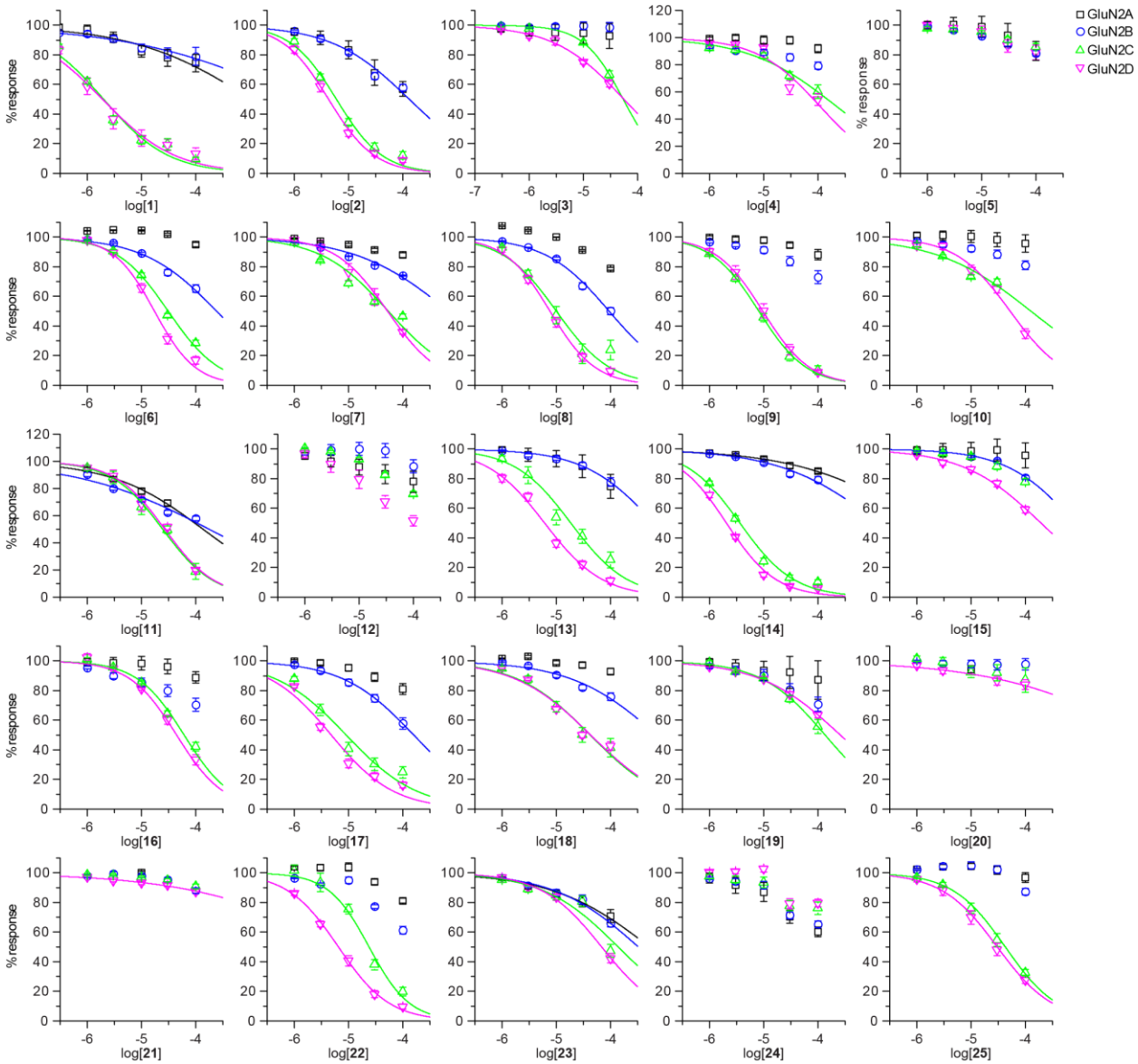
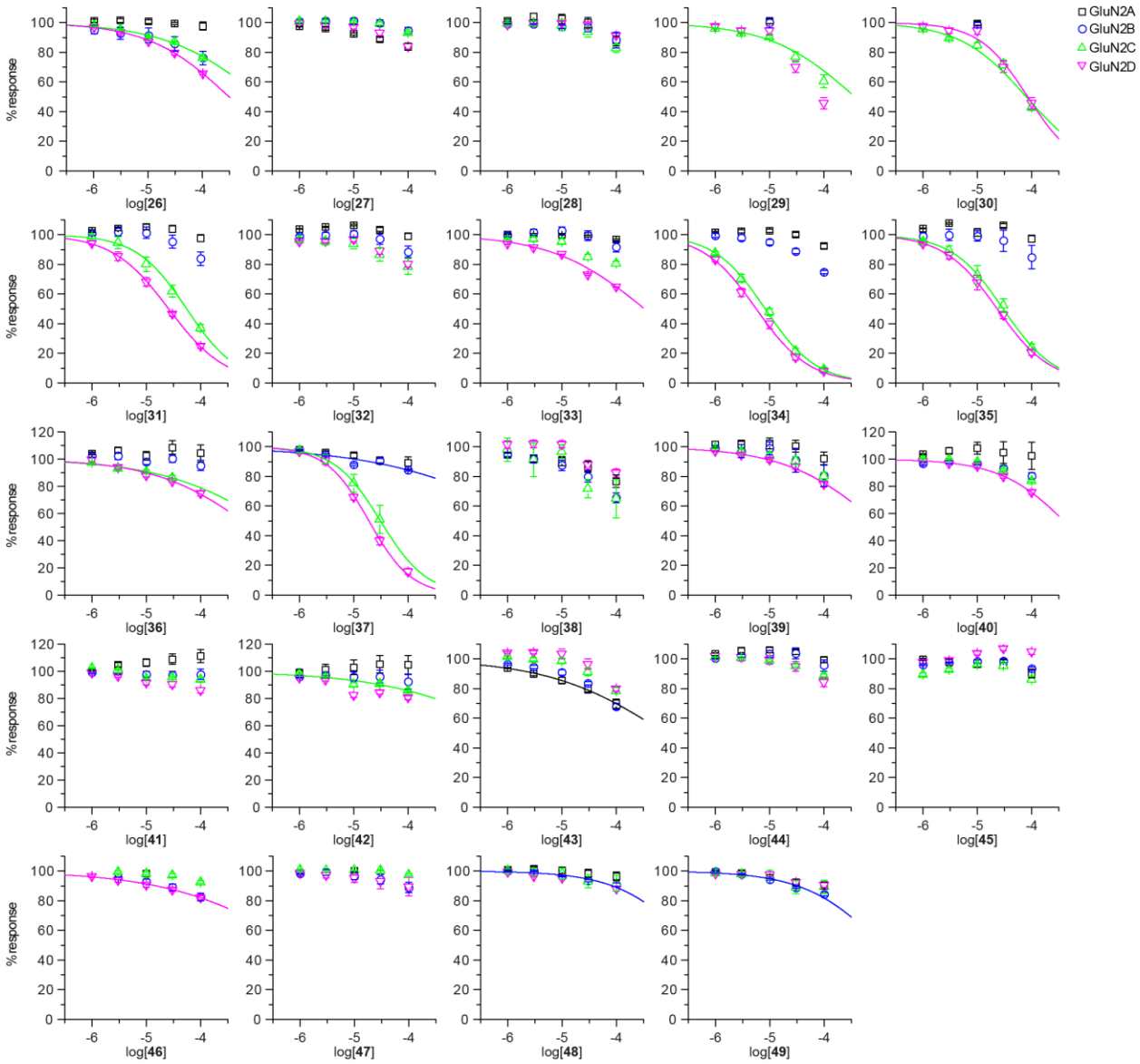
Supporting Information

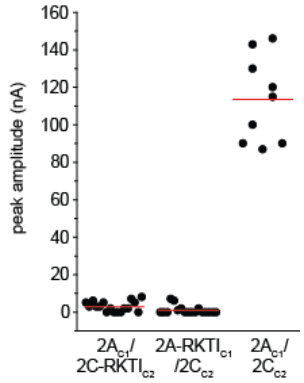
Contents: **Pages**



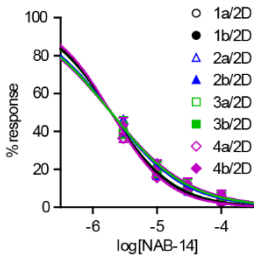
Supplementary Figure 1. Mean concentration-response data and fitted curves for the NAB series. Concentration-response data were plotted for each test compound as the mean percent (± s.e.m.) of the maximal response to 100 µM glutamate and 30 µM glycine in *Xenopus* oocytes expressing GluN1-1a with GluN2A-2D. The data were fit by the Hill equation, unless the 99% CI for the percent maximal response at 10 µM included 100%. Fitted IC_{50} values, percent maximal response at 10 µM, and compound structures are in **Tables 1** and **2,** and **Supplementary Table 1**.



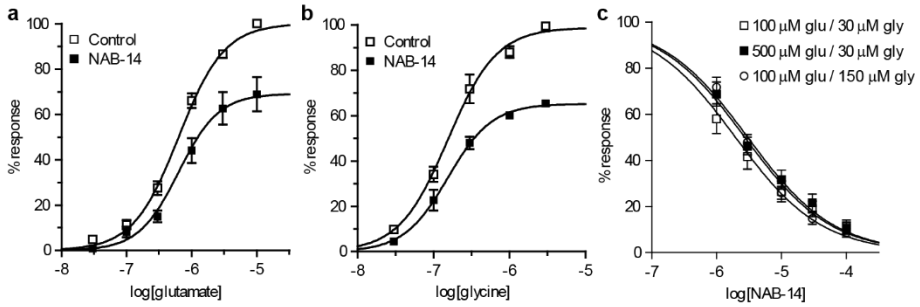
Supplementary Figure 2. Mean concentration-response data and fitted curves for the NAB series (continued). Concentration-response data were plotted for each test compound as the mean percent (± s.e.m.) of the maximal response to 100 µM glutamate and 30 µM glycine in *Xenopus* oocytes expressing GluN1-1a with GluN2A-2D. The data were fit by the Hill equation, unless the 99% CI for the percent maximal response at 10 µM included 100%. Fitted IC_{50} values, percent maximal response at 10 µM, and compound structures are in **Supplementary Tables 1–5**.



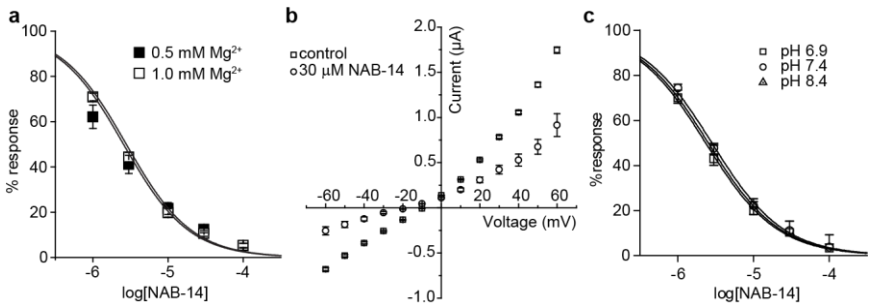
Supplementary Figure 3. Diheteromeric receptors contribute minimal current to GluN1/2A$_{C1}$/2C$_{C2}$ responses. Current responses to glutamate and glycine were recorded from oocytes expressing GluN1/2A$_{C1}$/2C$_{C2}$, GluN1/2A$_{C1}$/2C-RKTI$_{C2}$, or GluN1/2A-RKTI$_{C1}$/2C$_{C2}$. GluN1/2A$_{C1}$/2C-RKTI$_{C2}$ or GluN1/2A-RKTI$_{C1}$/2C$_{C2}$ receptors cannot be activated as GluN2-RKTI subunits do not effectively bind glutamate; therefore, the current responses in these cells are mediated by diheteromeric GluN1/2A$_{C1}$/2A$_{C1}$ and GluN1/2C$_{C2}$/2C$_{C2}$ that have "escaped" the ER. The sum of the GluN1/2A$_{C1}$/2A$_{C1}$ and GluN1/2C$_{C2}$/2C$_{C2}$ "escape" current amplitudes constitutes the diheteromeric receptor contribution, which was determined to be 4.2% of the response amplitude in oocytes expressing GluN1/2A$_{C1}$/2C$_{C2}$. Data points from all experiments are shown, and the red line is the mean.



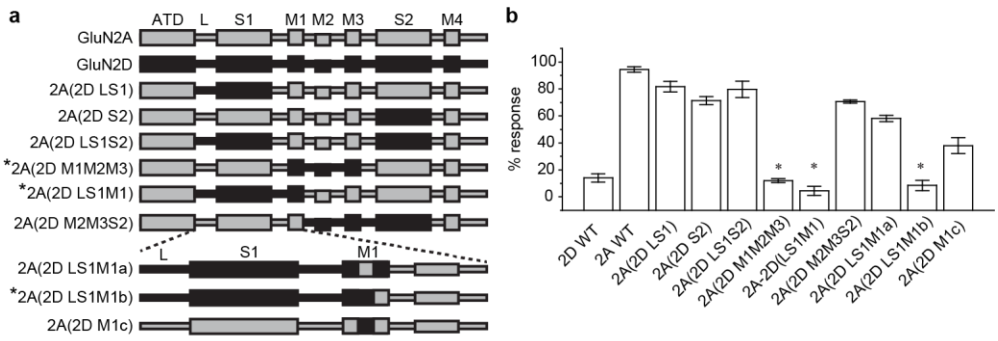
Supplementary Figure 4. NAB-14 inhibits NMDARs containing each of the GluN1 splice variants. Current responses to 100 µM glutamate and 30 µM glycine were recorded from *Xenopus* oocytes expressing GluN2D with one of the eight GluN1 splice variants (1a, 1b, 2a, 2b, 3a, 3b, 4a, 4b) in the presence of increasing concentrations of NAB-14. The concentration-response data are presented as percent of the maximal response to glutamate and glycine (mean ± s.e.m.) and were fit by the Hill equation. See **Supplementary Table 6** for IC_{50} values and statistics.



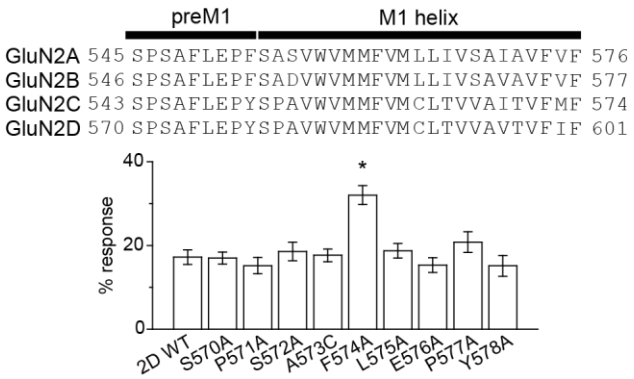
Supplementary Figure 5. NAB-14 is a non-competitive antagonist. Concentration-response data were plotted for current responses to increasing concentrations of (**a**) glutamate (30 μM glycine in all solutions) or (**b**) glycine (100 μM glutamate in all solutions). Current responses were recorded from *Xenopus* oocytes expressing GluN1/GluN2D in the presence of 0.1 % DMSO (control) or 3 μM NAB-14. The data (mean ± s.e.m.) were plotted and fit by the Hill equation. (**c**) Concentration-response data for NAB-14 were acquired in three different concentrations of glutamate (glu) and glycine (gly), as stated in the legend, and plotted as a percent of the maximal response (mean ± s.e.m.). See **Supplementary Table 7** for fitted IC_{50} values. The data were fit with the Hill equation, and the pIC_{50} values were compared by F-tests [glutamate: $F(1,84) = 0.644$, $p = 0.425$, glycine: $F(1,77) = 0.026$, $p = 0.873$, NAB-14: $F(2,123) = 2.17$, $p = 0.118$].



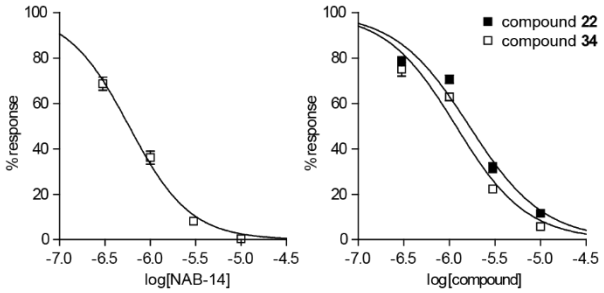
Supplementary Figure 6. Mg^{2+} concentration, voltage, and pH have no significant effects on NAB-14 activity. **(a)** Concentration-response data for NAB-14 was recorded in solutions containing 0.5 or 1.0 mM Mg^{2+}, and the data were fit by the Hill equation to determine the IC_{50} values (0.5 mM Mg^{2+}: 2.0 µM, pIC_{50} = -5.70 (-5.77,-5.63); 1.0 mM Mg^{2+}: 2.4 µM, pIC_{50} = -5.62 (-5.69,-5.55); $F(1,77) = 2.311$, $p = 0.110$). **(b)** The current-voltage relationship for GluN1/GluN2D receptors was determined in oocytes in the absence and presence of 30 µM NAB-14. The reversal potentials for control (0.119 ± 0.004) and NAB-14 (0.146 ± 0.008) were compared by a paired t-test ($p = 0.109$). **(c)** Concentration-response data for NAB-14 at GluN1/GluN2D receptors were acquired in oocytes with recording solutions at pH 6.9, 7.4, and 8.4. These data were plotted (mean ± s.e.m.) and fit by the Hill equation. The pIC_{50} values were compared across the different pH levels by a F-test [pH 6.9: 2.5 µM, pIC_{50} = -5.60 (-5.65,-5.54); pH 7.4: 2.3 µM, pIC_{50} = -5.63 (-5.68,-5.58); pH 8.4: 2.8 µM, pIC_{50} = -5.55 (-5.60,-5.50); $F(2,106) = 2.994$, $p = 0.054$].



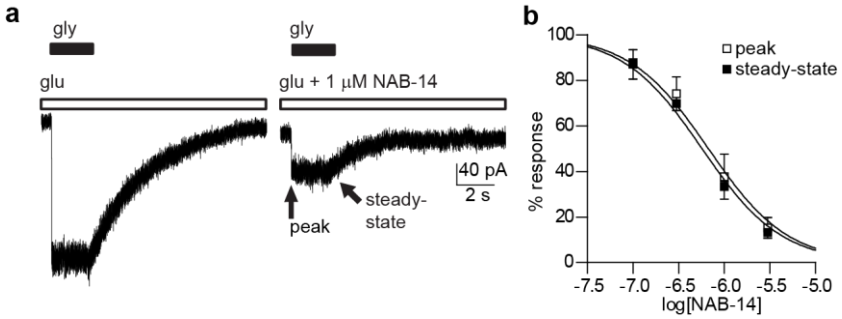
Supplementary Figure 7. The M1 transmembrane helix of GluN2D can transfer NAB-14 activity to GluN2A. **(a)** Domains from GluN2D were substituted for GluN2A domains to test whether NAB-14 activity could be transferred to GluN2A. The domains listed are: amino-terminal domain (ATD), linker (L), S1 and S2 are two portions of the polypeptide chain that form the agonist binding domain, and M1–M4 are the four transmembrane domains. **(b)** NAB-14 activity was tested on the chimeric GluN2 subunits expressed with GluN1 in *Xenopus* oocytes. Current responses to maximal glutamate and glycine in the absence and presence of 10 μM NAB-14 were measured by TEVC. The current response amplitude in NAB-14 is expressed as a percentage of the control response to glutamate (100 μM) and glycine (30 μM). The data were compared by one-way ANOVA and post hoc Bonferroni tests were performed to compare each chimera to GluN2A-WT and GluN2D-WT [$F(10,46) = 98.096$, $p < 0.001$, *significantly different from GluN2A and not significantly different from GluN2D; see **Supplementary Table 11** for mean comparison results].



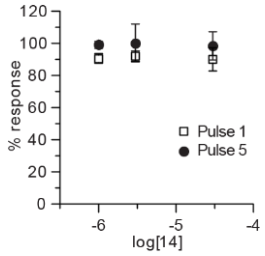
Supplementary Figure 8. Structural determinants of NAB-14 may include part of the pre-M1 region. NAB-14 activity was tested on GluN1/GluN2D receptors containing alanine mutations at pre-M1 residues in *Xenopus* oocytes. Current responses to 100 μM glutamate and 30 μM glycine in the absence and presence of 10 μM NAB-14 were measured by TEVC. The response in NAB-14 is expressed as a percent of the maximal response to glutamate and glycine. The data were compared by one-way ANOVA with post hoc Dunnett's tests compared to GluN2D-WT [$F(9,81) = 7.148$, $p < 0.001$, $^*p < 0.05$, see **Supplementary Table 13** for mean comparison results].



Supplementary Figure 9. NAB series compounds have enhanced potency at GluN1/GluN2D receptors expressed in HEK cells. Glutamate (100 μM) and glycine (30 μM) plus increasing concentrations of NAB-14, compound **22**, or compound **34** were co-applied to HEK cells transiently expressing GluN1/GluN2D using a rapid solution exchange system. Current responses were recorded by whole-cell voltage-clamp. Concentration-response data were plotted as a percentage of the maximal response and fit by the Hill equation.

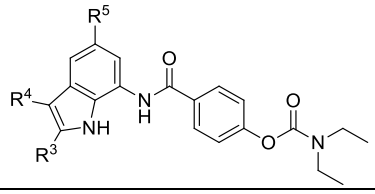


Supplementary Figure 10. NAB-14 activity is unaffected by glycine binding. 100 μM glutamate or 100 μM glutamate plus increasing concentrations of NAB-14 were applied to HEK cells expressing GluN1/GluN2D, then 30 μM glycine was applied for 15 s in the continuing presence of glutamate and NAB-14. Concentration-response data measured from the peak (initial) and steady-state responses to glycine applications were plotted and fit by the Hill equation. The pIC_{50} values were compared by F-tests [peak IC_{50} = 680 nM, pIC50 = -6.17 (-6.23,-6.11); steady-state IC_{50} = 580 nM, pIC_{50} = -6.24 (-6.28,-6.19); F(1,44) = 3.242, p = 0.077].



Supplementary Figure 11. NAB-14 does not inhibit GluN1/GluN2A receptor current responses in HEK cells. HEK cells were transfected with GluN1 and GluN2A and current repsones to pressure pulses of NMDA/glycine were recorded at by whole-cell voltage-clamp at -60 mV. The peak amplitude of responses to the first and fifth pulses were measured and plotted. The mean percent of the control response and 99% CI at 30 μM NAB-14 for pulse 1 was 91% (71,110) and pulse 5 was 99% (69,130).

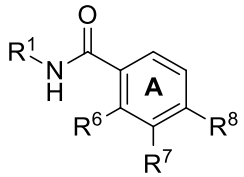
Supplementary Table 1. Optimization of Indole Substituents



#	R^3	R^4	R^5	IC_{50}, mean (μM) pIC_{50}, mean (95% CI) % control at 10 μM, mean (99% CI) GluN2A	GluN2B	GluN2C	GluN2D	N
14	H	H	H	5170 -2.36 (-2.58,-2.13) 93 (88,98)	3010 -2.69 (-2.97,2.41) 91 (87,95)	3.7 -5.45 (-5.54,5.37) 24 (18,31)	2.2 -5.68 (-5.74,-5.61) 15 (10,20)	12
22	H	H	Me	104 (88,120)	95 (87,103)	24 -4.65 (-4.80,-4.49) 75 (64,87)	6.8 -5.19 (-5.31,-5.07) 41 (28,53)	4–8
23	H	Me	Me	1200 -3.07 (-3.81,-2.33) 86 (73,99)	289 -3.55 (-3.86,-3.27) 86 (74,99)	85 (68,101)	84 -4.16 (-4.31,-4.01) 84 (77,90)	3–10
24	H	Me	CO_2Me	87 (49,125)	92 (77,107)	94 (72,115)	103 (89,109)	4–8
25	H	Me	H	104 (92,117)	105 (91,119)	42 -4.41 (-4.56,-4.26) 76 (64,88)	33 -4.55 (-4.76,-4.34) 70 (55,85)	4–9
26	Me	H	H	101 (93,109)	91 (62,120)	1100 -3.00 (-3.33,-2.66) 90 (88,92)	315 -3.51 (-3.61,-3.39) 87 (82,92)	4

Current responses to 100 μM glutamate and 30 μM glycine co-applied with increasing concentrations of compound were recorded in *Xenopus* oocytes expressing GluN1 with GluN2A, GluN2B, GluN2C, or GluN2D. The data were fit by the Hill equation, unless the 99% CI of the mean percent maximal response at 10 μM included 100%. Data for compound **14**, reported in Table 1, are included here for comparison.

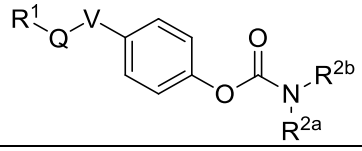
Supplementary Table 2. Optimization of A-Ring Substituent Position and Identity

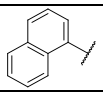
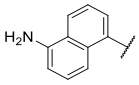
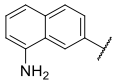


#	R^1	R^6	R^7	R^8	IC_{50}, mean (μM) pIC_{50}, mean (95% CI) % control at 10 μM, mean (99% CI) GluN2A	GluN2B	GluN2C	GluN2D	N
2		H	H	$OC(O)NEt_2$	83 (61,106)	172 -3.82 (-4.00,-3.64) 82 (77,86)	6.7 -5.21 (-5.33,-5.10) 35 (27,42)	5.0 -5.38 (-5.49,-5.27) 27 (21,33)	7–21
14		H	H	$OC(O)NEt_2$	5170 -2.36 (-2.58,-2.13) 93 (88,98)	3010 -2.69 (-2.97,2.41) 91 (87,95)	3.7 -5.45 (-5.54,5.37) 24 (18,31)	2.2 -5.68 (-5.74,-5.61) 15 (10,20)	12
27		H	$OC(O)NEt_2$	H	NF 92 (88,97)	101 (90,112)	100 (95,106)	97 (89,105)	4
28		$OC(O)NEt_2$	H	H	103 (85,120)	97 (92,102)	98 (77,119)	100 (93,106)	4
29		H	F	$OC(O)NEt_2$	101 (94,108)	104 (84,116)	234 -3.70 (-4.41,-2.99) 90 (81,99)	95 (78,111)	3-5
30		H	Cl	$OC(O)NEt_2$	99 (92,107)	96 (87,110)	79 -4.11 (-4.27,-3.95) 85 (74,96)	64 -4.21 (-4.41,-4.01) 89 (82,97)	4-7
31		H	Cl	$OC(O)NEt_2$	105 (94,116)	101 (79,123)	54 -4.29 (-4.45,-4.13) 80 (62,98)	26 -4.60 (-4.67,-4.52) 68 (58,78)	4–8
32		H	I	$OC(O)NEt_2$	106 (103,110)	100 (91,109)	94 (74,114)	97 (88,105)	4
33		H	OMe	$OC(O)NEt_2$	100 (97,104)	103 (87,118)	96 (86,105)	316 -3.50 (-3.52,-3.48) 87 (86,87)	4
34		Cl	H	$OC(O)NEt_2$	103 (96,110)	95 (86,103)	8.7 -5.08 (-5.18,-4.98) 48 (41,55)	6.3 -5.24 (-5.37,-5.12) 40 (30,50)	4–12

Current responses to 100 μM glutamate and 30 μM glycine co-applied with increasing concentrations of compound were recorded in *Xenopus* oocytes expressing GluN1 with GluN2A, GluN2B, GluN2C, or GluN2D. The data were fit by the Hill equation, unless the 99% CI of the mean percent maximal response at 10 μM included 100%. NF: the 99% CI did not include 100%, but the data could not be fit by the Hill equation. Data for compounds **2** and **14**, reported in Table 1, are included here for comparison.

