Supplementary Information

Tetrahydro-3H-pyrazolo[4,3-a]phenanthridine-based CDK inhibitor

1. Supplemental Figures

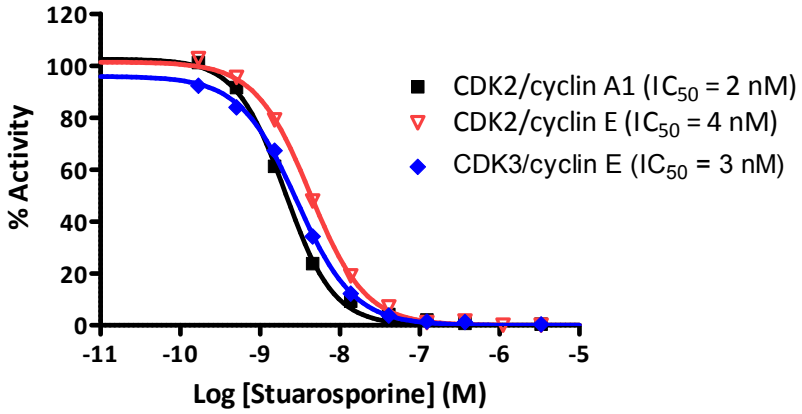

Figure S1. Dose-response curves of the inhibition of the indicated CDKs by staurosporine

Table S1. *In vitro* kinase selectivity of **HSD992**

Entry	Kinase	% inhibition
1	CDK3/cyclin E	89
2	CDK2/cyclin E	87
3	CDK2/Cyclin A1	84
4	CDK2/cyclin O	76
5	CDK9/cyclin K	72
6	CDK2/cyclin A	68
7	PKG1b	67
8	DYRK2	67
9	GCK/MAP4K2	67
10	CLK1	66
11	EPHB3	65
12	EPHB1	63
13	CDK9/cyclin T2	63
14	CLK2	63
15	RIPK2	62
16	PKCd	62
17	PKCeta	57
18	CLK4	57
19	MAK	57
20	PBK/TOPK	57
21	DMPK2	53
22	p70S6K/RPS6KB1	52
23	STK39/STLK3	50
24	ROCK2	49
25	LOK/STK10	48
26	EPHB4	47
27	DDR1	45
28	PRKX	44
29	VRK1	44
30	RSK4	43
31	TAOK2/TAO1	42
32	MUSK	42
33	NEK1	41
34	PIM1	40
35	TNIK	36
36	TAOK1	34
37	Aurora A	34
38	KHS/MAP4K5	34
39	AXL	34
40	LKB1	33
41	ROCK1	31
42	CDK19/cyclin C	31
43	BRK	31
44	ERK7/MAPK15	31
45	SLK/STK2	30
46	CDK9/cyclin T1	29
47	PYK2	28
48	CDK1/cyclin A	28
49	STK32C/YANK3	26
50	RSK1	26
51	c-Kit	26
52	CDK17/cyclin Y	26
53	STK32B/YANK2	26
54	RET	25
55	TYK1/LTK	25
56	HIPK4	24
57	CK2a2	24
58	ALK	24
59	c-MER	23
60	CDK1/cyclin B	23
61	CDK1/cyclin E	22
62	CDK5/p25	22
63	Aurora B	22
64	MLCK/MYLK	21
65	PDGFRb	21
66	EPHA1	20
67	STK16	20
68	p70S6Kb/RPS6KB2	20
69	EPHA4	20
70	PKCb2	19
71	FGFR1	19
72	RIPK5	19
73	EPHA5	19
74	FLT4/VEGFR3	18
75	PHKg1	18
76	NEK9	18
77	EPHA7	18
78	FGFR2	17
79	IR	17
80	HIPK1	17
81	SIK1	17
82	AKT1	17
83	FYN	17
84	c-Src	16
85	MLCK2/MYLK2	16
86	AKT3	16
87	HIPK2	16
88	MYO3A	16
89	PAK2	16
90	HGK/MAP4K4	15
91	PLK4/SAK	15
92	CDC7/DBF4	15
93	CAMKK1	15
94	FGR	15
95	NEK3	14
96	CDK5/p35	14
97	JNK1	14
98	PKCtheta	14
99	TAK1	14
100	STK33	14
101	MST1/STK4	14
102	RAF1	13
103	GRK4	13
104	DMPK	13
105	EPHA3	13
106	DCAMKL1	13
107	GLK/MAP4K3	13
108	STK38/NDR1	12
109	MNK1	12
110	CDK4/cyclin D3	12
111	STK38L/NDR2	12
112	NEK8	12
113	MSSK1/STK23	12
114	NEK6	12
115	TXK	12
116	MLK2/MAP3K10	12
117	Aurora C	12
118	FMS	12
119	DLK/MAP3K12	11
120	P38g	11
121	CDK18/cyclin Y	11
122	PDGFRa	11
123	ABL2/ARG	11
124	HCK	11
125	SRPK1	10
126	ARK5/NUAK1	10
127	CAMK2g	10
128	PKCb1	10
129	FGFR3	10
130	CAMK4	10
131	TAOK3/JIK	10
132	ULK3	10
133	PKA	10
134	PEAK1	10
135	ULK1	10
136	CDK7/cyclin H	10
137	c-MET	10
138	TBK1	10
139	TESK1	9
140	WNK2	9
141	MST2/STK3	9
142	CSK	9
143	MLK1/MAP3K9	9
144	CDK4/cyclin D1	8
145	ASK1/MAP3K5	8
146	BRSK2	8
147	IKKe/IKBKE	8
148	ULK2	8
149	NEK4	8
150	BTK	8
151	PKCa	8
152	ERK2/MAPK1	8
153	LCK	8
154	CLK3	8
155	SGK1	8
156	LIMK1	7
157	LCK2/ICK	7
158	IRAK4	7
159	MKK6	7
160	CK1d	7
161	PLK2	7
162	FES/FPS	7
163	GRK1	7
164	SRPK2	6
165	CK1epsilon	6
166	MST4	6
167	GRK6	6
168	PAK6	6
169	STK22D/TSSK1	6
170	PKN2/PRK2	6
171	KDR/VEGFR2	6
172	TYK2	6
173	ARAF	6
174	CK2a	6
175	HIPK3	5
176	PLK1	5
177	P38d/MAPK13	5
178	ZAK/MLTK	5
179	FAK/PTK2	5
180	PKAcb	5
181	CDK6/cyclin D1	5
182	MYO3b	5
183	MRCKb/CDC42BPB	4
184	SIK2	4
185	CK1g1	4
186	EPHA8	4
187	MARK3	4
188	TSSK2	3
189	CK1g2	3
190	PKD2/PRKD2	3
191	ABL1	3
192	JAK3	3
193	IRAK1	3
194	CDK6/cyclin D3	3
195	HPK1/MAP4K1	3
196	FER	2
197	ERK1	2
198	CHK1	2
199	SNARK/NUAK2	2
200	MKK4	2
201	SSTK/TSSK6	2
202	CAMK2a	2
203	BLK	1
204	MARK2/PAR-1Ba	1
205	AKT2	1
206	MAPKAPK3	1
207	ERBB2/HER2	1
208	IGF1R	1
209	CAMK1g	1
210	EPHB2	0
211	MINK/MINK1	0
212	JAK1	0
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214	COT1/MAP3K8	0
215	ALK2/ACVR1	0
216	SBK1	0
217	RIPK3	0
218	P38a/MAPK14	0
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236	ITK	0
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238	TTBK2	0
239	MST3/STK24	0
240	MRCKa/CDC42BPA	0
241	ALK3/BMPR1A	0
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243	KSR2	0
244	PLK3	0
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251	ZAP70	0
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260	MEKK1	0
261	STK25/YSK1	0
262	PKAcg	0
263	BRAF	0
264	MAPKAPK5/PRAK	0
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274	GRK5	0
275	TIE2/TEK	0
276	LYN B	0
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281	MEK1	0
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283	NEK2	0
284	DAPK1	0
285	IRR/INSRR	0
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287	PDK1/PDPK1	0
288	PIM2	0
289	DCAMKL2	0
290	MKK7	0
291	PAK1	0
292	IKKa/CHUK	0
293	NEK7	0
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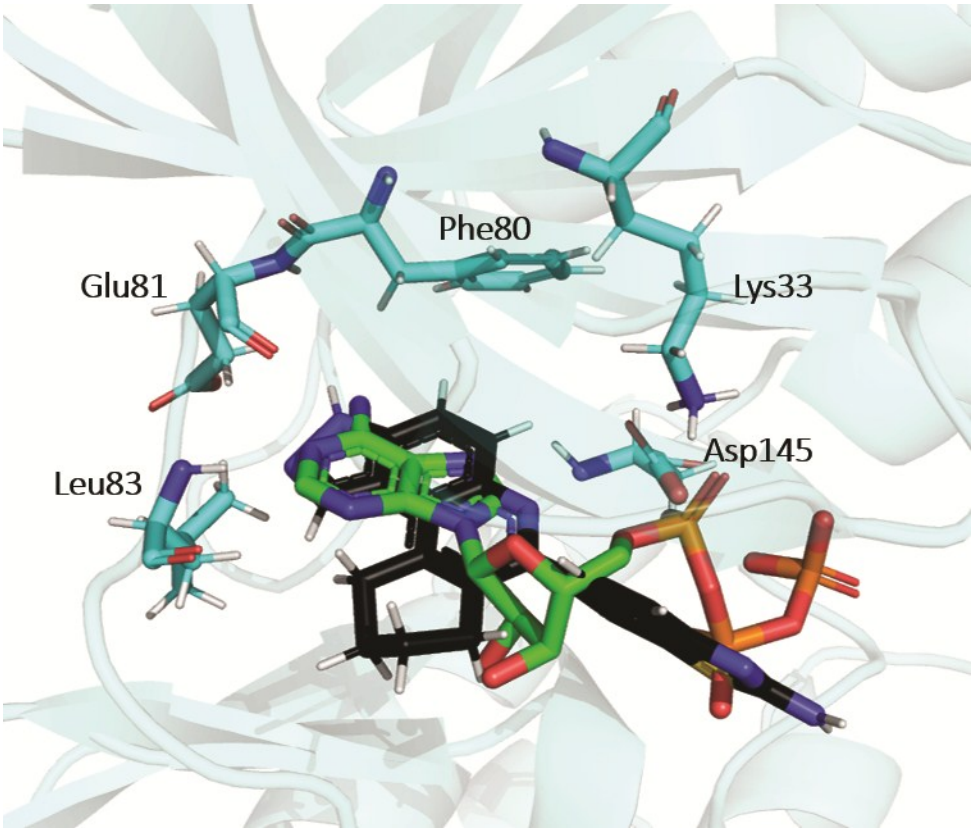


Figure S2. Overlay of ATP (green) and HSD992 (black) in the catalytic pocket of CDK2 (PDB entry 1HCK). Some residues in the active site have been shown and labeled. Figure generated in PyMOL visualization software (The PyMOL Molecular Graphics System, Version 2.0 Schrödinger, LLC).

