

Supporting Information

**One-pot Total Synthesis of Evodiamine and Its Analogues through a
Continuous Biscyclization Reaction**

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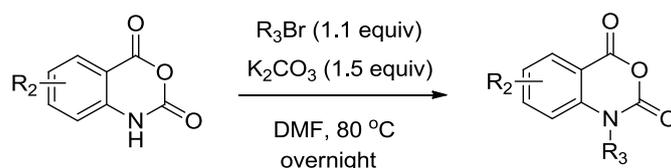
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1. General

Unless otherwise stated, all starting materials and catalysts were obtained from commercial suppliers and used without further purification. All new compounds were fully characterized. TLC analysis was performed using precoated glass plates. Column chromatography was performed using aluminium oxide basic (200–300 mesh). IR spectra were recorded as KBr pellets with absorption in cm^{-1} . ^1H NMR spectra were recorded in CDCl_3 or $\text{DMSO}-d_6$ on 400/600 MHz spectrometers and resonances (δ) are given in ppm relative to TMS (internal standard). ^{13}C NMR spectra were recorded in CDCl_3 or $\text{DMSO}-d_6$ on 100/150 MHz NMR spectrometers. HRMS were obtained on a 7.0T FTMS equipped with ESI. Melting points were determined using an electrothermal capillary melting point apparatus and not corrected.

2. General procedure for the synthesis

General Method A: Typical Experimental Procedure for Synthesis of 1- Alkyl -1*H*-benzo[*d*][1,3]oxazine-2,4-dione (N-Alkylisatoic anhydride).



1-Alkyl-1*H*-benzo[*d*][1,3]oxazine-2,4-dione (N-Alkylisatoic anhydride) were synthesized according to a previously known procedure.^[1]

General Method B:

➤ for **3** (**3a** as an example)

A mixture of tryptamine **1a** (1.0 mmol), N-Alkylisatoic anhydride **2a** (1.0 mmol), TFAA (1.0 mmol) in triethoxymethane and DMA (1.0 mL) (2:1) were added in a pressure vessel, then DABCO (1.5 mmol) was added and stirred at 100 °C for 5 h. Then added 50 mL water and 30 mL saturated brine solution to the mixture and extracted with EtOAc 3 times (3 × 50 mL). The extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (eluent: petroleum ether/EtOAc=4/1) to afford the product **3a** as white solid.

Reference:

[1] Ilangoan, A. and Satish, G. *J. Org. Chem.* **2014**, 79, 4984 – 4991.

3. Crystallographic data and molecular structure

14-propyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3I)

X-ray structure determination was obtained via slow evaporation of compound **3I** in EtOAc at room temperature.

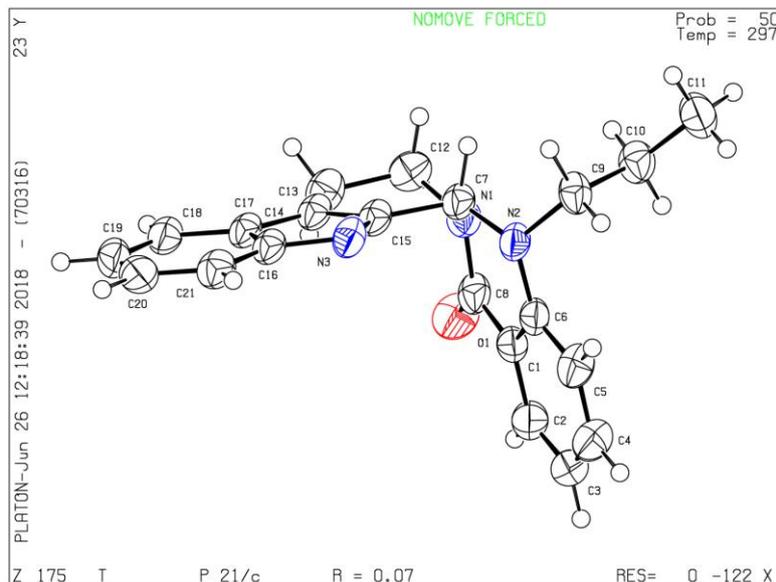
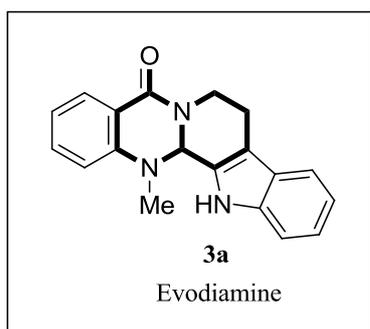


Figure S1. X-ray crystal structure of 3I;

Table S1. Crystal data and structure refinement for compound 3I (CCDC 1856975)

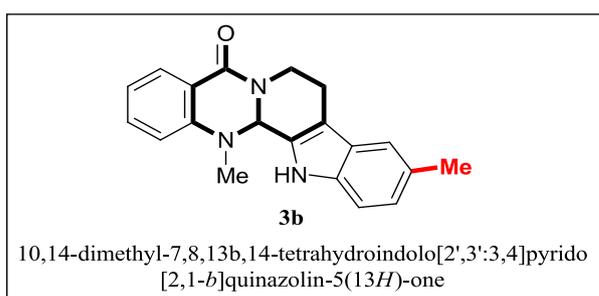
Bond precision:	C-C = 0.0062 Å	Wavelength=0.71073	
Cell:	a=15.913 (6)	b=8.626 (4)	c=13.089 (5)
	alpha=90	beta=113.649 (6)	gamma=90
Temperature:	297 K		
Volume	Calculated	Reported	
	1645.8 (12)	1645.7 (12)	
Space group	P 21/c	P 21/c	
Hall group	-P 2ybc	-P 2ybc	
Moiety formula	C21 H20 N3 O	?	
Sum formula	C21 H20 N3 O	C21 H20 N3 O	
Mr	330.40	330.40	
Dx, g cm ⁻³	1.333	1.333	
Z	4	4	
Mu (mm ⁻¹)	0.084	0.084	
F000	700.0	700.0	
F000'	700.25		
h, k, lmax	18, 10, 15	18, 10, 15	
Nref	2899	2870	
Tmin, Tmax	0.992, 0.993		
Tmin'	0.992		
Correction method=	Not given		
Data completeness=	0.990	Theta(max)= 24.996	
R(reflections)=	0.0720 (2506)	wR2(reflections)= 0.2288 (2870)	
S =	1.102	Npar= 230	

