

Table 1: Series 1: Variation at R₁

Code	R ₁	R ₂	R ₃	IC ₅₀ for Icmt inhibition ¹ μ M	IC ₅₀ for cell viability ² (μ M)	ClogP ³
Cys	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.5	21.8	7.00
J23	2'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.0	20.1	6.25
J24	4'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.4	> 25	7.00
J9	3'-OCH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.9	22.9	6.42
J8	3'-OC ₂ H ₅ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.3	19.1	6.95
J14	C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.8	25.3	6.5
J15	H	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	6.5	>25	4.61

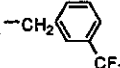
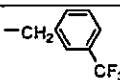
¹ Method is described in 6.1. Mean $\pm$ SD ($n \geq 3$). If no SD is given, $n = 2$.

² Human breast cancer cells (MDA-MB231) were used, Method is described in Example 7

³ Determined from Chem Draw Ultra 10.0

Figure 1

Table 2: Series 2: Variation at R₂

Code	R ₁	R ₂	R ₃	IC ₅₀ for Icmt inhibition ¹ μM	IC ₅₀ for cell viability ² (μM)	ClogP ³
Cys	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.5	21.8	7.0
J16	3'-CH ₃ -C ₆ H ₅	H	-CH ₂ CONH ₂	33	>100	2.83
J10	3'-CH ₃ -C ₆ H ₅		-CH ₂ CONH ₂	2.5	17.2	6.39
J21	3'-CH ₃ -C ₆ H ₅	Isoprenyl	-CH ₂ CONH ₂	7.7	28.5	5.00
J22	3'-CH ₃ -C ₆ H ₅	geranyl	-CH ₂ CONH ₂	1.1	10.6	7.03
J11	3'-CH ₃ -C ₆ H ₅		CH ₂ CON(C ₂ H ₅) ₂	22.9	>50	7.52

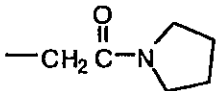
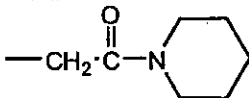
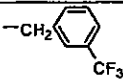
¹ Method is described in 6.1. Mean $\pm$ SD ($n \geq 3$). If no SD is given, $n = 2$.

² Human breast cancer cells (MDA-MB 231) were used, Method is described in Example 7.

³ Determined from Chem Draw Ultra 10.0

Figure 2

Table 3: Series 3: Variations at R₃ (tertiary amides)

Code	R ₁	R ₂	R ₃	IC ₅₀ for Icmt inhibition n ¹ μM	IC ₅₀ for cell viability ² (μM)	ClogP ³
Cys	3'-CH ₃ - C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.5	21.8	7.0
J5	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CON(CH ₃) ₂	1.5	31.1	7.51
J1	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CON(C ₂ H ₅) ₂	1.4	27	8.57
J7	3'- OCH ₃ C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CON(C ₂ H ₅) ₂	0.8	51.8	7.99
J6	3'- OC ₂ H ₅ C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CON(C ₂ H ₅) ₂	1.0	26.8	8.52
J4	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇		1.2	15.6	9.71
J2	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇		1.8	28.9	10.27
J11	3'-CH ₃ -C ₆ H ₅		-CH ₂ CON(C ₂ H ₅) ₂	22.9	>50	7.52

¹ Method is described in 6.1. Mean ± SD (n ≥ 3). If no SD is given, n = 2.² Human breast cancer cells (MDA-MB 231) were used, Method is described in Example 7³ Determined from Chem Draw Ultra 10.0

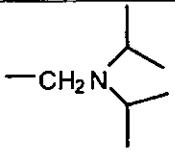
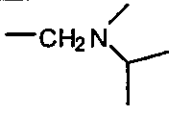
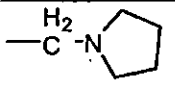
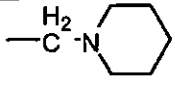
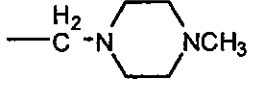
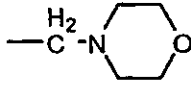
Figure 3

