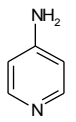
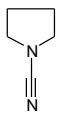
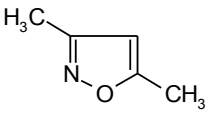
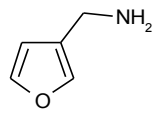
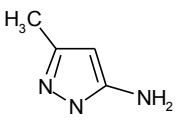
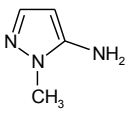
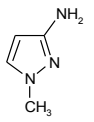
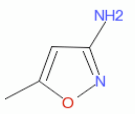
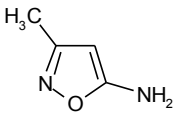
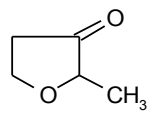
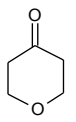
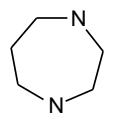
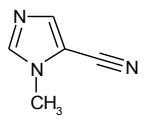
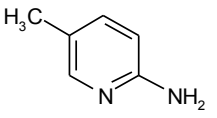
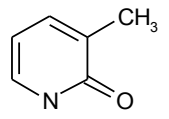
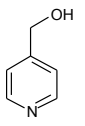
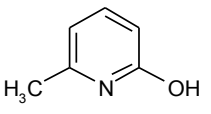
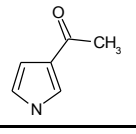
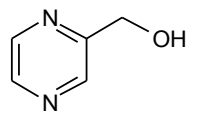
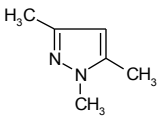
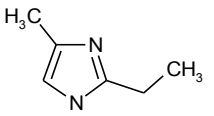
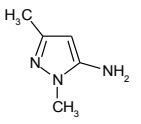
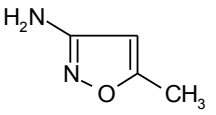
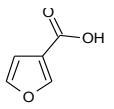
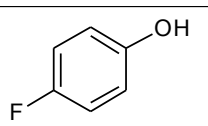
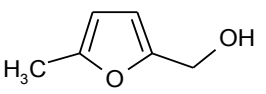
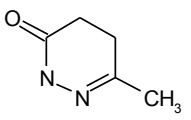
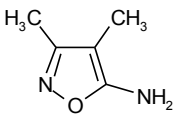
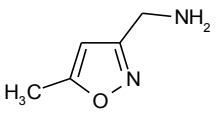
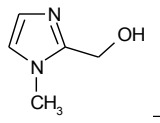
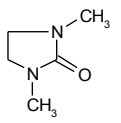
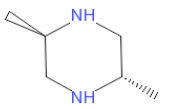
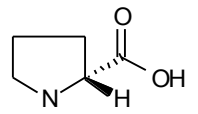
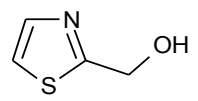
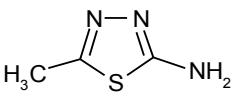
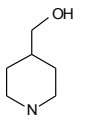
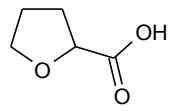
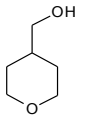
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

Library number[a]	CAS number[b]	Molecular Structure	Product Name	*Tb* Ino1 Tm Shift[c] [˚C]	*T. brucei* Alamar Blue[d]	HeLa Cells Alamar Blue[d]	A549 Cells Alamar Blue[e]
1	N/A	N/A	Control	-0.005 ± 0.152 f	99.5 ± 11	99.2 ± 10.8	100 ± 14
2	504-24-5		pyridin-4-amine	-0.22 ± 0.07	**98.8 ± 6.7**	102.7 ± 2.2	105.9
3	1530-88-7		pyrrolidine-1-carbonitrile	-0.19 ± 0.06	82.5 ± 12.8	**88.5 ± 1.3**	114.9
4	300-87-8		3,5-dimethylisoxazole	-0.4 ± 0.08	**116.6 ± 5.1**	107.7 ± 5.3	123.1
5	4543-47-9		3-furylmethylamine	0.3 ± 0.06	**79.2 ± 7.9**	101.3 ± 5.3	112.7
6	31230-17-8		3-methyl-1H-pyrazol-5-amine	0.2 ± 0.06	94.9 ± 3.6	102.2 ± 3.3	121.4
7	1192-21-8		1-methyl-1H-pyrazol-5-ylamine	0.12 ± 0.06	96.4 ± 2.6	106.5 ± 6.2	123.6
8	1904-31-0		1-methyl-1H-pyrazol-3-amine	0.09 ± 0.07	93.4 ± 0.9	106.6 ± 7.8	122.1
9	1072-67-9		5-methylisoxazol-3-amine	0.13 ± 0.06	97 ± 14.3	**105 ± 6.2**	112.2
10	14678-02-5		3-methylisoxazol-5-amine	-0.02 ± 0.07	67.7 ± 8.7	66 ± 4.6	87.2
11	3188-00-9		2-methyltetrahydrofuran-3-one	0.77 ± 0.06	**97.8 ± 15.4**	100.7 ± 5.4	85.3
12	29943-42-8		tetrahydro-4H-pyran-4-one	0.23 ± 0.07	103 ± 17.2	100.3 ± 3.5	97.4
13	505-66-8		1,4-diazepane	0.4 ± 0.07	101.5 ± 15.4	88.5 ± 11.1	82.4
15	66121-66-2		1-methyl-1H-imidazole-5-carbonitrile	0.08 ± 0.07	93.4 ± 4.5	100.6 ± 9.5	90
16	1603-41-4		5-methylpyridin-2-amine	0.12 ± 0.06	66.2 ± 6.2	100.6 ± 1.1	89.4
17	1003-56-1		3-methyl-1,2-dihydropyridin-2-one	0.81 ± 0.08	**93.6 ± 17.8**	105.6 ± 11.4	87.2
18	586-95-8		4-pyridinylmethanol	0.36 ± 0.07	**101.2 ± 1.3**	103.5 ± 3.9	102
19	3279-76-3		6-methylpyridin-2-ol	0.09 ± 0.08	94.5 ± 12.2	102.6 ± 7.6	85.6
20	1072-82-8		1-(1H-pyrrol-3-yl)ethan-1-one	1.88 ± 0.08	**36.8 ± 9.7**	101.8 ± 4.3	121.3

Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

23	6705-33-5		2-pyrazinylmethanol	0.27 ± 0.07	110.3 ± 11.8	77.5 ± 12.3	75.9
24	1072-91-9		1,3,5-trimethyl-1H-pyrazole	-0.02 ± 0.07	**114 ± 12.5**	99.7 ± 11.5	88.5
25	931-36-2		2-ethyl-4-methyl-1H-imidazole	-0.09 ± 0.06	89.6 ± 2.5	98 ± 7.8	83.9
26	3524-32-1		1,3-dimethyl-1H-pyrazol-5-amine	0.54 ± 0.07	**97.8 ± 4.7**	85.5 ± 9.4	70.1
27	88-14-2		2-furoic acid	0.17 ± 0.06	**21.3 ± 1**	95.7 ± 9.4	106.6
28	488-93-7		3-furoic acid	3.72 ± 0.08	**59.7 ± 5.5**	48.2 ± 11.8	111
29	371-41-5		4-fluorophenol	0.23 ± 0.08	85.3 ± 12.3	96.2 ± 7.7	88.4
30	3857-25-8		(5-methyl-2-furyl)methanol	3.79 ± 0.08	45 ± 14.1	23.3 ± 18.6	23.7
31	5157-08-4		6-methyl-2,3,4,5-tetrahydropyridazin-3-one	0.22 ± 0.07	**110.1 ± 12.1**	85.4 ± 6.1	68.2
32	19947-75-2		3,4-dimethylisoxazol-5-amine	-0.01 ± 0.07	96.2 ± 10.7	**76.4 ± 5.7**	71.7
33	154016-48-5		(5-methyl-3-isoxazolyl)methylamine	-0.07 ± 0.07	**75.7 ± 13.5**	64.3 ± 18.4	75.6
34	17334-08-6		(1-methyl-1H-imidazol-2-yl)methanol	-0.16 ± 0.07	**133.4 ± 1.6**	97 ± 14	72.1
35	80-73-9		1,3-dimethylimidazolidin-2-one	0.04 ± 0.07	92.2 ± 13	101.1 ± 6.6	92.7
36	2815-34-1		2,5-dimethylpiperazine	0.18 ± 0.08	81.1 ± 18.6	91.3 ± 12.1	76.6
37	344-25-2		D-proline	0.41 ± 0.06	**102.9 ± 8.2**	94.8 ± 10.1	78.6
38	14542-12-2		1,3-thiazol-2-ylmethanol	0.18 ± 0.09	**87.9 ± 9**	99.4 ± 4.1	95
39	108-33-8		5-methyl-1,3,4-thiadiazol-2-amine	0.31 ± 0.08	102.8 ± 12	104.8 ± 14.5	72.3
40	6457-49-4		4-piperidylmethanol	-1.35 ± 0.1	**72.2 ± 8.1**	84.3 ± 9	104.2
42	16874-33-2		tetrahydro-2-furancarboxylic acid	0.3 ± 0.08	**107.5 ± 16.4**	81.9 ± 17	75.1
43	14774-37-9		tetrahydro-2H-pyran-4-ylmethanol	-0.02 ± 0.08	112.7 ± 18.4	91.9 ± 5.9	79.2

