(2C), 124.2, 124.0, 121.9, 115.9, 114.0, 110.4, 48.3; HPLC: 97.7 %, Column: X-Bridge C18 (4.6X100mm) 3.5 μ m, mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/10, 3/90, 11.5/98&12/10. Column Temp : 30°C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80:20) V/V ; UV 215 nm, retention time 7.8 min; Mass: m/z (CI) 436 ($M + 1$, 100%).

8-Benzyl-7-butyl-8H-indolo[3,2-a]phenazine(2n)

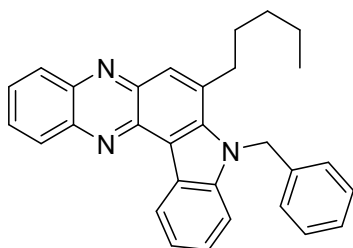


Chemical Formula: $C_{29}H_{25}N_3$
Exact Mass: 415.2048

Brown solid; Yield: 76%; mp: 150-155 °C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR : 2924, 1505, 1442, 1336, 1076, 738 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 9.41 (d, J =8 Hz, 1H), 8.43 (d, J = 8 Hz, 1H), 8.27 (d, J = 8 Hz, 1H), 7.90 (s, 1H), 7.87-7.78 (m, 2H), 7.54-7.49 (m, 3H), 7.28-7.23 (m, 3H), 6.96 (d, J = 7.6 Hz, 2H), 5.92 (s, 2H), 3.11 (t, J =8.4 Hz, 2H), 1.85-1.78 (m, 2H), 1.48-1.42 (m, 2H), 0.92 (t, J =7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.8, 141.2, 141.1, 141.0,

140.3, 138.6, 137.7, 135.4, 129.5, 129.4, 129.2, 129.0 (2C), 128.5, 127.5, 126.9, 125.2 (2C), 125.1, 124.2, 123.9, 121.8, 115.6, 109.8, 48.6, 32.9, 32.5, 22.4, 13.8 ; HPLC: 95.0 %, Column: X-SELECT CSH C18 (4.6X150mm) 5 μ m, mobile phase A: 0.05% Formic acid in MliQwater, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/5, 1.5/5, 4/50, 10/80, 15/98, 18/98, 20/5. Column Temp: 35 $^{\circ}$ C, flow rate: 1 ml/min, Diluent: (ACN : WATER); UV 215 nm, retention time 17.3 min; Mass: m/z (CI) 416 (M + 1, 100%).

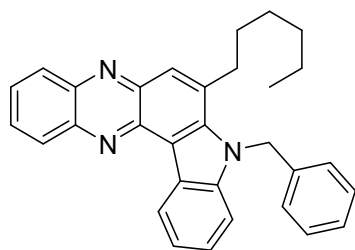
8-Benzyl-7-pentyl-8*H*-indolo[3,2-*a*]phenazine(2o)



Chemical Formula: C₃₀H₂₇N₃
Exact Mass: 429.2205

Yellow solid; Yield: 76%; mp: 150-155 $^{\circ}$ C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR: 1511, 1454, 1336, 1082, 771 cm^{-1} ; ^1H NMR (400 MHz, CDCl₃) δ 9.41 (d, J = 7.2 Hz, 1H), 8.43 (d, J = 8 Hz, 1H), 8.28 (d, J = 8 Hz, 1H), 7.90 (s, 1H), 7.88-7.80 (m, 2H), 7.54-7.49 (m, 3H), 7.26-7.23 (m, 3H), 6.96 (d, J = 7.2 Hz, 2H), 5.91 (s, 2H), 3.10 (t, J = 8 Hz, 2H), 1.85-1.81 (m, 2H), 1.45-1.36 (m, 2H), 1.33-1.25 (m, 2H), 0.88 (t, J = 7.6 Hz, 3H) ; ^{13}C NMR (100 MHz, CDCl₃): δ 142.8, 141.2, 140.3, 138.6, 137.7, 135.5, 129.5, 129.4, 129.2, 129.0 (2C), 128.5, 127.5, 126.9, 126.9, 125.2 (2C), 125.1, 124.2, 123.9, 121.8, 115.6, 114.0, 109.8, 48.6, 33.2, 31.5, 29.7, 22.4, 13.9; HPLC: 99.2 %, Column: X-Bridge C18 (4.6X100mm) 3.5 μ m, mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/10, 3/90, 11.5/98&12/10. Column Temp : 30 $^{\circ}$ C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80:20) V/V ; UV 215 nm, retention time 8.9 min; Mass: m/z (CI) 430 (M + 1, 100%).

