Supporting Information

Structure-Activity Relations in the Binding of Chemically Derivatized CD4 to HIV gp120

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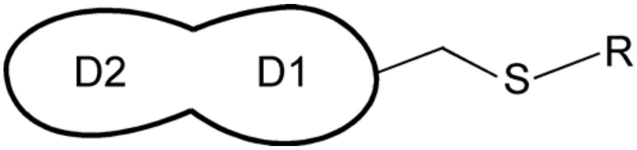
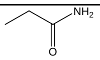
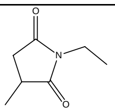
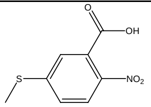
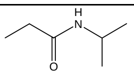
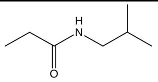
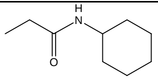
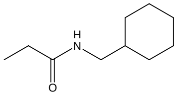
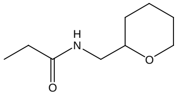
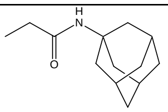
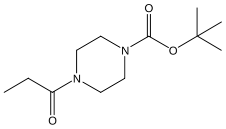
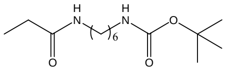
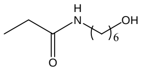
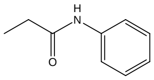
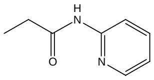
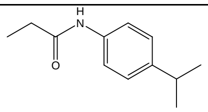
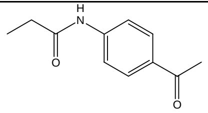
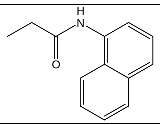
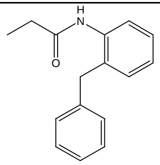
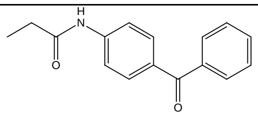
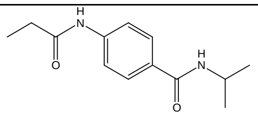
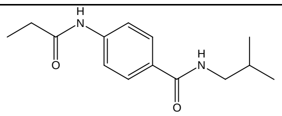
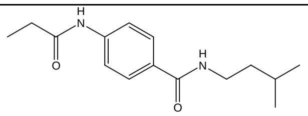
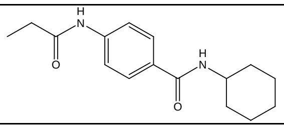
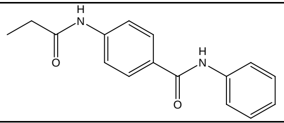
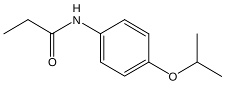
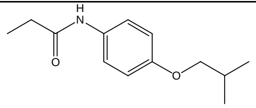
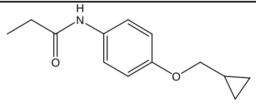
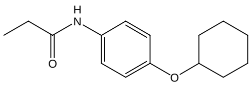
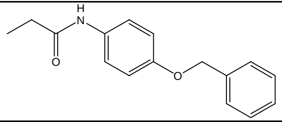
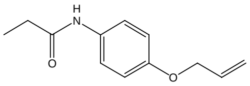
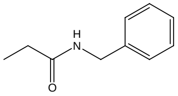
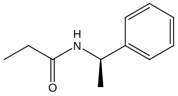
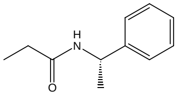
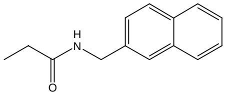
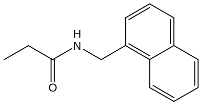
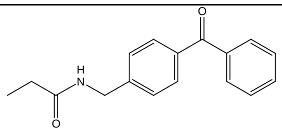
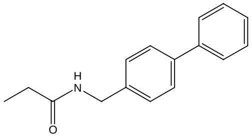
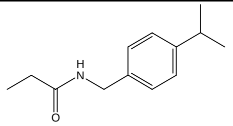
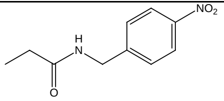
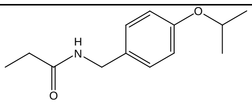
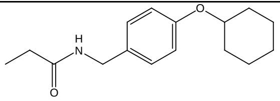
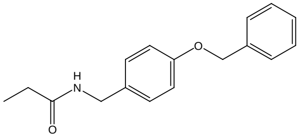
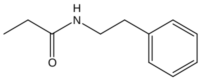
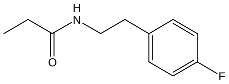
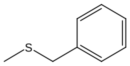
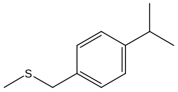
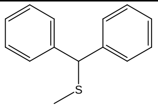
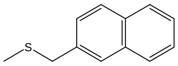
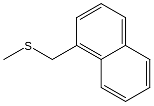
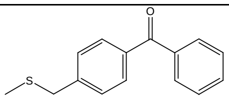
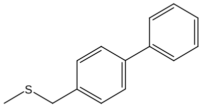
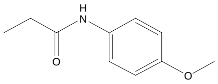
SUPPLEMENT TABLE 1. Chemical structures of modification groups (identified by compound numbers followed by their code numbers in parentheses) on D1D2F43C from all 94 cysteine modifying compounds, completeness of the modification and IC_{50} values of the correspondingly derivatized D1D2F43C in inhibiting the binding of D1D2 to YU2 gp120. All compounds designed for this study are listed including the compounds that failed to react with D1D2F43C. The correction factors for converting estimated IC_{50} to corrected IC_{50} are also listed when applicable. The IC_{50} values are presented as the mean ± SD values from two to three independent experiments. For haloacetamide compounds, the corrected IC_{50} values of their derivatives are given, whereas the measured IC_{50} values (colored in red) are used for disulfide-compound generated derivatives. N/D stands for “not determined”.

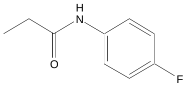
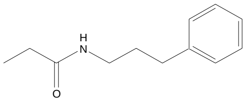
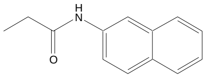
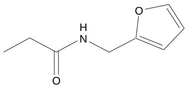
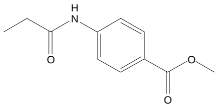
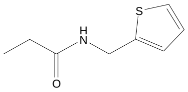
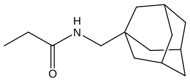
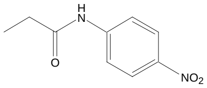
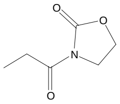
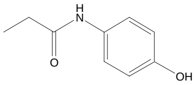
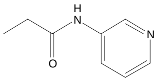
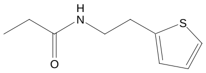
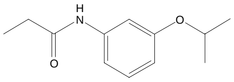
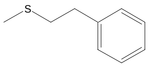


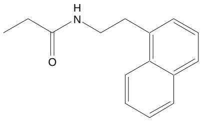
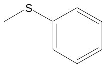
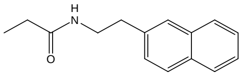
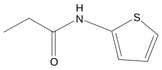
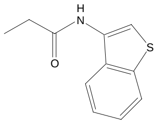
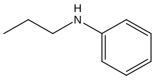
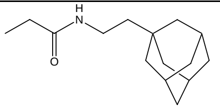
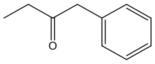
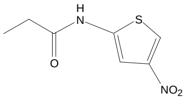
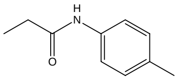
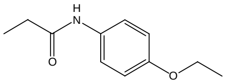
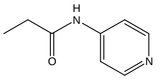
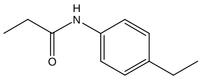
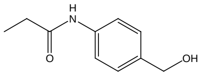
Compound	R	Completeness (%)	Correction Factor	IC_{50} ± SD of Derivatized D1D2 (nM)
Iodoacetamide		>98	0.98	33.3 ± 5.5
N-Ethylmaleimide (NEM)		>98	N/D	3220 ± 2330
DTNB		80	N/D	3580 ± 1640
1 (**SNS-1**)		>98	1.00	184 ± 39
2 (**SNS-2**)		>98	1.00	29.4 ± 2.2
3 (**SNS-3**)		>98	1.00	13.0 ± 2.1
4 (**SNS-4**)		>98	1.00	7.79 ± 2.08
5 (**SNS-5**)		>98	1.00	17.0 ± 2.5
6 (**SNS-6**)		>98	1.00	223 ± 49
7 (**SNS-7**)		>98	1.00	1860 ± 320

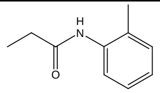
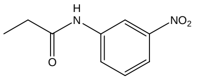
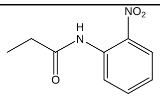
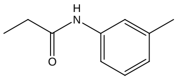
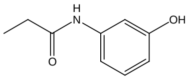
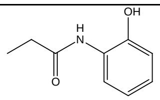
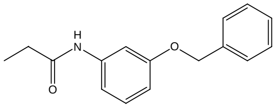
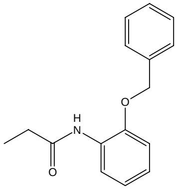
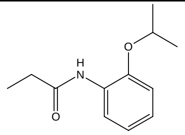
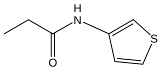
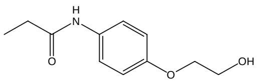
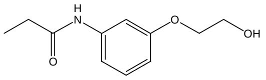
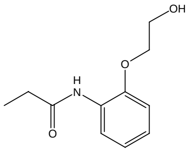
Compound	R	Completeness (%)	Correction Factor	IC$_{50}$ ± SD of Derivatized D1D2 (nM)
8 (**SNS-8**)		>98	1.00	1680 ± 500
9 (**SNS-9**)		>98	1.00	33.0 ± 9.7
10 (**SNS-10**)		>98	0.88	7.76 ± 0.83
11 (**SNS-11**)		>98	0.69	12.3 ± 0.77
12 (**SNS-12**)		>98	0.85	4.84 ± 0.83
13 (**SNS-13**)		>98	0.51	8.14 ±0.4
14 (**SNS-14**)		>98	0.75	10.4 ± 0.8
15 (**SNS-15**)		>98	1.00	51.9 ± 6.3
16 (**SNS-16**)		>98	0.52	46.2 ± 1.3
17 (**SNS-17**)		>98	0.50	402 ± 68
18 (**SNS-18**)		>98	0.59	4180 ± 2630
19 (**SNS-19**)		>98	0.56	3340 ± 510
20 (**SNS-20**)		>98	0.90	921 ± 206
21 (**SNS-21**)		>98	0.69	456 ± 89

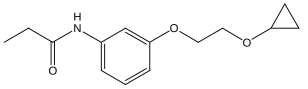
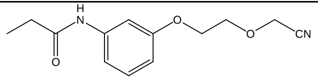
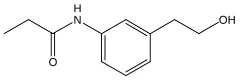
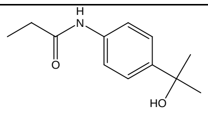
Compound	R	Completeness (%)	Correction Factor	IC_{50} ± SD of Derivatized D1D2 (nM)
22 (**SNS-22**)		>98	0.92	1500 ± 330
23 (**SNS-23**)		>98	0.91	637 ± 202
24 (**SNS-24**)		>98	0.93	764 ± 207
25 (**SNS-25**)		>98	0.95	470 ± 205
26 (**SNS-26**)		>98	0.93	290 ± 84
27 (**SNS-27**)		>98	0.92	1210 ± 340
28 (**SNS-28**)		>98	1.00	15.2 ± 0.7
29 (**SNS-29**)		>98	1.00	88.7 ± 1.5
30 (**SNS-30**)		>98	1.00	166 ± 22
31 (**SNS-31**)		>98	0.87	12.2 ± 0.8
32 (**SNS-32**)		>98	0.72	75.7 ± 11.2
33 (**SNS-33**)		>98	0.56	421 ± 9
34 (**SNS-34**)		25	N/D	N/D
35 (**SNS-35**)		>98	1.00	7.95 ± 0.09

Compound	R	Completeness (%)	Correction Factor	IC_{50} ± SD of Derivatized D1D2 (nM)
36 (**SNS-36**)		>98	0.67	14.9 ± 0.0
37 (**SNS-37**)		>98	0.94	25.7 ± 6.4
38 (**SNS-38**)		>98	0.95	350 ± 41
39 (**SNS-39**)		10	N/D	N/D
40 (**SNS-40**)		>98	1.00	10.6 ± 2.9
41 (**SNS-41**)		>98	1.00	10.6 ± 0.7
42 (**SNS-42**)		>98	N/D	11.5 ± 1.8
43 (**SNS-43**)		>98	N/D	9.14 ± 1.99
44 (**SNS-44**)		>98	N/D	1380 ± 100
45 (**SNS-45**)		>98	N/D	14.3 ± 0.6
46 (**SNS-46**)		20	N/D	N/D
47 (**SNS-47**)		90	N/D	27.0 ± 1.6
48 (**SNS-48**)		>98	N/D	14.9 ± 0.0
49 (**DN-10**)		30	0.75	N/D

Compound	R	Completeness (%)	Correction Factor	IC_{50} ± SD of Derivatized D1D2 (nM)
50 (**DN-12**)		>98	0.89	7.08 ± 1.24
51 (**DN-22**)		>98	1.00	16.4 ± 2.6
52 (**DN-26**)		25	0.78	N/D
53 (**DN-28**)		>98	1.00	18.3 ± 2.1
54 (**DN-30**)		>98	0.52	9.87 ± 0.67
55 (**DN-34**)		>98	1.00	18.8 ± 0.5
56 (**DN-40**)		>98	1.00	42.3 ± 5.9
57 (**DN-52**)		>98	0.72	4.14 ± 0.03
58 (**DN-54**)		30	N/D	N/D
59 (**DN-60**)		>98	0.75	11.4 ± 0.2
60 (**DN-64**)		0	N/D	N/D
61 (**DN-143**)		40	N/D	N/D
62 (**DN-144**)		20	N/D	N/D
63 (**DN-146**)		>98	N/D	24.7 ± 8.6

Compound	R	Completeness (%)	Correction Factor	IC$_{50}$ ± SD of Derivatized D1D2 (nM)
64 (**DN-149**)		>98	0.83	69.3 ± 1.8
65 (**DN-150**)		0	N/D	N/D
66 (**DN-152**)		80	0.85	146 ± 4
67 (**DN-155**)		>98	0.70	18.2 ± 1.8
68 (**DN-170**)		>98	0.81	13.1 ± 0.5
69 (**DN-171**)		0	N/D	N/D
70 (**DN-179**)		0	N/D	N/D
71 (**DN-180**)		>98	1.00	26.4 ± 3.9
72 (**DN-182**)		30	N/D	N/D
73 (**DN-183**)		>98	0.79	7.07 ± 1.51
74 (**DN-185**)		>98	0.75	7.23 ± 0.14
75 (**DN-187**)		>98	0.47	8.31 ± 0.07
76 (**DN-189**)		>98	0.81	5.87 ± 0.17
77 (**DN-199**)		>98	0.81	10.6 ± 3.0

Compound	R	Completeness (%)	Correction Factor	IC$_{50}$ ± SD of Derivatized D1D2 (nM)
78 (**DN-209**)		>98	0.96	24.5 ± 1.0
79 (**DN-210**)		>98	0.73	7.12 ± 1.3
80 (**DN-213**)		>98	0.80	17.8 ± 4.0
81 (**DN-218**)		>98	0.84	6.59 ± 0.89
82 (**DN-222**)		>98	0.81	9.82 ± 1.92
83 (**DN-229**)		>98	0.82	9.06 ± 0.41
84 (**DN-231**)		>98	0.97	14.3 ± 0.25
85 (**DN-234**)		>98	0.94	8.87 ± 1.09
86 (**DN-238**)		>98	0.86	12.9 ± 1.4
87 (**DN-242**)		>98	0.83	7.40 ± 1.04
88 (**DN-248**)		>98	0.74	16.4 ± 0.7
89 (**DN-260**)		>98	0.80	14.9 ± 0.4
90 (**DN-261**)		>98	0.82	17.6 ± 1.7

Compound	R	Completeness (%)	Correction Factor	IC$_{50}$ ± SD of Derivatized D1D2 (nM)
91 (**DN-263**)		>98	0.83	36.2 ± 6.5
92 (**DN-265**)		>98	0.87	22.0 ± 0.4
93 (**DN-268**)		>98	0.86	11.4 ± 0.1
94 (**DN-271**)		>98	0.88	10.9 ± 1.3

SYNTHESES AND CHARACTERIZATION OF TWO LIBRARIES OF THIOL-REACTIVE REAGENTS

General Remarks. The compound code numbers instead of compound numbers are used in this section. Please refer to table above for their concordance. All reactions were carried out under argon with HPLC grade solvents. All other commercially available materials were used as received. Reactions were monitored by thin layer chromatography (TLC) using 0.25 mm Merck pre-coated silica gel plates. Flash column chromatography was performed with the indicated solvents on silica gel-60 (particle size 0.040–0.060 µm; Merck and Silicycle). Yields refer to chromatographically and spectroscopically pure compounds, unless stated otherwise. All melting points were determined on a Thomas-Hoover apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 500 and 125 MHz, respectively, on a Brüker AMX-500 spectrometer and obtained at 298 K. Chemical shifts are reported relative to chloroform (δ 7.24 for proton and δ 77.0 for carbon-13) or the residual solvent peak of the indicated solvent. Optical rotations were obtained with a Perkin-Elmer model 241 polarimeter (Na lamp, 589 nm, 25 ˚C) in the solvent indicated. Infrared spectra were recorded with a Midac M-1200 FTIR spectrometer. High-resolution mass spectra were obtained at the University of Pennsylvania Mass Spectrometry Center on a VG micromass 70/70H high-resolution double-focusing electron impact/high-resolution mass spectrometer.

Synthesis of the First Generation Library of Bromoacetamides

1. Compounds Synthesized from Commercially Available Amines

General Procedure for Preparation of 2-Bromoanilides

Aniline (200 mg, 2.15 mmol), 2-bromo-acetic acid (299 mg, 2.15 mmol), and 1-(3-dimethylaminpropyl)-3-ethylcarbodiimide hydrochloride (EDC, 412 mg, 2.15 mmol) were combined in methylene chloride (5 mL) at 0 ˚C. The reaction mixture was warmed to ambient temperature and stirred for 1 h. The reaction mixture was then diluted with EtOAc (25 mL) and washed with 1M HCl (25 mL), saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo.

***N*-Isopropyl-2-bromo-acetamide (SNS-1).** FTIR ($CHCl_3$) 3285 (br s), 3078 (w), 3014 (w), 2972 (w), 1646 (s), 1559 (m), 1463 (w), 1419 (w), 1215 (w), 1130 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.28 (br, 1 H), 4.07 (heptet, *J* = 6.7 Hz, 1 H), 3.85 (s, 2 H), 1.19 (d, *J* = 6.7 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 42.3, 29.4, 22.4; low resolution mass spectrum (CI, CH_4) *m/z* 180 and 182 $[(M+H)^+]$; calcd for $C_5H_{11}BrNO$: 180 and 182].

***N*-Isobutyl-2-bromo-acetamide (SNS-2).** FTIR ($CHCl_3$) 3295 (br m), 3088 (br w), 2961 (m), 2929 (w), 2872 (w), 1655 (s), 1560 (m), 1467 (w), 1419 (w), 1389 (w), 1160 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.57 (br, 1 H), 3.89 (s, 2H), 3.13 (dd, *J* = 6.5 and 6.7 Hz, 2 H), 1.86–1.80 (m, 1 H), 0.94 (d, *J* = 6.7 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 47.4, 29.4, 28.3, 20.0; low resolution mass spectrum (CI, CH_4) *m/z* 194.0 and 196.0 $[(M+H)^+]$; calcd for $C_6H_{13}BrNO$: 194.0 and 196.0].

***N*-Cyclohexyl-2-bromo-acetamide (SNS-3).** FTIR ($CHCl_3$) 3283 (br m), 3075 (br w), 2938 (m), 2929 (w), 2854 (w), 1646 (s), 1558 (m), 1445 (w), 1417 (w), 1211 (w), 1190 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.33 (br, 1 H), 3.86 (s, 2 H), 3.82–3.71 (m, 1 H), 1.94–1.90 (m, 2 H), 1.74–1.70 (m, 2 H), 1.64–1.60 (m, 1 H), 1.43–1.34 (m, 2 H), 1.24–1.15 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 49.0, 32.7, 29.5, 25.4, 24.7; low resolution mass spectrum (CI, CH_4) *m/z* 220.0 and 222.0 $[(M+H)^+]$; calcd for $C_8H_{15}BrNO$: 220.0 and 222.0].

***N*-Cyclohexylmethyl-2-bromo-acetamide (SNS-4).** FTIR ($CHCl_3$) 3289 (br s), 3099 (br w), 2928 (s), 2929 (m), 1648 (s), 1569 (m), 1446 (m), 1329 (w), 1221 (w), 1161 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.54 (br, 1 H), 3.89 (s, 2 H), 3.15 (dd, *J* = 6.5 and 6.5 Hz, 2 H), 1.75–1.65 (m, 5 H), 1.52–1.48 (m, 1 H), 1.28–1.14 (m, 3 H), 0.99–0.91 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 46.3, 37.7, 30.7, 29.5, 26.3, 25.7; low resolution mass spectrum (CI, CH_4) *m/z* 234 and 236 $[(M+H)^+]$; calcd for $C_9H_{17}BrNO$: 234 and 236].