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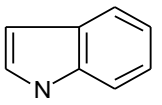
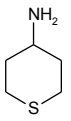
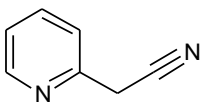
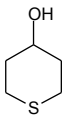
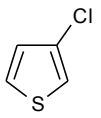
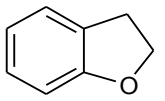
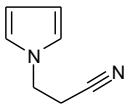
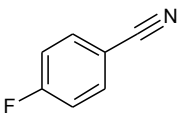
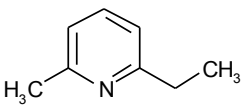
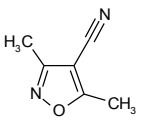
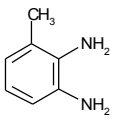
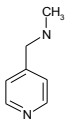
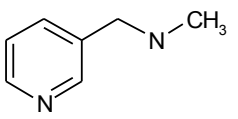
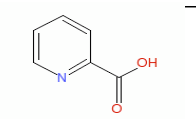
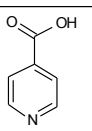
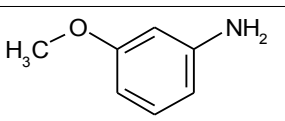
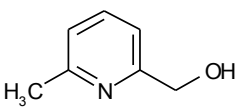
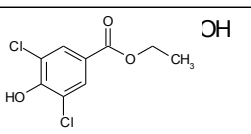
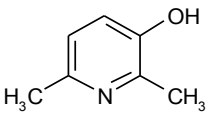
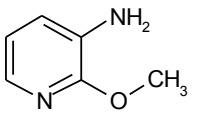
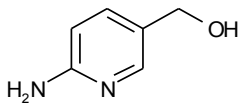
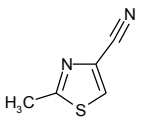
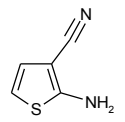
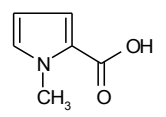
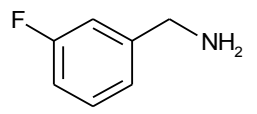
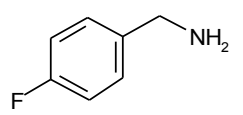
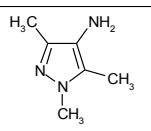
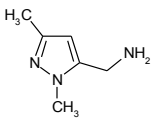
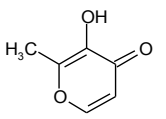
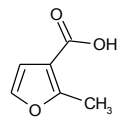
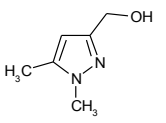
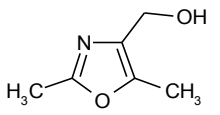
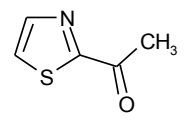
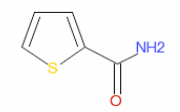
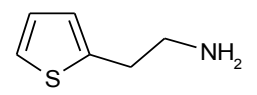
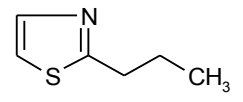
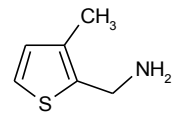
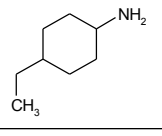
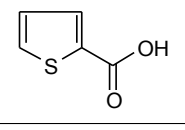
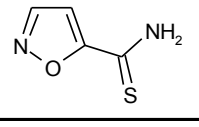
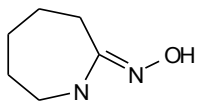
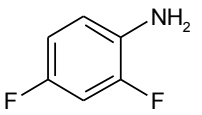
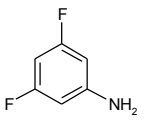
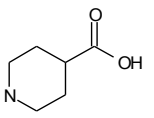
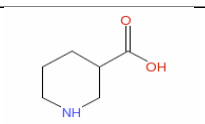
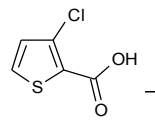
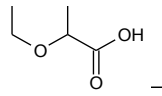
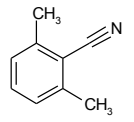
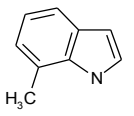
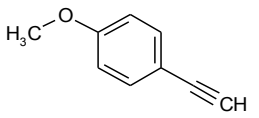
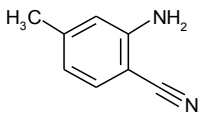
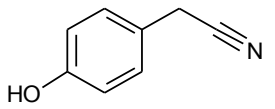
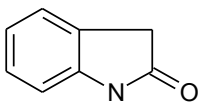
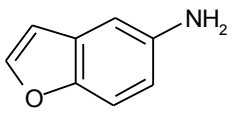
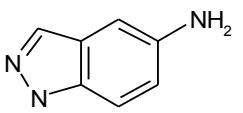
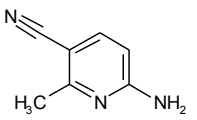
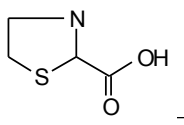
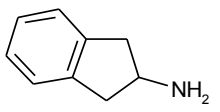
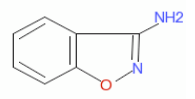
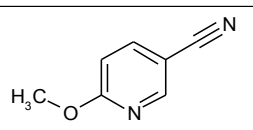
44	120-72-9		1H-indole	0.11 ± 0.06	28.4 ± 12	85.7 ± 19.3	75.7
45	21926-00-1		tetrahydrothiopyran-4-ylamine	0.24 ± 0.07	103.4 ± 13.8	88.6 ± 3.1	95.6
46	2739-97-1		2-(2-pyridyl)acetonitrile	1.11 ± 0.24	44.1 ± 16.1	63.2 ± 17.9	82.6
47	29683-23-6		tetrahydro-2H-thiopyran-4-ol	-0.07 ± 0.07	**113.4 ± 7.5**	95 ± 10	74.9
48	17249-80-8		3-chlorothiophene	-0.2 ± 0.08	108.2 ± 17.8	95.5 ± 2	101
49	496-16-2		2,3-dihydrobenzo[b]furan	-1.08 ± 0.12	104.3 ± 18.1	102.1 ± 8.6	87.3
50	43036-06-2		3-(1H-pyrrol-1-yl)propanenitrile	-0.67 ± 0.17	**90.7 ± 10.3**	**75.4 ± 6.4**	140.2
51	1194-02-1		4-fluorobenzonitrile	0.1 ± 0.08	85.3 ± 5.2	90.9 ± 7.5	64.2
52	1122-69-6		2-ethyl-6-methylpyridine	0.4 ± 0.08	80.8 ± 14	**89.7 ± 9.7**	70.8
53	31301-46-9		3,5-dimethyl-4-isoxazolecarbonitrile	0.52 ± 0.09	85 ± 13.8	89.3 ± 2.8	84.5
55	2687-25-4		3-methylbenzene-1,2-diamine		30.7 ± 8.3	11.2 ± 7.2	26.5
56	6971-44-4		N-methyl-N-(4-pyridinylmethyl)amine	0.01 ± 0.08	**86.8 ± 7.8**	87.9 ± 9.9	78.5
57	20173-04-0		N-methyl-N-(3-pyridylmethyl)amine	-0.07 ± 0.07	**111.2 ± 6.8**	89.3 ± 9.6	79
58	98-98-6		2-pyridinecarboxylic acid	-0.36 ± 0.08	**63 ± 15.4**	87.3 ± 6.1	97.9
60	55-22-1		isonicotinic acid	-1.64 ± 0.13	90.7 ± 13.8	**98.3 ± 12.5**	117.5
61	536-90-3		3-methoxyaniline	0.19 ± 0.07	**67.4 ± 6.7**	48.7 ± 8.9	69.2
62	1122-71-0		(6-methylpyridin-2-yl)methanol	-0.01 ± 0.07	95.7 ± 17.2	98.6 ± 7.3	67.5
63	6293-56-7		2-(3-pyridyl)ethan-1-ol	-0.07 ± 0.07	84.6 ± 9.4	104.8 ± 13.1	76.9
64	1122-43-6		2,6-dimethylpyridin-3-ol	0.13 ± 0.07	**110.6 ± 6.3**	103.4 ± 13.2	80.6
65	20265-38-7		2-methoxypyridin-3-amine	1.46 ± 0.07	40 ± 11.5	**66.6 ± 18.7**	75.4