4. Characterization data for target compound



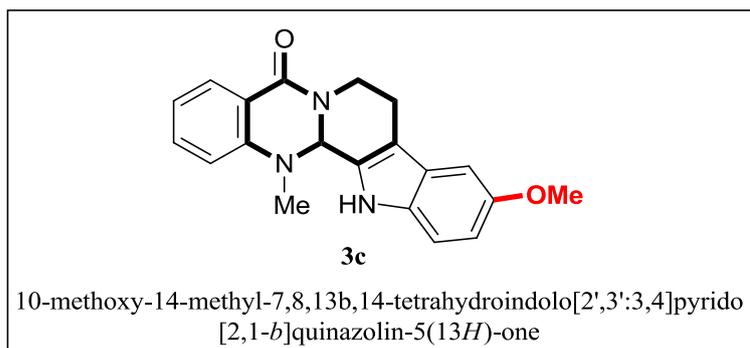
14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one

(Evodiamine) (3a): Yield 71%; 215.1 mg; white solid; mp = 302–303 °C; IR (KBr) ν_{max} : 3424, 2361, 2252, 2126, 1639, 1509, 1451, 1389, 1051, 1027, 1005, 825 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.08 (s, 1H), 7.84–7.77 (m, 1H), 7.48 (s, 2H), 7.40–7.33 (m, 1H), 7.14–7.09 (m, 1H), 7.07–7.03 (m, 1H), 7.03–6.99 (m, 1H), 6.98–6.94 (m, 1H), 6.13 (s, 1H), 4.69–4.59 (m, 1H), 3.22–3.16 (m, 1H), 2.94–2.84 (m, 4H), 2.80–2.78 (m, 1H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.3, 148.8, 136.5, 133.5, 130.6, 128.0, 126.0, 121.9, 120.3, 119.2, 119.0, 118.3, 117.5, 111.7, 111.5, 69.8, 40.9, 36.5, 19.5. HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{18}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 304.1447, found 304.1444.

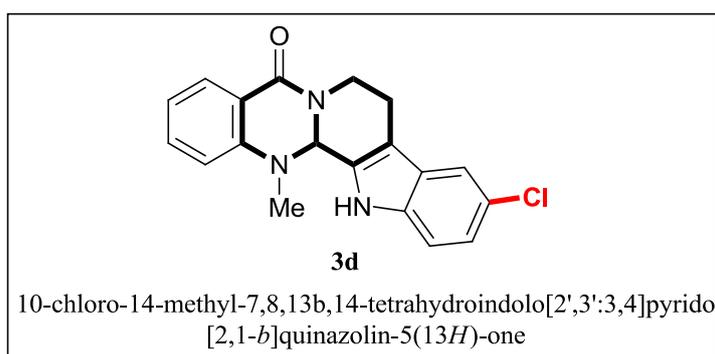


10,14-dimethyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one

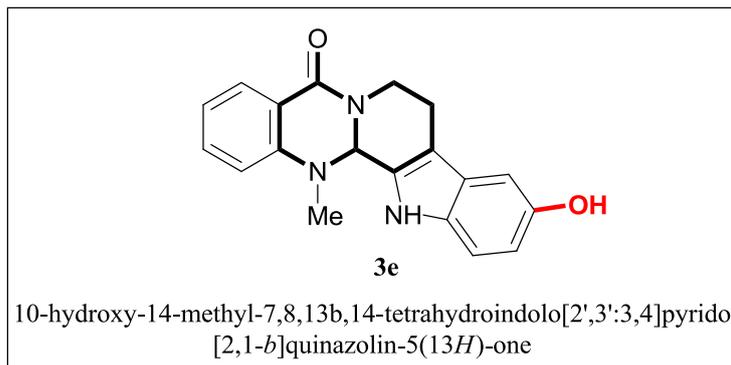
(3b): Yield 43%; 136.3 mg; white solid; mp = 284–285 °C; IR (KBr) ν_{max} : 3427, 3230, 2361, 1631, 1608, 1511, 1471, 1453, 1390, 1280, 1027, 824 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.06 (s, 1H), 7.93 (d, $J = 7.8$ Hz, 1H), 7.61 (t, $J = 7.8$ Hz, 1H), 7.42–7.35 (m, 2H), 7.18 (d, $J = 8.4$ Hz, 1H), 7.13–7.05 (m, 2H), 6.24 (s, 1H), 4.80–4.71 (m, 1H), 3.35–3.30 (m, 1H), 3.02 (s, 4H), 2.91–2.86 (m, 1H), 2.67–2.62 (m, 3H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.3, 148.7, 134.8, 133.5, 130.7, 128.0, 127.4, 126.2, 123.5, 120.2, 119.2, 117.9, 117.4, 111.4, 111.0, 69.9, 41.0, 36.4, 21.2, 19.5. HRMS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 318.1605, found 318.1601.



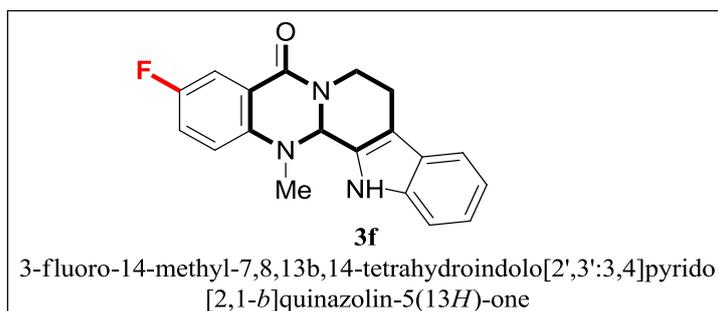
10-methoxy-14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3c): Yield 56%; 186.5 mg; white solid; mp = 312–314 °C; IR (KBr) ν_{max} : 3428, 2361, 2338, 2253, 1633, 1511, 1459, 1438, 1391, 1211, 1027, 825 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 10.89 (s, 1H), 7.79 (d, $J = 7.8$ Hz, 1H), 7.47 (t, $J = 7.8$ Hz, 1H), 7.25 (d, $J = 9.0$ Hz, 1H), 7.03 (d, $J = 8.4$ Hz, 1H), 6.98–6.90 (m, 2H), 6.75 (d, $J = 8.4$ Hz, 1H), 6.10 (s, 1H), 4.66–4.59 (m, 1H), 3.75 (s, 3H), 3.20–3.15 (m, 1H), 2.89 (s, 4H), 2.77–2.73 (m, 1H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.3, 153.4, 148.7, 133.5, 131.5, 131.3, 128.0, 126.3, 120.2, 119.1, 117.3, 112.4, 112.0, 111.4, 100.1, 69.9, 55.4, 41.1, 36.4, 19.6. HRMS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}_2^+$ ($\text{M}+\text{H}$) $^+$ 334.1548, found 334.1550.