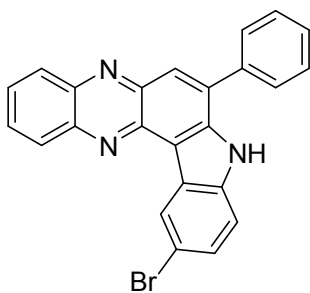
8-Benzyl-7-hexyl-8*H*-indolo[3,2-*a*]phenazine(2p)



Chemical Formula: $C_{31}H_{29}N_3$
Exact Mass: 443.2361

Brown solid; Yield: 81%; mp: 95-100°C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR: 1514, 1430, 1335, 1152, 753 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$): δ 9.22 (s, 1H), 8.57-8.51 (m, 2H), 8.15 (s, 1H), 8.01 (t, J = 4.4 & 5.2 Hz, 2H), 7.55 (d, J = 4 Hz, 3H), 7.27 (t, J = 5.6 & 4.8 Hz, 3H), 6.93 (t, J = 2.4 & 5.2 Hz, 2H), 5.93 (s, 2H), 3.14 (t, J = 8 & 8 Hz, 2H), 1.82-1.76 (m, 2H), 1.45-1.40 (m, 2H), 1.33-1.25 (m, 4H), 0.88 (t, J = 6.4 & 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 142.8, 142.0, 140.6, 138.2, 136.8, 132.7, 132.1, 131.6, 130.8, 129.6, 129.2 (2C), 127.9, 126.6, 125.1 (2C), 123.8, 123.2, 122.9 (2C), 119.1, 115.4, 110.3, 48.9, 33.6, 31.4, 30.1, 29.7, 22.5, 14.0. HPLC: 98.8 %, Column: X-Bridge C18 (4.6X100mm) 3.5 μ m, mobile phase A: 0.05% Formic acid in Mli-Q-water, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/10, 3/90, 11.5/98&12/10. Column Temp : 30°C, flow rate: 1.0 mL/min, Diluent : ACN : Mli-Q-water (80:20) V/V ; UV 215 nm, retention time 9.9 min; Mass: m/z (CI) 444 ($M + 1$, 100%).

11-Bromo-7-phenyl-8H-indolo[3,2-a]phenazine(2q)

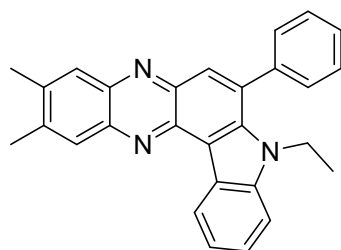


Chemical Formula: $C_{24}H_{14}BrN_3$
Exact Mass: 423.0371

Light yellow solid; Yield: 81%; mp: 255-260°C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR: 2925, 1551, 1154, 751 cm^{-1} ; 1H NMR (400 MHz, $DMSO-d_6$): δ 12.09 (s, 1H), 9.11 (s, 1H), 8.37 (d, J = 8 Hz, 1H), 8.21 (d, J = 8 Hz, 1H), 7.99 (s, 1H), 7.94-7.83 (m, 4H), 7.68-7.65 (m, 3H), 7.62-7.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.3, 142.2, 141.5, 141.3, 140.9, 138.3, 138.0, 136.8,

