Supporting Information

3-Hydroxypyrimidine-2,4-diones as a New Inhibitor Scaffold of HIV Integrase

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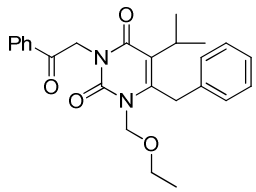
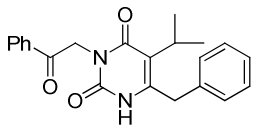
Chemistry Experimental

General Procedures. All commercial chemicals were used as supplied unless otherwise indicated. Dry solvents (THF, Et_2O, CH_2Cl_2 and DMF) were dispensed under argon from an anhydrous solvent system with two packed columns of neutral alumina or molecular sieves. Flash chromatography was performed on a Teledyne Combiflash RF-200 with RediSep columns (silica) and indicated mobile phase. All reactions were performed under inert atmosphere of ultra-pure argon with oven-dried glassware. ^1H and ^{13}C NMR spectra were recorded on a Varian 600 MHz spectrometer. Mass data were acquired on an Agilent TOF II TOS/MS spectrometer capable of ESI and APCI ion sources. Analysis of sample purity was performed on a Varian Prepstar SD-1 HPLC system with a Varian Microsorb-MW 100-5 C18 column (250mm x 4.6 mm). All tested compounds have a purity ≥ 96%.

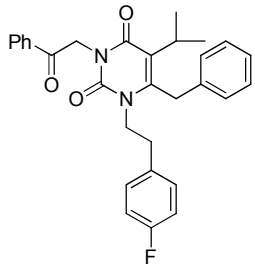


6-Benzyl-1-(ethoxymethyl)-5-isopropyl-3-(2-oxo-2-phenylethyl)pyrimidine-2,4(1H,3H)-dione (34). [S1] To the solution of compound **6** (1.0 g, 3.30 mmol) in 30 mL CH_3CN, was added 2-bromoacetophenone (857 mg, 4.30 mmol) and K_2CO_3 (594 mg, 4.30 mmol), this reaction mixture was heated to reflux for 3 h, After cooling to rt, removed the solvent and the residue was dissolved into water and extracted with EtOAc (10 mL x 3), combined the organic phase. The organic layer was washed with aqueous 1 N HC1 (10 mL), H_2O (10 mL) and dried over Na_2SO_4, then concentrated under reduced pressure. The resultant residue residue was purified by combiflash to give (1.18 g, yield: 84%) as white solid; ^{1}HNMR (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 2 H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.2 Hz. 2H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 2H), 5.36 (s, 2H), 5.11

(s, 2H), 4.17 (s, 2H), 3.56 (q, *J* = 6.6 Hz, 2H), 3.02 (septet, *J* = 7.2 Hz, 1H), 2.84 (septet, *J* = 7.2 Hz, 1H), 1.22 (d, *J* = 7.2 Hz, 6H), 1.13 (t, *J* = 6.6 Hz, 3H); MS (ESI-) m/z: 419.50 (M-1).

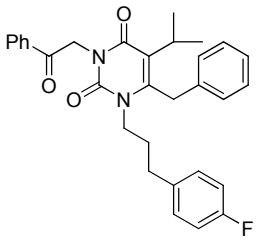


6-Benzyl-5-isopropyl-3-(2-oxo-2-phenylethyl)pyrimidine-2,4(1H,3H)-dione (35). [S1] Compound **34** (1.18 g, 2.80 mmol) was dissolved in 5 mL of TFA:H_2O (9:1), and the reaction mixture was heated under reflux for 2 h. Then solvent was removed and the residue was crystallized from EtOH to give **35** (760 mg, 76%) as white solid; ^{1}HNMR (600 MHz $CDCl_3$) δ 8.03 (d, *J* = 8.4 Hz, 2 H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.60 (t, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 3H), 5.34 (s, 2H), 3.87 (s, 2H), 2.97 (septet, *J* = 7.2 Hz, 1H), 1.16 (d, *J* = 7.2 Hz, 6H); MS (ESI-) m/z: 361.42 (M-1).