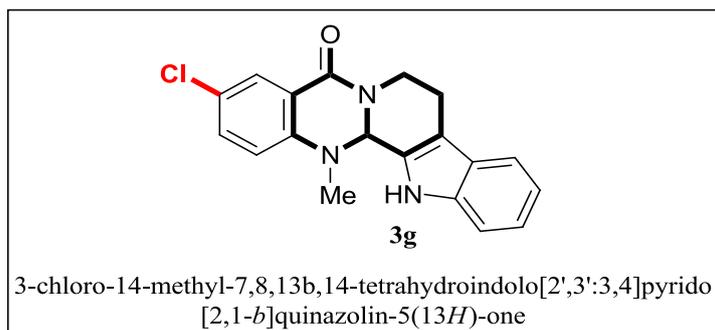
10-chloro-14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3d): Yield 68%; 229.2 mg; white solid; mp = 312–313 °C; IR (KBr) ν_{max} : 3444, 2361, 2339, 1699, 1634, 1508, 1456, 1392, 1027, 1002 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.29 (s, 1H), 7.78 (d, $J = 7.8$ Hz, 1H), 7.52 (s, 1H), 7.47 (t, $J = 7.8$ Hz, 1H), 7.36 (d, $J = 8.4$ Hz, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 7.03 (d, $J = 8.4$ Hz, 1H), 6.95 (t, $J = 7.2$ Hz, 1H), 6.15 (s, 1H), 4.64–4.58 (m, 1H), 3.21–3.16 (m, 1H), 2.94–2.86 (m, 4H), 2.79–2.74 (m, 1H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.3, 148.6, 134.9, 133.6, 132.8, 128.0, 127.2, 123.6, 121.8, 120.3, 119.0, 117.6, 117.3, 113.2, 111.4, 69.8, 41.0, 36.7, 19.3. HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{17}\text{ClN}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 338.1057, found 338.1055.



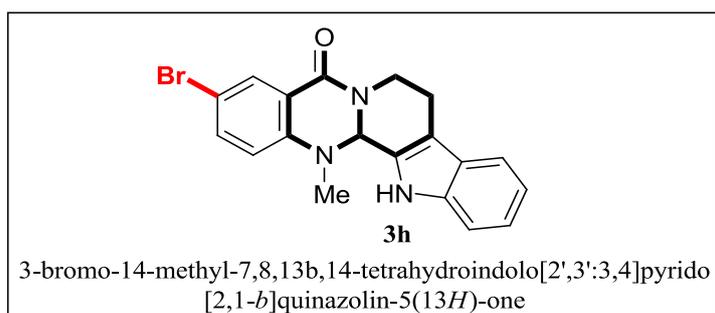
10-hydroxy-14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3e) : Yield 28%; 89.3 mg; white solid; mp = 276–277 °C; IR (KBr) ν_{max} : 3444, 3259, 2361, 2338, 1634, 1457, 1219, 1110, 1045, 1024, 1002 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 10.73 (s, 1H), 8.75 (s, 1H), 7.80 (d, $J = 7.8$ Hz, 1H), 7.46 (t, $J = 7.2$ Hz, 1H), 7.17 (d, $J = 8.4$ Hz, 1H), 7.01 (d, $J = 8.4$ Hz, 1H), 6.96–6.92 (m, 1H), 6.78 (s, 1H), 6.67–6.62 (m, 1H), 6.08 (s, 1H), 4.65–4.59 (m, 1H), 3.21–3.16 (m, 1H), 2.94–2.83 (m, 4H), 2.69–2.64 (m, 1H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.5, 150.8, 148.7, 133.6, 131.3, 131.0, 128.1, 126.8, 120.1, 118.9, 117.0, 112.2, 110.7, 102.3, 70.1, 41.2, 36.5, 19.6. HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{18}\text{N}_3\text{O}_2^+$ ($\text{M}+\text{H}$) $^+$ 320.1398, found 320.1394.



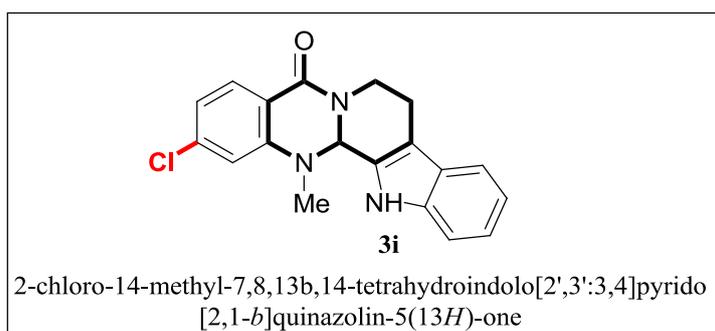
3-fluoro-14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3f) : Yield 42%; 134.8 mg; white solid; mp = 223–224 °C; IR (KBr) ν_{max} : 3426, 2361, 1635, 1580, 1483, 1445, 1417, 1266, 1050, 1027, 1004, 827 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.21 (s, 1H), 7.62–7.55 (m, 1H), 7.52–7.47 (m, 1H), 7.43–7.34 (m, 2H), 7.21–7.17 (m, 1H), 7.15–7.10 (m, 1H), 7.06–7.00 (m, 1H), 6.08 (s, 1H), 4.69–4.59 (m, 1H), 3.24–3.16 (m, 1H), 2.85 (s, 2H), 2.66 (s, 3H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 163.1, 157.3 (d, $J = 236.9$ Hz, $^1J_{\text{CF}}$), 146.1, 136.7, 129.6, 125.9, 122.2 (d, $J = 6.3$ Hz, $^3J_{\text{CF}}$), 122.0, 121.9 (d, $J = 7.7$ Hz, $^3J_{\text{CF}}$), 120.6 (d, $J = 23.6$ Hz, $^2J_{\text{CF}}$), 119.0, 118.4, 113.5 (d, $J = 22.4$ Hz, $^2J_{\text{CF}}$), 111.7, 69.3, 40.4, 36.6, 19.6. HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{17}\text{FN}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 322.1355, found 322.1350.