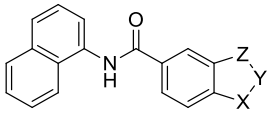
Supplementary Table 3. Optimization of Linker A



#	R^1	R^{2a} and R^{2b}	Q	V	IC_{50}, mean (μM) pIC_{50}, mean (95% CI) % control at 10 μM, mean (99% CI) GluN2A	GluN2B	GluN2C	GluN2D	N
1		Et	NH	C=O	1070 -3.60(-4.98,-2.22) 82 (69,96)	2320 -2.98 (-3.71,-2.25) 85 (76,93)	2.6 -5.65 (-5.80,-5.50) 27 (17,36)	1.4 -5.91 (-6.10,-5.72) 16 (5,28)	7–10
35		Et	C=O	NH	102 (92,111)	99 (83,115)	31 -4.59 (-4.85,-4.32) 73 (52,94)	25 -4.64 (-4.80,-4.48) 68 (52,84)	7-8
36		iPr	O	C=O	102 (90,114)	98 (89,107)	2070 -2.78 (-3.64,-1.92) 91 (83,98)	1260 -2.99 (-3.50,-2.49) 88 (80,96)	4-7
37		iPr	O	C=O	94 (84,104)	6510 -2.21 (-2.45,-1.96) 88 (84,92)	258 -4.34 (-4.96,-3.72) 75 (56,95)	194 -4.73 (-4.83,-4.63) 66 (60,72)	4-10

Current responses to 100 μM glutamate and 30 μM glycine co-applied with increasing concentrations of compound were recorded in *Xenopus* oocytes expressing GluN1 with GluN2A, GluN2B, GluN2C, or GluN2D. The data were fit by the Hill equation, unless the 99% CI of the mean percent maximal response at 10 μM included 100%. Data for compound **1**, reported in Table 1, are included here for comparison.

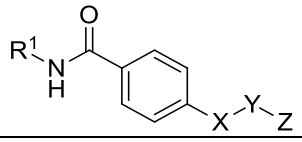
Table 4. Optimization of Linker B

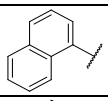
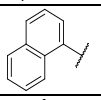
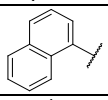
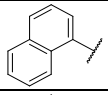
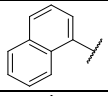
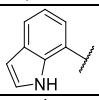
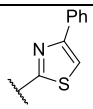
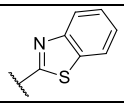


#	X	Y	Z	IC_{50}, mean (μM) pIC_{50}, mean (95% CI) % control at 10 μM, mean (99% CI) GluN2A	GluN2B	GluN2C	GluN2D	N
38	O	C=O	NH	90 (72,108)	87 (67,108)	97 (78,115)	102 (91,112)	4-6
39	O	C=O	NMe	102 (81,123)	99 (79,119)	94 (81,106)	754 -3.13 (-3.28,-2.98) 91 (84,98)	4

Current responses to 100 μM glutamate and 30 μM glycine co-applied with increasing concentrations of compound were recorded in *Xenopus* oocytes expressing GluN1 with GluN2A, GluN2B, GluN2C, or GluN2D. The data were fit by the Hill equation, unless the 99% CI of the mean percent maximal response at 10 μM included 100%.

Supplementary Table 5. Optimization of Linker B



#	R^1	X	Y	Z	IC_{50}, mean (μM) pIC_{50}, mean (95% CI) % control at 10 μM, mean (99% CI) GluN2A	GluN2B	GluN2C	GluN2D	N
1		O	C=S	NEt_2	1070 -3.60(-4.98,-2.22) 82 (69,96)	2320 -2.98 (-3.71,-2.25) 85 (76,93)	2.6 -5.65 (-5.80,-5.50) 27 (17,36)	1.4 -5.91 (-6.10,-5.72) 16 (5,28)	7–10
2		O	C=O	NEt_2	83 (61,106)	172 -3.82 (-4.00,-3.64) 82 (77,86)	6.7 -5.21 (-5.33,-5.10) 35 (27,42)	5.0 -5.38 (-5.49,-5.27) 27 (21,33)	7–21
40		NH	C=O	NEt_2	108 (82,134)	97 (90,104)	98 (94,102)	95 (89,100)	4-7
41		O	C=O	CEt_2	106 (89,124)	98 (85,110)	NF 95 (93,97)	92 (82,101)	4
42		O	C=O	Cyclo-propyl	103 (49,157)	96 (77,116)	NF 90 (83,98)	NF 83 (72,93)	3-4
43		OCH_2	C=O	NEt_2	1490 -3.05 (-3.68,-2.37) 86 (74,97)	91 (81,101)	99 (89,108)	103 (71,136)	4
44		CH_2O	C=O	NEt_2	106 (86,126)	103 (89,117)	99 (95,103)	99 (82,117)	3-4
45		CH_2O	C=O	NEt_2	97 (82,111)	98 (93,104)	96 (86,106)	104 (96,111)	4
46		-	C=O	NEt_2	98 (93,104)	93 (83,102)	98 (93,104)	91 (81,100)	4
47		-	C=O	OH	100 (98,102)	97 (73,120)	100 (99,101)	95 (78,112)	3-4
48		O			100 (88,113)	NF 96 (94,99)	98 (77,120)	96 (91,100)	4
49		O			96 (86,106)	2470 -2.64 (-2.96,-2.31) 94 (91,98)	97 (79,116)	98 (88,108)	4

Current responses to 100 μM glutamate and 30 μM glycine co-applied with increasing concentrations of compound were recorded in *Xenopus* oocytes expressing GluN1 with GluN2A, GluN2B, GluN2C, or GluN2D. The data were fit by the Hill equation, unless the 99% CI of the mean percent maximal response at 10 μM included 100%. NF: the 99% CI did not include 100%, but the data could not be fit by the Hill equation. Data for compound **1** and **2**, reported in Table 1, are included here for comparison.

Supplementary Table 6. NAB-14 inhibits NMDARs containing GluN1 splice variants similarly.

splice variant	IC_{50}	pIC_{50} (95% CI)	% response (100 μM) mean ± s.e.m.	N
GluN1-1a	1.8	-5.73 (-5.81,-5.65)	2.8 ± 1.0	4
GluN1-1b	2.0	-5.70 (-5.77,-5.62)	6.4 ± 0.3	4
GluN1-2a	2.5	-5.61 (-5.66,-5.56)	4.8 ± 0.9	4
GluN1-2b	2.1	-5.67 (-5.81,-5.53)	3.7 ± 1.1	4
GluN1-3a	1.7	-5.77 (-5.87,-5.67)	3.6 ± 0.8	4
GluN1-3b	2.0	-5.69 (-5.87,-5.51)	5.3 ± 2.4	5
GluN1-4a	1.5	-5.84 (-5.98,-5.69)	3.8 ± 2.3	4
GluN1-4b	1.9	-5.71 (-5.91,-5.51)	6.9 ± 2.1	4

Concentration-response data were fit by the Hill equation, and the pIC50 values were compared between groups using an F-test [$F(7,116) = 1.055$, $p = 0.397$]. See **Supplementary Figure 4** for concentration-response curves and experimental details.

Supplementary Table 7. NAB-14 potency is not affected by agonist concentration.

[glutamate] / [glycine]	IC_{50} (μM)	pIC_{50} (95% CI)	N
100 μM / 30 μM	2.0	-5.71 (-6.35,-5.07)	6
500 μM / 30 μM	3.0	-5.52 (-6.17,-4.87)	10
100 μM / 150 μM	2.7	-5.57 (-6.21,-4.92)	10

Current responses were recorded from *Xenopus* oocytes expressing GluN1/GluN2D receptors, and concentration-response data for NAB-14 were acquired for different concentrations of glutamate and glycine. The data were fit by the Hill equation.

Supplementary Table 8. Deactivation time constants for STN EPSCs.

	Control	Vehicle	Control	NAB-14
τ_{FAST} (ms)	34 ± 2.7	32 ± 5.0	45 ± 24	33 ± 20
τ_{SLOW} (ms)	264 ± 7.8	297 ± 11	276 ± 20	152 ± 81
% τ_{FAST}	62 ± 1.8	65 ± 2.8	67 ± 15	65 ± 20
τ_W (ms)	120 ± 4.0	125 ± 6.6	122 ± 42	79 ± 21
N	4		4	

Supplementary Table 9. Membrane properties of hippocampal interneurons.

Group/Cell #	Capacitance (pF)	Input Resistance (MΩ)
Vehicle		
Cell 1	41	374
Cell 2	36	269
Cell 3	42	147
Cell 4	24	135
NAB-14		
Cell 5	39	277
Cell 6	48	283
Cell 7	26	372
Cell 8	41	154
Cell 9	28	176

Supplementary Table 10. Deactivation time constants for hippocampal EPSCs.

		Control	Vehicle	Control	NAB-14
Pyramidal Neuron	**τ_{FAST} (ms)**	44 ± 6.0	41 ± 10	58 ± 9.5	53 ± 16
	τ_{SLOW} (ms)	226 ± 51	216 ± 39	239 ± 21	233 ± 13
	% τ_{FAST}	64 ± 5.0	62 ± 7.0	72 ± 9.6	67 ± 11
	τ_W (ms)	109 ± 26	112 ± 31	111 ± 12	118 ± 9.8
	N	3		4	
Interneuron	**τ_{FAST} (ms)**	69 ± 29	59 ± 22	69 ± 7.4	62 ± 16
	τ_{SLOW} (ms)	265 ± 54	283 ± 38	288 ± 25	217 ± 39
	% τ_{FAST}	58 ± 18	60 ± 18	62 ± 2.6	71 ± 9.0
	τ_W (ms)	157 ± 22	151 ± 27	150 ± 12	101 ± 14
	N	4		5	

Supplementary Table 11. Means comparisons for GluN2A-2D chimeras in **Supplementary Figure 7**.

	p value	
Chimera	**vs 2D WT**	**vs 2A WT**
2D WT	-	<0.001
2A WT	<0.001	-
2A (2D LS1)	<0.001	0.482
2A (2D S2)	<0.001	<0.001
2A (2D LS1S2)	<0.001	0.155
2A (2D LS1M1)	0.999	<0.001
2A (2D M1M2M3)	0.999	<0.001
2A (2D M2M3S2)	<0.001	<0.001
2A (2D LS1M1a)	<0.001	<0.001
2A (2D LS1M1b)	0.999	<0.001
2A (2D M1c)	0.002	<0.001

Supplementary Table 12. Means comparisons for GluN2A-2D mutants in **Figure 2**.

Mutant	P value
2D-C590L	<0.001
2D-T592I	>0.99
2D-V594S	0.20
2D-T597A	>0.99
2A-L565C	<0.001
2A-1567T	0.02
2A-S569V	0.55
2A-572T	>0.99
2D(S579A)	0.32
2D(P580A)	0.20
2D(A581C)	0.04
2D(V582A)	0.004
2D(W583A)	0.001
2D(W584A)	0.97
2D(M585A)	0.40
2D(M586A)	<0.001
2D(F587A)	<0.001
2D(V588A)	>0.99
2D(M589A)	>0.99
2D(C590A)	<0.001
2D(L591A)	<0.001
2D(T592A)	>0.99
2D(V593A)	>0.99
2D(T594A)	<0.001
2D(A595C)	<0.001
2D(V596A)	>0.99
2D(T597A)	>0.99
2D(V598A)	0.25
2D(F599A)	0.81
2D(I600A)	>0.99
2D(F601A)	0.55

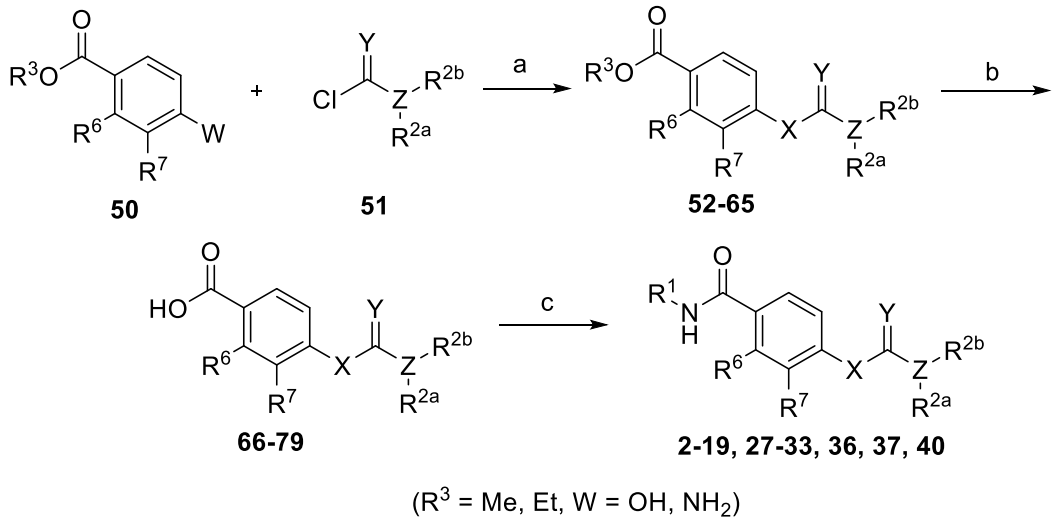
Supplementary Table 13. Mean comparisons for pre-M1 GluN2D mutants in **Supplementary Figure 8**.

Mutant	P value
2D(S570A)	>0.99
2D(P571A)	>0.99
2D(S572A)	>0.99
2D(A573C)	>0.99
2D(F574A)	<0.001
2D(L575A)	>0.99
2D(E576A)	0.97
2D(P577A)	0.72
2D(Y578A)	>0.99

Chemistry Methods

The synthetic route towards thiocarbamate (X=O, Y=S, Z=N), carbamate (X=O, Y=O, Z=N), and urea (X=NH, Y=O, Z=N) analogs is illustrated in Scheme 1. Reaction of ester **50** with the appropriately substituted thiocarbamoyl chloride or carbamoyl chloride reagent (**51**) generated the corresponding thiocarbamate, carbamate, and urea analogs (**52-65)**. Saponification of the ester afforded carboxylic acids **66-79**, which were subsequently subjected to standard coupling conditions to give the desired amide.

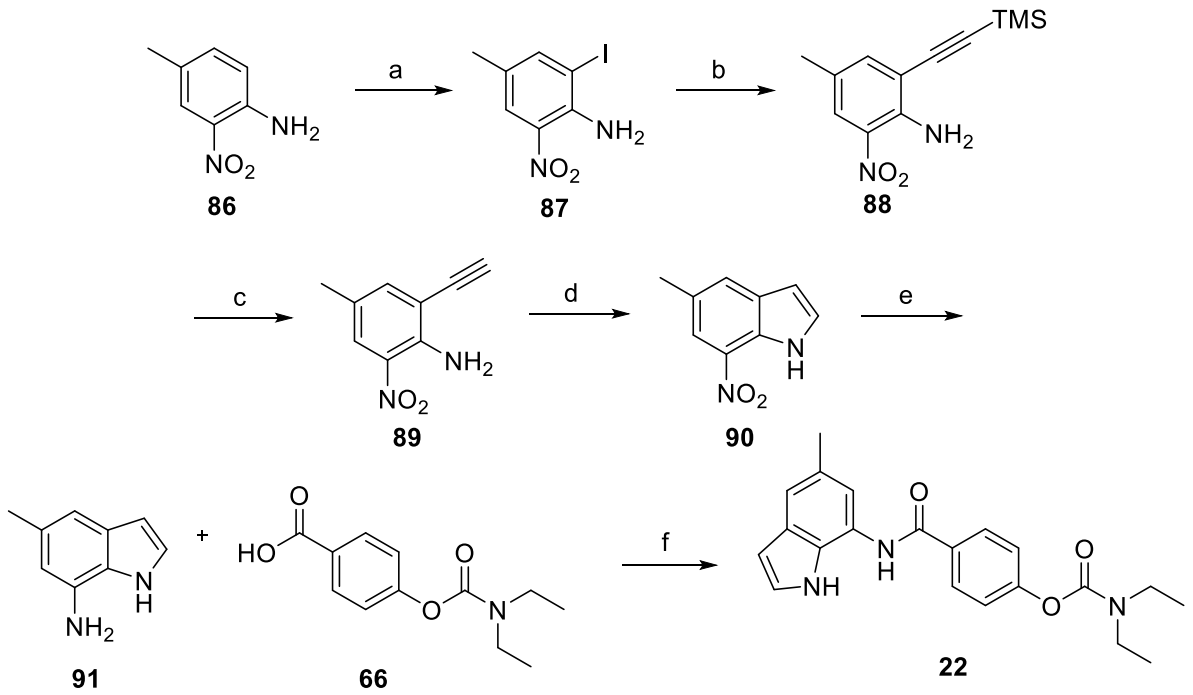
Scheme 1. Route for the Synthesis of Thiocarbamate, Carbamate, and Urea Analogs [a]



[a] *Reaction conditions:* (a) K_2CO_3, DMF, 71-95%; (b) NaOH, MeOH, rt, 12 hrs, 71-96%; (c) EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 32->99%.

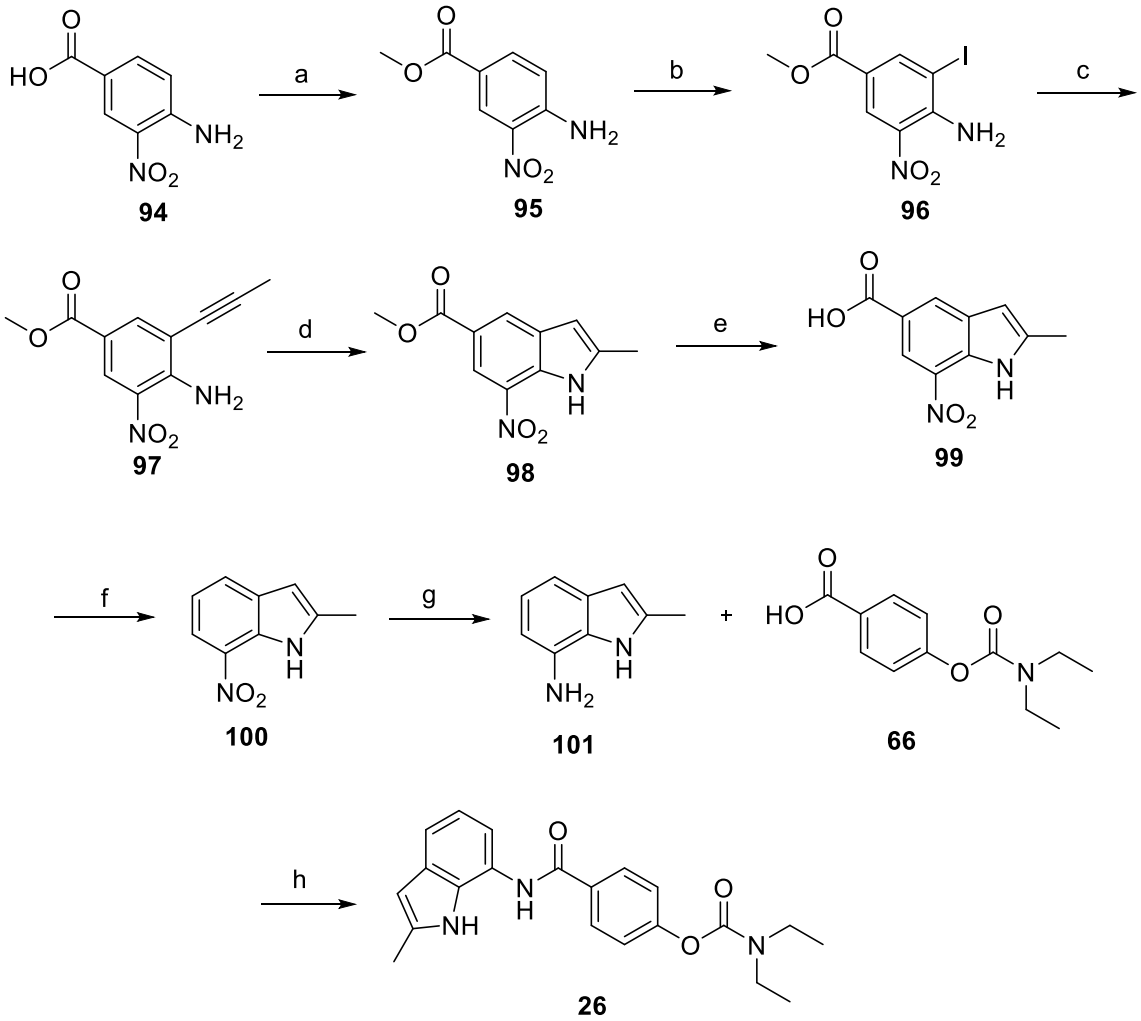
Analogs containing substituted indoles at R^1 were synthesized using two methodologies. In the first method, the 2-substituted indoles were generated by iodonizing 4-methyl-2-nitroaniline with ICl. In method 2, iodination of methyl-4-amino-3-nitrobenzoate, which was prepared *via* standard esterification, was performed with iodine and silver sulfate. The iodonitro-anilines were then coupled to the desired alkyne under Sonogashira conditions followed by 5-endo-dig cyclization (Schemes 2 and 3). The ester-containing compounds could then be saponified and de-carboxylated (Scheme 3) to afford the desired nitro-indole. Each of the nitro-indole compounds could be reduced to the appropriate aniline and coupled to the desired partner, as described above.

Scheme 2. Synthesis of 5-Substituted Indole Analog 22 via Sonogashira Reaction [a]



[a] *Reaction Conditions:* (a) ICl, rt, 1 hr, 66%; (b) ethynyltrimethylsilane, TEA, CuI, $Pd(Cl_2(PPh_3)_2)$, 0 °C to rt, 2 hrs, 67%; (c) TBAF, rt, 1 hr, 71%; (d) K-*t*-BuOH, NMP, rt, 1 ½ hrs, 50%; (e) H_2, 10% Pd/C, MeOH, 40 psi, rt, 45 min., 97%; (f) EDCI, DMAP, DCM, 0 °C to rt,, 12 hrs, 22%.

Scheme 3. Route to Access 2-Substituted Indole Analog 26 [a]

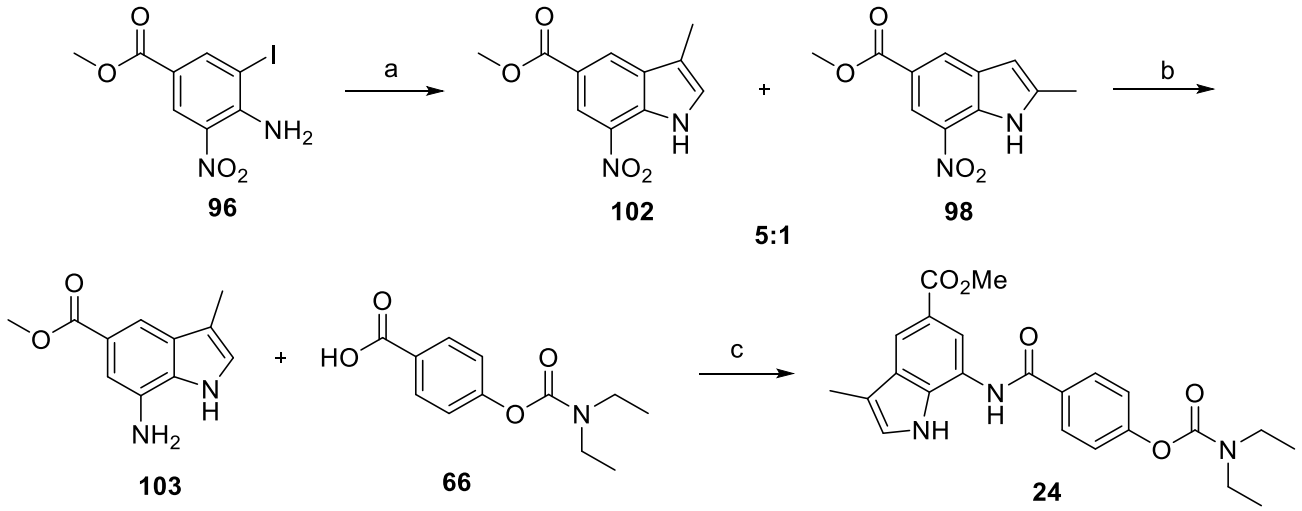


[a] *Reaction conditions:* (a) $SOCl_2$, MeOH, rt, 2 hrs, 87%; (b) I_2, Ag_2SO_4, rt, 36 hrs, 43%; (c) prop-1-yne, TEA, $Pd(Cl_2(PPh_3)_2)$, CuI, 62%; (d) K-*t*-BuO, NMP, rt, 12 hrs, 30%; (e) NaOH, MeOH, 120 °C M.W., 10 min, 87%; (f) Cu_2O, phenanthroline, NMP, quinoline, 170 °C, 41%; (g) H_2, 10% Pd/C, MeOH, 40 psi, rt, 45 min, >99%; (h) EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 30%.