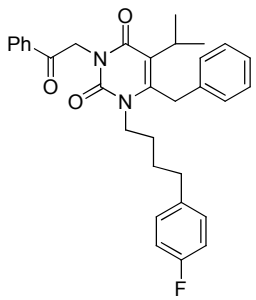


6-Benzyl-1-(4-fluorophenethyl)-5-isopropyl-3-(2-oxo-2-phenylethyl)pyrimidine-2,4(1H,3H)-dione (36). To a solution of **35** (180 mg, 0.50 mmol) in 2 mL of DMF, was added Cs_2CO_3 (242 mg, 0.75 mmol) and 1-(2-bromoethyl)-4-fluorobenzene (121 mg, 0.60 mmol), this reaction mixture was heated at 80 ^oC for 3 h. Then removed the solvent and dissolved the residue into water and extracted with EtOAc (15 mL x 3), the organic layer was washed with aqueous 1 N HC1 (10 mL), H_2O (10 mL) and dried over Na_2SO_4, then concentrated under reduced pressure. The resultant residue residue was purified by combiflash to give (74 mg, 31 %) as white solid; ^{1}HNMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.8 Hz), 7.23 (t, *J* =

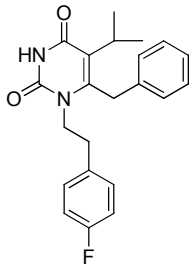
7.8 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 2H), 6.96 (m, 2H), 6.89 (m, 2H), 5.40 (s, 2H), 3.79 (t, *J* = 7.2 Hz, 2H), 3.73 (s, 2H), 2.84 (septet, *J* = 7.2 Hz, 1H), 2.72 (t, *J* = 7.8 Hz, 2H), 1.21 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) 191.1, 161.6, 160.4, 156.0, 150.5, 146.1, 134.1 (d, *J* = 7.4 Hz), 132.6, 132.5 (d, *J* = 3.4 Hz), 129.4 (d, *J* = 7.8 Hz), 128.4, 127.7, 127.1, 126.4, 117.1, 114.6 (d, *J* = 21.2 Hz), 46.3, 46.2, 33.4, 33.1, 27.7, 19.5; MS (ESI-) m/z: 483.22 (M-1).



6-bBnzyl-1-(3-(4-fluorophenyl)propyl)-5-isopropyl-3-(2-oxo-2-phenylethyl)pyrimidine-2,4(1H,3H)-dione (37). This compound was prepared as a white solid following the procedure described for the preparation of **36.** Yield: 61%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.8 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.21 (m, 4H), 7.13 (m, 1H), 6.88 (m, 2H), 6.80 (t, *J* = 8.4 Hz, 2H), 5.30 (s, 2H), 4.20 (t, *J* = 6.6 Hz, 2H), 3.82 (s, 2H), 3.08 (septet, *J* = 7.2 Hz, 1H), 2.43 (t, *J* = 7.8 Hz, 2H), 1.81 (quintet, *J* = 7.2 Hz, 2H), 1.19 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.0, 162.4, 161.6, 160.8, 151.8, 147.1, 136.6 (d, *J* = 2.9 Hz), 135.3 (d, *J* = 21.8 Hz), 133.8, 129.9 (d, *J* = 7.8 Hz), 129.4, 128.9, 127.6, 127.5, 7.2 Hz), 118.3, 115.6(d, *J* = 20.7 Hz), 47.4, 45.3, 34.6, 32.3, 30.7, 29.2, 20.2; MS (ESI-) m/z: 497.58 (M-1).

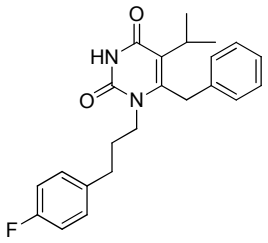


6-Benzyl-1-(4-(4-fluorophenyl)butyl)-5-isopropyl-3-(2-oxo-2-phenylethyl)pyrimidine-2,4(1H,3H)-dione (38). This compound was prepared as a white solid following the procedure described for the preparation of **36**. Yield: 63%; ^{1}HNMR (600 MHz, $CDCl_3$) δ7.93 (d, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.28 (t, *J* = 7.8 Hz), 7.21 (t, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.2 Hz, 2H), 6.96 (m, 2H), 6.84 (m, 2H), 5.35 (s, 2H), 3.92 (t, *J* = 7 .2 Hz, 2H), 3.64 (t, *J* = 7.2 Hz, 2H), 2.81 (septet, *J* = 7.2 Hz, 1H), 2.43 (t, *J* = 7.2 Hz, 2H), 1.50 (quintet, *J* = 7.2 Hz, 2H), 1.44 (quintet, *J* = 7.2 Hz, 2H), 1.20 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) 192.4, 162.3, 161.6, 160.7, 151.9, 147.2, 137.6 (d, *J* = 2.7 Hz), 135.5 (d, *J* = 18.5 Hz), 133.8, 129.9 (d, *J* = 8.0 Hz), 129.5, 128.9, 128.3, 127.6, 118.3, 115.4 (d, *J* = 20.6 Hz), 47.5, 45.5, 34.7, 29.1, 29.0, 28.8, 20.8; MS (ESI-) m/z: 511.61 (M-1).

