Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Electronic Supporting Information

Efficient Syntheses of 2, 3-Disubstituted Natural Quinazolinones via Iridium Catalysis

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EXPERIMENTAL SECTION

All the solvents were dried and purified using standard techniques. Reactions were monitored by HPLC. Separations by flash chromatography were performed on silica gel (200-300 mesh). ^{1}H and ^{13}C NMR spectra were recorded with an instrument operated at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR. DMSO-d6 and $CDCl_3$ were used as solvents in NMR experiments. Chemical shifts (δ) are given in parts per million (ppm). HRMS spectra were carried out in ESI mode.

Synthesis of 3-methyl-2-phenylquinazolin-4(3H)-one (3):

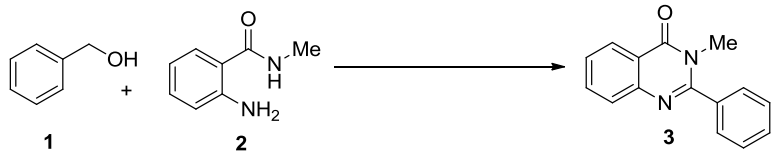


Table 1[a]: **Optimization of Reaction Conditions**

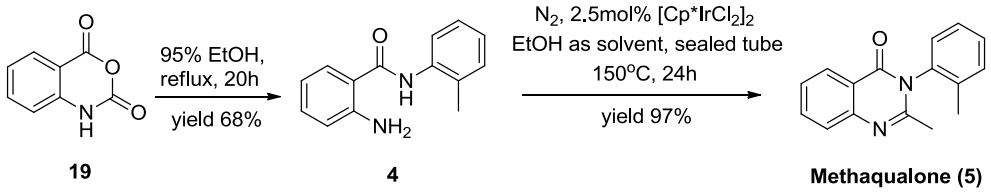
	Catalyst	Additive	Solvent	Yield[b]	Conversion	Time
1	$[Cp^*IrCl_2]_2$	AcOH[c]	xylene	69%	76%	24h
2	$[Cp^*IrCl_2]_2$	NaOH	xylene	74%	90%	24h
3	$[Cp^*IrCl_2]_2$	*t*-BuONa	xylene	68%	91%	24h
4	$[Cp^*IrCl_2]_2$	K_2CO_3	xylene	33%	80%	24h
5	$[Cp^*IrCl_2]_2$	No Base	xylene	93%[d]	100%	24h
6	$[Cp^*IrCl_2]_2$	No Base	DMF	47%	82%	24h
7	$[Cp^*IrCl_2]_2$	No Base	DMSO[f]	8%	57%	24h
8	$[Cp^*IrCl_2]_2$	No Base	toluene	25%	28%	24h
9	$[Cp^*IrCl_2]_2$[e]	No Base	xylene	97%[d]	100%	24h
10	$[Cp^*IrI_2]_2$[e]	No Base	xylene	65%	72%	24h
11	$IrCl_3$[i]	No base	xylene	trace	7%	24h
12	$[Ir(cod)Cl]_2$[h]	KOH	xylene	65%	100%	24h
13	$RuCl_2(PPh_3)_3$[e]	KOH	xylene	70%	100%	24h
14	$[Ru(p\text{- cymene})Cl_2]_2$[g]	K_2CO_3	xylene	16%	25%	24h

[a] Conditions: **1** (1 mmol), **2** (1 mmol), catalyst (1.25 mol%), base (20 mol%) in refluxing temperature of solvent under N_2. [b] H-NMR yield. [c] 5 mol% AcOH. [d] Isolated yield. [e] 2.5 mol% catalyst was used. [f] Reaction temperature was 140 ℃. [g] 2.5 mol% dppf was added. [h] 2.0 mol% catalyst was used. [i] 2.5 mol% catalyst and 7.5 mol% PPh_3 was used.