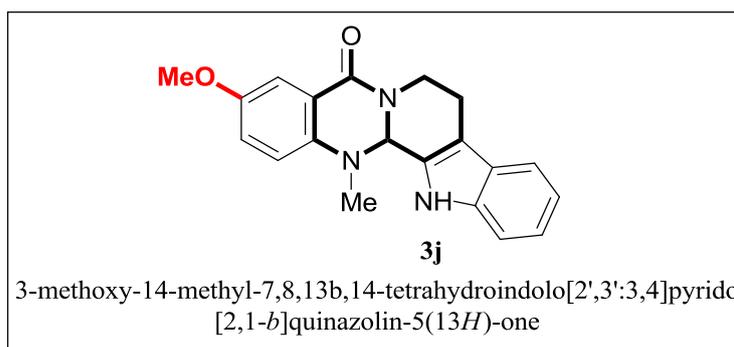
3-chloro-14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3g) : Yield 74%; 249.4 mg; white solid; mp = 307–308 °C; IR (KBr) ν_{max} : 3445, 3253, 2360, 2337, 1631, 1599, 1504, 1453, 1340 cm^{-1} ; ^1H NMR (600 MHz, DMSO- d_6) δ 10.95 (s, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.37 (d, J = 8.4 Hz, 1H), 7.11 (t, J = 7.8 Hz, 1H), 7.02–6.97 (m, 2H), 6.87 (d, J = 8.4 Hz, 1H), 6.22 (s, 1H), 4.65–4.62 (m, 1H), 3.24–3.19 (m, 1H), 3.11 (s, 3H), 2.99–2.94 (m, 1H), 2.75–2.70 (m, 1H). ^{13}C NMR (150 MHz, DMSO- d_6) δ 163.8, 148.8, 138.4, 136.3, 131.2, 129.8, 126.1, 122.0, 119.0, 118.8, 118.2, 116.1, 114.6, 111.7, 111.5, 70.6, 41.8, 36.4, 19.3. HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{17}\text{ClN}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 338.1052, found 338.1055.



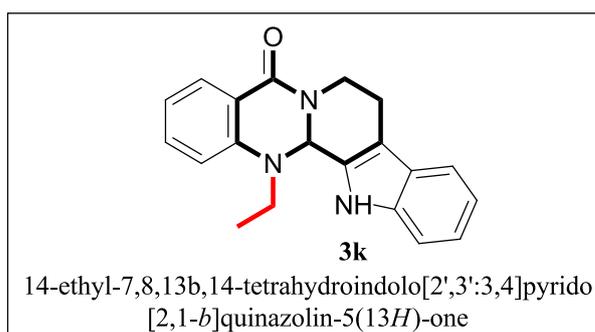
3-bromo-14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3h) : Yield 68%; 259.8 mg; white solid; mp = 200–201 °C; IR (KBr) ν_{max} : 3445, 2361, 2339, 1638, 1456, 1435, 1398, 1027, 1002 cm^{-1} ; ^1H NMR (600 MHz, DMSO- d_6) δ 11.06 (s, 1H), 7.85–7.79 (m, 1H), 7.63–7.58 (m, 1H), 7.48–7.43 (m, 1H), 7.37–7.31 (m, 1H), 7.14–7.07 (m, 1H), 7.04–6.95 (m, 2H), 6.19–6.13 (m, 1H), 4.63–4.55 (m, 1H), 3.23–3.19 (m, 1H), 2.99–2.87 (m, 4H), 2.80–2.74 (m, 1H). ^{13}C NMR (150 MHz, DMSO- d_6) δ 163.1, 147.6, 136.4, 136.0, 130.4, 130.0, 126.0, 122.0, 120.3, 119.1, 119.0, 118.3, 111.7, 111.5, 111.3, 69.9, 41.3, 36.3, 19.4. HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{17}\text{BrN}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 382.0545, found 382.0550.



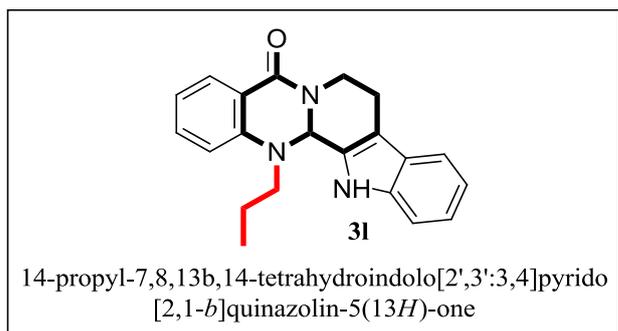
2-chloro-14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3i) : Yield 46%; 155.0 mg; white solid; mp = 291–292 °C; IR (KBr) ν_{max} : 3428, 2361, 2252, 1642, 1487, 1456, 1436, 1051, 1027, 1005, 946, 822 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.09 (s, 1H), 7.71 (s, 1H), 7.53–7.45 (m, 2H), 7.37–7.33 (m, 1H), 7.13–7.06 (m, 2H), 7.03–6.99 (m, 1H), 6.18–6.14 (m, 1H), 4.64–4.58 (m, 1H), 3.24–3.19 (m, 1H), 2.96–2.88 (m, 4H), 2.81–2.75 (m, 1H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 163.8, 148.9, 138.4, 136.3, 131.2, 129.8, 126.1, 122.0, 119.0, 118.8, 118.2, 116.1, 114.7, 111.8, 111.5, 70.6, 41.8, 36.5, 19.3. HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{17}\text{ClN}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 338.1052, found 338.1055.