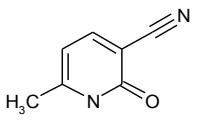
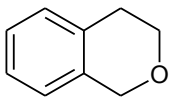
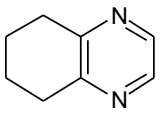
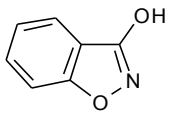
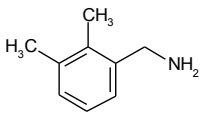
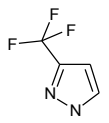
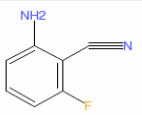
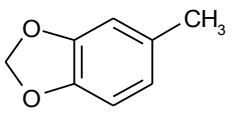
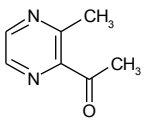
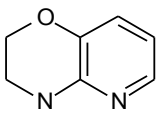
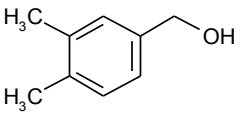
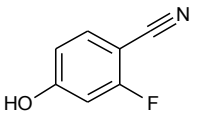
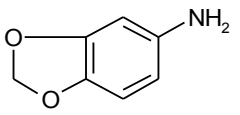
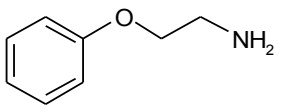
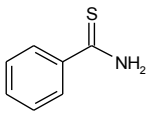
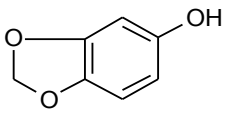
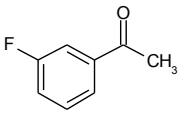
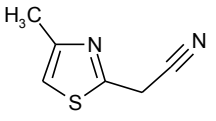
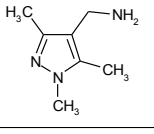
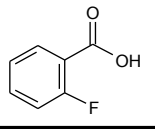
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

66	113293-71-3		(6-amino-3-pyridinyl)methanol	0.24 ± 0.09	29.6 ± 6.1	80.3 ± 9.7	85.1
67	21917-76-0		2-methyl-1,3-thiazole-4-carbonitrile	0.01 ± 0.07	106.5 ± 18	96.1 ± 9.2	89.7
68	4651-82-5		2-aminothiophene-3-carbonitrile		30.3 ± 11	**101.9 ± 3.1**	136.3
69	6973-60-0		1-methyl-1H-pyrrole-2-carboxylic acid	-0.57 ± 0.08	99.1 ± 18.5	95.3 ± 2.5	70.2
70	100-82-3		3-fluorobenzylamine	-1.88 ± 0.11	67.7 ± 18.9	104 ± 17.4	104.4
71	140-75-0		4-fluorobenzylamine	-0.17 ± 0.07	73.4 ± 16.8	93.3 ± 10.3	109.7
72	28466-21-9		1,3,5-trimethyl-1H-pyrazol-4-amine	1.19 ± 0.08	20.8 ± 6.2	**78.5 ± 0.8**	70.9
73	499770-63-7		(1,3-dimethyl-1H-pyrazol-5-yl)methylamine	-0.08 ± 0.07	80 ± 15.5	**91.3 ± 0.6**	107.6
74	118-71-8		3-hydroxy-2-methyl-4H-pyran-4-one	1.13 ± 0.08	**44.5 ± 21.1**	106.7 ± 10.5	105.3
75	6947-94-0		2-methyl-3-furoic acid	3.89 ± 0.07	**62.2 ± 10.6**	63.3 ± 5.9	110.4
76	153912-60-8		(1,5-dimethyl-1H-pyrazol-3-yl)methanol	0.56 ± 0.08	**85.4 ± 1.3**	**99.6 ± 4.5**	100.3
78	92901-94-5		(2,5-dimethyl-1,3-oxazol-4-yl)methanol	0.13 ± 0.08	103.4 ± 10.5	92.7 ± 11.5	110.1
79	24295-03-2		1-(1,3-thiazol-2-yl)ethan-1-one	-0.16 ± 0.07	113.9 ± 19.2	103.4 ± 16.6	94.5
80	5813-89-8		thiophene-2-carboxamide	-0.23 ± 0.07	99.6 ± 2.4	106.5 ± 17.5	90.3
81	30433-91-1		2-(2-thienyl)ethylamine	0.09 ± 0.07	**72.3 ± 9**	**116.8 ± 8.9**	119.2
82	17626-75-4		2-propyl-1,3-thiazole	0.22 ± 0.07	81.1 ± 11.9	96.8 ± 11	114.2
83	104163-35-1		(3-methyl-2-thienyl)methylamine	0.43 ± 0.06	**95.7 ± 2.4**	95.4 ± 10	124.1
84	23775-39-5		4-ethylcyclohexanamine	0.44 ± 0.06	**95.1 ± 12.8**	90.7 ± 14.2	118.3
85	527-72-0		thiophene-2-carboxylic acid	0.24 ± 0.06	**101.1 ± 12.4**	100.2 ± 7.4	119
86	175334-72-2		isoxazole-5-carbothioamide	0.94 ± 0.08	101.1 ± 3.2	101.9 ± 3.4	105.4