Optimized conditions: 2-amino-N-methylbenzamide (**2**) (1 mmol) and $[Cp^*IrCl_2]_2$ (0.025 mmol) were added to an oven-dried carousel tube, followed by benzyl alcohol (**1**) (1 mmol) in anhydrous xylene (2 mL). And then the system was degassed and filled with nitrogen. The reaction mixture was stirred and heated to reflux and the progress of the reaction was monitored by HPLC. After completion of the reaction, the resulting solution was cooled to room temperature, and the solvent was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (3:1 to 1:1) as eluent to provide the desired product **3-methyl-2-phenylquinazolin-4(3H)-one (3)**: White solid, mp: 128 - 129 °C (Lit.[1] 128 - 130 °C), 229 mg, 97%

yield, ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.18 (d, J = 8.0 Hz, 1H, ArH), 7.83 (t, J = 8.0 Hz, 1H, ArH), 7.66-7.68 (m, 3H, ArH), 7.53-7.57 (m, 4H, ArH), 3.36 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 161.6, 156.1, 147.0, 135.3, 134.3, 129.7, 128.3, 128.2, 127.1, 126.8, 126.0, 120.1, 33.8.

Synthesis of Methaqualone (5)



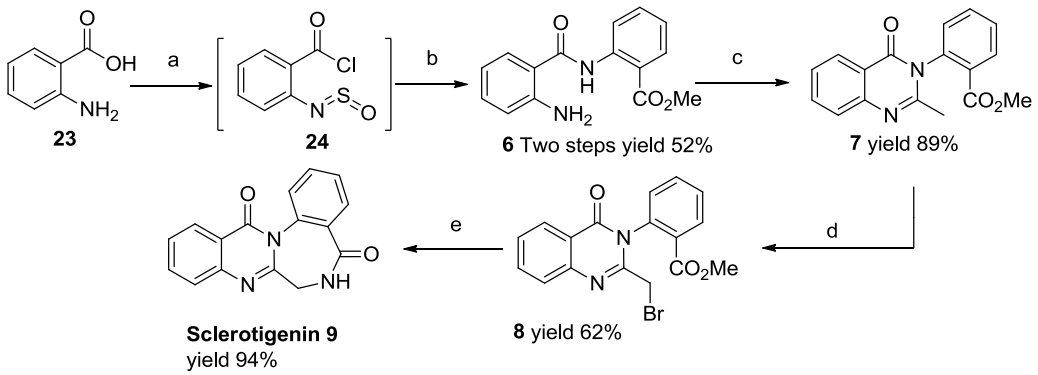
19 **4** **Methaqualone (5)**

A suspension of 1H-benzo[d][1,3]oxazine-2,4-dione **19** (4.89 g, 33 mmol), *o*-toluidine (3.53 g, 33 mmol) and 95% EtOH (40 mL) was stirred and heated to reflux for 20 h. The reaction was stopped and solvent was removed, 0.06 N aqueous HCl (160 mL) was added and stirred vigorously. The suspended solid was filtered, Na_2CO_3 was added to adjust the pH=9, filtered again, the solid of two time was dried and recrystallized (2-propanol:H_2O = 2:1).

2-amino-N-(o-tolyl)benzamide (4)[2]: White solid, mp: 108 - 109°C (Lit.[3] mp: 109 - 110 °C), 4.25 g, 67% yield, ^{1}H NMR (DMSO-d_6, 400 MHz): δ 9.61 (s, br, 1H, NH), 6.69 (d, J = 8.0 Hz, 1H, ArH), 7.25 (d, J = 8.0 Hz, 1H, ArH), 7.84 (t, J = 8.0 Hz, 1H, ArH), 7.12-7.21 (m, 3H, ArH), 6.74 (d, J = 8.0 Hz, 1H, ArH), 6.57 (t, J = 8.0 Hz, 1H, ArH), 6.38 (s, br, 2H, NH_2), 2.22 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6, 100 MHz): δ. 167.7, 149.9, 136.5, 133.7, 132.0, 130.1, 128.6, 126.6, 125.8, 125.7, 116.4, 114.6, 114.5, 17.9.