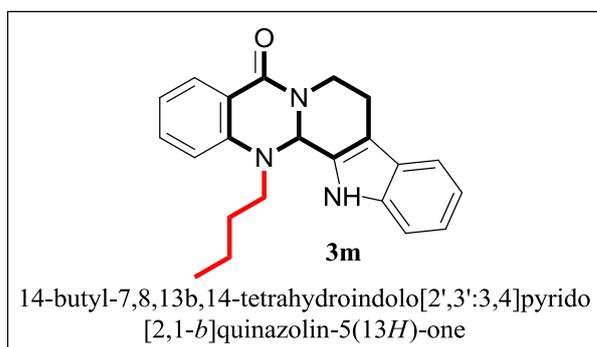
3-methoxy-14-methyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3j) : Yield 40%; 133.2 mg; white solid; mp = 222–224 °C; IR (KBr) ν_{max} : 3439, 2362, 2338, 1638, 1498, 1435, 1026, 999, 827 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.29 (s, 1H), 7.53 (d, J = 7.8 Hz, 1H), 7.48–7.36 (m, 2H), 7.24–7.11 (m, 3H), 7.09–7.02 (m, 1H), 6.03 (s, 1H), 4.76–4.64 (m, 1H), 3.79 (s, 3H), 3.25–3.16 (m, 1H), 2.95–2.80 (m, 2H), 2.57–2.46 (m, 3H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 163.7, 155.0, 143.8, 136.8, 129.5, 125.8, 123.1, 123.0, 121.9, 120.7, 118.9, 118.4, 111.7, 111.6, 110.7, 69.1, 55.5, 40.0, 36.9, 19.8. HRMS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}_2^+$ ($\text{M}+\text{H}$) $^+$ 334.1552, found 334.1550.



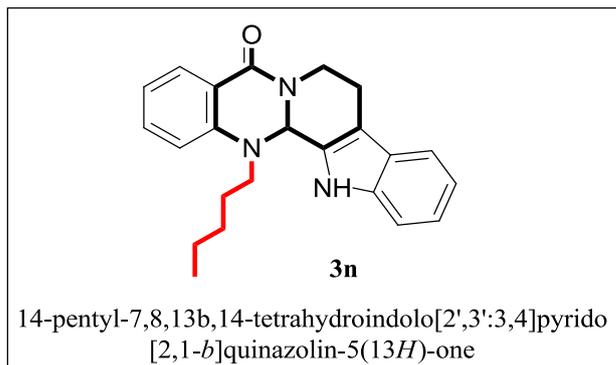
14-ethyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3k) : Yield 72%; 228.2 mg; white solid; mp = 299–300 °C; IR (KBr) ν_{max} : 3446, 2361, 2339, 1699, 1638, 1558, 1506, 1489, 1472, 1456, 1418, 1397 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 11.08 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.49–7.41 (m, 2H), 7.39–7.33 (m, 1H), 7.15–7.07 (m, 2H), 7.03–6.92 (m, 2H), 6.16 (s, 1H), 4.76–4.59 (m, 1H), 3.37–3.17 (m, 3H), 2.99–2.90 (m, 1H), 2.81–2.74 (m, 1H), 1.03 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.5, 147.1, 136.3, 133.2, 131.0, 128.0, 126.2, 121.7, 120.3, 118.8, 118.5, 118.1, 111.6, 111.0, 68.9, 44.8, 41.1, 19.4, 13.5. HRMS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{20}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 318.1602, found 318.1601.



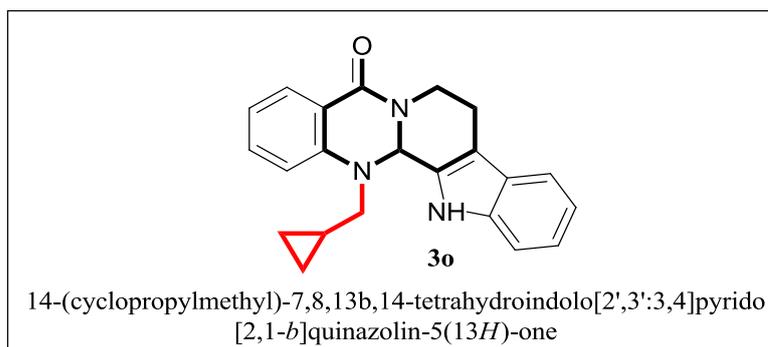
14-propyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (31) : Yield 51%; 168.8 mg; white solid; mp = 297–298 °C; IR (KBr) ν_{max} : 3445, 2926, 2361, 1636, 1458, 1390, 1261, 1159, 738 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.02 (s, 1H), 7.76 (d, $J = 7.8$ Hz, 1H), 7.46–7.39 (m, 2H), 7.37–7.33 (m, 1H), 7.11–7.05 (m, 2H), 6.99 (t, $J = 7.2$ Hz, 1H), 6.87 (t, $J = 7.2$ Hz, 1H), 6.18 (s, 1H), 4.65–4.59 (m, 1H), 3.51–3.44 (m, 1H), 3.30–3.23 (m, 2H), 2.99–2.93 (m, 1H), 2.75–2.70 (m, 1H), 1.57–1.49 (m, 2H), 0.80 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.8, 147.0, 136.2, 133.3, 131.6, 128.1, 126.3, 121.7, 119.4, 118.9, 118.8, 118.1, 117.2, 111.7, 111.0, 69.6, 51.6, 41.6, 21.1, 19.3, 11.3. HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{22}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 332.1755, found 332.1757.



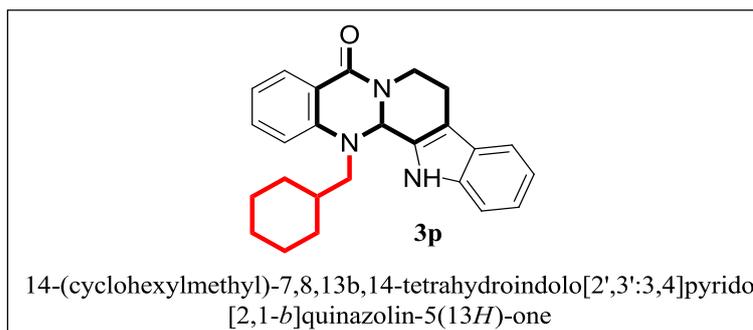
14-butyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3m) : Yield 49%; 169.1 mg; white solid; mp = 225–227 °C; IR (KBr) ν_{max} : 3432, 2361, 2252, 1637, 1471, 1418, 1052, 1027, 1005, 825 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 8.52 (s, 1H), 8.09 (d, $J = 7.8$ Hz, 1H), 7.55 (d, $J = 7.8$ Hz, 1H), 7.45–7.38 (m, 2H), 7.22 (t, $J = 7.8$ Hz, 1H), 7.17–7.13 (m, 1H), 7.12–7.06 (m, 2H), 5.92 (s, 1H), 4.90–4.83 (m, 1H), 3.30–3.23 (m, 1H), 3.06–2.97 (m, 3H), 2.93–2.88 (m, 1H), 1.46–1.37 (m, 2H), 1.19–1.07 (m, 2H), 0.76–0.71 (m, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 165.1, 148.4, 136.4, 132.7, 128.9, 126.4, 123.3, 123.0, 122.8, 121.5, 119.8, 118.8, 113.2, 111.3, 69.5, 50.8, 40.5, 30.6, 20.2, 19.9, 13.7. HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{24}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 346.1912, found 346.1914.