Alternatively, the Larock indole synthesis was envisioned to access 3-substituted indole-containing compounds (Schemes 4 and 5). However, the methyl 4-amino-3-iodo-5-nitrobenzoate reaction with trimethyl-(prop-1-yn-1-yl)-silane under Larock conditions yielded a 5:1 mixture of 2- and 3-methyl substituted indoles which could not be separated. The mixture of methyl-3-methyl-7-nitro-1H-indole-5-carboxylate and methyl 2-methyl-7-nitro-1H-indole-5-carboxylate was carried forward through reduction of the nitro-group and coupling to the desired partner (also an inseparable mixture, 5:1). Similarly, de-

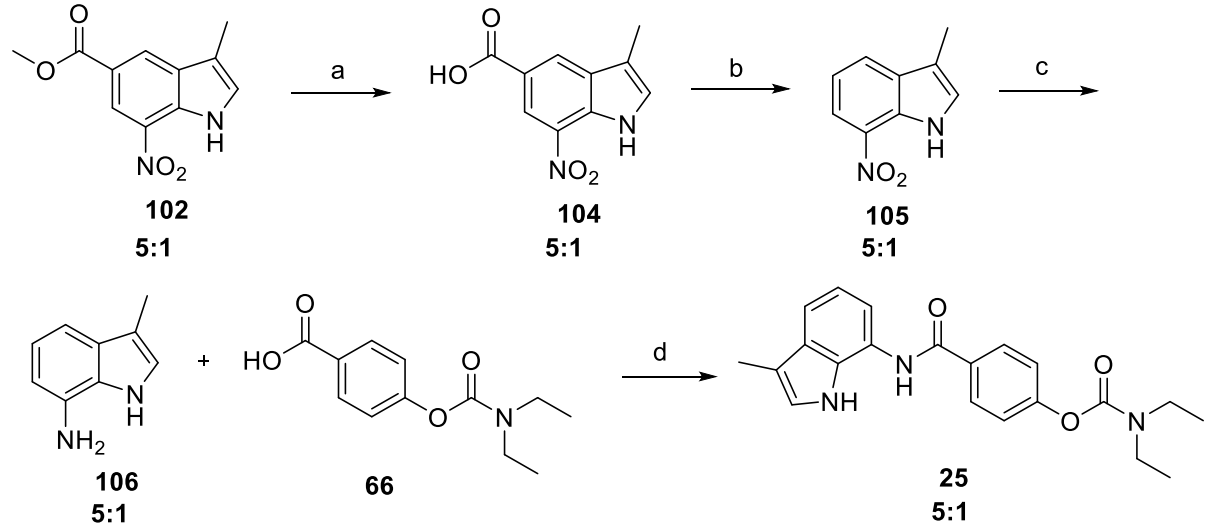
carboxylation of the 3-methyl-7-nitro-1H-indole-5-carboxylate and methyl 2-methyl-7-nitro-1H-indole-5-carboxylate resulted in an inseparable mixture of 3-methyl-7-nitro indole and 2-methyl-7-nitro indole, which remained inseparable throughout the subsequent steps (Scheme 5).

Scheme 4. Route to Access Di-Substituted Indole Analog 24 [a]



[a] *Reaction conditions:* (a) trimethyl(prop-1-ynyl)silane, LiCl, $Pd(OAc)_2$, K_2CO_3, 100 °C, 5 hrs, 48%, 5:1; (b) H_2, 10% Pd/C, MeOH, 40 psi, rt, 45 min, 88%, 5:1; (c) EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 32%, 5:1.

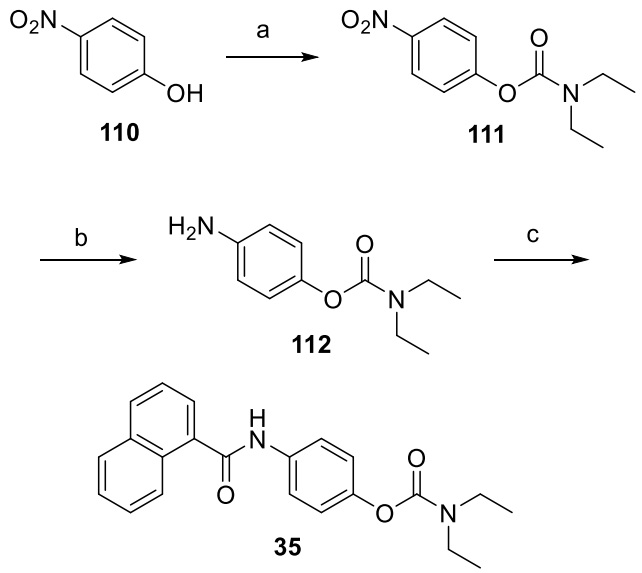
Scheme 5. Synthesis of 3-Substituted Indole Analog 25 via Larock Indole Synthesis [a]



[a] *Reaction Conditions:* (a) NaOH, MeOH, 120 °C M.W, 10 min, 87%, 5:1; (b) Cu_2O, phenanthroline, NMP, quinoline, 170 °C, 39%, 5:1; (c) H_2, 10% Pd/C, MeOH, 40 psi, rt, 45 min, 89%, 5:1; (d) EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 15%, 5:1.

An analog in which the amide linker between R^1 and the A-ring was reversed was synthesized by first forming the diethyl carbamate with 4-nitrophenol, followed by reduction of the nitro-group and coupling to 1-naphthoic acid as depicted in Scheme 6.

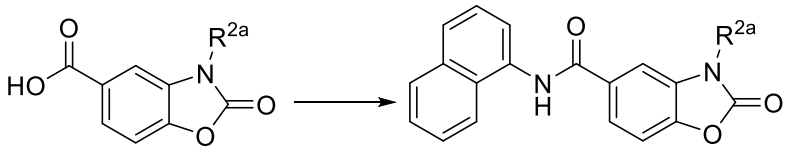
Scheme 6. Synthesis of Modified Linker A Analog 35 [a]



[a] *Reaction Conditions:* (a) diethyl carbamoyl chloride, pyridine, 180 °C M.W., 15 min, 41%; (b) H_2, 10% Pd/C, MeOH, 40 psi, rt, 45 min, 92%; (c) 1-naphthylamine, EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 41%.

Oxazolidinone analogs **38** and **39** were available commercially as the carboxylic acid **113** and were therefore prepared in a single step via EDCI coupling (Scheme 7).

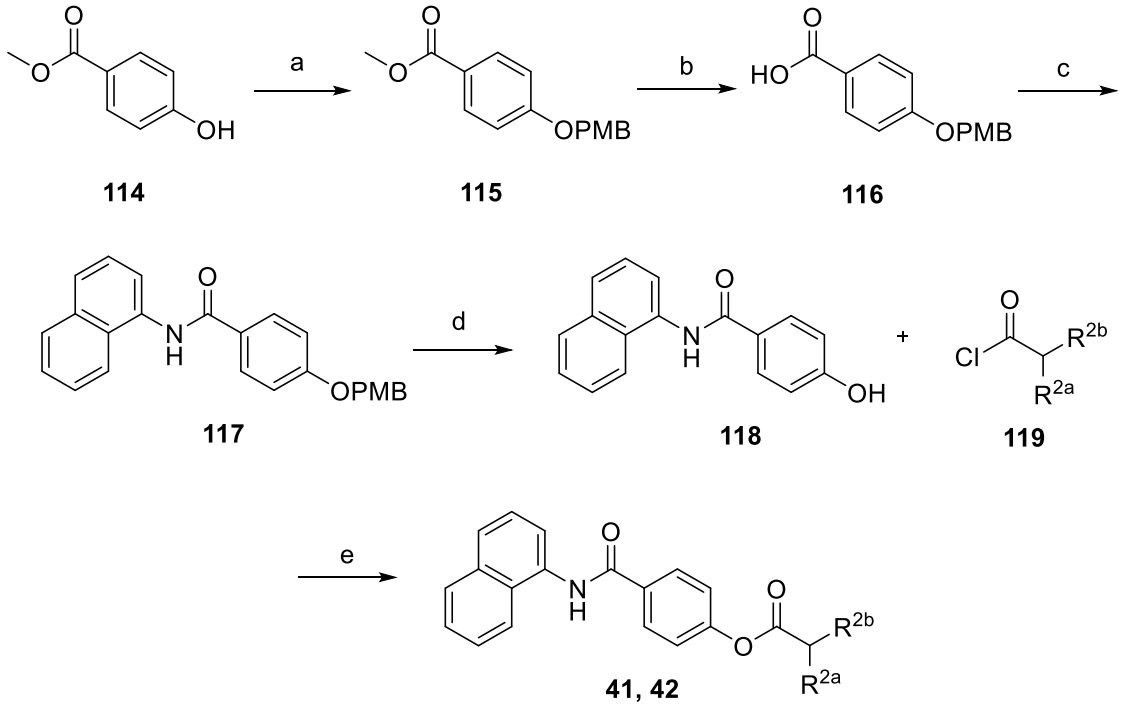
Scheme 7. Synthesis of Oxazolidinones 38 and 39 [a]



[a] *Reaction conditions:* 1-naphthylamine, EDCI, DMAP, DMF 0 °C to rt, 12 hrs, 7-19%.

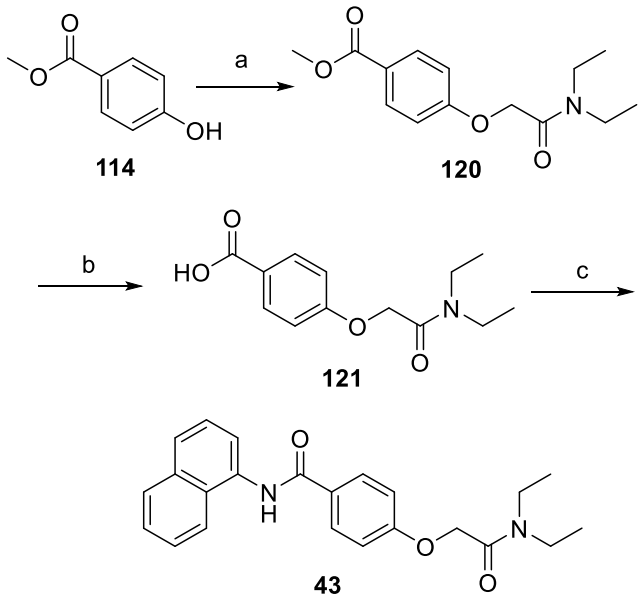
The synthetic route employed to access analogs containing modified B linkers was dependent upon the identity of linker positions X, Y and Z. Thus, protection of phenol **114** as the *p*-methoxybenzyl (PMB) ester afforded **115**, which was then saponified to yield benzoic acid **116** (Scheme 8). Amide coupling followed by PMB deprotection with trifluoroacetic acid (TFA) afforded phenol **118**. Final analogs were prepared via acylation of **118** with the desired acyl chloride. Ether **43** was prepared by reaction of 2-chloro-*N*,*N*-diethylacetamide with phenol to yield ether **120** (Scheme 9). Saponification generated acid **121**, which was then coupled to 1-naphthylamine to afford the desired analog **43**. Amide **46** was prepared from commercially available benzoic acid **122** (Scheme 10). Standard conditions afforded the acid chloride, which was reacted with diethylamine to yield amide **123**. Saponification of the ester afforded acid **124**. Final amide analog **46** was prepared by EDCI coupling of acid **124** with the desired amine. Analogs **44** and **45**, which contain an extended carbamate linker, were prepared as illustrated in Scheme 11. Commercially available alcohol **125** was treated with diethyl carbamoyl chloride to generate carbamate **126**. Saponification and amide coupling afforded analogs **44** and **45**.

Scheme 8. Synthetic Route to Access Ester Analogs 41 and 42 [a]



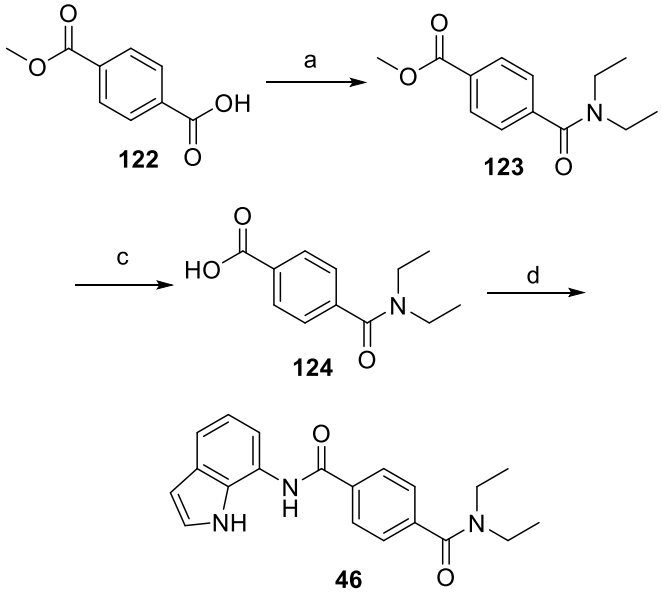
[a] *Reaction Conditions:* (a) PMBCl, K_2CO_3, DMF, rt, 12 hrs, 87%; (b) NaOH, MeOH, reflux, 12 hrs, 99%; (c) 1-naphthylamine, EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 70%; (d) TFA, rt, 30 min, 58%; (e) K_2CO_3, DMF, rt, 12 hrs, 20-80%.

Scheme 9. Route for the Synthesis of Ether Linker B Analog 43 [a]



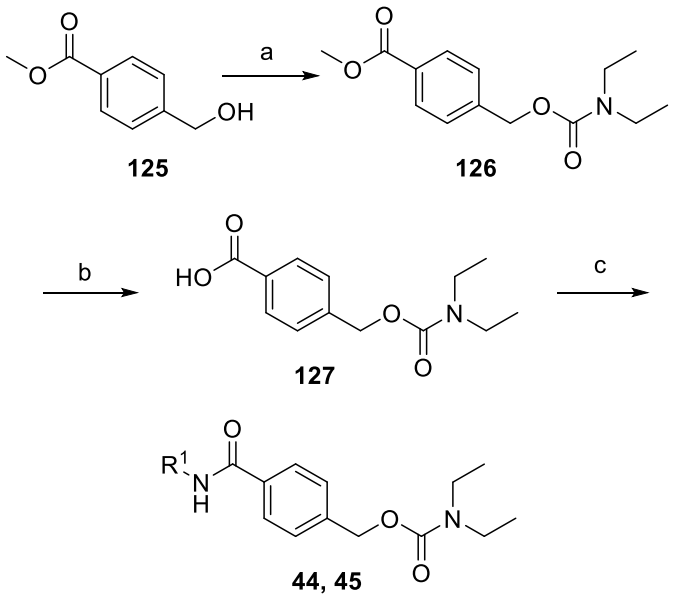
[a] *Reaction Conditions:* (a) *N*,*N*-diethylacetamide, K_2CO_3, DMF, rt, 12 hrs, >99%; (b) NaOH, MeOH, rt, 12 hrs, 93%; (c) 1-naphthylamine, EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 26%.

Scheme 10. Synthesis of Amide Linker B Analog 46



[a] *Reaction Conditions:* (a) $SOCl_2$, reflux, 1 hr, 94%; (b) diethylamine, TEA, DCM, rt, 20 min, 69%; (c) NaOH, MeOH, rt, 12 hrs, 59%; (d) 1*H*-indol-7-amine, EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 15%.

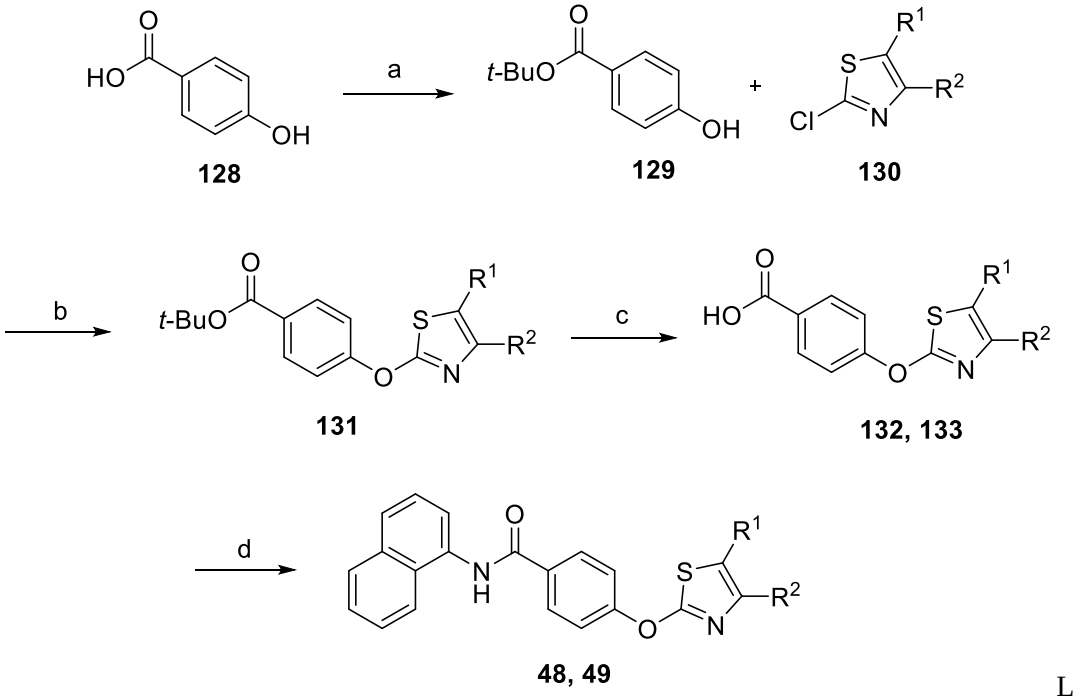
Scheme 11. Route for the Synthesis of Modified Linker B Analogs 44 and 45 [a]



[a] *Reaction Conditions:* (a) diethyl carbamoyl chloride, Cs_2CO_3, 24 hrs, >99%; (b) NaOH, MeOH, rt, 12 hrs, 95%; (c) R^1NH_2, EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 52%.

The synthetic route to access thiazole derivatives is shown in Scheme 12. Briefly, coupling of acid **128** with *tert*-butanol afforded phenol **129**, which was then heated with the desired thiazole (**130**) in a microwave reactor to yield ester **131**. De-esterification with trifluoroacetic acid yielded benzoic acid **132** and **133**. Last, thiazole analogs were generated by reacting acid **132** and **133** with 1-napthylamine under standard carbodiimide coupling conditions to yield **48** and **49**. Similarly, 2-chloro-4-hydroxybenzoate was converted to the tert-butyl-2-chloro-4-hydroxybenzoate, converted to the carbamate as above, de-protected with TFA and coupled to 7-aminoindole.

Scheme 12. Synthetic Routes to Access Thiazole Analogs 48 and 49[a]



L

[a] *Reaction Conditions:* (a) *t*-BuOH, DCC, DMAP, rt, 12 hrs, 66%; (b) K_2CO_3, DMF, 200 °C M.W., 15 min, 70-71%; (c) TFA, rt, 1 hr, 45-55%; (d) 1-naphthylamine, EDCI, DMAP, DMF, 0 °C to rt, 12 hrs, 32-62%.

General Chemistry Procedures

General Preparation of Thiocarbamate and Carbamate Compounds (Procedure I). To a solution of the corresponding hydroxybenzoate or aniline (1.0 mmol) in DMF (0.26 M) was added finely ground potassium carbonate (2.0 eq), which had been oven dried for 24 hrs. The mixture stirred at 24 °C for 1 hr before carbamoyl chloride (1.1 eq) was added. After stirring for 24 hrs, the mixture was diluted with distilled water and extracted with Et_2O (2x). Upon separating the organic phase, the solution was washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was then purified using flash column chromatography on SiO_2 (Hexanes/EtOAc: 6/1).

General Preparation of Carboxylic Acid Compounds (Procedure II). To a solution of the corresponding methyl ester (1.0 mmol) in MeOH (0.063 M) was added 1.0 M NaOH (3.8 eq). The reaction mixture stirred for 24 hrs before being acidified to a pH 3 using a 1.0 M solution of HCl and extracted in EtOAc (2x). The combined organic layers were washed with brine, filtered and concentrated *in vacuo* to give the desired product.

General Preparation of Phenyl Alkylcarbamothioates and Alkylcarbamates (Procedure III). To a solution of the corresponding carboxylic acid (1.0 mmol) in DMF (0.16 M) at 0 °C was added DMAP (1.1 eq) and EDCI (1.0 eq). The reaction mixture was allowed to continue stirring at 0 °C for 45 min. The mixture was then treated with the corresponding amine (1.1 eq) before slowly warming to room temperature and stirring 24 hrs. The reaction was concentrated *in vacuo* and partitioned between 1.0 M HCl and EtOAc. The resulting biphasic solution was extracted with EtOAc (2x). The organic layers were combined and washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was then purified using flash column chromatography on SiO_2 (Hexanes/EtOAc: 2/1).

General Preparation of Aminoindoles (Procedure IV). An appropriately substituted nitro-indole was dissolved in MeOH (0.1 M) and 10% wet Pd/C (0.1 eq) was added. The reaction was carried out at 40 psi on a hydrogenator for 45 min. The solution was then filtered over celite, dried *in vacuo*, and characterized unless otherwise noted.

General Preparation of Iodoindoles (Procedure V). To a solution of the corresponding nitro-aniline in 6% aq. HCl (100 mL) at 60 °C was added 0.1 M ICl (2.9 eq). The reaction mixture was stirred for 1 h before being poured onto sodium sulfite in crushed ice and neutralized with NaOH. The precipitate was filtered, rinsed with water and MeOH, dried *in vacuo*, and characterized unless otherwise noted.

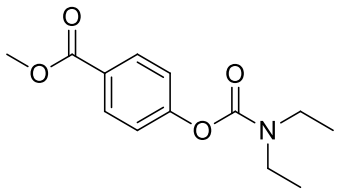
General Preparation of Iodoindoles (Procedure VI). To a solution of the corresponding nitro-aniline in EtOH (0.1 M) was added silver sulfate (1.4 eq) and iodine (1.4 eq). The resulting mixture was stirred at rt for 36 h before being concentrated under vacuum, dissolved in DCM, and washed with brine (3x). The organic layers were combined and washed with brine, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was then purified using flash column chromatography as noted.

General Preparation of Indoles via Larock Indole Synthesis (Procedure VII). To a solution of the corresponding nitro-aniline (1.0 eq) in DMF (0.1 M) was added LiCl (1.0 eq), the corresponding alkyne (5.0 eq), finely ground K_2CO_3 (5.0 eq), and palladium acetate (0.1 eq). The reaction mixture was heated to 100 °C for 5 h before being concentrated *in vacuo*, dissolved in DCM, and washed with brine (3x). The organic layers were combined, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was then purified using flash column chromatography on SiO_2 (0-5% MeOH/DCM, unless otherwise noted.

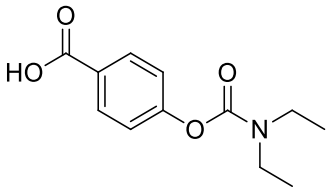
General Preparation of Indoles via Sonogashira Coupling Conditions (Procedure VIII). In a flame dried flask, an appropriately substituted iodo-aniline was dissolved in THF (1.4 M) with CuI (0.05 eq),

NEt_3 (1.0 eq), and palladium (bis-triphenylphosphine)(di-chloride) (0.05 eq). The mixture was cooled to 0 °C and an appropriate alkyne (1.1 eq) was added dropwise to the flask. The mixture was allowed to warm to rt and stirred for 2 h. The THF was removed *in vacuo* and Et_2O added to the residue. The organic layers were combined, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was then purified using flash column chromatography on SiO_2 (0-20% EtOAc/Hexanes, unless otherwise noted).

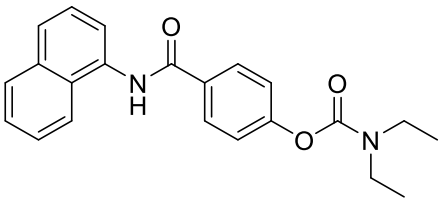
Chemical Synthesis



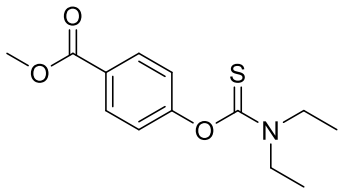
*Methyl 4-(diethylcarbamoyloxy)benzoate (**52**).* Compound **52** was prepared via Procedure I from methyl 4-hydroxybenzoate (1.0 g, 6.6 mmol) and *N*,*N*-diethylcarbamoyl chloride (0.96 mL, 7.7 mmol, 1.1 eq) to give a colorless oil (1.5 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 8.9 Hz, 2H), 3.78 (s, 3H), 3.30-3.27 (m, 4H), 1.16-1.08 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 155.1, 153.1, 130.7, 126.6, 121.4, 51.8, 42.1, 41.8, 14.0, 13.1.



*4-(Diethylcarbamoyloxy)benzoic acid (**66**).* Compound **66** was prepared via Procedure II from **52** (1.5 g, 6.0 mmol) to give a white solid (1.2 g, 87%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.98 (br s, 1H), 7.97 (d, *J* = 9.0 Hz, 2H), 7.24 (d, *J* = 8.6 Hz, 2H), 3.41-3.30 (m, 4H), 1.19 (t, *J* = 6.7 Hz, 3H), 1.12 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.8, 154.9, 152.7, 130.7, 127.5, 121.9; HRMS calcd for $C_{12}H_{15}NO_4$ 238.10804; found 238.21147 $[M+H]^+$.

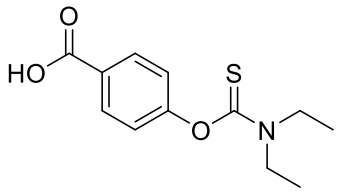


*4-(Naphthalen-1-ylcarbamoyl)phenyl diethylcarbamate (**2**).* Compound **2** was prepared via Procedure III from **66** (0.50 g, 2.1 mmol) and 1-naphthylamine (0.33 g, 2.3 mmol) to give a white solid (0.43 g, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.89 (d, *J* = 8.6 Hz, 2H), 7.85-7.82 (m, 2H), 7.70 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 154.1, 135.7, 134.2, 132.9, 131.3, 128.8, 128.5, 128.4, 126.1, 126.0, 125.6, 122.6, 122.0, 121.7, 42.6, 42.0, 14.2, 13.2; HRMS calcd for $C_{22}H_{22}N_2O_3$ 386.17094; found 363.17081 $[M+H]^+$.

