Copper-catalyzed domino sequences: A new route to pyrido-fused quinazolinones from 2'-haloacetophenones and 2-aminopyridines

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Supporting information

Materials and instrumentation

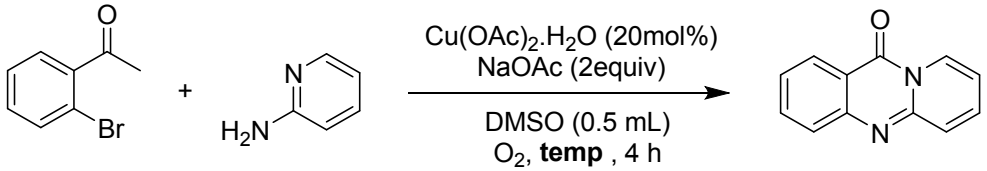
All reagents and starting materials were obtained commercially from Sigma-Aldrich and Merck, and were used as received without any further purification unless otherwise noted. Gas chromatographic (GC) analyses were performed using a Shimadzu GC 2010-Plus equipped with a flame ionization detector (FID) and an SPB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC analysis held samples at 120 ^{o}C for 0.5 min; heated them from 120 to 130 ^{o}C at 40 ^{o}C/min; held them at 130 ^{o}C for 1 min; heated them from 130 to 280 ^{o}C at 40 ^{o}C/min; and finally held them at 280 ^{o}C for 1.5 min. Inlet and detector temperatures were set constant at 280 ^{o}C. The GC yield was calculated using diphenyl ether as the internal standard. GC-MS analyses were analyzed on a Shimadzu GCMS-QP2010Ultra with a ZB-5MS column

(length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC-MS analysis held samples at 50 ^{o}C for 2 min; heated samples from 50 to 280^{o}C at 10 ^{o}C/min and held them at 280 ^{o}C for 10 min. Inlet temperature was set constant at 280 ^{o}C. MS spectra were compared with the spectra gathered in the NIST library. The ^{1}H NMR and ^{13}C NMR were recorded on Bruker AV 500 spectrometers using residual solvent peak as a reference.

Experimental procedure

To a 12-mL screw-cap vial containing DMSO (0.5 mL) was added 2'-bromoacetophenone (19.9 mg, 0.1 mmol), 2-aminopyridines (23.5 mg, 0.25 mmol), anhydrous NaOAc (16.4 mg, 0.2 mmol), $Cu(OAc)_2.H_2O$ (4.0 mg, 0.02 mmol) and diphenyl ether (0.1 mmol) as an internal standard. The catalyst concentration was calculated with respect to the copper/2'-bromoacetophenone molar ratio. The reactor was evacuated and back-filled with oxygen. The resulting mixture was then stirred at 120 ^{o}C for 4 h. After that, the mixture was slowly cooled to room temperature, then distilled water (5 mL) was added. The organic components were extracted with dichloromethane (20 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography on silica gel with hexane/ethyl acetate as eluent to give pure product. The product identity was further confirmed by GC-MS, ^{1}H NMR and ^{13}C NMR. The reaction yield was monitored by withdrawing aliquots from the reaction mixture, quenched with brine and the organic components were then extracted into ethyl acetate (2 mL), dried over anhydrous Na_2SO_4 and analyzed by GC with reference to diphenyl ether.

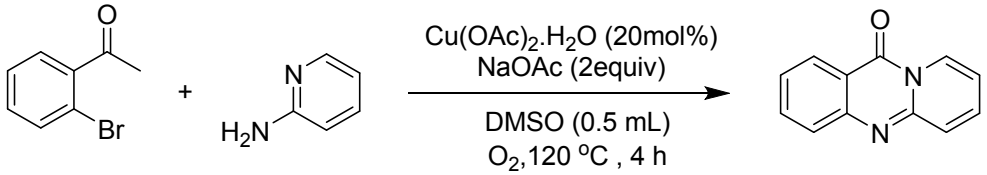
Table S1: Effect of varied temperature on the yield of 11H-pyrido[2,1-b]quinazolin-11-one:



Entry	Temperature (°C)	Yield[b] (%)
1	RT	0
2	80	46
3	100	58
4	**120**	**84**
5	140	57

[a]Reaction conditions: 2-bromoacetophenone (0.1 mmol); 2-aminopyridine (0.2mmol); DMSO (0.5 mL); $Cu(OAc)_2.H_2O$ (20 mol%); NaOAc (2 equiv); **temp**; oxygen atmosphere; 4 h.[b] GC yield of 11H-pyrido[2,1-b]quinazolin-11-one.

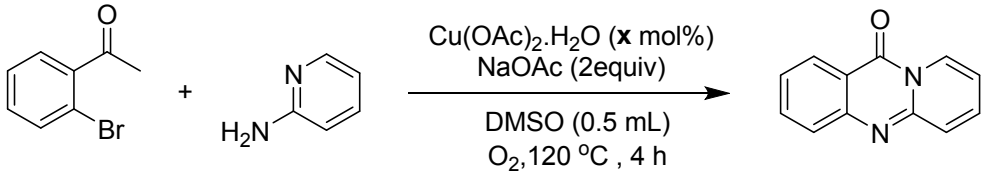
Table S2: Effect of diverse reactant mole proportions on the yield of 11H-pyrido[2,1-b]quinazolin-11-one:



Entry	Temperature (°C)	Yield[b] (%)
1	1:1	64
2	1:1.5	75
3	1:2	84
4	**1:2.5**	**90**
5	1:3	92
6	1.5:1	51
7	2:1	33

[a]Reaction conditions: 2-bromoacetophenone (0.1 mmol); DMSO (0.5 mL); $Cu(OAc)_2.H_2O$ (20 mol%); NaOAc (2 equiv); 120 °C; oxygen atmosphere; 4 h.[b] GC yield of 11H-pyrido[2,1-b]quinazolin-11-one.

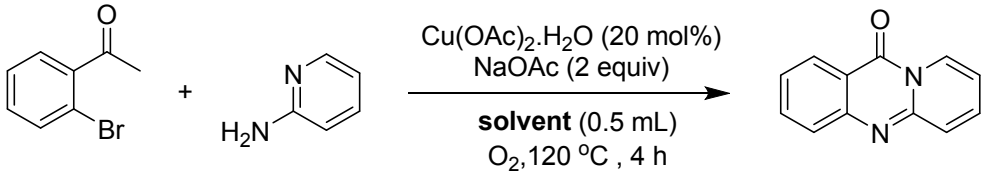
Table S3: Effect of different catalyst amounts on the yield of 11H-pyrido[2,1-b]quinazolin-11-one:



Entry	Catalyst amount (mol%)	Yield[b] (%)
1	0	0
2	5	39
3	10	45
4	15	67
5	**20**	**90**

[a]Reaction conditions: 2-bromoacetophenone (0.1 mmol); 2-aminopyridine (0.25 mmol); DMSO (0.5 mL); $Cu(OAc)_2.H_2O$ **(x mol%)**; NaOAc (2 equiv); 120 °C; oxygen atmosphere; 4 h.[b] GC yield of 11H-pyrido[2,1-b]quinazolin-11-one.

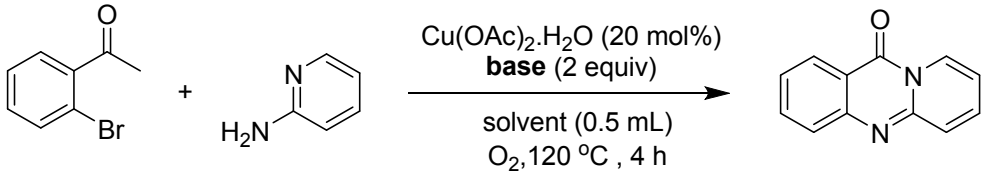
Table S4: Effect of diverse solvents on the yield of 11H-pyrido[2,1-b]quinazolin-11-one:



Entry	Solvent	Yield[b] (%)
1	Toluene	16
2	Xylene	46
3	Dioxane	48
4	Diglyme	63
5	NMP	75
6	DMF	41
7	DMAc	61
8	**DMSO**	**90**
9	DEG	25

[a]Reaction conditions: 2-bromoacetophenone (0.1 mmol); 2-aminopyridine (0.25 mmol); **solvent** (0.5 mL); $Cu(OAc)_2.H_2O$ (20 mol%); NaOAc (2 equiv); 120 °C; oxygen atmosphere; 4 h.[b] GC yield of 11H-pyrido[2,1-b]quinazolin-11-one.

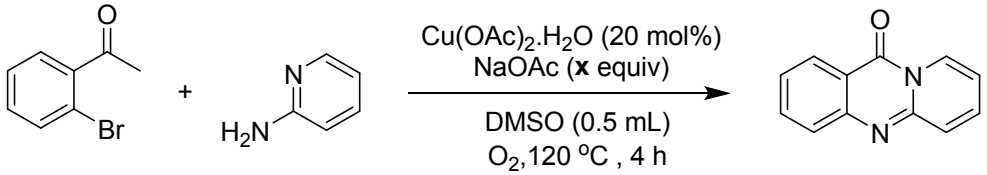
Table S5: Effect of different bases on the yield of 11H-pyrido[2,1-b]quinazolin-11-one:



Entry	Base	Yield[b] (%)
1	**NaOAc**	**90**
2	KOAc	80
3	NH_4OAc	14
4	$NaHCO_3$	19
5	K_2CO_3	6
6	K_3PO_4	4
7	KOH	8
8	Piperidine	23
9	Et_3N	2
10	DBU	0
11	Pyridine	11
12	DABCO	7
13	tBuOK	3
14	CsF	0
15	Cs_2CO_3	0

[a]Reaction conditions: 2-bromoacetophenone (0.1 mmol); 2-aminopyridine (0.25 mmol); DMSO (0.5 mL); $Cu(OAc)_2.H_2O$ (20 mol%); **base** (2 equiv); 120 °C; oxygen atmosphere; 4 h.[b] GC yield of 11H-pyrido[2,1-b]quinazolin-11-one.

