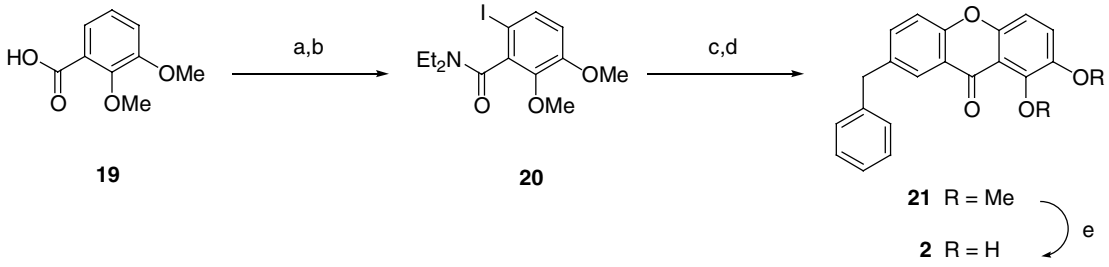
Supporting Materials

Experimentals for Preparation of Compounds **2**-**7**.

All commercially available chemicals and solvents were used without further purification. EM Science silica gel 60 was used for flash chromatography. ^{1}H NMR spectra were recorded on a Varian 400 MHz spectrometer. Chemical shifts are expressed in parts per million (ppm) relative to tetramethylsilane as the internal standard. Elemental analysis for carbon, hydrogen and nitrogen was determined on a Leeman Labs CEC 240XA and CE440 elemental analyzer. High resolution mass spectral data was obtained with a Bruker Daltonics BioApex 3T mass spectrometer.

Preparation of Catechol **2**.



Reagents: (a) $(COCl)_2$, DMF (cat.), $HNEt_2$, CH_2Cl_2, -45 C, 95%; (b) *sec*-BuLi, TMEDA, THF, then I_2, -78 C, 79%; (c) (i) 4-benzyl phenol, NaH, (ii) CuCl, Py, tris[2-(2-methoxyethoxy)ethyl]amine, 150 C, 53%; (d) LDA, THF, 0 C, 80%; (e) BBr_3, CH_2Cl_2, -78 C, 77%.

***N,N*-Diethyl-6-iodo-2,3-dimethoxy-benzamide (20).** To a solution of **19** (4.6 g, 25.2 mmol) and DMF (0.2 mL, 2.5 mmol) in CH_2Cl_2 (50 mL) was added oxalyl chloride (3.2 mL, 37.8 mmol) dropwise under argon. After stirring for 1 h, the solvent was removed and the residue was co-evaporated with benzene twice. The residue was redissolved in CH_2Cl_2 (50 mL) and cooled to 45 C before addition of Et_2NH (10.4 mL, 100.8 mmol). The reaction mixture was stirred overnight. The reaction mixture was diluted with CH_2Cl_2, washed with water, 1N HCl, brine, dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) gave an amide (5.7g, 95%

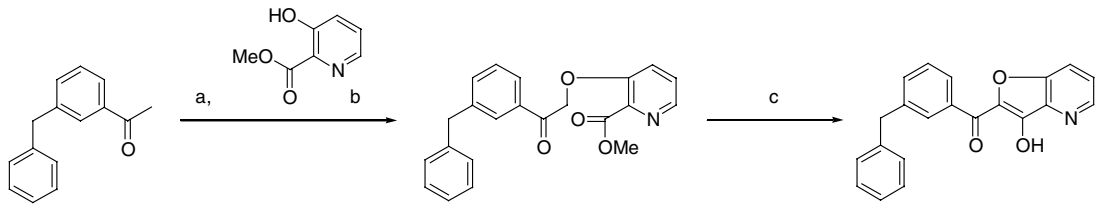
yield). ^{1}H NMR ($CDCl_3$) 7.07 (dd, *J* = 8.2, 7.7 Hz, 1H), 6.92 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.80 (dd, *J* = 7.5, 1.5 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 3.66-3.76 (m, 1H), 3.36-3.48 (m, 1H), 3.12-3.22 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.04 (t, *J* = 7.1 Hz, 3H). To a solution of TMEDA (1.67 mL, 11.1 mmol) in THF (100 mL) at –78 C was added *sec*-BuLi (1.3 M in cyclohexane, 8.5 mL, 11.1 mmol) under argon. After 5 min, the amide (2.5 g, 10.5 mmol) in THF (20 mL) was added dropwise. After 1 h at –78 C, I_2 (5.86 g, 23.1 mmol) in THF (20 mL) was added and the reaction mixture was allowed to warm to room temperature overnight. The reaction was quenched with $Na_2S_2O_3$ (5 g) in water (20 mL), diluted with AcOEt. The organic layer was washed with water, brine, dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) gave **20** (3.0g, 79% yield). ^{1}H NMR ($CDCl_3$) 7.47 (d, *J* = 8.8 Hz, 1H), 6.66 (d, *J* = 8.8 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 3.68-3.80 (m, 1H), 3.38-3.50 (m, 1H), 3.08-3.18 (m, 2H), 1.28 (t, *J* = 7.3 Hz, 3H), 1.10 (t, *J* = 7.3 Hz, 3H).