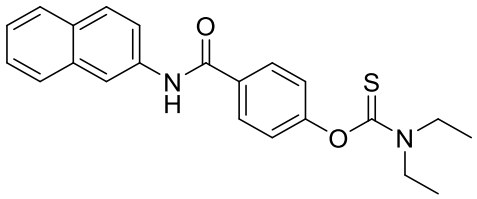


*Methyl 4-(diethylcarbamothioyloxy)benzoate **(53).*** Methyl-4-hydroxybenzoate (1.00 g, 6.57 mmol) and finely ground potassium carbonate (1.82 g, 13.1 mmol, 2.0 eq) were dissolved in DMF (25.0 mL). The mixture was stirred at room temperature for 1 hour to give an opaque suspension. Diethylthiocarbamoyl chloride (1.10 g, 7.23 mmol. 1.1 eq) was then added and the mixture was stirred at room temperature for 12 hours. The mixture was diluted with water (75 mL) and extracted with diethyl ether (2 x 100 mL). The combined organics were washed with water and brine, dried over MgSO4, and concentrated in vacuo to give a yellow solid. The crude material was purified using silica gel chromatography (ISCO, RediSep 12 g column, 1 EtOAc/6 Hexanes) to give an off-white solid (1.24 g, 71%). 1 H NMR (400 MHz, CDCl3) δ 8.07 (d, J = 8.6 Hz, 2H), 7.13 (d, J = 8.6 Hz, 2H), 3.90 (s, 3H), 3.87 (mult, 2H), 3.68 (quart, J = 7.0 Hz, 2H), 1.31 (t, J = 7.3 Hz, 3H). 13C NMR (100 MHz, CDCl3) δ 186.1, 166.5, 157.6, 131.0, 127.7, 123.0,

52.3, 48.5, 44.5, 13.7, 11.9. HRMS calcd for C13H17NO3S, 268.10084 [M+H]+ ; found, 268.10017 [M+H]+ .

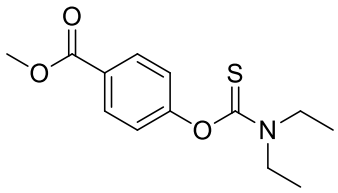


*4-(Diethylcarbamothioyloxy)benzoic acid **(67)**.* Methyl 4-(diethylcarbamothioyloxy)benzoate (0.933 g, 3.49 mmol) was dissolved in methanol (40.0 mL). To this solution, 1.0 N sodium hydroxide (13.3 mL, 13.3 mmol, 3.8 eq) was added. Immediately a solid precipitated. The mixture was stirred at room temperature for 12 hours, upon which all material went into solution. The pH was adjusted to ca. 3 with concentrated HCl. The mixture was then concentrated *in vacuo* to remove the methanol, upon which a white solid precipitated. The mixture was chilled at 4°C for 3 hours, and the product was collected by filtration and washed with hexanes to give a white solid (0.798 g, 90%). 1 H NMR (600 MHz, d6-DMSO) δ 7.98 (d, J = 9.1 Hz, 2H), 7.19 (d, J = 8.6 Hz, 2H), 3.81 (quart, J = 6.7 Hz, 2H), 3.67 (quart, J = 6.7 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H). 13C NMR (150 MHz, d6-DMSO) δ 184.9, 166.7, 157.0, 130.6, 128.1, 123.1, 123.0, 47.9, 44.2, 13.5, 13.4, 11.6, 11.5. HRMS calcd for C12H15NO3S, 254.08524 [M+H]+ ; found 254.08452 [M+H]+

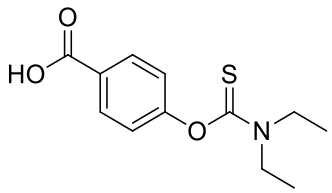


*O-4-(naphthalen-2-ylcarbamoyl)phenyl diethylcarbamothioate **(3)***: 4-(Diethylcarbamothioyloxy)benzoic acid (0.500 g, 1.97 mmmol) was dissolved in DMF (15.0 mL) and cooled to 0°C. To this solution, DMAP (0.265 g, 2.17 mmol, 1.1 eq), and EDC (0.378 g, 1.97 mmol, 1.0 378 eq) were added to give a colorless suspension. After stirring for 45 minutes, the solution became homogeneous. Finally, β-naphthylamine (0.311 g, 2.17 mmol, 1.1 eq) was added. The mixture was warmed to room temperature and stirred for 12

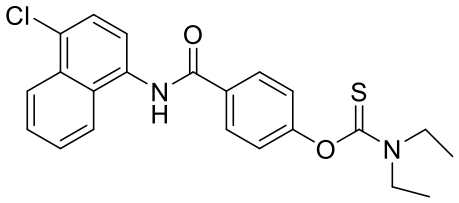
hours. The solvent was removed *in vacuo* and the residue was partitioned between 1.0 N HCl and EtOAc. The mixture was extracted with ethyl acetate (2x). The combined organics were washed with brine, dried with MgSO4, and concentrated *in vacuo* to give a white solid. The crude material was purified by silica gel chromatography (ISCO, RediSep 12 g column, 0-30% EtOAc/Hexanes gradient) to give a white solid. 1 H NMR (400 MHz, CDCl3) δ 8.34 (d, J = 2.3 Hz, 1H), 8.00 (bs, 1H), 7.95 (d, J = 9.0 Hz, 2H), 7.86-7.80 (mult, 3H), 7.59 (dd, J1 = 8.9 Hz, J2 = 2.3 Hz, 1H), 7.51-7.42 (mult, 2H), 7.22 (d, J = 8.6 Hz, 8.6 Hz, 2H), 3.92 (quart, J = 7.0 Hz, 2H), 3.72 (quart, J = 7.0 Hz, 2H), 1.38-1.34 (mult, 6H). 13C NMR (100 MHz, CDCl3) δ 186.2, 165.5, 156.7, 135.5, 134.0, 132.7, 131.0, 129.0, 128.5, 127.9, 127.7, 126.7, 125.3, 123.5, 120.3, 117.2, 48.7, 44.7, 13.8, 12.0. HRMS calcd for C22H22N2O2S, 379.14814 [M+H]+ ; found, 379.14712 [M+H]+ . Anal. (C22H22N2O2S) C, H, N.



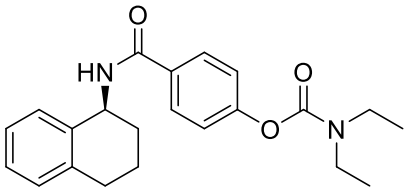
*Methyl 4-(diethylcarbamothioyloxy)benzoate (**54**).* Compound **54** was prepared via Procedure I from methyl 4-hydroxybenzoate (1.0 g, 6.6 mmol) and diethylthiocarbamoyl chloride (1.1 g, 7.2 mmol) to give an off-white solid (1.2 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.6 Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 3.90 (s, 3H), 3.87 (m, 2H), 3.68 (q, *J* = 7.0 Hz, 2H), 1.31 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.1, 166.5, 157.6, 131.0, 127.7, 123.0, 52.3, 48.5, 44.5, 13.7, 11.9; HRMZ calcd for $C_{13}H1_7NO_3S$ 268.10084; found 268.10017 $[M+H]^+$.



*4-(Diethylcarbamothioyloxy)benzoic acid (**68**).* Compound **68** was prepared via Procedure III from **54** (0.93 g, 3.5 mmol) to give a white solid (0.80 g, 90%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.98 (d, J = 9.1 Hz, 2H), 7.19 (d, J = 8.6 Hz, 2H), 3.81 (q, J = 6.7 Hz, 2H), 3.67 (q, J = 6.7 Hz, 2H), 1.25 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.9, 166.7, 157.0, 130.6, 128.1, 123.1, 123.0, 47.9, 44.2, 13.5, 13.4, 11.6, 11.5; HRMS calcd for $C_{12}H_{15}NO_3S$ 254.08524; found 24.08452 $[M+H]^+$.

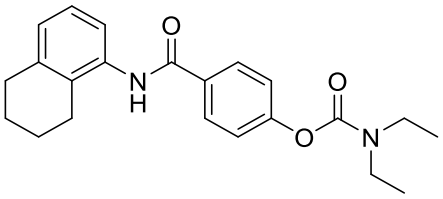


*O-(4-((4-Chloronaphthalen-1-yl)carbamoyl)phenyl) diethylcarbamothioate (**4**).* Compound **4** was prepared via Procedure III from **68** (0.40 g, 1.6 mmol) and 4-chloronaphthalen-1-amine (0.31 g, 1.7 mmol) to give a pink solid (0.21 g, 32%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.56 (s, 1H), 8.24 (dd, J = 8.3, 1.1 Hz, 1H), 8.17 – 8.06 (m, 3H), 7.81 – 7.59 (m, 4H), 7.32 – 7.23 (m, 2H), 3.85 (q, J = 7.1 Hz, 2H), 3.72 (q, J = 7.1 Hz, 2H), 1.27 (dt, J = 18.2, 7.1 Hz, 6H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 185.1, 165.6, 156.2, 133.6, 131.5, 130.3, 129.1, 129.0, 128.3, 127.8, 127.6, 127.1, 127.0, 126.1, 124.21, 124.1, 124.1, 123.9, 123.0, 122.9, 47.9, 44.1, 13.5, 13.4, 11.6, 11.5; HRMS calcd for $C_{22}H_{22}N_2O_2ClS$ 413.10850; found 413.10870 $[M+H]^+$.

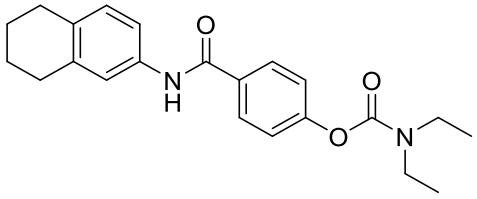


*(S)-4-(1,2,3,4-Tetrahydronaphthalen-1-ylcarbamoyl)phenyl diethylcarbamate (**5**).* Compound **5** was prepared via Procedure III from **66** (0.40 g, 1.7 mmol) and (*S*)-1,2,3,4-tetrahydronaphthalen-1-amine2-

methyl-1H-indol-5-amine (0.25 g, 1.7 mmol) to give a brown solid (0.26 g, 42%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.80 (d, J = 8.6 Hz, 1H), 7.98 – 7.90 (m, 2H), 7.24 – 7.08 (m, 6H), 5.29 – 5.19 (m, 1H), 3.46 – 3.25 (m, 4H), 2.87 – 2.69 (m, 2H), 2.05 – 1.91 (m, 2H), 1.88 – 1.69 (m, 2H), 1.20 (t, J = 7.0 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.8, 154.1, 153.6, 138.3, 137.9, 131.9, 129.5, 129.3, 128.5, 127.3, 126.5, 122.3, 122.1, 48.0, 47.8, 42.2, 30.6, 29.6, 21.2, 14.8, 13.9; HRMS calcd for $C_{22}H_{27}N_2O_3$ 367.20162; found 367.20144 $[M+H]^+$.

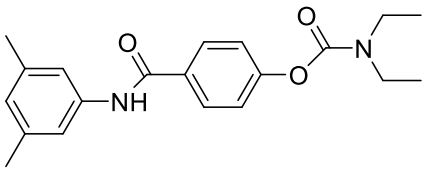


*4-((5,6,7,8-Tetrahydronaphthalen-1-yl)carbamoyl)phenyl diethylcarbamate (**6**).* Compound **6** was prepared via Procedure III from **66** (0.30 g, 1.3 mmol) and 5,6,7,8-tetrahydronaphthalen-1-amine (0.19 mL, 1.4 mmol, 1.1 eq) to give a pale pink solid (0.34 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.58 (s, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.18 (t, *J* = 8.0 Hz, 1H), 6.97 (d, *J* = 12 Hz, 1H), 3.48-3.39 (m, 4H), 2.82 (t, *J* = 6.4 Hz, 2H), 2.67 (t, *J* = 6.4 Hz, 2H), 1.89-1.86 (m, 2H), 1.82-1.78 (m, 2H), 1.30-1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 138.4, 135.6, 132.1, 128.5, 126.6, 126.1, 122.2, 120.7, 42.2, 30.0, 24.8, 23.1, 22.7, 14.5, 13.5; HRMS (APCI) calcd for $C_{22}H2_6O_3N_2$ 367. 20162; found 367.20128 $[M+H]^+$; Anal. ($C_{22}H_{26}O_3N_2$) C: 71.93, H: 7.10, N: 7.61.

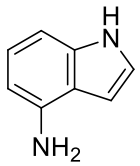


*4-((5,6,7,8-Tetrahydronaphthalen-2-yl)carbamoyl)phenyl diethylcarbamate (**7**).* Compound **7** was prepared via Procedure III from **66** (0.30 g, 1.3 mmol) and 5,6,7,8-tetrahydronaphthalen-2-amine (0.20 g, 1.4 mmol) to give a gray solid (0.29 g, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85-7.82 (m, 3H), 7.40 (s,

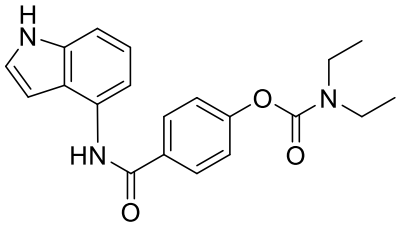
1H), 7.31 (dd, *J* = 1.6 Hz, *J* = 8.0 Hz, 1H), 7.22-7.20 (m, 2H), 7.05 (d, *J* = 8.4 Hz, 1H), 3.48-3.41 (m, 4H), 2.78-2.75 (m, 4H), 1.82-1.78 (m, 4H), 1.30-1.21 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 154.4, 138.1, 135.5, 135.1, 133.8, 132.1, 129.7, 128.5, 122.1, 120.9, 118.0, 42.6, 42.2, 29.8, 29.2, 23.4, 23.3, 14.5, 13.6; HRMS (APCI) calcd for $C_{22}H_{26}O_3N_2$ 367.20162; found 367.20138 $[M+H]^+$; Anal. ($C_{22}H_{16}O_3N_2$) C: 71.84, H: 7.09, N: 7.69.



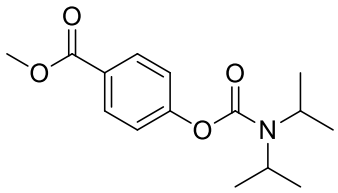
*4-((3,5-Dimethylphenyl)carbamoyl)phenyl diethylcarbamate (**8**).* Compound **8** was prepared via Procedure III from **66** (0.30 g, 1.3 mmol) and 3,5-dimethylaniline (0.17 g, 1.4 mmol) to give a white solid (0.30 g, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.84 (m, 2H), 7.73 (s, 1H), 7.28 (s, 2H), 7.25-7.23 (m, 2H), 6.81 (s, 1H), 3.50-3.38 (m, 4H), 2.34 (s, 6H), 1.32-1.22 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 154.3, 135.9, 138.8, 138.1, 132.1, 128.6, 126.4, 122.0, 118.2, 42.6, 42.2, 21.6, 14.4, 13.6; HRMS (APCI) calcd for $C_{20}H_{24}O_3N_2$ 341.18604; found 341.18597 $[M+H]^+$.



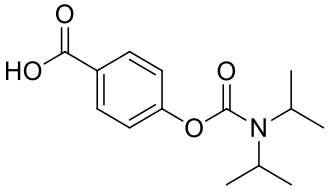
*1H-Indol-4-amine (**80**).* Compound **80** was prepared via Procedure IV from 4-nitro-1*H*-indole (1.0 g, 6.2 mmol) to give a white solid (0.70 g, 86%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (br s, 1H), 7.10 (t, *J* = 3.5 Hz, 1H), 7.00 (t, *J* = 7.8 Hz, 1H), 6.86 (t, *J* = 7.8 Hz, 1H), 6.85 (d, *J* = 6.45 Hz, 1H), 6.47-6.45 (m, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 3.91 (s, 2H); HRMS calcd for $C_8H_9N_2$ 133.07602; found; 133.07580 $[M+H]^+$.



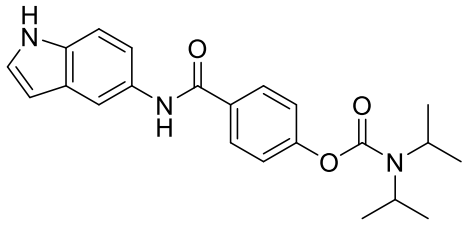
*4-(1H-Indol-4-ylcarbamoyl)phenyl diethylcarbamate (**9**).* Compound **9** was prepared via Procedure III from **66** (0.41 g, 1.7 mmol) and **80** (0.25 g, 1.8 mmol) to give an off-white solid (0.39 g, 65%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.14 (s, 1H), 10.10 (s, 1H), 8.03 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 7.6 Hz, 1H), 7.34 – 7.22 (m, 4H), 7.08 (t, J = 7.8 Hz, 1H), 6.59 (t, J = 2.5 Hz, 1H), 3.43 (q, J = 7.3 Hz, 2H), 3.36 – 3.28 (m, 2H), 1.18 (dt, J = 34.8, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 153.6, 153.0, 136.8, 131.9, 130.2, 129.2, 124.4, 122.2, 121.7, 120.9, 113.2, 108.5, 100.0, 41.8, 14.2, 13.3; HRMS calcd for $C_{20}H_{22}N_3O_3$ 352.16557; found 352.16537 $[M+H]^+$.



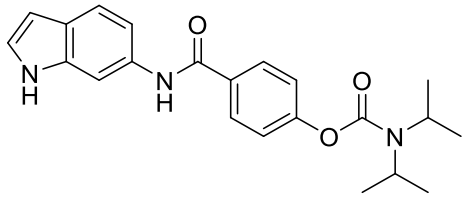
*Methyl 4-(diisopropylcarbamoyloxy)benzoate (**55**).* Compound **55** was prepared via Procedure I from methyl 4-hydroxybenzoate (1.0 g, 6.6 mmol) and *N*,*N*-diisopropylcarbamoyl chloride (0.77 mL, 7.2 mmol, 1.1 eq) to give a white solid (1.0 g, 53%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 9.0 Hz, 2H), 7.20 (d, *J* = 9.0 Hz, 2H), 4.20-3.91 (m, 2H), 3.89 (s, 3H), 1.41-1.28 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 155.3, 153.1, 131.1, 126.8, 121.7, 52.2, 47.1, 46.4, 21.6, 20.5; HRMS calcd for $C_{12}H_{21}NO_4$ 280.15500; found 280.15421 $[M+H]^+$.



*4-(Diisopropylcarbamoyloxy)benzoic acid (**69**).* Compound **69** was prepared via Procedure II from **55** (0.98 g, 3.5 mmol) to give a white solid (0.65 g, 70%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.96 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 3.98-3.65 (m, 2H), 1.46-1.25 (m, 12H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.9, 154.9, 152.3, 130.9, 127.5, 122.9, 45.6, 43.9, 21.4, 20.2; HRMS calcd for $C_{14}H_{19}NO_4$ 266.13935; found 266.13856 $[M+H]^+$.

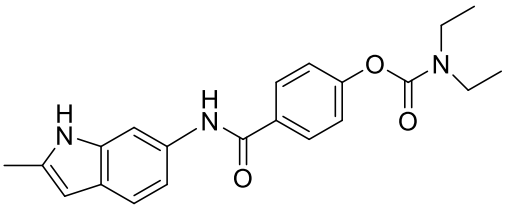


*4-((1H-Indol-5-yl)carbamoyl)phenyl diisopropylcarbamate (**10**).* Compound **10** was prepared via Procedure II from **69** (0.400g, 1.51 mmol) and 1H-indol-5-amine (0.219 g, 1.66 mmol) to give a white solid (0.19 g, 33%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.05 (s, 1H), 10.09 (s, 1H), 8.04 – 7.96 (m, 3H), 7.43 – 7.30 (m, 3H), 7.25 (d, J = 8.3 Hz, 2H), 6.41 (t, J = 2.3 Hz, 1H), 4.02 (p, J = 7.0 Hz, 2H), 1.32 – 1.23 (m, 12H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.0, 154.1, 153.0, 133.6, 132.6, 131.6, 130.1, 129.6, 129.5, 129.0, 128.1, 126.6, 126.5, 122.2, 122.2, 122.1, 116.8, 112.9, 112.8, 111.7, 111.6, 101.8, 47.0, 46.5, 22.0, 20.8; HRMS calcd for $C_{22}H_{26}N_3O_3$ 380.19687; found 380.19695; $[M+H]^+$.

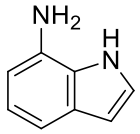


*4-((1H-Indol-6-yl)carbamoyl)phenyl diisopropylcarbamate (**11**).* Compound **11** was prepared via Procedure III from **69** (0.40 g, 1.5 mmol) and 1H-indol-6-amine (0.22 g, 1.7 mmol) to give a white solid (0.32 g, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.27 (s, 1H), 8.13 (s, 1H), 7.97 – 7.88 (m, 2H), 7.58 (d, J = 8.4 Hz, 1H), 7.27 – 7.13 (m, 3H), 7.04 (dd, J = 8.5, 1.9 Hz, 1H), 6.51 (t, J = 2.5 Hz, 1H), 4.18

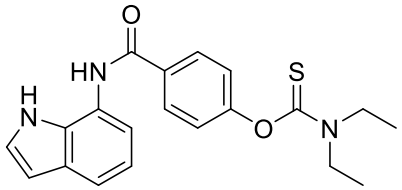
(tt, J = 7.2, 4.0 Hz, 1H), 4.03 (s, 1H), 1.44 – 1.34 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 154.3, 154.0, 136.4, 133.0, 132.5, 129.0, 125.5, 125.3, 122.5, 121.0, 114.2, 104.4, 102.3, 47.6, 46.8, 22.1, 20.9; HRMS calcd for $C_{22}H_{26}N_3O_3$ 380.19687; found 380.19717 $[M+H]^+$.



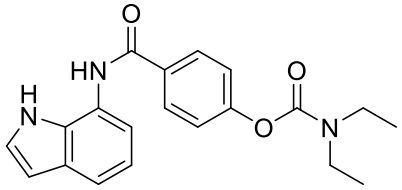
*4-(2-Methyl-1H-indol-6-ylcarbamoyl)phenyl diethylcarbamate (**12**).* Compound **12** was prepared via Procedure III from **66** (0.41 g, 1.7 mmol) and 2-methyl-1*H*-indol-6-amine (0.25 g, 1.7 mmol) to give a brown solid (0.21 g, 33%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.89 – 10.83 (m, 1H), 10.04 (s, 1H), 8.03 – 7.95 (m, 2H), 7.82 (d, J = 1.9 Hz, 1H), 7.33 – 7.18 (m, 4H), 6.13 – 6.07 (m, 1H), 3.42 (q, J = 7.1 Hz, 2H), 3.31 (t, J = 7.1 Hz, 2H), 2.37 (s, 3H), 1.18 (dt, J = 34.6, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.9, 154.1, 153.6, 136.9, 133.8, 132.8, 131.4, 129.5, 129.0, 122.3, 115.6, 112.0, 110.7, 99.9, 42.5, 42.2, 14.1, 13.9; HRMS calcd for $C_{21}H_{24}N_3O_3$ 366.18122; found 366.18144 $[M+H]^+$.



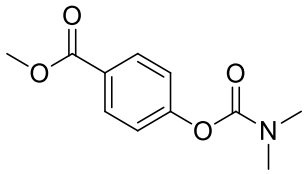
*7-Aminoindole (**81**).* Compound **81** was prepared via Procedure IV from 7-nitroindole (1.0 g, 6.2 mmol) to give a deep blue solid (0.8 g, 98 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.62 (br s, 1H), 7.24 (t, *J* = 2.74 Hz, 1H), 6.78-6.69 (m, 2H), 6.31-6.28, m, 2H), 5.04 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 133.7, 128.6, 123.8, 119.9, 108.6, 104.6, 101.5; HRMS calcd for $C_8H_9N_2$ 133.07602; found; 133.07580 $[M+H]^+$.



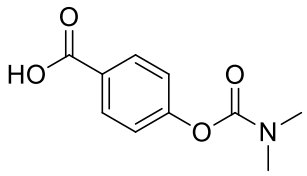
*O-(4-((1H-Indol-7-yl)carbamoyl)phenyl) diethylcarbamothioate (**13**).* Compound **13** was prepared via Procedure III from **68** (0.40 g, 1.7 mmol) and **81** (0.22 g, 1.7 mmol) to give a purple solid (0.34 g, 57%). ^{1}H NMR (400 MHz, DMSO-d6) δ 10.89 (s, 1H), 10.13 (s, 1H), 8.08 – 8.00 (m, 2H), 7.38 (d, J = 7.9 Hz, 1H), 7.34 – 7.18 (m, 4H), 6.96 (t, J = 7.7 Hz, 1H), 6.44 (dd, J = 3.1, 1.9 Hz, 1H), 3.81 (q, J = 7.0 Hz, 2H), 3.68 (q, J = 7.0 Hz, 2H), 1.23 (dt, J = 18.5, 7.0 Hz, 6H); ^{13}C NMR (151 MHz, dmso) δ 185.8, 165.5, 156.6, 132.8, 130.5, 129.8, 129.8, 125.9, 125.9, 123.7, 123.4, 123.4, 119.4, 119.3, 118.0, 116.6, 116.6, 102.1, 102.0, 48.5, 44.8, 14.2, 14.1, 12.3, 12.2; HRMS calcd for $C_{20}H_{22}N_3O_2S$ 368.14272; found 368.14281 $[M+H]^+$.



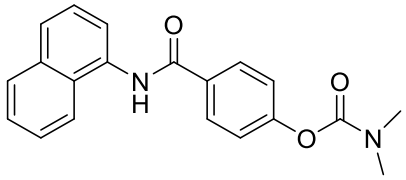
*4-((1H-Indol-7-yl)carbamoyl)phenyl diethylcarbamate (**14**).* Compound **14** was prepared via Procedure III from **66** (0.40 g, 1.7 mmol) and **81** (0.22 g, 1.7 mmol) to give a purple solid (0.34 g, 57%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.91 (s, 1H), 10.14 (s, 1H), 8.11 – 8.03 (m, 2H), 7.42 (d, J = 7.8 Hz, 1H), 7.34 (dd, J = 5.4, 2.5 Hz, 1H), 7.30 (d, J = 8.8 Hz, 3H), 7.00 (t, J = 7.7 Hz, 1H), 6.47 (t, J = 2.4 Hz, 1H), 3.44 (q, J = 7.1 Hz, 2H), 3.33 (q, J = 7.1 Hz, 2H), 1.23 (t, J = 7.0 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 153.7, 153.0, 131.6, 129.8, 129.3, 129.2, 123.1, 121.7, 118.7, 117.4, 116.0, 101.4, 41.8, 41.6, 14.3, 13.3; HRMS calcd for $C_{20}H_{22}N_3O_3$ 352.16557; found 352.16948 $[M+H]^+$.



*Methyl 4-(dimethylcarbamoyloxy)benzoate (**56**).* Compound **56** was prepared via Procedure I from methyl 4-hydroxybenzoate (1.0 g, 6.6 mmol) and *N*,*N*-dimethylcarbamoyl chloride (0.66 mL, 7.2 mmol, 1.1 eq) to give a white solid (1.4 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 3.84 (s, 3H), 3.03 (s, 3H), 2.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 155.2, 154.0, 130.9, 126.8, 121.6, 52.1, 36.6, 36.4; HRMS calcd for $C_{11}H_{13}NO_4$ 224.09240; found 224.09163 $[M+H]^+$.