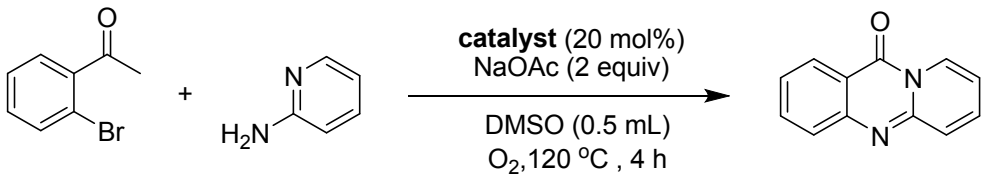
Table S6: Effect of varied base amounts on the yield of 11H-pyrido[2,1-b]quinazolin-11-one:



Entry	Base amount (equiv.)	Yield[b] (%)
1	0	23
2	0.5	43
3	1	65
4	1.5	81
5	**2**	**90**
6	2.5	**77**
7	3	76

[a]Reaction conditions: 2-bromoacetophenone (0.1 mmol); 2-aminopyridine (0.25 mmol); DMSO (0.5 mL); $Cu(OAc)_2.H_2O$ (20 mol%); NaOAc (**x** equiv); 120 ^oC; oxygen atmosphere; 4 h.[b] GC yield of 11H-pyrido[2,1-b]quinazolin-11-one.

Table S7: Effect of different catalysts on the yield of 11H-pyrido[2,1-b]quinazolin-11-one:



Entry	Catalysts	Yield[b] (%)
1	**$Cu(OAc)_2.H_2O$**	**90**
2	$Cu(OAc)_2$ anhydrous	79
3	$Cu(NO_3)_2.2H_2O$	36
4	$CuCl_2.2H_2O$	63
5	$Cu(NO_3)_2.3H_2O$	74
6	$Cu(acac)_2$	29
7	$CuBr_2$	64
8	CuBr	75
9	CuI	75
10	Cu powder	58
11	$CuSO_4$ anhydrous	36
12	CuO	26
13	Cu_2O	37
14	$Fe(OAc)_2$	0
15	$Ni(OAc)_2.4H_2O$	0

16	$Co(OAc)_2.4H_2O$	0
17	$Mn(OAc)_2.4H_2O$	0

[a]Reaction conditions: 2-bromoacetophenone (0.1 mmol); 2-aminopyridine (0.25 mmol); DMSO (0.5 mL); **catalyst** (20 mol%); NaOAc (2 equiv); 120 ^{o}C; oxygen atmosphere; 4 h.[b] GC yield of 11H-pyrido[2,1-b]quinazolin-11-one.

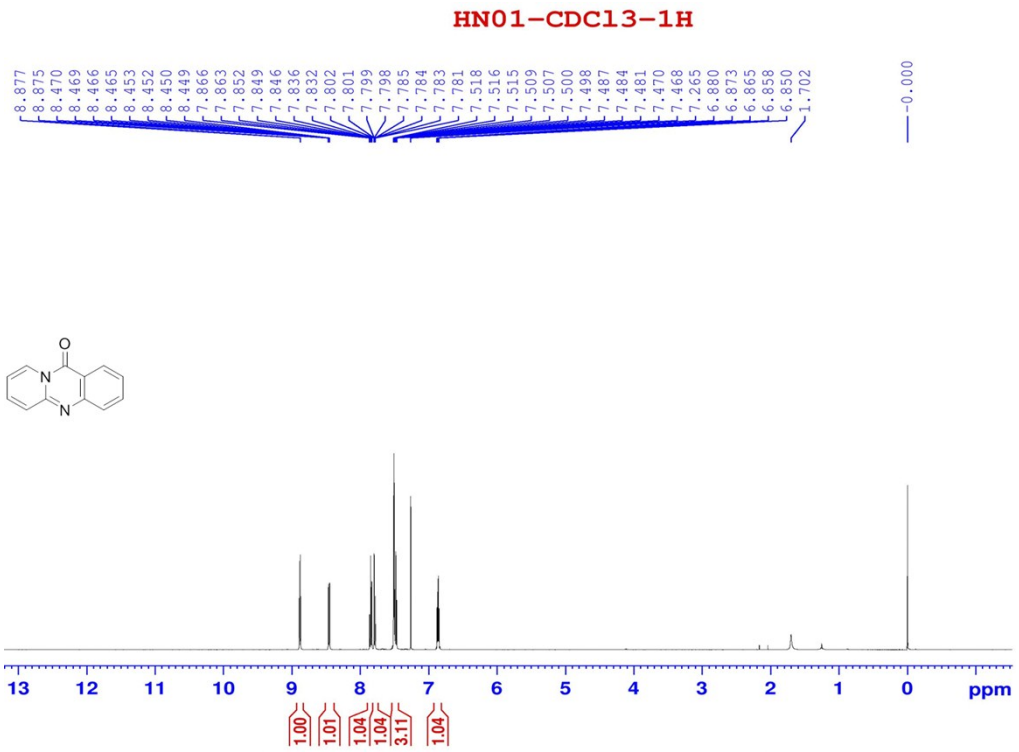


Fig.S1. [1]H-NMR spectra of 11*H*-pyrido[2,1-*b*]quinazolin-11-one.

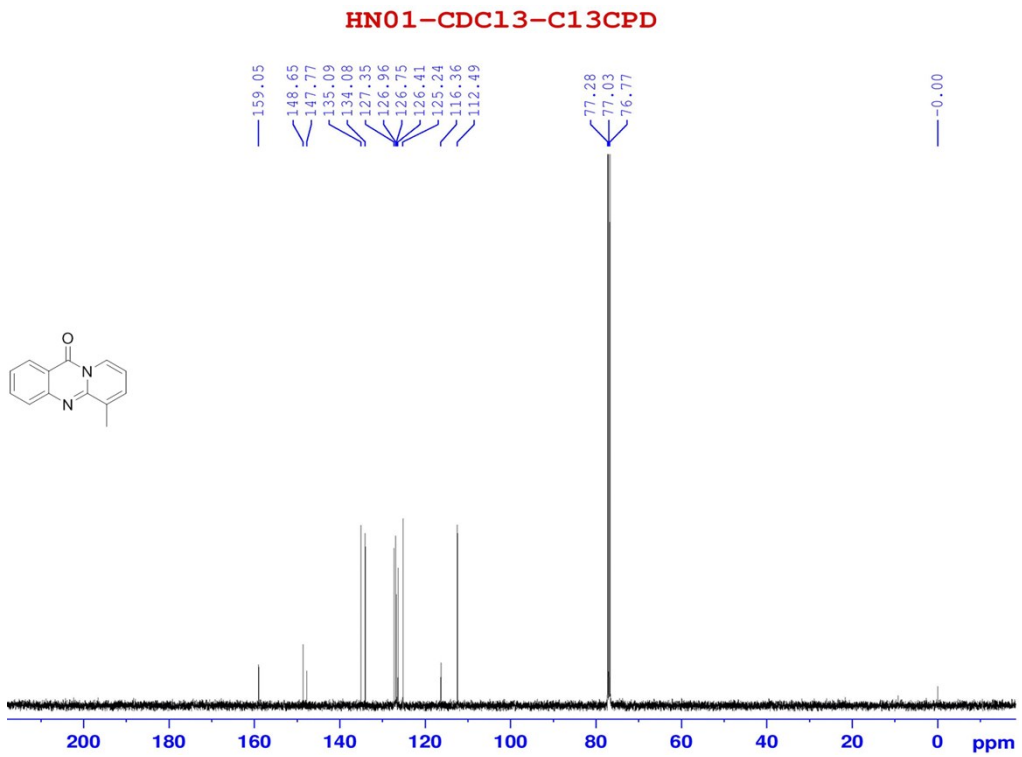


Fig.S2. ^{13}C-NMR spectra of 11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.4): Yellow solid, 87% yield (17 mg).^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 6.85–6.88 (m, 1H), 7.46–7.51 (m, 3H), 7.78-7.86 (m, 2H), 8.44-8.47 (m, 1H), 8.88 (dt, J = 7.5 Hz, 1.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 112.4, 116.3, 125.2, 126.4, 126.7, 126.9, 127.3, 134.0, 135.0, 147.7, 148.6, 159.0. HRMS calcd for $C_{12}H_8N_2O$ $(M+H)^+$: 197.0709, found $(M+H)^+$: 197.0701.

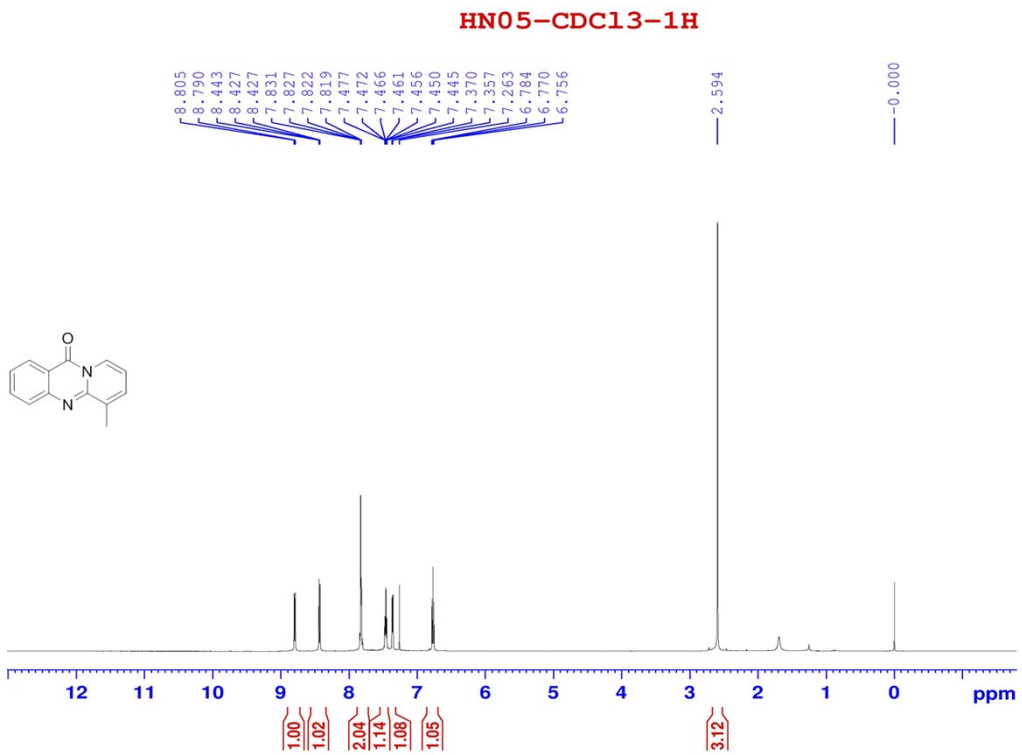


Fig.S3. ^{1}H-NMR spectra of 6-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