***N*-(1-Adamantyl)-2-bromo-acetamide (SNS-6).** FTIR ($CHCl_3$) 3317 (br m), 3074 (br w), 2907 (s), 2851 (m), 1653 (s), 1550 (s), 1453 (w), 1359 (w), 1308 (w), 1141 (w), 1192 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.11 (br, 1 H), 3.77 (s, 2 H), 2.10–2.08 (m, 3 H), 2.02–2.00 (m, 6 H), 1.69–1.67 (m, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0, 52.5, 41.1, 36.2, 29.8, 29.3; low resolution mass spectrum (CI, CH_4) *m/z* 272.0 and 274.0 $[(M+H)^+]$; calcd for $C_{12}H_{19}BrNO$: 272.0 and 274.0].

[6-(2-Bromo-acetylamino)-hexyl]-carbamic acid *tert*-butyl ester (SNS-8). FTIR ($CHCl_3$) 3317 (br m), 3083 (br w), 2851 (m), 1644 (s), 1610 (s), 1469 (w), 1352 (w), 1317 (w), 1192 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.53 (br, 1 H), 6.01 (br, 1 H), 3.97 (s, 2 H), 3.21 (t, *J* = 7.6 Hz, 2 H), 2.92 (t, *J* = 6.9 Hz, 2 H), 1.48-1.52 (m, 4 H), 1.22-1.27 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 159.2, 70.0, 44.2, 42.1, 37.2, 31.7, 28.7, 27.2, 26.4; low resolution mass spectrum (CI, CH_4) *m/z* 337.1 and 339.1 $[(M+H)^+]$; calcd for $C_{13}H_{26}BrN_2O_3$: 337.1 and 339.1].

2-Bromo-*N*-(6-hydroxy-hexyl)-acetamide (SNS-9). FTIR ($CHCl_3$) 3317-3150 (br m), 3044 (br w), 2854 (m), 1610 (s), 1469 (w), 1352 (w), 1317 (w), 1192 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.87 (br, 1 H), 4.05 (s, 2 H), 3.56 (t, *J* = 6.7 Hz, 2 H), 3.18 (t, J =2 H), 1.48-1.51 (m, 4 H), 1.28-1.30 (m, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 63.0, 42.3, 36.5, 33.7, 32.9, 27.2, 25.8; low resolution mass spectrum (CI, CH_4) *m/z* 238.0 and 240.0 $[(M+H)^+]$; calcd for $C_8H_{17}BrNO_2$: 238.0 and 240.0].

***N*-Phenyl-2-bromo-acetamide (SNS-10).** Mp = 129–131 ˚C; FTIR ($CHCl_3$) 3298 (m), 3204 (w), 3146 (w), 3101 (w), 1656 (s), 1608 (m), 1555 (m), 1498 (w), 1445 (m), 1336 (w), 1112 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (br s, 1 H), 7.53 (d, *J* = 7.7 Hz, 2 H), 7.36 (dd, *J* = 7.7 and 7.4 Hz, 2 H), 7.17 (t, *J* = 7.4 Hz, 1 H), 4.03 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 136.9, 129.1, 125.2, 120.0, 29.5; high resolution mass spectrum (CI) *m/z* 212.9800 $[(M)^+]$; calcd for C_8H_8BrNO: 212.9789].

***N*-(Pyridine-2-yl)-2-bromo-acetamide (SNS-11).** FTIR ($CHCl_3$) 3224 (m), 3112 (w), 3060 (w), 1684 (s), 1581 (s), 1541 (s), 1462 (w), 1432 (s), 1397 (w), 1330 (w), 1292 (w), 1276 (w), 1200 (w), 1154 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.82 (br s, 1 H), 8.32 (d, J = 4.9 Hz, 1 H), 7.74 (dd, J = 7.4 and 8.3 Hz, 1 H), 7.10 (dd, J = 4.9 and 7.4 Hz, 1 H), 4.02 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.9, 150.3, 148.0, 138.5, 120.6, 113.9, 28.9; low resolution mass spectrum (CI, CH_4) *m/z* 215 and 217 $[(M+H)^+$; calcd for $C_7H_8BrN_2O$: 215 and 217].

***N*-(4-Isopropyl-phenyl)-2-bromo-acetamide (SNS-12).** FTIR ($CHCl_3$) 3300 (br m), 3199 (w), 3132 (w), 3081 (w), 2958 (w), 2872 (w), 1669 (s), 1610 (s), 1547 (s), 1513 (m), 1414 (m), 1336 (w), 1244 (w), 1187 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (br s, 1 H), 7.43 (d, J = 8.3 Hz, 2 H), 7.21 (d, J = 8.3 Hz, 2 H), 4.01 (s, 2 H), 2.89 (heptet, J = 7.0 Hz, 1 H), 1.24 (d, J = 7.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 146.0, 134.6, 127.0, 120.3, 33.6, 29.5, 24.0; low resolution mass spectrum (CI, CH_4) *m/z* 255.0 and 277.0 $[(M)^+$; calcd for $C_{11}H_{14}BrNO$: 255.0 and 277.0].

***N*-(4-Acetyl-phenyl)-2-bromo-acetamide (SNS-13).** FTIR ($CHCl_3$) 3286 (br m), 3195 (w), 3107 (w), 1702 (m), 1653 (s), 1599 (s), 1538 (s), 1363 (w), 1334 (w), 1284 (m), 1250 (w), 1179 (m), 1164 (w) cm^{-1}; ^1H NMR (500 MHz, $CHCl_3$) δ 8.32 (br s, 1 H), 7.97 (d, J = 8.8 Hz, 2 H), 7.66 (d, J = 8.8 Hz, 2 H), 4.04 (s, 2H), 2.59 (s, 3 H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 196.8, 163.6, 141.1, 133.7, 129.7, 119.2, 29.3, 26.5; low resolution mass spectrum (CI, CH_4) *m/z* 255.0 and 277.0 $[(M)^+$; calcd for $C_{10}H_{10}BrNO_2$: 255.0 and 277.0].

***N*-(Naphthalene-1-yl)-2-bromo-acetamide (SNS-14).** FTIR ($CHCl_3$) 3254 (br m), 3051 (w), 1662 (s), 1554 (m), 1505 (w), 1393 (w), 1347 (w), 1189 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.68 (br s, 1 H), 7.96 (d, J = 7.5 Hz, 1 H), 7.90–7.86 (m, 2 H), 7.75 (d, J = 8.2 Hz, 1 H), 7.59–7.48 (m, 3 H), 4.19 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8, 134.1, 131.4, 128.9, 127.0, 126.7, 126.5, 126.2, 125.7, 120.6, 120.2, 29.9; low resolution mass spectrum (CI, CH_4) *m/z* 263.0 and 265.0 $[(M)^+$; calcd for $C_{12}H_{10}BrNO$: 263.0 and 265.0].

***N*-(2-Benzyl-phenyl)-2-bromo-acetamide (SNS-15).** FTIR ($CHCl_3$) 3268 (m), 3025 (w), 1658 (s), 1587 (w), 1539 (m), 1454 (m), 1251 (w), 1196 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.89 (br s, 1 H), 7.84 (d, J = 8.1 Hz, 1 H), 7.34–7.16 (m, 5 H), 7.36 (dd, J = 7.7 and 7.4 Hz, 2 H), 7.17 (t, J = 7.4 Hz, 1 H), 4.02 (s, 2 H), 3.89 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.5, 138.5, 135.0, 131.9, 128.9, 128.5, 127.6, 126.8, 126.0, 123.7, 38.2, 29.4; low resolution mass spectrum (CI, CH_4) *m/z* 304 and 306 $[(M+H)^+$; calcd for $C_{15}H_{15}BrNO$: 304 and 306].

***N*-(4-Benzoyl-phenyl)-2-bromo-acetamide (SNS-16).** FTIR ($CHCl_3$) 3285 (br m), 3056 (w), 1702 (m), 1653 (s), 1596 (s), 1532 (s), 1408 (w), 1318 (m), 1281 (m), 1252 (w), 1176 (w), 1151 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.33 (br s, 1 H), 7.85 (d, J = 8.7 Hz, 1 H), 7.78 (d, J = 8.1 Hz, 2 H), 7.68 (d, J = 8.7 Hz, 2 H), 7.59 (t, J = 7.3 Hz, 2 H), 7.49 (dd, J = 7.3 and 8.1 Hz, 2 H), 4.05 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 163.6, 140.7, 137.6, 134.0, 132.4, 131.6, 129.9, 128.3, 119.0, 29.3; high resolution mass spectrum (CI, CH_4) *m/z* 317.0038 $[(M)^+$; calcd for $C_{15}H_{12}BrNO_2$: 317.0051].

***N*-Benzyl-2-bromo-acetamide (SNS-28).** Mp = 105–107 ˚C; FTIR ($CHCl_3$) 3279 (s), 3071 (w), 3014 (w), 2955 (w), 1647 (s), 1556 (m), 1453 (w), 1423 (w), 1213 (w), 1005 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.28 (m, 5 H), 6.77 (br, 1 H), 4.48 (d, J = 15.2 Hz, 2 H), 3.93 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 137.2, 128.8, 127.8, 127.7, 44.2, 29.1; high resolution mass spectrum (CI) *m/z* 228.0032 $[(M+H)^+$; calcd for $C_9H_{11}BrNO$: 228.0024].

2-Bromo-*N*-(1R-phenyl-ethyl)-acetamide (SNS-29). $[\alpha]_D^{20}$ = + 42.4 (c = 0.50, $CHCl_3$); FTIR ($CHCl_3$) 3262 (s), 3068 (w), 3003 (w), 2955 (w), 1649 (s), 1572 (m), 1443 (w), 1213 (w), cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31–7.23 (m, 5 H), 6.54 (br, 1 H), 5.02 (q, J = 7.4 Hz, 1 H), 3.93 (s, 2 H), 1.61 (d, J = 7.4 Hz, 1 H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 140.9, 129.7, 128.3, 126.5, 46.4, 37.9, 22.8; low resolution mass spectrum (CI, CH_4) *m/z* 241.0 and 243.0 [$(M)^+$; calcd for $C_{10}H_{12}BrNO$: 241.0 and 243.0].

2-Bromo-*N*-(1S-phenyl-ethyl)-acetamide (SNS-30). $[\alpha]_D^{20}$ = -41.9 (*c* = 0.50, $CHCl_3$); Spectral data identical to the enantiomer **SNS-29** above.

2-Bromo-*N*-(4-nitro-benzyl)-acetamide (SNS-36). IR (thin film): 3274, 3233, 3165, 3103, 2955, 1684, 1622, 1559, 1506, 1335, 1251, 1112, 1029, 799 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 9.21 (br s, 1 H), 8.25 (d, *J* = 8.9 Hz, 2 H), 7.82 (d, *J* = 8.9 Hz, 2 H), 5.92 (s, 2 H), 4.10 (s, 2 H); ^{13}C NMR (125 MHz, acetone-d_6) δ 166.4, 145.6, 144.4, 125.7, 120.1, 58.2, 30.1; high resolution mass spectrum (CI) *m/z* 271.9785 [M^+; calcd for $C_8H_9BrN_2O_3$: 271.9797].

2. Synthesis of *N*-(4-Alkyloxy-phenyl)-2-bromoacetamides

General Procedure for Preparation of N-(4-Alkyloxy-phenyl)-2-bromo-acetamides.

4-Aminophenol (**49**, 250 mg, 2.29 mmol) was combined with di-*iso*-propylethylamine (DIEA, 597 μL, 3.44 mmol), tetrabutylammonium iodide (TBAI, 85 mg, 0.23 mmol) and 2-bromopropane (130 μL, 2.29 mmol) in DMF (3.0 mL). The reaction mixture was stirred at 60 ˚C for 8 h, then cooled to ambient temperature and diluted with CH_2Cl_2 (15 mL). The organic solution was washed with aqueous 1 N NaOH (15 mL) and then extracted with 1 M HCl (2 × 15 mL). Aqueous washings were basified with solid $NaHCO_3$ to pH 7–8, and the resulting solution was extracted with CH_2Cl_2 (2 × 15 mL). The organic layer was washed with brine (15 mL), treated with activated charcoal, filtered through a Celite® pad, and concentrated in vacuo. The amorphous residue was immediately dissolved in CH_2Cl_2 (3.0 mL) and combined with 2-bromo-acetic acid (239 mg, 1.72 mmol) and 1-ethyl-3-(3′-dimethylaminopropyl)-carbodiimide Hydrochloride (EDC, 330 mg, 1.72 mmol) at ambient temperature. The reaction mixture was stirred for 1 h, then diluted with EtOAc (25 mL) and washed with 1M HCl (25 mL), saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. Recrystallization from EtOAc/heptane gave **SNS-22** as an off-white crystalline solid in 49% yield after two steps (304 mg, 1.12 mmol).

***N*-(4-Isopropoxy-phenyl)-2-bromo-acetamide (SNS-22).** FTIR ($CHCl_3$) 3255 (br m), 2977 (w), 2930 (w), 1639 (s), 1511 (m), 1443 (m), 1351 (w), 1277 (m), 1229 (m), 1167 (w), 1116 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, *J* = 8.7 Hz, 2 H), 6.95 (d, *J* = 8.7 Hz, 2 H), 6.73 (br, 1 H), 4.94 (heptet, *J* = 6.8 Hz, 1 H), 3.58 (s, 2 H), 1.07 (d, *J* = 6.8 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 156.8, 131.0, 129.3, 116.3, 47.3, 28.0, 20.6; low resolution mass spectrum (CI, CH_4) *m/z* 272.0 and 274.0 [$(M+H)^+$; calcd for $C_{11}H_{15}BrNO_2$: 272.0 and 274.0].

***N*-(4-Isobutoxy-phenyl)-2-bromo-acetamide (SNS-23).** FTIR ($CHCl_3$) 3253 (br m), 2955 (m), 1643 (s), 1513 (s), 1448 (m), 1419 (m), 1272 (m), 1224 (m), 1147 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.7 Hz, 2 H), 6.95 (d, *J* = 8.7 Hz, 2 H), 6.65 (br, 1 H), 3.66 (s, 2H), 3.54 (d, *J* = 7.5 Hz, 2 H), 1.83–1.79 (m, 1 H), 0.93 (d, *J* = 6.7 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 156.5, 133.4, 128.9, 116.6, 57.1, 27.2, 26.6, 20.0; low resolution mass spectrum (ESI) *m/z* 308 and 310 [$(M+Na)^+$; calcd for $C_{12}H_{16}BrNNaO_2$: 308 and 310].

***N*-(4-Cyclopropylmethoxy-phenyl)-2-bromo-acetamide (SNS-24).** FTIR ($CHCl_3$) 3271 (br m), 3081 (w), 3007 (w), 1643 (s), 1513 (s), 1445 (m), 1273 (m), 1231 (m), 1156 (w), 1037 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.6 Hz, 2 H), 6.94 (d, *J* = 8.6 Hz, 2 H), 6.42 (br, 1 H), 3.67 (s, 2 H), 3.57 (d, *J* = 7.2 Hz, 2 H), 1.99–1.94 (m, 1 H), 0.45 (dd, *J* = 4.7 and 10.6 Hz, 2 H), 0.15 (dd, *J* = 4.7 and 9.9 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 156.4, 133.4, 129.4, 116.5, 54.5, 27.3, 9.5, 3.7;

low resolution mass spectrum (CI, CH_4) *m/z* 284 and 286 $[(M+H)^+$; calcd for $C_{12}H_{15}BrNO_2$: 284 and 286].

***N*-(4-Cyclohexyloxy-phenyl)-2-bromo-acetamide (SNS-25).** FTIR ($CHCl_3$) 3279 (br m), 2932 (m), 2856 (w), 1632 (s), 1512 (s), 1451 (m), 1330 (w), 1227 (m), 1057 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.7 Hz, 2 H), 6.93 (d, *J* = 8.7 Hz, 2 H), 6.63 (br s, 1 H), 4.54–4.50 (m, 1 H), 3.56 (s, 2H), 1.84–1.81 (m, 2 H), 1.75–1.72 (m, 2 H), 1.83–1.79 (m, 2 H), 1.39–1.35 (m, 2 H), 1.09–1.03 (m, 2 H), 0.93–0.89 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 156.7, 131.0, 130.0, 116.2, 55.2, 31.1, 27.9, 25.6, 25.2; low resolution mass spectrum (CI, CH_4) *m/z* 312 and 314 $[(M+H)^+$; calcd for $C_{14}H_{19}BrNO_2$: 312 and 314].

***N*-(4-Benzyloxy-phenyl)-2-bromo-acetamide (SNS-26).** FTIR ($CHCl_3$) 3285 (br m), 3030 (w), 2951 (w), 1641 (s), 1514 (s), 1443 (m), 1272 (m), 1226 (m), 1081 (w), 1028 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28–7.26 (m, 3 H), 7.20–7.18 (m, 2 H), 6.90 (d, *J* = 8.7 Hz, 2 H), 6.81 (d, *J* = 8.7 Hz, 2 H), 5.98 (br s, 1 H), 4.85 (s, 2 H), 3.68 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 156.1, 136.5, 133.5, 129.3, 128.9, 128.4, 127.6, 116.4, 53.8, 27.1; low resolution mass spectrum (CI, CH_4) *m/z* 320 and 322 $[(M+H)^+$; calcd for $C_{15}H_{14}BrNO_2$: 320 and 322].

***N*-(4-Allyloxy-phenyl)-2-bromo-acetamide (SNS-27).** FTIR ($CHCl_3$) 3285 (br m), 3030 (w), 2951 (w), 1641 (s), 1514 (s), 1443 (m), 1272 (m), 1226 (m), 1081 (w), 1028 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.6 Hz, 2 H), 6.92 (d, *J* = 8.6 Hz, 2 H), 5.84 (br, 1 H), 5.85 (ddt, *J* = 5.6, 10.1, and 17.1 Hz, 1 H), 5.16 (d, *J* = 10.1 Hz, 1 H), 5.11 (dd, *J* = 5.0 and 17.1 Hz, 1 H), 4.27 (dd, *J* = 5.0 and 5.6 Hz, 2 H), 3.67 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 156.5, 133.1, 132.0, 129.3, 118.9, 116.7, 53.2, 27.0; low resolution mass spectrum (CI, CH_4) *m/z* 270 and 272 $[(M)^+$; calcd for $C_{11}H_{12}BrNO_2$: 270 and 272].

3. Synthesis of 4-(2-Bromo-acetylamino)-*N*-alkyl-benzamides

General Procedure for Preparation of 4-(2-Bromo-acetylamino)-*N*-alkyl-benzamides

4-Aminobenzoic acid (**50**, 250 mg, 1.82 mmol) was combined with *N*-hydroxybenzotriazole (HOBt, 369 mg, 2.73 mmol) and DIEA (232 µL, 2.73 mmol) in CH_2Cl_2 (5.0 mL). After the reaction mixture was cooled to 0 ˚C, EDC (349 mg, 1.82 mmol) was added, and the solution was stirred for 3 h at 0 ˚C. The reaction mixture was diluted with EtOAc (15 mL) and extracted with 1 M HCl (2 × 15 mL). The aqueous layer was basified with solid $NaHCO_3$ to pH 7–8 and extracted with EtOAc (2 × 15 mL). The organic layer was washed with brine (15 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The solid residue was immediately dissolved in CH_2Cl_2 (2.5 mL) and combined with 2-bromo-acetic acid (253 mg, 1.82 mmol) and EDC (349 mg, 1.82 mmol) at ambient temperature. A white precipitate, which formed after stirring the reaction mixture for 1 h, was filtered, washed with large amounts of cold CH_2Cl_2, and recrystallized from MeOH-EtOAc to furnish 2-bromo-acetanilide **SNS-17** as a white solid in 73% yield after two steps (290 mg, 1.33 mmol).

4-(2-Bromo-acetylamino)-*N*-isopropyl-benzamides (SNS-17). FTIR (KBr) 3285 (br m), 2974 (w), 1670 (s), 1624 (s), 1526 (s), 1404 (w) cm^{-1}; ^1H NMR (500 MHz, MeOH-d_4) δ 7.80 (d, *J* = 8.8 Hz, 2 H), 7.67 (d, *J* = 8.8 Hz, 2 H), 4.19 (heptet, *J* = 6.6 Hz, 1 H), 3.98 (s, 2 H), 1.24 (d, *J* = 6.6 Hz, 6 H), ($N\underline{H}$ protons were not observed in MeOH-d_4 solvent); ^{13}C NMR (125 MHz, MeOH-d_4); ^{13}C NMR (125 MHz, MeOH-d_4) δ 168.7, 167.8, 142.5, 131.7, 129.2, 120.3, 43.1, 29.6, 22.6; high resolution mass spectrum (CI, CH_4) *m/z* 298.0304 $[(M)^+$; calcd for $C_{12}H_{15}BrN_2O_2$: 298.0317].

4-(2-Bromo-acetylamino)-*N*-isobutyl-benzamides (SNS-18). FTIR (KBr) 3299 (br s), 2956 (w), 1681 (s), 1632 (s), 1520 (m), 1400 (w), 1267 (w), 1154 (w) cm^{-1}; ^1H NMR (500 MHz, MeOH-d_4) δ 7.81

(d, J = 8.7 Hz, 2 H), 7.67 (d, J = 8.7 Hz, 2 H), 3.98 (s, 2H), 3.18 (d, J = 7.1 Hz, 2 H), 1.94–1.88 (m, 1 H), 0.95 (d, J = 6.7 Hz, 6 H), (*N<u>H</u>* protons were not observed in MeOH-*d*$_4$ solvent); ^{13}C NMR (125 MHz, MeOH-*d*$_4$); ^{13}C NMR (125 MHz, MeOH-*d*$_4$) δ 169.6, 167.8, 142.6, 131.6, 129.2, 120.4, 48.5, 29.8, 29.6, 20.6; low resolution mass spectrum (CI, CH_4) *m/z* 313.0 and 315.0 [(M+H)$^+$; calcd for $C_{13}H_{18}BrN_2O_2$: 313.0 and 315.0].