2-amino-N-(*o*-tolyl)benzamide **4** (113 mg, 0.5 mmol), $[Cp^*IrCl_2]_2$ (10 mg, 0.013 mmol) and EtOH (2.0 mL) were added to oven-dried thick-wall-tube, filled in nitrogen and sealed. The reaction mixture was stirred and heated to 150 °C (oil temperature) for 24 h. The resulting solution was cooled to room temperature, and the solvent was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (1:2) as eluent to provide the desired product **Methaqualone (5)**: White solid, mp: 112 - 114 °C (Lit.[4] mp: 114 - 115 °C), 121mg, 97% yield, ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.11 (d, J = 8.0 Hz, 1H, ArH), 7.84 (t, J = 8.0 Hz, 1H, ArH), 7.67 (d, J = 8.0 Hz, 1H, ArH), 7.52 (t, J = 8.0 Hz, 1H, ArH), 7.35-7.46 (m, 4H, ArH), 2.08 (s, 3H, CH_3), 2.02 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6, 100 MHz): δ. 160.7, 154.3, 147.4, 136.8, 134.9, 131.0, 129.2, 128.4, 127.7, 126.5, 126.3, 120.2, 23.5, 16.8. HRMS (ESI): $[M + H]^+$: $C_{16}H_{15}N_2O$ Calcd for 251.1184. Found: 251.1181.

Synthesis of Sclerotigenin



Reagents and conditions: (a) $SOCl_2$, toluene, reflux, 3 h (b) Toluene, r.t., 48 h (c) N_2, 2.5 mol% $[Cp^*IrCl_2]_2$, EtOH as solvent, sealed tube, 150 ^oC, 24 h (d) Br_2, AcOH, reflux, 3 h (e) NH_3/MeOH (7N), sealed tube, 65^oC, 4 h.

To a stirred suspension of 2-aminobenzoic acid **23** (8.22 g, 60 mmol) in anhydrous toluene (120 mL) was added freshly distilled $SOCl_2$ (17.5 mL, 240 mmol) under N_2 atmosphere, and the mixture was refluxed for 3 h. The excess $SOCl_2$ and toluene were distilled off by codistillation with toluene (20 mL) and the resulting residue of compound **24** (12.098 g) was dissolved in toluene (120 mL) and was immediately used.

To a stirred solution of freshly prepared N-sulfinylanthraniloyl chloride (12.098 g, 60 mmol) in toluene (120 mL) at r.t. under N_2 atmosphere was added methyl 2-aminobenzoate (7.054 g, 46.2 mmol) in toluene (120 mL) dropwise over 10 min, and the mixture was maintained at r.t. for 48 h. After completion of the reaction, the mixture was diluted with cold H_2O (300 mL) and extracted with DCM (2 x 200mL), The combined organic phases were washed with 10% aq $NaHCO_3$ (2 x 150mL) followed by H_2O (100 mL) and brine (60 mL), dried (Na_2SO_4) and concentrated under reduced pressure to afford a solid residue which was purified by column chromatography on silica gel (hexane-EtOAc, 98:2) to give **Methyl 2-(2-aminobenzamido)benzoate (6)**[5]: Light yellow solid, mp: 114 - 115^oC (Lit.[6] mp: 116 - 117 ^oC), 6.49 g, two steps, 52% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 11.39 (s, br, 1H, NH), 8.51 (d, J = 8.0 Hz, 1H, ArH), 7.99 (d, J = 8.0 Hz, 1H, ArH), 7.60-7.66 (m, 2H, ArH), 7.18-7.26 (m, 2H, ArH), 6.79 (d, J = 8.0 Hz, 1H, ArH), 6.64 (t, J = 8.0 Hz, 1H, ArH), 6.56 (s, br, 2H, NH_2), 3.87 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6, 100 MHz): δ. 168.0, 167.3, 150.4, 140.5, 134.1, 132.7, 130.6, 127.3, 122.8, 120.6, 117.0, 116.6, 115.1, 113.7, 52.5.