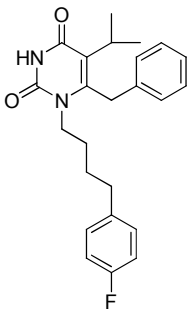


6-Benzyl-1-(4-fluorophenethyl)-5-isopropylpyrimidine-2,4(1H,3H)-dione (39). [S1] To a solution of **36** (64 mg, 0.13 mmol) in 1 mL of MeOH, was added AcOH (95 mg, 1.56 mmol) and Mg (19 mg, 0.79 mmol), The resulting mixture was stirred at rt for 30 min, TLC shows no start material left, then reaction mixture was filtered, and the filtrate was concentrated in vacuo. The residue was diluted with 5% $NaHCO_3$ (10 mL), extracted with EtOAc (10 mL x 2), combined the organic phase and dried over Na_2SO_4, then concentrated under reduced pressure. The resultant residue was purified with combiflash to give (22 mg, 48%) as white solid; ^{1}HNMR (600 MHz, $CDCl_3$) δ 8.89 (s, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.09 (d, *J* = 7.2 Hz, 2H), 7.01 (m, 2H), 6.98 (m, 2H), 3.83 (m, 4H), 2.88 (septet, *J* = 7.2 Hz, 1H), 2.79 (t, *J* = 7.8 Hz, 2H), 1.29 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ

162.8, 162.4, 161.2, 151.3, 148.8, 135.2, 133.7 (d, *J* = 3.3 Hz), 130.5 (d, *J* = 7.8 Hz), 129.6, 127.7 (d, *J* = 23.2 Hz), 119.2, 115.9 (d, *J* =21.3 Hz), 46.7, 34.7, 34.5, 28.3, 20.8; MS (ESI-) m/z: 365.43(M-1).

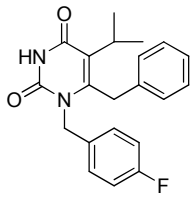


6-Benzyl-1-(3-(4-fluorophenyl)propyl)-5-isopropylpyrimidine-2,4(1H,3H)-dione (40). This compound was prepared as a white solid following the procedure described for the preparation of **39**. Yield: 53%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 9.20 (s, 1H), 7.24 (t, *J* = 7.2 Hz, 2H, 7.19 (d, *J* = 6.6 Hz, 1H), 6.97 (m, 2H), 6.89 (m, 2H), 6.84 (d, *J* = 6.6 Hz, 2H), 3.74 (s, 2H), 3.52 (t, *J* = 7.8 Hz, 2H), 2.78 (septet, *J* = 7.2 Hz, 1H), 2.48 (t, *J* = 7.2 Hz, 2H), 1.81 (quintet, *J* = 7.2 Hz, 2H), 1.21 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.6, 162.5, 160.9, 151.7, 148.6, 136.5, 135.1 (d, *J* = 3.5 Hz), 130.0 (d, *J* = 7.4 Hz), 129.4, 127.6 (d, *J* = 14.0 Hz), 119.2, 115.6 (d, *J* = 21.2 Hz), 44.4, 34.6, 32.3, 30.8, 28.8, 20.7; MS (ESI-) m/z: 379.45 (M-1).

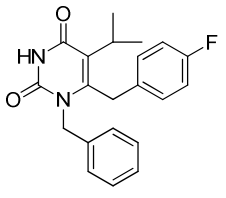


6-Benzyl-1-(4-(4-fluorophenyl)butyl)-5-isopropylpyrimidine-2,4(1H,3H)-dione (41). This compound was prepared as a white solid following the procedure described for the preparation of **39**. Yield: 57%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 9.27 (s, 1H), 7.36 (t, *J* = 7.2 Hz,

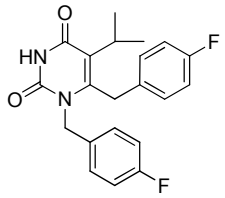
2H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 2H), 7.07 (m, 2H), 6.96 (m, 2H), 3.96 (s, 2H), 3.68 (t, *J* = 7.2 Hz, 2H), 2.84 (septet, *J* = 7.2 Hz, 1H), 3.53 (t, *J* = 7.2 Hz, 2H), 1.55 (m, 4H), 1.28 (d, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.7, 162.3, 160.7, 151.5, 148.7, 137.5 (d, *J* = 2.9 Hz), 135.4, 129.9 (d, *J* = 7.8 Hz), 129.5, 127.7(d, *J* = 17.3 Hz), 119.1, 115.4 (d, *J* = 21.2 Hz), 44.9, 34.7, 29.0, 28.8, 28.7, 20.7; MS (ESI-) m/z: 393.48 (M-1).