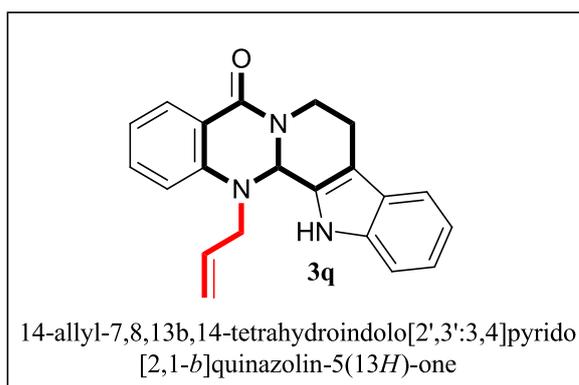
14-pentyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3n) : Yield 39%; 140.0 mg; white solid; mp = 227–229 °C; IR (KBr) ν_{max} : 3445, 3150, 2929, 2851, 2361, 2339, 1635, 1601, 1471, 1418, 1337, 1302, 1270, 1232, 1163 cm^{-1} ; ^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 11.03 (s, 1H), 7.76 (d, $J = 7.6$ Hz, 1H), 7.46–7.40 (m, 2H), 7.35 (d, $J = 8.0$ Hz, 1H), 7.11–7.05 (m, 2H), 7.02–6.96 (m, 1H), 6.87 (t, $J = 7.6$ Hz, 1H), 6.15 (s, 1H), 4.65–4.57 (m, 1H), 3.33–3.21 (m, 3H), 2.97–2.90 (m, 1H), 2.76–2.70 (m, 1H), 1.49 (s, 2H), 1.19–1.12 (m, 4H), 0.77–0.71 (m, 3H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.8, 147.2, 136.3, 133.3, 131.4, 128.2, 126.3, 121.7, 119.6, 119.3, 118.8, 118.1, 117.4, 111.7, 111.1, 69.5, 49.9, 41.5, 28.6, 27.5, 21.9, 19.4, 13.8. HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{26}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 360.2074, found 360.2070.



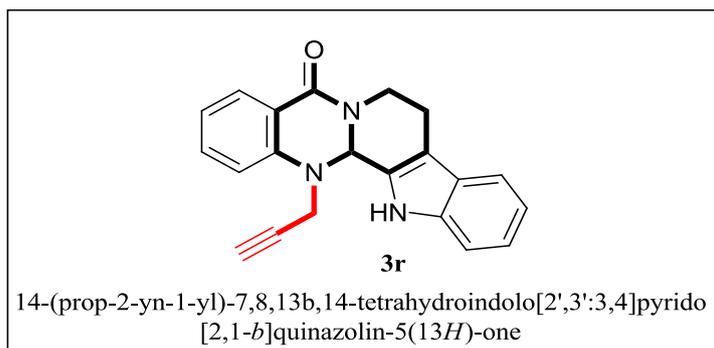
14-(cyclopropylmethyl)-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3o) : Yield 55%; 188.7 mg; white solid; mp = 284–285 °C; IR (KBr) ν_{max} : 3439, 2362, 2252, 2126, 1651, 1490, 1464, 1388, 1293, 1253, 1158, 1050, 1027, 1003, 825 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.07 (s, 1H), 7.83–7.78 (m, 1H), 7.49–7.42 (m, 2H), 7.38–7.33 (m, 1H), 7.22–7.17 (m, 1H), 7.13–7.08 (m, 1H), 7.02–6.94 (m, 2H), 6.20 (s, 1H), 4.69–4.62 (m, 1H), 3.29–3.22 (m, 2H), 3.13–3.06 (m, 1H), 2.97–2.91 (m, 1H), 2.81–2.75 (m, 1H), 1.01–0.94 (m, 1H), 0.38–0.28 (m, 2H), 0.03–0.08 (m, 2H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.7, 147.8, 136.3, 133.0, 131.0, 128.0, 126.1, 121.8, 120.6, 119.2, 118.9, 118.2, 111.7, 111.1, 69.1, 54.6, 41.1, 19.4, 10.1, 3.7, 3.5. HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{22}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 344.1755, found 344.1757.



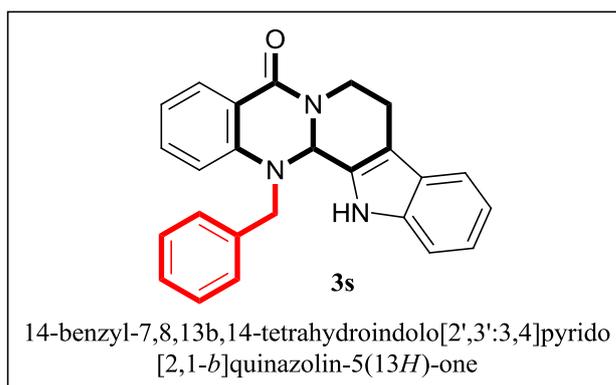
14-(cyclohexylmethyl)-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3p) : Yield 37%; 142.5 mg; white solid; mp = 242–244 °C; IR (KBr) ν_{max} : 3426, 2928, 2361, 1338, 1644, 1505, 1450, 1416, 1048, 1026, 1004 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 10.92 (s, 1H), 7.70 (s, 1H), 7.42–7.31 (m, 3H), 7.08 (s, 1H), 6.97 (s, 2H), 6.74 (s, 1H), 6.17 (s, 1H), 4.66–4.58 (m, 1H), 3.69 (s, 1H), 3.28 (s, 1H), 3.17–3.11 (m, 1H), 3.00 (s, 1H), 2.69–2.63 (m, 1H), 1.90–1.84 (m, 1H), 1.69–1.56 (m, 5H), 1.17–1.06 (m, 3H), 1.01–0.94 (m, 1H), 0.89–0.82 (m, 1H). ^{13}C NMR (100 MHz, $\text{DMSO-}d_6$) δ 165.2, 146.7, 136.0, 133.6, 132.4, 128.2, 126.4, 121.6, 118.8, 118.0, 117.0, 115.1, 111.7, 110.9, 70.9, 55.5, 42.5, 36.2, 30.4, 30.3, 26.1, 25.5, 25.4, 19.2. HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{28}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 386.2221, found 386.2227.