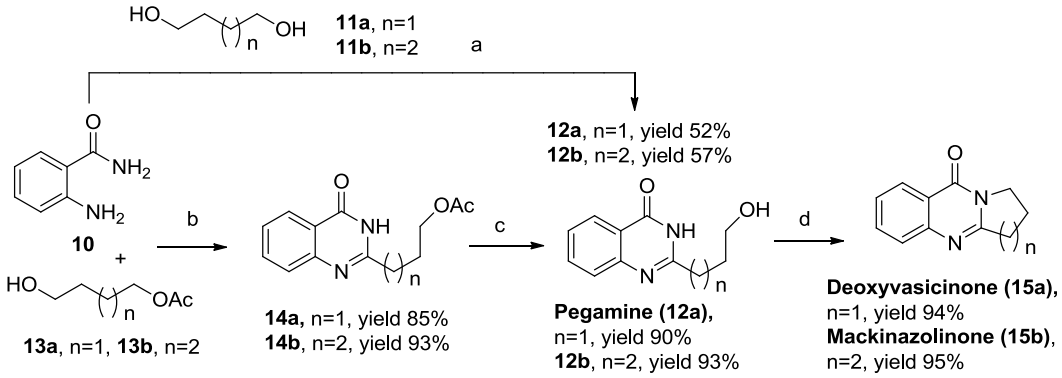
The procedure synthesis of **7** was similar to the preparation of **5**. **Methyl 2-(2-methyl-4-oxoquinazolin-3(4H)-yl)benzoate (7)**: White solid, mp: 135 - 137 ^oC (Lit.[7] mp: 139 - 140 ^oC), 130 mg, 89% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 8.20 (d, J = 8.0 Hz, 1H, ArH), 8.13 (d, J = 8.0 Hz, 1H, ArH), 7.92 (t, J = 8.0 Hz, 1H, ArH), 7.13-7.28 (m, 2H, ArH), 7.69 (d, J = 8.0 Hz, 1H, ArH), 7.58 (t, J = 8.0 Hz, 1H, ArH), 3.70 (s, 3H, CH_3), 2.15 (s, 3H, CH_3),. ^{13}C NMR (DMSO-d_6, 100 MHz): δ. 164.4,

161.3, 154.0, 147.3, 137.6, 134.6, 134.2, 131.4, 130.4, 129.7, 127.2, 126.6, 126.3, 126.2, 120.1, 52.3, 23.6.

Bromine (0.511 g, 3.2 mmol) was added dropwise to a solution of AcOH (10 mL) and compound **7** (0.942 g, 3.2 mmol) over 15 min, and the solution was heated to reflux for 3 h. The reaction was stopped and cooled to 0 °C, ice-water (10 mL) was added and filtered, the solid was purified by column chromatography to give **Methyl 2-(2-(bromomethyl)-4-oxoquinazolin-3(4H)-yl)benzoate (8)**[8]: brown solid, mp: 201 - 203 °C (Lit.[8] mp: 200 - 203 °C), 0.74 g, 62% yield, ^{1}H NMR ($DCCl_3$-d_1, 400 MHz): δ 8.27 (d, J = 8.0 Hz, 1H, ArH), 8.23 (d, J = 8.0 Hz, 1H, ArH), 7.76-7.81 (m, 3H, ArH), 7.66 (t, J = 8.0 Hz, 1H, ArH), 7.51-7.55 (m, 2H, ArH), 4.26 (d, J = 8.0 Hz, 1H, CH_aH_b), 3.91 (d, J = 8.0 Hz, 1H, CH_aH_b), 3.70 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6, 100 MHz): δ. 164.8, 162.3, 151.8, 147.2, 136.3, 134.7, 133.8, 132.1, 131.1, 130.1, 128.0, 127.7, 127.6, 127.1, 52.5, 29.7.

Compound **8** and NH_3/MeOH (5.0 mL, 35 mmol, 7 N) were added to thick-wall-bottle, the bottle was sealed and heated to 65 ℃ (oil temperature) for 4 h. The reaction was stopped and cooled to room temperature. The solvent was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel using DCM/MeOH (20:1) as eluent to provide the desired product **Sclerotigenin (9)**: light brown solid, mp: 268 – 270 °C (Lit.[9] mp: 270 - 273 °C), 74 mg, 94% yield, ^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.96 (t, J = 4.0, 1H, NH), 8.18 (d, J = 8.0 Hz, 1H, ArH), 7.89 (t, J = 8.0 Hz, 1H, ArH), 7.79 (d, J = 8.0 Hz, 1H, ArH), 7.71 (d, J = 8.0 Hz, 1H, ArH), 7.56-7.66 (m, 4H, ArH), 4.17 (dd, J = 4.0 Hz, 20.0 Hz, 1H, CH_aH_b), 3.99 (dd, J = 4.0 Hz, 20.0Hz, 1H, CH_aH_b). ^{13}C NMR (DMSO-d_6, 100 MHz): δ. 166.9, 160.9, 154.7, 146.1, 135.1, 133.3, 130.7, 130.6, 129.2, 128.7, 128.4, 127.5, 127.0, 126.8, 121.0, 46.1. HRMS (ESI): $[M + H]^+$: $C_{16}H_{12}N_3O_2$ Calcd for 278.0930. Found: 278.0918.