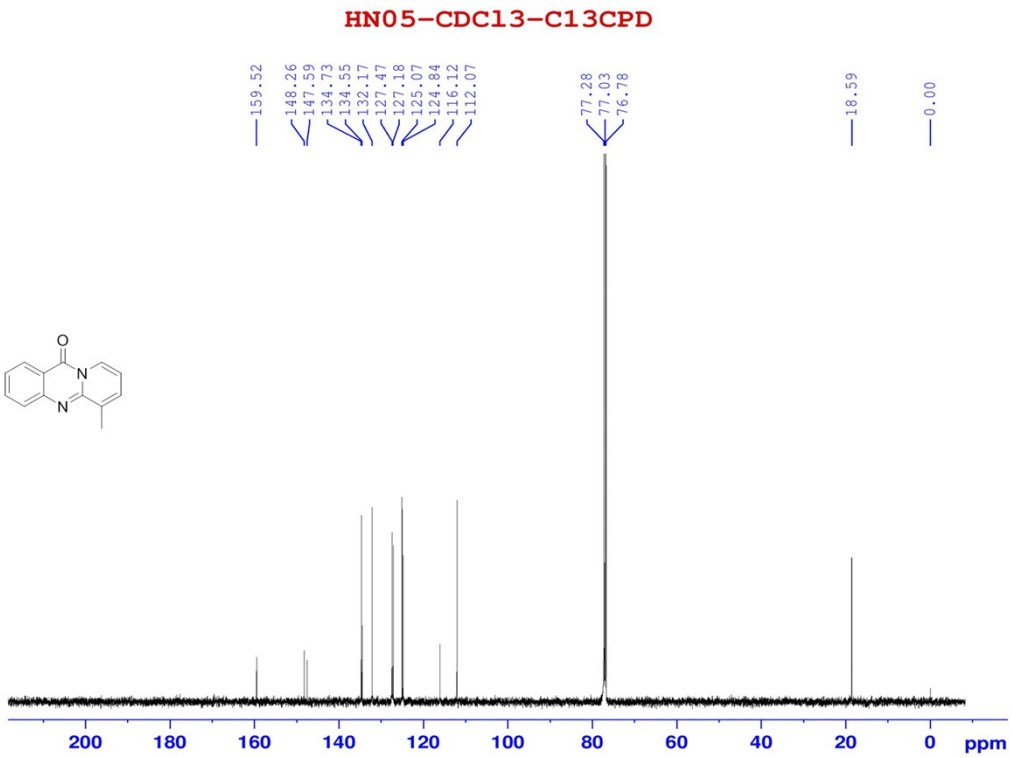


Fig.S4. ^{13}C-NMR spectra of 6-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 6-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.45): Yellow solid, 68% yield (14 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 2.59 (s, 3H), 6.77 (t, J = 7.0 Hz, 1H), 7.36 (d, J = 6.5 Hz, 1H), 7.44–7.47 (m, 1H), 7.81–7.83 (m, 2H), 8.43 (d, J = 8.0 Hz, 1H), 8.80 (d, J = 7.5 Hz, 1H).^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 18.5, 112.0, 116.1, 124.8, 125.0, 127.1, 127.4, 132.1, 134.5, 134.7, 147.5, 148.2, 159.5.

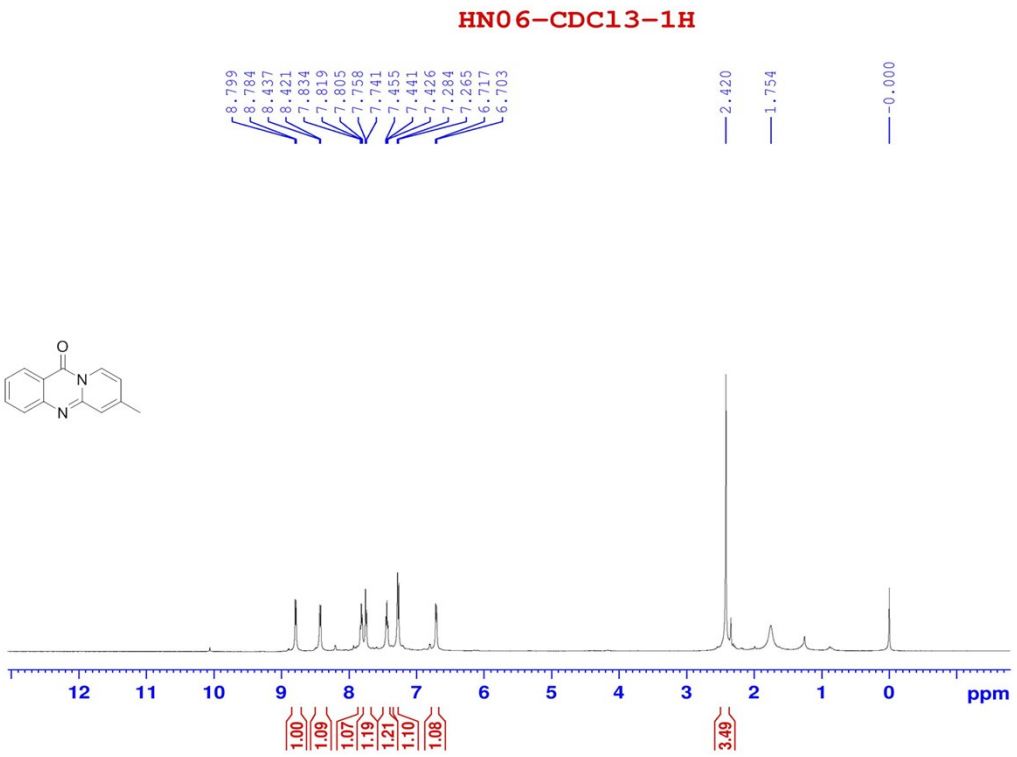


Fig.S5. ^{1}H-NMR spectra of 7-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

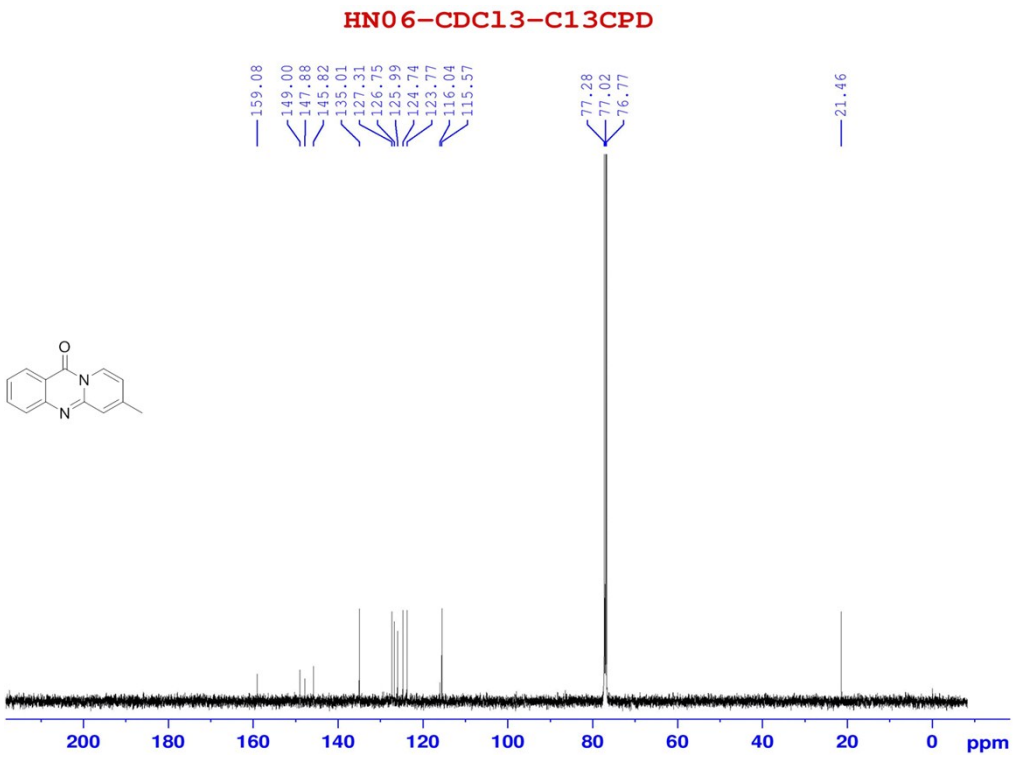


Fig.S6. ^{13}C-NMR spectra of 7-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 7-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.45): Yellow solid, 72% yield (15 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 2.42 (s, 3H), 6.70 (d, J = 7.5 Hz, 1H), 7.27 (d, J = 9.5 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.81 (t, J = 7.5 Hz, 1H), 8.43 (d, J = 9.5 Hz, 1H), 8.79 (d, J = 7.5 Hz, 1H) .^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 21.4, 115.5, 116.0, 123.7, 124.7, 125.9, 126.7, 127.3, 135.0, 145.8, 147.8, 149.0, 159.0.