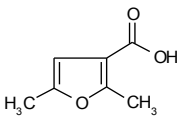
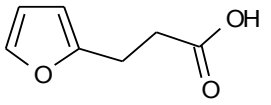
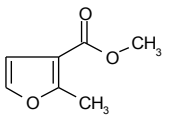
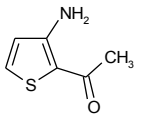
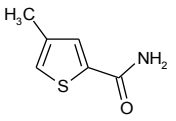
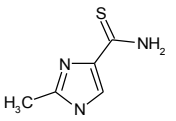
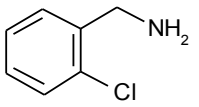
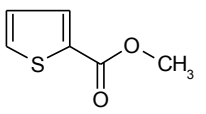
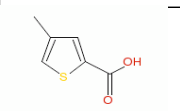
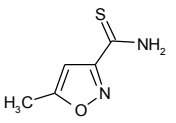
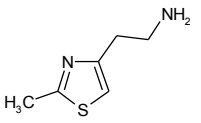
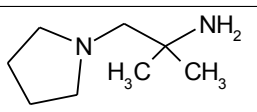
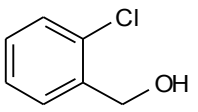
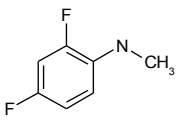
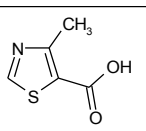
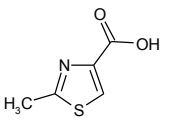
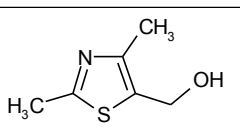
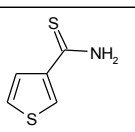
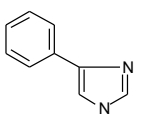
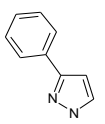
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

87	19214-08-5		azepan-2-one oxime	0.52 ± 0.06	56.3 ± 9.9	92.3 ± 17.4	115
88	367-25-9		2,4-difluoroaniline	1.11 ± 0.07	**45.4 ± 8.9**	**87.6 ± 10.6**	132
89	372-39-4		3,5-difluoroaniline	0.3 ± 0.07	**112.1 ± 10.7**	104.4 ± 10.5	132.4
90	498-94-2		piperidine-4-carboxylic acid	0.5 ± 0.06	**75.1 ± 12.4**	106.3 ± 2	131.7
91	498-95-3		3-piperidinecarboxylic acid	1.69 ± 0.1	36.1 ± 11	**76.6 ± 29.1**	102.7
92	5337-03-1		tetrahydro-2H-pyran-4-carboxylic acid	-0.35 ± 0.07	58.7 ± 14.3	78.4 ± 15.8	118.1
93	51673-83-7		tetrahydropyran-2-carboxylic acid	0.55 ± 0.06	**67.2 ± 12**	**97.5 ± 2.4**	107.4
94	6575-13-9		2,6-dimethylbenzonitrile	1.3 ± 0.06	86 ± 16.6	96.4 ± 13.9	114.4
95	933-67-5		7-methyl-1H-indole	-4.86 ± 0.12	24.1 ± 5.2	11.9 ± 8.8	13.4
96	768-60-5		1-eth-1-ynyl-4-methoxybenzene	0.48 ± 0.06	104 ± 18.1	94 ± 4.9	111
97	26830-96-6		2-amino-4-methylbenzonitrile	1.58 ± 0.07	**72.2 ± 14.4**	81.4 ± 7.4	96.2
98	14191-95-8		2-(4-hydroxyphenyl)acetonitrile	0.27 ± 0.05	**101.5 ± 0.9**	92.9 ± 6.5	114.9
99	59-48-3		indolin-2-one	2.04 ± 0.07	37.3 ± 9.2	66.6 ± 18.7	228.9
100	58546-89-7		1-benzofuran-5-amine	0.78 ± 0.05	38 ± 6.4	80.2 ± 12.5	109.6
101	19335-11-6		1H-indazol-5-amine		38.2 ± 11.6	31.7 ± 16.2	70.6
102	183428-90-2		6-amino-2-methylnicotinonitrile	0.27 ± 0.06	68.4 ± 19.6	69.4 ± 12.4	76.1
103	16310-13-7		1,3-thiazolane-2-carboxylic acid	2.63 ± 0.08	77.9 ± 15.6	**103.3 ± 6.4**	107.3
104	2975-41-9		indan-2-amine	0.89 ± 0.05	28.9 ± 6.4	70 ± 18.5	122.9
107	36216-80-5		1,2-benzisoxazol-3-amine	0.95 ± 0.06	26.5 ± 5.8	76.9 ± 10.5	103.5
108	15871-85-9		6-methoxynicotinonitrile	0.38 ± 0.07	**108.3 ± 14.1**	95 ± 10.2	125