7-Benzyl-1,2-dimethoxy-xanthen-9-one (21). To a suspension of NaH (60% in mineral oil, 1.08 g, 27.1 mmol) in THF (270 mL) was added 4-benzylphenol (5.0 g, 27.1 mmol) in portion at 0 C. After 30 min, the reaction mixture became a clear solution. The reaction was warmed to room temperature and solvent was removed to give a slightly pink solid (7.0 g). To a seal tube was cahrged with the slightly pink solid (2.9 g), **20** (1.5 g, 4.1 mmol), CuCl (203 mg, 2.0 mmol), tris[2-(2-methoxyethoxy)ethyl]amine (0.64 mL, 2.0 mmol) and pyridine (1 mL). The mixture was heated at 150 C for 2 h. After cooling to room temperature, the reaction mixture was partitioned between AcOEt and water. The organic layer was washed with 1N NaOH, brine, dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) gave a diaryl ether (900 mg, 53% yield). ^{1}H NMR ($CDCl_3$) 7.14-7.30 (m, 5H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 6.78 (d, *J* = 8.9 Hz, 1H), 6.59 (d, *J* = 8.8 Hz, 1H), 3.91 (s, 2H), 3.89 (s, 3H), 3.81 (s, 3H), 3.48-3.56 (m, 2H), 3.14-3.26 (m, 2H), 1.14 (t, *J* = 7.0 Hz, 3H), 1.07 (t, *J* = 7.0 Hz, 3H). To a solution of LDA (2.0 M, 0.6 mL, 1.2 mmol) in THF (1 mL) was added the diaryl ether (50 mg, 0.12 mmol) in THF (0.5 mL) at room temperature. After 30 min, the reaction was quenched with 1N HCl at 0 C. The reaction mixture was partitioned between AcOEt and water. The organic layer was washed with water, brine, dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) gave **21** (33 mg, 80% yield). ^{1}H NMR ($CDCl_3$) 8.14 (s, 1H), 7.18-7.50 (m, 9H), 4.07 (s, 2H), 4.00 (s, 3H), 3.92 (s, 3H).

7-Benzyl-1,2-dimethoxy-xanthen-9-one (2). To a solution of **21** (130 mg, 0.37 mmol) in CH_2Cl_2 (5 mL) was added BBr_3 (1.0 M in CH_2Cl_2, 1.87 mL, 1.87 mmol) dropwise at 78 C. The reaction mixture was stirred at 78 C for 30 min, then room temperature

10 min. The reaction was quenched with $NaHCO_3$ at 0 C. The reaction mixture was partitioned between CH_2Cl_2 and water. The organic layer was washed with water, brine, dried over Na_2SO_4, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) gave **2** (90 mg, 77% yield). ^{1}H NMR ($CDCl_3$) 12.60 (s, 1H), 8.10 (s, 1H), 7.56 (d, *J* = 8.6 Hz, 1H), 7.18-7.50 (m, 7H), 6.88 (d, *J* = 9.0 Hz, 1H), 5.44 (s, 1H), 4.10 (s, 2H). HRMS (ES) *m/z* 319.0976 (MH^+). Anal. ($C_{20}H_{14}O_4$ 0.3AcOEt 0.1Hexane) C, H.

Preparation of Furanopyridine **3**.



8 **22** **3**

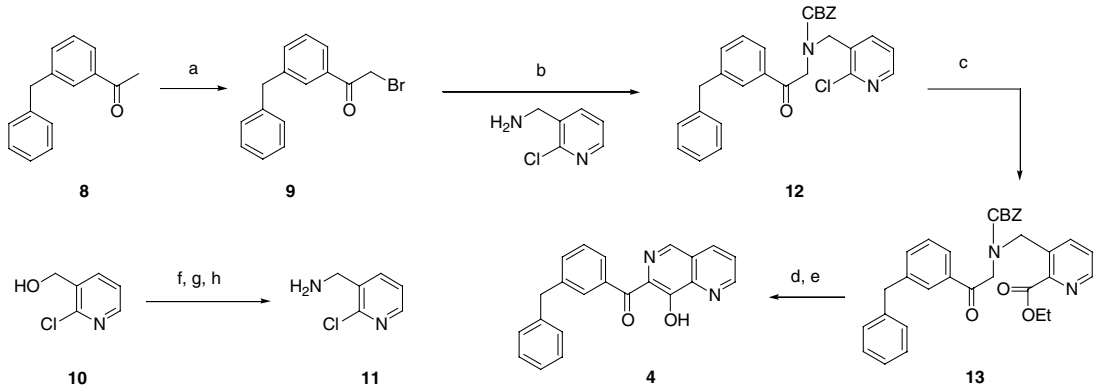
Reagents: (a) Br_2, $AlCl_3$ (cat.), AcOEt; (b) Cs_2CO_3, DMF, 87% for step a & b; (c) LDA, THF, -78 C, 41%.