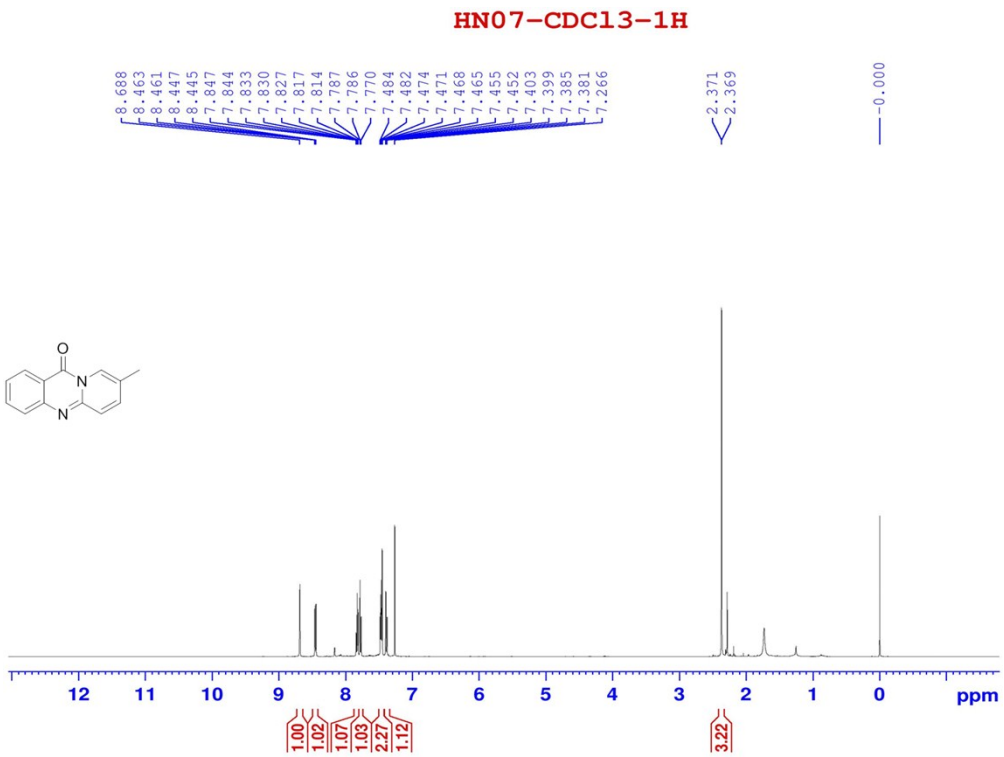


Fig.S7. ^{1}H-NMR spectra of 8-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

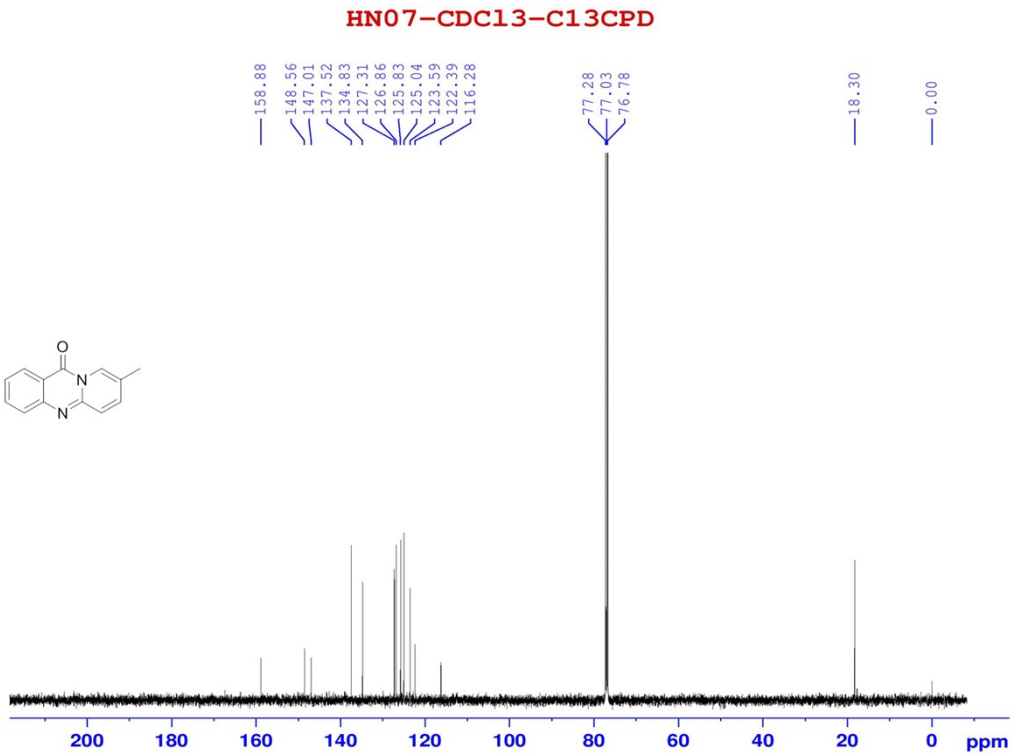


Fig.S8. ^{13}C-NMR spectra of 8-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 8-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.45): Yellow solid, 82% yield (17 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 2.37 (d, J = 1 Hz, 3H), 7.39 (dd, J = 9 Hz, 2 Hz, 1H), 7.45–7.48 (m, 2H), 7.78 (dd, J = 8.5 Hz, 0.5 Hz, 1H), 7.83 (td, J = 7.0 Hz, 1.5 Hz, 1H), 8.45 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 8.68 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 18.3, 116.2, 122.3, 123.5, 125.0, 125.8, 126.8, 127.3, 134.8, 137.5, 147.0, 148.5, 158.8.

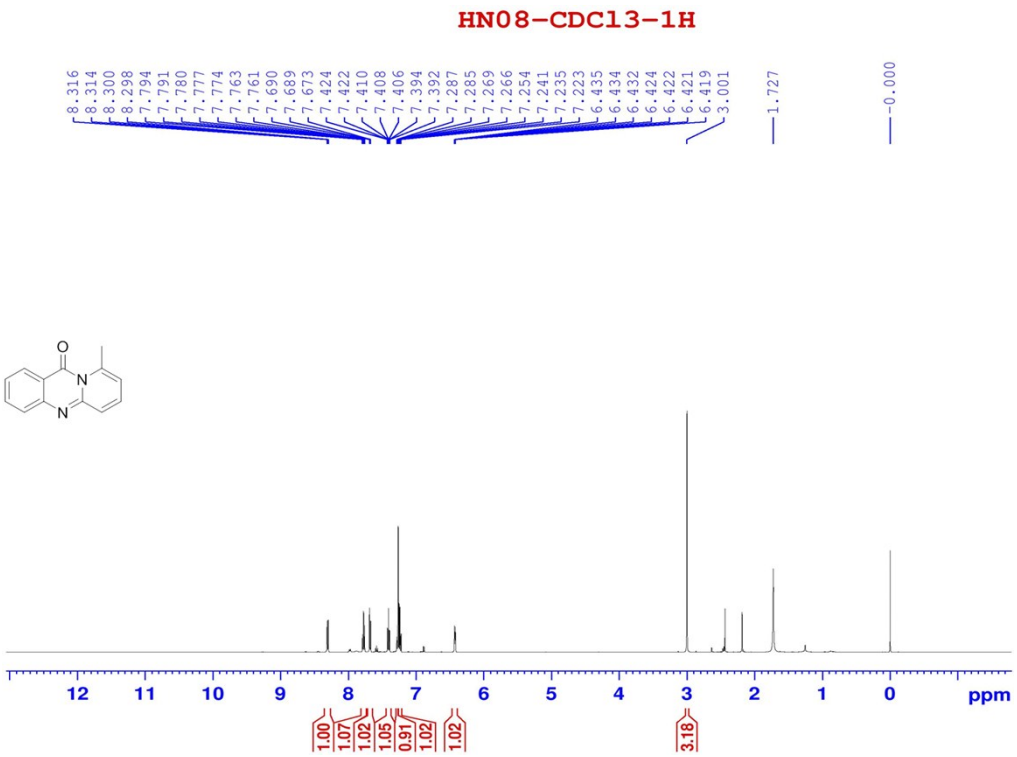


Fig.S9. ^{1}H-NMR spectra of 9-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

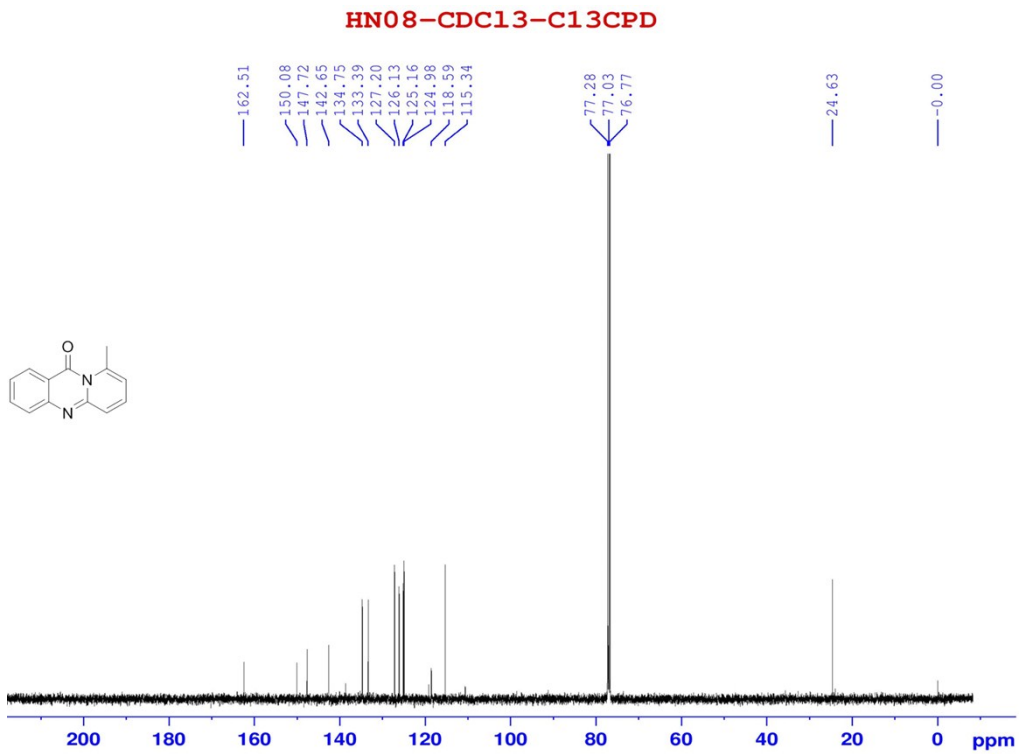


Fig.S10. ^{13}C-NMR spectra of 9-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 9-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.45): Yellow solid, 71% yield (15 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 3.00 (s, 3H), 6.43 (dt, J = 6.5 Hz, 1.0 Hz, 1H), 7.22–7.28 (m, 2H), 7.40 (td, J = 7.0 Hz, 1.0 Hz, 1H), 7.68 (dd, J = 8.5 Hz, 0.5 Hz, 1H), 7.79 (td, J = 8.5 Hz, 1.5 Hz, 1H), 8.31 (dd, J = 8.5 Hz, 1.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 24.6, 115.3, 118.5, 124.9, 125.1, 126.1, 127.2, 133.3, 134.7, 142.6, 147.7, 150.0, 162.5.