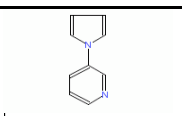
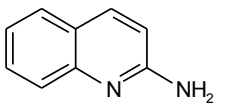
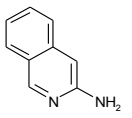
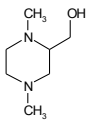
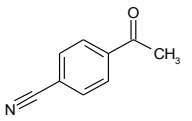
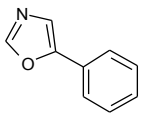
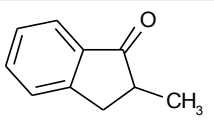
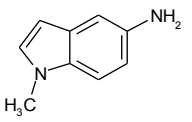
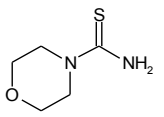
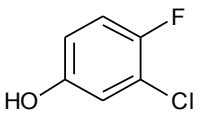
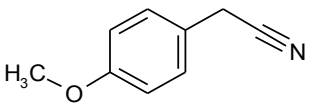
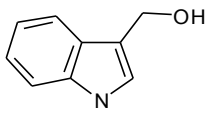
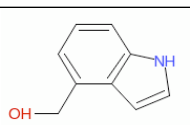
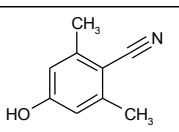
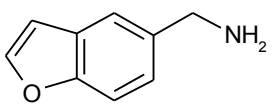
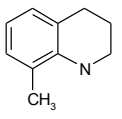
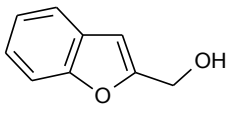
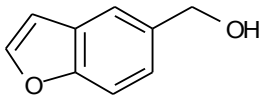
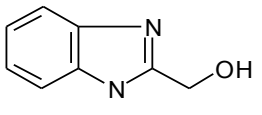
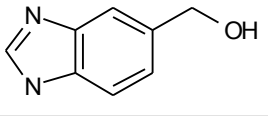
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

109	4241-27-4		6-methyl-2-oxo-1,2-dihydropyridine-3-carbonitrile	0.22 ± 0.06	**108.6 ± 5.1**	97.4 ± 2	118.7
110	493-05-0		3,4-dihydro-1H-benzo[c]pyran	0.34 ± 0.06	**109.8 ± 0.6**	88.7 ± 19.2	114.3
111	34413-35-9		5,6,7,8-tetrahydroquinoxaline	0.16 ± 0.06	**109.7 ± 17.6**	**95.6 ± 0.8**	96.1
112	21725-69-9		benzo[d]isoxazol-3-ol	0.23 ± 0.06	**100.2 ± 3**	83 ± 11.2	76.7
113	51586-20-0		2,3-dimethylbenzylamine	0.12 ± 0.07	**74.5 ± 13.2**	89.3 ± 15.9	83.6
114	20154-03-4		3-(trifluoromethyl)-1H-pyrazole	-0.07 ± 0.07	86.2 ± 19.7	85.9 ± 6.1	73.8
115	77326-36-4		2-amino-6-fluorobenzonitrile	0.17 ± 0.07	**90 ± 9.9**	**71.3 ± 0.6**	77.4
116	7145-99-5		5-methyl-1,3-benzodioxole	0.38 ± 0.06	**114.9 ± 5.4**	82.7 ± 15.6	109.4
117	23787-80-6		1-(3-methylpyrazin-2-yl)ethan-1-one	0.4 ± 0.06	**105.4 ± 17.6**	87.6 ± 11.3	88.3
118	20348-23-6		3,4-dihydro-2H-pyrido[3,2-b][1,4]oxazine	0.46 ± 0.06	**75.6 ± 3.7**	84.1 ± 18	92.3
119	6966-10-5		(3,4-dimethylphenyl)methanol	-0.28 ± 0.07	**102.7 ± 2.8**	84.7 ± 15.3	123.5
120	82380-18-5		2-fluoro-4-hydroxybenzonitrile	0.41 ± 0.06	39 ± 9.1	18.6 ± 10.7	72.6
121	14268-66-7		1,3-benzodioxol-5-amine	0.72 ± 0.07	42.4 ± 11.3	76.7 ± 16	109.9
122	1758-46-9		2-phenoxyethylamine	-0.03 ± 0.06	**64.6 ± 8.2**	73.6 ± 5.4	100.4
123	2227-79-4		benzene-1-carbothioamide	0.42 ± 0.06	107.2 ± 16.2	89 ± 10.9	87.9
124	533-31-3		1,3-benzodioxol-5-ol	2.1 ± 0.04	28.2 ± 7.1	39.7 ± 12.5	53.6
125	455-36-7		1-(3-fluorophenyl)ethan-1-one	-0.02 ± 0.07	**105.3 ± 17.2**	83 ± 14.8	101.3
126	19785-39-8		2-(4-methyl-1,3-thiazol-2-yl)acetonitrile	2.1 ± 0.09	**75.3 ± 15.4**	69.7 ± 10.3	98.4
128	352018-93-0		(1,3,5-trimethyl-1H-pyrazol-4-yl)methylamine	0.22 ± 0.06	**87 ± 9.9**	**80.3 ± 7**	87.7
129	445-29-4		2-fluorobenzoic acid	0.13 ± 0.07	**123.5 ± 7.6**	78.6 ± 14.2	126.3

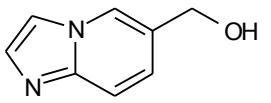
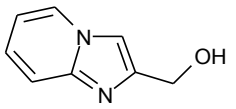
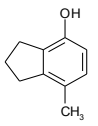
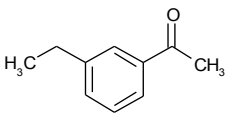
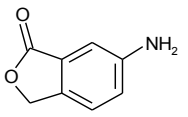
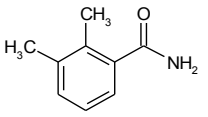
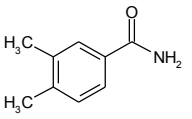
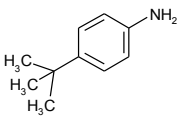
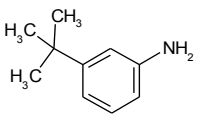
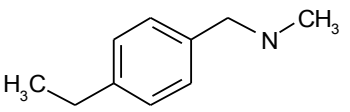
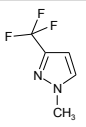
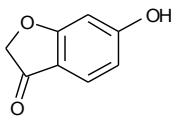
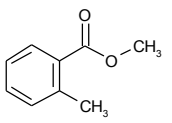
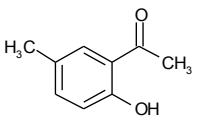
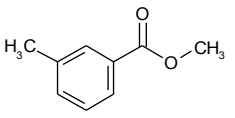
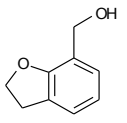
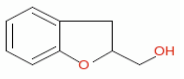
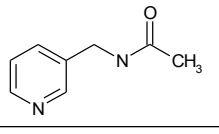
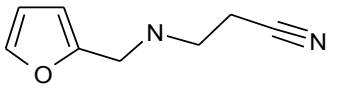
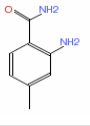
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