4-(2-Bromo-acetylamino)-*N*-isoamyl-benzamides (SNS-19). FTIR (KBr) 3369 (br m), 3303 (br m), 3043 (w), 2959 (w), 1683 (s), 1626 (s), 1531 (m), 1431 (w), 1406 (w), 1307 (w), 1256 (w), 1157 (w) cm^{-1}; ^{1}H NMR (500 MHz, MeOH-*d*$_4$) δ 7.79 (d, J = 8.8 Hz, 2 H), 7.67 (d, J = 8.8 Hz, 2 H), 3.98 (s, 2 H), 3.38 (t, J = 7.5 Hz, 2 H), 1.69–1.63 (m, 1 H), 1.50 (dt, J = 7.2 and 7.5 Hz, 2 H), 0.95 (d, J = 6.6 Hz, 6 H), (*N<u>H</u>* protons were not observed in MeOH-*d*$_4$ solvent); ^{13}C NMR (125 MHz, MeOH-*d*$_4$); ^{13}C NMR (125 MHz, MeOH-*d*$_4$) δ 169.4, 167.8, 142.5, 131.6, 129.2, 120.4, 39.3, 29.6, 27.1, 22.9; low resolution mass spectrum (CI, CH_4) *m/z* 327 and 329 [(M+H)$^+$; calcd for $C_{14}H_{20}BrN_2O_2$: 327 and 329].

4-(2-Bromo-acetylamino)-*N*-cyclohexyl-benzamides (SNS-20). FTIR (KBr) 3290 (br s), 3036 (w), 2987 (w), 1653 (s), 1598 (m), 1544 (s), 1436 (m) cm^{-1}; ^{1}H NMR (500 MHz, MeOH-*d*$_4$) δ 7.92 (d, J = 8.3 Hz, 2 H), 7.75 (d, J = 8.3 Hz, 2 H), 4.12 (s, 2 H), 3.42 (quintet, J = 9.2 Hz, 1 H), 1.65 – 1.51 (m, 10 H), (*N<u>H</u>* protons were not observed in MeOH-*d*$_4$ solvent); ^{13}C NMR (125 MHz, MeOH-*d*$_4$); ^{13}C NMR (125 MHz, MeOH-*d*$_4$) δ 170.2, 165.4, 145.7, 131.5, 128.2, 119.7, 45.6, 37.2, 33.3, 27.1, 21.9; low resolution mass spectrum (CI, CH_4), 338.1 and 340.1 [(M)$^+$; calcd for $C_{15}H_{19}BrN_2O_2$: 338.1 and 340.1].

4-(2-Bromo-acetylamino)-*N*-phenyl-benzamides (SNS-21). FTIR (KBr) 3302 (br s), 3048 (w), 1645 (s), 1601 (m), 1531 (s), 1443 (m), 1330 (w) cm^{-1}; ^{1}H NMR (500 MHz, MeOH-*d*$_4$) δ 7.93 (d, J = 8.7 Hz, 2 H), 7.73 (d, J = 8.7 Hz, 2 H), 7.67 (d, J = 8.5 Hz, 2 H), 7.35 (dd, J = 7.4 and 8.5 Hz, 2 H), 7.13 (t, J = 7.4 Hz, 1 H), 3.99 (s, 2H), (*N<u>H</u>* protons were not observed in MeOH-*d*$_4$ solvent); ^{13}C NMR (125 MHz, MeOH-*d*$_4$) δ 168.1, 167.9, 142.9, 139.9, 131.8, 129.8, 129.7, 125.6, 122.4, 120.4, 29.6; low resolution mass spectrum (CI, CH_4) *m/z* 334 and 336 [(M+H)$^+$; calcd for $C_{15}H_{14}BrN_2O_2$: 334 and 336].

4. Synthesis of *N*-(4-Alkyloxy-benzyl)-2-bromoacetamides

General Procedure for Preparation of *N*-(4-Alkyloxy-benzyl)-2-bromo-acetamides 4-Cyanophenol (51, 250 mg, 2.10 mmol) was combined with K_2CO_3 (1.04 g, 10.5 mmol), tetrabutylammonium iodide (78 mg, 0.21 mmol) and 2-bromopropane (197 μL, 2.10 mmol) in DMF (3.0 mL). The reaction mixture was heated at 100 ˚C for 3 h, then cooled to ambient temperature and diluted with CH_2Cl_2 (15 mL). The organic solution was washed with aqueous 1 N NaOH (15 mL) and brine (15 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The oily residue was dissolved in THF (3.0 mL) and treated with alane-*N*,*N*-dimethylamine complex in toluene (0.5 M, 4.20 mL) for 1 h at ambient temperature. The reaction mixture was quenched with 1N NaOH (ca. 0.5 mL) and extracted with CH_2Cl_2 (10 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was added as a CH_2Cl_2 solution (1.5 mL) to a pre-combined (ca. 10 min) mixture of 2-bromoacetic acid (220 mg, 1.58 mmol) and EDC (303 mg, 1.58 mmol) in CH_2Cl_2 (2.0 mL) at 0 ˚C. The reaction mixture was warmed to ambient temperature, stirred for 1 h, and then diluted with EtOAc (25 mL) and washed with 1M HCl (25 mL), saturated aqueous $NaHCO_3$ (25 mL) and brine (25 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. Flash chromatography (35% EtOAc in hexanes) and recrystallization from EtOAc/heptane furnished 2-bromo-acetamide SNS-37 as a white crystalline solid in 39% yield after three steps (176 mg, 0.82 mmol).

***N*-(4-Isopropoxy-benzyl)-2-bromo-acetamide (SNS-37).** FTIR ($CHCl_3$) 3339 (br s), 2976 (w), 2930 (w), 1640 (s), 1602 (s), 1509 (m), 1432 (w), 1371 (w), 1266 (m), 1245 (m), 1181 (w), 1123 (m), 1015 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.7 Hz, 2 H), 6.86 (d, *J* = 8.7 Hz, 2 H), 6.72 (br, 1 H), 4.53 (heptet, *J* = 6.9 Hz, 1 H), 4.41 (d, *J* = 5.6 Hz, 2 H), 3.91 (s, 2 H), 1.33 (d, *J* = 6.9 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 157.6, 129.2, 129.1, 116.1, 70.0, 43.8, 29.2, 22.0; low resolution mass spectrum (CI, CH_4) *m/z* 286 and 288 [(M+H)$^+$; calcd for $C_{12}H_{17}BrNO_2$: 286 and 288].

***N*-(4-Cyclohexyloxy-benzyl)-2-bromo-acetamide (SNS-38).** FTIR ($CHCl_3$) 3288 (br s), 3071 (w), 2935 (s), 2857 (m), 1652 (s), 1612 (w), 1536 (m), 1510 (s), 1448 (w), 1357 (w), 1298 (w), 1239 (s), 1174 (w), 1049 (m), 1022 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 6.69 (br, 1 H), 4.40 (d, *J* = 5.7 Hz, 2 H), 4.25–4.20 (m, 1 H), 3.91 (s, 2 H), 3.82–3.71 (m, 1 H), 1.99–1.96 (m, 2 H), 1.83–1.79 (m, 2 H), 1.57–1.48 (m, 2 H), 1.41–1.29 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 157.5, 129.2, 129.0, 116.3, 75.5, 43.8, 31.8, 29.2, 25.6, 23.7, 22.0; high resolution mass spectrum (CI, CH_4) *m/z* 348.0578 [(M+H)$^+$; calcd for $C_{15}H_{20}BrNNaO_2$: 348.0575].

***N*-(4-Benzyloxy-benzyl)-2-bromo-acetamide (SNS-39).** FTIR ($CHCl_3$) 3295 (br s), 2907 (w), 1642 (s), 1544 (s), 1512 (s), 1429 (w), 1380 (w), 1240 (s), 1175 (m), 1110 (w), 1009 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.0 Hz, 2 H), 7.39 (dd, *J* = 7.0 and 7.6 Hz, 2 H), 7.33 (t, *J* = 7.6 Hz, 1 H), 7.22 (d, *J* = 8.6 Hz, 2 H), 6.96 (d, *J* = 8.6 Hz, 2 H), 6.74 (br, 1 H), 5.07 (s, 2 H), 4.42 (d, *J* = 5.7 Hz, 2 H), 3.91 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 158.4, 136.8, 129.6, 129.2, 128.6, 128.0, 127.4, 115.2, 70.1, 43.7, 42.6, 29.1; low resolution mass spectrum (CI, CH_4) *m/z* 334 and 336 [(M+H)$^+$; calcd for $C_{16}H_{17}BrNO_2$: 334 and 336].

5. Bromoacetamides SNS-5, SNS-31, SNS-32, SNS-33, SNS-34, SNS-35, SNS-40, and SNS-41

General Procedure for the Gabriel Synthesis of the Required Amines

The alkyl bromide was combined with potassium phthallidamide (**52**, 1.5 equiv.) and dissolved in dry DMSO (0.5 M final concetration of alkyl bromide), followed by addition of TBAI (0.1 equiv.). The reaction mixture was stirred for 5 h, then diluted with EtOAc. The organic phase was successively washed with 1M HCl, saturated $NaHCO_3$ solution, brine, dried over $MgSO_4$, and concentrated in vacuo. The obtained product was dissolved in absolute EtOH (0.5 M), followed by careful addition of anhydrous hydrazine (1.5 equiv.). The flask was then heated to 60 °C for 3 h. Upon cooling to room temperature, the resulting solid was filtered off and washed with cold EtOH. The obtained amine was coupled with bromoacetic acid using the EDC coupling protocol described above.

***N*-(Tetrahydropyran-2-ylmethyl)-2-bromo-acetamide (SNS-5).** FTIR ($CHCl_3$) 3290 (br s), 3097 (br w), 2938 (m), 2848 (w), 1648 (s), 1569 (w), 1436 (w), 1208 (w), 1093 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.83 (br, 1 H), 4.01–3.97 (m, 1 H), 3.87 (s, 2 H), 3.59–3.52 (m, 1 H), 3.46–3.38 (m, 2 H), 3.12–3.06 (m, 1 H), 1.86–1.83 (m, 1 H), 1.61–1.45 (m, 4 H), 1.33–1.25 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 75.9, 68.4, 44.6, 29.1, 29.0, 25.8, 22.9; low resolution mass spectrum (CI, CH_4) *m/z* 236 and 238 [(M+H)$^+$; calcd for $C_8H_{15}BrNO_2$: 236 and 238].

***N*-(Naphthalene-2-ylmethyl)-2-bromo-acetamide (SNS-31).** FTIR ($CHCl_3$) 3276 (br s), 3052 (w), 2929 (w), 1647 (s), 1549 (m), 1416 (w), 1205 (w), 1123 (w), 1029 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CHCl_3$) δ 7.85–7.81 (m, 4 H), 7.74 (s, 1 H), 7.52–7.47 (m, 2 H), 6.85 (br, 1 H), 4.64 (d, *J* = 5.9 Hz, 2 H), 3.96 (s, 2 H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 165.3, 134.7, 133.3, 132.9, 128.7, 127.8, 127.7, 126.5, 126.4, 126.1, 125.7, 44.0, 29.2; high resolution mass spectrum (CI) *m/z* 278.0190 [(M+H)$^+$; calcd for $C_{13}H_{13}BrNO$: 278.0164].

***N*-(Naphthalene-1-ylmethyl)-2-bromo-acetamide (SNS-32).** FTIR ($CHCl_3$) 3282 (br s), 3042 (w), 1640 (s), 1542 (m), 1471 (w), 1419 (w), 1203 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.9 Hz, 1 H), 7.90 (d, *J* = 8.0 Hz, 1 H), 7.85 (d, *J* = 6.4 Hz, 1 H), 7.59–7.52 (m, 2 H), 7.46–7.43 (m, 2 H), 6.71 (br, 1 H), 4.93 (d, *J* = 5.5 Hz, 2 H), 3.93 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 133.8, 132.5, 131.3, 128.9, 128.8, 126.8, 126.7, 126.7, 126.1, 125.3, 123.1, 42.3, 29.0; low resolution mass spectrum (CI) *m/z* 278 and 280 $[(M+H)^+$; calcd for $C_{13}H_{13}BrNO$: 278 and 280].

***N*-(4-Phenyl-benzyl)-2-bromo-acetamide (SNS-34).** FTIR ($CHCl_3$) 3288 (br s), 1638 (s), 1542 (s), 1406 (w), 1265 (m), 1027 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59–7.57 (m, 4 H), 7.45 (dd, *J* = 7.5 and 7.9 Hz, 2 H), 7.38–7.36 (m, 3 H), 6.85 (br, 1 H), 4.54 (d, *J* = 5.9 Hz, 2 H), 3.95 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 140.8, 140.6, 136.2, 128.8, 128.2, 127.6, 127.4, 127.1, 43.9, 29.1; low resolution mass spectrum (CI, CH_4) *m/z* 304 and 306 $[(M+H)^+$; calcd for $C_{15}H_{15}BrNO$: 304 and 306].

***N*-(4-Isopropyl-benzyl)-2-bromo-acetamide (SNS-35).** FTIR ($CHCl_3$) 3289 (br s), 3053 (w), 3015 (w), 2957 (m), 2973 (w), 1648 (s), 1548 (s), 1458 (w), 1419 (w), 1362 (w), 1207 (w), 1059 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23–7.22 (m, 4 H), 6.73 (br, 1 H), 4.44 (d, *J* = 5.7 Hz, 2 H), 3.92 (s, 2 H), 2.91 (heptet, *J* = 6.9 Hz, 1 H), 1.25 (d, *J* = 6.9 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 148.6, 134.5, 127.8, 126.8, 44.0, 33.8, 29.1, 23.9; low resolution mass spectrum (CI, CH_4) *m/z* 270 and 272 $[(M+H)^+$; calcd for $C_{12}H_{17}BrNO$: 270 and 272].

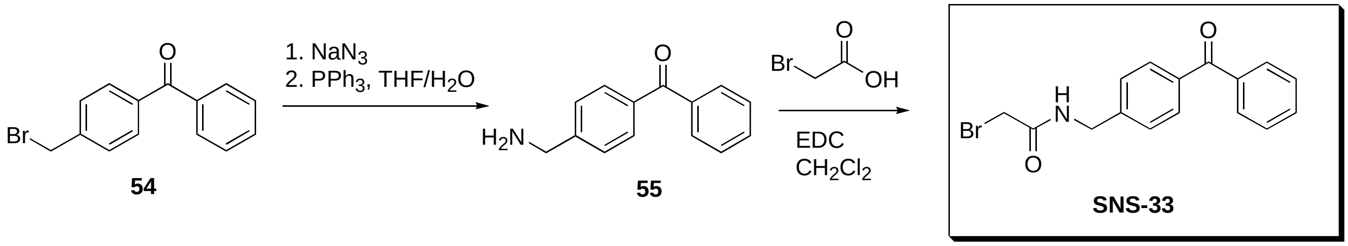
***N*-Phenethyl-2-bromo-acetamide (SNS-40).** FTIR ($CHCl_3$) 3289 (br s), 3085 (w), 3029 (w), 2934 (w), 2863 (w), 1655 (s), 1550 (s), 1496 (m), 1454 (w), 1364 (w), 1311 (w), 1212 (m), 1129 (w), 1030 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 7.4 and 8.0 Hz, 2 H), 7.25 (t, *J* = 8.0 Hz, 1 H), 7.21 (d, *J* = 7.4 Hz, 2 H), 6.49 (br, 1 H), 3.85 (s, 2 H), 3.55 (dt, *J* = 6.1 and 6.9 Hz, 2 H), 2.85 (t, *J* = 6.9 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 138.3, 128.8, 128.7, 126.7, 41.3, 35.4, 29.2; low resolution mass spectrum (CI, CH_4) *m/z* 242 and 244 $[(M+H)^+$; calcd for $C_{10}H_{13}BrNO$: 242 and 244].

***N*-(4-Fluorophenethyl)-2-bromo-acetamide (SNS-41).** FTIR ($CHCl_3$) 3331 (br s), 2937 (w), 1640 (s), 1540 (s), 1508 (s), 1438 (w), 1402 (w), 1296 (w), 1262 (m), 1219 (m), 1190 (w), 1156 (w), 1049 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.6 Hz, 2 H), 7.01 (dd, *J* = 8.6 and 8.6 Hz, 2 H), 6.59 (br, 1 H), 3.85 (s, 2 H), 3.54 (dt, *J* = 6.3 and 7.1 Hz, 2 H), 2.83 (t, *J* = 7.1 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 171.8 (J_{CF} = 244.9 Hz), 133.9, 130.2 (J_{CF} = 7.8 Hz), 115.5 (J_{CF} = 21.3 Hz), 42.6, 34.7, 29.2; low resolution mass spectrum (CI, CH_4) *m/z* 260 and 262 $[(M+H)^+$; calcd for $C_{10}H_{12}BrFNO$: 260 and 262].

6. Piperazine Derivative SNS-7

4-Bromoacetyl-piperazine-1-carboxylic acid *tert*-butyl ester (SNS-7). Piperidine (250 mg, 2.90 mmol) dissolved in 5.0 mL MeOH was cooled to -78 °C, followed by addition of $(Boc)_2O$ (576 mg, 2.64 mmol) in MeOH (1.0 M). The solution was warmed to room temperature over 1 h, after which the reaction mixture was poured into EtOAc. The organic layer was washed successively with saturated $NaHCO_3$ solution, water, and brine, dried over $MgSO_4$, and concentrated in vacuo. The product was coupled to bromoacetic acid utilizing EDC as described above to provide **SNS-7** in 61% yield (2 steps). FTIR ($CHCl_3$) 3083 (br w), 2851 (m), 1647 (s), 1616 (s), 1474 (w), 1369 (w), 1309 (w), 1183 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CHCl_3$) 4.13 (s, 2 H), 3.35 – 3.23 (m, 8 H), 1.42 (s, 9 H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 169.8, 156.2, 72.2, 50.4, 46.7, 35.2, 28.7; low resolution mass spectrum (CI, CH_4) *m/z* 306.1 and 308.1 $[(M)^+$; calcd for $C_{11}H_{19}BrN_2O_3$: 306.1 and 308.1].

7. Benzophenone Derivative SNS-33



***N*-(4-Benzoyl-benzyl)-2-bromo-acetamide (SNS-33).** A round bottom flask was charged with (4-Bromomethyl-phenyl)-phenyl-methanone (**54,** 250 mg, 0.91 mmol), tetrabutyl ammonium iodide (10 mol%) and NaN_3 (89 mg, 1.36 mmol) and dissolved in 3 mL of DMSO. The resulting clear solution was stirred at room temperature for 8 h. The reaction mixture was then poured into saturated $NaHCO_3$ solution, extracted 3 x with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The azide was subjected to the Staudinger reaction without further purification.

The resulting residue was dissolved in 0.25 mL H_2O and 0.50 mL MeOH, followed by addition of PPh_3 (357 mg, 1.36 mmol). The reaction was stirred for 8 h, then poured into 1M HCl, extracted with EtOAc. The aqueous layer is then basified with sat. $NaHCO_3$ and extracted 5 x with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to provide benzylic amine **55**.

Amine **55** was subjected to the EDC coupling protocol described above to provide **SNS-33** in 35% yield (3 steps). FTIR ($CHCl_3$) 3297 (br m), 3062 (br w), 1657 (s), 1607 (m), 1538 (m), 1413 (w), 1317 (m), 1279 (s), 1177 (w) 1027 (w) cm^{-1}; ^1H NMR (500 MHz, $CHCl_3$) δ 7.80–7.77 (m, 5 H), 7.59 (t, *J* = 7.5 Hz, 1 H), 7.48 (dd, *J* = 7.5 and 7.9 Hz, 2 H), 7.41 (d, *J* = 7.4 Hz, 1 H), 6.90 (br, 1 H), 4.58 (d, *J* = 6.0 Hz, 2 H), 3.96 (s, 2H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 196.2, 165.5, 141.9, 137.5, 137.1, 132.5, 130.6, 130.0, 128.3, 127.4, 43.5, 29.0; low resolution mass spectrum (CI) *m/z* 332 and 334 [$(M+H)^+$; calcd for $C_{16}H_{15}BrNO_2$: 332 and 334].

Synthesis of the Second Library of Bromoacetamides

Two methods for the synthesis of the requisite bromoacetamides were employed (Supplemental Scheme 8): (**A**) Acylation with bromoacetyl bromide and (**B**) Amide coupling reaction mediated by EDC. General procedures for each method, along with the method employed and full characterization data for each compound are given below.

Method A: Acylation with bromoacetyl bromide

Bromoacetyl bromide (1.1 equiv.) was dissolved in anhydrous CH_2Cl_2 (0.5 M) and the reaction mixture was cooled in an ice bath. Triethylamine (1.2 equiv.) was added, followed by addition of the corresponding amine (1.0 equiv., dissolved in minimum amount of CH_2Cl_2). The reaction mixture was stirred at 0 ^oC for 1 h, and then allowed to warm to room temperature. Water was added and the aqueous layer was extracted with 4x CH_2Cl_2. The combined organic layer was washed with 5% HCl, water, saturated $NaHCO_3$, and brine. After the organic layer was dried over $MgSO_4$, the solvent was removed in vacuo and the product was purified by flash chromatography.