134.8, 130.8, 129.7 (2C), 129.6, 129.4, 129.3, 129.1(2C), 127.7, 126.9, 125.7, 124.9, 115.1, 113.8, 113.2; HPLC: 92.4 %, Column: X-SELECT CSH C18 (4.6X150mm) 5 μ m, mobile phase A: 0.05% Formic acid in MliQwater, mobile phase B: 0.05% Formic acid in ACN; Gradient Time%B: 0/5, 1.5/5, 4/50, 10/80, 15/98, 18/98, 20/5. Column Temp : 35 $^{\circ}$ C, flow rate: 1 ml/min, Diluent : (ACN : WATER); UV 215 nm, retention time 16.3 min; Mass: m/z (CI) 424 (M + 1, 100%).

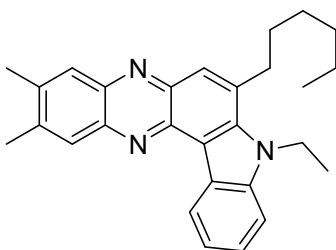
8-Ethyl-2,3-dimethyl-7-phenyl-8*H*-indolo[3,2-*a*]phenazine (2r)



Chemical Formula: C₂₈H₂₃N₃
Exact Mass: 401.1892

Light brown solid; Yield: 80%; mp: 205-210 $^{\circ}$ C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR: 3125, 1458, 1025, 755 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 9.21(d, J = 8 Hz, 1H), 8.21 (d, J = 5.6 Hz, 2H), 8.10 (s, 1H), 7.62-7.49 (m, 8H), 4.06-4.01 (m, 2H), 2.61 (s, 3H), 2.58 (s, 3H), 1.08 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 144.1, 143.1, 142.5, 141.4, 140.0, 138.6, 138.0, 136.7, 133.1, 132.4, 129.0, 128.7(2C), 128.6(2C), 128.1, 125.9, 124.0, 123.7, 122.7, 122.5, 122.1, 115.7, 110.2, 39.6, 20.9, 20.7, 14.7; Mass: m/z (CI) 402 (M + 1, 100%).

8-Ethyl-7-hexyl-2,3-dimethyl-8*H*-indolo[3,2-*a*]phenazine (2s)



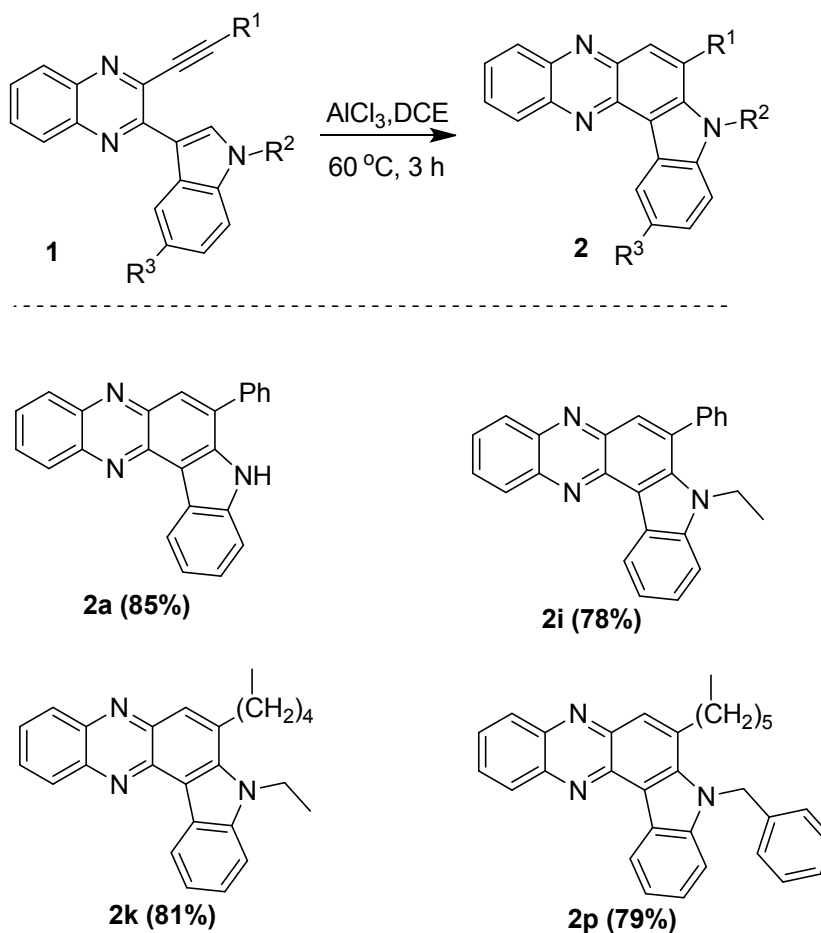
Light brown solid; Yield: 75%; mp: 170-175 $^{\circ}$ C; R_f = 0.6 (10% EtOAc/ *n*-hexane); IR: 1654, 1458, 1256, 712 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 9.22 (d, J = 8 Hz, 1H), 8.21 (d, J =4 Hz, 2H), 8.13 (s, 1H), 7.62-7.55 (m, 2H), 7.50 (t, J =8 Hz, 1H), 4.75-4.70 (m, 2H), 3.30 (t, J = 8 Hz,