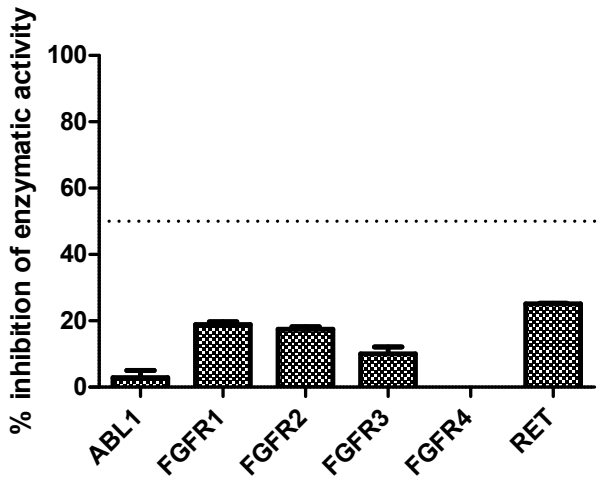


Figure S3. In vitro kinase inhibition by HSD992. The cell lines substantially inhibited by HSD992 are driven by ABL1, FGFR1-4 and RET kinases. However, HSD992 does not inhibit the *in vitro* activity of these driver kinases.

2. Experimental Section

Biology

In vitro kinase inhibition assay

The kinase inhibition assay was performed using the kinase profiling service of Reaction Biology Corporation (Malvern, PA, USA). Briefly, DMSO stock solutions of compounds were diluted into reaction mixture containing 100 μM ATP and kinase in a single dose mode at a concentration of 0.5 μM. Alternatively, compounds were tested in 10-dose IC50 duplicate mode with a 3-fold serial dilution starting at 3.33 μM. The kinase activity was determined relative to DMSO control. IC50 data were fit to a non-linear regression using GraphPad Prism 4 Software (GraphPad, La Jolla, CA, USA).

Cell culture

Purdue University compound ND992 was dissolved in DMSO in 20 mM stock. The reference compound staurosporine was dissolved in DMSO in 1 mM stock. Staurosporine was purchased from Sigma-Aldrich (Saint Louis, MI). Cell Titer-Glo® 2.0 Luminescent cell viability assay reagent was purchased from Promega (Madison, WI, USA). KMS-11 cell line was purchased from Japan Cell Bank. UACC-62 cell line was purchased from Addexbio. HCC-78 and NOMO-1 cell lines were purchased from Reactive-Bioarray. LC-2/Ad was purchased from Sigma-Aldrich. Other cell lines were purchased from American Type Culture Collection. Apart from DMS114, HLY-1, NCI-H1703, NCI-H520, and LC-2/Ad, all cell lines were tested at Reaction Biology Corporation. Cell culture media are listed in the following table. Media were routinely supplemented with 100 μg/mL of penicillin, and 100 μg/mL of streptomycin. Cultures were maintained at 37°C in a humidified atmosphere of 5% CO_2 and 95% air.

Table S1. Culture method for cell lines used in this study

Cell line	Medium
NK-92	EMEM without ribonucleosides and deoxyribonucleosides + 12.5%FBS + 12.5%Horse serum + 0.2mM Myo-inositol + 0.1mM B-mercaptoethanol + 0.02mM folic acid + 100unit/ml recombinant human IL-2 + 1.5g/L sodium bicarbonate
MDA-MB-361	DMEM/F12 + 10%FBS
MDA-MB-468	DMEM + 10%FBS
HS578T	DMEM + 10%FBS + 0.01mg/ml Bovine insulin
A549	F12K + 10%FBS
MDA-MB-157	F12K + 10%FBS
HS578Bst	Hybri-care + 10%FBS + EGF 30ng/ml
BT474	Hybri-Care + 1.5 g/L sodium bicarbonate + 10%FBS
HT-29	McCoy's 5A + 10%FBS
SK-BR-3	McCoy's 5A + 10%FBS
SK-OV3	McCoy's 5A + 10%FBS
Hep G2	EMEM + 10%FBS
U87MG	EMEM + 10%FBS
A-498	EMEM + 10%FBS
SK-MEL-2	EMEM + 10%FBS

ZR-75-1	RPMI + 10%FBS
SNU-182	RPMI + 10%FBS
KMS-11	RPMI + 10%FBS
UACC-62	RPMI + 10%FBS
SU-DHL-1	RPMI + 10%FBS
SU-DHL-6	RPMI + 10%FBS
Molt-4	RPMI + 10%FBS
HCC-78	RPMI + 10%FBS
NCI-H441	RPMI + 10%FBS
NOMO-1	RPMI + 10%FBS
LnCap	RPMI + 10%FBS
BT-549	RPMI + 10%FBS + 0.01mg/ml Bovine Insulin
OVCAR3	RPMI + 20%FBS + 0.01mg/ml Bovine Insulin
DMS114	Waymouth + 10%FBS
LC-2/Ad	RPMI/F12 + 10%FBS
NCI-H1703	RPMI + 10%FBS
NCI-H1755	RPMI + 10%FBS
NCI-H520	RPMI + 10%FBS
HLY-1	RPMI + 10%FBS
K562	IMDM + 10%FBS

Antiproliferative activity of compounds

Compound ND992 was diluted in DMSO solution with 10-dose and 3-fold dilution in a source plate starting at 20 mM. The reference compound staurosporine was diluted in DMSO solution with 10-dose and 3-fold dilution in a source plate starting at 10 mM (for adherent cell lines) and 1 mM (for suspension cell lines). 12.5 nL of each test compound was delivered from the source plate to each well of the 384-well cell culture plates by Echo 550 (Labcyte, San Jose, CA, USA). 25 µL of culture media containing 2000 cells was added to each of the wells in duplicates of the cell culture plate. The cells were incubated with the compounds at 37°C, 5% CO_2 for 72 hours. 25 µL of Cell Titer Glo 2.0 reagent was added to each well. The contents were mixed on an orbital shaker for 2 min and incubated at room temperature for 15 min to stabilize luminescent signal. Luminescence was recorded by Envision 2104 Multilabel Reader (PerkinElmer, Santa Clara, CA). The number of viable cells in culture was determined based on quantitation of the ATP present in each culture well. The IC50 curves were plotted and IC50 values were calculated using the GraphPad Prism 4 program based on a sigmoidal dose-response equation.

Molecular Docking with GOLD program

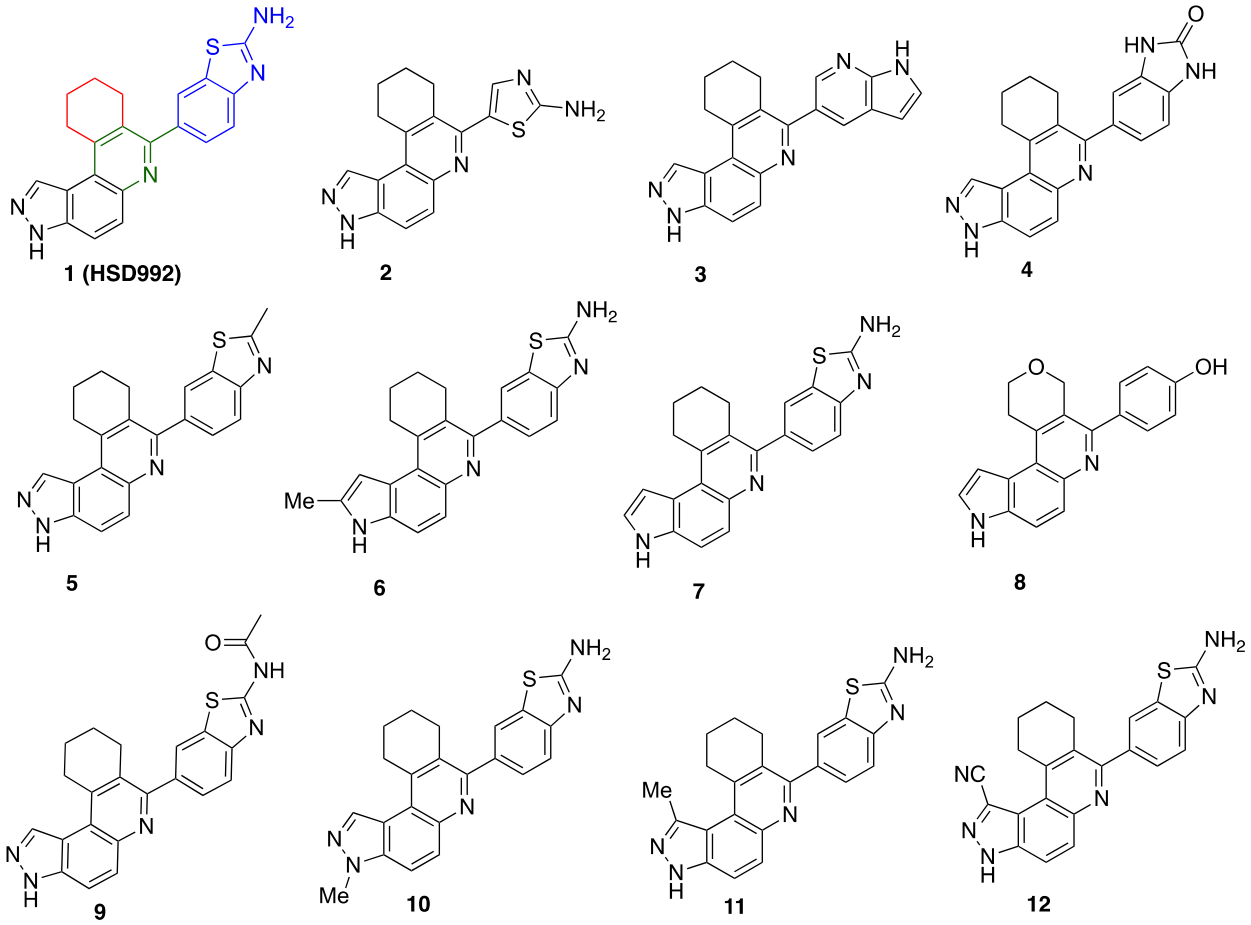
The PDB file for CDK2 (1HCK) was obtained from the RCSB Protein Data bank (www.rcsb.org). **HSD992** was drawn in ChemDraw Professional software version 16.0 and Chem3D software version 16.0 (PerkinElmer Informatics) was used to generate an energy minimized 3D structure saved as a mol2 file. GOLD docking was run from the Hermes visualizer. For protein preparation, the wizard option was used to add hydrogens, delete water molecules and the crystalized ligand. **HSD992** was then docked into

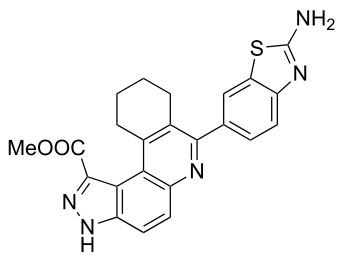
the binding site using the default 10 genetic algorithms and the ChemPLP scoring function. Following the docking, PyMOL visualization software (The PyMOL Molecular Graphics System, Version 2.0 Schrödinger, LLC) was used to generate the figures.

Chemistry

General Considerations General Considerations All reagents and solvents were purchased from commercial suppliers and used them as received, unless otherwise stated. The ^{1}H and ^{13}C NMR spectra were obtained in CD_3OD or $(CD_3)_2SO$ as solvent using a 500 MHz spectrometer with Me_4Si as an internal standard. Chemical shifts were reported in parts per million (δ) downfield from internal standard Me_4Si. Data for ^{1}H NMR spectra were reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, or combinations thereof. High resolution mass spectra (HRMS) were recorded using electron spray ionization (ESI) technique and as TOF mass analyzer. All the new synthesized compounds were characterized using ^{1}H NMR, ^{13}C NMR, and HRMS data. Substrate 2-amino-benzthiazole-6-carbaldehyde (95% purity) was purchased from Chemcia Scientific, LLC.