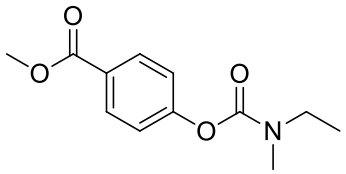


*4-(Dimethylcarbamoyloxy)benzoic acid (**70**).* Compound **70** was prepared via Procedure II from **56** (1.4 g, 6.1 mmol) to give a white solid (0.56 g, 44%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 3.04 (s, 3H), 2.92 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.8, 155.0, 153.5, 130.8, 127.6, 122.0, 36.4, 36.2; HRMS calcd for $C_{10}H_{11}NO_4$ 210.07675; found 210.07594 $[M+H]^+$.

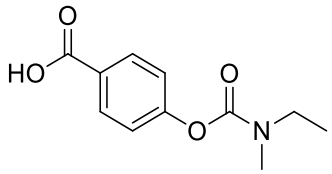


*4-(Naphthalen-1-ylcarbamoyl)phenyl dimethylcarbamate (**15**).* Compound **15** was prepared via Procedure III from **70** (0.40 g, 1.9 mmol) and 1-naphthylamine (0.30 g, 2.1 mmol) to give an off-white solid (0.43 g, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (br s, 1H), 7.94 (d, *J* = 8.2 Hz, 2H), 7.89-7.86 (m, 3H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.51-7.46 (m, 3H), 7.20 (d, *J* = 8.2 Hz, 2H), 3.08 (s, 3H), 2.92 (s, 3H); ^{13}C NMR (100

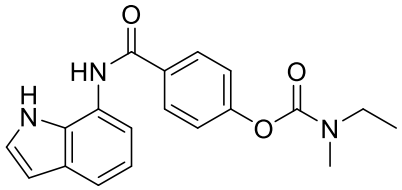
MHz, $CDCl_3$) δ 165.9, 155.44, 154.35, 134.3, 132.8, 131.7, 128.8, 128.7, 128.1, 126.4, 126.2, 125.8, 122.1, 122.0, 121.5, 36.8, 36.6; HRMS calcd for $C_{20}H_{18}N_2O_3$ 335.13968; found 335.13885 $[M+H]^+$.



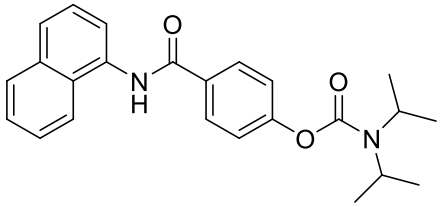
*Methyl 4-(ethyl(methyl)carbamoyloxy)benzoate (**57**).* Compound **57** was prepared via Procedure I from methyl 4-hydroxybenzoate (1.0 g, 6.6 mmol) and *N*-ethyl-*N*-methyl carbamoyl chloride (0.80 mL, 7.2 mmol, 1.1 eq) to give the desired benzoate (1.2 g, 77%). ^1H NMR (300 MHz, $CDCl_3$, 1:1 ratio of rotamers) δ 8.07-8.03 (mult, 4H), 7.20 (dd, *J* = 8.4, 2.7 Hz, 4H), 3.91 (s, 6H), 3.52-3.39 (mult, 4H), 3.08 (s, 3H), 3.00 (s, 3H), 1.30-1.19 (mult, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0, 166.7, 155.5, 131.2, 127.1, 121.8, 52.3, 44.4, 13.4, 12.6; HRMS Calcd for $C_{12}H_{15}NO_4$ 238.1074; found 238.1074 $[M+H]^+$.



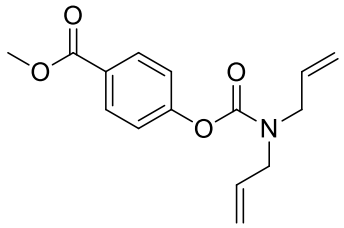
*4-(Ethyl(methyl)carbamoyloxy)benzoic acid (**71**).* Compound **71** was prepared via Procedure II from **57** (1.2 g, 5.1 mmol). After acidification, the residue was then diluted with distilled water and extracted with Et_2O (2x). The combined organic layers were washed with brine, filtered, and concentrated *in vacuo* to give a white solid (0.81 g, 72%). ^1H NMR (400 MHz, DMSO-d_6, 1:1 ratio of rotamers) δ 7.96-7.94 (mult, 4H), 7.24 (d, *J* = 8.4 Hz, 4H), 3.41 (q, *J* = 8.0 Hz, 2H), 3.34 (q, *J* = 7.2 Hz, 2H), 3.03 (s, 3H), 2.91 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.7, 166.7, 154.8, 130.7, 127.5, 121.9, 43.6, 17.2, 12.2; HRMS calcd for $C_{11}H_{13}NO_4$ 224.0917; found 224.0916.



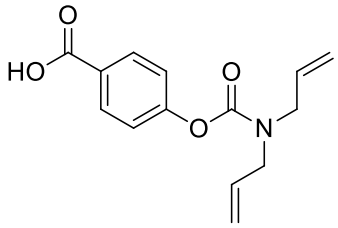
*4-(1H-Indole-7-ylcarbamoyl)phenyl ethyl(methyl)carbamate **(16).*** Compound **16** was prepared via Procedure III from **71** (0.11 g, 0.5 mmol) and **81** (0.066 g, 0.5 mmol, 1.0 eq) to give a pink solid (071 g, 42%). ^{1}H NMR (600 MHz, $CDCl_3$, 1:1 mixture of rotamers) δ 9.91 (br s, 2H), 8.21 (s, 2H), 8.11 (d, *J* = 9.0 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.28-7.23 (m, 4H), 7.07 (t, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 7.2 Hz, 2H), 6.59 (t, *J* = 1.8 Hz, 2H), 3.57-3.55 (m, 2H), 3.55-3.41 (m, 2H), 3.11 (d, *J* = 12.6 Hz, 3H), 3.04 (d, *J* = 11.4 Hz, 3H), 1.29-1.26 (m, 3H), 1.26-1.21 (m, 3H); ^{13}C NMR (150 MHz, DMSO-d_6, 1:1 mixture of rotamers) δ 165.0, 153.9, 153.4, 153.3, 131.8, 129.9, 129.5, 129.4, 129.3, 125,6, 125.0, 123.3, 123.2, 122.1, 121.5, 119.1, 118.6, 117.7, 117.2, 116.2, 115.7, 101.8, 101.4, 43.7, 34.0, 33.7, 13.3; HRMS calcd for $C_{19}H_{19}O_3N_3$ 338.1499; found 338.1499 $[M+H]^+$; Anal. ($C_{16}H_{19}O_3N_3$) C: 64.98, H: 6.20, N: 10.22.



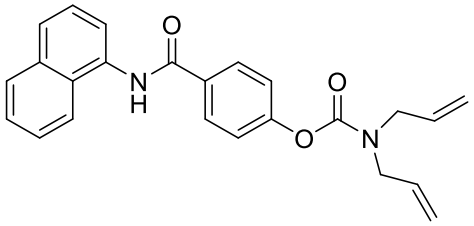
*4-(Naphthalen-1-ylcarbamoyl)phenyl diisopropylcarbamate (**17**).* Compound **17** was prepared via Procedure III from **69** (0.40 g, 1.5 mmol) and 1-naphthylamine (.024 g, 1.7 mmol) to give an off-white foam (0.37 g, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (br s, 1H), 7.98 (d, *J* = 8.5 Hz, 2H), 7.95 (d, *J* = 7.4 Hz, 1H), 7.91-7.88 (m, 2H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.54-7.49 (m, 3H), 7.26 (d, *J* = 8.5 Hz, 2H), 4.18-4.95 (m, 2H), 1.39-1.24 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 154.4, 153.4, 134.4, 132.7, 131.6, 129.0, 128.8, 127.9, 126.6, 126.4, 126.2, 126.0, 122.3, 121.8, 121.2, 47.3, 46.4, 21.8, 21.5; HRMS calcd for $C_{24}H_{26}N_2O_3$ 391.20228; found 391.20157 $[M+H]^+$.



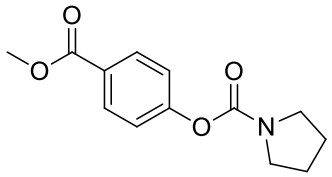
*Methyl 4-(diallylcarbamoyloxy)benzoate (**58**).* Compound **58** was prepared via Procedure I from methyl 4-hydroxybenzoate (1.0 g, 6.6 mmol) and *N*,*N*-diallylcarbamoyl chloride (1.1 mL, 7.2 mmol, 1.1 equiv) to give a colorless oil (1.7 g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.9 Hz, 2H), 7.16 (d, *J* = 8.9 Hz, 2H), 5.82-5.77 (m, 2H), 5.20-5.14 (m, 4H), 4.01-3.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 155.1, 153.6, 133.0, 132.8, 130.9, 126.9, 117.8, 117.0, 52.0, 49.5, 49.0; HRMS calcd for $C_{15}H_{17}NO_4$ 276.12370; found 276.12292 $[M+H]^+$.



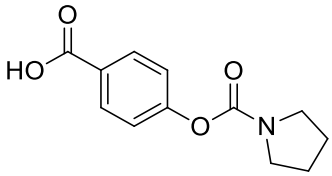
*4-(Diallylcarbamoyloxy)benzoic acid (**72**).* Compound **72** was prepared via Procedure II from **58** (1.7 g, 6.1 mmol) to give a white solid (1.2 g, 77%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.99 (br s, 1H), 8.00 (d, *J* = 7.4 Hz, 2H), 7.23 (d, *J* = 7.4 Hz, 2H), 5.99-5.76 (m, 2H), 5.25-5.16 (m, 4H), 3.90-3.72 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.8, 154.7, 153.2, 133.7, 130.8, 127.8, 121.9, 117.4, 116.7, 49.4, 49.1; HRMS calcd for $C_{14}H_{15}NO_4$ 262.10805; found 262.10727 $[M+H]^+$.



*4-(Naphthalen-1-ylcarbamoyl)phenyl diallylcarbamate (**18**).* Compound **18** was prepared via Procedure III from **72** (0.50 g, 1.9 mmol) and 1-naphthylamine (0.30 g, 2.1 mmol) to give an off-white solid (0.35 g, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (br s, 1H), 7.94 (d, *J* = 8.6 Hz, 2H), 7.89-7.83 (m, 3H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.51-7.45 (m, 3H), 7.02 (d, *J* = 8.6 Hz, 2H), 5.87-5.76 (m, 2H), 5.25-5.19 (m, 4H), 4.02-3.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 154.2, 154.1, 134.3, 133.1, 132.9, 132.7, 131.8, 128.8, 128.7, 128.3, 126.4, 126.2, 125.8, 122.1, 122.0, 121.5, 118.1, 117.3, 49.6, 49.2; HRMS calcd for $C_{24}H_{22}N_2O_3$ 387.17098; found 387.16989 $[M+H]^+$.

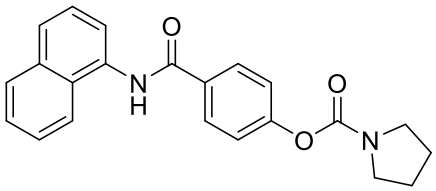


*4-(Methoxycarbonyl)phenyl pyrrolidine-1-carboxylate (**59**).* Compound **59** was prepared via Procedure I from methyl 4-hydroxybenzoate (1.0 g, 6.6 mmol) and pyrrolidine-1-carbonyl chloride (0.80 mL, 7.2 mmol, 1.1 eq) to give a white solid (1.4 g, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 3.89 (s, 3H), 3.55 (t, *J* = 6.7 Hz, 2H), 1.96-1.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 155.3, 152.4, 131.1, 126.9, 121.7, 52.2, 46.7, 46.6, 25.9, 25.1; HRMS calcd for $C_{13}H1_5NO_4$ 295.10805; found 250.10729 $[M+H]^+$.

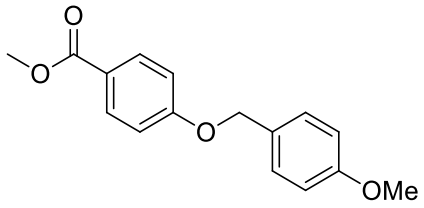


*4-(Pyrrolidine-1-carbonyloxy)benzoic acid (**73**).* Compound **73** was prepared via Procedure II from **59** (1.6 g, 6.3 mmol) to give a white solid (0.86 g, 58%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.97 (br s, 1H), 7.97 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 2H), 3.51-3.48 (m, 2H), 3.35-3.32 (m, 2H), 1.88-1.84 (m,

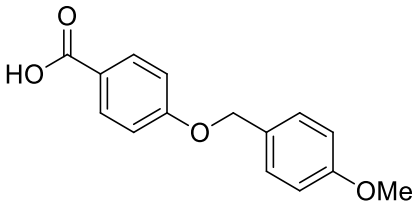
4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.8, 154.8, 151.6, 130.8, 127.5, 121.9, 46.4, 46.2, 25.3, 24.5; HRMS calcd for $C_{12}H_{13}NO_4$ 236.09240; found 236.09163 $[M+H]^+$.



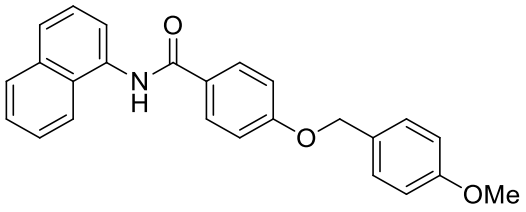
*4-(Naphthalen-1-ylcarbamoyl)phenyl pyrrolidine-1-carboxylate (**19**).* Compound **19** was prepared via Procedure III from **73** (0.50 g, 2.1 mmol) and 1-naphthylamine (0.34 g, 2.3 mmol) to give a pink solid (0.64 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (br s, 1H), 7.96 (d, *J* = 8.2 Hz, 2H), 7.89-7.84 (m, 3H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.51-7.46 (m, 3H), 7.23 (d, *J* = 8.2 Hz, 2H), 3.52 (t, *J* = 6.7 Hz, 2H), 3.31 (t, *J* = 6.7 Hz, 2H), 1.91 (quint, *J* = 6.7 Hz, 2H), 1.83 (quint, *J* = 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 154.3, 152.7, 134.3, 132.9, 131.5, 128.9, 126.2, 125.9, 122.2, 122.0, 121.6, 25.9, 25.1; HRMS calcd for $C_{20}H_{20}N_2O_3$ 361.15533; found 361.15430 $[M+H]^+$; Anal. ($C_{22}H_{20}N_2O_3$) C: 71.42, H: 5.47, N: 7.56.



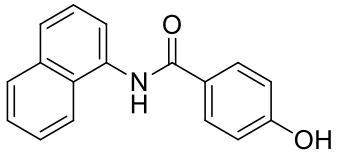
*Methyl 4-(4-methyoxybenzylocy)benzoate (**82**).* Methyl 4-hydroxybenzoate (12 g, 79 mmol) was dissolved in DMF (85 mL). 4-Methoxybenzyl chloride (14 mL, 103 mmol, 2.0 eq) was added, followed by potassium carbonate (22 g, 158 mmol). The mixture was stirred at rt for 12 h before being poured into an ice bath and warmed to rt. The white precipitate was collected via filtration and washed with hexanes (1.6 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 6.99 (d, *J* = 9.0 Hz, 2H), 6.93 (d, *J* = 8.6 Hz, 2H), 5.03 (s, 2H), 3.89 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 162.7, 159.7, 131.7, 129.5, 128.4, 122.8, 114.6, 70.0, 55.4, 52.0.



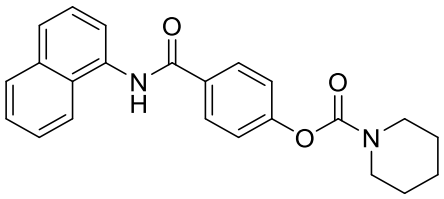
*4-(4-Methoxybenzyloxy)benzoic acid (**83**).* Compound **82** (1.0 g, 6.7 mmol) was dissolved in methanol (50 mL). To this solution, 1.0 N NaOH (14 mL, 14 mmol, 3.8 eq) was added. The solution was refluxed for 12 h. The pH was adjusted to 3 with concentrated HCl. The resultant white precipitate was obtained via filtration and washed with hexanes (0.94 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 9.0 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.05 (d, *J* = 9.0 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2h), 5.08 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 136.2, 159.3, 131.5, 129.9, 128.5, 123.2, 114.7, 114.0, 69.4, 55.2, 48.8.



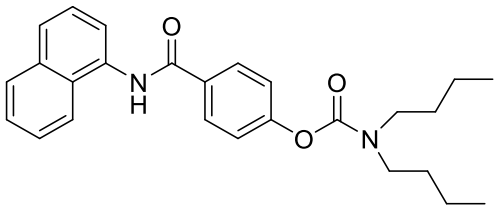
*4-(4-Methoxybenzyloxyl)-N-(naphthalen-1-yl)benzamide (**84**).* Compound **84** was prepared via Procedure III from **83** (5.0 g, 19 mmol) and 1-naphthylamine (3.1 g, 21 mmol) to give a white solid (5.2 g, 70%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.37 (br s, 2H), 8.15 (d, *J* = 8.2 Hz, 2H), 8.03-7.98 (m, 2H), 7.87 (d, *J* = 8.2 Hz, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 5.16 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.6, 161.1, 159.1, 134.1, 133.8, 129.8, 129.7, 129.4, 128.5, 128.1, 126.7, 126.2, 126.1, 125.9, 125.6, 123.9, 123.5, 114.6, 113.9, 69.3, 55.1.



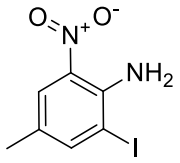
*4-Hydroxy-N-(naphthalene-1-yl)benzamide (**85**).* Compound **84** (0.50 g, 1.0 mmol) was dissolved in TFA (3.0 mL, 39 mmol, 30 eq). The mixture immediately turned purple, and was stirred at rt for 30 min. The solution was concentrated *in vacuo* to give a yellow residue. The residue was partitioned between EtOAc and water. The organics were separated and washed with sat. $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated *in vacuo* to give a white foam. The foam was taken up in DCM, upon which a white solid precipitated, which was collected via filtration. The crude material was purified using flash column chromatography on SiO_2 (EtOAc/DCM, 1/3) to give a white foam. The crude material was further purified using reverse phase preparative HPLC. The sample was dissolved in THF. Method: 40% MeOH/H_2O to 90% MeOH/H_2O over 40 min. at 10 mL/min, 1 min. ramp to 100% MeOH; 100% MeOH for 40 min. The product comes out near 80% MeOH (first peak). The title compound was obtained as a white solid (0.20 g, 58%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.20 (s, 2H), 10.14 (br s, 1h), 8.10-7.96 (m, 4H), 7.85 (d, J = 7.6 Hz, 1H), 7.60-7.53 (m, 4H), 6.92 (d, J = 8.5 Hz, 2H).



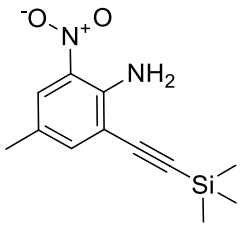
*4-(Naphthalen-1-ylcarbamoyl)phenyl piperidine-1-carboxylate (**20**).* Compound **20** was prepared via Procedure I from **85** (0.092 g, 0.35 mmol) and piperidine carbonyl chloride (0.048 mL, 0.38 mmol, 1.1 eq) to give a white solid (0.086 g, 66%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.46 (s, 1H), 8.12 (d, J = 7.9 Hz, 2H), 8.01 (br m, 2H), 7.88 (d, J = 7.9 Hz, 1H), 6.72-7.55 (m, 4H), 7.32 (d, J = 8.3 Hz, 2H), 3.60 (br s, 2H), 3.45 (br s, 2H), 1.62 (br m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.0, 154.5, 153.3, 134.3, 132.7, 131.6, 128.8, 128.8, 128.1, 126.4, 126.2, 125.8, 122.1, 121.5, 45.8, 45.3, 26.0, 25.5, 24.3; HRMS calcd for $C_{23}H_{22}N_2O_3$ 375.17094; found 375.16991 $[M+H]^+$; Anal. ($C_{23}H_{22}N_2O_3$) C: 71.58, H: 5.74, N: 7.36.



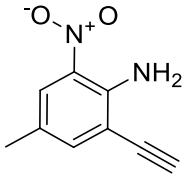
*4-(Naphthalen-1-ylcarbamoyl)phenyl dibutylcarbamate (**21**).* Compound **21** was prepared via Procedure I from **85** (0.085 g, 0.32 mmol) and dibutyl carbamoyl chloride (0.069 mL, 0.36 mmol, 1.1 eq) to give a colorless oil (0.11 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.92 (d, *J* = 8.6 Hz, 2H), 7.85-7.83 (m, 2H), 7.78 (d, *J* = 7.0 Hz, 2H), 3.21 (t, *J* = 7.4 Hz, 2H), 1.60-1.47 (m, 4H), 1.35-1.23 (m, 4H), 0.97-0.88 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 154.4, 154.2, 134.3, 132.8, 131.5, 128.9, 128.7, 128.3, 126.4, 126.1, 125.8, 122.2, 121.9, 121.7, 47.6, 47.3, 31.0, 30.1, 20.1, 14.0; HRMS calcd for $C_{26}H_{30}N_2O_3$ 419.23358; found 419.23261 $[M+H]^+$.



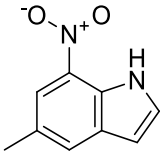
*2-Iodo-4-methyl-6-nitroaniline (**87**).* Compound **87** was prepared via Procedure V from 4-methyl-2-nitroaniline (1.0 g, 6.6 mmol) to give a pale solid (1.3 g, 71%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.94 (d, *J* = 1.96, 1H), 7.88 (s, 1H), 6.90 (bs, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.24, 142.64, 130.53, 126.90, 125.72, 88.19, 18.96; HRMS calcd for $C_7H_8N_2O_2I$ 278.96251; found 278.96241 $[M+H]^+$.



*4-Methyl-2-nitro-6-((trimethylsilyl)ethynyl)aniline (**88**).* Compound **88** was prepared via Procedure VIII from **87** (1.0 g, 3.6 mmol) and ethynyltrimethylsilane (0.39 g, 4.0 mmol) to give an orange solid (0.60 g, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 1H), 7.42 – 7.36 (m, 1H), 6.57 (s, 2H), 2.22 (t, *J* = 0.7 Hz, 3H), 0.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.8, 140.2, 126.6, 125.5, 112.2, 103.1, 99.3, 0.13; HRMS calcd for $C_{12}H_{17}N_2O_2Si$ 249.10538; found 205.10535 $[M+H]^+$.

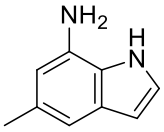


*2-Ethynyl-4-methyl-6-nitroaniline (**89**).* In a 25 mL round-bottomed flask, **88** (1.0 g, 4.0 mmol) was dissolved in THF (6.0 mL). TBAF (4.4 mL, 4.4 mmol) was added and the mixture was stirred at rt for 1 hr. The THF was removed *in vacuo* and the crude material washed with brine and DCM. The product was purified by flash chromatography on SiO_2 (20% EtOAc/Hexanes) to give the desired product (0.50 g, 71%). ^{1}H NMR (400 MHz) $CDCl_3$ δ 7.94 (s, 1H), 7.41(s, 1H), 6.58 (bs, 2H), 3.50 (s, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz) $CDCl_3$ δ 144.1, 140.5, 127.1, 125.3, 110.9, 85.2, 85.0, 78.6, 20.2.

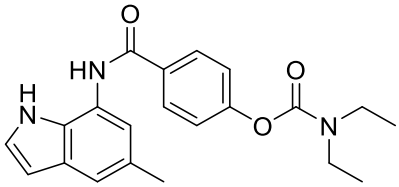


*5-Methyl-7-nitro-1H-indole (**90**).* In a 10 ml round-bottomed flask, potassium tert-butoxide (0.57 g, 5.1 mmol) was dissolved in NMP (1.4 mL). A solution of **89** (0.50 g, 2.8 mmol) in the remaining NMP was added dropwise to the basic solution at rt. The mixture was stirred for 1.5 h. Reaction performed under inert conditions. The reaction mixture was quenched with water, extracted with ether, and dried ($MgSO_4$). The product was purified using flash chromatography on SiO_2 (Hexanes/Ethyl Acetate, 0-20% gradient). The product was carried on without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80

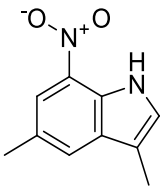
(br s, 1H), 7.94 (s, 1H), 7.20 (s, 1H), 7.32 (t, *J* = 2.74, 1H), 6.58-6.57 (m, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.0, 129.9, 129.2, 127.9, 126.9, 126.8, 120.1, 103.5, 21.1.



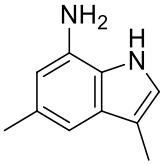
*5-Methy-1H-indol-7-amine (**91**).* Compound **91** was prepared via Procedure IV from **90** (0.25 g, 1.4 mmol) to give the desired indole (0.20 g, 97%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (br s, 1H), 7.17 (t, *J* = 2.74 Hz, 1H), 6.56 (s, 1H), 6.19-6.14 (m, 2H), 6.31-6.28, m, 2H), 4.93 (s, 2H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 133.3, 128.4, 128.2, 124.0, 123.7, 108.4, 106.3, 101.0, 21.6; HRMS calcd for $C_9H_{11}N_2$ 147.09168; found; 147.09160 $[M+H]^+$.



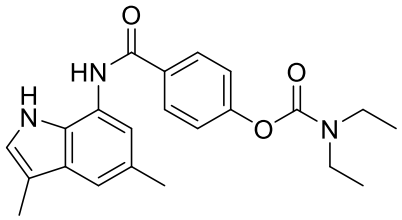
*4-(5-Methyl-1H-indol-7-ylcarbamoyl)phenyl diethylcarbamate (**22**).* Compound **22** was prepared via Procedure III from **66** (0.35 g, 1.5 mmol) and **91** (0.20 g, 1.4 mmol) to give a brown solid (0.10 g, 22%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.755 (br s, 1H), 10.07 (s, 1H), 7.31-7.22 (m, 3H), 7.19 (d, *J* = 3.91, 2H), 6.36 (q, *J* = 1.96, *J* = 2.74, 1H) 3.44-3.32 (m, 4H), 2.38 (s, 3H), dt (1.18, *J* = 6.85, *J* = 35.6, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 153.7, 153.0, 131.6, 139.4, 129.2, 128.1, 127.3, 122.7, 121.9, 116.9, 14.2, 13.3; HRMS (APCI) calcd for $C_{21}H_{23}N_3O_3$ 366.18122; found 366.18113 $[M+H]^+$.