2H), 2.61 (s, 3H), 2.60 (s, 3H), 1.95-1.88 (m, 2H), 1.59-1.53 (m, 5H), 1.43-1.35 (m, 4H), 0.93 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 143.5, 142.7, 141.8, 141.3, 139.6, 139.3, 137.4, 133.3, 133.1, 128.1, 125.7, 124.0, 123.8, 122.9, 122.0, 121.2, 115.4, 109.7, 40.1, 34.0, 31.6, 30.4, 29.2, 22.5, 20.9, 20.6, 15.9, 14.0; Mass: m/z (CI) 410 ($M + 1$, 100%).

References

1. K. S. Kumar, D. Rambabu, S. Sandra, R. Kapavarapu, G. R. Krishna, M.V. B. Rao, K. Chatti, C. M. Reddy, P. Misra, M. Pal, *Bioorg. Med. Chem.* 20 (2012) 1711–1722.

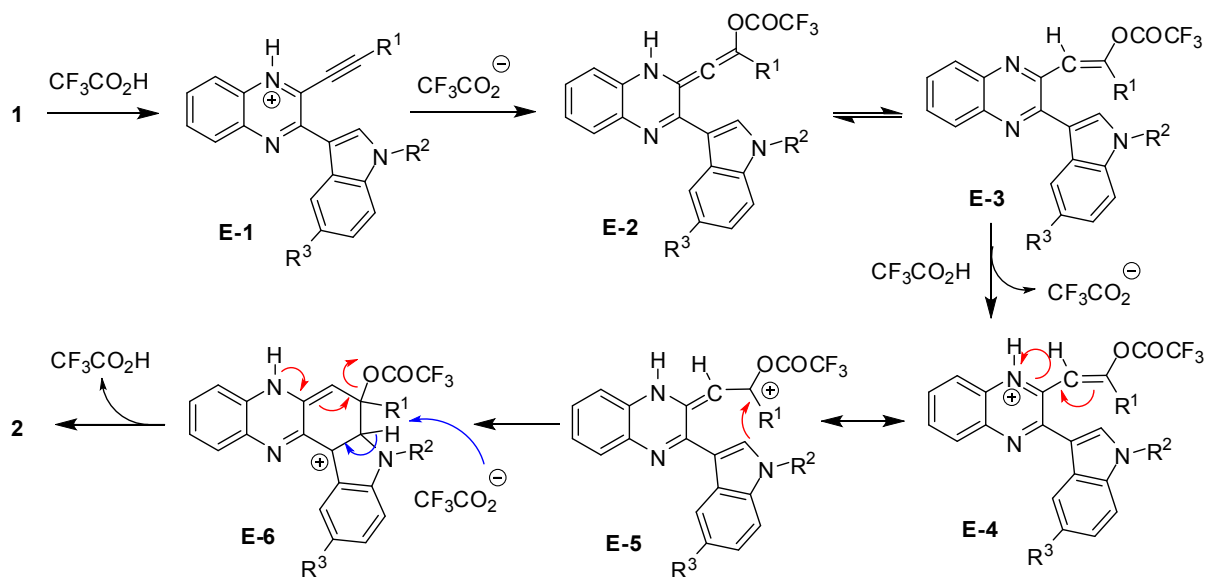
Table S-4. AlCl_3 mediated synthesis of indolophenazine (**2**)^{a,b}



