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Supplementary Material

Synthesis of a Rhodanine-Based Compound Library Targeting Bcl-XL and Mcl-1

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Experimental Section

Chemistry. General Experimental Section

All ^{1}H NMR and ^{13}C NMR spectra were acquired on a Bruker 400 UltraShield Spectrometer operating at 400 MHz and 100 MHz respectively. The proton spectra were referenced to the respective residual solvent peaks (MeOH-d_4: 3.20; DMSO-d_6: 2.50 ppm) except for those recorded in $CDCl_3$ which were referenced to TMS. Carbon spectra were referenced to the central peak of the respective residual solvents (MeOH-d_4: 49.0; DMSO-d_6: 39.5; $CDCl_3$: 77.0 ppm). Low-resolution and high-resolution electron impact mass spectra (EIMS) were measured using a Finnigan MAT95XP double-focusing mass spectrometer. Low-resolution electrospray ionization (ESI) mass spectra were recorded using Waters Quattro Micro™ API. High resolution ESI spectra were obtained using the Agilent 6210 Time-of-Flight LC/MS. Infrared (IR) spectra were measured on a BioRad FTIR spectrophotometer with samples analyzed as KBr discs, or as thin films on a KBr plate. All elemental analyses were carried out on a EuroEA3000 series CHNS Analyzer.

Experimental Details. General Procedure for the Synthesis of *N*-substituted Rhodanines (**7a-f**)

To a solution of the chosen amino acid (typically 5 g, 30 mmol) in water (100 mL) was added NaOH (2.4 g, 2 equiv.) and CS_2 (1.81 mL, 30 mmol). The reaction mixture was stirred for 16 h at room temperature after which a solution of sodium chloroacetate (2.82 g, 30 mmol) was added. The reaction mixture was stirred for a further 3 h at room temperature, then acidified with aqueous HCl (6 N, 30 mL). The resulting solution was refluxed for 16 h, then cooled to room temperature. The crude product was extracted from the aqueous layer with ethyl acetate (3 x 50 mL), and the combined organic layer was dried with $MgSO_4$, filtered, and the solvent removed in vacuo. The products were recrystallized from ethanol-water mixtures.

2-(4-oxo-2-thioxothiazolidin-3-yl)acetic acid (**7a**). Yellow solid, 89% yield. Mp 148 ºC (lit.[1]148 ºC). ^{1}H NMR ($CDCl_3$): δ 4.16 (s, 2H, NCH_2), 4.79 (s, 2H, SCH_2).

(S)-2-(4-oxo-2-thioxothiazolidin-3-yl)propanoic acid (**7b**). Yellow solid, 90% yield. Mp 152-153 ºC. (lit.[2]152-153 ºC). ^{1}H NMR ($CDCl_3$): δ 1.61 (d, *J* = 7 Hz, 3H, CH_3), 4.00 (d, *J* = 2 Hz, 2H, CH_2), 5.68 (q, *J* = 7 Hz, 1H, NCH).

(S)-3-methyl-2-(4-oxo-2-thioxothiazolidin-3-yl)butanoic acid (**7c**). Yellow solid, 92% yield. Mp 113-115 ºC. (lit.[3]113-115 ºC). ^{1}H NMR ($CDCl_3$): δ 0.81 (d, *J* = 7 Hz, 3H, CH_3), 1.24 (d, *J* = 7 Hz, 3H, CH_3), 2.80 (m, 1H, $CH_3\underline{CH}$), 4.03 (s, 2H, SCH_2), 5.25 (d, *J* = 9 Hz, 1H NCH), 9.60 (s, 1H, CO_2H).

(S)-4-methyl-2-(4-oxo-2-thioxothiazolidin-3-yl)pentanoic acid (**7d**). Pale yellow solid, 88% yield. Mp 100 ºC. (lit.[3] 99-101 ºC). ^{1}H NMR ($CDCl_3$): δ 0.91 (d, *J* = 7 Hz, 3H, CH_3), 0.95 (d, *J* = 7 Hz, 3H, CH_3), 1.51 (m, 1H, $CH_3\underline{CH}$), 2.09 (m, 2H, $NCHCH_2$), 3.98 (s, 2H, SCH_2), 5.66 (m, 1H, NCH).

(2S,3S)-3-methyl-2-(4-oxo-2-thioxothiazolidin-3-yl)pentanoic acid (**7e**). Pale yellow solid, 80% yield. Mp 74-76 ºC. ^{1}H NMR ($CDCl_3$): δ 0.86 (t, *J* = 7 Hz, 3H, CH_3), 0.97-1.06 (m, 1H, $C\underline{H_{2a}}CH_3$), 1.19 (d, *J* = 7 Hz, 3H, $\underline{CH}CH_3$), 1.22-1.28 (m, 1H, $C\underline{H_{2b}}CH_3$), 2.55 (m, 1H, $\underline{CH}CH_3$), 4.02 (s, 2H, SCH_2), 5.31 (d, *J* = 9 Hz, 3H, NCH). ^{13}C NMR ($CDCl_3$): δ 11.0, 17.5, 25.2, 33.4, 34.5, 61.9, 173.4, 173.6, 201.0. LR-ESI(-) *m/z* (%): 246 ($[M-H]^-$, 23), 172 (100).

(S)-2-(4-oxo-2-thioxothiazolidin-3-yl)-3-phenylpropanoic acid (**7f**). Yellow solid, 89% yield. Mp 170-172 ºC.

(lit.[4]170-173 ºC). ^{1}H NMR ($CDCl_3$): δ 3.52 (d, *J* = 7 Hz, 2H, CH_2Ph), 3.77 (s, 2H, SCH_2), 5.85 (br s, 1H, NCH), 7.13- 7.25 (m, 5H) 9.65 (s, 1H, CO_2H). LR-ESI(-) *m/z* (%): 280 ([M-H]$^-$, 75).