3-[2-(Benzyl-phenyl)-2-oxo-ethoxy]-pyridine-2-carboxylic methyl ester (22). To a mixture of **8** (670 mg, 3.19 mmol) and $AlCl_3$ (21.3 mg, 0.16 mmol) in AcOEt (5 mL) was added Br_2 (560 mg, 3.50 mmol). After 20 min, the solvent was removed and the residue was redissolved in DMF (17 mL). To this DMF solution was added 3-hydroxy piconilic acid methyl ester (800 mg, 5.2 mmol) and Cs_2CO_3 (1.69 g, 5.2 mmol). After stirring for 3 h, the reaction was quenched with saturated aqueous NH_4Cl. The reaction mixture was partitioned between AcOEt and water. The organic layer was washed with water, brine, dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) gave **22** (330 mg, 87% yield). ^{1}H NMR ($CDCl_3$) 8.32 (d, *J* = 4.4 Hz, 1H), 7.81-7.84 (m, 2H), 7.16-7.48 (m, 9 H), 5.38 (s, 2H), 4.05 (s, 2H), 3.96 (s, 3H).

(3-Benzyl-phenyl)-(3-hydroxy-furo[3,2-*b*]pyridin-2-yl)-methanone (3). To a solution of **22** (120 mg, 0.33 mmol) in THF (3 mL) was added LDA (2.0 M in haptane/THF/ethylbenzene, 0.25 mL, 0.5 mmol) at –78 C. The reaction was allowed to warm to room temperature slowly. The reaction mixture was partitioned between AcOEt and water. The organic layer was washed with water, brine, dried over Na_2SO_4, filtered

and concentrated to give a yellow powder. The yellow power was recrystalized with MeOH/Et_2O to give **3** (45 mg, 41% yield). ^{1}H NMR (CD_3OD) 8.64 (d, *J* = 4.6 Hz, 1H), 8.08 (d, *J* = 7.2 Hz, 1H), 8.05 (s, 1H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.61 (dd, *J* = 8.6, 4.6 Hz, 1H), 7.48-7.54 (m, 2H), 7.18-7.34 (m, 5H), 4.10 (s, 2H). HRMS (ES) *m/z* 330.1125 (MH^+). Anal. ($C_{21}H_{15}NO_3$ 0.1MeOH 0.05Et_2O) C, H, N.

Preparation of Naphthyridine **4**.



Reagents: (a) Br_2, $AlCl_3$ (cat.), 1,4-dioxane; (b) *i*-Pr_2NEt, CH_3CN; then CBZCl, 76% for steps a & b; (c) $Pd(II)(PPh_3)_2Cl_2$, Et_3N, CO (250 psi), EtOH, 50%; (d) NaHMDS, THF; (e) 48% HBr, CH_3CN; then air oxidation, 42% for steps d & e; (f) $SOCl_2$, toluene, 98%; (g) LiN_3, DMSO; (h) 5% Pt/C, H_2, EtOH, 51% for steps g & h.

***C*-(2-Chloro-pyridin-3-yl)-methylamine (11).** To a solution of **10** (7.4 g, 51.5 mmol) in a mixed solvent of toluene (250 mL) and CH_2Cl_2 (50 mL) was added $SOCl_2$ (5.64 mL, 77.3 mmol) at 0 C. The reaction was allowed to warm to room temperature overnight. The excess reagent and solvents were removed *in vacuo*. The residue was partitioned between AcOEt and aqueous $NaHCO_3$ solution. The organic layer was washed with water, brine, dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) gave a chloromethylpyridine (8.1 g, 98% yield). ^{1}H NMR ($CDCl_3$) 8.37 (d, *J* = 4.8 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.30 (dd, *J* = 7.5, 4.8 Hz, 1H), 4.70 (s, 2H). A mixture of the chloromethylpyridine (500 mg, 3.09 mmol) and LiN_3 (160 mg, 3.24 mmol) in DMSO (6 mL) was stirred overnight. The reaction mixture was partitioned between AcOEt and water. The organic layer was washed with water, brine, dried over $MgSO_4$, filtered and concentrated to give an azidomethylpyridine (483 mg, 95% yield). ^{1}H NMR ($CDCl_3$) 8.37 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.77 (dd, *J* = 7.6,

1.9 Hz, 1H), 7.30 (dd, *J* = 7.5, 4.8 Hz, 1H), 4.54 (s, 2H). A mixture of the azidomethylpyridine (240 mg, 1.43 mmol) and Pt/C (5% on carbon, 279 mg, 0.07 mmol) in EtOH (15 mL) was stirred under H_2. After 3 h, the reaction mixture was filtered through Celite then concentrated to give **11** (163 mg, 80% yield). ^{1}H NMR ($CDCl_3$) 8.30 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.79 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.26 (dd, *J* = 7.5, 4.8 Hz, 1H), 3.96 (s, 2H), 1.50 (s, 2H).