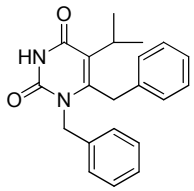
6-Benzyl-1-(4-fluorobenzyl)-5-isopropylpyrimidine-2,4(1H,3H)-dione (31). To a suspension of pyrimidine **5** (488 mg, 2 mmol) in 5 mL of anhydrous DCM, was added BSA (1.07 mL, 4.40 mmol) at room temperature under argon. The resulting mixture was stirred until a clear solution was achieved (ca. 30 min). then removed the solvent and 4-flurobenzyl bromide (0.975 mL, 6.00 mmol) and 1 mL of chlorobenzene were added followed by the addition of a catalytic amount of TBAI. The reaction mixture was stirred at rt for 10 min and then under microwave irradiation 160 ^{o}C for 1.5 h. After cooling, quenched this reaction by adding a saturated aqueous solution of $NaHCO_3$, The aqueous phase was extracted with DCM (10 mL x 3). The combined organic extracts were dried over Na_2SO_4 and concentrated under vacuum. The resultant residue was purified by combiflash (hexanes / EtOAc, 2:1) to afford (350 mg, 50 %) as white solid; ^{1}HNMR (600 MHz, $CDCl_3$) δ 8.52 (b, 1H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.26 (t, *J* = 7.8 Hz, 2H), 7.04 (m, 3H), 6.99 (t, *J* = 8.4 Hz, 2H), 4.80 (s, 2H), 3.80 (s, 2H), 2.78 (septet, *J* = 7.2 Hz, 1H), 1.22 (d, *J* = 7.2 Hz, 6H); MS (ESI-) m/z: 351.18 (M-1).



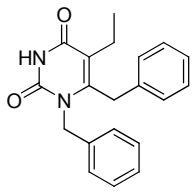
1-(4-Fluorobenzyl)-5-methylpyrimidine-2,4(1H,3H)-dione (57). This compound was prepared as a white solid following the procedure described for the preparation of **31.** Yield: 27%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 9.31 (b, 1H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 7.07 (m, 3H), 4.92 (s, 2H), 3.84 (s, 2H), 2.82 (septet, *J* = 7.2 Hz, 1H), 1.29 (d, *J* = 6.6 Hz, 6H); MS (ESI+) m/z: 353.16 (M+1).



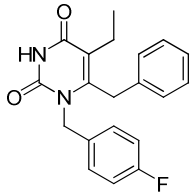
1,6-Bis(4-fluorobenzyl)-5-isopropylpyrimidine-2,4(1H,3H)-dione (58). This compound was prepared as a white solid following the procedure described for the preparation of **31.** Yield: 54%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 9.86 (b, 1H), 7.10 (dd, *J* = 3.0, 8.4 Hz, 2H), 7.06 (m, 6H), 4.88 (s, 2H), 3.84 (s, 2H), 2.82 (septet, *J* = 7.2 Hz, 1H), 1.26 (d, *J* = 6.6 Hz, 6H); MS (ESI-) m/z: 369.17 (M-1).



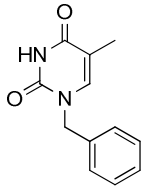
1,6-Dibenzyl-5-isopropylpyrimidine-2,4(1H,3H)-dione (59). This compound was prepared as a white solid following the procedure described for the preparation of **31**. Yield: 36% as white solid: ^{1}HNMR (600 MHz, $CDCl_3$) δ 8.19 (b, 1H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 2H), 7.11 (m, 4H), 7.05 (t, *J* = 8.4 Hz, 2H), 4.88 (s, 2H), 3.88 (s, 2H), 2.85 (septet, *J* = 7.2 Hz, 1H), 1.28 (d, *J* = 7.2 Hz, 6H); MS (ESI+) m/z: 335.18 (M+1)..