130	636-44-2		2,5-dimethyl-3-furoic acid	0.62 ± 0.08	**98.1 ± 6.8**	**84.7 ± 0.7**	120.6
131	935-13-7		3-(2-furyl)propanoic acid	1.22 ± 0.09	52.6 ± 15.5	**69.8 ± 21.4**	98.1
132	6141-58-8		methyl 2-methyl-3-furoate	1.64 ± 0.09	34.3 ± 8.4	71.3 ± 11.3	100.4
133	31968-33-9		1-(3-amino-2-thienyl)ethan-1-one	1.24 ± 0.07	**56.3 ± 21.4**	83 ± 12.2	100.4
134	83933-16-8		4-methylthiophene-2-carboxamide	0.61 ± 0.07	**73.7 ± 20.6**	83.1 ± 5.6	123.3
135	129486-91-5		2-methyl-1H-imidazole-4-carbothioamide	1.74 ± 0.09	115.5 ± 16.6	90.3 ± 10.9	101.5
136	89-97-4		2-chlorobenzylamine	0.02 ± 0.07	**113.2 ± 5.8**	53.3 ± 12.2	90.4
138	5380-42-7		methyl thiophene-2-carboxylate	0.31 ± 0.05	**110.9 ± 2.8**	**89.4 ± 9.3**	120.9
139	14282-78-1		4-methylthiophene-2-carboxylic acid	0.08 ± 0.07	**121.9 ± 1.1**	**70.9 ± 10.7**	120.9
140	77358-26-0		5-methylisoxazole-3-carbothioamide	0.2 ± 0.07	99.2 ± 19.8	89.2 ± 6.5	110.2
141	165115-15-1		2-(2-methyl-1,3-thiazol-4-yl)ethylamine	-0.02 ± 0.08	**82.8 ± 0.9**	98.9 ± 7.6	104.6
142	34155-39-0		2-methyl-1-(1-pyrrolidinyl)-2-propanamine	0.13 ± 0.07	**70.6 ± 6.5**	89.9 ± 8.9	96.3
143	17849-38-6		(2-chlorophenyl)methanol	0.46 ± 0.05	88.5 ± 19.7	93.3 ± 6.6	108.7
144	138564-16-6		N1-methyl-2,4-difluoroaniline	1.09 ± 0.06	**38.1 ± 11.4**	79.3 ± 10.3	109.6
145	20485-41-0		4-Methyl-thiazole-5-carboxylic acid	0.01 ± 0.07	**115.2 ± 9.7**	90.6 ± 16.1	114.5
146	35272-15-2		2-methyl-1,3-thiazole-4-carboxylic acid	0.1 ± 0.08	**102.5 ± 14.9**	87 ± 6.4	109
147	50382-32-6		(2,4-dimethyl-1,3-thiazol-5-yl)methanol	0.14 ± 0.08	98 ± 16.2	93.6 ± 4.3	118.5
148	24044-76-6		thiophene-3-carbothioamide	0.78 ± 0.08	74.6 ± 6.6	92.3 ± 7	99.6
149	670-95-1		4-phenyl-1H-imidazole	0.24 ± 0.06	**86.3 ± 13.6**	80.2 ± 11.7	99.1
150	2458-26-6		3-phenyl-1H-pyrazole	-0.45 ± 0.06	51.9 ± 12.6	74.6 ± 17.7	82

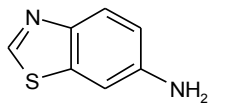
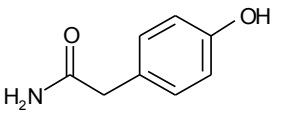
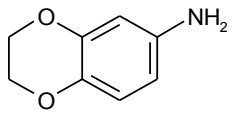
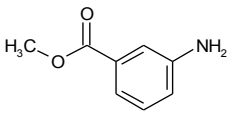
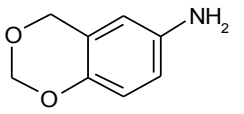
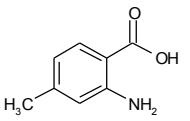
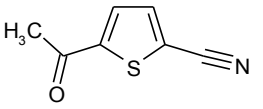
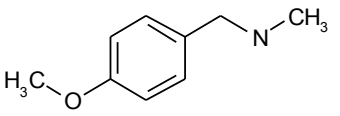
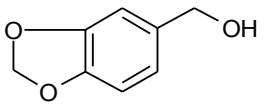
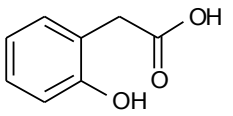
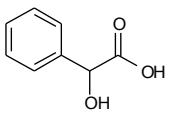
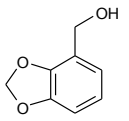
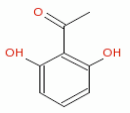
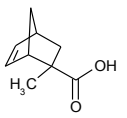
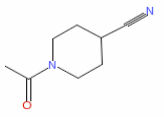
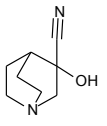
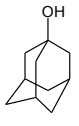
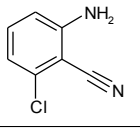
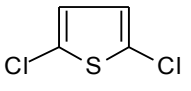
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