Method B: Amide formation with bromoacetic acid and EDC

Bromoacetic acid (1.1 equiv.) was dissolved in anhydrous CH_2Cl_2 (0.5 M) and the reaction mixture was cooled in an ice bath. 1-ethyl-3-(3′-dimethylaminopropyl)-carbodiimide hydrochloride (EDC, 1.1 equiv) was added as a neat solid, and the mixture was stirred at 0 °C until complete dissolution was achieved. The corresponding amine or aniline (1.0 equiv.) was added, followed by the addition of 2,6-lutidine (1.0 equiv.). After the reaction mixture was stirred at room temperature for 20 h, ethyl acetate and saturated $NaHCO_3$ solution were added. The organic layer was washed with additional saturated $NaHCO_3$, brine and dried over $MgSO_4$. After the solvent was removed, the residue was purified by flash chromatography.

1. Compounds Synthesized from Commercially Available Amines

2-Bromo-*N*-(4-methoxy-phenyl)-acetamide (DN-10). Method **A**, Yield: 59%; M.p. 125-126 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.43 (d, *J* = 8.9 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 4.02 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 157.0, 129.9, 122.0, 114.2, 114.1, 55.4, 29.5; IR (thin film): 3291, 2955, 1662, 1540, 1512, 1283, 1253, 1179, 1030, 828 cm^{-1}; high resolution mass spectrum (CI) *m/z* 242.9911 [M$^+$; calcd for $C_9H_{10}BrNO_2$: 242.9895].

2-Bromo-*N*-(4-fluoro-phenyl)-acetamide (DN-12). Method **A**, Yield: 52%; M.p. 133-136 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (br s, 1H), 7.47-7.50 (m, 2H), 7.02-7.06 (m, 2H), 4.01 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4, 160.8, 158.9, 132.9, 122.00, 121.93, 115.9, 115.7, 29.3; IR (thin film): 3270, 3220, 3162, 3103, 1652, 1621, 1566, 1506, 1431, 1407, 1209, 1109, 836 cm^{-1}; high resolution mass spectrum (CI) *m/z* 230.9702 [M$^+$; calcd for C_8H_7BrFNO: 230.9695].

2-Bromo-*N*-(3-phenyl-propyl)-acetamide (DN-22). Method **A**, Yield: 59%; M.p. 43-45 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15-7.31 (m, 5H), 6.51 (br s, 1H), 3.85 (s, 2H), 3.33 (q, *J* = 7.0 Hz, 2H), 2.67 (t, *J* = 7.5 Hz, 2H), 1.89 (quintet, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 141.0, 128.5, 128.3, 126.1, 39.8, 33.1, 30.7, 29.3; IR (thin film): 3287, 3087, 3025, 2936, 2861, 1653, 1559, 1453, 1310, 1211, 748, 699 cm^{-1}; high resolution mass spectrum (CI) *m/z* 256.0346 [(M+H)$^+$; calcd for $C_{11}H_{15}BrNO$: 256.0337].

2-Bromo-*N*-naphthalen-2-yl-acetamide (DN-26). Method **A**, Yield: 84%; M.p. 122-125 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (br s, 1H), 8.20 (d, *J* = 2.0 Hz, 1H), 7.80-7.84 (m, 3H), 7.42-7.51 (m, 3H), 4.09 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.5, 134.3, 133.6, 131.0, 129.0, 127.8, 127.6, 126.7, 125.5, 119.6, 117.1, 29.5; IR (thin film): 3289, 1681, 1654, 1583, 1558, 1360, 824, 742 cm^{-1}; high resolution mass spectrum (CI) *m/z* 262.9946 [M$^+$; calcd for $C_{12}H_{10}BrNO$: 262.9946].

2-Bromo-*N*-furan-2-ylmethyl-acetamide (DN-28). Method **A**, Yield: 64%; M.p. 70-72 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.37 (m, 1H), 6.83 (br s, 1H), 6.32-6.33 (m, 1H), 6.25 (d, *J* = 3.2 Hz, 1H), 4.47 (d, *J* = 5.6 Hz, 2H), 3.89 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 150.2, 142.5, 110.5, 107.9, 37.1, 28.9; IR (thin film): 3280, 3085, 1647, 1559, 1435, 1196, 1079, 1021, 746 cm^{-1}; high resolution mass spectrum (CI) *m/z* 217.9823 [(M+H)$^+$; calcd for $C_7H_9BrNO_2$: 217.9817].

4-(2-Bromo-acetylamino)-benzoic acid methyl ester (DN-30). Method **A**, Yield: 62%; M.p. 144-146 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (br s, 1H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 8.8 Hz, 2H), 4.03 (s, 2H), 3.90 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 163.7, 141.0, 130.8, 126.5, 119.0, 52.1, 29.3; IR (thin film): 3269, 3197, 3128, 3079, 2951, 1717, 1683, 1602, 1544, 1436, 1410, 1278, 1178, 1110, 1016, 798, 769 cm^{-1}; high resolution mass spectrum (CI) *m/z* 270.9832 [M$^+$; calcd for $C_{10}H_{10}BrNO_3$: 270.9844].

2-Bromo-*N*-thiophen-2-ylmethyl-acetamide (DN-34). Method **A**, Yield: 38%; M.p. 76-77 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.24-7.26 (m, 1H), 6.96-7.00 (m, 2H), 6.86 (br s, 1H), 4.63 (d, *J* = 5.6 Hz, 2H), 3.89 (s, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 165.1, 139.6, 127.0, 126.4, 125.5, 38.9, 28.9; IR (thin film): 3249, 3074, 3023, 1668, 1635, 1559, 1425, 1214, 1159, 1134, 1039, 851, 826, 696 cm^{-1}; high resolution mass spectrum (CI) *m/z* 233.9599 [(M+H)$^+$; calcd for C_7H_9BrNOS: 233.9588].

2-Bromo-*N*-tricyclo[3.3.1.10,0]dec-1-ylmethyl-acetamide (DN-40). Method **A**; Yield: 57%; M.p. 128-129 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.56 (br s, 1H), 3.91 (s, 2H), 2.98 (d, *J* = 6.3 Hz, 2H), 1.98 (s, 3H), 1.71 (d, *J* = 12.2 Hz, 3H), 1.62 (d, *J* = 11.8 Hz, 3H), 1.49 (s, 6H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 165.3, 51.6, 40.1, 36.8, 33.7, 29.7, 28.1; IR (thin film): 3340, 2900, 2846, 1645, 1553, 1448 cm^{-1}; high resolution mass spectrum (CI) *m/z* 285.0718 [M$^+$; calcd for $C_{13}H_{20}BrNO$: 285.0728].

2-Bromo-*N*-(4-nitro-phenyl)-acetamide (DN-52). Method **A**; Yield: 67%; M.p. 164-166 °C. ^{1}H NMR (500 MHz, acetone-d$_6$) δ 10.03 (br s, 1H), 8.23 (d, *J* = 9.2 Hz, 2H), 7.91 (d, *J* = 9.2 Hz, 2H), 4.10 (s, 2H); ^{13}C NMR (125 MHz, acetone-d$_6$) δ 166.4, 145.6, 144.4, 125.7, 120.1, 30.1; IR (thin film): 3274, 3233, 3165, 3103, 2955, 1684, 1622, 1559, 1506, 1335, 1251, 1112, 1029, 799 cm^{-1}; high resolution mass spectrum (CI) *m/z* 257.9647 [M$^+$; calcd for $C_8H_7BrN_2O_3$: 257.9640].

3-Bromoacetyl-oxazolidin-2-one (DN-54).[i] Method **A** (modified according to Ref. 1); Yield: 70%; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.03 (br s, 1H), 4.51 (s, 2H), 4.48 (t, *J* = 7.8 Hz, 2H), 4.07 (t, *J* = 8.3 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 166.0, 153.0, 62.5, 42.7, 27.6; IR (thin film): 2970, 1773, 1701, 1476, 1391, 1366, 1340, 1220, 1163, 1112, 1037, 959, 887, 759 cm^{-1}; high resolution mass spectrum (CI) *m/z* 206.9532 [M$^+$; calcd for $C_5H_6BrNO_3$: 206.9531].

2-Bromo-*N*-(4-hydroxy-phenyl)-acetamide (DN-60). Method **A** (DMF was used in place of CH_2Cl_2). Yield: 53%; M.p. 145-147 °C. ^{1}H NMR (500 MHz, acetone-d$_6$) δ 9.29 (br s, 1H), 8.21 (s, 1H), 7.45 (d, *J* = 8.9 Hz, 2H), 6.78 (d, *J* = 8.9 Hz, 2H), 3.98 (s, 2H); ^{13}C NMR (125 MHz, acetone-d$_6$) δ 164.6, 154.7, 131.6, 121.8, 115.8, 30.2; IR (thin film): 3310, 1662, 1545, 1516, 1439, 1258, 1173, 1106, 965, 832, 801 cm^{-1}; high resolution mass spectrum (CI) *m/z* 228.9744 [M$^+$; calcd for $C_8H_8BrNO_2$: 228.9738].

2-Bromo-*N*-pyridin-3-yl-acetamide (DN-64). Method **B**; Yield: 7%; ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.65 (d, *J* = 2.6 Hz, 1H), 8.44 (dd, *J* = 4.8 and 1.4 Hz, 1H), 8.29 (br s, 1H), 8.16 (ddd, *J* = 8.3, 2.5 and 1.5 Hz, 1H), 7.33 (dd, *J* = 8.4 and 4.8 Hz, 1H), 4.23 (s, 2H); high resolution mass spectrum (CI) *m/z* 214.9818 [(M+H)$^+$; calcd for $C_7H_8BrN_2O$: 214.9820].

2-Bromo-*N*-(2-thiophen-2-yl-ethyl)-acetamide (DN-143). Method **A**; Yield: 64%; M.p. 66-68 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.18 (dd, *J* = 5.2 and 1.1 Hz, 1H), 6.96-6.97 (m, 1H), 6.87 (d, *J* = 3.4 Hz, 1H), 3.87 (s, 2H), 3.58 (q, *J* = 6.5 Hz, 2H), 3.07 (t, *J* = 6.7 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 165.3, 140.5, 127.1, 125.5, 124.1, 41.4, 29.5, 29.1; IR (thin film): 3287, 3078, 2933, 1653, 1559, 1437, 1213, 697 cm^{-1}; high resolution mass spectrum (CI) *m/z* 247.9750 [(M+H)$^+$; calcd for $C_8H_{11}BrNOS$: 247.9745].

2-Bromo-*N*-(3-isopropoxy-phenyl)-acetamide (DN-144). Method **A**; Yield: 81%; M.p. 80-82 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.05 (br s, 1H), 7.21-7.24 (m, 2H), 6.98 (dd, *J* = 8.0 and 1.1 Hz, 1H), 6.69 (dd, *J* = 8.3 and 2.3 Hz, 1H), 4.56 (septet, *J* = 6.1 Hz, 1H), 4.01 (s, 2H), 1.33 (d, *J* = 6.1 Hz, 6H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 163.3, 158.6, 138.1, 129.8, 112.8, 112.0, 107.7, 70.1, 29.5, 22.0; IR (thin film): 3295, 2976, 1670, 1597, 1555, 1491, 1446, 1280, 1207, 1156, 1116, 773 cm^{-1}; high resolution mass spectrum (CI) *m/z* 271.0209 [M$^+$; calcd for $C_{11}H_{14}BrNO_2$: 271.0208].

2-Bromo-*N*-*p*-tolyl-acetamide (DN-183). Method **A**; Yield: 71%; M.p. 141-142 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.10 (br s, 1H), 7.40 (d, *J* = 8.3 Hz, 2H), 7.15 (d, *J* = 8.3 Hz, 2H), 4.01 (s, 2H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 134.9, 134.3, 129.5, 120.1, 29.4, 20.8; IR (thin film): 3292, 3200, 3135, 1652, 1611, 1553, 1511, 1431, 1105, 816 cm^{-1}; high resolution mass spectrum (CI) *m/z* 226.9942 [M$^+$; calcd for $C_9H_{10}BrNO$: 226.9946].

2-Bromo-*N*-pyridin-4-yl-acetamide (DN-187). Method **A**; Yield: 76%[ii]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 4.7 and 1.6 Hz, 2H), 8.30 (br s, 1H), 7.51 (dd, *J* = 4.8, 1.6 Hz, 2H), 4.03 (s, 2H); high resolution mass spectrum (CI) *m/z* 214.9816 [(M+H)$^+$; calcd for $C_7H_8BrN_2O$: 214.9820].

2-Bromo-*N*-(4-ethyl-phenyl)-acetamide (DN-189). Method **A**; Yield: 78%; M.p. 137-138 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (br s, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.4 Hz, 2H), 4.01 (s, 2H), 2.63 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 141.3, 134.5, 128.4, 120.2, 29.4, 28.3, 15.5; IR (thin film): 3293, 3197, 3135, 2956, 1652, 1615, 1549, 1513, 1430, 1414, 1107, 835 cm^{-1}; high resolution mass spectrum (CI) *m/z* 241.0100 [M$^+$; calcd for $C_{10}H_{12}BrNO$: 241.0102].

2-Bromo-*N*-*o*-tolyl-acetamide (DN-209). Method **A**; Yield: 68%; M.p. 107-109 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (br s, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.10-7.26 (m, 3H), 4.06 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 134.9, 130.5, 129.2, 126.8, 125.8, 122.5, 29.7, 17.5; IR (thin film): 3258, 3024, 2915, 1652, 1540, 1420, 1317, 1197 cm^{-1}; high resolution mass spectrum (CI) *m/z* 226.9947 [M$^+$; calcd for $C_9H_{10}BrNO$: 226.9946].

2-Bromo-*N*-(3-nitro-phenyl)-acetamide (DN-210). Method **A**; Yield: 58%; M.p. 110-112 °C. ^{1}H NMR (500 MHz, acetone-d_6) δ 9.91 (br s, 1H), 8.67 (s, 1H), 7.88-8.00 (m, 2H), 7.52-7.64 (m, 1H) ; ^{13}C NMR (125 MHz, acetone-d_6) δ 165.3, 148.5, 139.8, 130.0, 125.1, 118.4, 113.8, 29.1; IR (thin film): 3307, 3104, 1679, 1601, 1528, 1431, 1349, 1096 cm^{-1}; high resolution mass spectrum (CI) *m/z* 257.9648 [M$^+$; calcd for $C_8H_7BrN_2O_3$: 257.9640].

2-Bromo-*N*-(2-nitro-phenyl)-acetamide (DN-213). Method **A**; Yield: 56%; M.p. 67-68 °C. ^{1}H NMR (500 MHz, acetone-d_6) δ 8.50-8.52 (m, 1H), 8.20-8.22 (m, 1H), 7.76-7.80 (m, 1H), 7.36-7.39 (m, 1H), 4.26 (s, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 165.0, 138.1, 135.3, 133.3, 125.5, 124.4, 122.6, 29.5; IR (thin film): 3339, 3295, 3014, 1684, 1607, 1586, 1545, 1503, 1436, 1344, 1275, 1146, 789, 745 cm^{-1}; high resolution mass spectrum (CI) *m/z* 257.9644 [M$^+$; calcd for $C_8H_7BrN_2O_3$: 257.9640].

2-Bromo-*N*-*m*-tolyl-acetamide (DN-218). Method **A**; Yield: 56%; M.p. 79-81 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 7.36 (s, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 4.00 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 139.0, 136.8, 128.9, 126.0, 120.7, 117.1, 29.5, 21.4; IR (thin film): 3291, 3153, 3099, 1666, 1616, 1558, 1490, 1438, 1323, 1202, 782, 691 cm^{-1}; high resolution mass spectrum (CI) *m/z* 226.9939 [M$^+$; calcd for $C_9H_{10}BrNO$: 226.9946].

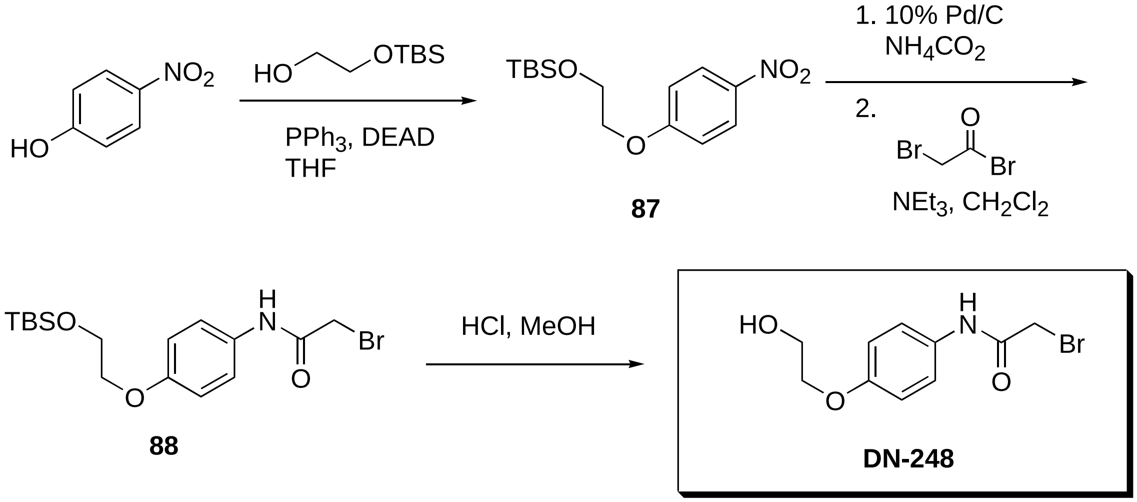
2-Bromo-*N*-(3-hydroxy-phenyl)-acetamide (DN-222). Method **A** (DMF used in place of CH_2Cl_2). Yield: 52%; M.p. 168-170 °C. ^{1}H NMR (500 MHz, acetone-d_6) δ 9.37 (br s, 1H), 8.32 (s, 1H), 7.33 (t, *J* = 2.1 Hz, 1H), 7.11 (t, *J* = 8.1 Hz, 1H), 7.01-7.03 (m, 1H), 6.57-6.59 (m, 1H), 3.99 (s, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 164.4, 157.7, 139.8, 129.5, 111.0, 110.5, 106.6, 29.5; IR (thin film): 3307 (br), 1669, 1616, 1554, 1496, 1452, 1279, 1206, 1157, 862, 774, 687 cm^{-1}; high resolution mass spectrum (CI) *m/z* 228.9758 [M$^+$; calcd for $C_8H_8BrNO_2$: 228.9738].

2-Bromo-*N*-(2-hydroxy-phenyl)-acetamide (DN-229). Method **A** (DMF used in place of CH_2Cl_2). Yield: 50%; M.p. 125-127 °C. ^{1}H NMR (500 MHz, acetone-d_6) δ 9.19 (br s, 1H), 8.96 (s, 1H), 7.89-7.90 (m, 1H), 6.97-7.01 (m, 1H), 6.91-6.93 (m, 1H), 6.82-6.85 (m, 1H), 4.19 (s, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 164.9, 147.2, 126.3, 125.1, 121.0, 119.8, 116.0, 29.2; IR (thin film): 3359, 3307 (br), 1648, 1619, 1592, 1554, 1459, 1369, 1282, 1228, 1196, 1108, 751, 744 cm^{-1}; high resolution mass spectrum (CI) *m/z* 228.9736 [M$^+$; calcd for $C_8H_8BrNO_2$: 228.9738].

***N*-(3-Benzyloxy-phenyl)-2-bromo-acetamide (DN-231).** Method **A**; Yield: 67%; M.p. 126-127 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (br s, 1H), 7.30-7.45 (m, 6H), 7.24 (t, *J* = 8.1 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.78-6.80 (m, 1H), 5.06 (s, 2H), 4.00 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4, 159.3, 138.1, 136.7, 129.8, 128.5, 128.0, 127.5, 112.4, 111.8, 106.7, 70.0, 29.5; IR (thin film): 3255, 3208, 3145, 3087, 1668, 1612, 1443, 1273, 1171, 1017, 976, 845, 789 cm^{-1}; low resolution mass spectrum (CI) *m/z* 319.0 [M$^+$; calcd for $C_{15}H_{14}BrNO_2$: 319.0].

***N*-(2-Benzyloxy-phenyl)-2-bromo-acetamide (DN-234).** Method **A**; Yield: 58%; M.p. 115-118 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.95 (br s, 1H), 8.34-8.37 (m, 1H), 7.35-7.48 (m, 5H), 6.90-7.15 (m, 3H), 5.14 (s, 2H), 4.00 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.0, 147.5, 136.2, 128.6, 128.3, 127.4, 127.3, 124.6, 121.4, 119.6, 111.7, 70.9, 29.7; IR (thin film): 3294, 3019, 1665, 1596, 1543, 1497, 1459, 1443, 1286, 1264, 1220, 1117, 1047, 751, 727 cm^{-1}; high resolution mass spectrum (CI) *m/z* 319.0208 [M$^+$; calcd for $C_{15}H_{14}BrNO_2$: 319.0217].