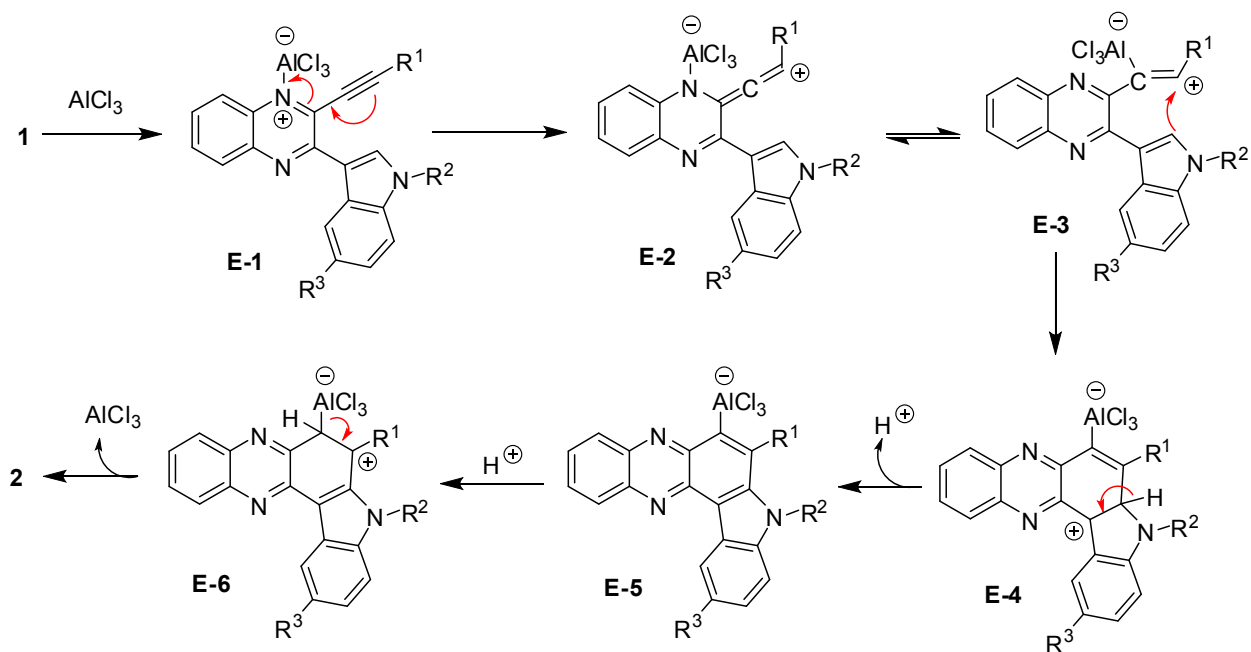
^aAll the reactions were carried out using compound **1** (1.0 equiv) and AlCl_3 (1.20 equiv) in a DCE (5 mL) at 60°C for 3 h. ^bIsolated yield.