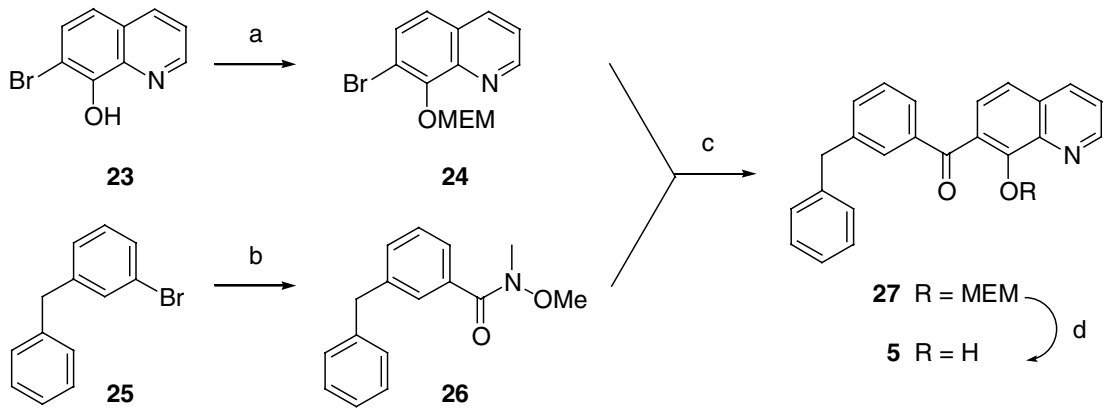
[2-(3-Benzyl-phenyl)-2-oxo-ethyl]-(2-chloro-pyridin-3-ylmethyl)-carbamic acid benzyl ester (12). To a mixture of **8** (1.25 g, 5.95 mmol) and $AlCl_3$ (78.6 mg, 0.59 mmol) in 1,4-dioxane (10 mL) was added Br_2 solution (0.62 M in 1,4-dioxane, 10 mL, 6.2 mmol) dropwise. After 1h, the solvent was removed *in vacuo*. The residue was dissolved in AcOEt (50 mL), washed with brine twice, dried over $MgSO_4$, filtered and concentrated to give **9** as an oil. To a solution of amine **11** (1.0 g, 5.95 mmol) and *i*-Pr_2NEt (4.2 mL, 45.6 mmol) in CH_3CN (50 mL) was added a solution of **9** (< 5.95 mmol) in CH_3CN (10 mL). After 1 h, CBZCl (1.71 mL, 12.0 mmol) was added. The reaction mixture was stirred overnight. The solvent was removed under reduced pressure. The residue was partitioned between AcOEt and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatograph (hexanes/ethyl acetate) to give **12** (2.2 g, 76%). ^{1}H NMR ($CDCl_3$) 8.34-8.41 (m, 1H), 8.00 (d, *J* = 7.6 Hz, 0.5H), 7.66-7.79 (m, 2.5H), 7.16-7.44 (m, 13H), 5.18 (s, 1H), 5.14 (s, 1H), 4.79 (s, 1H), 4.73 (s, 1H), 4.71 (s, 1H), 4.67 (s, 1H), 4.03 (s, 1H), 4.02 (s, 1H).

3-({Benzyloxycarbonyl-[2-(3-benzyl-phenyl)-2-oxo-ethyl]-amino}-methyl)-pyridine-2-carboxylic acid methyl ester (13). A mixture of **12** (1.0 g, 2.06 mmol), $Pd(PPh_3)_2Cl_2$ (140 mg, 0.2 mmol) and Et_3N (2 mL) in EtOH (30 mL) was charged into the glass liner of an autoclave. The mixture was purged with argon for 10 min. The autoclave was sealed, pressurized with CO to 250 psi and heated at 100 C for 48 h. After cooling to room temperature, the reaction mixture was filtered through Celite and concentrated. The resultant residue was purified by flash chromatograph (hexans/ethyl acetate) to give **13** (520 mg, 50% yield). ^{1}H NMR ($CDCl_3$) 8.58-8.63 (m, 1H), 8.04 (d, *J* = 8.0 Hz, 0.5H), 7.64-7.82 (m, 2.5H), 7.14-7.46 (m, 13H), 5.17 (s, 1H), 5.13 (s, 1H), 4.96 (s, 1H), 4.95 (s, 1H), 4.74 (s, 1H), 4.71 (s, 1H), 4.31-4.40 (m, 2H), 4.01 (s, 1H), 4.00 (s, 1H), 1.35 (q, *J* = 7.3 Hz, 3H).