Synthesized compounds





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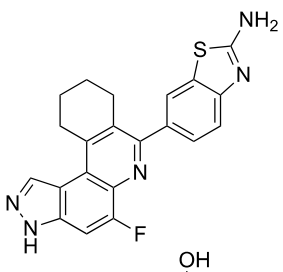

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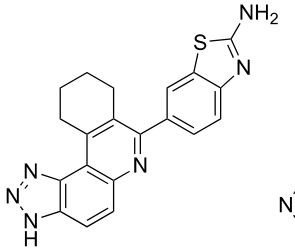

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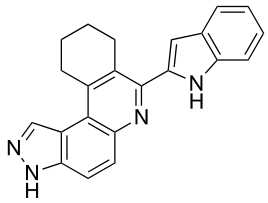

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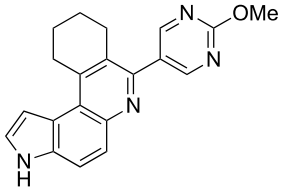

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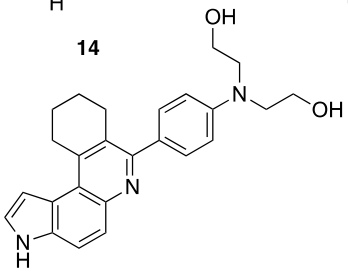

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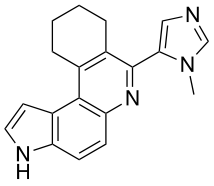

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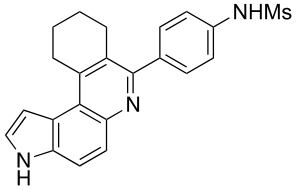

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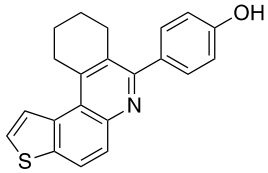

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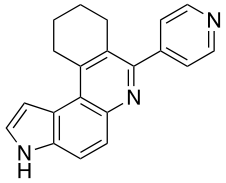

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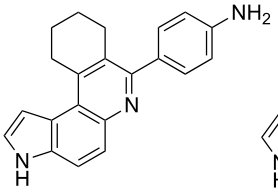

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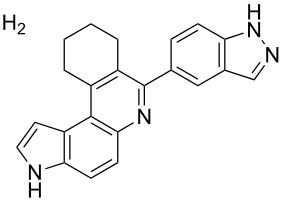

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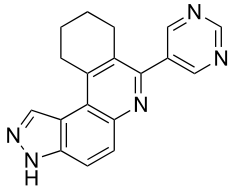

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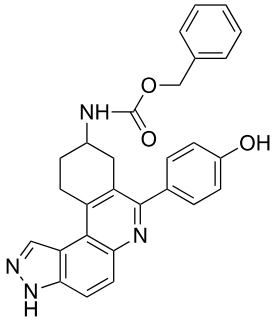

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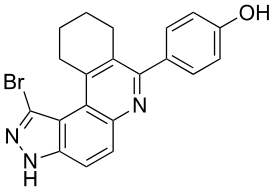

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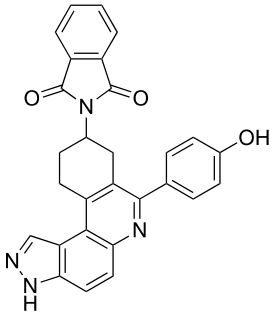

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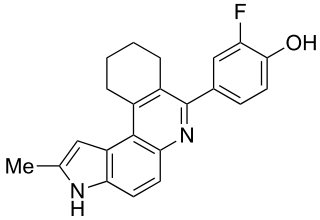

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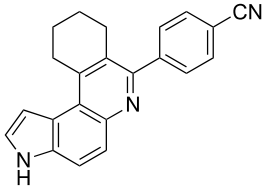

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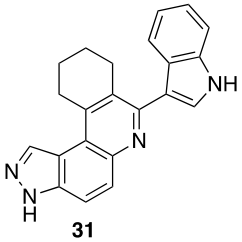
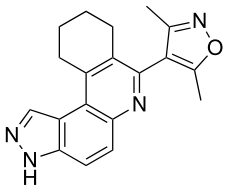
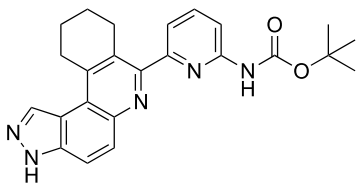


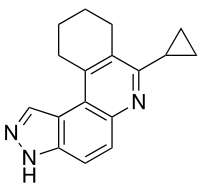
31



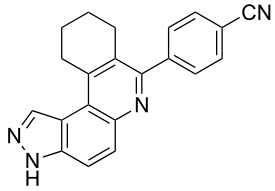
32



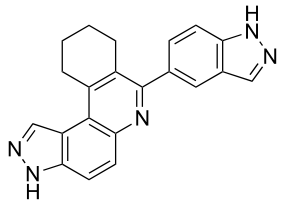
33



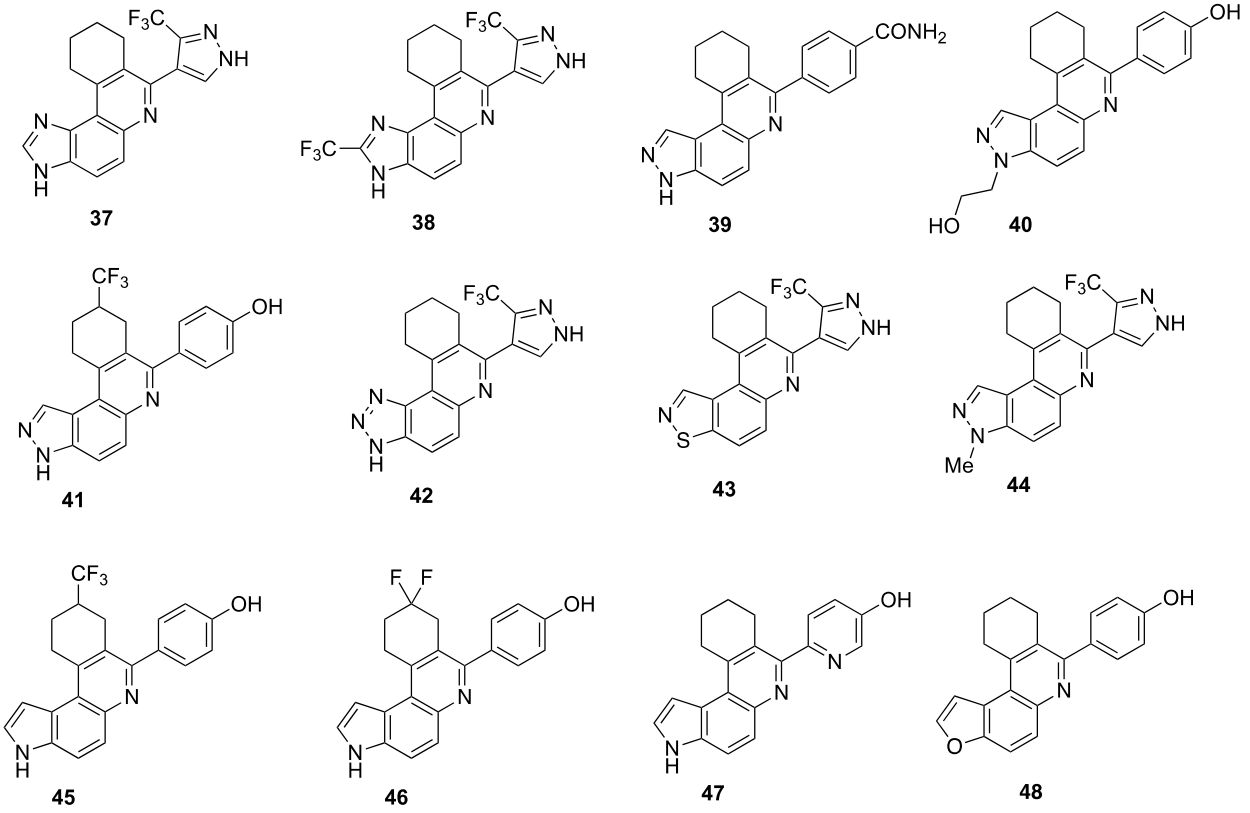
34



35



36

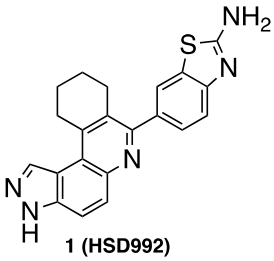


General procedure for the multicomponent reaction:

A screw capped 20 mL vial charged with amine (1 mmol) and aldehyde (1 mmol) in 5 mL of absolute ethanol was refluxed for 2 h. After complete conversion of substrates to imine, cyclic ketone (2.5 mmol) and a catalytic amount of conc. hydrochloric acid was added. The reaction was continued to reflux for 12 h. The resultant reaction mixture was concentrated under reduced pressure and was purified by flash silica gel chromatography (dichloromethane:methanol (99:01 to 80:20) to give the desired cyclized compound. (Note: In some cases, product may get precipitated out as solid after completion of reaction which was filtered, washed with ethanol and further purified using flash silica gel column chromatography).

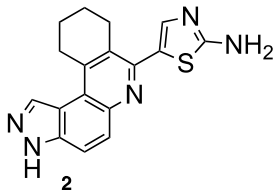
Compounds characterization data

5-(8,9,10,11-Tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-7-yl)benzo[d]thiazol-2-amine



Pale yellow solid (137 mg, 37%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H), 7.88 – 7.78 (m, 3H), 7.55 (s, 2H), 7.45 – 7.36 (m, 2H), 3.32 (s, 2H), 2.82 (t, *J* = 6.1 Hz, 2H), 1.99 (qq, *J* = 5.2, 2.7 Hz, 2H), 1.74 (dp, *J* = 9.1, 3.2, 2.8 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.61, 156.90, 152.94, 143.53, 142.39, 138.63, 136.32, 133.93, 131.17, 129.60, 127.25, 122.13, 121.64, 117.32, 116.50, 114.34, 29.75, 29.18, 22.66, 22.62; HRMS (ESI) m/z calcd for $C_{21}H_{18}N_5S$ $[M + H]^+$ 372.1283, found 372.1269.

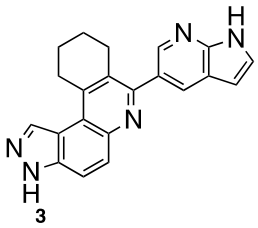
5-(8,9,10,11-Tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridin-7-yl)thiazol-2-amine



2

Yellow solid (166 mg, 52%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 (s, 1H), 7.79 (d, *J* = 9.1 Hz, 1H), 7.66 (d, *J* = 9.4 Hz, 1H), 7.51 (s, 1H), 7.23 (s, 2H), 3.28 – 3.22 (m, 2H), 2.96 (t, *J* = 6.2 Hz, 2H), 1.99 – 1.93 (m, 2H), 1.90 – 1.82 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 170.46, 148.47, 143.26, 142.39, 140.03, 138.39, 136.08, 129.21, 128.99, 128.03, 120.39, 116.44, 114.43, 29.95, 28.90, 22.52, 22.24; HRMS (ESI) m/z calcd for $C_{17}H_{16}N_5S$ $[M + H]^+$ 322.1126, found 322.1123.