Synthesis of Pegamine, Deoxyvasicinone and Mackinazolinone



Reagents and conditions: (a) 2.5mol% $[Cp^*IrCl_2]_2$, xylene, reflux, 22 h (b) 2.5mol% $[Cp^*IrCl_2]_2$, xylene, reflux, 48 h (c) K_2CO_3, methanol/H_2O (4:1), r.t., 4 h (d) DEAD, PPh_3, r.t., 3 h

2-Aminobenzamide (136 mg, 1 mmol) and $[Cp^*IrCl_2]_2$ (20 mg, 0.025 mmol) were added to oven dried carousel tube, followed by 5-hydroxypentyl acetate (146 mg, 1 mmol) in anhydrous toluene (2 mL). And then the system was gas-separated and filled with nitrogen. The reaction mixture was stirred and heated to reflux for 48h, monitored by HPLC. After completion of the reaction, the resulting solution was cooled to room temperature, and the solvent was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (3:1 to 1:1) as eluent to provide the desired product **4-(4-oxo-3,4-dihydroquinazolin-2-yl)butyl acetate (14b)**: White solid, mp: 135 - 137 ^oC, 242 mg, 93% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 12.17 (s, br, 1H, NH), 8.07 (d, *J* = 8.0 Hz, 1H, ArH), 7.76 (t, *J* = 8.0 Hz, 1H, ArH), 7.58 (d, *J* = 8.0 Hz, 1H, ArH), 7.44 (t, *J* = 8.0 Hz, 1H, ArH), 4.01 (t, *J* = 8.0, 2H, CH_2), 2.61 (t, *J* = 8.0, 2H, CH_2), 1.99 (s, 3H, CH_3), 1.73-1.80 (m, 2H, CH_2), 1.59-1.66 (m, 2H, CH_2). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 170.3, 161.7, 157.1, 148.8, 134.2, 126.7, 125.9, 125.6, 120.7, 63.5, 33.9, 27.5, 23.2, 20.6. HRMS (ESI): $[M + H]^+$: $C_{14}H_{17}N_2O_3$ Calcd for 261.1194. Found: 261.1211.

Similarly, the reaction of 4-hydroxybutyl acetate furnished 3-(4-oxo-3,4-dihydroquinazolin-2-yl) propyl acetate (**14a)**: White solid, mp: 169 - 170 ^oC, 209 mg, 85% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 12.19 (s, br, 1H, NH), 8.07 (d, *J* = 8.0 Hz, 1H, ArH), 7.76 (t, *J* = 8.0 Hz, 1H, ArH), 7.58 (d, *J* = 8.0 Hz, 1H, ArH), 7.45 (t, *J* = 8.0 Hz, 1H, ArH), 4.07 (t, *J* = 4.0, 2H, CH_2), 2.67 (t, *J* = 8.0, 2H, CH_2), 2.00-2.07 (m, 2H, CH_2), 1.94 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 170.2, 161.7, 156.4, 148.7, 134.2, 126.7, 125.9, 125.6, 120.8, 63.12, 30.96, 25.47, 20.60. HRMS (ESI): $[M + H]^+$: $C_{13}H_{15}N_2O_3$ Calcd for 247.1038. Found: 247.1058.