(3-Benzyl-phenyl)-(8-hydroxy-[1,6]naphthyridin-7-yl)-methone (4). To a solution of **13** (260 mg, 0.5 mmol) in THF (10 mL) was added NaHMDS (0.6 M in toluene, 1.2 mL, 0.72 mmol) at –78 C under agon. The reaction was allowed to warm to room temperature slowly. After 3 h, the reaction was quenched with aqueous NH_4Cl, extracted with AcOEt (2 50 mL). The combined organic phases were dried over Na_2SO_4, filtered

and concentrated. Preparative reverse phase HPLC purification provided a diketone (180 mg, 75% yield). ^{1}H NMR ($CDCl_3$) 8.86 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.76 (d, *J* = 7.4 Hz, 1H), 7.46-7.56 (m, 3H), 7.10-7.36 (m, 12H), 6.84 (d, *J* = 6.0 Hz, 1H), 4.95 (broad s, 2H), 4.60 (s, 2H), 4.00 (s, 2H). A solution of the ketone (50 mg, 0.1 mmol) in 48% HBr (3 mL) and CH_3CN (1 mL) was stirred under air at 35 C for 16 h. The excess reagents and solvents was removed under vacuum. The resultant residue was purified by preparative reverse phase HPLC to give **4** (25 mg, 56% yield). ^{1}H NMR (CD_3OD) 9.17 (dd, *J* = 4.3, 1.5 Hz, 1H), 8.90 (s, 1H), 8.61 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.98-8.02 (m, 2H), 7.89 (dd, *J* = 8.2, 4.3 Hz, 1H), 7.42-7.52 (m, 2H), 7.16-7.30 (m, 5H), 4.08 (s, 2H). HRMS (ES) *m/z* 341.1291 (MH^+). Anal. ($C_{22}H_{16}N_2O_2$ 0.4TFA 0.5H_20) C, H, N.

Preparation of quinloine **5**.



Reagents: (a) MEMCl, , *i*-Pr_2NEt, CH_2Cl_2, 42%; (b) $Pd(II)Cl_2$, PPh_3, MeNH(OMe) HCl, Et_3N, CO (200 psi), 73%; (c) *tert*-BuLi, THF, -78 C, 19%; (d) TFA, MeOH, 38%.

7-Bromo-8-(2-methoxy-ethoxymethoxy)-quinoline (24). To a solution of **23** (3.1 g, 13.8 mmol) and *i*-Pr_2NEt (7.2 mL, 41.5 mmol) in CH_2Cl_2 (100 mL) was added MEMCl (2.8 mL, 24.9 mmol) and the reaction mixture was stirred overnight. Water was added and two layers were separated. The aqueous layer was extracted with AcOEt twice. The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) provided **24** (1.8 g, 42% yield). ^{1}H NMR ($CDCl_3$) 8.90 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.68 (d, *J*

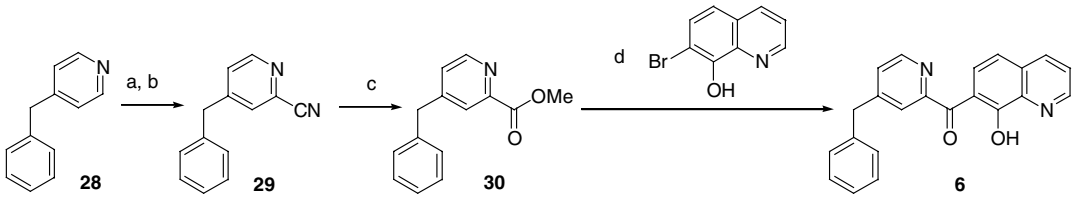
= 8.8 Hz, 1H), 7.46 (d, *J* = 9.0 Hz, 1H), 7.43 (dd, *J* = 8.3, 4.0 Hz, 1H), 5.75 (s, 2H), 4.18 (t, *J* = 4.7 Hz, 2H), 3.61 (t, *J* = 4.7 Hz, 2H), 3.37 (s, 3H).

3-Benzyl-*N*-methoxy-*N*-methyl-benzamide (26). A mixture of **25** (2.47 g, 10 mmol), PPh_3 (1.58 g, 6.0 mmol), MeNH(OMe) HCl (1.95 g, 20 mmol), $PdCl_2$ (180 mg, 1.0 mmol) and Et_3N (5.6 mL, 40 mmol) in 1-methyl-2-pyrrolidinone (35 mL) was charged into the glass liner of an autoclave. The mixture was purged with argon for 10 min. The autoclave was sealed, pressurized with CO to 200 psi and heated at 120 C for 40 h. After cooling to room temperature, the reaction mixture was filtered through Celite. The filtrate was partitioned between benzene (400 mL) and water (50 mL), washed with water three times, washed with brine, dried over $MgSO_4$, filtered and concentrated. The resultant residue was purified by flash chromatograph (hexans/ethyl acetate) to give **25** (1.86 g, 73% yield). ^{1}H NMR ($CDCl_3$) 7.50 (s, 1H), 7.20-7.40 (m, 8H), 4.01 (s, 2H), 3.50 (s, 3H), 3.32 (s, 3H).