Preparation of 2-Bromo-5-formylpyridine (**8**)

The compound was prepared following the literature procedure.[5] A suspension of 2-bromo-5-iodopyridine (3 g, 11 mmol) in dry Et_2O (100 mL) was cooled to -78 ºC prior to the addition of *n*-BuLi (2.2 M, 5.3 mL, 1.1 equiv.). The reaction mixture was stirred for 1 h at -78 ºC prior to the addition of dry DMF (1 mL). After stirring for 1 h, the reaction mixture was warmed to room temperature and quenched by the addition of dilute HCl (1 M, 20 mL). The organic layer was separated, and the aqueous layer was further extracted with Et_2O (2 x 20 mL). The ether layer was dried with $MgSO_4$, filtered, and the solvent removed in vacuo. Column chromatography on silica using a gradient (7-60% EtOAc, hexanes) yielded the pure product as a white solid (1.25 g, 64% yield). R_f (1:1 EtOAc/hexanes): 0.39. Mp 100-101ºC. (lit.[6]100ºC). ^{1}H NMR ($CDCl_3$): δ 7.69 (d, *J* = 8 Hz, 1H), 8.01 (dd, *J* = 8 Hz and 2 Hz, 1H), 8.83 (d, *J* = 2 Hz, 1H), 10.10 (s, 1H, CHO).

General Procedure for the Suzuki coupling of compound **8** to Boronic Acids **9a-d**

To a solution of **8** (0.1 g, 0.54 mmol) in 1,4-dioxane (5 mL) was added the requisite boronic acid (1.1 equiv.) and aqueous K_3PO_4 (0.23g in 1 mL H_2O, 2 equiv.). The reaction mixture was degassed for 1 min with argon before adding catalytic $Pd_2(dba)_3$ (10 mg, 2 mol%) and PCy_3HBF_4 (8 mg, 4 mol%). The reaction mixture was stirred at 100 °C for 16 h in a sealed tube. The reaction mixture was then cooled to room temperature, and the solvent was removed. The residue was partitioned between EtOAc (20 mL) and water (20 mL), and the aqueous phase was further extracted with EtOAc (2 × 20 mL). Column chromatography on silica (EtOAc/hexanes, 0-50%) yielded the desired products as white or pale yellow solids.

2-(2,3-dimethoxyphenyl)-5-formylpyridine (**10a**). Pale yellow solid (95 % yield). Mp 84 ºC.[7] ^{1}H NMR ($CDCl_3$): δ 3.72 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 7.04 (dd, *J* = 8 Hz and 2 Hz, 1H), 7.20 (t, *J* = 8 Hz, 1H), 7.44 (dd, *J* = 8 Hz and 2 Hz, 1H), 8.09 (d, *J* = 8 Hz, 1H), 8.20 (dd, *J* = 8 Hz and 2 Hz, 1H), 9.14 (d, *J* = 2 Hz, 1H), 10.14 (s, 1H). Anal ($C_{14}H_{13}NO_3$) C, H, N.

2-(3,4-methylenedioxyphenyl)-5-formylpyridine (**10b**). White solid (97 % yield). R_f (1: 3 EtOAc/hexanes): 0.33. Mp 133-138 ºC. ^{1}H NMR ($CDCl_3$): δ 6.06 (s, 2H, CH_2), 6.94 (d, *J* = 9 Hz, 1H), 7.63 (m, 2H), 7.80 (d, *J* = 9 Hz, 1H), 8.18 (dd, *J* = 8 Hz and 2 Hz, 1H), 9.06 (d, *J* = 1 Hz, 1H), 10.11 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$): δ 101.6, 107.7, 108.6, 119.8, 122.2, 129.4, 132.3, 136.4, 148.5, 149.7, 152.4, 161.5, 190.3. FTIR (cm^{-1}, KBr): 757 w, 818 m, 846 w, 895 m, 931 m, 1037 s, 1107 m, 1240 s, 1302 m, 1369 s, 1404 m, 1476 s, 1558 m, 1591 s, 1696 s. LR-ESI(+) *m/z* (%): 228 ([M+H]$^+$, 100). HR-ESI(+): Calcd 228.0655 for $C_{13}H_{10}NO_3$ [M+H]$^+$, found 228.0674. Anal ($C_{13}H_9NO_3$) C, H, N.

2-(3,4-dimethoxyphenyl)-5-formylpyridine (**10c**). Yellow crystals (77 % yield). Mp 107-108 ºC.[7] ^{1}H NMR ($CDCl_3$): δ 3.96 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 6.98 (d, *J* = 8 Hz, 1H), 7.63 (dd, *J* = 8 Hz and 2 Hz, 1H), 7.77 (d, *J* = 2 Hz, 1H), 7.86 (d, *J* = 8 Hz, 1H), 8.18 (dd, *J* = 8 Hz and 2 Hz, 1H), 9.07 (d, *J* = 2 Hz, 1H), 10.10 (s, 1H). Anal ($C_{14}H_{13}NO_3$) C, H, N.

2-(3-chloro-4-isopropoxyphenyl)-5-formylpyridine (**10d**). Colorless crystals (yield 93%). Mp 83 ºC. ^{1}H NMR ($CDCl_3$): δ1.43 (d, *J* = 6 Hz, 6H, 2 × CH_3), 4.68 (m, 1H, OCH), 7.05 (dd, *J* = 9 Hz, 1H), 7.82 (d, *J* = 8 Hz, 1H), 7.96 (dd, *J* = 8 Hz and 3 Hz, 1H), 8.15 (d, *J* = 3 Hz, 1H), 8.19 (dd, *J* = 8 Hz and 3 Hz, 1H), 9.07 (d, *J* = 2 Hz, 1H), 10.11 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 22.0, 72.0, 114.9, 119.7, 124.6, 126.9, 129.51, 129.57, 130.9, 136.5, 152.4, 155.5, 160.5, 190.3. HRMS (ESI$^+$): Calcd 276.0786 for $C_{15}H_{15}ClNO_2$ [M+H]$^+$, found 276.0785. Anal ($C_{15}H_{14}ClNO_2$) C, H, N.

General Procedure for the Knoevenagel Condensation of Aldehydes **10a-d** with Rhodanines **7a-f**

To a solution of the aldehydes **10a-d** (typically 100 mg, 0.30 mmol) in glacial acetic acid (1 to 5 mL) and sodium acetate (0.11 g, 4 equiv.) was added the desired rhodanine **7a-f** (2 equiv.). The mixture was refluxed for 3 h, then cooled to room temperature. The solvent was removed in vacuo, and aqueous HCl (1 M, 50 mL) was added and the resulting mixture was refluxed for a further 1 h. The reaction mixture was then cooled to room temperature, and the precipitate was collected via vacuum filtration. Recrystallization from hot 1 M HCl, or column chromatography on silica, gave the pure products **11a-x** (65-98% yields).