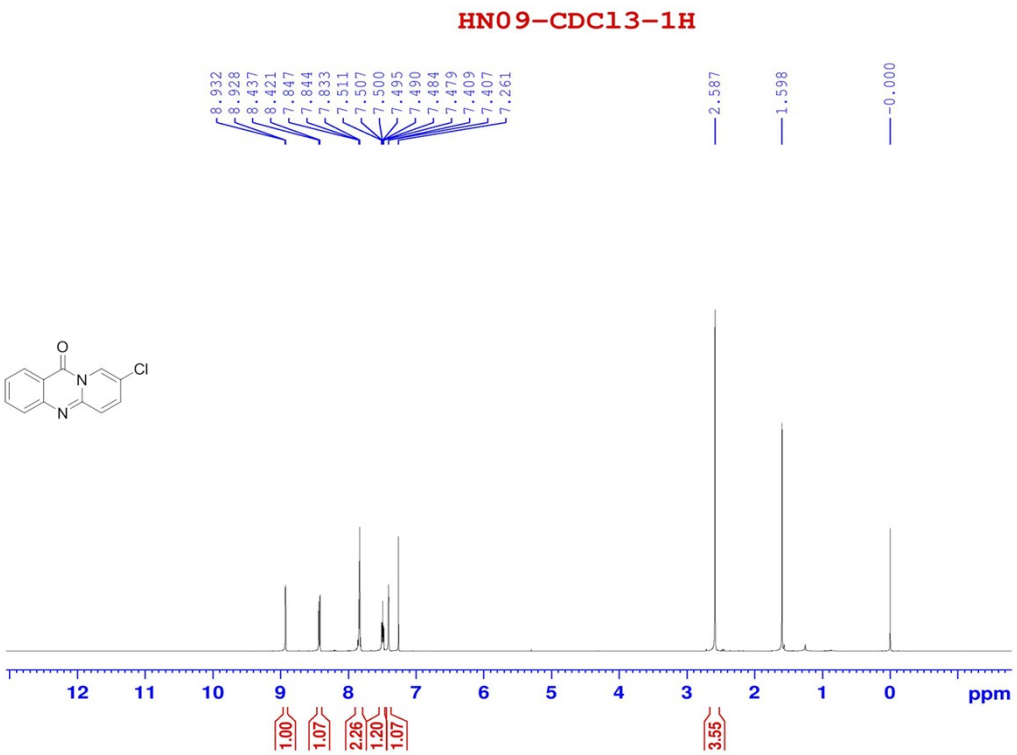


Fig.S11. ^{1}H-NMR spectra of 8-chloro-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

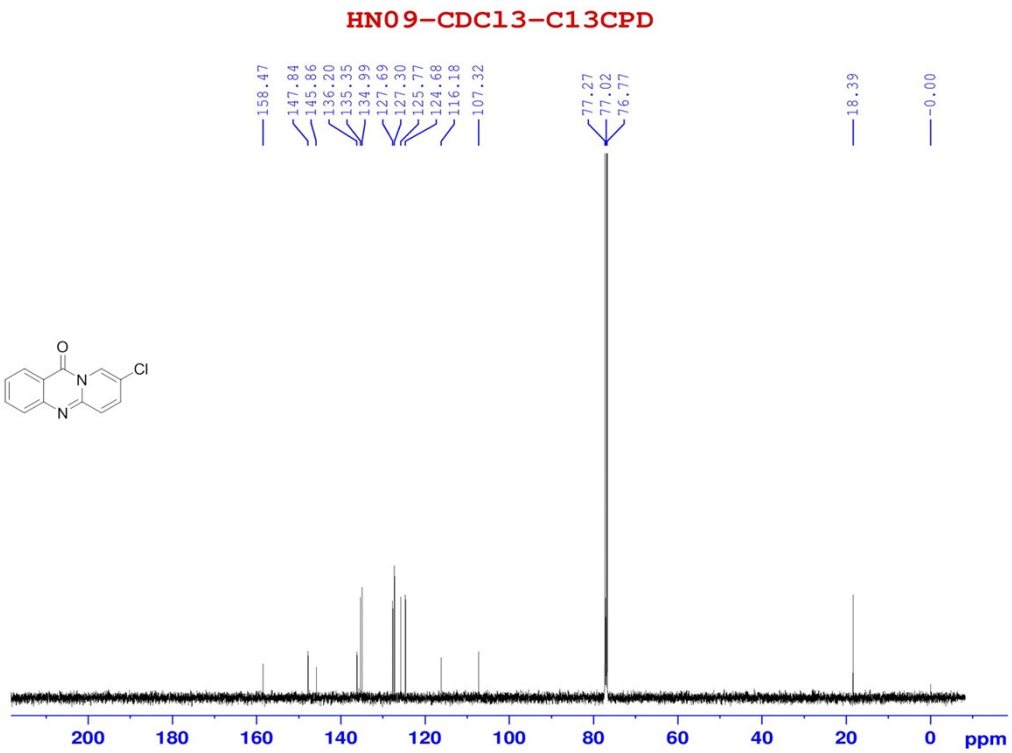


Fig.S12. ^{13}C-NMR spectra of 8-chloro-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 8-chloro-11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.4): Yellow solid, 55% yield (16 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 2.58 (s, 3H), 7.40 (s, 1H), 7.47–7.51 (m, 1H), 7.83–7.84 (m, 2H), 8.43 (d, J = 8.0 Hz, 1H), 8.93 (d, J = 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 18.3, 107.3, 116.1, 124.6, 125.7, 127.3, 127.6, 134.9, 135.3, 136.2, 145.8, 147.8, 158.4.

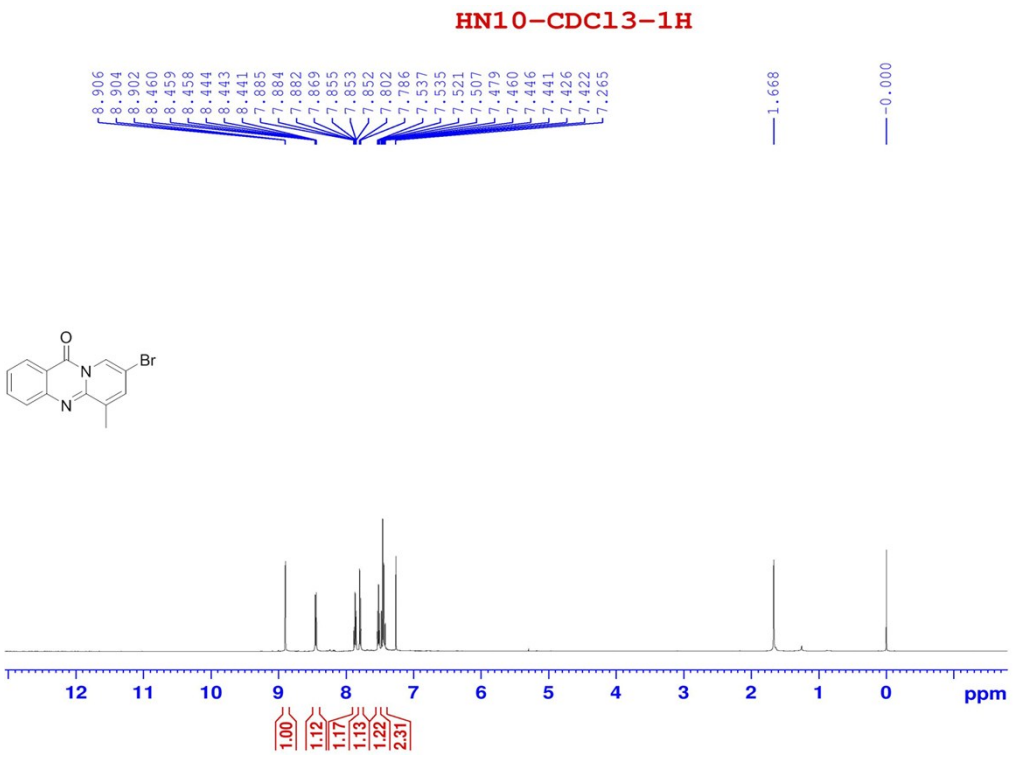


Fig.S13. ^{1}H-NMR spectra of 8-bromo-6-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

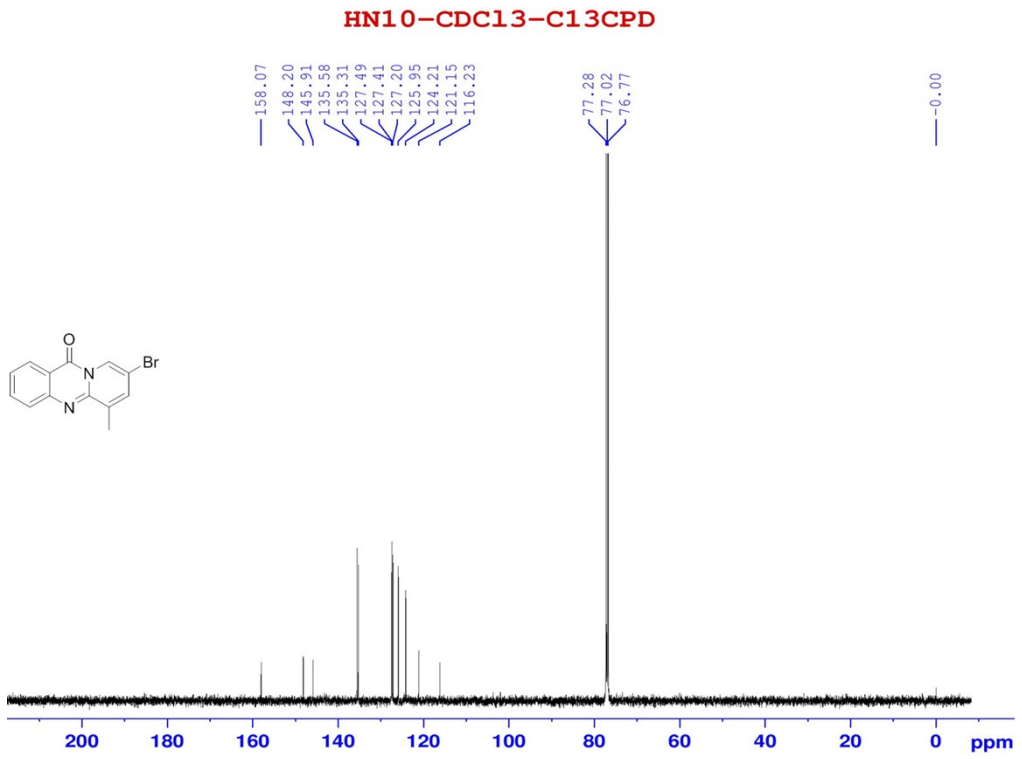


Fig.S14. ^{13}C-NMR spectra of 8-bromo-6-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 8-bromo-6-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.4): Yellow solid, 74% yield (17 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 7.42–7.47 (m, 2H), 7.86 (t, J = 7.0 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.86 (td, J = 7.5 Hz, 0.5 Hz, 1H), 8.45 (dt, J = 8.0 Hz, 0.5 Hz, 1H), 8.90–8.91 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 116.2, 121.1, 124.2, 125.9, 127.2, 127.4, 127.5, 135.3, 135.5, 145.9, 148.2, 158.0.