(3-Benzyl-phenyl)-(8-methoxy-quinolin-7-yl)-methanone (27). To a solution of **24** (0.76 g, 2.4 mmol) in THF (10 mL) was added *tert*-BuLi (1.5 M in pentane, 3.6 mL, 5.4 mmol) at –78 C under argon. After 15 min, a solution of **26** (0.62 g, 2.4 mmol) in THF (5 mL) was added. The reaction was allowed to warm to room temperature slowly and quenched with aqueous NH_4Cl. The reaction mixture was extracted with AcOEt. The organic phase was dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) provided **27** (0.2 g, 19% yield). ^{1}H NMR ($CDCl_3$) 8.97 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.19 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.85 (s, 1H), 7.15-7.75 (m, 11H), 5.55 (s, 2H), 4.13 (s, 2H), 3.51-3.59 (m, 2H), 3.17-3.25 (m, 2H), 3.22 (s, 3H).

(3-Benzyl-phenyl)-(8-hydroxy-quinolin-7-yl)-methanone (5). To a solution of **27** (0.2 g, 0.46 mmol) in MeOH (3 mL) was added TFA (1.0 mL, 14 mmol). After 72 h, the reaction mixture was treated with aqueous $NaHCO_3$ and extracted with AcOEt. The organic phase was dried over Na_2SO_4, filtered and concentrated. Preparative reverse phase HPLC purification provided **5** (60 mg, 38% yield). ^{1}H NMR ($CDCl_3$) 8.98 (dd, *J* = 4.7, 1.3 Hz, 1H), 8.19 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.54-7.70 (m, 4H), 7.18-7.43 (m, 8H), 4.07 (s, 2H). MS (ES) *m/z* 340 (MH^+). Anal. ($C_{23}H_{17}NO_2$ 0.80TFA 0.32$H_2$0) C, H, N.

Preparation of quinloine **6**.



Reagents: (a) AcOH, 30% H_2O_2, 80 C, 96%; (b) TMSCN, Et_3N, CH_3CN, reflux, 70%; (c) HCl(g), MeOH, 0 C, 80%; (d) NaH, *n*-BuLi, THF, -78 C, 31%.

4-Benzyl-pyridine-2-carbonitrile (29). A mixture of 4-benzyl pyridine **28** (15 mL, 94.0 mmol), AcOH (90 mL) and H_2O_2 (35% aqueous solution, 30 mL) was heated at 85 C overnight. After cooling to room temperature, the reaction mixture was treated with saturated aqueous $NaHCO_3$ (300 mL) and extracted with CH_2Cl_2 three times. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated to give a pyridine *N*-oxide (16.6 g, 96% yield). ^{1}H NMR ($CDCl_3$) 8.11 (d, J = 6.9 Hz, 2H), 7.26-7.36 (m, 3H), 7.16 (d, J = 6.7 Hz, 2H), 7.06 (d, J = 6.9 Hz, 2H), 4.01(s, 2H). To a solution of the pyridine N-oxide (14.0 g, 75.6 mmol) and Et_3N (16.0 mL) in CH_3CN (80 mL) was added TMSCN (25.0 mL, 187.5 mmol) dropwise. The reaction mixture was then refluxed overnight. After cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$, brine and dried over Na_2SO_4, filtered and evaporated *in vacuo*. The residue was purified by flash chromatography (hexanes/ethyl acetate) to give **29** (10.2 g, 70% yield). ^{1}H NMR ($CDCl_3$) 8.11 (d, J = 5.1 Hz, 1H), 7.49 (s, 1H), 7.27-7.38 (m, 4H), 7.16 (d, J = 7.2 Hz, 2H), 4.01 (s, 2H).

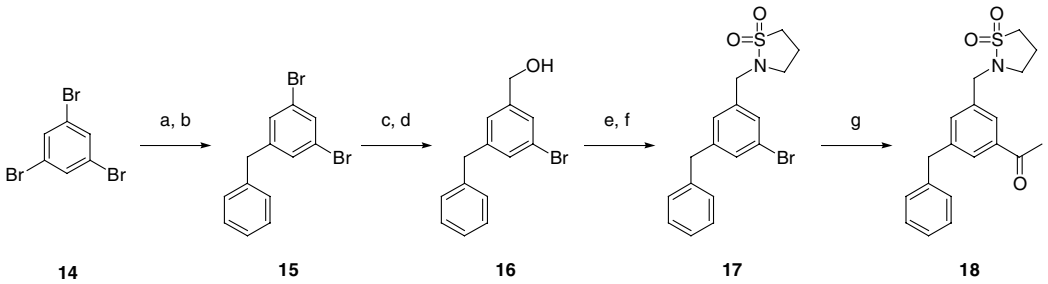
4-Benzyl-pyridine-2-carboxylic acid methyl ester (30). A solution of **29** (2.36 g, 12.1 mole) in MeOH (50 mL) at 0 °C under argon was bubbled with HCl gas till saturation. The reaction stirred at room temperature overnight. The solvent was removed under reduced pressure. The residue was treated with saturated aqueous $NaHCO_3$ and extracted with $CHCl_3$ four times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated. Chromatographic purification using ethyl acetate/hexanes as eluents afforded **30** (2.2 g, 80% yield). ^{1}H NMR ($CDCl_3$) 8.62 (d, J = 5.3 Hz, 1H), 8.00 (s, 1H), 7.26-7.36 (m, 4H), 7.18 (d, J = 6.7 Hz, 2H), 4.06 (s, 2H), 4.00 (s, 3H).