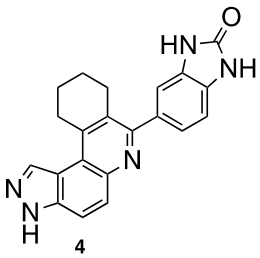
7-(1H-Pyrrolo[2,3-b]pyridin-5-yl)-8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridine



3

Off-white solid (203 mg, 60%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.09 (s, 1H), 8.78 (s, 1H), 8.54 (d, *J* = 2.1 Hz, 1H), 8.37 (d, *J* = 2.1 Hz, 1H), 8.17 (q, *J* = 9.2 Hz, 2H), 7.65 (t, *J* = 3.0 Hz, 1H), 6.61 (dd, *J* = 3.5, 1.8 Hz, 1H), 3.51 – 3.44 (m, 2H), 2.86 (t, *J* = 6.2 Hz, 2H), 2.09 – 2.01 (m, 2H), 1.86 – 1.73 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.20, 149.00, 143.45, 136.93, 132.02, 130.20, 128.42, 122.92, 122.10, 119.30, 115.16, 115.08, 101.14, 30.71, 28.46, 21.95, 21.88; HRMS (ESI) m/z calcd for $C_{21}H_{18}N_5$ $[M + H]^+$ 340.1562, found 340.1551.

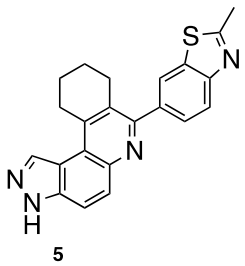
5-(8,9,10,11-Tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-7-yl)-1H-benzo[d]imidazol-2(3H)-one



4

Off-white solid (178 mg, 50%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H), 7.84 (d, *J* = 9.1 Hz, 1H), 7.78 (d, *J* = 9.1 Hz, 1H), 7.16 – 7.09 (m, 2H), 7.00 (d, *J* = 7.8 Hz, 1H), 3.28 (t, *J* = 6.5 Hz, 2H), 2.77 (t, *J* = 6.1 Hz, 2H), 2.00 – 1.95 (m, 2H), 1.73 – 1.66 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.16, 156.09, 143.72, 142.21, 139.73, 134.99, 133.77, 130.00, 129.94, 129.53, 129.35, 122.16, 121.65, 116.30, 115.27, 109.89, 108.18, 29.70, 29.28, 22.65, 22.62; HRMS (ESI) m/z calcd for $C_{21}H_{18}N_5O$ $[M + H]^+$ 356.1511, found 356.1507.

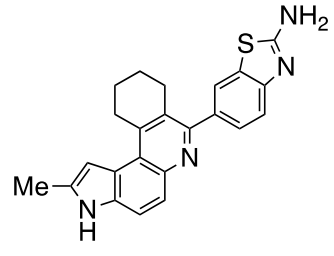
2-Methyl-6-(8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-7-yl)benzo[d]thiazole



5

Off-white solid (207 mg, 56%).^{1}H NMR (500 MHz, DMSO-d_6) δ 8.83 (s, 1H), 8.47 (d, *J* = 1.8 Hz, 1H), 8.26 (d, *J* = 9.2 Hz, 1H), 8.21 (d, *J* = 9.2 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.83 (dd, *J* = 8.4, 1.8 Hz, 1H), 3.51 (t, *J* = 6.4 Hz, 2H), 2.85 – 2.78 (m, 2H), 2.04 (dq, *J* = 8.8, 6.1, 4.4 Hz, 2H), 1.79 (tq, *J* = 9.4, 6.1, 4.2 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 170.38, 154.36, 150.99, 136.08, 135.88, 131.87, 129.54, 128.07, 124.74, 124.31, 123.33, 122.34, 122.00, 121.15, 115.41, 114.98, 112.01, 40.49, 40.32, 40.25, 40.16, 39.99, 39.82, 39.66, 39.49, 30.86, 28.22, 21.86, 21.70, 20.47; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_4S$ $[M + H]^+$ 371.1330, found 371.1320.

6-(2-Methyl-8,9,10,11-tetrahydro-3*H*-pyrrolo[3,2-*a*]phenanthridin-7-yl)benzo[*d*]thiazol-2-amine

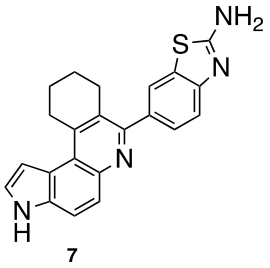


6

Pale yellow solid (76 mg, 20%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 7.72 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.67 (dd, *J* = 8.9, 0.7 Hz, 1H), 7.62 (d, *J* = 8.9 Hz, 1H), 7.49 (dd, *J* = 8.2, 0.6 Hz, 1H), 7.39 (dd, *J* = 8.2, 1.7 Hz, 1H), 6.87 (t, *J* = 0.9 Hz, 1H), 3.45 (t, *J* = 6.5 Hz, 2H), 2.76 (t, *J* = 6.2 Hz, 2H), 2.54 – 2.53 (m, 3H), 2.03 (ddt, *J* = 10.1, 7.4, 3.8 Hz, 2H), 1.84 – 1.74 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 168.99, 155.62, 151.48, 143.70, 142.35, 134.68, 133.75, 133.15, 130.60, 127.26, 126.73, 122.27, 121.26, 121.14, 120.64, 116.83, 115.28, 104.03, 29.95,

28.70, 22.51, 22.21, 12.08; HRMS (ESI) m/z calcd for $C_{23}H_{21}N_4S$ [M + H]$^+$ 385.1487, found 385.1495.

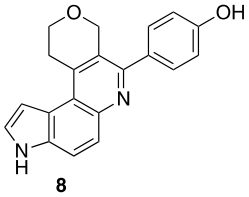
6-(8,9,10,11-Tetrahydro-3*H*-pyrrolo[3,2-*a*]phenanthridin-7-yl)benzo[*d*]thiazol-2-amine



7

Pale yellow solid (115 mg, 31%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.73 (d, *J* = 2.2 Hz, 1H), 7.83 (s, 1H), 7.77 (d, *J* = 8.9 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.52 (s, 2H), 7.48 (t, *J* = 2.9 Hz, 1H), 7.39 (s, 2H), 7.12 (t, *J* = 2.5 Hz, 1H), 3.38 (t, *J* = 6.5 Hz, 2H), 2.80 (t, *J* = 6.1 Hz, 2H), 2.02 – 1.92 (m, 2H), 1.77 – 1.67 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.48, 155.93, 152.75, 143.41, 142.23, 134.61, 133.18, 131.12, 127.69, 127.23, 124.12, 123.90, 122.33, 122.08, 120.38, 117.29, 116.41, 106.26, 30.01, 29.30, 22.94, 22.64; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_4S$ [M + H]$^+$ 371.1330, found 371.1327.

4-(1,2,4,9-Tetrahydropyrano[3,4-c]pyrrolo[3,2-f]quinolin-5-yl)phenol

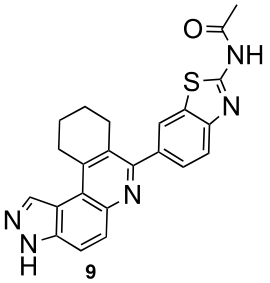


8

Yellow solid (193 mg, 61%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.36 (s, 1H), 8.22 (d, *J* = 9.0 Hz, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.81 (t, *J* = 2.9 Hz, 1H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.30 (t, *J* = 2.4 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 2H), 4.17 (t, *J* = 5.7 Hz, 2H), 3.61 (t, *J* = 5.8 Hz, 2H), 3.42 (s, 2H); ^{13}C NMR (126 MHz, DMSO) δ 159.90, 149.19, 133.51, 132.49, 131.49, 130.87, 127.07, 126.51, 122.13, 120.36, 119.93, 116.30, 115.93, 115.62, 105.92, 66.43, 64.15, 29.76; HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2O_2$ [M + H]$^+$ 317.1290, found 317.1290.

***N*-(6-(8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridin-7-yl)benzo[*d*]thiazol-2-yl)acetamide**

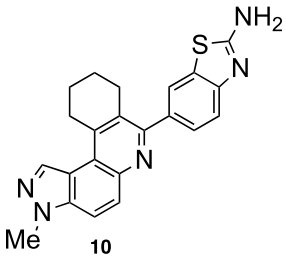
Compound **1** (HSD992) (93 mg, 0.25 mmol) was dissolved in a mixture of DMF (2 mL) and triethylamine (2 equiv), followed by addition of acetyl chloride (30 mg, 1.5 mmol). The reaction was continued for overnight at room temperature. After completion of reaction, reaction mixture was extracted with ethyl acetate (2 X 20 mL) and washed with brine solution and the crude was purified with dichloromethane:methanol (90:10) by flash coloumn chromatography to get the desired product as yellow solid (73 mg, 70%).



9

^{1}H NMR (500 MHz, Methanol-d_4) δ 8.76 (s, 1H), 8.38 (d, *J* = 9.3 Hz, 1H), 8.31 – 8.24 (m, 1H), 8.20 (d, *J* = 9.3 Hz, 1H), 7.88 – 7.84 (m, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 4.32 (s, 3H), 3.67 (t, *J* = 6.3 Hz, 2H), 2.95 (t, *J* = 6.1 Hz, 2H), 2.26 – 2.18 (m, 2H), 1.99 – 1.87 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 170.98, 155.22, 149.49, 141.56, 138.36, 135.15, 134.18, 132.65, 129.29, 127.49, 125.42, 124.19, 123.58, 118.90, 118.87, 115.92, 114.54, 35.36, 31.10, 27.83, 21.22, 21.15; HRMS (ESI) m/z calcd for $C_{23}H_{20}N_5O_2S$ [M + H]$^+$ 414.1389, found 414.1399.

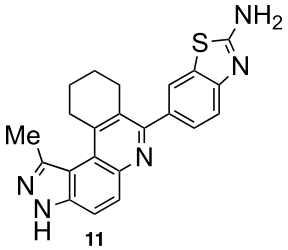
6-(3-methyl-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridin-7-yl)benzo[*d*]thiazol-2-amine



10

Off-white solid (138 mg, 36%).^{1}H NMR (500 MHz, DMSO-d_6) δ 8.50 (d, *J* = 0.9 Hz, 1H), 8.02 – 7.95 (m, 1H), 7.91 – 7.85 (m, 2H), 7.63 (s, 2H), 7.46 – 7.36 (m, 2H), 4.17 (s, 3H), 3.31 (t, *J* = 6.5 Hz, 2H), 2.82 (t, *J* = 6.1 Hz, 2H), 2.01 – 1.95 (m, 2H), 1.83 – 1.66 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.75, 156.84, 152.94, 143.09, 142.79, 138.18, 135.06, 133.62, 131.17, 129.90, 129.18, 127.28, 122.20, 121.53, 117.29, 117.17, 114.03, 36.31, 29.76, 29.17, 22.58, 22.54. HRMS (ESI) m/z calcd for $C_{22}H_{20}N_5S$ [M + H]$^+$ 386.1439, found 386.1435.

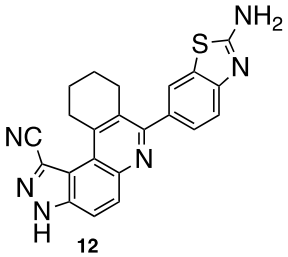
6-(1-Methyl-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridin-7-yl)benzo[*d*]thiazol-2-amine



11

Off-white solid (116 mg, 30%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 7.77 (d, *J* = 9.1 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.53 – 7.47 (m, 1H), 7.38 (dd, *J* = 8.2, 1.8 Hz, 1H), 3.52 – 3.42 (m, 2H), 2.90 (s, 3H), 2.81 (q, *J* = 4.3, 3.1 Hz, 2H), 1.89 – 1.82 (m, 4H); ^{13}C NMR (126 MHz, MeOD) δ 169.08, 156.70, 151.68, 143.60, 143.42, 143.25, 141.25, 133.99, 130.75, 128.98, 128.59, 126.61, 123.95, 121.19, 116.95, 115.76, 113.89, 31.88, 27.83, 22.07, 21.90, 17.96; HRMS (ESI) m/z calcd for $C_{22}H_{20}N_5S$ $[M + H]^+$ 386.1439, found 386.1447.