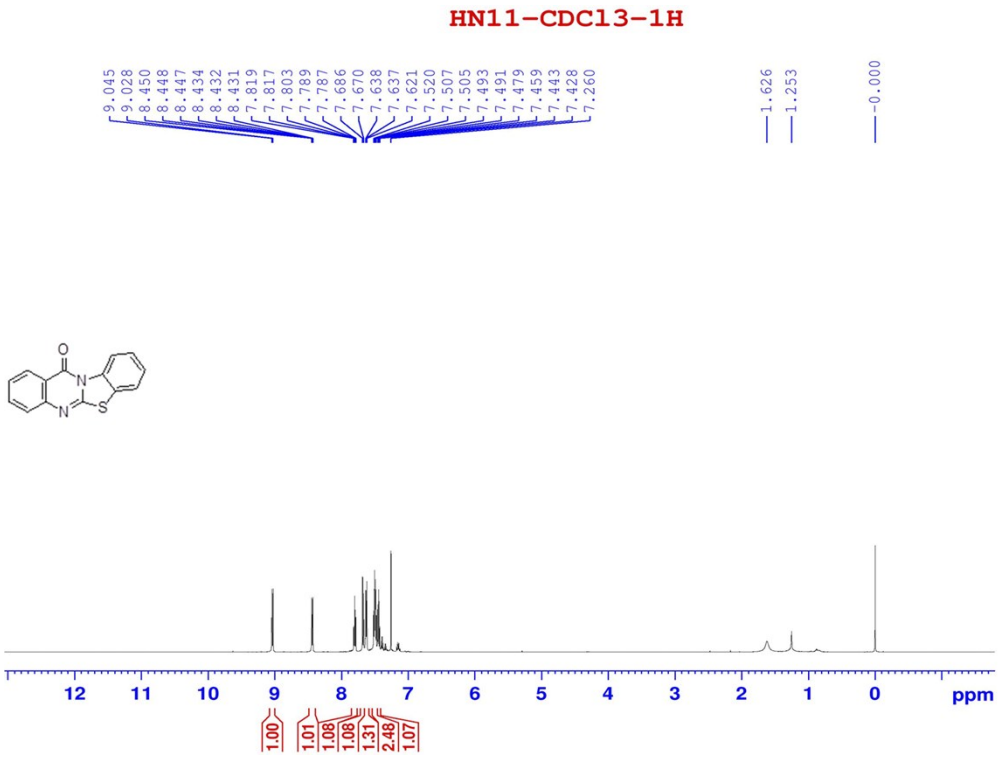


Fig.S15. ^{1}H-NMR spectra of 12*H*-benzo[4,5]thiazolo[2,3-*b*]quinazolin-12-one.

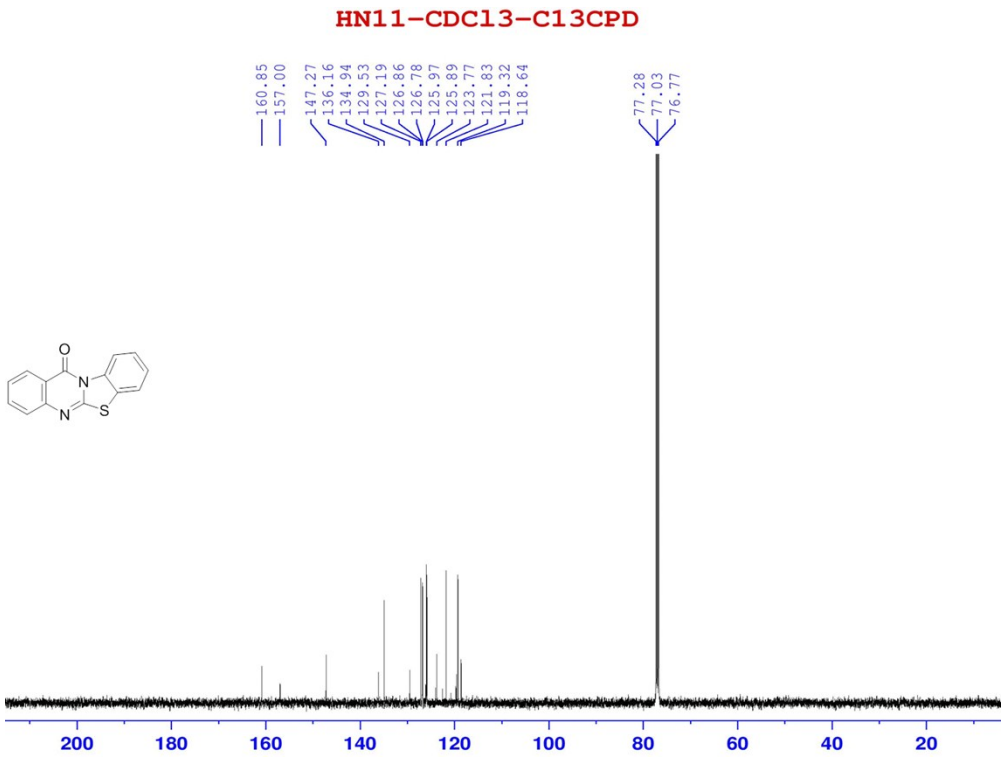


Fig.S16. ^{13}C-NMR spectra of 12*H*-benzo[4,5]thiazolo[2,3-*b*]quinazolin-12-one.

Characterization data for 12*H*-benzo[4,5]thiazolo[2,3-*b*]quinazolin-12-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:2 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.35): Yellow solid, 57% yield (15 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 7.44 (t, J = 8.0 Hz, 1H), 7.47–7.52 (m, 2H), 7.63 (d, J = 8.5 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.80 (t, J = 8.0 Hz, 1H), 8.44 (d, J = 8.0 Hz, 1H), 9.03 (d, J = 8.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 118.6, 119.3, 121.8, 123.7, 125.8, 125.9, 126.7, 126.8, 127.1, 129.5, 134.9, 136.1, 147.2, 160.8.

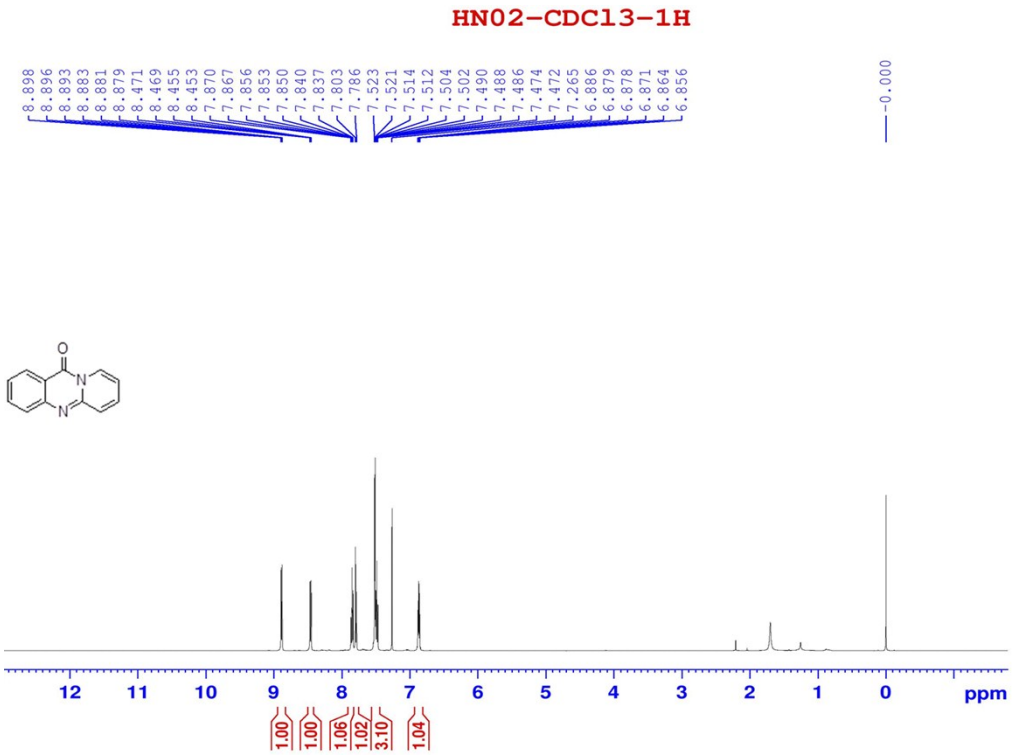


Fig.S17. ^{1}H-NMR spectra of 11*H*-pyrido[2,1-*b*]quinazolin-11-one.

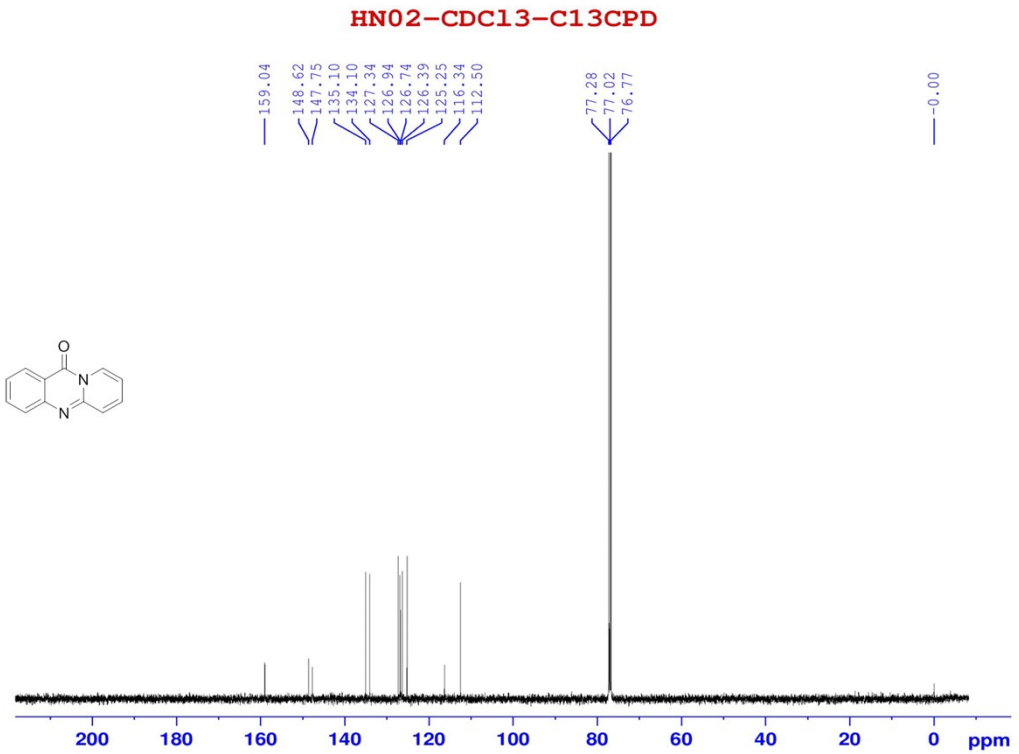


Fig.S18. ^{13}C-NMR spectra of 11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.4): Yellow solid, 89% yield (17 mg).^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 6.85–6.88 (m, 1H), 7.47–7.52 (m, 3H), 7.79 (d, J = 8.0 Hz, 1H), 7.83–7.86 (m, 1H), 8.46 (dd, J = 8.5 Hz, 1.0 Hz, 1H), 8.88 (dt, *J* = 8.5 Hz, 1.0 Hz, 1H).^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 112.5, 116.3, 125.2, 126.3, 126.7, 126.9, 127.3, 134.1, 135.1, 147.7, 148.6, 159.0