(4-Benzyl-pyridin-2-yl)-(8-hydroxy-quinolin-7-yl)-mathanone (6). To a suspension of NaH (60% in mineral oil, 106 mg, 2.65 mmol) in THF (15 mL) under argon was added **22** (350 mg, 1.56 mmol) in portion. After 1 h, the reaction mixture was cooled to –78 C

and *n*-BuLi (1.6 M in hexanes, 1.07 mL, 1.71 mmol) was added. After 1 h, a solution of **29** (800 mg, 3.52 mmol) in THF (5 mL) was added. The reaction mixture was warmed slowly to room temperature overnight. The reaction was quenched with saturated aqueous NH_4Cl and extracted with $CHCl_3$ three times. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated *in vacuo*. The residue was purified by preparative reverse phase HPLC to give **6** (220 mg, 13% yield). ^{1}H NMR (DMSO-d_6) 8.95 (d, J = 4.2 Hz, 1H), 8.56 (d, J = 5.0 Hz, 1H), 8.49 (d, J = 8.3 Hz, 1H), 7.92 (s, 1H), 7.72-7.76 (m, 2H), 7.57 (d, J = 5.0 Hz, 1H), 7.49 (d, J = 8.6 Hz, 1H), 7.23-7.38 (m, 5H), 4.15 (s, 2H). MS (ES) *m/z* 341 (MH^+). Anal. ($C_{22}H_{16}N_2O_2$ 1.90TFA 1.75H_20) C, H, N.

Preparation of Naphthyridine **7**.

(1) Preparation of ketone **18**.



Reagents:(a) *n*-BuLi, PhCHO, Et_2O, -78 C; (b) Et_3SiH, BF_3 OEt_2, CH_2Cl_2, 0 C, 82% for steps a & b; (c) *n*-BuLi, DMF, Et_2O, -78 C; (d) $NaBH_4$, MeOH, 77% for steps c & d; (e) PPh_3, CBr_4, CH_2Cl_2, 75%; (f) –sultam, K_2CO_3, CH_3CN, reflux, 99%; (g) Butyl vinyl ether, Pd(II)$(OAc)_2$, Tl(I)OAc, DPPP, Et_3N, DMF, 100 C; 1N HCl, THF, 90%.

3-Benzyl-1,5-dibromobenzene (15). To a suspension of **14** (31.5 g, 100 mmol) in Et_2O (450 mL) at –78 C was added *n*-BuLi (2.5 M in hexanes, 40 mL, 100 mmol) slowly under argon. The internal temperature was kept below –65 C. After 40 min, benzaldehyde (10.1 mL, 100 mmol) was added and the reaction mixture was allowed to warm to room temperature slowly overnight. The reaction was quenched with brine. The aqueous layer was extracted with Et_2O (100 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. The resultant residue was dissolved in CH_2Cl_2 (400 mL). Triethylsilane (108.9 mL, 400 mmol) was added and the solution was

cooled to 0 C. $BF_3 OEt_2$ (19 mL, 150 mmol) was added slowly (ca. 10 min) and the reaction mixture was allowed to warm to room temperature slowly overnight. The reaction was cooled to 0 C and quenched with aqueous $NaHCO_3$. The aqueous layer was extracted with hexanes. The combined organic phases were dried over $MgSO_4$, filtered and concentrated. The residue was eluted through a silica gel pad (400 mL) with hexanes to give **15** (26.4 g, 82% yield). ^{1}H NMR ($CDCl_3$) 7.50 (s, 1H), 7.22-7.34 (m, 5H), 7.16 (d, *J* = 7.3 Hz, 2H), 3.91 (s, 2H).

(3-Benzyl-5-bromo-phenyl)-methanol (16). To a solution of **15** (26.4 g, 81.5 mmol) in Et_2O (400 mL) at –78 C was added *n*-BuLi (2.5 M in hexanes, 32.6 mL, 81.5 mmol) slowly under argon. The internal temperature was kept below –65 C. After 40 min, DMF (7.6 mL, 97.8 mmol) was added and the reaction mixture was allowed to warm to room temperature slowly overnight. The reaction was quenched with brine. The aqueous layer was extracted with AcOEt (100 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated. The resultant residue was dissolved in MeOH (400 mL) and cooled to 0 C. $NaBH_4$ (3.7 g, 100 mmol) was added in portion and the reaction was allowed to warm to room temperature slowly overnight. The reaction was cooled to 0 C and quenched with 1N HCl. MeOH was removed *in vacuo*. The residue was extracted with AcOEt twice. The combined organic phases were dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) provided **16** (17.0 g, 77% yield). ^{1}H NMR ($CDCl_3$) 7.36 (s, 1H), 7.22-7.34 (m, 4H), 7.17 (d, *J* = 7.3 Hz, 2H), 7.11 (s, 1H), 4.60 (s, 2H), 3.91 (s, 2H).