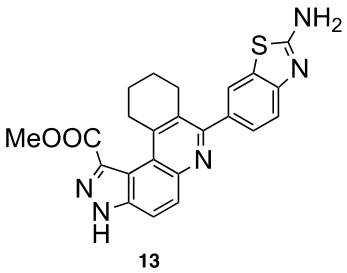
7-(2-Aminobenzo[*d*]thiazol-6-yl)-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridine-1-carbonitrile



12

Pale yellow solid (174 mg, 45%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.93 – 7.85 (m, 3H), 7.71 (s, 2H), 7.41 (d, *J* = 1.4 Hz, 2H), 3.50 (t, *J* = 6.5 Hz, 2H), 2.82 (t, *J* = 6.1 Hz, 2H), 1.91 (qd, *J* = 8.0, 6.6, 4.5 Hz, 2H), 1.74 (dp, *J* = 6.4, 4.3, 3.0 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.91, 158.23, 152.69, 144.42, 143.50, 139.88, 133.26, 131.59, 131.03, 129.99, 127.25, 122.19, 120.97, 120.20, 117.80, 117.26, 116.41, 114.67, 31.84, 28.91, 22.12, 21.96; HRMS (ESI) m/z calcd for $C_{22}H_{17}N_6S$ $[M + H]^+$ 397.1235, found 397.1245.

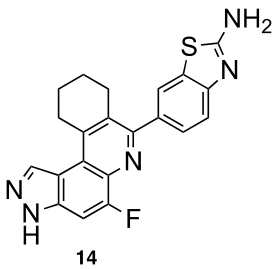
Methyl 7-(2-aminobenzo[*d*]thiazol-6-yl)-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridine-1-carboxylate



13

Off-white solid (126 mg, 30%); ^{1}H NMR (500 MHz, MeOD-d_4) δ 7.90 (d, *J* = 9.1 Hz, 1H), 7.80 (d, *J* = 9.1 Hz, 1H), 7.75 (d, *J* = 1.7 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 7.40 (dd, *J* = 8.2, 1.8 Hz, 1H), 4.03 (s, 3H), 3.15 (t, *J* = 6.1 Hz, 2H), 2.82 (t, *J* = 6.4 Hz, 2H), 1.87 – 1.80 (m, 2H), 1.79 – 1.72 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 169.18, 166.71, 157.69, 151.84, 144.55, 143.72, 142.35, 133.71, 130.80, 129.60, 128.44, 126.65, 121.94, 121.24, 116.99, 113.56, 112.70, 100.49, 51.92, 29.50, 27.49, 21.91, 21.88; HRMS (ESI) m/z calcd for $C_{23}H_{20}N_5O_2S$ $[M + H]^+$ 430.1338, found 430.1322.

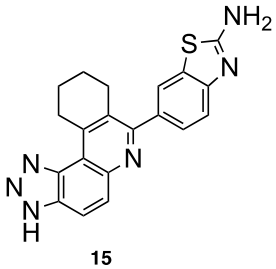
6-(5-Fluoro-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridin-7-yl)benzo[*d*]thiazol-2-amine



14

Off-white solid (148 mg, 38%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.56 (s, 1H), 7.91 – 7.84 (m, 1H), 7.70 (d, *J* = 9.8 Hz, 1H), 7.57 (d, *J* = 2.4 Hz, 2H), 7.45 – 7.38 (m, 2H), 3.36 – 3.32 (m, 2H), 2.84 (t, *J* = 6.1 Hz, 2H), 2.04 – 1.97 (m, 2H), 1.79 – 1.71 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.68, 158.36(d, *J* = 253.26 Hz), 157.08, 153.14, 142.83, 136.79, 136.49, 134.35, 133.64, 131.24, 131.14, 127.29, 122.53, 122.22, 117.37, 113.06, 98.20, 29.80, 29.24, 22.52, 22.44; HRMS (ESI) m/z calcd for $C_{21}H_{17}FN_5S$ $[M + H]^+$ 390.1189, found 390.1184.

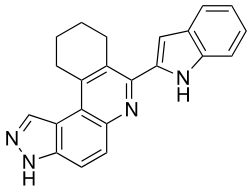
6-(8,9,10,11-Tetrahydro-3*H*-[1,2,3]triazolo[4,5-*a*]phenanthridin-7-yl)benzo[*d*]thiazol-2-amine



15

Off-white solid (112 mg, 30%).^{1}H NMR (500 MHz, DMSO-d_6) δ 8.03 (d, *J* = 9.1 Hz, 1H), 7.92 – 7.88 (m, 2H), 7.57 (s, 2H), 7.44 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 3.69 (t, *J* = 6.5 Hz, 2H), 2.85 (t, *J* = 6.2 Hz, 2H), 2.02 – 1.98 (m, 2H), 1.79 – 1.73 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 167.75, 158.87, 153.15, 145.33, 143.19, 139.18, 133.64, 131.24, 130.36, 130.18, 127.24, 122.15, 118.50, 117.37, 116.27, 29.93, 29.07, 22.66, 22.39. HRMS (ESI) m/z calcd for $C_{20}H_{17}N_6S$ $[M + H]^+$ 373.1235, found 373.1243.

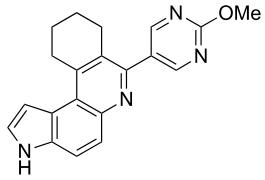
7-(1H-Indol-2-yl)-8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridine



16

Yellow solid (264 mg, 78%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.12 (s, 1H), 8.76 (s, 1H), 8.38 – 8.08 (m, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.57 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.09 (td, *J* = 7.4, 6.9, 1.0 Hz, 1H), 3.45 (t, *J* = 6.4 Hz, 2H), 3.18 – 3.15 (m, 2H), 2.11 – 1.99 (m, 2H), 1.92 – 1.81 (m, 2H);^{13}C NMR (126 MHz, DMSO) δ 143.78, 137.55, 134.89, 131.22, 130.49, 128.14, 124.23, 122.63, 121.72, 120.53, 119.45, 115.27, 112.54, 108.05, 30.84, 28.26, 21.91, 21.86, 21.86; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_4$ $[M + H]^+$ 339.1610, found 339.1618.

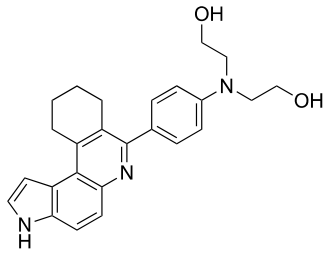
4-(2,3,4,8-Tetrahydro-1H-pyrrolo[3,2-b]phenanthridin-5-yl)phenol



17

Off white solid (178 mg, 54%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.85 (s, 2H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.51 (t, *J* = 2.8 Hz, 1H), 7.13 (t, *J* = 2.5 Hz, 1H), 3.99 (s, 3H), 3.37 (t, *J* = 6.5 Hz, 2H), 2.84 (t, *J* = 6.2 Hz, 2H), 1.99 – 1.91 (m, 2H), 1.75 (dd, *J* = 7.5, 4.3 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 164.77, 159.82, 149.96, 143.68, 142.81, 133.37, 129.18, 127.97, 124.12, 124.09, 122.80, 120.25, 116.84, 106.43, 55.22, 29.96, 28.70, 22.75, 22.49; HRMS (ESI) m/z calcd for $C_{20}H_{19}N_4O$ $[M + H]^+$ 331.1558, found 331.1553.

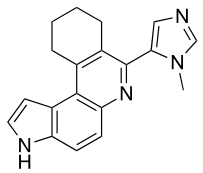
2,2'-((4-(8,9,10,11-Tetrahydro-3H-pyrrolo[3,2-a]phenanthridin-7-yl)phenyl)azanediyl)diethanol



18

Yellow solid (209 mg, 70%).^{1}H NMR (500 MHz, MeOD-d_4) δ 8.00 (d, *J* = 8.9 Hz, 1H), 7.77 (d, *J* = 8.9 Hz, 1H), 7.59 (d, *J* = 3.1 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.28 (d, *J* = 3.2 Hz, 1H), 6.95 (d, *J* = 8.9 Hz, 2H), 3.79 (t, *J* = 6.0 Hz, 4H), 3.65 (t, *J* = 6.0 Hz, 4H), 3.57 (t, *J* = 6.5 Hz, 2H), 2.90 (t, *J* = 6.2 Hz, 2H), 2.12 – 2.06 (m, 2H), 1.84 (td, *J* = 6.2, 3.2 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 152.36, 151.09, 149.41, 136.32, 133.50, 130.36, 129.04, 124.91, 122.68, 121.37, 120.18, 118.91, 115.34, 111.33, 106.08, 58.85, 53.41, 30.85, 28.37, 21.94, 21.66; HRMS (ESI) m/z calcd for $C_{25}H_{28}N_3O_2$ $[M + H]^+$ 402.2181, found 402.2179.

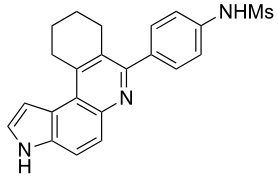
7-(1-Methyl-1H-imidazol-5-yl)-8,9,10,11-tetrahydro-3H-pyrrolo[3,2-a]phenanthridine



19

Off- white solid (151 mg, 50%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 7.79 (d, *J* = 7.9 Hz, 2H), 7.66 (d, *J* = 8.9 Hz, 1H), 7.40 (d, *J* = 3.1 Hz, 1H), 7.18 (s, 1H), 7.12 (d, *J* = 3.1 Hz, 1H), 3.60 (s, 3H), 3.38 (t, *J* = 6.5 Hz, 2H), 2.75 (t, *J* = 6.3 Hz, 2H), 2.00 – 1.94 (m, 2H), 1.81 (q, *J* = 6.0, 5.6 Hz, 2H). ^{13}C NMR (126 MHz, Methanol-d_4) δ 144.67, 144.01, 142.83, 138.47, 133.43, 130.97, 129.25, 128.07, 122.97, 122.14, 120.11, 116.34, 105.94, 31.45, 29.82, 27.83, 22.28, 21.90; HRMS (ESI) m/z calcd for $C_{19}H_{19}N_4$ $[M + H]^+$ 303.1609, found 303.1599.

***N*-(4-(8,9,10,11-Tetrahydro-3*H*-pyrrolo[3,2-*a*]phenanthridin-7-yl)phenyl)methanesulfonamide**

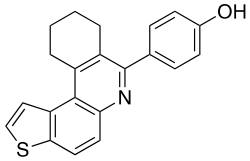


20

Pale yellow solid (245 mg, 74%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 7.78 (dd, *J* = 9.0, 0.8 Hz, 1H), 7.70 (d, *J* = 8.9 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.41 (d, *J* = 3.1 Hz, 1H), 7.39 – 7.34 (m, 2H), 7.18 (dd, *J* = 3.2, 0.9 Hz, 1H), 3.47 (t, *J* = 6.5 Hz, 2H), 2.75 (t, *J* = 6.2 Hz, 2H), 2.08 – 1.99 (m, 2H), 1.85 – 1.76 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 155.50, 143.69, 142.59, 139.11, 136.56, 133.23, 129.82,

127.48, 122.76, 121.96, 120.26, 119.66, 115.91, 105.76, 37.83, 29.92, 28.63, 22.47, 22.15; HRMS (ESI) m/z calcd for $C_{22}H_{22}N_3O_2S$ $[M + H]^+$ 392.1433, found 392.1435.