11a. Yellow powder. Mp 225-226 ºC. ^{1}H NMR (DMSO-d_6): δ 3.70 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 4.73 (s, 2H, NCH_2), 7.20 (m, 2H), 7.38 (dd, *J* = 7 Hz and 3 Hz, 1H), 7.98 (s, 1H), 8.01 (d, *J* = 8 Hz, 1H), 8.09 (dd, *J* = 8 Hz and 2 Hz, 1H), 9.01 (d, *J* = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 45.1, 55.9, 60.6, 114.1, 122.0, 125.5, 124.2, 124.7, 127.3, 130.4, 132.4, 136.7, 147.0, 152.1, 152.9, 156.5, 166.2, 167.2, 192.8. FTIR (cm^{-1}, KBr): 536 w, 584 w, 786 w, 835 w, 847 w, 1125 m, 1222 s, 1265 m, 1342 s, 1387 m, 1405 m, 1470 m, 1491 m, 1595 m, 1780 s, 2833 w, 2944 w, 2987 w. Anal ($C_{19}H_{16}N_2O_5S_2$) C, H, N, S.

11b. Orange powder. Mp 208 ºC. ^{1}H NMR (DMSO-d_6): δ 1.56 (d, J = 7 Hz, 3H, CHCH$_3$), 3.70 (s, 3H, OCH$_3$), 3.87 (s, 3H, OCH$_3$), 5.63 (q, J = 7 Hz, 1H, NCH), 7.20 (m, 2H), 7.38 (dd, J = 7 Hz and 3 Hz, 1H), 7.92 (s, 1H), 8.01 (d, J = 8 Hz, 1H), 8.06 (dd, J = 9 Hz and 2 Hz, 1H), 8.99 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 13.4, 52.9, 55.9, 60.6, 114.1, 122.0, 123.1, 124.1, 124.6, 127.3, 130.1, 132.4, 136.6, 147.0, 152.0, 152.8, 156.4, 166.0, 169.5, 192.4. FTIR (cm^{-1}, KBr): 534 w, 745 m, 1003 m, 1026 m, 1114 m, 1235 s, 1270 s, 1470 m, 1591 m, 1724 s, 1911 br w, 2916 w. LR-ESI(-) *m/z* (%):429 ([M-H]$^-$, 22), 386 (32), 271 (28), 126 (100). HR-ESI(-):Calcd. 429.0584 for $C_{20}H_{17}N_2O_5S_2$ [M-H]$^-$, found 429.0566. Anal ($C_{20}H_{18}N_2O_5S_2$) C, H, N, calculated S, 14.90; found S, 14.13.

11c. Brown-yellow solid. Mp 222-224 ºC. ^{1}H NMR (DMSO-d_6): δ 0.76 (d, J = 7 Hz, 3H, CH$_3$), 1.21 (d, J = 7 Hz, 3H, CH$_3$), 3.69 (s, 3H, OCH$_3$), 2.73 (m, 1H), 3.87 (s, 3H, OCH$_3$), 5.19 (d, J = 8 Hz, 1H), 7.19 (m, 2H), 7.38 (dd, J = 7 and 3 Hz, 1H), 7.96 (s, 1H), 8.00 (d, J = 8 Hz, 1H), 8.07 (dd, J = 8 and 2 Hz, 1H), 8.99 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 18.9, 21.6, 27.1, 55.8, 60.5, 62.1, 114.1, 122.0, 122.3, 124.1, 124.6, 127.2, 130.9, 132.4, 136.7, 147.0, 152.0, 152.8, 156.5, 166.4, 168.5, 193.0. FTIR (KBr, cm^{-1}) 3423 (br), 2971, 1722, 1609, 1478, 1248, 1029, 833, 796, 751. HRMS (ESI$^-$): Calcd 457.0897 for $C_{22}H_{21}N_2O_5S_2$ [M-H]$^-$ Found: 457.0873. Anal ($C_{22}H_{22}N_2O_5S_2$) H, N, S calculated C, 57.82; found C, 56.20.

11d. Yellow solid. Mp 167-169 ºC. ^{1}H NMR (CDCl$_3$): δ 0.95 (d, J = 6 Hz, 3H, CH$_3$), 1.00 (d, J = 6 Hz, 3H, CH$_3$), 1.57 (m, 1H), 2.16 (m, 1H), 2.30 (m, 1H), 3.71 (s, 3H, OCH$_3$), 3.93 (s, 3H, OCH$_3$), 5.78 (m, 1H, NCH), 7.03 (dd, J = 8 and 2 Hz, 1H), 7.21 (t, J = 8 Hz, 1H), 7.43 (dd, J = 8 and 2 Hz, 1H), 7.77 (s, 1H), 7.84 (dd, J = 8 and 3 Hz, 1H), 8.07 (d, J = 8 Hz, 1H), 8.88 (d, J = 3 Hz, 1H).^{13}C NMR (CDCl$_3$): δ 22.2, 23.0, 25.3, 36.9, 56.0, 56.1, 61.2, 113.9, 122.6, 124.3, 124.6, 125.6, 127.8, 129.1, 132.2, 136.6, 147.5, 151.4, 153.1, 156.6, 167.1, 172.1, 192.2. FTIR (KBr, cm^{-1}) 3440 (br), 2963, 1729, 1590, 1263, 1206, 1028, 828, 795, 749. HRMS (ESI$^-$): Calcd 471.1054 for $C_{23}H_{23}N_2O_5S_2$ [M-H]$^-$ Found: 471.1026. Anal. ($C_{23}H_{24}N_2O_5S_2$) C, H, N, S.