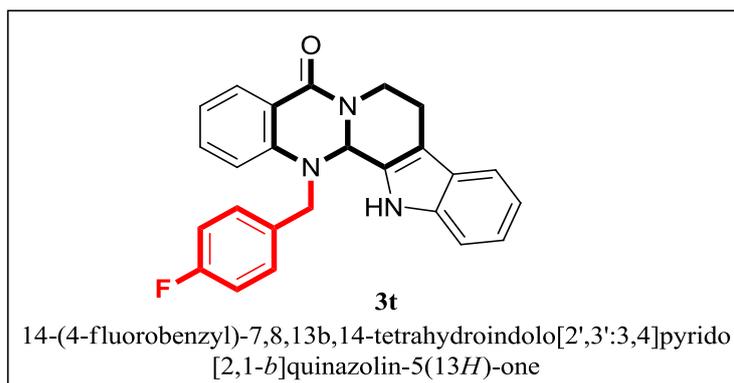
14-allyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3q) : Yield 52%; 171.1 mg; White solid; mp = 287–288 °C; IR (KBr) ν_{max} : 3446, 3212, 2361, 2338, 1633, 1454, 1405, 1341 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.10 (s, 1H), 7.79 (d, $J = 7.8$ Hz, 1H), 7.51–7.41 (m, 2H), 7.36 (d, $J = 7.8$ Hz, 1H), 7.14–7.06 (m, 2H), 7.03–6.97 (m, 1H), 6.97–6.92 (m, 1H), 6.15 (s, 1H), 5.89–5.81 (m, 1H), 5.09–5.01 (m, 2H), 4.66–4.59 (m, 1H), 3.97–3.90 (m, 2H), 3.27–3.19 (m, 1H), 2.98–2.89 (m, 1H), 2.80–2.73 (m, 1H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.5, 147.1, 136.3, 134.4, 133.1, 130.9, 128.0, 126.1, 121.8, 120.4, 119.9, 118.9, 118.5, 118.2, 117.1, 111.7, 111.3, 69.0, 52.6, 41.2, 19.3. HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{20}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 330.1605, found 330.1601.



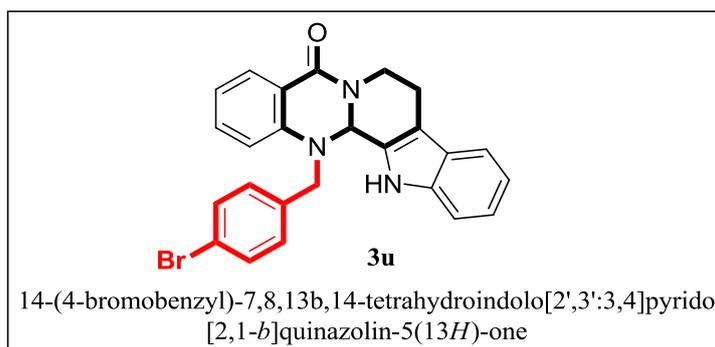
14-(prop-2-yn-1-yl)-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3r) : Yield 49%; 160.2 mg; white solid; mp = 168–170 °C; IR (KBr) ν_{max} : 3749, 3445, 2855, 2361, 1635, 1470, 1419, 1097, 924, 796, 750, 668 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.30 (s, 1H), 7.90 (s, 1H), 7.54 (s, 2H), 7.41–7.28 (m, 2H), 7.20–6.99 (m, 3H), 6.17 (s, 1H), 4.69–4.58 (m, 1H), 4.09–3.98 (m, 1H), 3.66–3.56 (m, 1H), 3.25–3.17 (m, 1H), 3.06 (s, 1H), 2.96–2.81 (m, 2H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 163.5, 147.1, 136.8, 132.8, 129.0, 128.0, 125.8, 123.4, 122.9, 122.1, 121.3, 119.0, 118.5, 112.2, 111.7, 80.0, 75.2, 68.1, 40.0, 39.0, 19.5. HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{18}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 328.1443, found 328.1444.



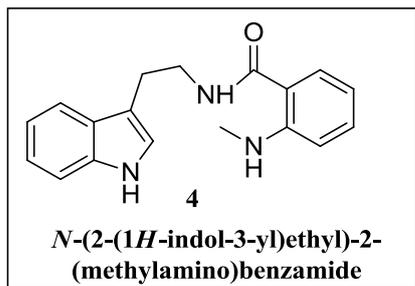
14-benzyl-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3s) : Yield 58%; 219.8 mg; white solid; mp = 251–252 °C; IR (KBr) ν_{max} : 3083, 2859, 2361, 1631, 1478, 1421, 1350, 1231, 1163, 1127, 927, 799, 742, 697 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.14 (s, 1H), 7.75 (d, $J = 7.8$ Hz, 1H), 7.44 (d, $J = 7.8$ Hz, 1H), 7.37 (d, $J = 8.4$ Hz, 1H), 7.33–7.26 (m, 5H), 7.24–7.20 (m, 1H), 7.10 (t, $J = 7.8$ Hz, 1H), 7.00 (t, $J = 7.2$ Hz, 1H), 6.87–6.81 (m, 2H), 6.33 (s, 1H), 4.70–4.64 (m, 1H), 4.63–4.57 (m, 2H), 3.27–3.22 (m, 1H), 2.95–2.89 (m, 1H), 2.74–2.69 (m, 1H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.8, 146.7, 138.2, 136.3, 133.2, 131.6, 128.4, 128.2, 127.6, 127.2, 126.3, 121.9, 119.8, 119.0, 118.2, 117.2, 111.7, 111.4, 70.3, 52.8, 41.8, 19.3. HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{22}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 380.1755, found 380.1757.