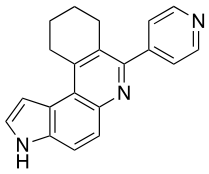
4-(8,9,10,11-Tetrahydrothieno[3,2-a]phenanthridin-7-yl)phenol



21

Off-white solid (245 mg, 74%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.96 (s, 1H), 8.36 (d, *J* = 8.9 Hz, 1H), 8.32 (d, *J* = 5.6 Hz, 1H), 8.08 (d, *J* = 5.5 Hz, 1H), 7.97 (d, *J* = 8.9 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 3.49 (q, *J* = 6.5 Hz, 2H), 2.80 (t, *J* = 6.2 Hz, 2H), 1.94 (dp, *J* = 6.6, 4.6, 2.8 Hz, 2H), 1.79 – 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 158.82, 139.74, 133.74, 131.22, 130.02, 128.68, 127.46, 125.78, 123.88, 115.49, 31.70, 29.13, 22.58, 21.88; HRMS (ESI) m/z calcd for $C_{21}H_{18}NOS$ $[M + H]^+$ 332.1109, found 332.1118.

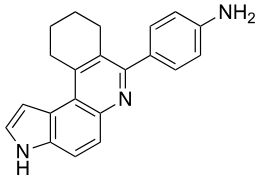
7-(Pyridin-4-yl)-8,9,10,11-tetrahydro-3H-pyrrolo[3,2-a]phenanthridine



22

Off white solid (183 mg, 61%).^{1}H NMR (500 MHz, DMSO-d_6) δ 11.81 (s, 1H), 8.67 (dt, *J* = 4.4, 1.5 Hz, 2H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 8.9 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.54 – 7.48 (m, 1H), 7.14 (s, 1H), 3.40 (t, *J* = 6.6 Hz, 2H), 2.77 (t, *J* = 6.1 Hz, 2H), 2.01 – 1.94 (m, 2H), 1.75 (q, *J* = 5.9 Hz, 2H); ^{13}C NMR (126 MHz, DMSO) δ 153.34, 149.84, 149.10, 143.44, 142.78, 133.41, 127.19, 124.49, 124.16, 124.08, 122.90, 120.26, 116.87, 106.42, 29.94, 28.67, 22.76, 22.39; HRMS (ESI) m/z calcd for $C_{20}H_{18}N_3$ $[M + H]^+$ 300.1500, found 300.1508.

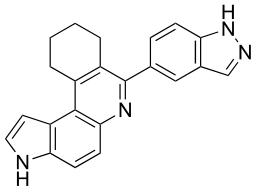
4-(8,9,10,11-Tetrahydro-3H-pyrrolo[3,2-a]phenanthridin-7-yl)aniline



23

Bright yellow solid (194 mg, 62%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.09 (d, *J* = 8.9 Hz, 1H), 7.93 (d, *J* = 8.8 Hz, 1H), 7.72 (s, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.26 (s, 1H), 6.75 (d, *J* = 8.3 Hz, 2H), 5.79 (s, 2H), 3.51 (t, *J* = 6.5 Hz, 2H), 3.32 (s, 2H), 2.85 (t, *J* = 6.2 Hz, 2H), 2.09 – 1.95 (m, 2H), 1.81 – 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 151.31, 133.58, 133.58, 131.48, 129.37, 129.33, 127.94, 126.34, 122.49, 120.03, 118.73, 113.57, 106.60, 31.13, 28.60, 22.25, 21.94; HRMS (ESI) m/z calcd for $C_{21}H_{20}N_3$ $[M + H]^+$ 314.1657, found 314.1651.

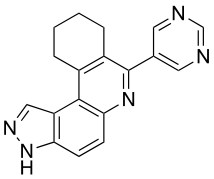
7-(1*H*-Indazol-5-yl)-8,9,10,11-tetrahydro-3*H*-pyrrolo[3,2-*a*]phenanthridine



24

White solid (173 mg, 51%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.76 (s, 1H), 8.12 (s, 1H), 7.91 (s, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H), 7.54 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.48 (t, *J* = 2.8 Hz, 1H), 7.11 (t, *J* = 2.6 Hz, 1H), 3.37 (d, *J* = 6.9 Hz, 2H), 2.77 (t, *J* = 6.2 Hz, 2H), 1.99 – 1.91 (m, 2H), 1.73 – 1.64 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 156.34, 143.43, 142.27, 139.73, 134.40, 134.08, 133.20, 128.24, 127.74, 124.12, 123.87, 123.10, 122.38, 121.28, 120.41, 116.42, 109.84, 106.27, 30.01, 29.35, 22.91, 22.62; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_4$ $[M + H]^+$ 339.1610, found 339.1618.

7-(Pyrimidin-5-yl)-8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridine

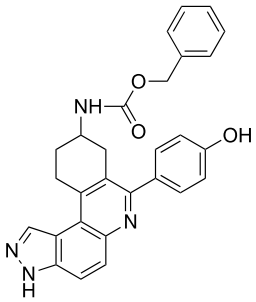


25

Yellow solid (144 mg, 48%). ^{1}H NMR (500 MHz, DMSO-d_6) δ ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.26 (s, 1H), 9.07 (s, 2H), 8.55 (s, 1H), 7.89 (d, *J* = 9.0 Hz, 1H), 7.84 (d, *J* = 9.0 Hz, 1H), 3.31 (s, 2H), 2.84 (t, *J* = 6.1 Hz, 2H), 2.03 – 1.94 (m, 2H), 1.80 – 1.71 (m, 2H);^{13}C NMR (126 MHz, DMSO) δ 158.00, 157.25, 150.89,

143.91, 142.97, 138.83, 136.49, 134.77, 129.84, 129.50, 122.42, 116.25, 114.94, 29.62, 28.44, 22.43, 22.38; HRMS (ESI) m/z calcd for $C_{19}H_{17}N_4$ $[M + H]^+$ 301.1453, found 301.1457.

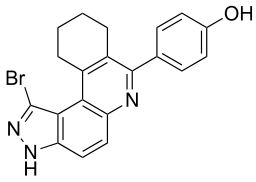
Benzyl (7-(4-hydroxyphenyl)-8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-9-yl)carbamate



26

Off-white solid (241 mg, 52%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 8.66 (d, *J* = 9.1 Hz, 1H), 8.08 (dd, *J* = 9.2, 6.3 Hz, 1H), 7.93 (dd, *J* = 9.3, 5.3 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.29 – 7.20 (m, 5H), 7.02 (d, *J* = 8.2 Hz, 2H), 5.01 (s, 2H), 3.97 – 3.84 (m, 1H), 3.67 – 3.56 (m, 1H), 3.54 – 3.41 (m, 1H), 3.18 – 3.08 (m, 1H), 2.95 – 2.82 (m, 1H), 2.42 – 2.29 (m, 1H), 2.11 – 2.01 (m, 1H). ^{13}C NMR (126 MHz, MeOD) δ 161.72, 159.87, 156.89, 152.70, 150.63, 139.58, 136.84, 136.35, 130.82, 129.46, 128.03, 127.56, 127.34, 123.73, 122.33, 120.83, 119.33, 118.00, 115.47, 114.97, 66.04, 48.13, 48.08, 47.96, 47.79, 47.62, 47.45, 47.28, 47.11, 45.66, 33.71, 29.28, 26.87; HRMS (ESI) m/z calcd for $C_{28}H_{25}N_4O_3$ $[M + H]^+$ 465.1927, found 465.1927

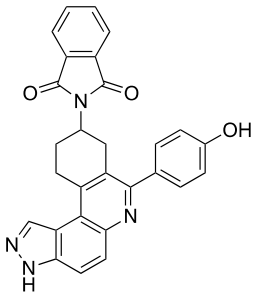
4-(1-Bromo-8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-7-yl)phenol



27

Off-white solid (153 mg, 39%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 8.18 (d, *J* = 9.1 Hz, 1H), 8.06 (d, *J* = 9.2 Hz, 1H), 7.57 (d, *J* = 8.3 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 3.99 (s, 2H), 2.97 (s, 2H), 1.97 (t, *J* = 3.5 Hz, 4H). ^{13}C NMR (126 MHz, MeOD) δ 160.37, 155.96, 154.60, 151.79, 141.55, 135.37, 132.94, 130.83, 127.59, 123.46, 121.93, 120.38, 119.25, 115.60, 114.56, 36.01, 27.02, 20.91, 20.80; HRMS (ESI) m/z calcd for $C_{20}H_{17}BrN_3O$ $[M + H]^+$ 394.0555, found 394.0556.

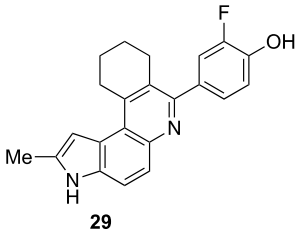
2-(7-(4-Hydroxyphenyl)-8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-9-yl)isoindoline-1,3-dione



28

Off-white solid (239 mg, 52%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.56 (s, 1H), 8.57 (s, 1H), 7.89 – 7.84 (m, 2H), 7.83 – 7.78 (m, 5H), 7.36 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 4.45 – 4.33 (m, 1H), 3.73 – 3.59 (m, 2H), 3.53 – 3.39 (m, 1H), 2.92 – 2.85 (m, 1H), 2.82 – 2.69 (m, 1H), 2.36 – 2.26 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 168.38, 157.66, 156.88, 143.84, 141.13, 138.66, 136.38, 134.76, 132.01, 131.67, 130.75, 129.58, 127.50, 123.38, 121.10, 116.54, 115.25, 114.60, 47.46, 32.19, 31.15, 26.15; HRMS (ESI) m/z calcd for $C_{28}H_{21}N_4O_3$ $[M + H]^+$ 461.1614, found 461.1619.

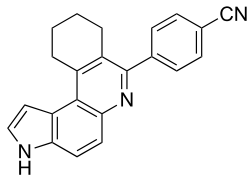
Methyl 4-(8,9,10,11-tetrahydro-3H-pyrrolo[3,2-a]phenanthridin-7-yl)benzoate



29

Off-white solid (105 mg, 30%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 7.68 (dd, *J* = 8.9, 0.8 Hz, 1H), 7.62 (d, *J* = 8.9 Hz, 1H), 7.22 (dd, *J* = 11.8, 2.0 Hz, 1H), 7.13 (ddd, *J* = 8.2, 2.1, 0.9 Hz, 1H), 7.03 (dt, *J* = 8.9, 8.2 Hz, 1H), 6.87 (s, 1H), 3.48 – 3.40 (m, 2H), 2.76 (t, *J* = 6.2 Hz, 2H), 2.54 (s, 3H), 2.07 – 1.99 (m, 2H), 1.86 – 1.75 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.38, 152.03 (*J* = 241.92 Hz), 144.97, 144.23, 141.91, 133.92, 133.16, 132.30, 127.16, 125.13, 122.28, 121.10, 120.18, 117.07, 116.57, 116.41, 115.50, 104.05, 29.98, 28.55, 22.44, 22.14, 12.07; HRMS (ESI) m/z calcd for $C_{22}H_{22}FN_2O$ $[M + H]^+$ 349.1716, found 349.1717.