11e. Orange powder. Mp 129-130 ºC. ^{1}H NMR (DMSO-d_6): δ 0.80 (t, J = 7 Hz, 3H, CH$_2$CH$_3$), 0.96 (m, 1H, CH$_{2a}$CH$_3$), 1.17 (d, J = 6 Hz, 3H, CHCH$_3$), 1.24 (m, 1H, CH$_{2b}$CH$_3$), 2.51 (m, 1H, CH$_3$CH), 3.69 (s, 3H, OCH$_3$), 3.87 (s, 3H, OCH$_3$), 5.21 (d, J = 9 Hz, 1H, NCHCO$_2$H), 7.20 (m, 2H), 7.39 (dd, J = 8 Hz and 1 Hz, 1H), 7.95 (s, 1H), 8.01 (m, 1H), 8.07 (dd, J = 9 Hz, 2H), 8.99 (d, J = 2 Hz, 1H). ^{13}C NMR (CDCl$_3$): δ 11.2, 17.6, 25.3, 33.8, 56.0, 61.1, 62.0, 113.8, 122.6, 123.9, 124.6, 125.5, 127.7, 129.5, 132.4, 136.4, 147.5, 151.8, 153.1, 156.8, 167.3, 171.2, 192.2. FTIR (cm^{-1}, KBr): 548 w, 687 w, 738 w, 1001 m, 1036 m, 1094 w, 1126 m, 1236 br s, 1261 s, 1327 m, 1427 w, 1468 m, 1585 m, 1719 s, 2361 w, 2933 m, 2965 m. LR-ESI(-) *m/z* (%):471 ([M-H]$^-$, 25), 428 (65), 357 (18), 168 (100). HR-ESI(-): Calcd. 471.1054 for $C_{23}H_{23}N_2O_5S_2$ [M-H]$^-$, found 471.1038. Anal ($C_{23}H_{24}N_2O_5S_2$) C, H, N, S.

11f. Yellow solid. Mp 160-162 ºC.[7] ^{1}H NMR (CDCl$_3$): δ 3.64 (d, J = 7 Hz, 2H), 3.70 (s, 3H, OCH$_3$), 3.92 (s, 3H, OCH$_3$), 6.00 (br s, 1H, NCH), 7.03 (d, J = 8 Hz, 1H), 7.20 (m, 6H), 7.40 (d, J = 8 Hz, 1H), 7.74 (s, 1H), 7.81 (d, J = 8 Hz, 1H), 8.04 (d, J = 8 Hz, 1H), 8.88 (s, 1H). Anal. ($C_{26}H_{22}N_2O_5S_2$) C, H, N, S.

11g. Pale orange powder. Mp 281-282 ºC. ^{1}H NMR (DMSO-d_6): δ 4.76 (s, 2H, NCH$_2$CO$_2$H), 6.12 (s, 2H, OCH$_2$O), 7.06 (d, J = 8 Hz, 1H), 7.74 (d, J = 2 Hz, 1H), 7.77 (dd, J = 8 Hz and 2 Hz, 1H), 7.95 (s, 1H), 8.02 (dd, J = 9 Hz and 2 Hz, 1H), 8.09 (d, J = 9 Hz, 1H), 8.92 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 45.1, 101.6, 106.8, 108.7, 119.9, 121.7, 122.8, 127.0, 130.5, 131.7, 137.5, 148.1, 149.1, 152.2, 156.6, 166.2, 167.2, 192.7. FTIR (cm^{-1}, KBr): 739 w, 807 w, 1037 m, 1105 m, 1196 s, 1251 m, 1270 m, 1328 s, 1393 m, 1439 m, 1472 s, 1584 s, 1712 s. LR-ESI(-) *m/z* (%): 399 ([M-H]$^-$,73); 301 (91). HR-ESI(-): Calcd 399.0115 for $C_{18}H_{11}N_2O_5S_2$ [M-H]$^-$, found: 399.0104. Anal ($C_{18}H_{12}N_2O_5S_2$) C, H, N, S.

11h. Orange-brown solid. Mp 251-252 ºC. ^{1}H NMR (DMSO-d_6): δ 1.55 (d, J = 7 Hz, 3H, CH$_3$), 5.62 (q, J = 7Hz, 1H, NCHCO$_2$H), 6.12 (s, 2H, OCH$_2$O), 7.07 (d, J = 8 Hz, 1H), 7.74 (d, J = 2 Hz, 1H), 7.77 (dd, J = 8 Hz and 2 Hz, 1H), 7.89 (s, 1H), 8.01 (dd, J = 9 Hz and 1 Hz, 1H), 8.10 (d, J = 8 Hz, 1H), 8.91 (d, J = 2 Hz, 1H).^{13}C NMR (DMSO-d_6): δ 13.4, 52.9, 101.6, 106.8, 108.7, 119.9, 121.7, 122.4, 127.0, 130.2, 131.7, 137.4, 148.1, 149.1, 152.1, 156.5, 166.0, 169.5, 192.3. Anal ($C_{19}H_{14}N_2O_5S_2$) Calcd C, 55.80; H, 4.21; N, 6.17; S, 14.90. Found C, 53.04; H, 4.25; N, 6.01; S, 15.16. FTIR (cm^{-1}, KBr): 467 w, 549 w, 597 w, 636 w, 686 w, 764 w, 808 m, 846 w, 894 m, 917 m, 935 m, 1001 w, 1036 m, 1053 m, 1108 m, 1144 w, 1246 s, 1257 s, 1305 m, 1348 s, 1391 m, 1442 m, 1476 s, 1501 m, 1591 m, 1608 m, 1700 s, 1740 m.LR-ESI(-) *m/z* (%): 413 ([M-H]$^-$, 8); 249 (13); 155 (32); 123 (100); 69 (57). HRMS: Calcd 413.0271 for $C_{19}H_{13}N_2O_5S_2$ [M-H]$^-$; found 413.0286. Anal ($C_{19}H_{14}N_2O_5S_2$) C, H, N, S.