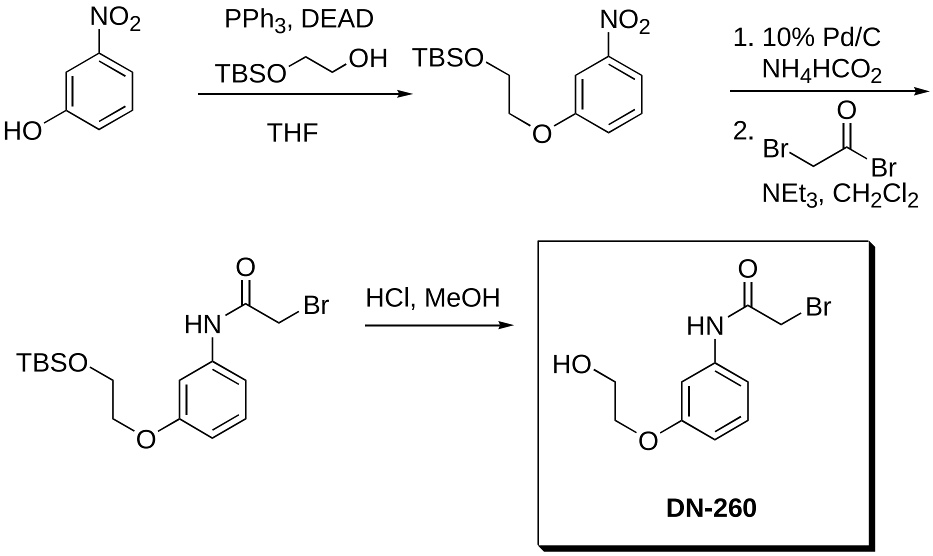
2. Synthesis of *N*-(Alkyloxy-phenyl)-2-bromoacetamides



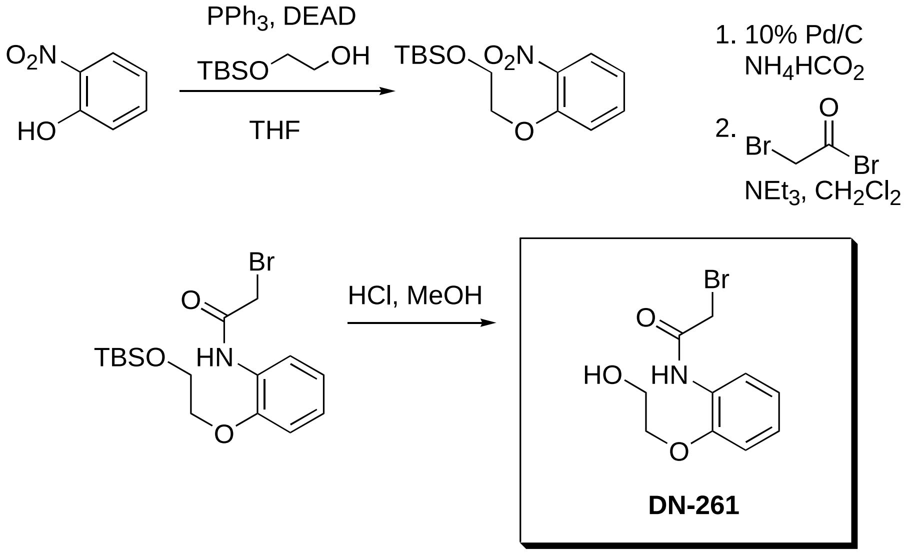
2-Bromo-*N*-[4-(2-hydroxy-ethoxy)-phenyl]-acetamide (DN-248). A round bottom flask was changed with 4-nitrophenol (300 mg, 2.16 mmol), 2-(*tert*-butyldimethylsilyloxy)ethanol[iii] (380 mg, 2.16 mmol), PPh_3 (848 mg, 3.24 mmol) and anhydrous THF (6 mL). Diethyl azodicarboxlate (DEAD) (0.513 mL, 3.24 mmol) was added dropwise and the resulting mixture was stirred at room temperature for 20 h. The solvent was removed in vacuo and the crude product was purified by flash chromatography (20% EtOAc in hexanes) to give 350 mg (55%) of **87**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 9.3 Hz, 2H), 6.97 (d, *J* = 9.3 Hz, 2H), 4.14 (t, *J* = 5.2 Hz, 2H), 4.00 (t, *J* = 4.7 Hz, 2H), 0.90 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0, 141.5, 125.8, 114.5, 70.1, 61.6, 25.8, 18.3, -5.3.

To a round bottom flask flushed with argon was added 10% Pd/C (100 mg) and 3 mL of MeOH. Compound **87** (300 mg, 1.01 mmol) dissolved in 2 mL of MeOH was added, followed by addition of NH_4HCO_2 (293 mg, 4.65 mmol). After the reaction mixture was stirred for 15 min at room temperature, TLC analysis showed complete consumption of the starting material. The reaction mixture was filtered through Celite and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$ and concentrated. The residue was dissolved in anhydrous CH_2Cl_2 (1 mL) and added dropwise to a mixture of bromoacetyl bromide (0.175 mL, 2.02 mmol), Et_3N (0.31 mL, 2.22 mmol) and CH_2Cl_2 (4 mL) at 0 °C. After the mixture was stirred for 1 h at 0 °C and 1 h at room temperature, water was added and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with saturated $NaHCO_3$ and brine. After drying over $MgSO_4$, the solvent was evaporated and the product was purified by flash chromatography to give 250 mg (64%) of bromoacetamide **88**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (br s, 1H), 7.40-7.45 (m, 2H), 6.85-6.90 (m, 2H), 4.00-4.05 (m, 4H), 3.92-4.00 (m, 2H), 0.91 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 156.4, 129.9, 121.9, 114.9, 69.6, 62.0, 29.5, 25.9, 18.4, -5.2.

To a flask containing **88** (250 mg, 0.64 mmol) and MeOH (5 mL) was added 1N HCl (1 mL). The mixture was stirred for 30 min, at which point TLC showed complete consumption of the starting material. Saturated $NaHCO_3$ was added to neutralize the mixture and the product was extracted with EtOAc. The organic layer was dried over $MgSO_4$ and concentrated. The crude solid was purified by flash chromatography (100% EtOAc) to give 140 mg (80%) of **DN-248**. M.p. 132-133 °C. ^{1}H NMR (500 MHz, CD_3OD) δ 7.45 (d, *J* = 9.0 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 4.02 (t, *J* = 5.1 Hz, 2H), 3.94 (s, 2H), 3.85 (t, *J* = 4.6 Hz, 2H); ^{13}C NMR (125 MHz, CD_3OD) δ 165.9, 156.1, 131.1, 121.5, 114.4, 69.4, 60.2, 28.2; IR (thin film): 3270, 3045, 1664, 1605, 1559, 1505, 1452, 1219, 1078, 1054, 910, 830 cm^{-1}; high resolution mass spectrum (CI) *m/z* 272.9991 [M$^+$; calcd for $C_{10}H_{12}BrNO_3$: 273.0001].

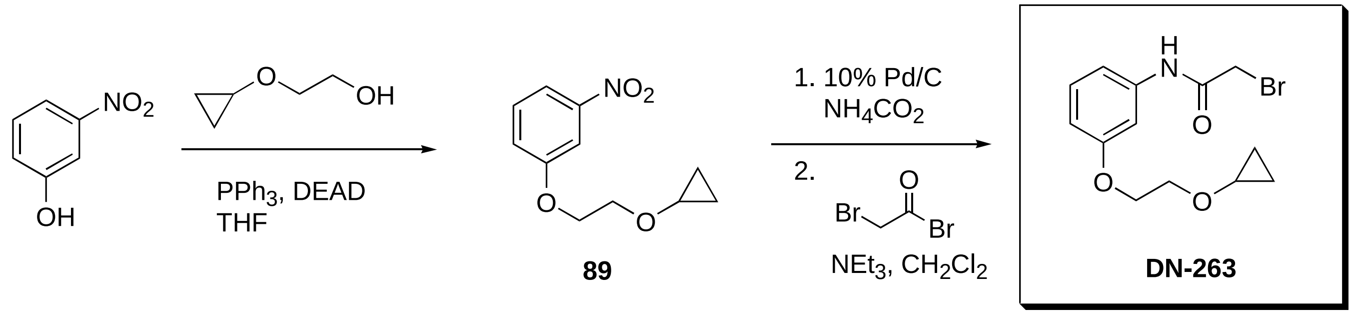


2-Bromo-*N*-[3-(2-hydroxy-ethoxy)-phenyl]-acetamide (DN-260). Starting from 3-nitrophenol, DN-260 was prepared using analogous procedures described above for **DN-248**. Yield: 28% (4 steps). M.p. 85-87 °C. ^{1}H NMR (500 MHz, acetone-d_6) δ 9.46 (br s, 1H), 7.41 (t, *J* = 2.2 Hz, 1H), 7.20 (t, *J* = 8.1 Hz, 1H), 7.11-7.13 (m, 1H), 6.67-6.69 (m, 1H), 4.04 (t, *J* = 5.1 Hz, 2H), 4.01 (s, 2H), 3.97 (t, *J* = 5.9 Hz, 1H), 3.83-3.87 (m, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 164.5, 159.6, 139.9, 129.4, 111.6, 110.0, 106.0, 69.6, 60.4, 29.5; IR (thin film): 3307 (br), 2930, 2879, 1673, 1602, 1555, 1492, 1452, 1281, 1206, 1159, 1076 cm^{-1}; high resolution mass spectrum (CI) *m/z* 273.0003 [M$^+$; calcd for $C_{10}H_{12}BrNO_3$: 273.0001].



DN-261

2-Bromo-*N*-[2-(2-hydroxy-ethoxy)-phenyl]-acetamide (DN-261). Starting from 2-nitrophenol, **DN-261** was prepared using analogous procedures described above for **DN-248**. Yield: 24% (4 steps). M.p. 98-100 °C. ^{1}H NMR (500 MHz, acetone-d_6) δ 9.13 (br s, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.04-7.07 (m, 2H), 6.93-7.00 (m, 1H), 4.14-4.17 (m, 2H), 4.11 (s, 2H), 3.87-3.91 (m, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 164.0, 148.2, 128.2, 124.3, 121.0, 120.0, 112.8, 71.2, 60.3, 29.7; IR (thin film): 3355, 3200-3600 (br), 3019, 2929, 1674, 1601, 1539, 1489, 1453, 1255, 1213, 1118, 1079, 1047, 917, 750 cm^{-1}; high resolution mass spectrum (CI) *m/z* 273.0004 [M$^+$; calcd for $C_{10}H_{12}BrNO_3$: 273.0001].



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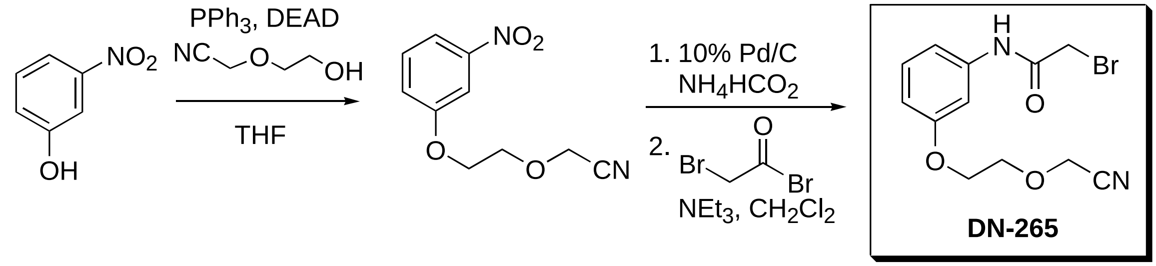
DN-263

2-Bromo-*N*-[3-(2-cyclopropoxy-ethoxy)-phenyl]-acetamide (DN-263). A round bottom flask was changed with 3-nitrophenol (613 mg, 4.41 mmol), 2-cyclopropoxylethanol[iv] (450 mg, 4.41 mmol), PPh_3 (1.73 g, 6.62 mmol) and anhydrous THF (10 mL). Diethyl azodicarboxlate (DEAD) (1.04 mL, 6.62 mmol) was added dropwise and the resulting mixture was stirred at room temperature for 20 h. The solvent was removed in vacuo and the crude product was purified by flash chromatography (20% EtOAc/hexanes) to give 110 mg (11%) of **89**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.83 (m, 1H), 7.74 (t, J = 2.3 Hz, 1H), 7.41 (t, J = 8.2 Hz, 1H), 7.22-7.27 (m, 1H), 4.17 (t, J = 4.7 Hz, 2H), 3.88 (t, J = 4.5 Hz, 2H), 3.35-3.44 (m, 1H), 0.61-0.65 (m, 2H), 0.45-0.53 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 149.1, 129.8, 121.7, 115.8, 108.9, 68.6, 67.8, 53.7, 5.6.

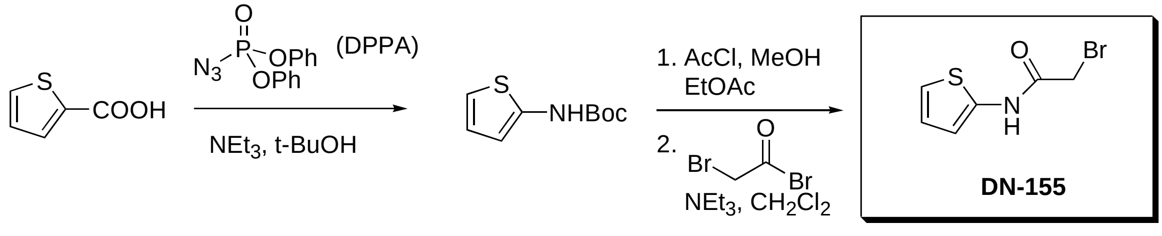
To a round bottom flask flushed with argon was added 10% Pd/C (30 mg) and 2 mL of MeOH. Compound **89** (50 mg, 0.22 mmol) dissolved in 1 mL of MeOH was added, followed by addition of NH_4HCO_2 (65 mg, 1.04 mmol). After the reaction mixture was stirred for 15 min at room temperature, TLC analysis showed complete consumption of the starting material. The reaction mixture was filtered through Celite and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated. The residue was dissolved in anhydrous CH_2Cl_2 (0.5 mL) and added dropwise to a mixture of bromoacetyl bromide (0.040 mL, 0.45 mmol), Et_3N (0.070 mL, 0.49 mmol) and CH_2Cl_2 (1.5 mL) at 0 ^{o}C. After the mixture was stirred for 1 h at 0 ^{o}C and 1 h at room temperature, water was added and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with saturated $NaHCO_3$ and brine. After drying over $MgSO_4$, the solvent was evaporated and the product was purified by flash chromatography (40% EtOAc in hexanes) to give 40 mg (58%) of **DN-263**. M.p. 58-60 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 7.26-7.28 (m, 1H), 7.22 (t, J = 8.2 Hz, 1H), 7.01 (dd, J = 8.0 and 1.2 Hz, 1H), 6.73 (dd, J = 8.3 and 2.3 Hz, 1H), 4.10 (t, J = 5.0 Hz, 2H), 3.99 (s, 2H), 3.85 (t, J = 4.6 Hz, 2H), 3.37-3.40 (m, 1H), 0.60-0.64 (m, 2H), 0.46-0.50 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 159.3, 138.0, 129.7, 112.3, 111.6, 106.5, 68.9, 67.2, 53.6, 29.4, 5.6; IR (thin film): 3290, 3089, 2930, 1671, 1600, 1557, 1493, 1446, 1280, 1209, 1160, 1085, 875, 772, 688 cm^{-1}; high resolution mass spectrum (CI) m/z 313.0306 [M^+; calcd for $C_{13}H_{16}BrNO_3$: 313.0314].



DN-265

2-Bromo-*N*-[3-(2-cyanomethoxy-ethoxy)-phenyl]-acetamide (DN-265). Starting from 3-nitrophenol and 2-(2-hydroxyethoxy)acetonitrile[v] **DN-265** with analogous procedures described above for the synthesis of **DN-263**. Yield: 23% (3 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 7.33 (t, J = 2.2 Hz, 1H), 7.23-7.27 (m, 2H), 7.01 (dd, J = 7.9 and 1.3 Hz, 1H), 6.74 (dd, J = 8.7 and 2.1 Hz, 1H), 4.38 (s, 2H), 4.16-4.29 (m, 2H), 4.01 (s, 2H), 3.95-3.97 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 158.9, 138.1, 129.9, 115.7, 112.6, 111.5, 106.4, 69.8, 67.1, 56.7, 29.4; IR (thin film): 3319, 2927, 2871, 1682, 1601, 1557, 1493, 1445, 1279, 1123, 860, 774 cm^{-1}; high resolution mass spectrum (CI) m/z 313.0183 [$(M+H)^+$; calcd for $C_{12}H_{14}BrN_2O_3$: 313.0188].

3. Synthesis of Thiophene-containing Bromoacetamides

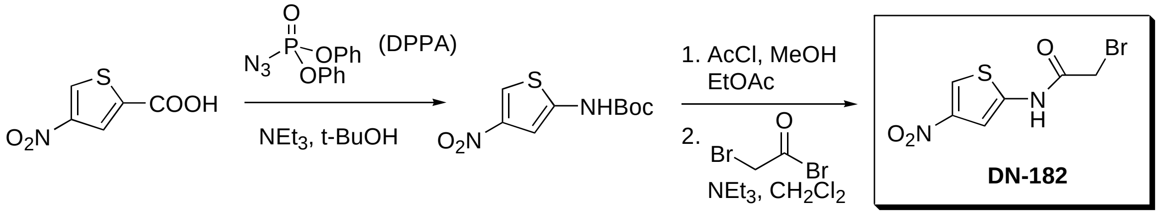


DN-155

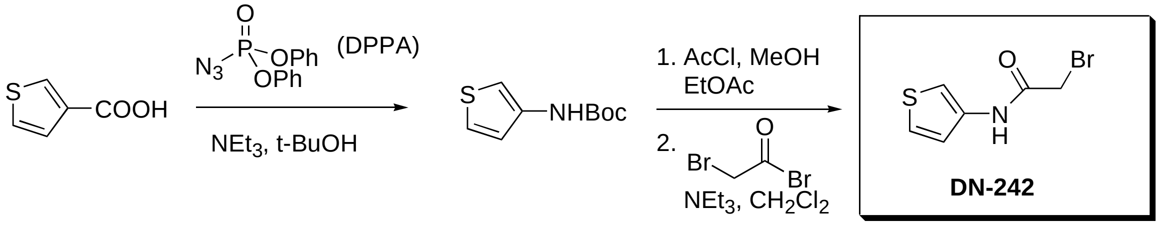
2-Bromo-*N*-thiophen-2-yl-acetamide (DN-155). Thiophene-2-carboxylic acid (300 mg, 2.34 mmol), diphenylphosphoryl azide (DPPA) (0.53 mL, 2.46 mmol) and triethylamine (0.34 mL, 2.46 mmol) were dissolved in *t*-butyl alcohol (7 mL). The reaction mixture was refluxed for 20 h. After the mixture was allowed to cool to room temperature, the solvent was removed in vacuo. The residue was dissolved in benzene and washed with 5% citric acid, water, saturated $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and evaporated. The crude product was passed through a plug of silica gel, eluted with 40% EtOAc in hexanes, to give 280 mg (60%) of 2-*tert*-butoxycarbonyl-aminothiophene.[vi] M.p.

147-148 °C; ^{1}H NMR (500 MHz, CDCl3) δ 7.12 (br s, 1H), 6.75-6.85 (m, 2H), 6.50-6.55 (m, 1H), 1.52 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.5, 140.3, 124.4, 117.0, 111.3, 81.3, 28.4; IR (thin film): 3301, 2976, 1676, 1564, 1500, 1447, 1365, 1346, 1285, 1235, 1153, 1056, 678 cm^{-1}.

A round bottom flask was changed with anhydrous EtOAc (4 mL) and MeOH (0.203 mL, 5 mmol). The mixture was cooled in an ice bath. Acetyl chloride (0.36 mL, 5 mmol) was added dropwise at 0 °C. 2-*tert*-butoxycarbonyl-aminothiophene (100 mg, 0.50 mmol) dissolved in EtOAc (1 mL) was added dropwise to the reaction mixture, and the resulting solution was stirred for 16 h (the ice bath was allowed to melt during this time). The volatiles were evaporated in vacuo. To the residue was added anhydrous CH_2Cl_2 (5 mL) and the suspension was cooled in an ice bath. Triethylamine (0.21 mL, 1.51 mmol) was added, resulting in complete dissolution. Bromoacetyl bromide (0.087 mL, 1.01 mmol) was added dropwise at 0 °C and the reaction mixture was stirred for 2 h at 0 °C, and 1 h at room temperature. Saturated $NaHCO_3$ was added and the organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by flash chromatography (40% EtOAc in hexanes) to give 40 mg (37%) of **DN-155**. M.p. 151-152 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (br s, 1H), 6.94 (dd, *J* = 5.5 and 1.3 Hz, 1H), 6.87-6.89 (m, 1H), 6.77 (dd, *J* = 3.8 and 1.3 Hz, 1H), 4.06 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 138.0, 124.2, 119.0, 113.5, 28.4; IR (thin film): 3221, 3131, 3064, 2923, 1644, 1587, 1428, 1321, 1233, 1098 cm^{-1}; high resolution mass spectrum (CI) *m/z* 218.9379 [M$^+$; calcd for C_6H_6BrNOS: 218.9353].