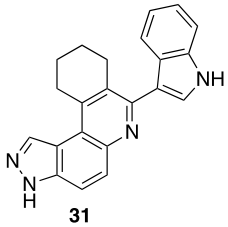
4-(8,9,10,11-Tetrahydro-3H-pyrrolo[3,2-a]phenanthridin-7-yl)benzonitrile



30

Off-white solid (195 mg, 60%).^{1}H NMR (500 MHz, DMSO-d_6) δ 11.80 (s, 1H), 7.92 (d, *J* = 8.5 Hz, 1H), 7.81 (dd, *J* = 8.9, 0.8 Hz, 1H), 7.75 (d, *J* = 8.9 Hz, 2H), 7.64 (d, *J* = 8.9 Hz, 1H), 7.51 (t, *J* = 2.8 Hz, 1H), 7.15 – 7.11 (m, 1H), 3.38 (t, *J* = 6.1 Hz, 2H), 2.73 (t, *J* = 6.1 Hz, 2H), 2.00 – 1.93 (m, 2H), 1.76 – 1.68 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 154.08, 146.45, 143.42, 142.77, 133.40, 132.39, 130.61, 127.28, 124.14, 124.07, 122.82, 120.26, 119.41, 116.85, 110.74, 106.41, 29.95, 28.81, 22.76, 22.41; HRMS (ESI) m/z calcd for $C_{22}H_{20}N_3$ $[M + H]^+$ 326.1657, found 326.1662.

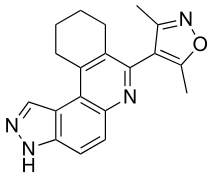
7-(1*H*-indol-3-yl)-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridine



31

White solid (183 mg, 54%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 8.72 (s, 1H), 8.14 (d, *J* = 8.7 Hz, 1H), 8.04 – 7.93 (m, 2H), 7.61 – 7.52 (m, 2H), 7.30 – 7.16 (m, 2H), 3.49 (t, *J* = 6.2 Hz, 2H), 2.99 (t, *J* = 6.1 Hz, 2H), 2.22 – 2.10 (m, 2H), 1.87 (q, *J* = 5.7 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 152.83, 147.51, 136.55, 135.07, 132.76, 128.62, 125.73, 122.77, 122.39, 120.99, 119.61, 118.86, 115.08, 112.11, 107.22, 30.80, 27.71, 21.46, 21.29; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_4$ $[M + H]^+$ 339.1610, found 339.1618.

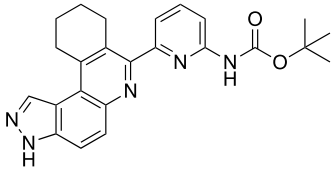
3,5-Dimethyl-4-(8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-7-yl)isoxazole



32

White solid (229 mg, 72%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 8.92 (s, 1H), 8.35 (d, *J* = 9.3 Hz, 1H), 8.06 (dd, *J* = 9.2, 2.4 Hz, 1H), 3.71 – 3.64 (m, 2H), 2.86 – 2.77 (m, 2H), 2.45 (s, 3H), 2.25 – 2.20 (m, 5H), 2.06 – 1.98 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 170.18, 158.64, 155.86, 140.72, 140.00, 135.64, 134.42, 134.28, 124.70, 121.79, 118.93, 114.70, 108.54, 30.94, 26.68, 21.17, 20.88, 10.39, 8.99; HRMS (ESI) m/z calcd for $C_{19}H_{19}N_4O$ $[M + H]^+$ 319.1559, found 319.1563.

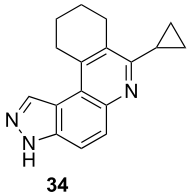
***tert*-Butyl (6-(8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-7-yl)pyridin-2-yl)carbamate**



33

White solid (245 mg, 51%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 8.79 (s, 1H), 8.23 (d, *J* = 9.3 Hz, 1H), 8.12 – 8.05 (m, 3H), 7.65 (dd, *J* = 5.7, 2.6 Hz, 1H), 3.53 (d, *J* = 6.0 Hz, 2H), 3.08 (t, *J* = 6.1 Hz, 2H), 2.21 – 2.14 (m, 2H), 1.99 – 1.91 (m, 2H), 1.58 (s, 9H); ^{13}C NMR (126 MHz, MeOD) δ 154.62, 153.09, 153.05, 147.37, 146.93, 140.49, 139.57, 134.87, 134.39, 132.10, 124.03, 120.98, 119.75, 119.68, 114.62, 114.29, 80.98, 30.97, 27.41, 27.15, 21.16, 21.06; HRMS (ESI) m/z calcd for $C_{24}H_{26}N_5O_2$ $[M + H]^+$ 416.2087, found 416.2089.

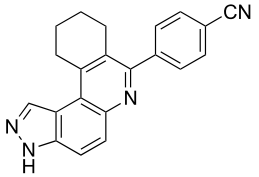
7-Cyclopropyl-8,9,10,11-tetrahydro-3H-pyrazolo[4,3-a]phenanthridine



34

Off-white solid (181 mg, 69%).^{1}H NMR (500 MHz, DMSO-d_6) δ 8.45 (s, 1H), 7.73 (d, *J* = 9.0 Hz, 1H), 7.64 (d, *J* = 9.1 Hz, 1H), 3.18 (q, *J* = 5.3, 4.6 Hz, 2H), 2.94 (t, *J* = 6.2 Hz, 2H), 2.21 (tt, *J* = 8.1, 4.9 Hz, 1H), 1.96 – 1.88 (m, 2H), 1.86 – 1.81 (m, 2H), 1.10 – 0.99 (m, 2H), 0.97 – 0.87 (m, 2H) ; ^{13}C NMR (126 MHz, DMSO) δ 157.71, 143.33, 140.97, 138.28, 135.75, 129.57, 129.38, 120.82, 116.55, 113.67, 29.49, 26.38, 22.40, 22.37, 13.67, 9.14; HRMS (ESI) m/z calcd for $C_{17}H_{18}N_3$ $[M + H]^+$ 264.1501, found 264.1509.

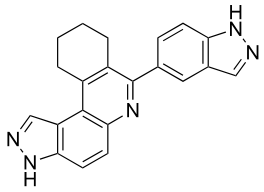
4-(8,9,10,11-Tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridin-7-yl)benzonitrile



35

Off-white solid (182 mg, 56%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.78 (s, 1H), 8.20 (t, *J* = 7.4 Hz, 2H), 8.10 (d, *J* = 8.1 Hz, 2H), 7.94 (d, *J* = 8.2 Hz, 2H), 3.48 – 3.44 (m, 2H), 2.73 (t, *J* = 6.2 Hz, 2H), 2.07 – 1.97 (m, 2H), 1.84 – 1.72 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 150.26, 140.30, 138.64, 136.93, 135.01, 132.87, 131.23, 130.97, 123.45, 122.31, 119.99, 118.89, 115.01, 113.13, 30.63, 28.01, 21.85, 21.68; HRMS (ESI) m/z calcd for $C_{21}H_{17}N_4$ $[M + H]^+$ 325.1453, found 325.1455.

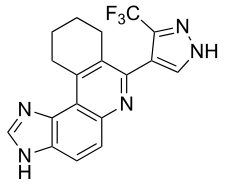
7-(1*H*-Indazol-5-yl)-8,9,10,11-tetrahydro-3H-pyrazolo[4,3-*a*]phenanthridine



36

Off-white solid (224 mg, 65%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.56 (s, 1H), 8.12 (s, 1H), 7.92 (s, 1H), 7.83 (d, *J* = 5.8 Hz, 2H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.55 (d, *J* = 8.6 Hz, 1H), 3.32 – 3.26 (m, 2H), 2.78 (t, *J* = 6.1 Hz, 2H), 2.01 – 1.92 (m, 2H), 1.74 – 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.30, 143.71, 142.28, 139.80, 138.66, 136.27, 134.45, 133.55, 129.66, 129.54, 128.17, 123.07, 121.71, 121.43, 116.44, 114.31, 109.93, 29.69, 29.22, 22.64, 22.59; HRMS (ESI) m/z calcd for $C_{21}H_{18}N_5$ $[M + H]^+$ 340.1562, found 340.1565.

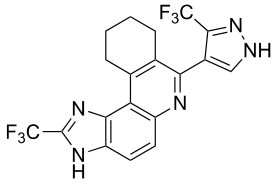
7-(3-(Trifluoromethyl)-1*H*-pyrazol-4-yl)-8,9,10,11-tetrahydro-3*H*-imidazo[4,5-*a*]phenanthridine



37

Off-white solid (75 mg, 21%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 8.30 (s, 1H), 7.99 (d, *J* = 1.2 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 1H), 7.83 (d, *J* = 8.9 Hz, 1H), 3.68 (d, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.3 Hz, 2H), 2.08 – 1.98 (m, 2H), 1.91 – 1.83 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 149.00, 145.68, 143.27, 142.66, 140.11, 130.25, 130.05, 124.01, 122.80 (q, *J* = 270.51 Hz), 118.99, 118.30, 115.91, 112.78, 94.71, 29.26, 27.75, 22.04, 21.86. HRMS (ESI) m/z calcd for $C_{18}H_{15}F_3N_5$ $[M + H]^+$ 358.1280, found 358.1286.

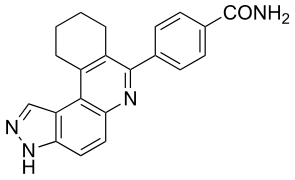
2-(Trifluoromethyl)-7-(3-(trifluoromethyl)-1*H*-pyrazol-4-yl)-8,9,10,11-tetrahydro-3*H*-imidazo[4,5-*a*]phenanthridine



38

Off-white solid (106 mg, 25%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 7.99 (s, 1H), 7.90 (d, *J* = 9.1 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H), 3.91 – 3.75 (m, 2H), 2.68 (t, *J* = 6.3 Hz, 2H), 2.07 – 1.92 (m, 2H), 1.94 – 1.77 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 149.46, 144.26, 143.57, 140.04, 139.76, 137.30, 131.82, 130.86, 130.17, 126.46, 124.94(q, *J* = 269.64 Hz), 120.67, 120.32(q, *J* = 268.64 Hz), 118.93, 114.85, 29.42, 27.82, 21.99, 21.94. HRMS (ESI) m/z calcd for $C_{19}H_{14}F_6N_5$ $[M + H]^+$ 426.1153, found 426.1155.

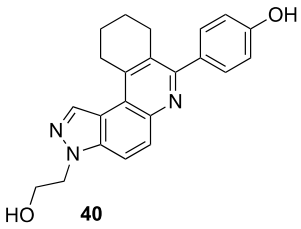
4-(8,9,10,11-Tetrahydro-3H-pyrazolo[4,3-a]phenanthridin-7-yl)benzamide



39

Off-white solid (172 mg, 50%).^{1}H NMR (500 MHz, DMSO-d_6) δ 8.60 (s, 1H), 8.05 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 2H), 7.86 (d, *J* = 9.1 Hz, 1H), 7.81 (d, *J* = 9.1 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.41 (s, 1H), 3.39 – 3.34 (m, 2H), 2.77 (t, *J* = 6.1 Hz, 2H), 2.04 – 1.98 (m, 2H), 1.79 – 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 168.13, 156.17, 144.02, 143.77, 142.55, 133.95, 129.63, 129.40, 129.29, 127.64, 122.07, 116.23, 29.68, 28.86, 22.58, 22.49; HRMS (ESI) m/z calcd for $C_{21}H_{21}N_4O$ $[M + H]^+$ 345.1715, found 345.1719.