Table 4: Series 4: Variations at R₃ (other than tertiary amides) •

Code	R ₁	R ₂	R ₃	IC ₅₀ for Icmt inhibition ¹ μM	IC ₅₀ for cell viability ² (μM)	ClogP ³
Cys	3'-CH ₃ - C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.5	21.8	7.0
J3	3'-CH ₃ - C ₆ H ₅	-n-C ₈ H ₁₇	-H	> 100	> 50	8.69
J20	3'-CH ₃ - C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CH ₂ CONH ₂	1.2	20.4	7.77
J12	3'-CH ₃ - C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ COOCH ₃	76	>100	8.37
J13	3'-CH ₃ C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ COOC ₂ H ₅	>100	>100	8.90
J19G	3'-CH ₃ C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ NHCOCH ₃	1.8	30.4	7.50
J28G	3'-CH ₃ C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ NH ₂ SO ₂ CH ₃	1.2	17.1	7.36

¹ Method is described in 6.1. Mean ± SD (n ≥ 3). If no SD is given, n = 2.² Human breast cancer cells (MDA-MB 231) were used. Method is described in Example 7³ Determined from Chem Draw Ultra 10.0**Figure 4**

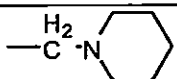
Table 5: Series 5: Variations at R₃ (amines)

Code	R ₁	R ₂	R ₃	IC ₅₀ for Icmt inhibition ¹ (μM)	IC ₅₀ for cell viability ² (μM)	ClogP ³
Cys	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.5	21.8	7.0
J18	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ NH ₂	0.7	2.9	7.64
J25G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ N(CH ₃) ₂	1.3	6.86	8.52
J17G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ N(C ₂ H ₅) ₂	0.7	3.6	9.58
J27G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ N(C ₃ H ₇) ₂	0.8	13	10.64
J26G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇		1.7	20.1	10.20
J29G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇		0.9	5.3	9.36
J31G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇		0.5	5.1	9.16
J32G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇		0.7	4.9	9.72
J30G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇		0.9	6.1	8.88
J34G	3'-CH ₃ -C ₆ H ₅	-n-C ₈ H ₁₇		2.7	25	8.44

¹ Method is described in 6.1. Mean ± SD (n ≥ 3). If no SD is given, n = 2.² Human breast cancer cells (MDA-MB 231) were used, Method is described in Example 7³ Determined from Chem Draw Ultra 10.0. As compounds are tertiary amines, a more useful gauge of lipophilicity would be log D (pH 7.4). This value would be lower than ClogP because the amino side chain will be protonated at pH 7.4.

Figure 5

Table 6: Series 6: Variations at R₁ and R₂, with R₃ = amino

Code	R ₁	R ₂	R ₃	IC ₅₀ for Icmt inhibition ¹ (μM)	IC ₅₀ for cell viability ² (μM)	ClogP ³
Cys	3'-CH ₃ - C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ CONH ₂	1.5	21.8	7.0
J17G	3'-CH ₃ - C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ N(C ₂ H ₅) ₂	0.7	3.6	9.58
J36G	2'- CH ₃ C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ N(C ₂ H ₅) ₂	0.6	5.5	9.28
J37G	4'- CH ₃ C ₆ H ₅	-n-C ₈ H ₁₇	-CH ₂ N(C ₂ H ₅) ₂	0.6	3.4	9.58
J40G	F	-n-C ₈ H ₁₇	-CH ₂ N(C ₂ H ₅) ₂	4.1	7.2	7.38
J38G	3'-CH ₃ - C ₆ H ₅	isoprenyl	-CH ₂ N(C ₂ H ₅) ₂	2.4	3.8	7.58
J39G	3'-CH ₃ - C ₆ H ₅	isoprenyl		2.1	3.9	7.71
J35G	H	isoprenyl	-CH ₂ N(C ₂ H ₅) ₂	67	74	5.19
J41G	F	isoprenyl	-CH ₂ N(C ₂ H ₅) ₂	35	32	5.38

¹ Method is described in 6.1. Mean ± SD (n ≥ 3). If no SD is given, n = 2.² Human breast cancer cells (MDA-MB 231) were used, Method is described in Example 7³ Determined from Chem Draw Ultra 10.0