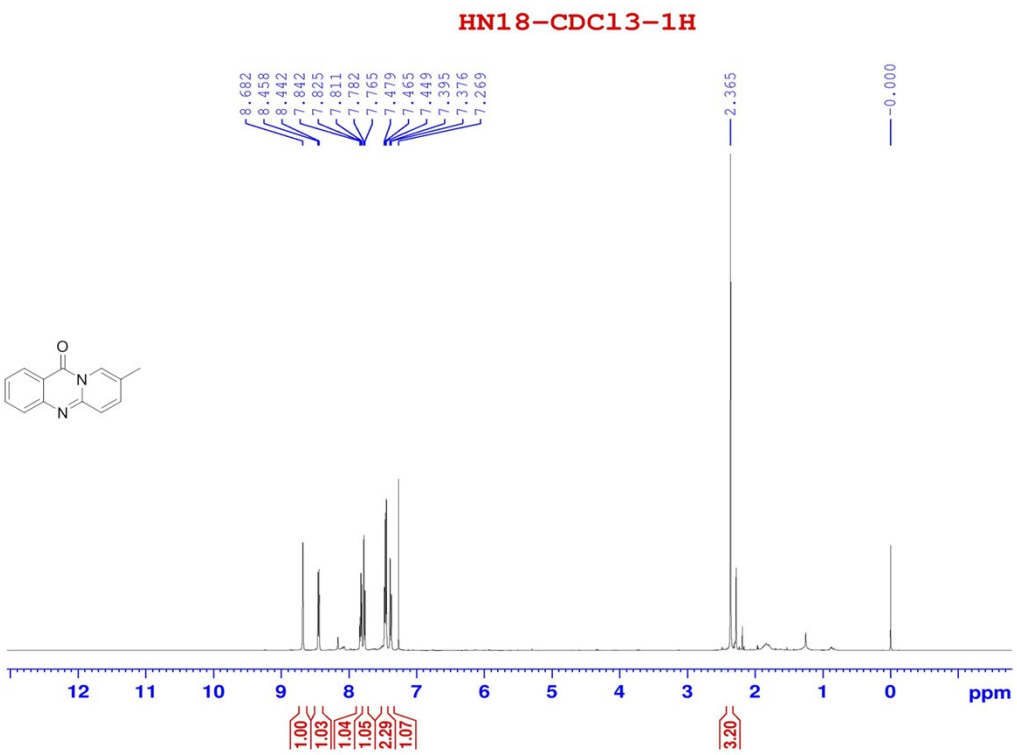


Fig.S19. [1]H-NMR spectra of 8-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

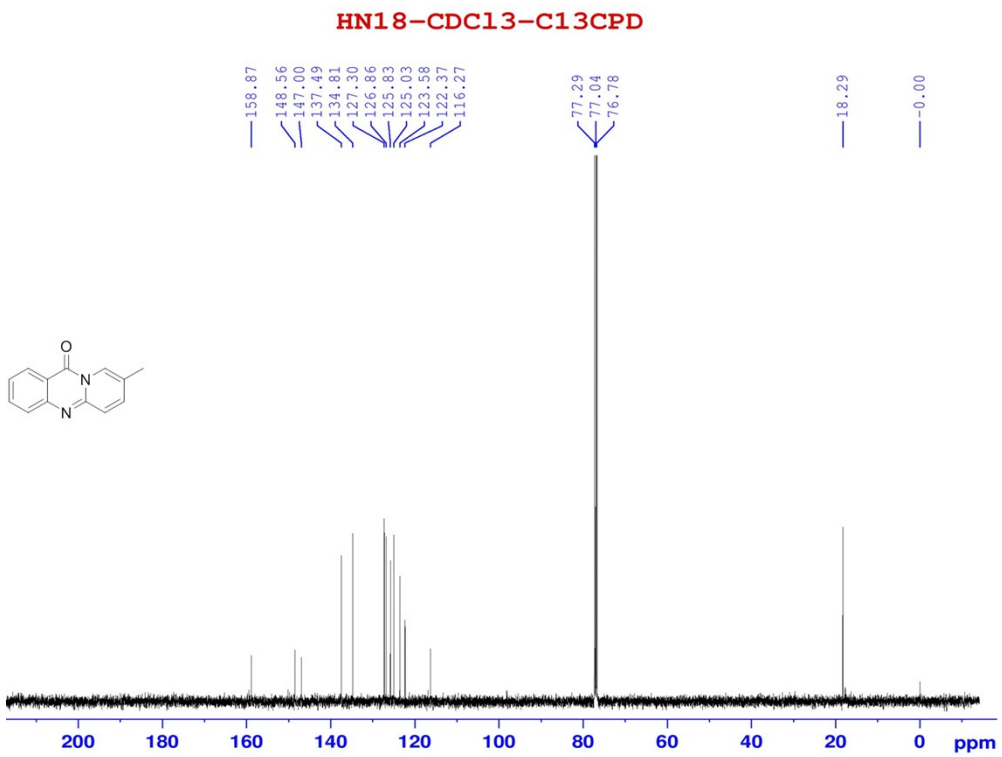


Fig.S20. ^{13}C-NMR spectra of 8-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 8-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.45): Yellow solid, 87% yield (18 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 2.36 (s,3H), 7.38 (d, J = 9.5 Hz, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 8.5 Hz, 1H), 7.81 – 7.84 (m, 1H), 8.45 (d, J = 8.0 Hz, 1H), 8.68 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 18.2, 116.2, 122.3, 123.5, 125.0, 125.8, 126.8, 127.3, 134.8, 137.4, 147.0, 148.5, 158.8

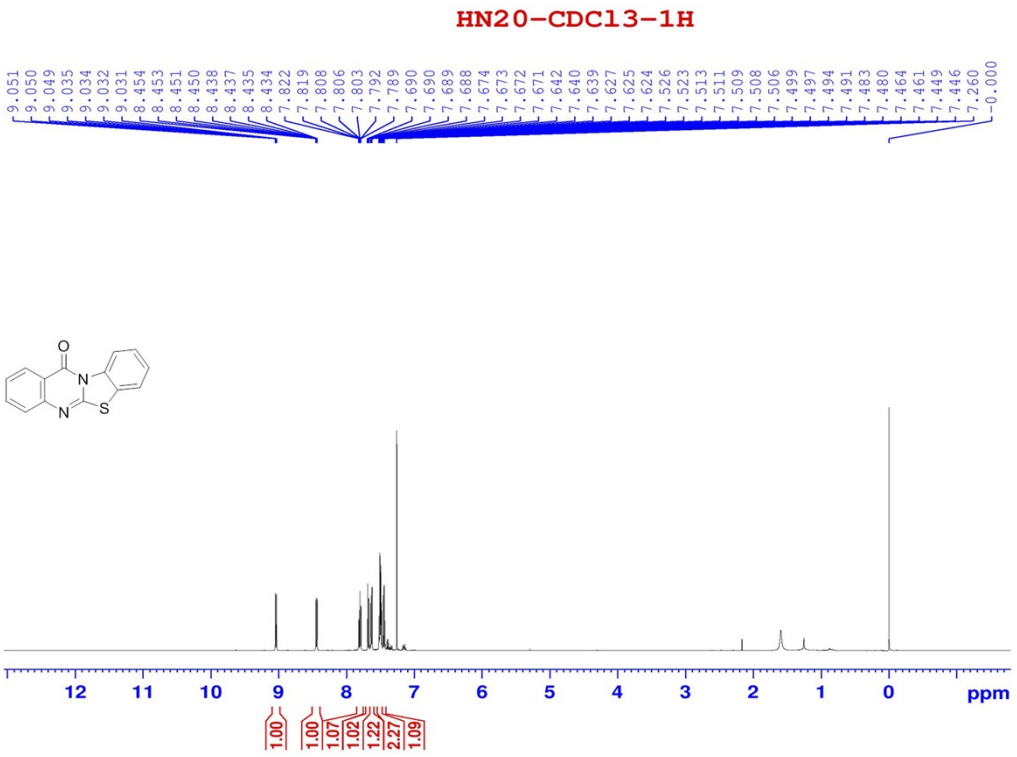


Fig.S21. ^{1}H-NMR spectra of 12*H*-benzo[4,5]thiazolo[2,3-*b*]quinazolin-12-one.