*3,5-Dimethyl-7-nitro-1H-indole (**92**).* Compound **92** was prepared via Procedure VII from **87** (2.0 g, 7.2 mmol) and trimethyl(prop-1-ynyl)silane (4.0 g, 36 mmol). The product was obtained as a 9:1 mixture of the desired 3-substituted indole to the undesired 2-substituted indole (0.62 g, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.99 – 7.93 (m, 1H), 7.71 – 7.66 (m, 1H), 7.09 (s, 1H), 2.50 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 128.8, 128.7, 127.8, 124.6, 124.5, 120.4, 120.4, 113.1, 21.7, 10.0; HRMS calcd for $C_{10}H_{11}N_2O_4$ 191.08150; found 191.08139 $[M+H]^+$.

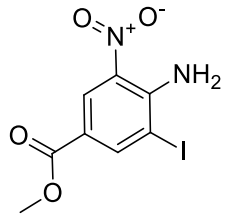


*3,5-Dimethyl-1H-indol-7-amine (**93**).* Compound **93** was prepared via Procedure IV from **92** (0.62 g, 3.3 mmol). The title compound was isolated after column chromatography using a 20-80% gradient of EtOAc in hexanes (0.46 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 6.92 (s, 1H), 6.73 (s, 1H), 6.32 (s, 1H), 3.60 (s, 2H), 2.40 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.0, 129.4, 129.3, 125.2, 121.8, 121.7, 111.6, 110.4, 110.3, 110.0, 110.0, 21.4, 9.7; HRMS calcd for $C_{10}H_{13}N_2$ 161.10733; found 161.10693 $[M+H]^+$.

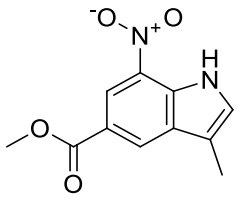


*4-(3,5-Dimethyl-1H-indol-7-ylcarbamoyl)phenyl diethylcarbamate (**23**).* Compound **23** was prepared via Procedure III from **66** (0.74 g, 3.1 mmol) and **93** (0.46 g, 2.9 mmol) to give a brown solid (0.33 g, 33%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.43 – 10.37 (m, 1H), 10.04 (s, 1H), 8.09 – 8.01 (m, 2H), 7.33 – 7.25 (m, 2H), 7.20 (d, J = 1.4 Hz, 1H), 7.13 (s, 1H), 7.06 (t, J = 1.7 Hz, 1H), 3.43 (q, J = 7.1 Hz, 2H), 3.38 – 3.28 (m, 2H), 2.40 (s, 3H), 2.24 (s, 3H), 1.23 (t, J = 7.0 Hz, 3H), 1.14 (t, J = 7.0 Hz, 3H); ^{13}C NMR (150

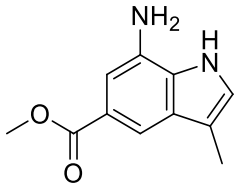
MHz, DMSO-d_6) δ 165.4, 154.4, 153.6, 132.3, 130.29, 129.9, 128.9, 127.3, 123.5, 123.3, 123.2, 122.3, 122.3, 117.9, 117.8, 115.9, 115.8, 109.8, 42.5, 42.2, 22.0, 21.9, 14.9, 14.8, 14.0, 13.9, 10.4, 10.3; HRMS calcd for $C_{22}H_{26}N_3O_3$ 380.19687; found 380.19642 $[M+H]^+$.



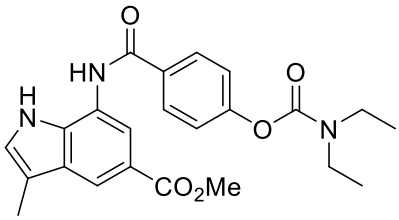
*Methyl 4-amino-3-iodo-5-nitrobenzoate (**96**).* Compound **96** was prepared via Procedure VI from methyl-4-amino-3-nitrobenzoate (4.7 g, 24 mmol). The title compound was isolated via column chromatography using DCM as a yellow/orange solid (3.3 g, 43%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.59 – 8.52 (m, 1H), 8.43 – 8.37 (m, 1H), 7.60 (s, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.7, 147.3, 144.9, 130.0, 128.2, 117.9, 87.9, 52.4; HRMS calcd for $C_8H_8N_2O_4I$ 322.95234; found 322.95221 $[M+H]^+$.



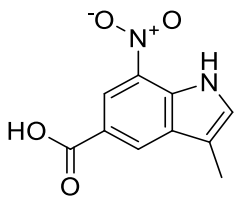
*Methyl 3-methyl-7-nitro-1H-indole-5-carboxylate (**102**).* Compound **102** was prepared via Procedure VII from **96** (0.75 g, 2.3 mmol). The product was obtained as a 5:1 mixture of 2- and 3-substituted indole which was carried forward (0.26 g, 48%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.00 (s, 1H), 8.58 – 8.49 (m, 2H), 7.42 (s, 1H), 3.92 (s, 3H), 2.35 (d, J = 1.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.6, 132.4, 132.0, 130.2, 127.8, 127.4, 119.6, 118.9, 113.4, 52.4, 9.1; HRMS calcd for $C_{11}H_{11}N_2O_4$ 235.07133; found 235.07132 $[M+H]^+$.



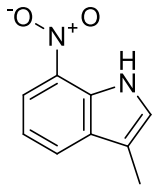
*Methyl 7-amino-3-methyl-1H-indole-5-carboxylate (**103**).* Compound **103** was prepared via Procedure IV from **102** (0.26 g, 1.1 mmol) to give the desired product as a 5:1 mixture (0.20 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.94 – 7.87 (m, 1H), 7.25 (d, J = 1.4 Hz, 1H), 6.97 – 6.91 (m, 1H), 3.90 (s, 3H), 3.75 (s, 2H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 131.0, 130.2, 129.0, 122.8, 122.6, 122.1, 114.5, 114.4, 114.2, 109.1, 109.1, 52.2, 10.0; HRMS calcd for $C_{11}H_{13}N_2O_2$ 205.09715; found; 205.09721 $[M+H]^+$.



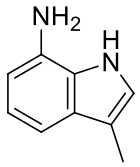
*Methyl 7-(4-(diethylcarbamoyloxy)benzamido)-3-methyl-1H-indole-5-carboxylate (**24**).* Compound **24** was prepared via Procedure III from **66** (0.25 g, 1.1 mmol) and **103** (0.20 g, 0.98 mmol) to give a brown solid (0.38 g, 32%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.00 (s, 1H), 10.24 (s, 1H), 8.08 (d, J = 8.5 Hz, 3H), 8.02 (s, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.26 (s, 1H), 3.86 (s, 3H), 3.43 (q, J = 7.1 Hz, 2H), 3.33 (q, J = 7.2 Hz, 2H), 2.32 (s, 3H), 1.23 (t, J = 7.0 Hz, 3H), 1.14 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.1, 164.9, 153.9, 152.9, 132.6, 131.3, 129.3, 129.3, 129.0, 124.5, 124.4, 122.8, 121.7, 119.8, 118.1, 116.5, 111.4, 51.8, 41.8, 41.6, 14.2, 13.3, 9.5; HRMS calcd for $C_{23}H_{26}N_3O_5$ 423.18670; found 423.18661 $[M+H]^+$.



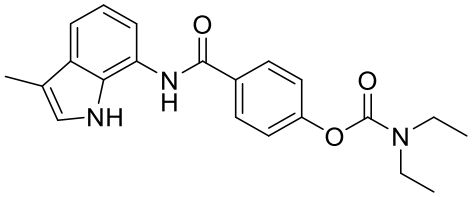
*3-Methyl-7-nitro-1H-indole-5-carboxylic acid (**104**).* Methyl 3-methyl-7-nitro-1H-indole-5-carboxylate (1.2 g, 5.1 mmol) was dissolved in MeOH (13 mL) and 1N NaOH (8.0 mL) and heated to 120 °C in the microwave for 10 minutes. The mixture was acidified to pH 3 and then filtered to give the product as a yellow solid (1.0 g, 89%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.13 (s, 1H), 11.96 (s, 1H), 8.58 (d, J = 2.0 Hz, 1H), 8.55 – 8.53 (m, 1H), 7.44 – 7.39 (m, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.4, 166.7, 132.4, 132.0, 130.2, 127.5, 120.9, 119.3, 113.3, 9.1; HRMS calcd for $C_{10}H_7O_4N_2$ 219.04113; found 219.04112 $[M-H]^-$.



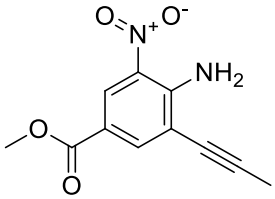
*3-Methyl-7-nitro-1H-indole (**105**).* A flame-dried flask was charged with 1,10-phenanthroline (0.082 g, 0.45 mmol), **104** (1.0 g, 4.5 mmol), and copper (I) oxide (0.032 g, 0.23 mmol). *N*-Methylpyrolidone (5.8 mL, 60 mmol) and quinoline (1.9 mL, 16 mmol) were added via syringe into the flask and the mixture was heated to 170 °C. The reaction was stirred and monitored by TLC until completion. The reaction mixture was poured onto 2N HCl (5 mL), and extracted with diethyl ether. The organics were washed with brine, dried ($MgSO_4$), filtered and dried *in vacuo*. The product was purified using column chromatography (EtOAc/Hexanes, 0-20% gradient) (0.31 g, 39%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.62 (s, 1H), 8.09 (dd, J = 8.7, 3.9 Hz, 1H), 8.06 – 7.99 (m, 1H), 7.31 (s, 1H), 7.25 – 7.19 (m, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 132.4, 132.3, 128.4, 127.1, 126.1, 118.5, 118.0, 111.6, 9.2; HRMS calcd for $C_9H_7O_2N_2$ 175.05130; found 175.05104 $[M-H]^-$.



*3-Methyl-1H-indol-7-amine (**106**).* Compound **106** was prepared via Procedure IV from **105** (0.31 g, 1.8 mmol) to give the desired indole (0.23 g, 89%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 7.00 (s, 1H), 6.75 – 6.59 (m, 2H), 6.33 – 6.26 (m, 1H), 4.94 (s, 2H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 133.6, 128.5, 125.8, 121.1, 119.3, 109.5, 104.6, 99.6, 9.9; HRMS calcd for $C_{19}H_{11}N_2$ 147.09168; found 147.09152 $[M+H]^+$.

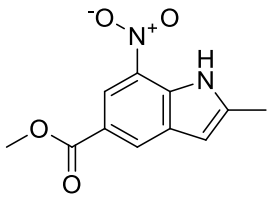


*4-(3-Methyl-1H-indol-7-ylcarbamoyl)phenyl diethylcarbamate (**25**).* Compound **25** was prepared via Procedure III from **66** (0.33 g, 1.4 mmol) and **106** (0.20 g, 1.4 mmol) to give a pink solid (0.075 g, 15%) as 6:1 mixture (3-substituted: 2-substituted indole product). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 10.09 (s, 1H), 8.06 (d, J = 8.2 Hz, 2H), 7.38 – 7.19 (m, 4H), 7.12 (s, 1H), 6.99 (t, J = 7.5 Hz, 1H), 3.49 – 3.39 (m, 2H), 3.38 – 3.28 (m, 2H), 2.27 (s, 3H), 1.27 – 1.10 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 153.7, 153.0, 152.2, 131.6, 130.1, 130.0, 129.5, 129.3, 122.9, 122.7, 121.7, 115.9, 115.5, 109.6, 41.8, 41.6, 14.3, 13.3, 9.7; HRMS calcd for $C_{21}H_{24}N_3O_3$ 366.18122; found 366.18095 $[M+H]^+$.

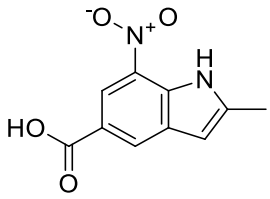


*Methyl 4-amino-3 nitro-5-(prop-1-ynyl)benzoate (**97**).* In a flame-dried, 100 mL round-bottomed flask, triethylamine (1.7 mL, 12 mmol), copper (I) iodide (0.24 g, 1.2 mmol), palladium(bis-

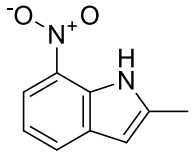
triphenylphosphine)(di-chloride) (0.43 g, 0.62 mmol), and **96** (2.0 g, 6.2 mmol) were added and stirred at rt. Prop-1-yne (0.27 g, 6.8 mmol) was bubbled in for 10 minutes and the mixture was stirred at rt until TLC indicated completion, within an hour. The solvents were removed *in vacuo*, and ether was added to the mixture prior to filtering over a pad of celite. The organics were washed with brine (3x), dried ($MgSO_4$) and concentrated *in vacuo*. The title compound was obtained after column chromatography using 20% EtOAc in hexanes as yellow solid (Ghilagaber et al., 2007). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (d, J = 2.0 Hz, 1H), 7.89 (d, J = 2.0 Hz, 1H), 7.73 (s, 2H), 3.82 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.3, 148.1, 137.1, 130.5, 127.3, 115.9, 112.9, 96.0, 73.3, 52.2, 4.6; HRMS calcd for $C_{11}H_9N_2O_4$ 233.05678; found 233.05652 $[M-H]^-$.



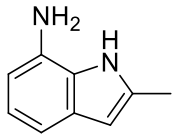
*Methyl 2-methyl-7-nitro-1H-indole-5-carboxylate (**98**).* A flame-dried round-bottomed flask was charged with potassium *t*-butoxide (2.5 g, 22 mmol) and *N*-methylpyrolidone (5.0 mL). A solution of **97** (2.9 g, 4.3 mmol) in *N*-methylpyrolidone (6.0 mL) was added dropwise to the basic solution at rt. The mixture was stirred overnight. Reaction performed under inert conditions. The reaction was quenched with water and DCM was added to the mixture. After several washes, the organics were combined and dried *in vacuo*. The mixture was purified using column chromatography (0-20% EtOAc/Hexanes gradient). The final product was obtained by crystallization in EtOAc/Hexanes; 1:9 ratio of solvents (0.60 g, 21%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.74 (d, J = 1.4 Hz, 1H), 8.58 – 8.48 (m, 1H), 6.46 (dq, J = 2.1, 1.1 Hz, 1H), 3.95 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 139.6, 132.8, 132.0, 129.0, 121.9, 119.7, 103.2, 103.1, 52.56, 14.0; HRMS calcd for $C_{11}11O_4N_2$ 235.07133; found 235.07134 $[M+H]^+$.



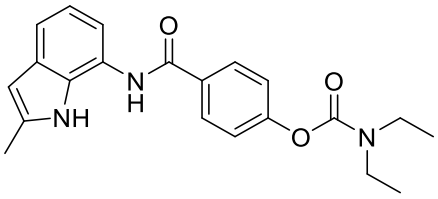
*2-Methyl-7-nitro-1H-indole-5-carboxylic acid (**99**).* **98** (0.60 g, 2.6 mmol) was dissolved in MeOH (10 mL) and 1N NaOH (4.3 mL) was added and heated to 120 °C in the microwave for 10 minutes. The mixture was acidified to pH 3 and filtered to give the desired product (0.49 g, 87%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.13 (s, 1H), 12.07 (s, 1H), 8.50 (s, 1H), 8.47 (s, 1H), 6.57 (s, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.7, 141.4, 132.8, 131.5, 130.4, 128.0, 121.3, 118.1, 102.5, 13.4; HRMS calcd for $C_{10}H_7O_4N_2$ 219.04113; found 219.04103 $[M-H]^-$.



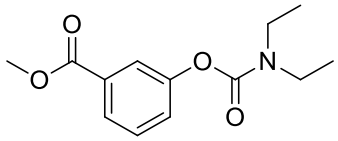
*2-Methyl-7-nitro-1H-indole (**100**).* A flame-dried flask was charged with 1,10-phenanthroline (0.04 g, 0.22 mmol), **99** (0.49 g, 2.2 mmol), and copper (I) oxide (0.016 g, 0.11 mmol). NMP (2.8 mL, 29 mmol) and quinoline (0.94 mL, 7.9 mmol) were added via syringe into the flask and the mixture was heated to 170 °C. The reaction was stirred and monitored by TLC until completion. The reaction mixture was poured onto 2N HCl (5 mL) and extracted with diethyl ether. The organics were washed with brine, dried ($MgSO_4$), filtered and dried *in vacuo*. The product was purified using column chromatography (EtOAc/Hexanes, 0-20% gradient) (0.16 g, 41%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.74 (s, 1H), 8.04 – 7.88 (m, 2H), 7.22 – 7.11 (m, 1H), 6.47 – 6.40 (m, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 139.8, 132.9, 132.8, 131.9, 128.5, 127.4, 118.5, 117.2, 101.1, 101.0, 13.4; HRMS calcd for $C_{19}H_7O_2N_2$ 175.05130; found 175.05130 $[M-H]^-$.



*2-Methyl-1H-indole-7-amine (**101**).* Compound **101** was prepared via Procedure IV from **100** (0.16 g, 0.91 mmol) to give the desired indole in quantitative yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.17 – 7.02 (m, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.49 (t, *J* = 6.7 Hz, 1H), 6.15 (d, *J* = 7.1 Hz, 1H), 3.56 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.2, 130.3, 130.1, 127.1, 120.4, 112.1, 108.3, 101.2, 13.7; HRMS calcd for $C_{19}H_{11}N_2$ 147.09168; found 147.09150 $[M+H]^+$.

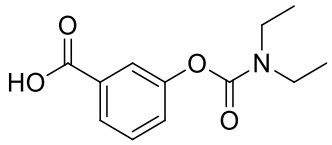


*4-(2-Methyl-1H-indol-7-ylcarbamoyl)phenyl diethylcarbamate (**26**).* Compound **26** was prepared via Procedure III from **66** (0.22 g, 0.91 mmol) and **101** (0.13 g, 0.91 mmol) to give an off-white solid (0.18 g, 54%). ^{1}H NMR (400 MHz DMSO-d_6) δ 10.71 (s, 1H), 10.04 (s, 1H), 8.06 (d, *J* = 8.2 Hz, 2H), 7.33 – 7.19 (m, 4H), 6.92 (t, *J* = 7.7 Hz, 1H), 6.15 (s, 1H), 3.43 (q, *J* = 7.2 Hz, 2H), 3.38 – 3.28 (m, 2H), 2.39 (s, 3H), 1.23 (t, *J* = 6.9 Hz, 3H), 1.14 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.8, 153.7, 153.0, 135.5, 131.7, 130.1, 130.0, 129.3, 122.2, 121.7, 116.3, 115.4, 99.5, 41.8, 41.6, 13.4, 13.3; HRMS calcd for $C_{21}H_{24}N_3O_3$ 366.18122; found 366.18094 $[M+H]^+$.

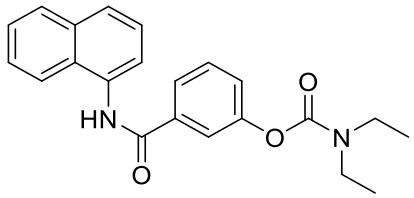


*Methyl 3-(diethylcarbamoyloxy)benzoate (**60**).* Compound **60** was prepared via Procedure I using methyl 3-hydroxybenzoate (1.0 g, 6.6 mmol) and diethylcarbamoyl chloride (0.92 mL, 7.2 mmol, 1.1 eq) to yield

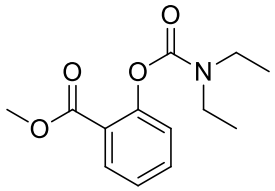
a colorless oil (1.5 g, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (dt, *J* = 7.5, 1.5 Hz, 1H), 7.79 (t, *J* = 6.3 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.35 (dq, *J* = 8.4, 1.2 Hz, 1H), 3.92 (s, 3H), 3.43 (q, *J* = 7.2 Hz, 4H), 1.30-1.19 (mult, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 153.8, 151.5, 131.4, 129.2, 126.5, 126.2, 123.0, 52.1, 42.3, 42.9, 14.2, 13.3; HRMS Calcd for $C_{13}H_{17}NO_4$ 252.1230; found 252.1231 $[M+H]^+$.



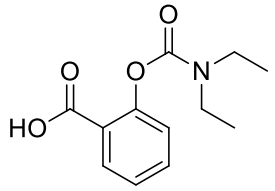
*3-(Diethylcarbamoyloxy)benzoic acid (**74**).* Compound **74** was prepared via Procedure II from **60** (1.5 g, 6.1 mmol) to give a colorless oil (1.3 g, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (br s, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.85 (s, 1H), 7.49-7.37 (mult, 2H), 3.52-3.40 (mult, 4H), 1.30-1.20 (mult, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.0, 154.2, 151.7, 130.9, 129.5, 127.6, 127.1, 123.7, 42.6, 42.2, 14.4, 13.5; HRMS Calcd for $C_{12}H_{15}NO_4$ 238.1074; found 238.1074 $[M+H]^+$.



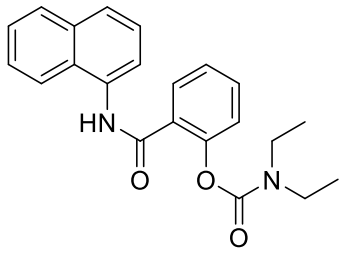
*3-(Napthalen-1-ylcarbamoyl)phenyl diethylcarbamate **(27).*** Compound **27** was prepared via Procedure III from **74** (1.1 g, 4.5 mmol) and 1-napthylamine (0.70 g, 4.9 mmol, 1.1 eq). Upon concentrating on high vacuum for 72 hrs, a viscous, pink oil was obtained (0.82 g, 50%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (br s, 1H), 7.94-786 (m, 3H), 7.80-7.75 (m, 3H), 7.54-7.48 (m, 3H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.38-7.34 (m, 1H), 3.49-3.38 (m, 4H), 1.31-1.20 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 154.0, 151.6, 135.9, 134.1, 132.6, 129.4, 128.44, 128.38, 126.4, 126.1, 126.0, 125.6, 125.2, 123.9, 122.5, 121.9, 121.2, 42.3, 42.0, 14.2, 13.3; HRMS calcd for $C_{22}H_{22}N_2O_3$ 363.1703; found 363.1704 $[M+H]^+$; Anal. ($C_{22}H_{22}N_2O_3$) C: 69.13, H: 6.33, N: 7.19.



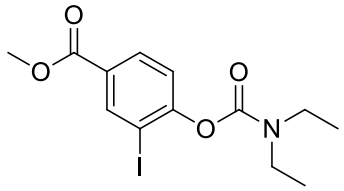
*Methyl 2-(diethylcarbamoyloxy)benzoate (**61**).* Compound **61** was prepared via Procedure I using methyl 2-hydroxybenzoate (1.0 g, 6.6 mmol) and diethylcarbamoyl chloride (0.92 mL, 7.2 mmol, 1.1 eq) to yield a colorless oil (1.7 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.53 (td, *J* = 7.8, 1.8 Hz, 1H), 7.27 (td, *J* = 7.5, 0.9 Hz, 1H), 7.16 (dd, *J* = 8.1, 1.2 Hz, 1H), 3.86 (s, 3H), 3.51 (q, *J* = 7.2 Hz, 2H), 3.40 (q, *J* = 6.9 Hz, 2H), 1.32-1.20 (mult, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 153.6, 150.9, 133.1, 131.1, 124.9, 123.8, 51.7, 42.0, 41.7, 13.7, 13.0; HRMS calcd for $C_{13}H_{17}NO_4$ 252.1230; found 252.1231 $[M+H]^+$.



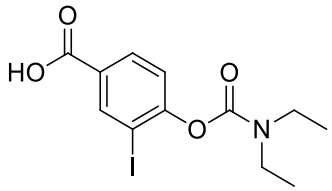
*2-(Diethylcarbamoyloxy)benzoic acid (**75**).* Compound **75** was prepared via Procedure II from **61** (1.6 g, 6.2 mmol). After acidification, the residue was then diluted with distilled water and extracted with Et_2O (2x). The combined organic layers were washed with brine, filtered and concentrated *in vacuo* to give a colorless oil (1.5 g, 71%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.59 (td, *J* = 8.1, 1.8 Hz, 1H), 7.30 (td, *J* = 7.8, 0.9 Hz, 1H), 7.19 (dd, *J* = 8.4, 0.9, 1H), 3.50 (q, *J* = 7.2 Hz, 2H), 3.40 (q, *J* = 7.2 Hz, 2H), 1.31-1.19 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 154.0, 151.7, 134.2, 132.0, 125.3, 124.2, 123.3, 42.2, 41.9, 13.9, 13.2; HRMS Calcd for $C_{12}H_{15}NO_4$ 238.1074; found 238.1074 $[M+H]^+$.



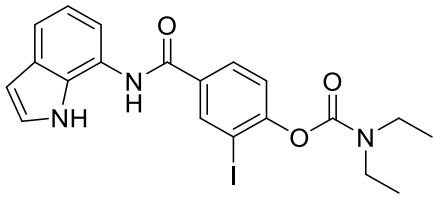
*2-(Napthalen-1-ylcarbamoyl)phenyl diethylcarbamate **(28).*** Compound **28** was prepared via Procedure III from **75** (1.0 g, 4.4 mmol) and 1-napthylamine (0.69 g, 4.8 mmol, 1.1 eq). The crude product was purified using flash column chromatography (Hexanes/EtOAc: 2/1). Triturating with diethyl ether gave a pink solid (0.66 g, 42%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.84 (br s, 1H), 8.19 (d, *J* = 7.5 Hz, 1H), 7.98-7.94 (m, 1H), 7.90-7.87 (m, 2H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.56-7.49 (m, 4H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 1H), 3.42 (q, *J* = 6.9 Hz, 2H), 3.29 (q, *J* = 7.2 Hz, 2H), 1.15 (t, *J* = 7.2 Hz, 3H), 0.97 (t, *J* = 6.9 Hz, 3H; ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.3, 154.9, 148.5, 134.3, 132.8, 132.0, 130.7, 130.3, 128.8, 127.0, 126.40, 126.36, 126.1, 126.0, 125.8, 123.4, 121.2, 120.2, 42.6, 42.3, 14.2, 13.2; HRMS calcd for $C_{22}H_{22}N_2O_3$ 363.1703; found 363.1704 $[M+H]^+$.