Figure 6

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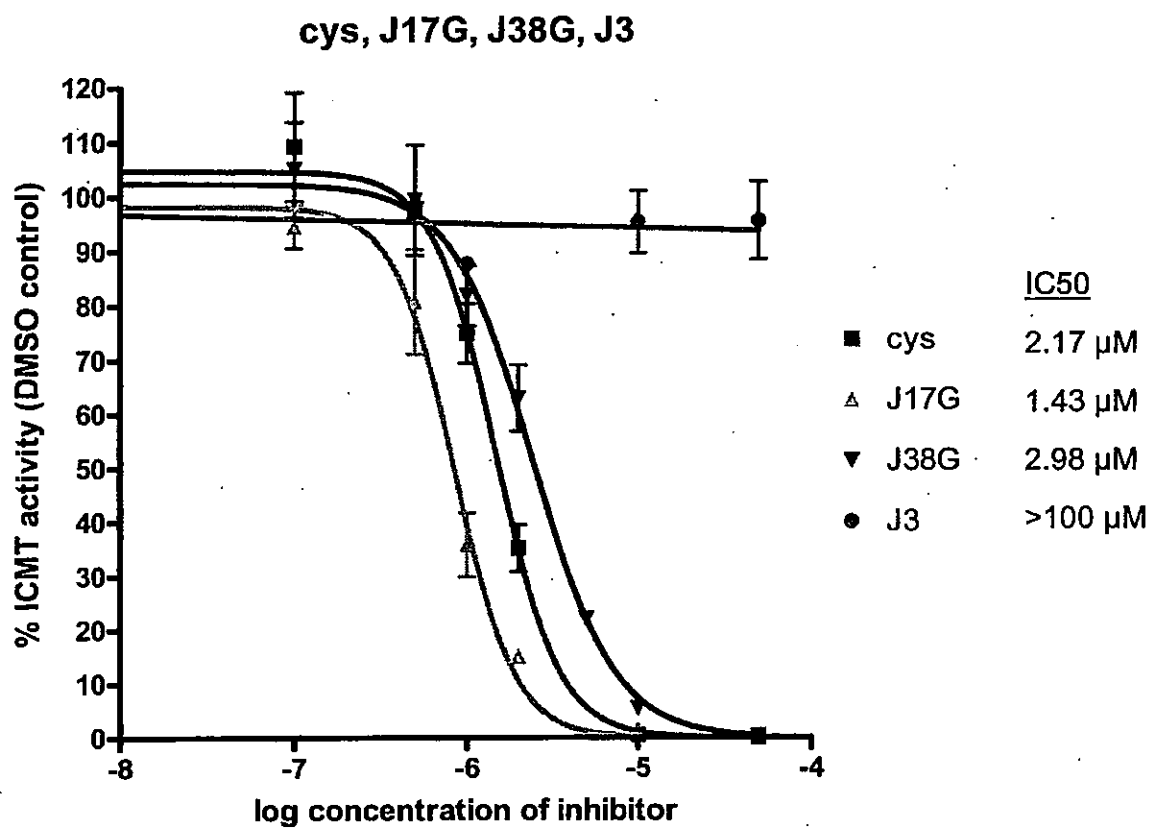