11i. Yellow solid. Mp 248 ºC. ^{1}H NMR (DMSO-d_6): δ 0.76 (d, J = 7 Hz, 3H, CH$_3$), 1.21 (d, J = 7 Hz, 3H, CH$_3$), 2.74 (m, 1H, CH(CH$_3$)$_2$), 5.18 (d, J = 7 Hz, 1H, NCHCO$_2$H) 6.12 (s, 2H, OCH$_2$O), 7.07 (d, J = 8 Hz, 1H), 7.75 (d, J = 2 Hz, 1H), 7.78 (dd, J = 8 Hz and 2 Hz, 1H), 7.94 (s, 1H), 8.03 (dd, J = 9 Hz and 2 Hz, 1H), 8.11 (d, J = 9 Hz, 1H), 8.92 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 18.9, 21.6, 27.1, 62.1, 101.6, 106.7, 108.6, 119.8, 121.5, 121.7, 126.9, 131.0, 131.6, 137.5, 148.1, 149.1, 152.2, 156.6, 166.4, 168.5, 192.9. FTIR (cm^{-1}, KBr): 547 w, 808 w, 1037 m, 1201 m, 1237 s, 1330 m, 1347 m, 1475 s, 1591 m, 1607 m, 1702 s, 1734 s, 2973 w. LR-ESI (-) *m/z* (%): 441

([M-H]$^-$, 50); 398 (100); 342 (30). HRMS: Calcd 441.0584 for $C_{21}H_{17}N_2O_5S_2$ [M-H]$^-$; found 441.0568. Anal ($C_{21}H_{18}N_2O_5S_2$) C, H, N, S.

11j. Yellow solid. Mp 233 ºC. ^{1}H NMR (DMSO-d_6): δ 0.87 (d, J = 7 Hz, 3H, CH_3), 0.92 (d, J = 7 Hz, 3H, CH_3), 1.48 (m, 1H, $\underline{CH_{2a}}$CH), 2.03 (m, 1H, $\underline{CH}(CH_3)_2$), 2.21 (m, 1H, $\underline{CH_{2b}}$CH), 5.60 (br s, 1H, N$\underline{CH}CO_2H$), 6.12 (s, 2H, OCH_2O), 7.07 (d, J = 8 Hz, 1H), 7.74 (d, J = 2 Hz, 1H), 7.76 (dd, J = 8 Hz and 2 Hz, 1H), 7.91 (s, 1H), 8.01 (dd, J = 9 Hz and 2 Hz, 1H), 8.09 (d, J = 9 Hz, 1H), 8.91 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 21.9, 22.8, 24.8, 36.3, 55.9, 101.6, 106.7, 108.6, 119.9, 121.7, 121.9, 127.0, 130.6, 131.6, 137.5, 148.1, 149.1, 152.2, 156. 6, 166.4, 169.3, 193.0. FTIR (cm^{-1}, KBr): 747 w, 813 m, 1036 s, 1226 s, 1249 s, 1268 s, 1337 s, 1390 m, 1475 s, 1593 m, 1608 m, 1699 s, 1734 br m, 2364 w, 2905 w. LR-ESI(-) *m/z* (%): 455 ([M-H]$^-$, 22); 339 (12); 325 (52); 297 (14); 243 (15); 192 (43). HR-ESI(-): Calcd 455.0741 for $C_{22}H_{19}N_2O_5S_2$ [M-H]$^-$, found 455.0724. Anal ($C_{22}H_{20}N_2O_5S_2$) C, H, N, S.

11k. Yellow-orange flakes. Mp 221-222 ºC. ^{1}H NMR (DMSO-d_6): δ 0.80 (t, J = 7 Hz, 3H, $CH_2\underline{CH_3}$), 0.95 (m, 1H, $\underline{CH_{2a}}CH_3$), 1.16 (d, J = 7 Hz, 3H, $\underline{CH}CH_3$), 1.23 (m, 1H, $\underline{CH_{2b}}CH_3$), 2.51 (m, 1H, $CH_3\underline{CH}$), 5.22 (d, J = 9 Hz, 1H, N$\underline{CH}CO_2H$), 6.12 (s, 2H, OCH_2O), 7.07 (d, J = 8 Hz, 1H), 7.74 (d, J = 2 Hz, 1H), 7.78 (dd, J = 8 Hz and 2 Hz, 1H), 7.93 (s, 1H), 8.02 (dd, J = 9 Hz and 2 Hz, 1H), 8.11 (d, J = 8 Hz, 1H), 8.92 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 10.9, 17.5, 24.9, 33.0, 61.6, 79.1, 101.6, 106.8, 108.7, 119.9, 121.5, 127.0, 131.0, 131.7, 137.6, 148.2, 149.2, 152.2, 156.6, 166.5, 168.6, 193.0. FTIR (cm^{-1}, KBr): 547 w, 583 w, 660 w, 691 w, 740 w, 808 m, 845 w, 893 w, 936 w, 958 w, 1037 m, 1102 m, 1132 m, 1201 m, 1237 s, 1305 m, 1330 m, 1347 m, 1391 m, 1440 m, 1475 s, 1501 m, 1555 w, 1591 m, 1607 m, 1702 s, 1734 m, 2363 m, 2929 m, 2973 m. LR-ESI(-) *m/z* (%): 445 ([M-H]$^-$, 33); 412 (78); 341 (22); 256 (25); 168 (75). HR-ESI(-): Calcd 455.0741 for $C_{22}H_{19}N_2O_5S_2$ [M-H]$^-$, found: 455.0739. Anal ($C_{22}H_{20}N_2O_5S_2$) C, H, N, S.

11l. Yellow powder. Mp 229 ºC. ^{1}H NMR (DMSO-d_6): δ 3.52 (d, J = 5 Hz, 2H, CH_2Ph), 5.90 (br s, 1H, N$\underline{CH}CO_2H$), 6.11 (s, 2H, OCH_2O), 7.05 (d, J = 8 Hz, 1H), 7.13-7.23 (m, 5H), 7.73 (d, J = 2 Hz, 1H), 7.76 (dd, J = 8 Hz and 2 Hz, 1H), 7.86 (s, 1H), 7.95 (dd, J = 9 Hz and 2 Hz, 1H), 8.06 (d, J = 9 Hz, 1H), 8.88 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 33.0, 58.2, 101.6, 106.7, 108.6, 119.8, 121.5, 121.7, 126.7, 126.8, 128.3, 128.9, 130.5, 131.6, 136.4, 137.5, 148.1, 149.1, 152.2, 156.6, 166.3, 168.6, 192.2. FTIR (cm^{-1}, KBr): 839 w, 1035 m, 1170 m, 1235 s, 1266 s, 1338 s, 1475 s, 1592 m, 1609 m, 1706 s, 1732 br m, 2890 w. LR-ESI(-) *m/z* (%): 489 ([M-H]$^-$, 100); 445 ([M-C_3H_8]$^-$, 85); 354 (28); 311 (43); 243 (32); 219 (16). HR-ESI(-): Calcd 489.0584 for $C_{25}H_{17}N_2O_5S_2$ [M-H]$^-$, found 489.0593. Anal ($C_{25}H_{18}N_2O_5S_2$) C, H, N, S.