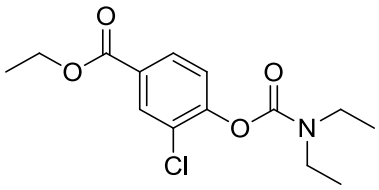
*Methyl 4-((diethylcarbamoyl)oxy)-3-iodobenzoate **(62).*** Compound **62** was prepared via Procedure I from methyl 4-hydroxy-3-iodobenzoate (1.0 g, 3.6 mmol) to give a white solid (1.24 g, 91%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.1 Hz, 1H), 8.02 (dd, J_1 = 2.1 Hz, J_2 = 8.7 Hz, 1H), 7.28 (d, *J* = 8.7 Hz, 1H), 3.91 (s, 3H), 3.53 (q, *J* = 7.5 Hz, 2H), 3.41 (q, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 6.9 Hz, 3H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 155.6, 152.5, 140.8, 130.9, 128.7, 123.1, 90.5, 52.6, 42.6, 42.4, 14.6, 13.5; HRMS Calcd for $C_{13}H_{16}INO_4$ 378.0197; found 378.0198 $[M+H]^+$.



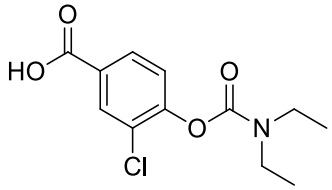
*4-((Diethylcarbamoyl)oxy)-3-iodobenzoic acid (**76**).* Compound **76** was prepared via Procedure II from **62** (0.95 g, 2.5 mmol). After concentrating *in vacuo*, the crude product was then purified using flash column chomatography on SiO_2 (Hexanes/EtOAc: 2/1) to give a white solid (0.81 g, 88%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.33 (d, J = 1.2 Hz, 1H), 7.94 (dd, J_1 = 1.8 Hz, J_2 = 8.4 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 3.47 (q, J = 7.2 Hz, 2H), 3.32 (q, J = 7.2 Hz, 2H), 1.28 (t, J = 7.2 Hz, 3H), 1.14 (t, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.5, 155.1, 151.8, 139.7, 130.5, 129.5, 123.6, 92.0, 42.0, 41.8, 14.3, 13.2; HRMS Calcd for $C_{12}H_{14}INO_4$ 361.9895; found 361.9893 $[M-H]^+$.



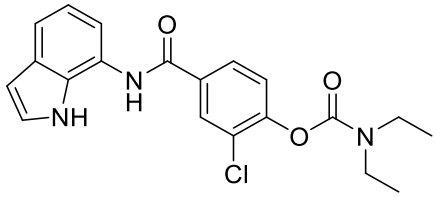
*4-((1H-Indol-7-yl)carbamoyl)-2-iodophenyl diethylcarbamate **(29).*** Compound **29** was prepared via Procedure III from **76** (0.34 g, 0.94 mmol) and **81** (0.14 g, 1.0 mmol, 1.1 eq) to give a pale yellow solid (0.14 g, 32%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.81 (br s, 1H), 8.34-8.31 (m, 2H), 7.82 (dd, J_1 = 1.8 Hz, J_2 = 8.4 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.27-7.25 (m, 2H), 7.07 (t, J = 7.8 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.58 (t, J = 3.0 Hz, 1H), 3.57 (q, J = 7.2 Hz, 2H), 3.46 (q, J = 6.6 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.2, 163.8, 154.6, 153.1, 138.8, 133.1, 130.8, 128.7, 125.2, 123.3, 122.5, 119.6, 118.6, 114.4, 102.8, 91.2, 42.7, 42.5, 14.6, 13.6; HRMS calcd for $C_{20}H_{20}IN_3O_3$ 478.0622; found 478.0619 $[M+H]^+$.



*Ethyl 3-chloro-4-((diethylcarbamoyl)oxy)benzoate (**63**).* Compound **63** was prepared via Procedure I from ethyl 3-chloro-4-hydroxybenzoate (1.0 g, 5.0 mmol) to give a white solid (1.1 g, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 2.0 Hz, 1H), 7.95 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.32 (d, J = 8.4 Hz, 1H), 4.37 (q, J = 6.8 Hz, 2H), 3.49 (q, J = 6.8 Hz, 2H), 3.40 (q, J = 7.2 Hz, 2H), 1.39 (t, J = 7.2 Hz, 3H), 1.30 (t, J = 7.2 Hz, 3H), 1.22 (t, J = 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 152.6, 151.5, 131.6, 129.1, 128.7, 127.5, 124.1, 61.5, 42.7, 42.3, 14.6, 14.3, 13.4; HRMS Calcd for $C_{14}H_{18}ClNO_4$ 300.0997; found 300.1000 $[M+H]^+$.

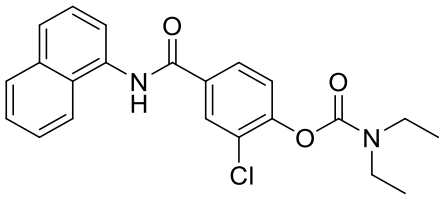


*3-Chloro-4-((diethylcarbamoyl)oxy)benzoic acid (**77**).* Compound **77** was prepared via Procedure II from **63** to give a white solid (0.78 g, 89%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.01 (d, J = 1.6 Hz, 1H), 7.91 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 3.44 (q, J = 6.4 Hz, 2H), 3.31 (q, J = 7.2 Hz, 2H), 1.24 (t, J = 6.8 Hz, 3H), 1.12 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.6, 151.7, 150.7, 130.6, 129.4, 129.3, 126.6, 124.8, 42.0, 41.7, 14.1, 13.2; HRMS calcd for $C_{12}H_{14}ClNO_4$ 270.0539; found 270.0538 $[M-H]^+$.

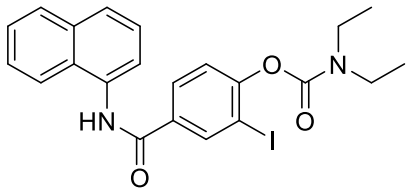


*4-((1H-Indol-7-yl)carbamoyl)-2-chlorophenyl diethylcarbamate (**30**).* Compound **30** was prepared via Procedure III from **77** (0.55 g, 2.0 mmol) and **81** (0.29 g, 2.2 mmol) to give a gray solid (0.78 g, >99%).

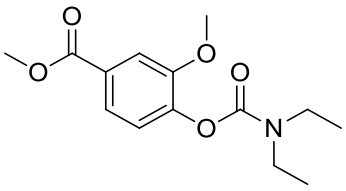
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (br s, 1H), 8.31 (br s, 1H), 7.98 (d, *J* = 2.0 Hz, 1H), 7.77 (dd, J_1 = 1.6 Hz, J_2 = 8.8 Hz, 1H) 7.55 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.58 (d, *J* = 2.0 Hz, 1H), 3.53 (q, *J* = 6.8 Hz, 2H), 3.45 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 6.8 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 153.1, 150.6, 132.7, 130.9, 129.8, 128.5, 128.1, 126.9, 125.3, 124.4, 122.5, 119.6, 118.7, 114.2, 102.8, 42.8, 42.5, 14.3, 13.5; HRMS calcd for $C_{20}H_{20}ClN_3O_3$ 386.1266; found 386.1268 $[M+H]^+$.



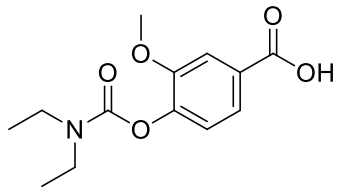
*2-Chloro-4-(naphthalen-1-ylcarbamoyl)phenyl diethylcarbamate (**31**).* Compound **31** was prepared via Procedure III from **77** (0.24 g, 1.3 mmol) and 1-naphthylamine (0.20 g, 1.4 mmol) to give the desired product (0.21 g, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (br s, 1H), 8.00 (d, *J* = 1.8 Hz, 1H), 7.82 (d, *J* = 8.7 Hz, 2H), 7.75-7.68 (m, 2H), 7.59 (dd, *J* = 2.7 Hz, *J* = 6.6 Hz, 1H), 7.48-7.37 (m, 3H), 7.16 (dd, *J* = 1.8 Hz, *J* = 1.8 Hz, 1H), 3.45 (q, *J* = 6.9 Hz, 2H), 3.27 (q, *J* = 7.2 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.05 (t, *J* = 7.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 152.8, 150.2, 134.2, 132.7, 132.6, 129.8, 128.6, 128.4, 127.5, 126.8, 126.7, 126.2, 126.0, 125.5, 123.9, 123.0, 122.2, 42.5, 42.2, 14.1, 13.2; HRMS (APCI) calcd for $C_{22}H_{21}ClN_2O_3$ 397.13135; found 397.13105; Anal. ($C_{22}H_{21}ClN_2O_3$) C: 66.78, H: 5.26, N: 6.79.



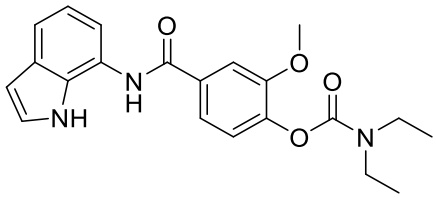
2-Iodo-4-(naphthalen-1-ylcarbamoyl)phenyl diethylcarbamate (**32**). Compound **32** was prepared via Procedure III from **76** (0.36 g, 0.99 mmol) and 1-naphthylamine (0.16 g, 1.1 mmol) to give the desired product (0.077 g, 16%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (br s, 1H), 8.41 (d, *J* = 2.1 Hz, 1H, 7.87-7.84 (m, 3H), 7.73 (d, *J* = 8.7 Hz, 2H), 7.52-7.43 (m, 3H), 7.22 (d, *J* = 8.4 Hz, 1H), 3.52 (q, *J* = 7.2 Hz, 2H), 3.34 (q, *J* = 6.9 Hz, 2H), 1.33 (t, *J* = 6.9 Hz, 3H), 1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 154.5, 152.8, 138.8, 134.3, 133.3, 132.6, 128.7, 128.5, 128.4, 126.7, 126.4, 126.2, 125.7, 123.2, 122.6, 121.8, 91.1, 42.6, 42.3, 14.5, 13.3; HRMS (APCI) calcd for $C_{22}H_{21}IN_2O_3$ 489.06614; found 489.06633.



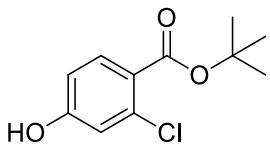
*Methyl 4-(diethylcarbamoyloxy)-3-methoxybenzoate (**64**).* In a 50 mL round-bottomed flask, methyl 4-hydroxy-3-methoxybenzoate (2.5 g, 14 mmol), and potassium carbonate (3.8 g, 27 mmol) were stirred in DMF (31 mL) for 1 hr at rt to give an opaque suspension. Diethylcarbamic chloride (1.7 mL, 14 mmol) was added. The mixture was stirred overnight at rt The reaction mixture was dried *in vacuo* and then diluted with water (75 mL) and extracted with DCM. The combined extracts were washed with water and brine and then dried ($MgSO_4$) and concentrated to give the title compound without further purification (3.5 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.59 (d, *J* = 1.9 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.39 (dq, *J* = 28.2, 7.1 Hz, 4H), 1.21 (dt, *J* = 27.3, 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.75, 153.60, 151.74, 144.80, 128.09, 123.31, 122.73, 113.47, 56.30, 56.18, 52.46, 52.33, 42.52, 42.28, 14.20, 13.57. HRMS calcd for $C_{14}H_{20}O_5N$ 282.13360; found 282.13349 $[M+H]^+$.



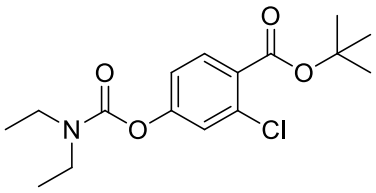
*4-((Diethylcarbamoyl)oxy)-3-methoxybenzoic acid (**78**).* **64** (3.5 g, 12 mmol) was dissolved in MeOH (13 mL) and 1N NaOH (8.00 mL) was added and heated to 120 °C in the microwave for 10 minutes. The mixture was checked by TLC which indicated completion. The mixture was acidified to pH 3 and then filtered to give the product as a white solid (2.5 g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.60 (m, 2H), 7.17 (d, *J* = 8.2 Hz, 1H), 3.87 (s, 3H), 3.41 (dq, *J* = 26.7, 7.1 Hz, 4H), 1.23 (dt, *J* = 26.9, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 153.7, 151.8, 145.4, 127.4, 123.6, 113.9, 56.3, 56.2, 42.6, 42.4, 14.2, 13.5; HRMS calcd for $C_{13}H_{17}O_5NNa$ 290.09989; found 290.09981 $[M+Na]^+$.



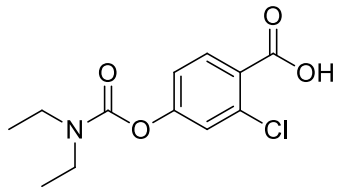
*4-(1H-Indol-7-ylcarbamoyl)-2-methoxyphenyl diethylcarbamate (**33**).* Compound **33** was prepared via Procedure III from **78** (2.4 g, 9.0 mmol) and **81** (1.2 g, 9.0 mmol) to give an off-white solid (1.6 g, 46%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.55 (s, 1H), 7.50 (dd, *J* = 7.1, 1.7 Hz, 1H), 7.45 (d, *J* = 2.1 Hz, 1H), 7.36 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.29 – 7.20 (m, 1H), 7.08 – 6.97 (m, 3H), 6.55 (dd, *J* = 3.1, 2.1 Hz, 1H), 3.74 (s, 3H), 3.52 – 3.37 (m, 4H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 125.1, 123.4, 119.8, 119.6, 118.3, 114.1, 112.0, 102.7, 56.0, 42.6, 42.4, 14.2, 13.7; HRMS calcd for $C_{21}H_{24}N_3O_4$ 382.17613; found 382.17599 $[M+H]^+$.



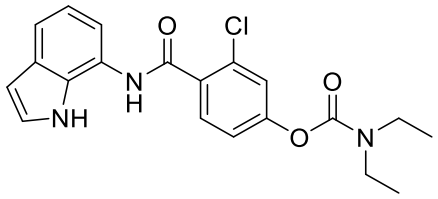
*tert-Butyl 2-chloro-4-hydroxybenzoate (**107**).* 2-Chloro-4-hydroxybenzoic acid (2.5 g, 14 mmol) was dissolved in DCM (60 mL) and combined with DMAP (0.069 g, 0.57 mmol) and *t*-BuOH (40 mL, 14 mmol) under Argon at 24 °C. DCC (22 mL, 21.7 mmol) was added in to the solution dropwise. The reaction was stirred overnight before being filtered and concentrated. The mixture was diluted with EtOAc and washed with sodium bicarbonate (2x). The combined organic layers were then washed with brine, dried ($MgSO_4$), filtered and concentrated. The crude product was then dry loaded on a 120 g RediSep column (10/3 Hexanes/EtOAc) to give the desired product (0.50 g, 15%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.67 (m, 1H), 6.92 (d, J = 2.4 Hz, 1H), 6.81 – 6.71 (m, 1H), 6.62 (s, 1H), 1.60 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.2, 135.4, 133.5, 123.5, 118.2, 114.0, 82.6, 28.4; HRMS calcd for $C_{11}H_{12}O_3Cl$ 227.04805; found 227.04803 $[M-H]^-$.



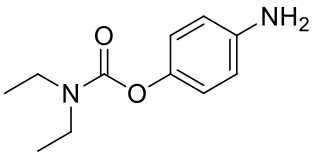
*tert-Butyl 2-chloro-4-(diethylcarbamoyloxy)benzoate (**108**).* In a 10 mL round-bottomed flask, **107** (0.50 g, 2.2 mmol), and pottasium carbonate (0.60 g, 4.4 mmol) were stirred in DMF (5.0 mL) for 1 hr at rt to give an opaque suspension. Diethylcarbamic chloride (0.28 mL, 2.2 mmol) was added. The mixture was stirred for 4 h at rt. The reaction mixture was dried *in vacuo* and then diluted with water (75 mL) and extracted with DCM. The combined extracts were washed with water and brine and then dried ($MgSO_4$) and concentrated. The title compound was obtained by column chromatography using 0-20% EtOAc in hexanes (0.32 g, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.6 Hz, 1H), 7.22 (d, *J* = 2.3 Hz, 1H), 7.07 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.38 (dq, *J* = 14.4, 7.1 Hz, 4H), 1.57 (s, 9H), 1.20 (dt, *J* = 15.9, 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 153.9, 153.2, 134.3, 132.2, 128.6, 124.4, 124.3, 120.1, 82.5, 42.6, 42.2, 28.4, 28.3, 14.4, 13.5; HRMS calcd for $C_{12}H_{15}O_4NCl$ 272.06841; found 272.06840 $[M+H]^+$.



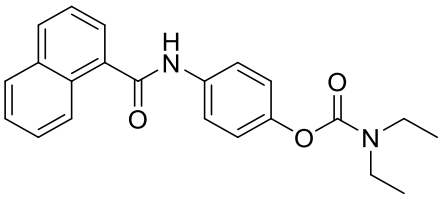
*2-Chloro-4-(diethylcarbamoyloxy)benzoic acid (**109**).* In a 10 mL round-bottomed flask, **108** (0.32 g, 0.98 mmol) was dissolved in TFA (3.9 mL). The mixture was stirred until TLC indicated completion. The reaction mixture was diluted with diethyl ether, washed with brine (3x), dried ($MgSO_4$) and concentrated. The residue was then partitioned between sodium bicarbonate and DCM and washed with sodium bicarbonate (3x). The organics were dried ($MgSO_4$) and concentrated to yield the desired product (0.15 g, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.01 (d, *J* = 8.7 Hz, 1H), 7.28 (d, *J* = 2.3 Hz, 1H), 7.13 (dd, *J* = 8.7, 2.3 Hz, 1H), 3.47 – 3.32 (m, 4H), 1.28 – 1.15 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 154.9, 153.6, 136.1, 133.8, 125.2, 125.0, 124.9, 120.4, 42.8, 42.4, 14.3, 13.3; HRMS calcd for $C_{12}H_{13}O_4NCl$ 270.05386; found 270.05432 $[M-H]^-$.



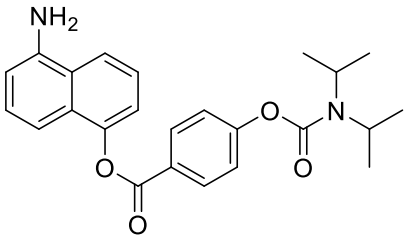
*4-(1H-Indol-7-ylcarbamoyl)-3-chlorophenyl diethylcarbamate (**34**).* Compound **34** was prepared via Procedure III from **109** (0.15 g, 0.55 mmol) and **81** (0.07 g, 0.55 mmol) to give a brown solid (0.063 g, 30%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.78 (s, 1H), 10.28 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 2.3 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.29 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.00 (t, *J* = 7.7 Hz, 1H), 6.47 (dd, *J* = 3.0, 1.9 Hz, 1H), 3.43 (q, *J* = 6.9 Hz, 2H), 3.33 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.5, 152.7, 152.4, 133.7, 130.5, 130.0, 129.2, 128.2, 125.3, 123.3, 123.0, 120.9, 118.9, 117.1, 113.9, 41.9, 41.6, 14.1, 13.2; HRMS calcd for $C_{20}H_{20}N_3O_3Cl$ 386.12660; found 386.12640 $[M+H]^+$.



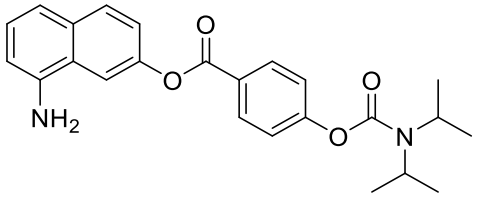
*4-Aminophenyl diethylcarbamate (**112**).* Compound **112** was prepared via Procedure IV from 4-nitrophenyl diethylcarbamate (0.25 g, 1.1 mmol). The title compound was obtained using flash chromatography with a 20%-50% EtOAc in hexanes gradient (0.20 g, 92%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.84 – 6.68 (m, 2H), 6.55 – 6.46 (m, 2H), 4.96 (s, 2H), 3.34 (s, 4H), 1.20 – 1.04 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 143.9, 143.6, 122.4, 122.4, 115.6, 115.51, 77.5, 77.2, 76.9, 42.2, 41.8, 14.3, 13.5; HRMS calcd for $C_{11}H_{17}N_2O_2$ 209.12845 found; 209.12836 $[M+H]^+$.



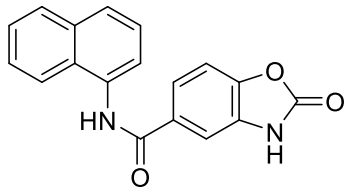
*4-(1-Naphthamido)phenyl diethylcarbamate (**35**).* Compound **35** was prepared via Procedure III from **112** (0.18 g, 0.84 mmol) and 1-naphthoic acid (0.15 g, 0.84 mmol) to give an off-white solid (0.12 g, 41%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.63 (s, 1H), 8.23 – 8.15 (m, 1H), 8.09 (d, J = 8.2 Hz, 1H), 8.06 – 8.01 (m, 1H), 7.80 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 6.9 Hz, 1H), 7.67 – 7.54 (m, 3H), 7.12 (d, J = 8.7 Hz, 2H), 3.52 – 3.22 (m, 4H), 1.21 (t, J = 7.0 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.2, 153.5, 147.0, 136.4, 134.7, 133.2, 130.2, 130.1, 129.6, 128.4, 127.0, 126.4, 125.5, 125.2, 125.1, 122.2, 122.2, 122.1, 120.5, 41.7, 41.5, 14.2, 13.3; HRMS calcd for $C_{22}H_{23}N_2O_3$ 363.17032; found 363.16994 $[M+H]^+$.



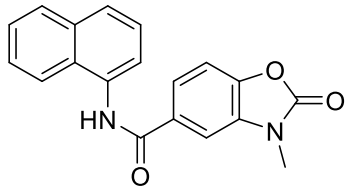
*5-Aminonaphthalen-1-yl 4-((diisopropylcarbamoyl)oxy)benzoate (**36**).* Compound **36** was prepared via Procedure III from **69** (0.40 g, 1.5 mmol) and 5-aminonaphthalen-1-ol (0.26 g, 1.7 mmol) to give a red solid (0.11 g, 18%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.23 (d, J = 8.4 Hz, 2H), 8.02 (d, J = 8.4 Hz, 1H), 7.43 – 7.28 (m, 4H), 7.19 (t, J = 7.9 Hz, 1H), 6.95 (d, J = 8.3 Hz, 1H), 6.69 (d, J = 7.5 Hz, 1H), 5.88 (s, 2H), 4.06 – 3.94 (m, 2H), 1.25 (d, J = 15.7 Hz, 12H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.8, 156.4, 152.7, 147.1, 145.9, 132.2, 132.0, 128.4, 128.3, 128.3, 125.9, 124.5, 123.6, 123.0, 122.9, 121.4, 119.0, 118.9, 108.7, 108.5, 108.3, 47.1, 46.7, 21.9, 20.7; HRMS calcd for $C_{24}H_{27}N_2O_4$ 407.19653; found 407.19718 $[M+H]^+$.



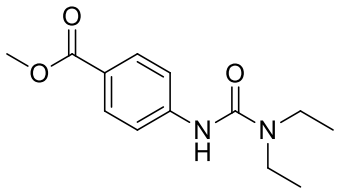
*7-Aminonaphthalen-1-yl 4-((diisopropylcarbamoyl)oxy)benzoate (**37**).* Compound **37** was prepared via Procedure III from **69** (0.4 g, 1.5 mmol) and 8-aminonaphthalen-2-ol (0.26 g, 1.7 mmol) to give a brown solid (0.31 g, 51%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.30 – 8.22 (m, 2H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.46 – 7.30 (m, 4H), 7.23 (t, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 8.3 Hz, 1H), 6.72 (d, *J* = 7.4 Hz, 1H), 5.92 (s, 2H), 4.09 – 3.97 (m, 2H), 1.33 – 1.22 (m, 12H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 164.8, 156.4, 152.7, 147.1, 145.9, 132.2, 132.0, 128.4, 128.4, 128.3, 125.9, 124.5, 123.63, 123.0, 122.9, 121.4, 119.0, 118.9, 108.7, 108.5, 108.3, 47.1, 46.6, 21.9, 20.7; HRMS calcd for $C_{24}H_{27}N_2O_4$ 407.19653; found 407.19653 $[M+H]^+$.



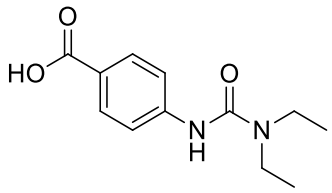
N-(Napthalen-1—yl)-2-oxo—2,3,-dihydrobenzo[d]oxazole-5-carboxamide ***(38).*** Compound **38** was prepared via Procedure III from 2-oxo-2,3-dihydrobenzo[*d*]oxazole-5-carboxylic acid (0.18 g, 1.0 mmol) and 1-napthylamine (0.14 g, 1.0 mmol, 1.0 eq) to afford a brown solid (0.058 g, 19%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.40 (br s, 1H), 7.96-7.95 (m, 2H), 7.85 (t, *J* = 7.8 Hz, 2H), 7.76 (s, 1H), 7.55-7.52 (m, 4H), 7.44 (d, *J* = 8.4 Hz, 1H), 3.33 (br s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 165.5, 154.5, 145.7, 133.9, 133.8, 130.5, 130.2, 129.3, 128.1, 126.4, 126.1, 126.0, 125.6, 124.0, 123.4, 122.4, 109.29, 109.27; HRMS calcd for $C_{18}H_{12}N_2O_3$ 305.0921; found 305.0921 $[M+H]^+$; Anal. ($C_{18}H_{12}N_2O_3$) C: 62.35, H: 3.32, N: 8.26.



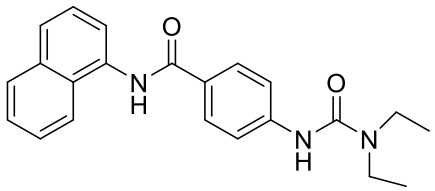
3-Methyl-N-(napthyalen-1-yl)-2-oxo-2,3-dihydrobenzo[d]oxazole-5-carboxamide ***(39)***. Compound **39** was prepared via Procedure III from 3-methyl-2-oxo-2,3-dihydrobenzo[*d*]oxazole-5-carboxylic acid (0.19 g, 1.0 mmol) and 1-napthylamine (0.14 g, 1.0 mmol, 1.0 eq) to afford a white solid (0.0066 g, 2%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.42 (br s, 1H), 8.0 (m, 2H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 7.2 Hz, 1H), 7.77 (s, 1H), 7.60-7.55 (m, 3H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.42 (d, *J* = 9.0 Hz, 1H), 3.43 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 182.2, 165.4, 154.1, 144.3, 133.8, 132.0, 130.3, 129.2, 128.1, 126.4, 126.1, 126.0, 125.6, 124.0, 123.3, 122.5, 109.2, 108.7, 28.3; HRMS calcd for $C_{19}H_{14}N_2O_3$ 319.1077; found 319.1077 $[M+H]^+$.