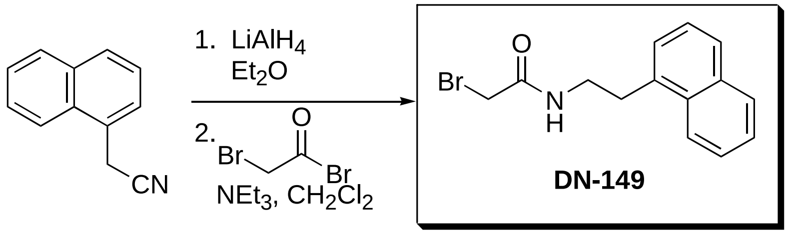


2-Bromo-*N*-(4-nitro-thiophen-2-yl)-acetamide (DN-182). Starting with 4-nitrothiophene-2-carboxylic acid[vii] **DN-182** was synthesized using analogous procedures described for **DN-155**. Yield: 9% (3 steps); M.p. 166-168 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (br s, 1H), 7.91 (dd, *J* = 1.8 and 0.6 Hz, 1H), 7.27 (d, *J* = 1.8 Hz, 1H), 4.09 (s, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 164.5, 145.6, 140.4, 119.6, 105.3, 27.3; IR (thin film): 3267, 3117, 3034, 2975, 2924, 2855, 1665, 1580, 1510, 1472, 1420, 1388, 1332, 1239, 1124, 1085, 991, 825, 782, 725, 689 cm^{-1}; high resolution mass spectrum (CI) *m/z* 263.9199 [M$^+$; calcd for $C_6H_5BrN_2O_3S$: 263.9204].



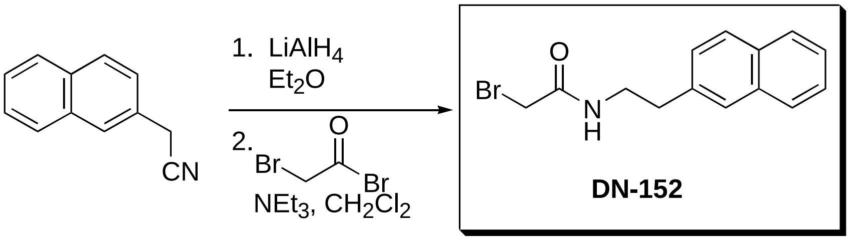
2-Bromo-*N*-thiophen-3-yl-acetamide (DN-242). Starting from commercially available thiophene-3-carboxylic acid, **DN-242** was synthesized using analogous procedures described above for **DN-155**. Yield: 40% (3 steps); M.p. 118-120 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (br s, 1H), 7.58 (dd, *J* = 3.2 and 1.3 Hz, 1H), 7.24-7.26 (m, 1H), 7.04 (dd, *J* = 5.2 and 1.4 Hz, 1H), 4.00 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.0, 134.6, 124.9, 120.9, 111.3, 29.0; IR (thin film): 3278, 3145, 3106, 1652, 1588, 1539, 1435, 1304, 1158, 1105, 969, 776 cm^{-1}; high resolution mass spectrum (CI) *m/z* 218.9358 [M$^+$; calcd for C_6H_6BrNOS: 218.9353].

4. Synthesis of *N*-Naphthylethyl Bromoacetamides



2-Bromo-*N*-(2-naphthalen-1-yl-ethyl)-acetamide (DN-149). A round bottom flask was charged with $LiAlH_4$ (91 mg, 2.39 mmol) and anhydrous diethyl ether (4 mL). To the above suspension was added commercially available 2-(naphthalen-1-yl)acetonitrile (200 mg, 1.20 mmol) dissolved in diethyl ether (1 mL) dropwise. The resulting suspension was stirred overnight at room temperature. Water was cautiously added until gas evolution ceased, followed by addition of 1M NaOH until the solution became basic (pH > 9). The aqueous layer was extracted with ether (1 x). The combined organic layer was washed with brine and dried over $MgSO_4$. After evaporation of the organic solvent, the crude amine was isolated as a viscous oil (160 mg, 78%) and used in the next step without further purification.

Bromoacetyl bromide (0.152 mL, 1.75 mmol) was dissolved in 4 mL of anhydrous CH_2Cl_2 and cooled in an ice bath. Triethylamine (0.270 mL, 1.93 mmol) was added, followed by the above amine dissolved in 1 mL of CH_2Cl_2. The resulting mixture was stirred for 1 h at 0 ^oC. The ice bath was removed and the mixture was stirred for 1 h at room temperature. Water (15 mL) was added and the aqueous layer was extracted with another potion of CH_2Cl_2. The combined organic layer was washed with 5% HCl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography (1:1 EtOAc/hexanes) to give 173 mg (68% from crude amine) of **DN-149**. M.p. 109-111 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.77 (d, J = 8.2 Hz, 1H), 7.48-7.57 (m, 2H), 7.44 (t, J = 7.1 Hz, 1H), 7.33 (d, J = 6.9 Hz, 1H), 6.62 (br s, 1H), 3.81 (s, 2H), 3.65 (q, J = 6.3 Hz, 2H), 3.32 (t, J = 7.1 Hz, 2H),; ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 134.4, 133.9, 131.8, 128.8, 127.5, 126.8, 126.2, 125.7, 125.4, 123.4, 40.7, 32.4, 29.1; IR (thin film): 3250, 3078, 2927, 1652, 1576, 1436, 1300, 1214, 800, 781 cm^{-1}; high resolution mass spectrum (CI) *m/z* 291.0277 [M^+; calcd for $C_{14}H_{14}BrNO$: 291.0259].

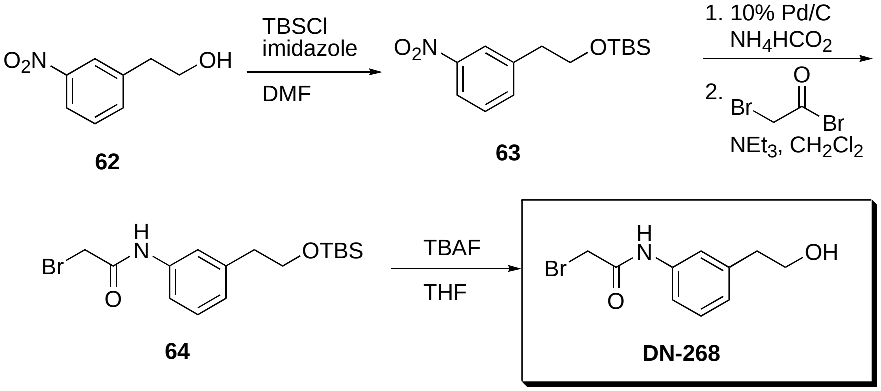


2-Bromo-*N*-(2-naphthalen-2-yl-ethyl)-acetamide (DN-152). Starting from commercially available 1-(naphthalen-1-yl)acetonitrile, **DN-152** was synthesized using analogous procedures described above for **DN-149**, except anhydrous THF was used instead of diethyl ether in the first step due to solubility issues. Yield: 50% (2 steps); M.p. 100-102 ^oC. ^1H NMR (500 MHz, $CDCl_3$) δ 7.79-7.83 (m, 3H), 7.66 (s, 1H), 7.45-7.49 (m, 2H), 7.35 (dd, J = 8.4 and 1.8 Hz, 1H), 6.52 (br s, 1H), 3.84 (s, 2H), 3.64 (q, J = 6.9 Hz, 2H), 3.01 (t, J = 6.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 135.7, 133.5, 132.3, 128.4, 127.6, 127.4, 127.2, 127.0, 126.2, 125.6, 41.1, 35.5, 29.2; IR (thin film): 3302, 3055, 2928, 1652, 1539, 1210, 823, 741 cm^{-1}; high resolution mass spectrum (CI) *m/z* 292.0269 [$(M+H)^+$; calcd for $C_{14}H_{15}BrNO$: 292.0337].

5. Synthesis of (2-Bromo-ethyl)-phenyl-amine (DN-171)

DN-171 was synthesized according to a known literature procedure.[viii]

6. Synthesis of DN-268



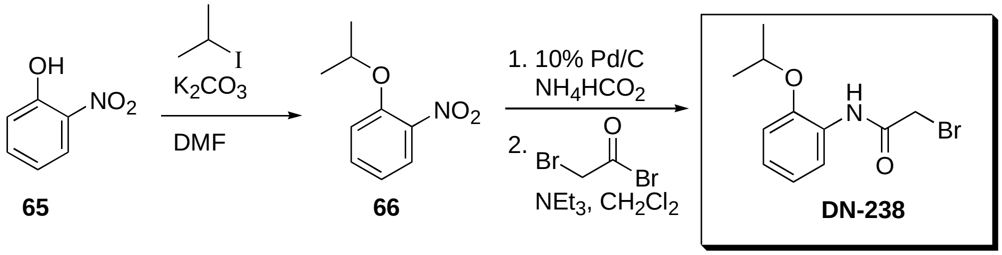
2-Bromo-*N*-[3-(2-hydroxy-ethyl)-phenyl]-acetamide (DN-268). A round bottom flask was charged with commercially available 2-(3-nitrophenyl)ethanol (**62**, 300 mg, 1.79 mmol), TBSCl (325 mg, 2.15 mmol), imidazole (244 mg, 3.59 mmol), and anhydrous DMF (3 mL). The reaction mixture was stirred at room temperature for 30 min. Water was added and the product was extracted with ether (3x). The organic layer was washed with saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. After solvent evaporation, the product was purified by flash chromatography (10% EtOAc in hexanes) to give 475 mg (94%) of TBS ether **63**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05-8.15 (m, 2H), 7.55 (d, J = 7.6 Hz, 1H), 7.44 (t, J = 7.8 Hz, 1H), 3.85 (t, J = 6.3 Hz, 2H), 2.91 (t, J = 6.4 Hz, 2H), 0.85 (s, 9H), -0.04 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 141.6, 135.5, 128.8, 124.0, 121.2, 63.4, 38.9, 25.7, 18.1, -5.6.

To a round bottom flask flushed with argon was added 10% Pd/C (100 mg) and 6 mL of MeOH. Compound **63** (475 mg, 1.69 mmol) dissolved in 2 mL of MeOH was added, followed by addition of NH_4HCO_2 (521 mg, 8.26 mmol). After the reaction mixture was stirred for 15 min at room temperature, the reaction mixture was filtered through Celite and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated. The residue was dissolved in anhydrous CH_2Cl_2 (2.5 mL) and added dropwise to a mixture of bromoacetyl bromide (0.31 mL, 3.60 mmol), NEt_3 (0.63 mL, 4.49 mmol) and CH_2Cl_2 (8 mL) at 0 ^{o}C. After the mixture was stirred for 1 h at 0 ^{o}C and 1 h at room temperature, water was added and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with saturated $NaHCO_3$ and brine. After drying over $MgSO_4$, the solvent was evaporated and the product was purified by flash chromatography (30% EtOAc in hexanes) to give 240 mg (38%) of **64**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 (br s, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.36 (s, 1H), 7.26 (t, J = 7.9 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 4.01 (s, 2H), 3.80 (t, J = 6.9 Hz, 2H), 2.81 (t, J = 6.9 Hz, 2H), 0.87 (s, 9H), -0.01 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 140.5, 136.8, 128.8, 126.1, 120.7, 117.8, 64.1, 39.4, 29.4, 25.8, 18.2, -5.5.

TBS ether **64** (180 mg, 0.48 mmol) was dissolved in THF (3 mL). *tetra*-butyl ammonium floride (0.58 mL, 0.58 mmol, 1M in THF) was added dropwise and the resulting mixture was stirred at room temperature for 3 h. The solvent was removed in vacuo and the product was purified by flash chromatography (100% EtOAc) to give 96 mg (77%) of **DN-268**. ^{1}H NMR (500 MHz, acetone-d_6) δ

9.40 (br s, 1H), 7.45-7.55 (m, 2H), 7.15-7.25 (m, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 4.01 (s, 2H), 3.73-3.76 (m, 2H), 3.66 (t, *J* = 5.5 Hz, 1H), 2.78 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 164.4, 140.4, 138.7, 128.5, 124.7, 119.9, 117.1, 62.8, 39.3, 29.2; IR (thin film): 3303 (br), 3091, 2932, 2867, 1672, 1615, 1595, 1561, 1489, 1445, 1326, 1274, 1045, 789, 698 cm^{-1}; high resolution mass spectrum (CI) *m/z* 257.0065 [M$^+$; calcd for $C_{10}H_{12}BrNO_2$: 257.0051].

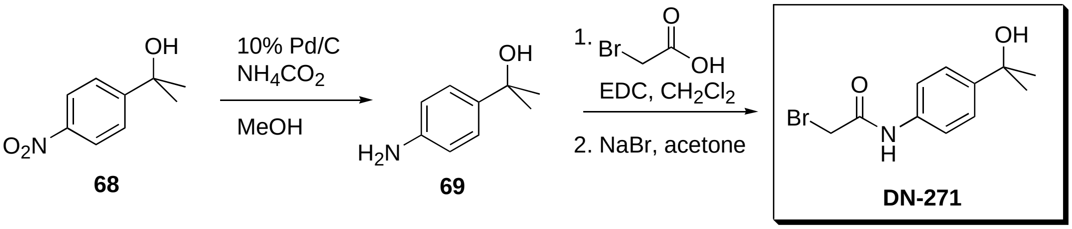
7. Synthesis of Bromoacetamide DN-238



2-Bromo-*N*-(2-isopropoxy-phenyl)-acetamide (DN-238). A round bottom flask was charged with 2-nitrophenol **65** (300 mg, 2.16 mmol), 2-iodopropane (0.43 mL, 4.32 mmol), K_2CO_3 (1.49 g, 10.8 mmol), and anhydrous DMF (5 mL). The reaction mixture was heated at 60 °C for 16 h. Water (10 mL) was added and the product was extracted with diethyl ether. The organic layer was washed with water and brine, and dried over $MgSO_4$. After removal of the solvent in vacuo, the product **66** (290 mg, 74%) was sufficiently pure and used in the next step without further purification. Its spectral data were in agreement with those reported in the literature.[ix]

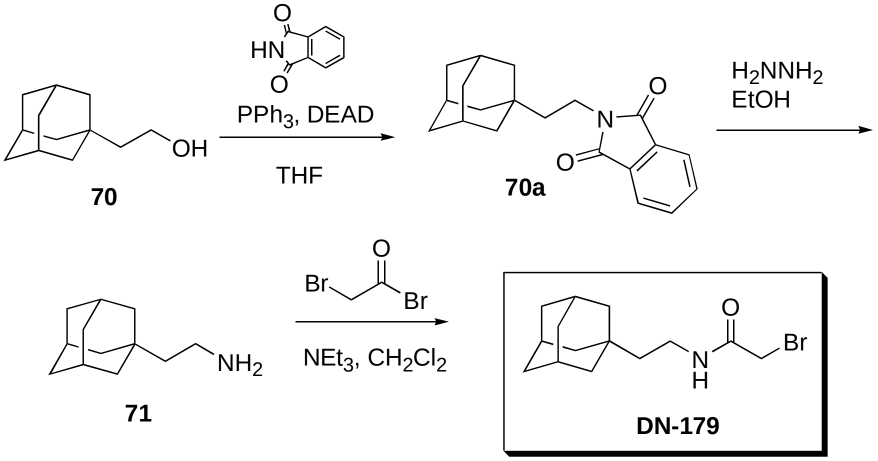
To a round bottom flask flushed with argon was added 10% Pd/C (100 mg) and 5 mL of MeOH. Compound **66** (280 mg, 1.55 mmol) dissolved in 5 mL of MeOH was added, followed by addition of NH_4HCO_2 (453 mg, 7.12 mmol). After stirring for 15 min at room temperature, the reaction mixture was filtered through Celite and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated. The residue was dissolved in anhydrous CH_2Cl_2 (4 mL) and added dropwise to a mixture of bromoacetyl bromide (0.27 mL, 3.09 mmol), NEt_3 (0.47 mL, 3.40 mmol) and CH_2Cl_2 (4 mL) at 0 °C. After the mixture was stirred for 1 h at 0 °C and 1 h at room temperature, water was added and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with saturated $NaHCO_3$ and brine. After drying over $MgSO_4$, the solvent was evaporated and the product was purified by flash chromatography (1:1 EtOAc/hexanes) to give 288 mg (69%) of **DN-238**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.00 (br s, 1H), 8.32-8.33 (m, 1H), 6.90-7.07 (m, 3H), 4.60 (septet, *J* = 6.0 Hz, 1H), 4.03 (s, 2H), 1.38 (d, *J* = 6.1 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 146.5, 128.0, 124.4, 121.0, 119.4, 112.9, 71.7, 29.9, 22.1; IR (thin film): 3371, 2977, 2932, 1683, 1598, 1538, 1482, 1456, 1331, 1289, 1252, 1119, 953, 749 cm^{-1}; high resolution mass spectrum (CI) *m/z* 271.0199 [M$^+$; calcd for $C_{11}H_{14}BrNO_2$: 271.0208].

8. Synthesis of Bromoacetamide DN-271



2-Bromo-*N*-[4-(1-hydroxy-1-methyl-ethyl)-phenyl]-acetamide (DN-271). To a round bottom flask flushed with argon was added 10% Pd/C (50 mg) and 4 mL of MeOH. Alcohol **68**[x] (190 mg, 1.05 mmol) dissolved in 1 mL of MeOH was added, followed by addition of NH_4HCO_2 (304 mg, 4.83 mmol). After stirring for 15 min at room temperature, the reaction mixture was filtered through Celite and the filtrate was concentrated. The residue was dissolved in EtOAc and washed with saturated $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated. The residue (crude **69**) was dissolved in anhydrous CH_2Cl_2 (1 mL) and added to a mixture of bromoacetic acid (175 mg, 1.26 mmol) and EDC (241 mg, 1.26 mmol) in CH_2Cl_2 (5 mL) at 0 ^{o}C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. EtOAc (20 mL) was added to dilute the mixture and the organic layer was washed with saturated $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and concentrated. Purification of the crude product by flash chromatography (1:1 EtOAc/hexanes) gave 100 mg of bromoacetamide **DN-271**, contaminated with the corresponding chloroacetamide (Cl/Br ratio = 3:1 by ^{1}H NMR analysis). The mixture was dissolved in acetone (3 mL) and refluxed in the presence of NaBr (380 mg, 3.7 mmol) for 48 h. The suspension was filtered and concentrated to give 62 mg (22%) of **DN-271**, free of chloroacetamide. ^{1}H NMR (500 MHz, acetone-d_6) δ 9.41 (br s, 1H), 7.57 (d, J = 8.6 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H), 4.01 (s, 2H), 1.49 (s, 6H); ^{13}C NMR (125 MHz, acetone-d_6) δ 164.3, 146.3, 136.8, 124.9, 118.9, 70.8, 31.4, 29.5; IR (thin film): 3311 (br), 2959, 2929, 2871, 1721, 1674, 1600, 1534, 1273, 1121, 1072, 836 cm^{-1}.

9. Synthesis of Adamantyl Substituted Bromoacetamide DN-179

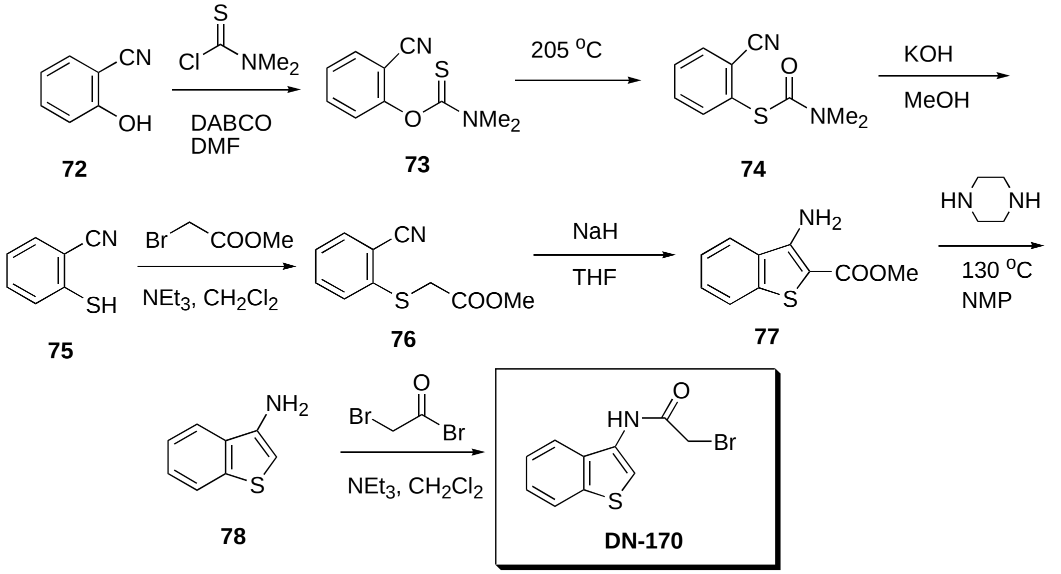


2-Bromo-*N*-(2-adamandt-1-yl-ethyl)-acetamide (DN-179). A round bottom flask was charged with commercially available alcohol **70** (200 mg, 1.11 mmol), phthalimide (245 mg, 1.66 mmol), PPh_3 (726 mg, 2.77 mmol) and anhydrous THF (10 mL). Diethyl azadicarboxylate (0.45 mL, 2.77 mmol) was added dropwise and the mixture was stirred overnight at room temperature. The solvent was evaporated and the residue was purified by flash chromatography (35% EtOAc in hexanes) to give 320 mg (93%) of the corresponding *N*-substituted phthalimide **70a**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73-7.79 (m, 2H), 7.58-7.65 (m, 2H), 3.61-3.70 (m, 2H), 1.92 (s, 3H), 1.66 (d, *J* = 12.1 Hz, 3H), 1.60 (d, *J* = 11.8 Hz, 3H), 1.54 (s, 6H), 1.35-1.43 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1, 133.6, 132.2, 122.9, 42.2, 42.0, 37.0, 33.1, 31.8, 28.5.