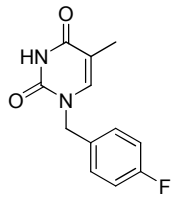
1,6-Dibenzyl-5-ethylpyrimidine-2,4(1H,3H)-dione (60). This compound was prepared as a white solid following the procedure described for the preparation of **31**. Yield: 55%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 10.28 (b, 1H), 7.33 (m, 4H), 7.39 (m, 4H), 7.07 (d, *J* = 7.2 Hz, 2H), 4.66 (s, 2H), 4.15 (s, 2H), 2.47 (q, *J* = 7.8 Hz, 2H), 1.07 (t, *J* = 7.8 Hz, 3H); MS (ESI+) m/z: 321.16 (M+1).



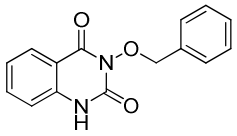
6-Benzyl-5-ethyl-1-(4-fluorobenzyl)pyrimidine-2,4(1H,3H)-dione (61). This compound was prepared as a white solid following the procedure described for the preparation of **31.** Yield: 50%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 10.12 (b, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.15 (m, 4H), 7.04 (t, *J* = 8.4 Hz, 2H), 4.87 (s, 2H), 3.86 (s, 2H), 2.48 (q, *J* = 7.2 Hz, 2H), 1.06 (t, *J* = 7.2 Hz, 3H); MS (ESI+) m/z: 339.15 (M+1).



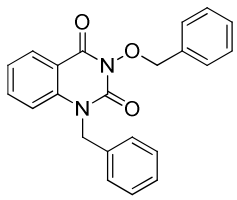
1-Benzyl-5-methylpyrimidine-2,4(1H,3H)-dione (62). This compound was prepared as a white solid following the procedure described for the preparation of **31**. Yield: 79%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 9.18 (b, 1H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 7.2 Hz, 2H), 6.97 (s, 1 H), 4.89 (s, 2H), 1.88 (s, 3 H); MS (ESI-) m/z: 215.07 (M-1).



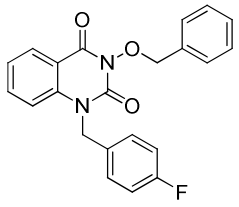
1-(4-Fluorobenzyl)-5-methylpyrimidine-2,4(1H,3H)-dione (63). This compound was prepared as a white solid following the procedure described for the preparation of **31**. Yield: 77%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 9.20 (b, 1H), 7.30 (dd, *J* = 5.4, 8.4 Hz, 2H), 7.07 (t, *J* = 8.4 Hz, 2H), 6.97 (s, 1H), 4.85 (s, 2H), 1.89 (s, 3H); MS (ESI-) m/z: 233.07 (M-1).



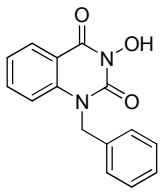
3-(Benzyloxy)quinazoline-2,4(1H,3H)-dione (72). [S2] To a solution of ortho amino ester (760 mg, 5.00 mmol) in 50 mL of toluene, was added CDI (1.02 g 6.25 mmol), This reaction mixture was refluxed for 2 hour. Then NH_2OBn (923 mg, 7.50 mmol) was added and refluxing was continued for 2 hour. This reaction mixture was concentrated and re-dissolved into 25 mL of EtOH and treated with 2 N NaOH, This reaction was heated to reflux for 2 hours and then cooled to room temperature, the desired compound was precipitated by acidification with HOAc. Then filtrated and washed the solid with water and Et_2O. Then recrystallized in MeOH to get (710 mg, 53%) as white solid; ^{1}HNMR (600 MHz, DMSO) δ 8.03 (d, *J* = 7.8 Hz, 1H), 7.74 (t, *J* = 7.2 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.49 (m, 3H), 7.30 (m, 3H), 5.16 (s, 2H); MS (ESI-) m/z: 267.27 (M-1).



1-Benzyl-3-(benzyloxy)quinazoline-2,4(1H,3H)-dione (73). [S2] To a solution of compound **72** (200 mg 0.75 mmol) in 3 mL of anhydrous DMF, was added Cs_2CO_3 (489 mg, 1.50 mmol) and benzyl bromide (153 mg, 0.90 mmol), this reaction mixture was heated at 80 ^oC for 4 hours, after cooling to room temperature, filtrated and the filtrate was washed with water and extracted with EtOAc (15 mL x 3), combined the organic phase. The organic layer was washed with aqueous 1 N HC1 (10 mL), H_2O (10 mL) and dried over Na_2SO_4, filtered, and concentrated to dryness. The residue was purified by combiflash to give (156 mg, yield 58%) as white solid. ^{1}HNMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.8 Hz, 1H), 7.58 (m, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.32 (m, 3H), 7.27 (m, 2H), 7.22 (d, *J* = 7.2 Hz, 1H), 7.19 (m, 1H), 7.13 (d, *J* = 7.2 Hz, 2H), 7.05 (d, *J* = 9.0 Hz, 1H), 5.30 (s, 2H), 5.22 (s, 2H); MS (ESI-) m/z: 358.39 (M-1).