11m. Orange solid. Mp 177-178 ºC (dec). ^{1}H NMR (DMSO-d_6): δ 3.84 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 4.77 (s, 2H, NCH_2), 7.10 (d, J = 8 Hz, 1H), 7.79 (m, 2H), 7.97 (s, 1H), 8.04 (dd, J = 8 Hz and 2 Hz, 1H), 8.15 (d, J = 8 Hz, 1H), 8.95 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 45.1, 55.5, 55.6, 110.0, 111.8, 120.2, 120.3, 122.9, 127.0, 129.2, 130.3, 138.0, 149.0, 151.0, 151.5, 156.3, 166.2, 167.2, 192.6. FTIR (KBr, cm^{-1}) 3445, 2939, 2843, 1722, 1586, 1516, 1332, 1201, 1058, 842, 734, 609. HRMS (ESI$^-$): Calcd 415.0428 for $C_{19}H_{15}N_2O_5S_2$ [M-H]$^-$ Found: 415.0418. Anal ($C_{19}H_{16}N_2O_5S_2$) Calcd C, 54.79; H, 3.87; N, 6.73; S, 15.40. Found C, 45.84; H, 3.72; N, 5.61; S, 12.99.

11n. Brown-yellow solid. Mp 243-244 ºC. ^{1}H NMR (DMSO-d_6): δ 1.56 (d, J = 7 Hz, 3H, CH_3), 3.83 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 5.63 (q, J = 7 Hz, 1H, NCH), 7.10 (d, J = 8 Hz, 1H), 7.77 (m 2H), 7.90 (s, 1H), 8.00 (dd, J = 8 and 2 Hz, 1H), 8.14 (d, J = 8 Hz, 1H), 8.92 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 13.4, 52.8, 55.5, 55.6, 109.9, 111.7, 119.8, 120.0, 122.2, 126.8, 129.9, 130.4, 137.4, 149.0, 150.8, 152.8, 156.9, 166.0, 169.5, 192.3. FTIR (KBr, cm^{-1}) 3424 (br), 2938, 2361, 1721, 1584, 1287, 1238, 814, 731, 669. HRMS (ESI$^-$): Calcd 429.0584 for $C_{20}H_{17}N_2O_5S_2$ [M-H]$^-$ Found: 429.0573. Anal ($C_{20}H_{18}N_2O_5S_2$) Calcd C, 55.80; H, 4.21; N, 6.51; S, 14.90. Found C, 53.04; H, 4.25; N, 6.01; S, 15.16.

11o. Brown-yellow solid. Mp 182-184 ºC. ^{1}H NMR (DMSO-d_6): δ 0.76 (d, J = 7 Hz, 3H, CH_3), 1.21 (d, J = 6 Hz, 3H, CH_3), 2.75 (m, 1H, CH), 3.84 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 5.19 (d, J = 9 Hz, 1H, NCH), 7.11 (d, J = 8 Hz, 1H), 7.78 (m, 2H), 7.95 (s, 1H), 8.04 (dd, J = 9 and 2 Hz, 1H), 8.16 (d, J = 9 Hz, 1H), 8.94 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 19.0, 21.7, 27.2, 55.5, 55.6, 62.2, 109.9, 111.8, 119.8, 120.1, 121.4, 126.8, 130.0, 131.2, 137.6, 149.0, 150.9, 152.3, 157.0, 166.5, 168.6, 193.0. FTIR (KBr, cm^{-1}) 3550 (br), 2965, 2363, 1726, 1585, 1244, 1026, 836, 737. HRMS (ESI$^-$): Calcd 457.0897 for $C_{22}H_{21}N_2O_5S_2$ [M-H]$^-$ Found: 457.0882. Anal ($C_{22}H_{22}N_2O_5S_2$) Calcd C, 57.62; H, 4.84; N, 6.11;S, 13.99. Found C, 52.40; H, 5.25; N, 5.04; S, 17.93.

11p. Yellow solid. Mp 162-164 ºC. ^{1}H NMR ($CDCl_3$): δ 0.95 (d, J = 7 Hz, 3H, CH_3), 1.00 (d, J = 7 Hz, CH_3), 1.56 (m, 1H), 2.15 (m, 1H), 2.30 (m, 1H), 3.95 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 5.80 (m, 1H, NCH), 6.97 (d, J = 9 Hz, 1H), 7.56 (dd, J = 9 Hz and 1 Hz, 1H), 7.69 (br s, 1H), 7.73 (s, 1H), 7.81 (br s, 2H), 8.82 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 22.2, 23.0, 25.2, 36.9, 56.00, 56.03, 56.1, 110.0, 111.1, 120.3, 120.4, 123.3, 127.2, 129.4, 130.4, 137.1, 149.5, 151.1, 152.0, 157.8, 167.0, 172.5, 192.1. FTIR (KBr, cm^{-1}) 3450 (br), 2959, 1722, 1584, 1275, 1208, 1025,

834, 770, 738. HRMS (ESI$^-$): Calcd 471.1054 for $C_{23}H_{23}N_2O_5S_2$ [M-H]$^-$ Found: 471.1033. Anal ($C_{23}H_{24}N_2O_5S_2$) C, H, N, S.