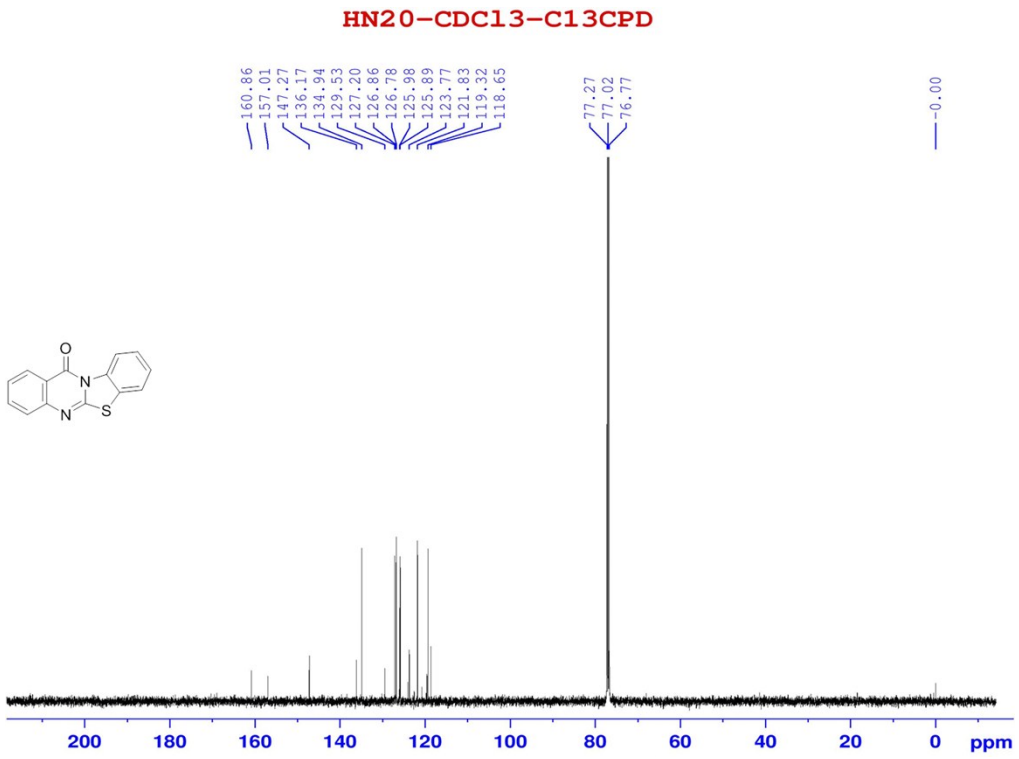


Fig.S22. ^{13}C-NMR spectra of 12*H*-benzo[4,5]thiazolo[2,3-*b*]quinazolin-12-one.

Characterization data for 12*H*-benzo[4,5]thiazolo[2,3-*b*]quinazolin-12-one

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.35): Yellow solid, 63% yield (16.5 mg). ^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 7.44 (td, J = 7.5 Hz, 1.5 Hz, 1H), 7.48 – 7.52 (m, 2H), 7.62 – 7.64 (m, 1H), 7.67 – 7.69 (m, 1H), 7.78 – 7.82 (m, 1H), 9.03 – 9.05 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 118.6, 119.3, 121.8, 123.7, 125.8, 125.9, 126.7, 126.8, 127.2, 134.9, 136.1, 147.2, 157.0, 160.8

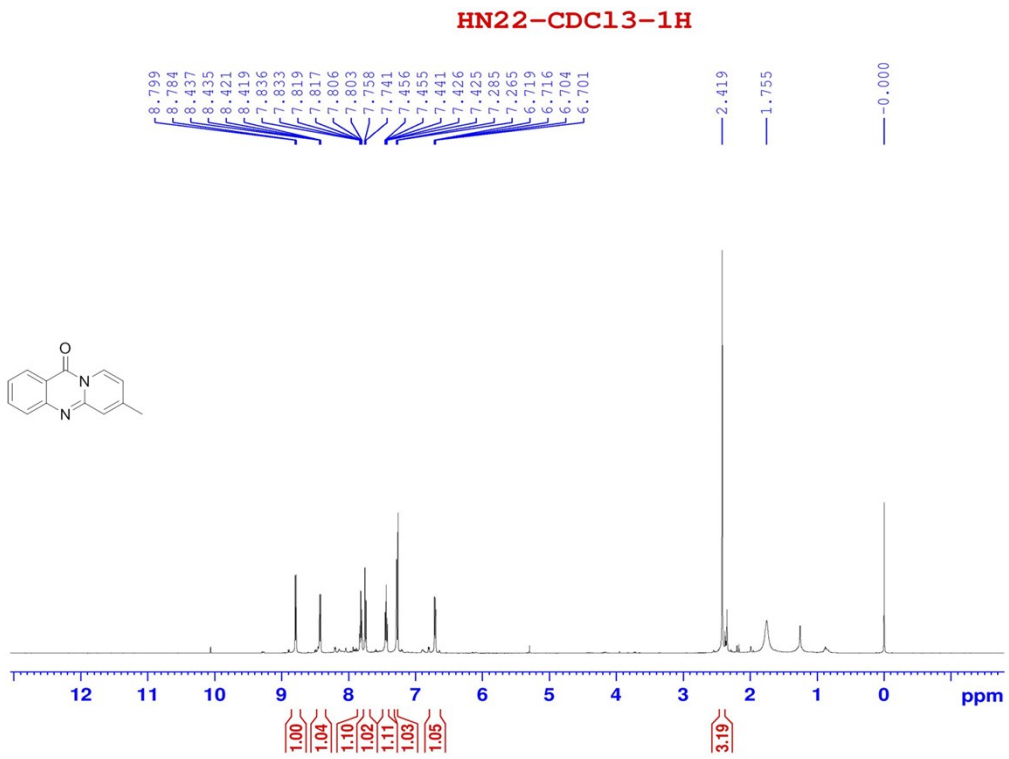


Fig.S23. ^{1}H-NMR spectra of 7-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

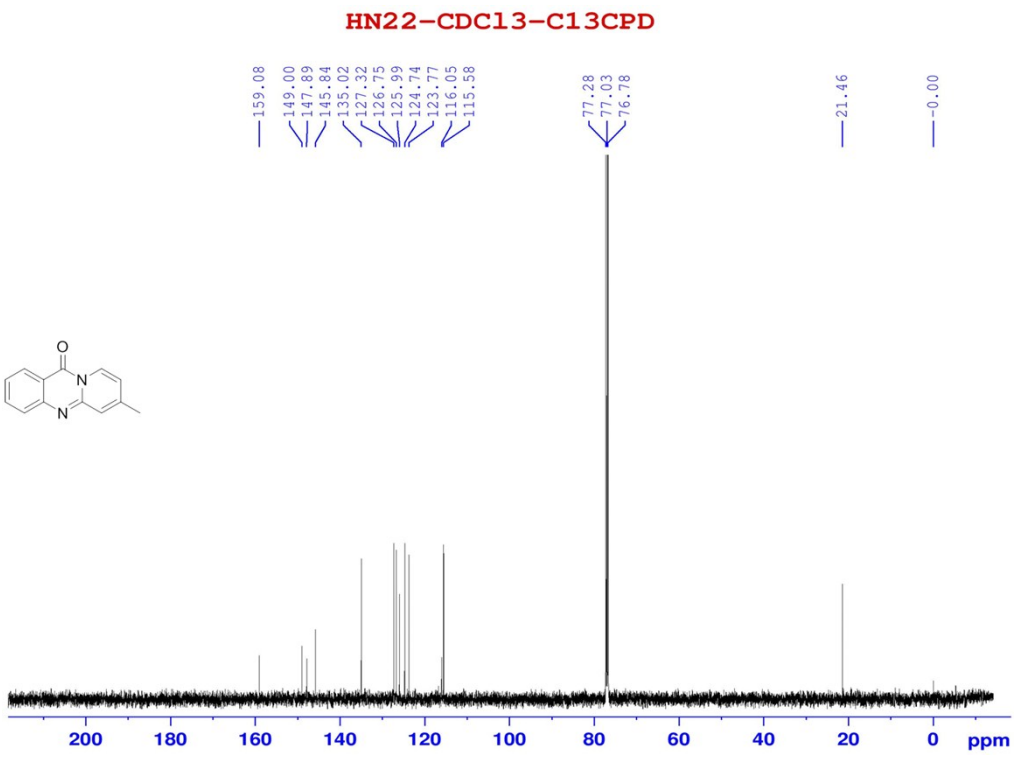
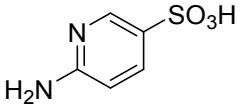
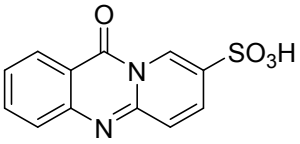
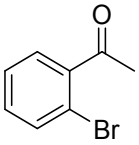
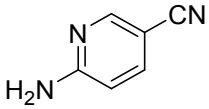
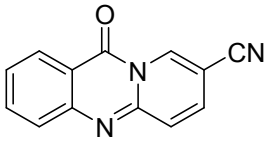
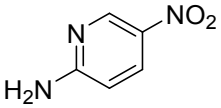
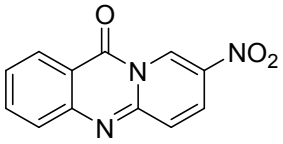
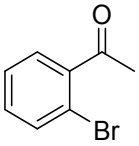
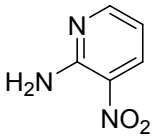
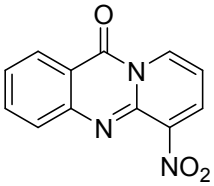


Fig.S24. ^{13}C-NMR spectra of 7-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one.

Characterization data for 7-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (HN22 – Entry 12)

Prepared as shown in the general experimental procedure and purified on silica gel (230-400 mesh or 37-63 μm, ethyl acetate/hexane = 1:1 (v./v.), TLC silica gel 60 F_{254}, R_f = 0.45): Yellow solid, 78% yield (16.3 mg).^{1}H-NMR (500 MHz, $CDCl_3$) δ(ppm) 2.41 (s,3H), 6.70 (d, J = 1.5 Hz, 1H), 7.26 – 7.28 (m, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.75 (d, J = 9.0 Hz, 1H), 7.81 (td, J = 9.0 Hz, 1.5 Hz, 1H), 8.43 (dd, J = 7.5 Hz, 1Hz, 1H), 8.79 (d, J = 7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ(ppm) 21.4, 115.5, 116.0, 123.7, 124.7, 125.9, 126.7, 127.3, 135.0, 145.8, 147.8, 149.0, 159.0

Table S8: Effect of strong electron-withdrawing substituents on 2-aminopyridine[a]

Entry	Reactant 1	Reactant 2	Product	Isolated Yield (%)
1				Trace
2				Trace
3				Trace
4				Trace

[a] [a]Reaction conditions: 2'-bromoacetophenone (0.1 mmol); 2-aminopyridines (0.25 mmol); NaOAc (0.2 mmol); DMSO (0.5 mL); $Cu(OAc)_2.H_2O$ catalyst (20 mol%); oxygen atmosphere; 120 ^oC; 4 h.