To a flask containing **70a** (200 mg, 0.65 mmol) was added absolute EtOH (5 mL) and hydrazine (1 mL).[xi] The mixture was brought to reflux and a white precipitate began to form. After 1 h of reflux, the solution was decanted and concentrated to give 100 mg (86%) of amine **71**, which was used in the next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.63-2.70 (m, 2H), 1.90 (s, 3H), 1.67 (d, *J* = 12.0 Hz, 3H), 1.59 (d, *J* = 12.2 Hz, 3H), 1.46 (s, 6H), 1.41 (br s, 2H), 1.16-1.23 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 48.8, 42.6, 37.1, 36.4, 31.9, 28.6.

Bromoacetyl bromide (0.146 mL, 1.68 mmol) was dissolved in 3 mL of CH_2Cl_2 and cooled to 0 °C. Et_3N (0.235 mL, 1.68 mmol) was added dropwise, followed by addition of amine **71** (100 mg, 0.56 mmol) dissolved in 1 mL of CH_2Cl_2. The resulting mixture was stirred for 1 h at 0 °C and 1 h at room temperature. Water was added and the aqueous layer was extracted with another portion of CH_2Cl_2. The combined organic layer was washed with 5% HCl, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography (40% EtOAc/hexanes) to give 100 mg (60%) of **DN-179**. M.p. 154-155 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.36 (br s, 1H), 3.86 (s, 2H), 3.28-3.32 (m, 2H), 1.96 (s, 3H), 1.71 (d, *J* = 12.1 Hz, 3H), 1.61 (d, *J* = 11.8 Hz, 3H), 1.52 (s, 6H), 1.30-1.33 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 43.4, 42.3, 36.9, 35.3, 31.9, 29.3, 28.5; IR (thin film): 3272, 3069, 2900, 2847, 1648, 1554, 1451, 1210 cm^{-1}; high resolution mass spectrum (CI) *m/z* 300.0949 $[(M+H)^+$; calcd for $C_{14}H_{23}BrNO$: 300.0963].

10. Synthesis of Benzothiophene Derivative DN-170.



***N*-Benzo[*b*]thiophen-3-yl-2-bromo-acetamide (DN-170).** 2-Cyanophenol **72** (500 mg, 4.20 mmol) and 1,4-diazabicyclo[2.2.2]octane (DABCO) (1.28 g, 10.5 mmol) were dissolved in anhydrous DMF (5 mL). Dimethylthiocarbamoyl chloride (680 mg, 5.46 mmol) was added and the reaction mixture was stirred at 75 °C for 2 h. The reaction mixture was allowed to cool to room temperature. EtOAc (20 mL) and water (20 mL) were added to the mixture, and the aqueous layer was extracted with additional EtOAc (3 x). The combined organic layer was dried over $MgSO_4$ and concentrated. The product was purified by flash chromatography (60% EtOAc in hexanes) to give 680 mg (79%) of thiocarbamate **73**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58-7.70 (m, 2H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.26 (d, *J* = 8.3 Hz, 1H), 3.47

(s, 3H), 3.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.9, 155.4, 133.5, 132.9, 126.2, 124.9, 115.2, 108.2, 43.5, 39.0.

Thiocarbamate **73** (680 mg, 3.30 mmol) was placed in a round bottom flask under an argon atmosphere. The flask was immersed in an oil bath at 205 °C and the reaction was monitored by TLC. After 3 h of heating, most of the starting material was consumed. The heating bath was removed and the flask was allowed to cool to room temperature. The product was purified by flash chromatography (60% EtOAc in hexanes) to give 420 mg (62%) of isothiocarbamate **74**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (dd, J = 7.6 and 1.2 Hz, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.59 (dt, J = 7.6 and 1.3 Hz, 1H), 7.51 (t, J = 8.2 Hz, 1H), 3.14 (s, 3H), 3.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 137.3, 133.5, 132.9, 132.6, 129.5, 119.7, 117.1, 37.0.

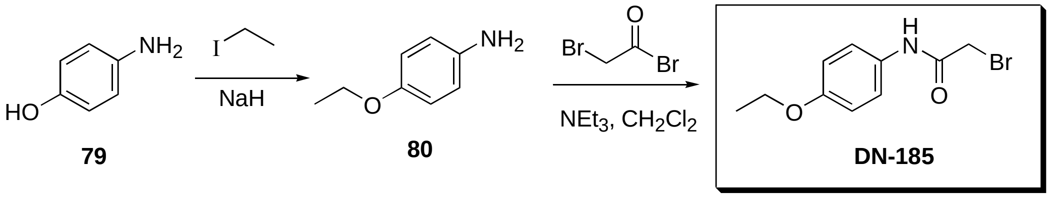
Isothiocarbamate **74** (400 mg, 1.94 mmol) was dissolved in THF (4 mL). KOH (240 mg, 4.27 mmol) dissolved in 1 mL of MeOH was added and the resulting mixture was stirred at room temperature for 16 h. The reaction mixture was poured over crushed ice and acidified to pH 2 with concentrated HCl. The product was extracted with EtOAc, and the organic layer was dried over $MgSO_4$. The solvent was evaporated in vacuo and the crude product was purified by flash chromatography (60:40 EtOAc/hexanes) to give 200 mg (76%) of 2-cyanothiophenol (**75**). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55-7.63 (m, 1H), 7.35-7.45 (m, 2H), 7.16-7.27 (m, 1H), 4.08 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.3, 133.4, 132.9, 129.3, 125.7, 117.3, 111.9; IR (thin film): 3062, 2561, 2223, 1589, 1469, 1434, 1284, 1271, 1199, 1166, 1133, 1074, 1037, 932, 756, 712, 673 cm^{-1}.

2-cyanothiophenol (**75**) (670 mg, 4.96 mmol) was dissolved in anhydrous CH_2Cl_2 (15 mL). NEt_3 (0.83 mL, 5.96 mmol) was added to the reaction mixture, followed by the addition of methyl bromoacetate (0.56 mL, 5.96 mmol). The reaction mixture was stirred for 2 h at room temperature. The mixture was diluted with CH_2Cl_2 (30 mL) and washed with water, 1M HCl and brine. The organic layer was dried over $MgSO_4$ and concentrated to give 650 mg (64%) of **76**, which was sufficiently pure and used in the next step without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61-7.68 (m, 1H), 7.48-7.57 (m, 2H), 7.25-7.33 (m, 1H), 3.72 (s, 2H), 3.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.1, 139.2, 133.7, 133.1, 130.8, 127.4, 116.8, 114.6, 52.7, 35.9.

Ester **76** (650 mg, 3.14 mmol), dissolved in 5 mL of anhydrous THF, was added to a suspension of NaH (263 mg, 6.59 mmol, 60% dispersion in mineral oil) in THF (10 mL). The resulting mixture was refluxed for 6 h. After the mixture has come to room temperature, saturated NH_4Cl was cautiously added to quench the excess NaH. The product was extracted with EtOAc (2 x) and the organic layer was washed with brine and dried over $MgSO_4$. The solvent was removed in vacuo and the residue, benzothiophene **77**, was transferred to a flask containing piperazine (1.18 g, 13.6 mmol) and *N*-methylpyrrolidinone (NMP) (12 mL). The mixture was heated to 130°C and stirred at this temperature for 16 h. The reaction mixture was allowed to come to room temperature, and water (30 mL) was added. The aqueous layer was extracted with EtOAc (3 x). The combined organic layer was washed with brine and dried over $MgSO_4$. After the solvent was removed in vacuo, the residue was passed through a plug of silica gel, eluting with 40% EtOAc in hexanes to give aminothiophene **78**, which was still contaminated with NMP as judged by NMR analysis. Without further purification, aminothiophene **78** was re-dissolved in anhydrous CH_2Cl_2 and added dropwise to a mixture of bromoacetyl bromide (0.51 mL, 5.91 mmol), NEt_3 (0.91 mL, 6.50 mmol) and CH_2Cl_2 (5 mL) at 0 °C. The reaction mixture was stirred for 1 h at 0 °C and 1 h at room temperature. Water was added and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with 5% HCl, saturated $NaHCO_3$ solution, and brine. After drying over $MgSO_4$, the solvent was evaporated and the residue was purified by flash chromatography (35% EtOAc/hexanes) to give 400 mg (47% from **76**) of **DN-170**. M.p. 132-133 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (br s, 1H), 7.98 (s, 1H) 7.85 (dd, J = 7.0 and 1.7 Hz, 1H), 7.62 (dd, J = 6.8 and 1.5 Hz, 1H), 7.39-7.45 (m, 2H), 4.12 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

163.1, 137.9, 132.2, 127.5, 125.0, 124.2, 123.2, 118.6, 113.3, 29.3; IR (thin film): 3277, 3052, 1661, 1597, 1538, 1460, 1433, 1204, 755, 730 cm^{-1}; high resolution mass spectrum (CI) *m/z* 268.9508 [M$^+$; calcd for $C_{10}H_8BrNOS$: 268.9510].

11. Synthesis of Bromoacetamide DN-185.

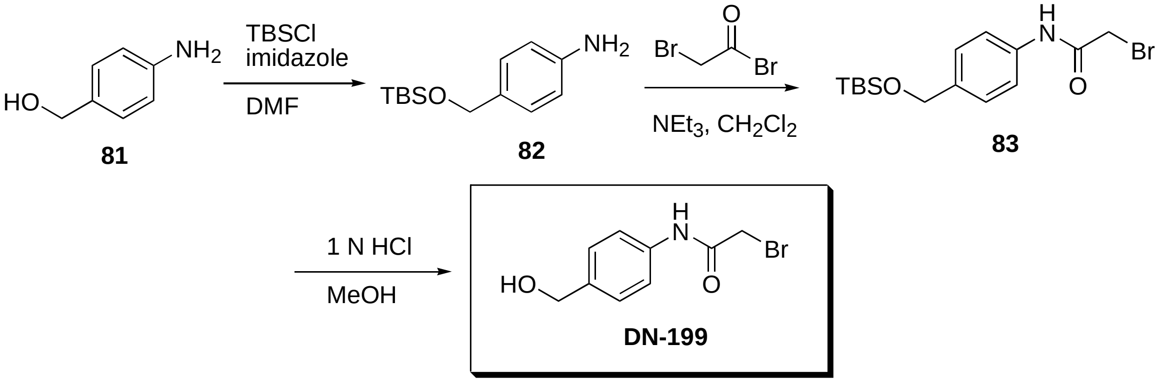


79 **80** **DN-185**

2-Bromo-*N*-(4-ethoxy-phenyl)-acetamide (DN-185). To a flask containing NaH (120 mg, 3.03 mmol, 60% dispersion in mineral oil) anhydrous DMF (5 mL) and 4-aminophenol **79** (300 mg, 2.75 mmol) were added and the mixture was stirred for 30 min at room temperature. Ethyl iodide (0.24 mL, 3.03 mmol) was added dropwise and the resulting mixture was stirred at room temperature for 20 h. Water (10 mL) was added and the aqueous layer was extracted with EtOAc (3x). The combined organic layer was washed with water, brine, and dried over $MgSO_4$. After the solvent was evaporated, the product was purified by flash chromatography (30% EtOAc/hexanes) to give 135 mg (36%) of 4-ethoxyaniline (**80**). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.72-6.78 (m, 2H), 6.61-6.68 (m, 2H), 3.96 (q, *J* = 7.0 Hz, 2H), 3.43 (br s, 2H), 1.37 (t, *J* = 7.0 Hz, 3H).

Aniline **80** (135 mg, 0.99 mmol) was dissolved in 1 mL of anhydrous CH_2Cl_2 and added to a mixture of bromoacetyl bromide (0.17 mL, 1.97 mmol), Et_3N (0.30 mL, 2.17 mmol), and CH_2Cl_2 (4 mL) at 0 ^{o}C. The reaction mixture was stirred for 1 h at 0 ^{o}C and 1 h at room temperature. Water was added and the aqueous layer was extracted with another potion of CH_2Cl_2. The combined organic layer was washed with 5% HCl, saturated $NaHCO_3$, and brine. After drying over $MgSO_4$, the solvent was evaporated and the residue was purified by flash chromatography (40% EtOAc in hexanes) to give 174 mg (68%) of **DN-185**. M.p. 134-136 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (br s, 1H), 7.39 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 4.02 (q, *J* = 6.9 Hz, 2H), 3.99 (s, 2H), 1.38 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 156.4, 129.8, 122.0, 114.8, 63.7, 29.4, 14.7; IR (thin film): 3267, 3205, 3143, 3100, 2973, 2924, 2879, 1657, 1612, 1557, 1511, 1393, 1234, 1174, 1113, 1046, 824 cm^{-1}; high resolution mass spectrum (CI) *m/z* 257.0061 [M$^+$; calcd for $C_{10}H_{12}BrNO_2$: 257.0051].

12. Synthesis of Bromoacetamide DN-199



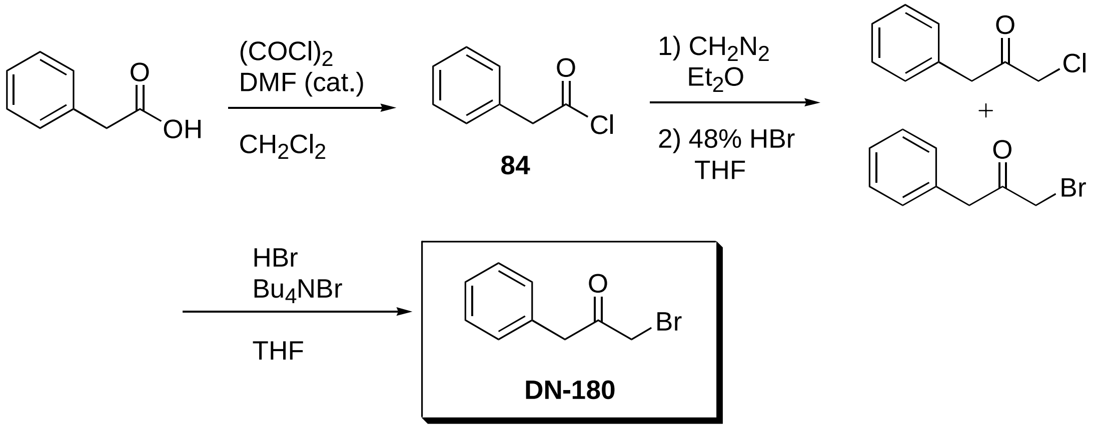
81 **82** **83** **DN-199**

2-Bromo-*N*-(4-hydroxymethyl-phenyl)-acetamide (DN-199). 4-aminobenzyl alcohol (**81**) (300 mg, 2.44 mmol), TBSCl (368 mg, 2.44 mmol), and imidazole (332 mg, 4.88 mmol) were dissolved in anhydrous DMF (5 mL). The reaction mixture was stirred at room temperature for 30 min. Water (10 mL) was added and the product was extracted with EtOAc (3 x). The organic layer was washed with saturated $NaHCO_3$, water, and brine. After drying over $MgSO_4$, the solvent was evaporated and the residue was purified by flash chromatography (30% EtOAc/hexanes) to give 394 mg (68%) of TBS ether **82**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.3 Hz, 2H), 6.66 (d, *J* = 8.3 Hz, 2H), 4.62 (s, 2H), 3.60 (br s, 2H), 0.93 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.3, 131.6, 127.7, 115.0, 65.0, 26.0, 18.4, -5.1.

TBS ether **82** (394 mg, 1.66 mmol) was dissolved in 1 mL of anhydrous CH_2Cl_2 and added to a mixture of bromoacetyl bromide (0.29 mL, 3.32 mmol), Et_3N (0.51 mL, 3.66 mmol), and CH_2Cl_2 (4 mL) at 0 ^{o}C. The reaction mixture was stirred for 1 h at 0 ^{o}C and 1 h at room temperature. Water was added and the aqueous layer was extracted with another potion of CH_2Cl_2. The combined organic layer was washed with saturated $NaHCO_3$ and brine. After drying over $MgSO_4$, the solvent was evaporated and the residue was purified by flash chromatography (35% EtOAc in hexanes) to give 341 mg (57%) of bromoacetamide **83**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (br s, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 4.71 (s, 2H), 4.02 (s, 2H), 0.94 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 138.5, 135.6, 126.8, 119.9, 64.5, 29.5, 25.9, 18.4, -5.3.

TBS ether **83** (80 mg, 0.22 mmol) was dissolved in 10 mL of MeOH. 1N HCl (5 mL) was added dropwise and the resulting mixture was stirred at room temperature for 30 min. EtOAc (20 mL) was added to dilute the mixture and the organic layer was washed with saturated $NaHCO_3$ and brine. After drying over $MgSO_4$, the organic layer was concentrated and the residue was purified by flash chromatography (100% EtOAc) to give 50 mg (92%) of **DN-199**. M.p. 101-103 ^{o}C. ^{1}H NMR (500 MHz, acetone-d_6) δ 9.43 (br s, 1H), 7.59 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 4.57 (d, *J* = 5.6 Hz, 2H), 4.11 (t, *J* = 5.8 Hz, 1H), 4.01 (s, 2H); ^{13}C NMR (125 MHz, acetone-d_6) δ 165.3, 139.2, 138.4, 127.9, 120.1, 64.3, 30.4; IR (thin film): 3300-2700 (br), 3295, 3204, 3137, 1657, 1611, 1545, 1415, 1335, 1105, 1038, 826 cm^{-1}; high resolution mass spectrum (CI) *m/z* 242.9898 [M$^+$; calcd for $C_9H_{10}BrNO_2$: 242.9895].

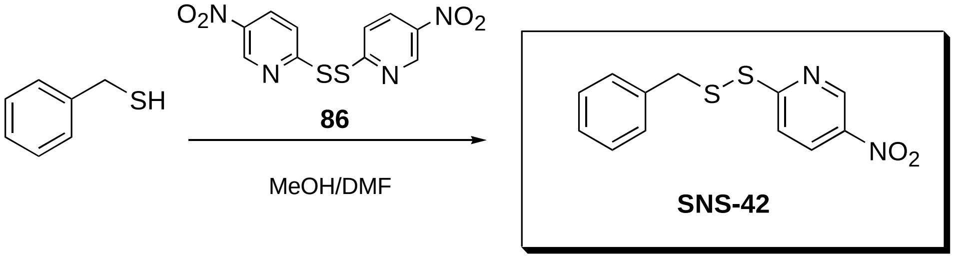
13. Synthesis of Bromoketone DN-180



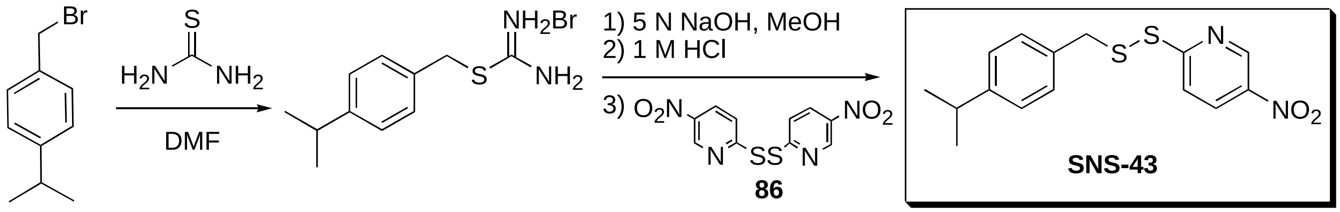
1-Bromo-3-phenyl-propan-2-one (DN-180). Phenylacetic acid (200 mg, 1.47 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) and cooled in an ice bath. Oxalyl chloride (0.26 mL, 2.94 mmol) was added, followed by 2 drops of DMF. The ice bath was removed and the mixture was stirred at room temperature for 1.5 h (until gas evolution ceased). The solvent and excess oxalyl chloride were removed in vacuo. The residue (acid chloride **84**) was dissolved in anhydrous ether and cooled to 0 °C. An ethereal solution of CH_2N_2 (prepared from *N*-methyl-*N*-nitrosourea and KOH)[xii] was added dropwise and the resulting mixture was stirred at 0 °C for 3 h. The solvent was evaporated in vacuo and the residue was dissolved in THF (5 mL). 48% HBr (1 mL) was then added dropwise. The reaction mixture was concentrated and the residue was taken up in EtOAc (10 mL). The organic layer was washed with saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. After removal of the solvent in vacuo, the crude oil was purified by flash chromatography (40% EtOAc in hexanes) to give 100 mg of a mixture of **DN-180** and the corresponding chloro- analog in ~ 1:1 ratio as judged by ^{1}H NMR analysis.

The above mixture of bromo- and chloroketones were dissolved in 2 mL of CH_2Cl_2, followed by addition of tetrabutylammonium bromide (60 mg, 0.18 mmol) and 48% HBr (1 g, 5.9 mmol). The resulting mixture was refluxed for 16 h. After cooling to room temperature, CH_2Cl_2 (10 mL) was added and the organic layer was washed with water, saturated $NaHCO_3$, and brine. The organic layer was dried over $MgSO_4$ and concentrated. The ratio of DN-180 to chloroketone was improved to 3 : 1. The same reaction conditions were therefore applied, with three times the amount of tetrabutylammonium bromide and aq. HBr. After aqueous workup, the crude product was purified by flash chromatography (40% EtOAc hexanes) to give 25 mg (8%, 4 steps) of **DN-180**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23-7.36 (m, 5H), 3.95 (s, 2H), 3.91 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.3, 133.1, 129.4, 128.9, 127.4, 46.7, 33.4; IR (thin film): 3059, 3030, 2936, 1725, 1495, 1453, 1391, 1181, 1045, 739, 699 cm^{-1}; high resolution mass spectrum (CI) *m/z* 211.9836 [M^+; calcd for C_9H_9BrO: 211.9837].