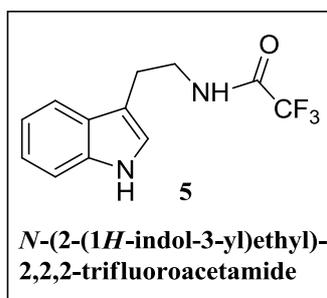
14-(4-fluorobenzyl)-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3t) : Yield 73%; 289.8 mg; white solid; mp = 263–264 °C; IR (KBr) ν_{max} : 3444, 3248, 2361, 1644, 1602, 1507, 1467, 1410, 1302, 1222, 1025, 1004 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.27 (s, 1H), 7.83–7.73 (m, 1H), 7.47–7.28 (m, 5H), 7.11 (s, 3H), 7.00 (s, 1H), 6.87 (s, 2H), 6.33 (s, 1H), 4.68–4.52 (m, 3H), 3.28–3.19 (m, 1H), 2.97–2.88 (m, 1H), 2.78–2.70 (m, 1H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.7, 161.4 (d, $J = 241.7$ Hz, $^1J_{\text{CF}}$), 146.8, 136.3, 134.4, 133.2, 131.2, 129.6 (d, $J = 8.0$ Hz, $^3J_{\text{CF}}$), 128.2, 126.2, 121.9, 120.3, 119.5, 118.9, 118.2, 117.7, 115.1 (d, $J = 21.2$ Hz, $^2J_{\text{CF}}$), 111.7, 111.5, 70.1, 52.1, 41.6, 19.3. HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{21}\text{FN}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 398.1667, found 398.1663.



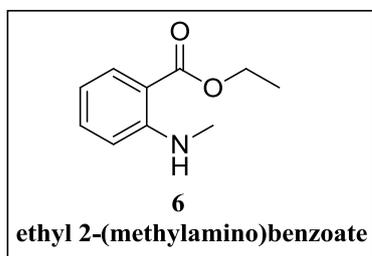
14-(4-bromobenzyl)-7,8,13b,14-tetrahydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(13*H*)-one (3u) : Yield 70%; 319.9 mg; white solid; mp = 255–257 °C; IR (KBr) ν_{max} : 3443, 2361, 2338, 1646, 1051, 1027, 1005, 825 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 11.22 (s, 1H), 7.77 (d, $J = 7.8$ Hz, 1H), 7.50–7.43 (m, 3H), 7.38–7.31 (m, 2H), 7.26–7.20 (m, 2H), 7.10 (t, $J = 7.2$ Hz, 1H), 7.01–6.97 (m, 1H), 6.90–6.83 (m, 2H), 6.33 (s, 1H), 4.65–4.53 (m, 3H), 3.26–3.21 (m, 1H), 2.94–2.89 (m, 1H), 2.75–2.70 (m, 1H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 164.7, 146.7, 137.8, 136.3, 133.3, 131.3, 129.8, 128.2, 126.2, 121.9, 120.2, 120.1, 119.2, 119.0, 118.2, 117.4, 111.7, 111.5, 70.2, 52.2, 41.7, 19.3. HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{21}\text{BrN}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 458.0866, found 458.0863.



***N*-(2-(1*H*-indol-3-yl)ethyl)-2-(methylamino)benzamide (4)** : Yield 86%; 252.0 mg; yellow solid; mp = 109–111 °C; IR (KBr) ν_{max} : 3434, 3329, 3260, 1628, 1578, 1518, 1455, 1417, 1334, 1282, 1224, 1169, 737, 701, 558, 525, 476 cm^{-1} ; ^1H NMR (600 MHz, $\text{DMSO-}d_6$) δ 10.85 (s, 1H), 8.46 (s, 1H), 7.72 (s, 1H), 7.61–7.52 (m, 2H), 7.38–7.28 (m, 2H), 7.19 (s, 1H), 7.10–7.00 (m, 2H), 6.63–6.54 (m, 2H), 3.54–3.48 (m, 2H), 2.98–2.92 (m, 2H), 2.78 (s, 3H). ^{13}C NMR (150 MHz, $\text{DMSO-}d_6$) δ 169.1, 150.1, 136.3, 132.3, 128.2, 127.3, 122.7, 121.0, 118.4, 118.3, 115.3, 114.0, 112.0, 111.5, 110.5, 29.4, 25.3. HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{20}\text{N}_3\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 294.16009, found 294.16049.



***N*-(2-(1*H*-indol-3-yl)ethyl)-2,2,2-trifluoroacetamide (5)** : Yield 24%; 61.4 mg; yellow solid; mp = 94–96 °C; IR (KBr) ν_{max} : 3398, 3325, 1702, 1628, 1559, 1451, 1201, 1170, 747, 701, 501 cm^{-1} ; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 10.86 (s, 1H), 9.62–9.50 (m, 1H), 7.59–7.52 (m, 1H), 7.39–7.34 (m, 1H), 7.20–7.16 (m, 1H), 7.12–7.06 (m, 1H), 7.04–6.96 (m, 1H), 3.52–3.42 (m, 2H), 2.98–2.89 (m, 2H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 156.2 (q, $J = 35.7$ Hz, $^2J_{\text{CF}}$), 136.3, 127.1, 122.8, 121.0, 118.3, 118.1, 116.0 (q, $J = 286.5$ Hz, $^1J_{\text{CF}}$), 111.4, 111.0, 40.1, 24.2. HRMS (ESI) m/z calcd for $\text{C}_{12}\text{H}_{12}\text{F}_3\text{N}_2\text{O}^+$ ($\text{M}+\text{H}$) $^+$ 257.08962, found 257.08929.



ethyl 2-(methylamino)benzoate (6): Yield 75%; 134.2 mg; yellow oil; IR (KBr) ν_{max} : 3378, 1679, 1606, 1579, 1518, 1428, 1325, 1239, 1167, 1132, 1087, 751, 702, 529 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.95–7.91 (m, 1H), 7.69 (s, 1H), 7.39–7.34 (m, 1H), 6.69–6.58 (m, 2H), 4.34–4.28 (m, 2H), 2.92–2.89 (m, 3H), 1.40–1.35 (m, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 168.6, 151.9, 134.5, 131.5, 114.2, 110.6, 110.1, 60.1, 29.5, 14.3. HRMS (ESI) m/z calcd for $\text{C}_{10}\text{H}_{14}\text{NO}_2^+$ ($\text{M}+\text{H}$) $^+$

180.10191, found 180.10182.

5. Copies of ^1H NMR, ^{13}C NMR Spectra