Compound **14b** (2.09 g, 8.04 mmol), K_2CO_3 (1.65 g, 12.05 mmol) and 40 mL solvent ($MeOH:H_2O$=4:1) were added to 100 mL three-neck-bottle at room temperature, the solution was stirred for 4 h. The reaction was stopped and the solvent was removed with the aid of a rotary evaporator directly, the residue was purified by column chromatography on silica gel using methanol/ethyl acetate 1:99) as eluent to provide the desired product **2-(4-hydroxybutyl)quinazolin-4(3H)-one (12b)**: White solid, mp: 173 - 175 ^oC (lit.[10] mp: 175 - 177 ^oC), 1.63 g, 93% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 12.16 (s, br, 1H, NH), 8.07 (d, *J* = 8.0 Hz, 1H, ArH), 7.76 (t, *J* = 8.0 Hz, 1H, ArH), 7.58 (d, *J* = 8.0 Hz, 1H, ArH), 7.44 (t, *J* = 8.0 Hz, 1H, ArH), 4.41 (t, *J* = 8.0, 1H, OH), 3.41 (q, *J* = 8.0, *J* = 12.0, 2H, CH_2), 2.59 (t, *J* = 8.0, 2H, CH_2), 1.70-1.78 (m, 2H, CH_2), 1.43-1.51 (m, 2H, CH_2). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 161.7, 157.4, 148.9, 134.2, 126.7, 125.8, 125.6, 120.7, 60.3, 34.2, 31.8, 23.4. HRMS (ESI): $[M + H]^+$: $C_{12}H_{15}N_2O_2$ Calcd for 219.1089. Found: 219.1110.

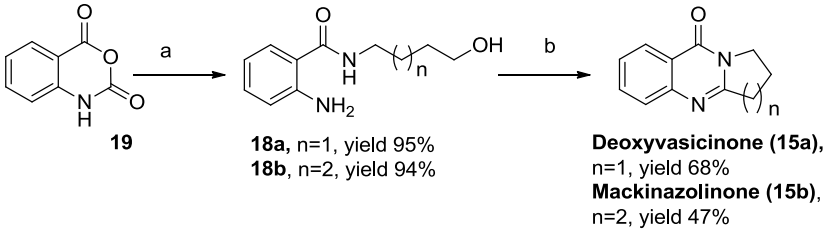
Similarly, the reaction of **14a** furnished **Pegamine (12a)**: White solid, mp: 161 - 163 ^oC (lit.[11] mp: 163 - 165 ^oC), 1.47 g, 90% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 12.15 (s, br, 1H, NH), 8.06 (d, *J* = 8.0 Hz, 1H, ArH), 7.76 (t, *J* = 8.0 Hz, 1H, ArH), 7.58 (d, *J* = 8.0 Hz, 1H, ArH), 7.44 (t, *J* = 8.0 Hz, 1H, ArH), 4.55 (s, 1H, OH), 3.46 (t, *J* = 8.0, CH_2), 2.64 (t, *J* = 8.0, 2H, CH_2), 1.83-1.90 (m, 2H, CH_2). ^{13}C

NMR (DMSO-d_6, 100 MHz): δ 161.7, 157.4, 148.8, 134.2, 126.7, 125.8, 125.6, 120.7, 60.0, 31.2, 29.8. HRMS (ESI): $[M + H]^+$: $C_{11}H_{13}N_2O_2$ Calcd for 205.0932. Found: 205.0952.

To a solution of (**12b)** (218 mg, 1.0 mmol) and triphenylphosphine (340 mg, 1.3 mmol) in THF (3.0 mL) was added a solution of DEAD (190 mg, 1.1 mmol) in THF (2.0 mL) in a dropwise fashion with continuous stirring at room temperature, and the reaction mixture was further stirred for 3.0 h. The reaction mixture was concentrated, and the residue was chromatographed on silica gel using petroleum ether and ethyl acetate (1:1) to obtain **Mackinazolinone (15b)**: White solid, mp: 98 - 100 ^oC (lit.[10] mp: 99 - 101 ^oC), 190 mg, 95% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 8.09 (d, J = 8.0 Hz, 1H, ArH), 7.76 (t, J = 8.0 Hz, 1H, ArH), 7.55 (d, J = 8.0 Hz, 1H, ArH), 7.44 (t, J = 8.0 Hz, 1H, ArH), 3.94 (t, J = 8.0, 2H, CH_2), 2.90 (t, J = 8.0, 2H, CH_2), 1.89-1.94 (m, 2H, CH_2), 1.80-1.84 (m, 2H, CH_2). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 161.1, 155.5, 147.1, 134.1, 126.2, 125.9, 125.8, 119.9, 41.7, 31.2, 21.3, 18.5. HRMS (ESI): $[M + H]^+$: $C_{12}H_{13}N_2O_1$ Calcd for 201.0983. Found: 201.1011.