11q. Orange solid. Mp 157-158 ^{o}C. ^{1}H NMR (DMSO-d_6): δ 0.80 (t, J = 7 Hz, 3H, CH_3), 0.95 (m, 1H), 1.16 (d, J = 6 Hz, 3H, CH_3), 1.24 (m, 1H), 2.54 (m, 1H), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 5.24 (d, J = 9 Hz, 1H, NCH), 7.10 (d, J = 8 Hz, 1H), 7.79 (m, 2H), 7.94 (s, 1H), 8.03 (dd, J = 9 and 2 Hz, 1H), 8.15 (d, J = 9 Hz, 1H), 8.93 (d, J = 2 Hz, 1H), 13.29 (br s, 1H, CO_2H). ^{13}C NMR (DMSO-d_6): δ 10.9, 17.5, 24.8, 33.0, 55.5, 55.6, 61.6, 109.9, 111.7, 119.8, 120.1, 121.3, 126.8, 129.9, 131.2, 137.5, 149.0, 150.8, 152.3, 157.0, 166.5, 168.6, 193.0. FTIR (KBr, cm^{-1}) 3480 (br), 2963, 2361, 1716, 1583, 1235, 1026, 836, 770, 736. HRMS (ESI$^-$): Calcd 471.1054 for $C_{23}H_{23}N_2O_5S_2$ [M-H]$^-$ Found: 471.1040. Anal. ($C_{23}H_{24}N_2O_5S_2$) C, H, N, S.

11r. Orange solid. Mp 202-203 ^{o}C.[7] ^{1}H NMR (DMSO-d_6): δ 3.53 (d, J= 4 Hz, 2H, $PhCH_2$), 3.83 (s, 3H, CH_3), 3.86 (s, 3H, CH_3), 5.86 (br s, 1H, NCH), 7.09 (d, J= 8 Hz, 1H), 7.15-7.23 (m, 5H), 7.77 (m, 2H), 7.86 (s, 1H), 7.98 (dd, J= 2 and 9 Hz, 1H), 8.13 (d, J= 9 Hz, 1H), 8.90 (d, J= 2 Hz, 1H). Anal ($C_{26}H_{23}ClN_2O_5S_2$) C, H, N, S.

11s. Brown-yellow solid. Mp 236-237 ^{o}C. ^{1}H NMR (DMSO-d_6): δ 1.34 (d, J = 6 Hz, 6H, 2 × CH_3), 4.76 (s, 2H, NCH_2), 4.81 (m, 1H), 7.32 (d, J = 9 Hz, 1H), 7.97 (s, 1H), 8.06 (dd, J = 9 and 2 Hz, 1H), 8.15 (dd, J = 9 and 2 Hz, 1H), 8.18 (d, J = 9 Hz, 1H), 8.26 (d, J = 2 Hz, 1H), 8.96 (d, J = 2 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 21.8, 45.1, 71.3, 115.2, 119.9, 122.9, 123.0, 127.0, 127.3, 128.5, 130.5, 137.6, 152.3, 154.5, 155.5, 166.2, 167.3, 192.6. FTIR (KBr, cm^{-1}) 2980, 1708, 1582, 1321, 1199, 1109, 951, 812, 743, 617. HRMS (ESI$^-$): Calcd 447.0246 for $C_{20}H_{16}ClN_2O_4S_2$ [M-H]$^-$ Found: 447.0231. Anal ($C_{20}H_{17}ClN_2O_4S_2$) Calcd C, 53.51; H, 3.82; N, 6.24; S, 14.28. Found C, 52.14; H, 3.85; N, 5.82; S, 13.30.

11t. Yellow solid. Mp 182-183 ^{o}C. ^{1}H NMR (DMSO-d_6): δ1.34 (d, J = 7 Hz, 6H, 2 × CH_3), 1.56 (d, J = 7 Hz, 3H, CH_3), 4.81 (m, 1H), 5.63 (q, J = 7 Hz, 1H, NCH), 7.32 (d, J = 9 Hz, 1H), 7.91 (s, 1H), 8.04 (dd, J = 8 and 2 Hz, 1H), 8.13 (m, 2H), 8.26 (d, J = 2 Hz, 1H), 8.94 (d, J = 2 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 13.7, 22.0, 53.1, 72.1, 115.1, 120.2, 123.9, 124.7, 126.8, 127.5, 129.3, 129.4, 130.6, 137.4, 151.9, 155.4, 156.7, 166.6, 172.6, 191.4. FTIR (KBr, cm^{-1}) 2978, 2361, 1711, 1582, 1475, 1247, 1109, 950, 811, 736. HRMS (ESI$^-$): Calcd 461.0402 for $C_{21}H_{18}ClN_2O_4S_2$ [M-H]$^-$ Found: 461.0377. Anal ($C_{21}H_{19}ClN_2O_4S_2$) C, H, N, S.

11u. Yellow solid. Mp 223-225 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 0.85 (d, J = 7 Hz, 3H, CH_3), 1.29 (d, J = 6 Hz, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 2.91 (m, 1H), 4.66 (m, 1H), 5.38 (d, J = 9 Hz, 1H, NCH), 7.04 (d, J = 9 Hz, 1H), 7.73 (s, 1H), 7.78 (d, J = 8 Hz, 1H), 7.83 (dd, J = 9 and 2 Hz, 1H), 7.90 (dd, J = 8 and 2 Hz, 1H), 8.06 (d, J = 2 Hz, 1H), 8.82 (d, J = 2 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ19.1, 21.7, 22.0, 27.7, 62.4, 72.1, 115.1, 120.2, 123.6, 124.7, 126.8, 127.5, 129.35, 129.37, 130.6, 137.4, 152.0, 155.4, 156.7, 167.2, 171.9, 192.1. HRMS (ESI$^-$): Calcd: 489.0715 for $C_{23}H_{22}ClN_2O_4S_2$ [M-H]$^-$ Found: 489.0738. Anal ($C_{23}H_{23}ClN_2O_4S_2$) C, H, N, S.