Reaction mechanism

1) TFA mediated reaction



2) AlCl_3 mediated reaction



Single crystal X-ray data

The X-ray data collection was monitored by SMART program (Bruker, 2003). All the data were corrected for Lorentzian, polarization and absorption effects using SAINT and SADABS programs (Bruker, 2003). SHELX-97 was used for structure solution and full matrix leastsquares refinement on F². Molecular and packing diagrams were generated using ORTEP-3 and Mercury-3.0. Geometrical calculations were performed using SHELXTL (Bruker, 2003) and PLATON.

Crystal data of (2h): CCDC 1503459, Single crystals suitable for X-ray diffraction of **2h** were grown from MeOH. Molecular formula = C₂₅H₂₅N₃, Formula weight = 367.48, Crystal system = Monoclinic, space group = P 2₁/c, a = 8.4926(2) Å, b = 7.9538(2) Å, c = 28.9887(7) Å, V = 1957.78(8) Å³, T = 296(2) K, Z = 4, D_c = 1.247 Mg/m³, 15774 Reflections collected, 3844 [R(int) = 0.0283] independent reflections, Goodness of fit = 1.019

Crystal data of (2l): CCDC 1503460, Single crystals suitable for X-ray diffraction of **2l** were grown from MeOH:DCM (1:1). Molecular formula = C₂₆H₂₇N₃, Formula weight = 381.50, Crystal system = Monoclinic, space group = P 2₁/n, a = 15.8218(7) Å, b = 8.1579(3) Å, c = 16.5439(7) Å, V = 2099.39(15) Å³, T = 296(2) K, Z = 4, D_c = 1.207 Mg/m³, 17282 Reflections collected, 4117 [R(int) = 0.0286] independent reflections, Goodness of fit = 1.028.

Pharmacology

Cell proliferation Assay

The anti-proliferative activity and cancer cell selectivity of the synthesized compounds on normal and cancer cells was evaluated using the SRB (Sulforhodamine B) cell proliferation assay. This assay was chosen because of its sensitivity, large dynamic range and the ability to measure cell proliferation over three days with normalization to initial cell number as well as to vehicle-treated cells. Further, this assay is the standardized assay of choice for anticancer compound screening at the National Cancer Institute (NIH). The SRB assay provides a colorimetric readout which can be spectrophotometrically measured and does not involve antibodies or toxic reagents. The assay is based on detection of total protein content of cells, which increases or decreases in proportion with cell number.

In brief, the assay was performed as follows: TZM-BL (Human cervical carcinoma cells) and A549 (human lung carcinoma cell) were seeded in 96-well plates and incubated overnight. The optimum cell numbers to be seeded were determined by a growth curve analysis for each cell line. In the initial (single dose) screen, compounds (dissolved in 100% DMSO to a stock concentration of 100 mM) were added to the adhered cells at a final concentration of 10 μ M. After 72 h of treatment, the cells were washed with phosphate-buffered saline and ice-cold 10% trichloroacetic acid added to the cells to precipitate all proteins for 1h at 4 °C. The cells were then washed with water and air-dried. Cellular proteins were then stained using 0.4% SRB solution in 1% acetic acid for 10 min at room temperature. The unbound dye was washed away by destaining with 1% acetic acid and bound dye solubilized with 10 μ M Tris solution. Absorbance of solubilized dye was measured at a wavelength of 590 nm. Percentage growth was determined by the formula $[(At-A0)/(Ac-A0)] \times 100$, where At=absorbance after 72h of test compound treatment, A0=Absorbance at time 0, Ac=Absorbance after 72h without treatment.

References

1. Rubinstein, L.V., et al., *Comparison of in vitro anticancer-drug-screening data generated with a tetrazolium assay versus a protein assay against a diverse panel of human tumor cell lines*. J Natl Cancer Inst, 1990. **82**(13): p. 1113-8.
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