Similarly, the reaction of **12a** furnished **Deoxyvasicinone (15a)**: White solid, mp: 105 - 107 ^oC (lit.[11] mp: 106 - 108 ^oC), 175 mg, 94% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 8.09 (d, J = 8.0 Hz, 1H, ArH), 7.77 (t, J = 8.0 Hz, 1H, ArH), 7.60 (d, J = 8.0 Hz, 1H, ArH), 7.46 (t, J = 8.0 Hz, 1H, ArH), 4.05 (t, J = 8.0, 2H, CH_2), 3.07 (t, J = 8.0, 2H, CH_2), 2.14-2.20 (m, 2H, CH_2). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.3, 159.9, 149.0, 134.0, 126.6, 125.8, 125.6, 120.1, 46.3, 31.8, 18.9. HRMS (ESI): $[M + H]^+$: $C_{11}H_{11}N_2O_1$ Calcd for 187.0827. Found: 187.0864.

Synthesis of Deoxyvasicinone and Mackinazolinone



Reagents and conditions: (a) **20a**, or **20b**, 1, 4-dioxane, r.t., 6h (b) **18a** (0.5 mmol) in xylene (4ml), 2.5 mol% $[Cp^*IrCl_2]_2$, 10mol% TfOH, reflux, 24h; **18b** (0.5 mmol) in xylene (4 ml), 5.0 mol% $[Cp^*IrCl_2]_2$, 20 mol% TfOH, reflux, 36h.

4-Amino-butanol **20a** (1.86 g, 20.8 mmol) was added dropwise to a solution of 1H-benzo[d] [1,3]oxazin-2,4-dione **19** (3.1 g, 19 mmol) in l,4-dioxane (40 mL) and the solution was stirred at 30 ^oC for 6 h. Reaction mixture was then concentrated and purified by silica gel column. The solid product was dried under vacuum. **2-amino-N-(4-hydroxybutyl)benzamide (18a)**[12]: White solid, mp: 88-90 ^oC, 3.76 g, 95% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 8.23 (s, br, 1H, NH), 7.51 (d, J = 8.0 Hz, 1H, ArH), 7.18 (t, J = 8.0 Hz, 1H, ArH), 6.73 (d, J = 8.0 Hz, 1H, ArH), 6.55 (t, J = 8.0 Hz, 1H, ArH). 6.42 (s, br, 2 H, NH_2), 4.46 (s, br, 1H, OH), 3.47 (t, J = 8.0 Hz, 2H, CH_2), 3.23-3.27 (m, 2H, CH_2), 1.47-

1.60 (m, 4H, CH_2). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 168.7, 149.4, 131.4, 127.9, 116.2, 115.0, 114.5, 60.4, 38.6, 29.9, 25.8.

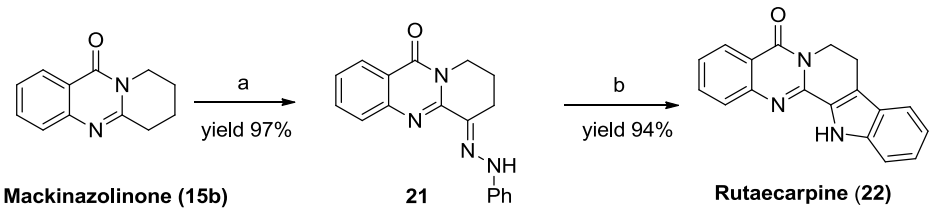
Similarly, the reaction of 5-aminopentan-1-ol furnished 2-amino-N-(5-hydroxypentyl) benzamide (**18b**)

2-amino-N-(5-hydroxypentyl) benzamide (18b): Thick oil, 3.96 g, 94% yield, ^1H NMR (DMSO-d_6, 400 MHz): δ 8.15 (s, br, 1H, NH) 7.44 (d, J = 8.0 Hz, 1H, ArH), 7.11 (t, J = 8.0 Hz, 1H, ArH), 6.67 (d, J = 8.0 Hz, 1H, ArH), 6.49 (t, J = 8.0 Hz, 1H, ArH). 6.35 (s, br, 2 H, NH_2), 4.35 (s, br, 1H, OH), 3.38-3.40 (m, 2H, CH_2), 3.16-3.21 (m, 2H, CH_2), 1.42-1.53 (m, 4H, CH_2), 1.28-1.32 (m, 2H, CH_2). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 168.7, 149.4, 131.4, 127.9, 116.2, 115.0, 114.5, 60.6, 32.2, 29.0, 23.1. HRMS (ESI): $[M + H]^+$: $C_{12}H_{19}N_2O_2$ Calcd for 223.1368. Found: 223.1422.