11v. Yellow solid. Mp 213-216 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 0.94 (d, J = 7 Hz, 3H, CH_3). 0.99 (d, J = 7 Hz, 3H, CH_3), 1.41 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.56 (m, 1H), 2.15 (m, 1H), 2.31 (m, 1H), 4.66 (m, 1H, OCH), 5.80 (m, 1H, NCH), 7.04 (d, J = 9 Hz, 1H), 7.80 (d, J = 8 Hz, 1H), 7.72 (s, 1H), 7.82 (dd, J = 8 and 2 Hz, 1H), 7.91 (dd, J = 9 and 2 Hz, 1H), 8.08 (d, J = 2 Hz, 1H), 8.81 (d, J = 2.2 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 22.0, 22.2, 23.0, 25.2, 36.9, 56.0, 72.1, 115.1, 120.1, 123.7, 124.7, 126.7, 127.5, 129.2, 129.3, 130.6, 137.4, 151.9, 155.4, 156.7, 167.0, 172.8, 192.0. FTIR (KBr, cm^{-1}) 2962, 1720, 1584, 1475, 1281, 1208, 1107, 952, 814, 736. HRMS (ESI$^-$): Calcd 503.0872 for $C_{24}H_{24}ClN_2O_4S_2$ [M-H]$^-$ Found: 503.0897. Anal. ($C_{24}H_{25}ClN_2O_4S_2$)C, H, N, S.

11w. Yellow solid. Mp 157-159 ^{o}C. ^{1}H NMR ($CDCl_3$): δ 0.88 (t, J = 7Hz, 3H), 1.07 (m, 1H), 1.25 (d, J = 7 Hz, 3H, CH_3), 1.31 (m, 1H), 1.43 (d, J = 6 Hz, 6H, 2 × CH_3), 2.66 (m, 1H), 4.67 (m, 1H), 5.44 (d, J = 9 Hz, 1H, NCH), 7.05 (d, J = 9 Hz, 1H), 7.74 (s, 1H), 7.79 (d, J = 9 Hz, 1H), 7.83 (dd, J = 9 and 2 Hz, 1H), 7.92 (dd, J = 9 and 2 Hz, 1H), 8.07 (d, J = 2 Hz, 1H), 8.81 (d, J = 2 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 11.1, 17.6, 22.0, 25.3, 33.7, 61.9, 72.1, 115.1, 120.1, 123.5, 124.7, 126.7, 127.5, 129.3, 129.4, 130.6, 137.3, 152.0, 155.4, 156.7, 167.2, 171.8, 192.1. FTIR (KBr, cm^{-1}) 2973, 2361, 1721, 1584, 1475, 1236, 1106, 951, 813, 734, 688. HRMS (ESI$^-$): Calcd 503.0872 for $C_{24}H_{24}ClN_2O_4S_2$ [M-H]$^-$ Found: 503.0853. Anal ($C_{24}H_{25}ClN_2O_4S_2$) C, H, N, S.

11x. Yellow solid. Mp 181-183 ^{o}C. ^{1}H NMR (DMSO-d_6): δ 1.33 (d, J = 6 Hz, 6H, 2 × CH_3), 3.53 (d, J = 5 Hz, 2H), 4.78 (m, 1H, OCH), 5.90 (br s, 1H, NCH), 7.18 (m, 5H), 7.29 (d, J = 9 Hz, 1H), 7.86 (s, 1H), 7.97 (dd, J = 9 and 2 Hz, 1H), 8.10 (dd, J = 9 and 3 Hz, 1H), 8.11 (d, J = 9 Hz, 1H), 8.23 (d, J = 2 Hz, 1H), 8.89 (d, J = 3 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 21.7, 33.0, 58.2, 71.2, 115.1, 119.8, 121.7, 122.8, 126.7, 126.9, 127.1, 128.2, 128.4, 128.9, 130.4, 136.5, 137.6, 152.3, 154.5, 155.4, 166.3, 168.6, 192.2. FTIR (KBr, cm^{-1}) 2978, 1720, 1583, 1475, 1279, 1107, 950, 815, 736. HRMS (ESI$^-$): Calcd 537.0715 for $C_{27}H_{22}ClN_2O_4S_2$ [M-H]$^-$ Found: 537.0695. Anal. ($C_{27}H_{23}ClN_2O_4S_2$) C, H, N, S.

Molecular Docking

The X-ray crystal structures of Bcl-XL and Mcl-1 with the Bim-BH3 peptide were downloaded from the PDB database (PDB IDs 3DFL and 2PQK). Sequence aligments and percent identity were confirmed using the matchmaker scripts in UCSF Chimera version 1.3.[8] The 3D structures of the inhibitors were generated using ChemBio 3D Ultra followed by MMFF energy minimization. AutoDock 4.0.1 and ADT were used for generating the docking models.[9, 10] Grid maps covering the entire BH3 binding site of both proteins were used in AutoDock calculations using the standard grid spacing of 0.375 Å. The GA-LS algorithm was adopted using the default setting except for the maximum number of energy evaluations which was set to 1,000,000. For each docking job, 100 hybrid GA-LS runs were employed. A total of 100 possible binding conformations were generated and grouped into clusters using a 1.0 Å root-mean-square tolerance. The lowest energy clusters were selected to create the docking poses, and the results were analyzed using ADT.

Biology. Fluorescence Polarization Assay

The Flu-Bak-BH3 peptide was purchased from Mimotopes (Clayton, Victoria, Australia). The peptide was prepared as 1 mM stock solution in DMSO, and stock solutions of the test compounds (4 mM in DMSO) were used for serial dilutions (250 μM to 0.65μM final concentrations). The assay was carried out in a total volume of 100 μL/well containing 3 μg glutathione *S*-transferase (GST)-hBcl_{XL}ΔC19 or 3 μg glutathione *S*-transferase (GST)-hMcl-1ΔC20 and 60 nM labeled peptide in buffer (50 mM Tris, pH 8, 150 mM NaCl and 0.1% bovine serum albumin). In each well was added 10 μL of the test compounds, and the reaction mixture was incubated at room temperature for 1 h. Each compound was tested in quadruplicate. The fluorescence polarization values were determined using Tecan GeniosPro plate reader using the excitation/emission wavelengths 485/535 nm. The data was analyzed using GraphPad Prism 5 and the results were fitted to a dose-response curve to obtain the IC_{50} values and standard deviations. The K_i values were calculated using an online calculator[11] using the following parameters: [L]= 0.06 μM for Flu-Bak, [Bcl-XL]=1.1 μM, and [Mcl-1]= 1.6 μM. The dissociation constants employed were K_d (Bcl-XL)= 0.14 μM and K_d (Mcl-1)= 1.1 μM.

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