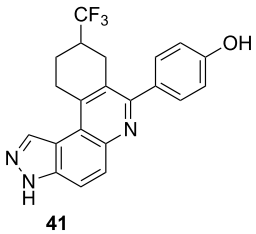
4-(3-(2-Hydroxyethyl)-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridin-7-yl)phenol



40

Off-white solid (177 mg, 49%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.59 (s, 1H), 8.51 (s, 1H), 7.96 (d, *J* = 9.1 Hz, 1H), 7.81 (d, *J* = 9.1 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 6.86 – 6.82 (m, 2H), 4.55 (t, *J* = 5.6 Hz, 2H), 3.88 – 3.82 (m, 2H), 3.32 – 3.27 (m, 2H), 2.79 (t, *J* = 6.2 Hz, 2H), 2.01 – 1.96 (m, 2H), 1.77 – 1.70 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.58, 157.01, 143.57, 142.09, 138.61, 135.29, 131.97, 130.89, 129.53, 129.38, 121.31, 117.15, 115.09, 114.17, 60.84, 51.76, 29.69, 29.23, 22.64; HRMS (ESI) m/z calcd for $C_{12}H_{24}N_3O_2$ $[M + H]^+$ 362.1869, found 362.1871.

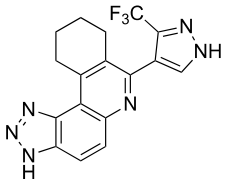
4-(9-(Trifluoromethyl)-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridin-7-yl)phenol



41

Off-white solid (165 mg, 43%).^{1}H NMR (500 MHz, DMSO-d_6) δ 10.27 (s, 1H), 8.60 (s, 1H), 8.11 – 7.90 (m, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.03 (d, *J* = 8.3 Hz, 2H), 3.54 – 3.43 (m, 1H), 3.40 – 3.28 (m, 1H), 3.10 – 2.97 (m, 1H), 2.90 – 2.82 (m, 1H), 2.79 – 2.68 (m, 1H), 2.39 – 2.30 (m, 1H), 1.94 – 1.79 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 159.74, 152.87, 148.17, 137.78, 131.71, 129.43(q, *J* = 278.46 Hz), 127.87, 122.81, 121.71, 115.86, 115.01, 37.62(q, *J* = 26.46 Hz), 29.44, 27.22, 20.90; HRMS (ESI) m/z calcd for $C_{21}H_{19}F_3N_3O$ $[M + H]^+$ 386.1480, found 386.1484.

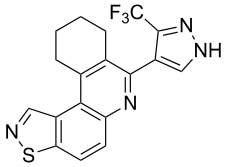
7-(3-(Trifluoromethyl)-1*H*-pyrazol-4-yl)-8,9,10,11-tetrahydro-3*H*-[1,2,3]triazolo[4,5-*a*]phenanthridine



42

Off-white solid (72 mg, 20%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 8.40 (d, *J* = 9.2 Hz, 1H), 8.33 (s, 1H), 8.05 (d, *J* = 9.2 Hz, 1H), 4.01 (t, *J* = 6.4 Hz, 2H), 2.82 (t, *J* = 6.3 Hz, 2H), 2.13 (dp, *J* = 9.3, 3.1 Hz, 2H), 2.02 – 1.93 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 154.39, 145.35, 140.07, 139.75, 138.56, 137.77, 134.33, 132.14, 122.37(q, *J* = 269.6 Hz), 121.20, 120.95, 116.39, 111.31, 30.87, 27.26, 21.12, 21.07; HRMS (ESI) m/z calcd for $C_{17}H_{14}F_3N_6$ $[M + H]^+$ 359.1232, found 359.1239.

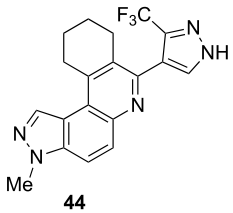
7-(3-(Trifluoromethyl)-1*H*-pyrazol-4-yl)-8,9,10,11-tetrahydroisothiazolo[4,5-*a*]phenanthridine



43

Off-white solid (120 mg, 32%). ^{1}H NMR (500 MHz, MeOD-d_4) δ 9.94 (s, 1H), 8.78 (d, *J* = 8.9 Hz, 1H), 8.41 (s, 1H), 8.21 (d, *J* = 8.9 Hz, 1H), 3.85 (t, *J* = 6.1 Hz, 2H), 2.87 (t, *J* = 6.1 Hz, 2H), 2.24 – 2.13 (m, 2H), 2.00 (td, *J* = 11.2, 9.5, 5.6 Hz, 2H); ^{13}C NMR (126 MHz, MeOD) δ 156.17, 155.87, 155.79, 145.11, 140.04, 139.75, 136.42, 135.01, 132.65, 129.80, 125.95, 125.43, 121.58, 120.19, 118.46, 109.79, 32.51, 27.76, 21.37, 20.63; HRMS (ESI) m/z calcd for $C_{18}H_{14}F_3N_4S$ $[M + H]^+$ 375.0891, found 375.0899.

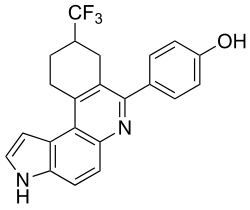
3-Methyl-7-(3-(trifluoromethyl)-1*H*-pyrazol-4-yl)-8,9,10,11-tetrahydro-3*H*-pyrazolo[4,3-*a*]phenanthridine



44

Off-white solid (148 mg, 40%).^{1}H NMR (500 MHz, MeOD-d_4) δ 8.77 (d, *J* = 0.9 Hz, 1H), 8.42 (dd, *J* = 9.3, 0.9 Hz, 1H), 8.38 (d, *J* = 0.9 Hz, 1H), 8.07 (d, *J* = 9.3 Hz, 1H), 4.32 (s, 3H), 3.68 (t, *J* = 6.3 Hz, 2H), 2.82 (t, *J* = 6.2 Hz, 2H), 2.22 – 2.12 (m, 2H), 2.05 – 1.92 (m, 2H); ^{13}C NMR (126 MHz, MeOD) δ 155.03, 142.35, 140.13 (q, *J* = 37.8 Hz), 138.47, 135.21, 134.39, 134.19, 132.52, 124.04, 122.33 (q, *J* = 269.6 Hz), 119.30, 118.65, 115.97, 109.85, 35.32, 30.84, 27.26, 21.19, 20.86; HRMS (ESI) m/z calcd for $C_{19}H_{17}F_3N_5$ $[M + H]^+$ 372.1436, found 372.1438.

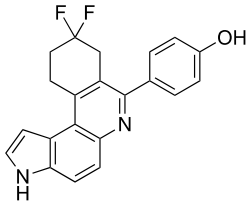
4-(9-(Trifluoromethyl)-8,9,10,11-tetrahydro-3H-pyrrolo[3,2-a]phenanthridin-7-yl)phenol



45

Off-white solid (157mg, 41%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.93 (s, 1H), 9.74 (s, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.67 (s, 1H), 7.60 – 7.50 (m, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.21 – 7.07 (m, 1H), 6.99 – 6.83 (m, 2H), 3.65 (dd, *J* = 18.1, 5.8 Hz, 1H), 3.01 – 2.93 (m, 1H), 2.89 – 2.81 (m, 1H), 2.78 – 2.65 (m, 1H), 2.43 – 2.31 (m, 1H), 1.92 – 1.77 (m, 1H); ^{13}C NMR (126 MHz, DMSO) δ 157.87, 155.35, 133.27, 131.96, 130.83, 129.75, 127.53, 124.57, 124.44, 121.71, 120.23, 117.24, 115.32, 106.11, 37.63 (q, *J* = 26.6 Hz), 29.04, 27.78, 21.66; HRMS (ESI) m/z calcd for $C_{22}H_{20}F_3N_2O$ $[M + H]^+$ 385.1528, found 385.1532.

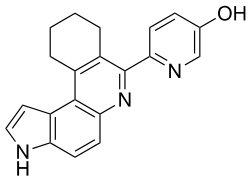
4-(9,9-Difluoro-8,9,10,11-tetrahydro-3H-pyrrolo[3,2-a]phenanthridin-7-yl)phenol



46

Off-white solid (180 mg, 49%).^{1}H NMR (500 MHz, DMSO-d_6) δ 11.84 (s, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 8.8 Hz, 1H), 7.53 (d, *J* = 3.0 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 3.1 Hz, 1H), 6.88 (d, *J* = 8.1 Hz, 2H), 3.63 (t, *J* = 7.1 Hz, 2H), 3.33 (t, *J* = 14.5 Hz, 2H), 2.48 – 2.38 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 157.78, 155.53, 143.87, 139.53, 133.29, 131.52, 130.80, 125.76, 124.38, 123.95, 123.87, 122.78, 121.98, 121.20, 120.23, 117.15, 115.32, 106.13, 37.50(*J* =26.46 Hz), 29.55(*J* =23.94 Hz), 28.22; HRMS (ESI) m/z calcd for $C_{21}H_{19}F_2N_2O$ $[M + H]^+$ 353.1465, found 353.1470.

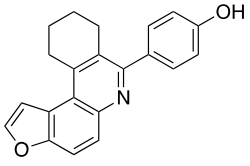
6-(8,9,10,11-Tetrahydro-3*H*-pyrrolo[3,2-*a*]phenanthridin-7-yl)pyridin-3-ol



47

Off-white solid (107 mg, 34%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.74 (s, 1H), 10.03 (s, 1H), 8.18 (d, *J* = 2.8 Hz, 1H), 7.77 (d, *J* = 8.9 Hz, 1H), 7.64 (dd, *J* = 12.0, 8.7 Hz, 2H), 7.49 (t, *J* = 2.8 Hz, 1H), 7.29 (dd, *J* = 8.5, 2.9 Hz, 1H), 7.12 (d, *J* = 2.5 Hz, 1H), 3.40 – 3.35 (m, 2H), 2.95 (t, *J* = 6.3 Hz, 2H), 1.96 – 1.92 (m, 2H), 1.78 – 1.69 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 153.80, 153.32, 151.06, 142.98, 142.40, 136.29, 133.31, 128.21, 125.55, 124.11, 123.92, 123.07, 122.67, 120.36, 116.37, 106.28, 30.10, 28.50, 22.89, 22.51; HRMS (ESI) m/z calcd for $C_{20}H_{18}N_3O$ $[M + H]^+$ 316.1450, found 316.1453.

4-(8,9,10,11-Tetrahydrofuro[3,2-a]phenanthridin-7-yl)phenol



48

Off-white solid (218 mg, 69%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.47 (d, *J* = 2.1 Hz, 1H), 8.36 (q, *J* = 9.2 Hz, 2H), 7.79 (d, *J* = 2.2 Hz, 1H), 7.61 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 3.56 (t, *J* = 6.4 Hz, 2H), 2.82 (t, *J* = 6.2 Hz, 2H), 2.00 (dq, *J* = 8.7, 5.8, 4.5 Hz, 2H), 1.86 – 1.65 (m, 2H); ^{13}C NMR (126 MHz, DMSO) δ 160.63, 153.59, 153.01, 148.23, 132.05, 131.37, 122.86, 121.34, 119.47, 116.00, 110.37, 30.67, 28.32, 21.74, 21.57; HRMS (ESI) m/z calcd for $C_{21}H_{18}NO_2$ $[M + H]^+$ 316.1337, found 316.1343.