Compound **18a** (104 mg, 0.5 mmol), $[Cp^*IrCl_2]_2$ (10 mg, 0.013 mmol), xylene (4.0 mL) and trifluoro-methansulfonic acid (8 mg, 0.05 mmol) were added to an oven-dried carousel tube, and then the system was vacuumed and filled with nitrogen. The reaction mixture was stirred and heated to reflux for 24 h, monitored by HPLC. After completion of the reaction, the resulting solution was cooled to room temperature, and the solvent was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (1:1) as eluent to provide the desired product (**15a**) 63 mg, 68% yield.

Compound **18b** (0.5mmol) under the conditions of xylene (4ml), 5.0mol% $[CpIrCl_2]_2$, 20mol% TfOH, reflux, 36 h gave Deoxyvasicinone (**15b**) in 47% yield (47 mg).

Synthesis of Rutaecarpine from Mackinazolinone



Mackinazolinone (15b) 21 Rutaecarpine (22)

Reagents and conditions: (a) aniline, 30% HCl, $NaNO_2$, AcOH, -5 to 5 ^oC, 5h (b) PPA, 180 ^oC, 1h.

Phenyldiazonium chloride was prepared from aniline (512 mg, 5.5 mmol) in 30% hydrochloric acid (5 mL) at 0 ^oC added dropwise a solution of sodium nitrite (380 mg, 5.5 mmol) in water (5 mL). The reaction mixture was stirred for 10 min and diluted with acetic acid (5 mL) and then was adjusted to pH=4 using sodium acetate. To this solution of phenyldiazonium chloride was added dropwise a solution of the quinazolinone (**15b)** (1.00 g, 5.0 mmol) in 50% acetic acid (10 mL) at 0 ^oC over a period of 15 min. The reaction mixture was further stirred at 0 ^oC for 5 h and then allowed to stand overnight in a refrigerator. The precipitated crystalline compound was filtered off, washed with cold

water, dried in vacuum to obtain crude product **(E)-6-(2-phenylhydrazono)-8,9-dihydro-6H-pyrido[2,1-b]quinazolin-11(7H)-one (21)**, 1.47 g, 97% yield, it was used directly without further purification.

To an oven-dried carousel tube, hydrazone (**21)** (304 mg, 1.0 mmol) and PPA (3379 mg, 10mmol) were added, and the stirred solution was heated to 180 ^{o}C for 1 h. The reaction mixture was cooled to room temperature, H_2O (30 mL) was added dropwise and extracted by AcOEt (20 mL x 3), the organic phase was dried by anhydrous Na_2SO_4. Solvent was removed and the residue was chromatographed on silica gel using petroleum ether and ethyl acetate (4:1) to obtain **Rutaecarpine (22)**: light yellow solid, mp: 257 - 258 ^{o}C (lit.[10] mp: 257 - 259 ^{o}C), 270 mg, 94% yield, ^{1}H NMR (DMSO-d_6, 400 MHz): δ 11.87 (s, 1H, NH), 8.16 (d, *J* = 8.0 Hz, 1H, ArH), 7.81 (t, *J* = 8.0 Hz, 1H, ArH), 7.68 (d, *J* = 8.0 Hz, 1H, ArH), 7.65 (d, *J* = 8.0 Hz, 1H, ArH), 7.46-7.50 (m, 2H, ArH), 7.26 (t, *J* = 8.0, 1H, ArH), 7.09 (t, *J* = 8.0, 1H, ArH), 4.45 (t, *J* = 8.0, 2H, CH_2), 3.18 (t, *J* = 8.0, 2H, CH_2). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 160.6, 147.3, 145.3, 138.6, 134.4, 127.1, 126.4, 125.9, 124.8, 124.7, 120.6, 119.9, 119.7, 117.8, 112.5, 40.8, 18.8. HRMS (ESI): $[M + H]^+$: $C_{18}H_{14}N_3O_1$ Calcd for 288.1137. Found: 288.1131.

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