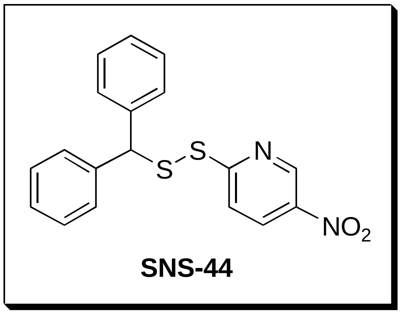
Synthesis of Sulfenyl Transfer Agents In Both Libraries



Preparation of 2-Benzyldisulfanyl-5-nitropyridine (SNS-42). To a stirred solution of 2,2'-dithiobis(5-nitropyridine) (**86**, 150 mg, 0.48 mmol) in 1:1 MeOH/DMF (4 mL), benzyl mercaptan, dissolved in 1:1 MeOH/DMF (0.64 mL, 0.5 M), was added dropwise over 15 min under argon atmosphere at ambient temperature. The intensely yellow solution was stirred for another 30 min, then diluted with EtOAc (10 mL) and washed with saturated aqueous $NaHCO_3$ (3 × 10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. Flash chromatography (20:80 EtOAc/hexanes), followed by recrystallization from EtOAc/heptane, gave **SNS-42** in 87% yield (77 mg, 0.277 mmol) as a white crystalline solid: mp = 106–108 °C; FTIR ($CHCl_3$) 3085 (w), 3050 (w), 2915 (w), 1585 (s), 1563 (s), 1516 (s), 1435 (m), 1344 (s), 1269 (w), 1147 (w), 1095 (m), 1006 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (dd, J = 2.6 and 0.5 Hz, 1 H), 8.15 (dd, J = 8.9 and 2.6 Hz, 1 H), 7.50 (dd, J = 8.9 and 0.5 Hz, 1 H), 7.29–7.20 (m, 5 H), 4.04 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 144.7, 135.9, 131.0, 129.3, 128.6, 127.8, 118.9, 43.7; high resolution mass spectrum (CI) *m/z* 278.0177 [$(M+H)^+$; calcd for $C_{12}H_{11}N_2O_2S_2$: 278.0184].



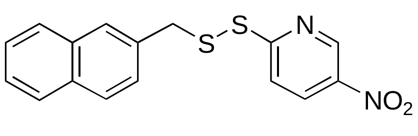
2-(4-Isopropyl-benzyldisulfanyl)-5-nitropyridine (SNS-43). 4-Isopropylbenzyl bromide (500 mg, 2.35 mmol) was combined with thiourea (268 mg, 3.52 mmol) in DMF (5.0 mL). The mixture was heated at 60 ˚C for 1 h, then cooled to ambient temperature and poured into ice-cold Et_2O (15 mL). The resulting precipitate was washed with Et_2O (2 × 10 mL) and then recrystallized from MeOH-EtOAc to give the isothiourea hydrobromide intermediate as a white crystalline solid in 90% yield (612 mg, 2.12 mmol): mp = 166–168 ˚C; FTIR (KBr) 3307 (w), 3260 (w), 3165 (br m), 3065 (br m), 2958 (w), 1656 (s), 1644 (s), 1414 (m), 1247 (w), 1153 (w), 1052 (w) cm^{-1}; ^{1}H NMR (500 MHz, MeOH-*d*$_4$) δ 7.24 (d, *J* = 8.2 Hz, 2 H), 4.40 (s, 2H), 2.90 (heptet, *J* = 6.9 Hz, 1 H), 1.23 (d, *J* = 6.9 Hz, 6 H), isothiourea *NH*'s were not observed in MeOH-*d*$_4$ solvent; ^{13}C NMR (125 MHz, MeOH-*d*$_4$) δ 172.3, 150.7, 132.3, 130.2, 128.1, 36.2, 35.1, 24.3; low resolution mass spectrum (ESI) *m/z* 209 $[(M+H)^+$; calcd for $C_{11}H_{17}N_2S$: 209]. The isothiourea (300 mg, 1.04 mmol) was dissolved in MeOH (3.0 mL). The solution was thoroughly deoxygenated by sparging with argon, and NaOH solution (5 N, 416 μL) was added. The reaction mixture was stirred under argon atmosphere until complete conversion to a thiol (ca. 30 min), as indicated by staining with Ellman Reagent (1 mg/mL in PBS, pH 7.0). The mixture was neutralized to pH 7.0 with 1 M HCl (1.04 mL) and canulated into a solution of **86** (323 mg, 1.04 mmol) in 1:1 MeOH/DMF (5 mL). The resulting intensely yellow solution was stirred for 30 min, diluted with EtOAc (10 mL), and washed with saturated aqueous $NaHCO_3$ (3 × 10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated in vacuo. Flash chromatography (20:80 EtOAc/hexanes), followed by recrystallization from EtOAc/heptane, gave **SNS-43** in 59% yield (195 mg, 0.614 mmol) as a beige crystalline solid: mp = 79–81 ˚C; FTIR ($CHCl_3$) 3030 (w), 2957 (m), 2925 (w), 2867 (w), 1586 (s), 1564 (s), 1514 (s), 1442 (m), 1349 (s), 1255 (w), 1147 (w), 1100 (m), 1051 (w), 1008 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.16 (d, *J* = 2.6 Hz, 1 H), 8.10 (dd, *J* = 8.9 and 2.6 Hz, 1 H), 7.47 (d, *J* = 8.9, 1 H), 7.19 (d, *J* = 8.0, 2 H), 7.05 (d, *J* = 8.0, 2 H), 4.01 (s, 2 H), 2.90 (heptet, *J* = 7.0 Hz, 1 H), 1.15 (d, *J* = 7.0 Hz, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 148.9, 144.6, 141.6, 133.2, 130.8, 129.4, 126.7, 118.9, 43.6, 33.7, 23.9; high resolution mass spectrum (CI) *m/z* 321.0618 $[(M+H)^+$; calcd for $C_{15}H_{17}N_2O_2S_2$: 321.0653].



SNS-44

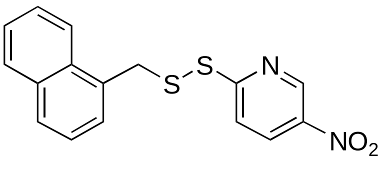
2-Benzhydryldisulfanyl)-5-nitropyridine (SNS-44). Chlorodiphenylmethane (500 mg, 2.47 mmol) was combined with thiourea (282 mg, 3.70 mmol) in DMF (5.0 mL). The mixture was heated at 100 ˚C for 1 h, then cooled to ambient temperature and poured into ice-cold Et_2O (15 mL). The resulting precipitate was washed with Et_2O (2 × 10 mL) and then recrystallized from MeOH-EtOAc to give the isothiourea hydrochloride intermediate as a white crystalline solid in 83% yield (570 mg, 2.05 mmol): mp = 196–198 ˚C; FTIR (KBr) 3202 (br w), 3027 (br s), 1637 (s), 1491 (m), 1448 (m), 1077 (w) cm^{-1};

^{1}H NMR (500 MHz, MeOH-d_4) δ 7.48 (d, *J* = 7.6 Hz, 4 H), 7.39 (dd, *J* = 7.3 and 7.6 Hz, 4 H), 7.33 (d, *J* = 7.3 Hz, 2 H), 6.30 (s, 1 H), isothiourea *N<u>H</u>*'s were not observed in MeOH-d_4 solvent; ^{13}C NMR (125 MHz, MeOH-d_4) δ 170.5, 139.2, 130.2, 129.6, 129.3, 55.3; low resolution mass spectrum (ESI) *m/z* 243 [(M+H)$^+$; calcd for $C_{14}H_{15}N_2S$: 243]. Disulfide **SNS-44** was prepared as described for **SNS-43**. Flash chromatography (20:80 EtOAc/hexanes), followed by recrystallization from EtOAc/heptane, gave **SNS-44** in 74% yield (319 mg, 0.903 mmol) as a white solid: mp = 112–114 ˚C; FTIR (CHCl$_3$) 3061 (w), 3027 (w), 1587 (s), 1565 (s), 1516 (s), 1494 (w), 1449 (m), 1342 (s), 1267 (w), 1132 (w), 1096 (m), 1030 (w), 1007 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 9.19 (d, *J* = 2.6 Hz, 1 H), 8.19 (dd, *J* = 2.6 and 8.5 Hz, 1 H), 7.56 (d, *J* = 8.5, 1 H), 7.42 (d, *J* = 7.5, 4 H), 7.30 (t, *J* = 7.5 Hz, 4 H), 7.25 (d, *J* = 7.3, 2 H), 5.41 (s, 1 H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.4, 144.8, 141.8, 138.9, 131.0, 128.7, 128.7, 128.0, 61.0; high resolution mass spectrum (CI) *m/z* 355.0564 [(M+H)$^+$; calcd for $C_{18}H_{15}N_2O_2S_2$: 355.0575].



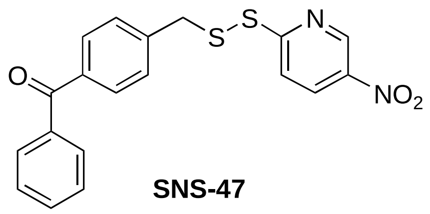
SNS-45

2-(Naphthalene-2-ylmethyldisulfanyl)-5-nitropyridine (SNS-45). Isothiourea **SNS-45** was prepared as described for **SNS-43**, using 2-bromomethylnaphthalene (500 mg, 2.26 mmol). Recrystallization from MeOH-EtOAc furnished isothiourea hydrobromide intermediate as a white crystalline solid in 95% yield (639 mg, 2.15 mmol): mp = 186–188 ˚C; FTIR (KBr) 3273 (br s), 3073 (br s), 2728 (br w), 1636 (s), 1437 (m), 1364 (w), 1242 (w), 1061 (w) cm^{-1}; ^{1}H NMR (500 MHz, MeOH-d_4) δ 7.91–7.84 (m, 4 H), 7.53–7.49 (m, 4 H), 4.61 (s, 2 H), isothiourea *N<u>H</u>*'s were not observed in MeOH-d_4 solvent; ^{13}C NMR (125 MHz, MeOH-d_4) δ 172.1, 134.7, 134.5, 132.6, 130.0, 129.3, 128.8, 128.8, 127.7, 127.7, 127.5, 36.7; low resolution mass spectrum (ESI) *m/z* 217 [(M+H)$^+$; calcd for $C_{12}H_{13}N_2S$: 217]. Disulfide **SNS-45** was prepared as described for **SNS-43**, using the isothiourea intermediate (300 mg, 1.01 mmol). Flash chromatography (20:80 EtOAc/hexanes), followed by recrystallization from EtOAc/heptane, gave the title compound in 47% yield (156 mg, 0.475 mmol) as a yellow powder: mp = 167–169 ˚C; FTIR (CHCl$_3$) 3082 (w), 3055 (w), 1585 (s), 1560 (s), 1509 (s), 1432 (m), 1340 (s), 1252 (w), 1091 (w), 1004 (w) cm^{-1}; ^{1}H NMR (500 MHz, CHCl$_3$) δ 8.96 (d, *J* = 2.6 Hz, 1 H), 7.81 (dd, *J* = 2.6 and 8.8 Hz, 1 H), 7.71 (dd, *J* = 6.0 and 8.2 Hz, 1 H), 7.62 (d, *J* = 8.8, 1 H), 7.59 (s, 1 H), 7.42–7.38 (m, 4 H), 7.32 (d, *J* = 8.8 Hz, 1 H), 4.18 (s, 2 H); ^{13}C NMR (125 MHz, CHCl$_3$) δ 168.2, 144.3, 141.0, 133.0, 132.7, 132.6, 130.5, 128.7, 128.7, 127.6, 127.5, 127.0, 126.5, 126.4, 118.7, 44.4; high resolution mass spectrum (CI) *m/z* 328.0328 [(M)$^+$; calcd for $C_{16}H_{12}N_2O_2S_2$: 328.0340].



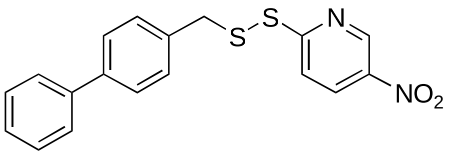
SNS-46

Preparation of 2-(Naphthalene-1-ylmethyldisulfanyl)-5-nitropyridine (SNS-46). Disulfide **SNS-46** was prepared as described for **SNS-43**. Flash chromatography (20:80 EtOAc/hexanes), followed by recrystallization from EtOAc/heptane, gave the title compound in 53% yield (175 mg, 0.535 mmol) as yellow crystalline plates: mp = 125–127 ˚C; FTIR ($CHCl_3$) 3084 (w), 1589 (s), 1565 (s), 1512 (m), 1434 (m), 1343 (s), 1266 (w), 1214 (w), 1132 (w), 1096 (m), 1008 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.02 (d, *J* = 2.6 Hz, 1 H), 8.15 (d, *J* = 8.4, 1 H), 7.80 (d, *J* = 8.1, 1 H), 7.75 (dd, *J* = 2.6 and 8.9 Hz, 1 H), 7.64–7.60 (m, 2 H), 7.54 (dd, *J* = 7.1 and 8.9 Hz, 1 H), 7.32 (d, *J* = 6.9 Hz, 1 H), 7.20 (dd, *J* = 7.6 and 7.7 Hz, 1 H), 7.07 (d, *J* = 8.9 Hz, 1 H), 4.50 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 144.3, 141.4, 133.9, 131.0, 131.0, 130.4, 128.9, 128.9, 128.8, 126.6, 126.2, 125.0, 123.3, 118.9, 41.5; high resolution mass spectrum (CI) *m/z* 328.0317 [(M)$^+$; calcd for $C_{16}H_{12}N_2O_2S_2$: 328.0340].



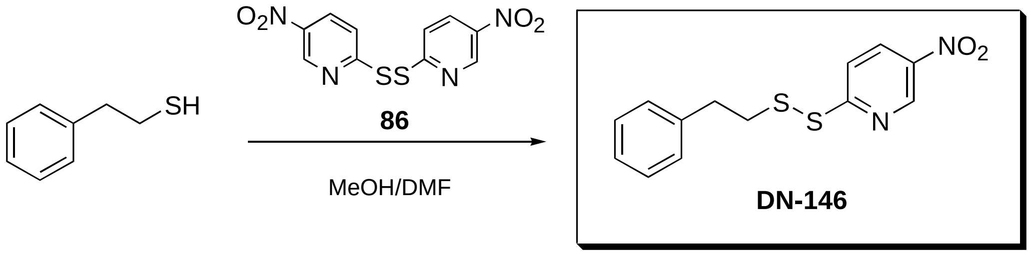
SNS-47

2-(4-Benzoyl-benzyldisulfanyldisulfanyl)-5-nitropyridine (SNS-47). Disulfide **SNS-47** was prepared as described for **SNS-43**. Flash chromatography (30:70 EtOAc/hexanes), followed by recrystallization from EtOAc/heptane, gave the title compound in 55% yield (248 mg, 0.65 mmol) as a white crystalline solid: mp = 115–117 ˚C; FTIR ($CHCl_3$) 3062 (w), 1654 (s), 1587 (s), 1564 (s), 1516 (s), 1446 (w), 1342 (s), 1277 (m), 1214 (w), 1179 (w), 1132 (w), 1096 (m), 1008 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (d, *J* = 2.6 Hz, 1 H), 8.24 (dd, *J* = 2.6 and 8.9 Hz, 1 H), 7.70 (d, *J* = 7.0, 2 H), 7.68 (d, *J* = 8.2 Hz, 2 H), 7.60 (d, *J* = 8.9 Hz, 1 H), 7.59 (t, *J* = 7.5 Hz, 1 H), 7.47 (dd, *J* = 7.0 and 7.5 Hz, 2 H), 7.40 (d, *J* = 8.2 Hz, 2 H), 4.11 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.8, 168.1, 144.9, 141.9, 140.5, 137.3, 137.1, 132.6, 131.2, 130.4, 129.9, 129.3, 128.3, 119.2, 43.1; high resolution mass spectrum (ESI) *m/z* 405.0355 [(M+Na)$^+$; calcd for $C_{19}H_{14}N_2NaO_3S_2$: 405.0344].



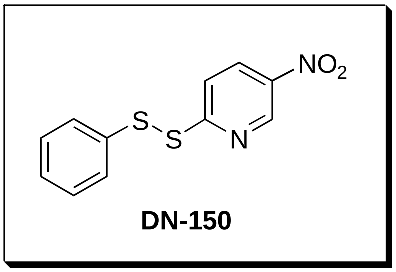
SNS-48

2-(4-Phenylbenzyldisulfanyl)-5-nitropyridine (SNS-48). Disulfide **SNS-48** was prepared as described for **SNS-43**. Flash chromatography (10:90 EtOAc/hexanes), followed by recrystallization from EtOAc/heptane, gave the title compound in 69% yield (219 mg, 0.62 mmol) as a white crystalline solid: mp = 121–123 ˚C; FTIR ($CHCl_3$) 3031 (w), 1593 (s), 1566 (s), 1525 (m), 1487 (w), 1436 (m), 1405 (w), 1343 (s), 1267 (w), 1133 (w), 1096 (m), 1007 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (d, *J* = 2.6 Hz, 1 H), 8.12 (dd, *J* = 2.6 and 8.9 Hz, 1 H), 7.54–7.40 (m, 6 H), 7.35–7.28 (m, 4 H), 4.08 (s, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 144.7, 141.7, 141.0, 140.2, 134.8, 131.0, 129.9, 128.9, 127.6, 127.3, 126.9, 119.1, 43.4; high resolution mass spectrum (CI) *m/z* 354.0482 [(M)$^+$; calcd for $C_{18}H_{14}N_2O_2S_2$: 354.0497].



DN-146

5-Nitro-2-phenethyldisulfanyl-pyridine (DN-146). Disulfide **86** (200 mg, 0.64 mmol) was dissolved in 5 mL of MeOH:DMF (1:1) solution under argon. 2-Phenylethanethiol (60 mg, 0.43 mmol) dissolved in 0.8 mL of MeOH:DMF (1:1) was added over 30 min. After the addition was complete, the reaction mixture was stirred at room temperature for 30 min. EtOAc (15 mL) was added and the organic layer was washed with saturated $NaHCO_3$ (3x) and brine (1x). The organic layer was dried over $MgSO_4$ and concentrated. The crude product was purified by flash chromatography (20% EtOAc/hexanes) to give 90 mg (71%) of **DN-146**. M.p. 91-93°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.26 (d, *J* = 2.5 Hz, 1H), 8.34 (dd, *J* = 8.9 and 2.6 Hz, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.18-7.32 (m, 5H), 3.13 (t, *J* = 7.7 Hz, 2H), 3.02 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 145.0, 142.0, 139.0, 131.5, 128.6, 128.5, 126.7, 119.1, 40.1, 35.2; IR (thin film): 3086, 3026, 2925, 2847, 1588, 1567, 1516, 1436, 1343, 1267, 1097, 855, 749, 701 cm^{-1}; low resolution mass spectrum (CI) *m/z* 293.0 [$(M+H)^+$; calcd for $C_{13}H_{13}N_2O_2S_2$: 293.0].



DN-150

5-Nitro-2-phenyldisulfanyl-pyridine (DN-150). The title compound was prepared with phenylthiol using identical procedures described above for **DN-146**. Yield: 56%. M.p. 92-94°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.26 (d, *J* = 2.6 Hz, 1H), 8.37 (dd, *J* = 8.9 and 2.6 Hz, 1H), 7.85 (d, *J* = 8.8 Hz, 1H), 7.50-7.52 (m, 2H), 7.26-7.34 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 145.0, 142.1, 134.6, 131.8, 129.4, 128.09, 128.05, 119.2; IR (thin film): 3066, 1589, 1565, 1517, 1477, 1438, 1343, 1267, 1097, 855, 749, 687 cm^{-1}; high resolution mass spectrum (CI) *m/z* 264.0027 [M^+; calcd for $C_{11}H_8N_2O_2S_2$: 264.0027].

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(ii) Ether was used as the solvent and Et_3N was eliminated. Instead of an aqueous workup, the resulting suspension (HBr salt) was filtered, washed with ether, and submitted to the Hendrickson laboratory for CD4 derivatization. A small amount was deprotonated (K_2CO_3/CH_2Cl_2) and analyzed by ^1H NMR and high resolution mass spectrometry. The yield reported is for the HBr salt.

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(xi) Anhydrous hydrazine gave the best results. Neither the HCl salt of hydrazine nor hydrazine monohydrate gave the desired product.

(xii) Preparation of ethereal solution of CH_2N_2: To a round bottom flask containing 10 mL of ether and 10 mL of 40% aqueous KOH solution was added *N*-methyl-*N*-nitrosourea (605 mg, 5.88 mmol) at 0^oC. The biphasic mixture was stirred at 0^oC for 30 min. The ethereal layer containing CH_2N_2 was separated and used immediately.