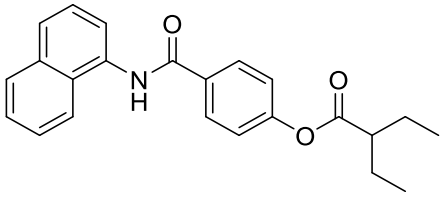
*Methyl 4-(3,3-diethylureido)benzoate (**65**).* To a solution of methyl 4-aminobenzoate (0.30 g, 2.0 mmol) and DIPEA (3.5 mL, 20 mmol, 10 eq) in THF (20 mL) was added diethylcarbamoyl chloride (2.5 mL, 20 mmol, 10 eq). The mixture was refluxed for 16 h. The reaction was poured into water and extracted with DCM. The organics were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to give an orange residue. The crude material was purified using flash column chromatography on SiO_2 (0-30% EtOAc/Hexanes) to give a white solid (0.12 g, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 9.0 Hz, 2H), 7.48 (d, *J* = 9.0 Hz, 2H), 6.75 (br s, 1H), 3.86 (s, 3H), 3.36 (q, *J* = 7.4 Hz, 4H), 1.20 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 154.2, 144.1, 130.8, 123.9, 118.6, 52.0, 41.8, 14.1; HRMS calcd for $C_{13}H_{18}N_2O_3$ 251.13968; found 251.13899 $[M+H]^+$.



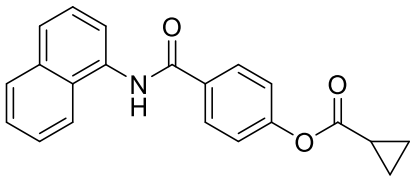
*4-(3,3-Diethylureido)benzoic acid (**79**).* Compound **79** was prepared via Procedure II from **65** (0.12 g, 0.50 mmol) to give a white solid (0.065 g, 56%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (s, 1H), 7.81 (d, *J* = 9.0 Hz, 2H), 7.63 (d, *J* = 9.0 Hz, 2H), 3.36 (q, *J* = 7.0 Hz, 4H), 1.10 (t, *J* = 7.0 Hz, 6H); HRMS calcd for $C_{12}H_{16}N_2O_3$ 237.12403; found 237.12554 $[M+H]^+$.



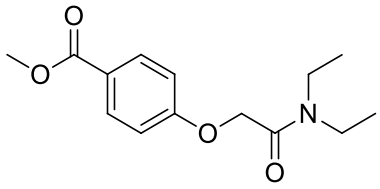
*4-(3,3-Diethylureido-N-(naphthalene-1-yl)benzamide (**40**).* Compound **40** was prepared via Procedure III from **79** (0.062 g, 0.26 mmol) and 1-naphthylamine (0.041 g, 0.29 mmol) to give a brown solution. The mixture was warmed to rt and stirred for 12 h. The solvent was removed *in vacuo* and the resultant residue treated with 1.0 N HCl, upon which a solid precipitated out. The precipitate was obtained by filtration and washed with ether. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (br s, 1H), 8.02 (d, *J* = 7.4 Hz, 1H), 7.95-7.89 (m, 3H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.59-7.50 (m, 6H), 6.59 (br s, 1H), 3.39 (q, *J* = 7.0 Hz, 4H), 1.25 (d, *J* = 7.0 Hz, 6H); CARBON; HRMS calcd for $C_{22}H_{23}N_3O_2$ 362.18697; found 362.18614 $[M+H]^+$.



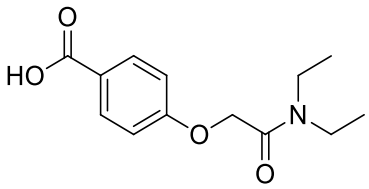
*4-(Naphthalen-1-ylcarbamoyl)phenyl 2-ethylbutanoate (**41**).* Compound **41** was prepared via Procedure I from **85** (0.10 g, 0.38 mmol) and 2-ethylbutyryl chloride (0.057 mL, 0.42 mmol, 1.1 eq) to give a colorless oil (0.028 g, 20%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (br s, 1H), 7.97 (d, *J* = 7.9 Hz, 3H), 7.88 (d, *J* = 9.0 Hz, 2H), 7.74 (d, *H* = 8.3 Hz, 1H), 7.55-7.49 (m, 3H), 7.26 (d, *J* = 9.0 Hz, 2H), 3.63-3.59 (m, 2H), 3.49-3.44 (m, 2H), 1.79-1.69 (m, 4H); HRMS calcd for $C_{23}H_{23}NO_3$ 362.17573; found 362.17475 $[M+H]^+$.



*4-(Naphthalen-1-ylcarbamoyl)phenyl cyclopropanecarboxylate (**42**).* Compound **42** was prepared via Procedure I from **85** (0.10 g, 0.38 mmol) and cyclopropanecarbonyl chloride (0.035 mL, 0.38 mmol, 1.0 eq) to give a white solid (0.028 g, 22%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (br s, 1H), 7.98 (d, *J* = 8.6 Hz, 2H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.91-7.87 (m, 2H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.55-7.48 (m, 3H), 7.24 (d, *J* = 8.6 Hz, 2H), 1.91-1.84 (m, 1H), 1.22-1.19 (m, 2H), 1.10-1.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 153.8, 134.4, 132.5, 132.4, 129.1, 128.9, 127.7, 126.7, 126.5, 126.3, 126.0, 122.3, 121.6, 121.0, 29.9, 13.3, 9.79; HRMS calcd for $C21H_{17}NO_3$ 332.12878; found 332.12802 $[M+H]^+$.

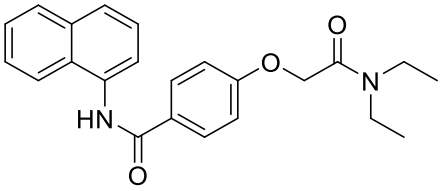


*Methyl 4-(2-(diethylamino)-2-oxoethoxy)benzoate (**120**).* Compound **120** was prepared via Procedure I from methyl 4-hydroxybenzoate (0.15 g, 1.0 mmol) and 2-chloro-*N*,*N*-diethylacetamide (0.17 g, 1.1 mmol, 1.1 eq). After stirring for 24 h, the mixture was diluted with distilled water and extracted with Et_2O (2x). Upon separating the organic phase, the solution was washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to give the desired benzoate (0.29 g, >99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.95 (mult, 2H), 6.96-6.93 (mult, 2H), 4.71 (s, 2H), 3.85 (s, 3H), 3.39-3.35 (mult, 4H), 1.20 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 166.4, 161.9, 131.7, 123.5, 114.4, 67.4, 52.0, 41.7, 40.5, 14.4, 12.9; HRMS Calcd for $C_{14}H_{19}NO_4$ 266.1387; found 266.1384 $[M+H]^+$.

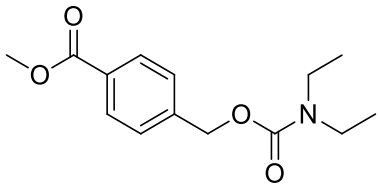


*4-(2-(Diethylamino)-2-oxoethoxy)benzoic acid (**121**).* Compound **121** was prepared via Procedure II from **120** (0.29 g, 1.1 mmol) to give a white solid (0.25 g, 93 %). ^{1}H NMR (600 MHz, DMSO – d_6) δ 7.87-

7.86 (mult, 2H), 6.98-6.96 (mult, 2H), 4.89 (s, 2H), 3.80 (br s, 1H), 3.32 (q, *J* = 7.2 Hz, 2H), 3.28 (q, *J* = 7.2 Hz, 2H), 1.15 (t, *J* = 7.2 Hz, 3H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.7, 166.7, 162.3, 132.3, 131.7, 123.0, 114.43, 114.39, 67.2, 41.7, 40.6, 14.3, 12.8; HRMS Calcd for $C_{13}H_{17}NO_4$ 252.1230; found 252.1230 $[M+H]^+$.

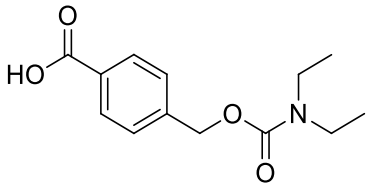


4-(2-(Diethylamino)-2-oxoethoxy)-N-(naphthalen-1-yl)benzamide ***(43).*** Compound **43** was prepared via Procedure III from **121** (0.25 g, 1.0 mmol) and 1-napthylamine to give the desired benzamide (0.097 g, 25%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.25 (br s, 1H), 8.00-7.96 (m, 3H), 7.91 (t, *J* = 7.8 Hz, 2H), 7.74 (d, *J* = 9.0 Hz, 1H), 7.53-7.52 (m, 3H), 7.06 (d, *J* = 8.4 Hz, 2H), 4.76 (s, 2H), 3.42-3.40 (m, 4H), 1.24 (t, *J* = 6.6 Hz, 3H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 161.3, 146.4, 134.4, 129.4, 129.0, 128.1, 126.6, 126.2, 126.17, 126.0, 121.5, 121.0, 119.1, 115.0, 109.6, 67.5, 41.8, 40.6, 14.6, 13.0; HRMS calcd for $C_{23}H_{24}N_2O_3$ 377.1860; found 377.1856 $[M+H]^+$; Anal. ($C_{23}H_{24}N_2O_3$) C: 71.94, H: 6.58, N: 6.93.

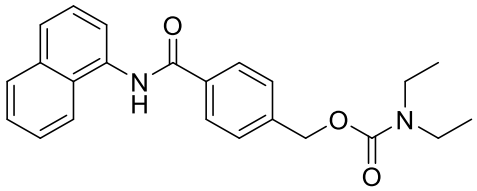


Methyl 4-(((diethylcarbamoyl)oxy)methyl)benzoate ***(126).*** To a solution of methyl 4-(hydroxymethyl)benzoate (0.17 g, 1.0 mmol) in acetonitrile (3 mL) was added cesium carbonate (0.80 g, 4.2 mmol). The reaction was allowed to stir at rt for 3 h before diethyl carbamoyl chloride (0.11 mL, 0.83 mmol, 1.0 eq) was added. The reaction continued to stir at rt for 24 h. At this time, the mixture was diluted with sat. NH_4Cl and extracted with EtOAc (2x). The combined organic layers were dried

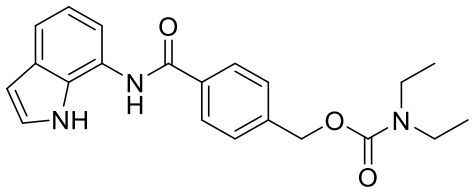
($MgSO_4$), filtered and concentrated *in vacuo* to give a white solid (0.23 g, >99%) which was carried on without purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 5.18 (s, 2H), 3.91 (s, 3H), 3.31 (q, *J* = 5.2 Hz, 4H), 1.13 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 155.7, 142.5, 129.9, 129.7, 127.4, 66.1, 52.3, 42.2, 41.5, 14.3, 13.6; HRMS (APCI) calcd for $C_{14}H_{19}NO_4$ 266.13868; found 266.13852 $[M+H]^+$.



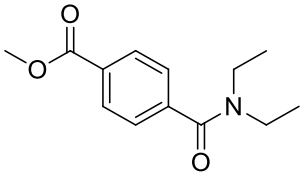
*4-(((Diethylcarbamoyl)oxy)methyl)benzoic acid (**127**).* Compound **127** was prepared via Procedure II from **126** (0.69 g, 2.6 mmol) to give a white solid (0.62 g, 95%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.93 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 5.13 (s, 2H), 3.24 (m, 4H), 1.06 (m, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.4, 154.7, 141.9, 130.8, 129.4, 65.4, 41.5, 40.9, 14.1, 13.4; HRMS (APCI) calcd for $C_{13}H_{17}NO_4$ 250.10848; found 250.10839.



*4-(Naphthalen-1-ylcarbamoyl)benzyl diethylcarbamate (**44**).* Compound **44** was prepared via Procedure III from **127** (0.26 g, 1.0 mmol) and 1-naphthylamine (0.16 g, 1.1 mmol) to give the desired product (0.19 g, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (br s, 1H), 7.95-7.86 (m, 5H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.49-7.38 (m, 5H), 5.16 (s, 2H), 3.32 (q, *J* = 6.8 Hz, 4H), 1.14 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, CDCl3) δ 182.2, 174.2, 155.7, 141.2, 134.3, 132.7, 130.4, 128.8, 127.8, 127.7, 127.3, 126.4, 126.2, 125.8, 121.9, 121.3, 66.2, 42.1, 41.5, 14.3, 13.6; HRMS (APCI) calcd for $C_{23}H_{24}N_2O_3$ 377.18597; found 377.18577; Anal. ($C_{23}H_{24}N_2O_3$) C: 72.87, H: 6.60, N: 7.38.

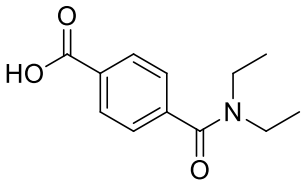


*4-((1H-Indol-7-yl)carbamoyl)benzyl diethylcarbamate **(45).*** Compound **45** was prepared via Procedure III from **127** (0.26 g, 1.0 mmol) and **81** (0.15 g, 1.1 mmol, 1.1 eq) to give a white solid (0.20 g, 52%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.98 (br s, 1H), 8.16 (br s, 1H), 7.93 (d, *J* = 7.8 Hz, 2H), 7.56-7.50 (m, 3H), 7.29 (t, *J* = 2.4 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.59 (t, *J* = 2.4 Hz, 1H), 5.22 (s, 2H), 3.40-3.39 (m, 4H), 1.17 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.2, 165.9, 155.8, 141.3, 134.0, 130.8, 128.5, 127.7, 125.1, 122.7, 119.6, 118.5, 114.1, 102.7, 66.2, 42.2, 41.5, 14.3, 13.6; HRMS calcd for $C_{21}H_{23}N_3O_3$ 366.1812; found 366.1809 $[M+H]^+$; Anal. ($C_{21}H_{23}N_3O_3$) C: 68.82, H: 6.52, N: 11.25.

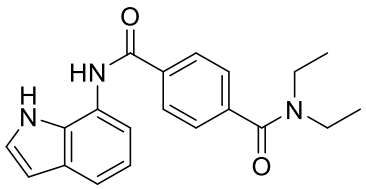


*Methyl 4-(diethylcarbamoyl)benzoate (**123**).* Thionyl chloride (2.8 mL, 5.6 mmol, 2.0 M) was added to 4-(methoxycarbonyl)benzoic acid (1.0 g, 5.6 mmol) and the reaction was brought to reflux. After refluxing for 1 h, the resulting mixture was concentrated *in vacuo*. To a stirred solution of acyl chloride (0.96 g, 4.9 mmol) in DCM (9.7 mL, 0.5 M) was added diethylamine (0.55 mL, 5.3 mmol, 1.1 eq) and TEA (0.85 mL, 6.1 mmol, 1.25 eq). The reaction was allowed to stir for 20 min at rt before being treated with DCM and diluted with distilled water. After extracting with DCM (2x), the combined organic layers were washed with brine, dried over ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was then purified using flash column chromatography on SiO_2 (Hexanes/EtOAc: 6/1) to yield a pale pink oil (0.79 g, 69%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 8.1, 0.9 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 3.75 (s, 3H), 3.38 (q, *J* = 6.3 Hz, 2H), 3.03 (q, *J* = 6.9 Hz, 2H), 1.07 (t, *J* = 6.6 Hz, 3H), 0.914 (t, *J* = 6.3 Hz, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$) δ 170.4, 166.6, 141.7, 130.8, 129.9, 126.4, 52.4, 43.4, 39.5, 14.3, 13.01; HRMS Calcd for $C_8H_6BrFO_2$ 232.9608; found 232.9609 $[M+H]^+$.

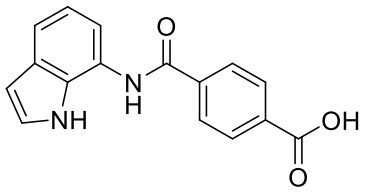


*4-(Diethylcarbamoyl)benzoic acid (**124**).* Compound **124** was prepared via Procedure II from **123** (0.79 g, 3.4 mmol). After acidification the mixture was concentrated *in vacuo*. Distilled water was added to create a suspension. The suspension was stored at 0 °C for approximately 30 min before being filtered. Washing the crystals with distilled water afforded a white solid (0.44 g, 59%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.1 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 3.58 (q, *J* = 6.6 Hz, 2H), 3.23 (q, *J* = 6.9, 2H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.12 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.3, 142.0, 130.6, 130.5, 126.5, 43.6, 39.7, 14.4, 13.1; HRMS calcd for $C_{12}H_{15}NO_3$ 222.1125; found 222.1128 $[M+H]^+$.

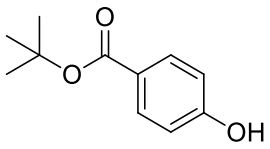


*N^1,N^1-Diethyl-N^4-(1H-indol-7-yl)terephthalamide **(46).*** Compound **46** was prepared via Procedure III from **124** (0.34 g, 1.6 mmol) and **81** (0.21 g, 1.6 mmol) to give a brown solid (0.076 g, 14%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.04 (br s, 1H), 9.13 (br s, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.23-7.17 (m, 4H), 7.01 (t, *J* = 8.0 Hz, 1H), 6.51 (t, *J* = 2.4 Hz, 1H), 3.49 (q, *J* = 6.8 Hz, 2H), 3.12 (q, *J* = 6.8 Hz, 2H), 1.19 (t, *J* = 6.8 Hz, 3H), 1.02 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 165.6, 139.8, 135.6, 130.8, 128.3, 128.1, 126.5, 125.1, 123.1, 119.7, 118.4, 114.1, 102.8, 43.7, 39.8, 14.4,

13.1; HRMS calcd for $C_{20}H_{21}N_3O_2$ 336.1707; found 336.1709 $[M+H]^+$; Anal. ($C_{20}H_{21}N_3O_2$) C: 68.40, H: 6.24, N: 11.36.

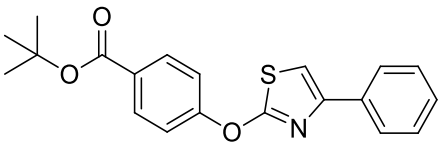


4-((1H-indol-7-yl)carbamoyl)benzoic acid ***(47).*** Methyl 4-((1H-indol-7-yl)carbamoyl)benzoate (0.2951 g, 1.003 mmol) in Methanol (Volume: 15.92 ml) under Argon was combined with Sodium Hydroxide (3.81 ml, 3.81 mmol) at rt and allowed to stir overnight. The mixture was monitored to completion by TLC. The pH of the reaction was then adjusted to 3.0 using conc. HCl. The resulting mixture was concentrated and added H2O to create a suspension. The suspension was placed in the fridge for approx. 30 minutes before filtering to collect the solid. The crystals were washed with H2O. 1H NMR (400 MHz, DMSO): 10.916, 10.307, 8.090-8.159 (4H, q), 7.428-7.447 (1H, d), 7.350-7.363 (1H, t), 7.318-7.336 (1H, d), 6.990-7.028 (1H, t), 6.473-6.485 (1H, t). 13C NMR (400MHz, CDCl3): 166.863, 138.682, 133.219, 129.855, 129.251, 128.197, 125.306, 122.799, 118.740, 117.602, 116.077, 101.468. HRMS calculated: 281.09207 for [M+H]+; found, 281.09232.

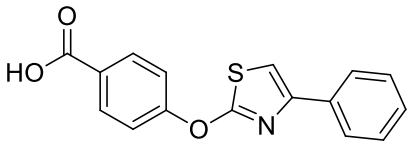


*tert-Butyl 4-hydroxybenzoate (**129**).* To a solution of methyl 4-hydroxybenzoate (2.5 g, 18 mmol) in DCM (75 mL, 0.24 M) was added DMAP (0.090 g, 0.71 mmol, 0.039 eq) and *t*-BuOH (50 mL, 18 mmol, 0.36 M). A 1.0 M solution of DCC in DCM (27 mL, 27.2 mmol, 1.5 eq) was added dropwise and the reaction mixture was stirred for 24 h. The mixture was filtered and concentrated *in vacuo*. The resulting residue

was diluted with EtOAc and washed with saturated aqueous sodium bicarbonate (2x). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was then purified using flash column chomatography on SiO_2 (Hexanes/EtOAc: 10/3) to yield a white solid (2.9 g, 82%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92-7.88 (mult, 2H), 6.87-6.84 (mult, 2H), 1.61 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 160.2, 131.9, 124.20, 115.30, 81.2, 28.45; HRMS Calcd for $C_{11}H_{14}O_3$ 193.0870; found 193.0869 $[M-H]^+$.

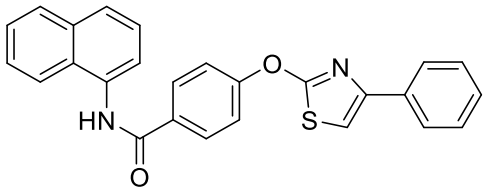


*tert-Butyl 4-(4-phenylthiazole-2-yloxy)benzoate (**131**).* To a solution of **129** (0.97 g, 5.0 mmol) in DMF (19 mL) was added finely ground potassium carbonate (1.4 g, 10.0 mmol) which had been oven dried for 24 h. The reaction mixture stirred at rt for 1 h before 2-chloro-4-benzylthiazole (1.1 g, 5.5 mmol) was added. Heating for 15 min at 200 °C μW afforded a liquid which was diluted with distilled water and extracted with Et_2O (2x). The organic phase was separated and was washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford a colorless oil (0.2 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97-7.94 (mult, 2H), 7.70-7.67 (mult, 2H), 7.30-7.18 (mult, 5H), 6.90 (s, 1H) 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 158.7, 150.0, 134.2, 131.60, 129.0, 128.9, 128.8, 128.4, 126.3, 126.1, 119.3, 114.4, 107.1, 81.4, 28.4; HRMS Calcd for $C_{20}H_{19}NO_3S$ 354.1158; found 354.1158 $[M+H]^+$.

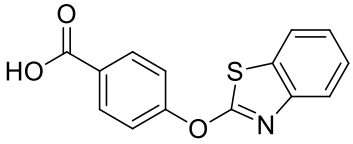


*4-(4-Phenylthiazol-2-yloxy)benzoic acid (**132**).* A solution of **131** (1.3 g, 3.6 mmol) in TFA (14.5 mL) was allowed to stir for 1 h at rt. The reaction mixture was filtered while washing with DCM to afford a white solid (0.56 g, 55%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.06 (d, J = 8.7 Hz, 2H), 7.83 (d, J = 7.5 Hz,

2H), 7.73 (s, 1H), 7.53 (d, *J* = 9.0 Hz, 2H), 7.44-7.33 (mult, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 170.9, 166.5, 158.2, 148.6, 133.7, 131.6, 128.8, 128.2, 125.6, 119.7, 110.8, 109.2; HRMS Calcd for $C_{16}H_{11}NO_3S$ 298.0532; found 298.0532 $[M+H-C_4H_8]^+$.

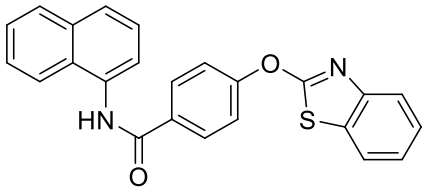


N-(Napthalen-1-yl)-4-(4-phenylthiazol-2-yloxy)benzamide ***(48).*** Compound **48** was prepared via Procedure III from **132** (0.51 g, 1.7 mmol) to give a white solid (0.45 g, 62%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.214 (br s, 1H), 8.08-8.01 (m, 3H), 7.94-7.91 (m, 2H), 7.85-7.76 (m, 3H), 7.56-7.51 (m, 5H), 7.44-7.34 (m, 3H), 7.101 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 181.4, 171.4, 165.3, 157.3, 148.6, 133.8, 132.0, 130.1, 129.2, 128.8, 128.2, 128.1, 126.4, 126.1, 126.0, 125.7, 125.6, 123.9, 123.4, 119.8, 110.8, 108.9; HRMS calcd for $C_{26}H_{18}N_2O_2S$ 423.1162; found 423.1164 $[M+H]^+$; Anal. ($C_{26}H_{18}N_2O_2S$) C: 73.07, H: 4.26, N: 6.54.



4-(Benzo[d]thiazol-2-yloxy)benzoic acid ***(133).*** To a solution of **129** (0.97 g, 5.0 mmol) in DMF (19 mL) was added finely ground potassium carbonate (1.4 g, 10 mmol) which had been oven dried for 24 h. The reaction mixture stirred at rt for 1 h before 2-chloro-benz[*d*]thiazole (0.68 mL, 5.5 mmol, 1.1 eq) was added. Heating for 15 min at 200 °C μW afforded a liquid which was diluted with distilled water and extracted with Et_2O (2x). The organic phase was separated and was washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo* to afford a yellow oil which was dissolved in TFA (14 mL) and allowed to stir for 1 h at rt. The reaction mixture was filtered while washing with DCM to afford a white

solid (0.96 g, 45%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.5 (br s, 1H), 8.05 (d, J = 8.7 Hz, 2H), 7.98 (d, J = 7.8 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 8.7 Hz, 2H), 7.45 (t, J = 7.8 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.2, 175.9, 170.4, 158.8, 148.5, 132.6, 127.0, 126.7, 124.8, 122.2, 121.6, 120.5; HRMS Calcd for $C_{14}H_9NO_3S$ 272.0376; found 272.0377 $[M+H]^+$.



4-(Benzo[d]thiazol-2-yloxy)-N-(napthalen-1-yl)benzamide ***(49).*** Compound **49** was prepared via Procedure III from **133** (0.33 g, 1.2 mmol). Upon purification using flash column chromatography, a white solid was obtained (0.15 g, 30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (br s, 1H), 8.096 (d, J = 9.0 Hz, 2H), 8.03 (d, J = 7.5 Hz, 1H), 7.94-7.91 (m, 2H), 7.79-7.73 (m, 3H), 7.58-7.52 (m, 5H), 7.47-7.41 (m, 1H), 7.37-7.31 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.1, 186.7, 171.0, 157.3, 149.0, 134.4, 132.6, 132.4, 129.4, 129.1, 127.8, 126.72, 126.66, 126.6, 126.3, 126.0, 124.7, 122.1, 121.7, 121.6, 121.0, 120.9; HRMS calcd for $C_{24}H_{16}N_2O_2S$, 397.1005; found 397.1006 $[M+H]^+$; Anal. ($C_{24}H_{16}N_2O_2S$) C: 72.04, H: 3.86, N: 6.96.