Figure 7

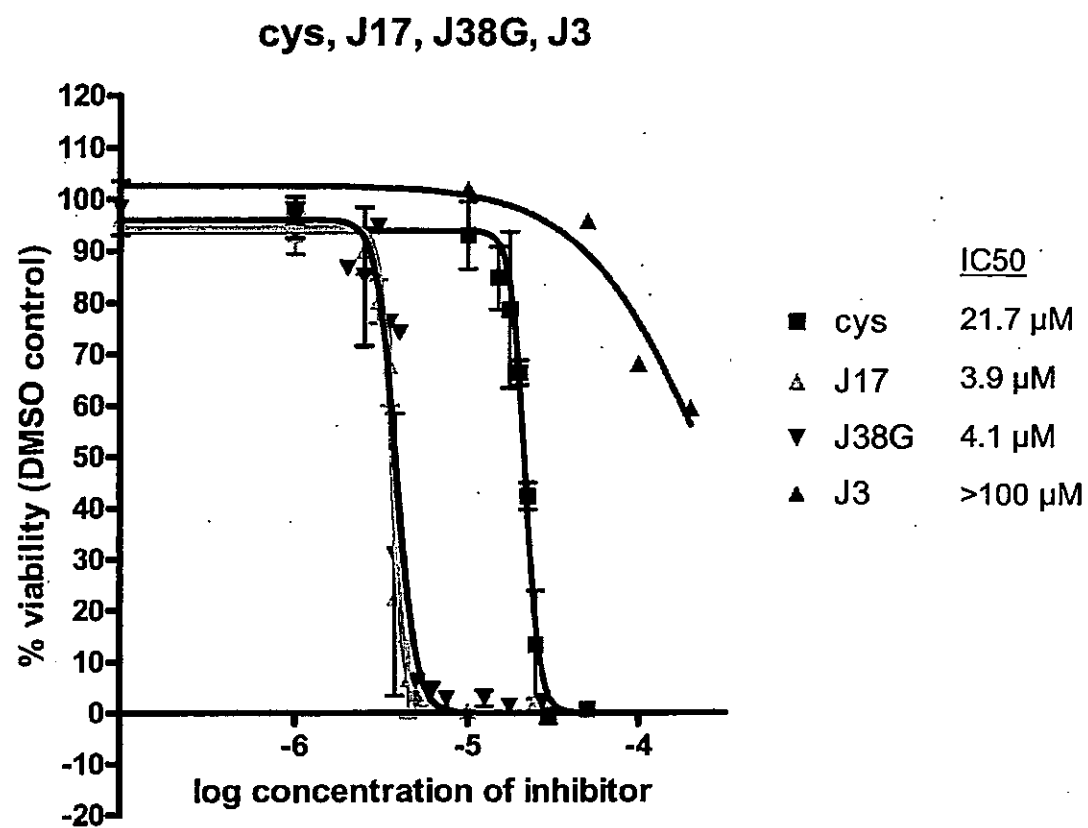


Figure 8

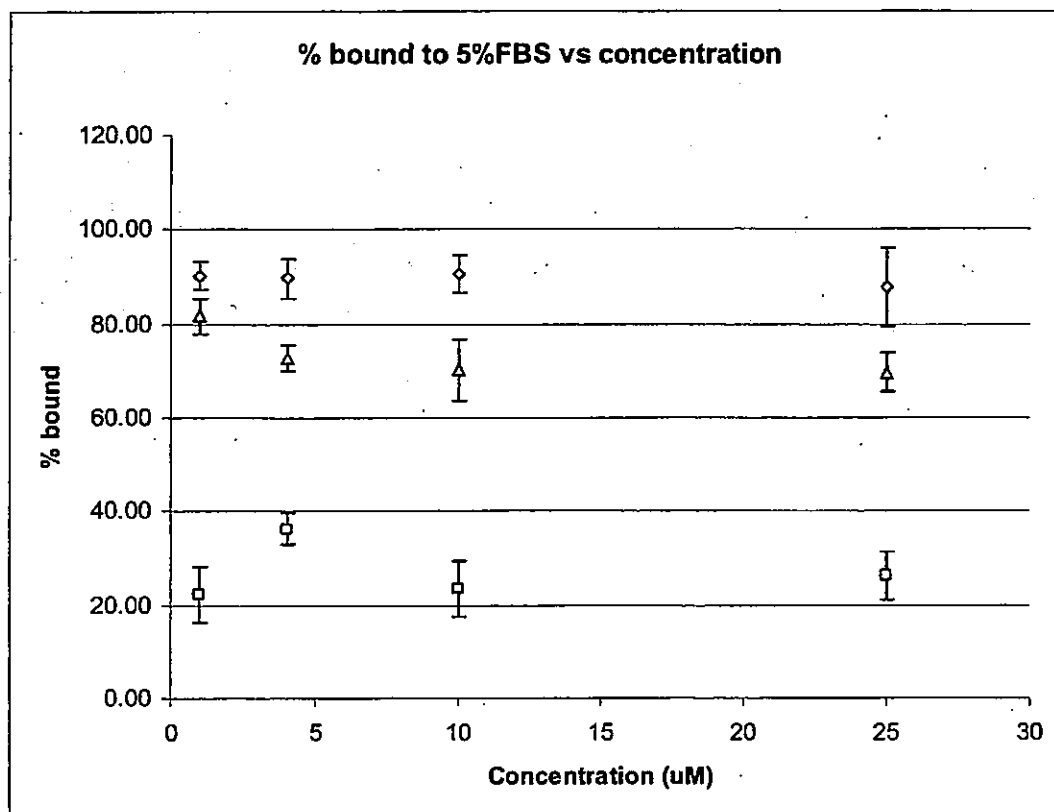


Figure.9