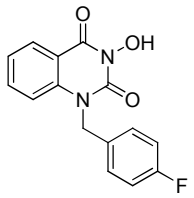


3-(Benzyloxy)-1-(4-fluorobenzyl)quinazoline-2,4(1H,3H)-dione (74). This compound was prepared as a white solid following the procedure described for the preparation of **73.** Yield: 67%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* =3.6 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.39 (m, 3H), 7.27 (s, 1H), 7.19 (m, 2H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.03 (t, *J* = 8.4 Hz, 2H), 5.32 (s, 2H), 5.28 (s, 2H); MS (ESI-) m/z: 375.38 (M-1).



Benzyl-3-hydroxyquinazoline-2,4(1H,3H)-dione (75). [S2] Compound **73** (80 mg, 0.22 mmol) was partitioned between 1 mL of 48% HBr and 1 mL of AcOH and heated to reflux

for 1 hour, after cooling to room temperature, concentrated under vacuo to give the solid which was recrystallized with MeOH to get (46 mg, yield 77%) as white solid. ^{1}HNMR (600 MHz, $CDCl_3$) δ 8.27 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.31 (m, 4H), 7.20 (d, *J* = 8.4 Hz, 1H), 5.43 (s, 2H); HRMS (ESI+) calcd. for $C_{15}H_{12}N_2O_3$ $[M+H]^+$ 269.0921, found 269.0927 (E = -2.35 ppm).



1-(4-Fluorobenzyl)-3-hydroxyquinazoline-2,4(1H,3H)-dione (76). This compound was prepared as a white solid following the procedure described for the preparation of **75**. Yield: 78%; ^{1}HNMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.25 (t, *J* = 7.8 Hz, 1H), 7.20 (m, 2H), 7.12 (d, *J* = 9.0 Hz, 1H), 7.03 (t, *J* = 8.4 Hz, 2H), 5.32 (s, 2H); HRMS (ESI+) calcd. for $C_{15}H_{11}FN_2O_3$ $[M+H]^+$ 287.0826, found 287.0826 (E = 0.16 ppm).

HPLC Analysis of Final Compounds

Table S1 HPLC Analysis of Compounds*

Compound	t_{ret} *(min)*	*Purity (%)*
63	10.63	99.2
65	10.73	98.7
61	10.68	98.6
62	8.75	98.3
64	10.63	97.7
65	11.95	97.5
53	5.81	98.8
66	5.73	98.7

67	5.01	98.4
73	7.48	96.2
72	7.83	97.0
42	9.56	98.4
43	11.5	98.8
44	10.1	97.1
28	11.6	99.8
29	9.35	97.9
30	9.33	98.0
13	9.76	97.9
12	9.41	99.4

* General conditions: reverse-phase Varian Microsorb-MW 100-5 C18 column with detection at 254 nm; solvent A = H_2O, solvent B = MeCN; flow rate = 1.0 mL/min; Method: linear 30-95% (B) over 25 min.

References

S1 Tanaka, H.; Takashima,H.; Ubasawa, M.; Sekiya, K.; Inouye, N.; Baba, M.; Shigeta, R.; Walker, T. R.; Clercq, E.; Miyasakat, T.; "Synthesis and Antiviral Activity of 6-Benzyl Analogs of 1-[(2 Hydroxyethoxy)methyl]- 6-(phenylthio)t hymine (HEPT)a s Potent and Selective Anti-HIV 1 Agents." *J. Med. Chem.* **1995***, 38,* 2860-2865.

S2 Tumey, L. N.; Bom, D.; Huck, B.; Gleason, E.; Wang, J.; Silver, D.; Brunden, K.; Boozer, S.; Rundlett, S.; Sherf, B.; Murphy, S.; Dent, T.; Leventhal, C.; Bailey, A.; Harrington, J.; Bennani, L. Y.; "The identification and optimization of a N-hydroxy urea series of flap endonuclease 1 inhibitors." *Bioorg. Med. Chem. Lett.* **2005**, *15,* 277–281.