2-(3-Benzyl-5-bromo-benzyl)-isothiazolidine 1,1-dioxide (17). To a solution of **16** (17.0 g, 61.4 mmol) and CBr_4 (22.4 g, 67.5 mmol) in CH_2Cl_2 (200 mL) was added a solution of PPh_3 (17.6 g, 67.5 mmol) in CH_2Cl_2 (20 mL) slowly at 0 C. The reaction was allowed to warm to room temperature overnight. CH_2Cl_2 was removed *in vacuo*. The residue was purified by flash chromatography with hexanes/ethyl acetate as eluents to give a bromide (17.6 g, 85% yield). ^{1}H NMR ($CDCl_3$) 7.38 (s, 1H), 7.22-7.34 (m, 4H), 7.16 (d, *J* = 7.3 Hz, 2H), 7.12 (s, 1H), 4.40 (s, 2H), 3.91 (s, 2H). A mixture of the bromide (5.0 g, 14.7 mmol), -sultam (3.65 g, 30.1 mmol) and K_2CO_3 (4.05 g, 29.3 mmol) in CH_3CN (60 mL) was refluxed for 36 h. After cooling to room temperature, the CH_3CN was removed *in vacuo*. The residue was partitioned between AcOEt and water. The AcOEt layer was dried over $MgSO_4$, filtered and concentrated. Flash chromatography purification (hexanes/ethyl acetate) provided **17** (5.5 g, 99% yield). ^{1}H NMR ($CDCl_3$) 7.34 (s, 1H), 7.22-7.33 (m, 4H), 7.16 (d, *J* = 7.3 Hz, 2H), 7.10 (s, 1H), 4.10 (s, 2H), 3.91 (s, 2H), 3.19 (t, *J* = 7.3 Hz, 2H), 3.09 (t, *J* = 6.8 Hz, 2H), 2.31 (quintet, *J* = 7.1 Hz, 2H).

1-[3-Benzyl-5-(1,1-dioxo-1 ^{6}-isothiazolidin-2-ylmethyl)-phenyl]-ethanone (18). A seal tube was charged with **17** (5 g, 13.2 mmol), Tl(I)OAc (4.16 g, 15.8 mmol), DPPP (0.98 g, 2.38 mmol), Et_3N (7.35 mL, 52.8 mmol) and DMF (20 mL). This mixture was purged with argon for 10 min. $Pd(OAc)_2$ (0.44 g, 1.98 mmol) and butyl vinyl ether (8.5 mL) were then added and the reaction mixture was stirred at 100 C overnight. After cooling to room temperature, the reaction mixture was filtered through Celite. DMF was removed under vacuum. The residue was redissolved in THF (200 mL) and treated with 1N HCl (200 mL). After 1 h, the reaction mixture was extracted with AcOEt twice. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatograph (hexanes/ethyl acetate) to give **18** (4.1 g, 90% yield). ^{1}H NMR ($CDCl_3$) 7.76 (s, 1H), 7.72 (s, 1H), 7.40 (s, 1H), 7.16-7.32 (m, 5H), 4.19 (s, 2H), 4.04 (s, 2H), 3.19 (t, *J* = 7.3 Hz, 2H), 3.08 (t, *J* = 6.8 Hz, 2H), 2.57 (s, 3H), 2.32 (quintet, *J* = 7.1 Hz, 2H).

(2) Naphthyridine **7** was prepared from ketone **18** in a similar manner as naphthyridine **4** from ketone **8**.

[3-Benzyl-5-(1,1-dioxo-1 ^{6}-isothiazolidin-2-ylmethyl)-phenyl]-(8-hydroxy-[1,6]naphthyridin-7-yl)-methanone (7). ^{1}H NMR (DMSO-d_6) 12.0 (broad s, 1H), 9.20 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.93 (s, 1H), 8.65 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.88 (dd, *J* = 8.3, 4.3 Hz, 1H), 7.74 (s, 1H), 7.72 (s, 1H), 7.52 (s, 1H), 7.16-7.32 (m, 5H), 4.13 (s, 2H), 4.03 (s, 2H), 3.21 (t, *J* = 7.6 Hz, 2H), 3.09 (t, *J* = 6.6 Hz, 2H), 2.20 (quintet, *J* = 7.2 Hz, 2H). HRMS (ES) *m/z* 474.1502 (MH^+). Anal. ($C_{26}H_{23}N_3O_4S$ 1.05TFA 0.7H_20) C, H, N.