151	72692-99-0		3-(1H-pyrrol-1-yl)pyridine	0.43 ± 0.06	**56.6 ± 19.2**	90.3 ± 6	90.1
152	580-22-3		quinolin-2-amine	-0.43 ± 0.08	33.4 ± 6.7	38.2 ± 3	56.9
153	25475-67-6		isoquinolin-3-amine	0.27 ± 0.06	**44.8 ± 5**	**88.5 ± 16.5**	117.6
154	14675-44-6		(1,4-dimethyl-2-piperazinyl)methanol	-0.04 ± 0.07	89.2 ± 16.1	96.9 ± 6.4	117.2
155	1443-80-7		4-acetylbenzonitrile	0.19 ± 0.06	**99.3 ± 17.3**	87.3 ± 16.6	130.8
156	1006-68-4		5-phenyl-1,3-oxazole	0.95 ± 0.06	35.1 ± 3.8	**77.5 ± 18.3**	104.2
157	17496-14-9		2-methylindan-1-one	0.14 ± 0.07	**108.6 ± 10.3**	94.7 ± 3.5	125.5
158	102308-97-4		1-methyl-1H-indol-5-amine	-0.82 ± 0.1	42.7 ± 9.7	12.5 ± 9.1	59.3
159	14294-10-1		morpholine-4-carbothioamide	0.21 ± 0.05	113.3 ± 16.8	93.8 ± 9.3	108.6
160	2613-23-2		3-chloro-4-fluorophenol	0.02 ± 0.05	50.8 ± 16.5	94.9 ± 15.3	77.4
161	104-47-2		2-(4-methoxyphenyl)acetonitrile	-0.04 ± 0.08	100.9 ± 1.7	107.7 ± 3.1	88.7
162	700-06-1		1H-indol-3-ylmethanol	2.31 ± 0.06	32.5 ± 5.9	16.3 ± 10.6	41.6
163	1074-85-7		1H-indol-4-ylmethanol	1.9 ± 0.06	**34.8 ± 0.8**	**103.3 ± 8.7**	47
164	58537-99-8		4-hydroxy-2,6-dimethylbenzonitrile	0.26 ± 0.08	84.7 ± 2.4	55.8 ± 12.1	90
165	37798-08-6		1-benzofuran-5-ylmethylamine	-0.26 ± 0.07	**81.5 ± 6.3**	**92.6 ± 8.6**	90.7
166	52601-70-4		8-methyl-1,2,3,4-tetrahydroquinoline	0.06 ± 0.07	**55.8 ± 21.7**	**95.5 ± 1.6**	76
167	55038-01-2		1-benzofuran-2-ylmethanol	-0.24 ± 0.09	**89.8 ± 4.7**	**84.9 ± 19.3**	78.2
168	31823-05-9		1-benzofuran-5-ylmethanol	0.39 ± 0.08	34.7 ± 8	**119.6 ± 11.4**	75.1
169	4856-97-7		1H-benzimidazol-2-ylmethanol	0.04 ± 0.07	86.5 ± 2.7	**121.3 ± 15**	81.7
170	106429-29-2		1H-benzimidazol-5-ylmethanol	0.15 ± 0.07	98.8 ± 1.6	**98.3 ± 4.2**	92

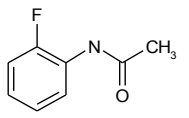
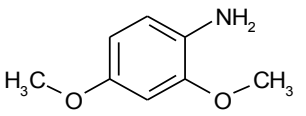
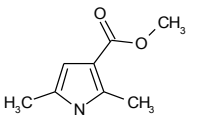
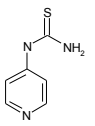
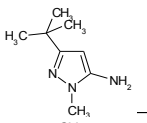
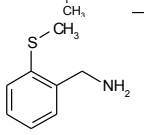
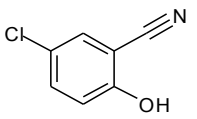
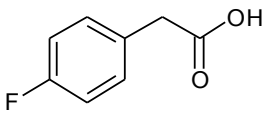
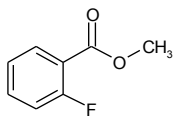
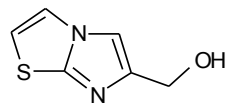
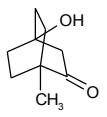
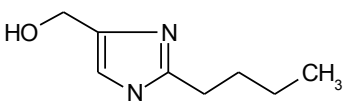
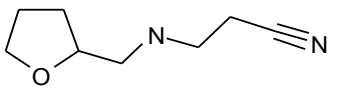
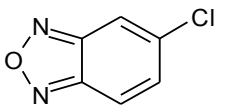
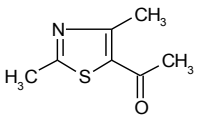
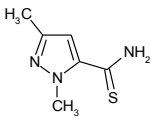
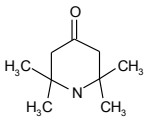
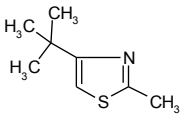
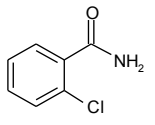
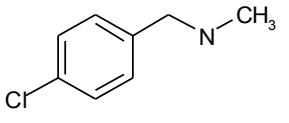
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

171	132213-07-1		imidazo[1,2-a]pyridin-6-ylmethanol	0.84 ± 0.09	**81.7 ± 2.5**	94.1 ± 15.6	99.4
172	82090-52-6		imidazo[1,2-a]pyridin-2-ylmethanol	0.44 ± 0.08	47.6 ± 14.2	**86.6 ± 15.1**	97.5
173	16400-13-8		7-methylindan-4-ol	-0.53 ± 0.05	29.6 ± 6	**43.2 ± 15.6**	53.7
174	22699-70-3		1-(3-ethylphenyl)ethan-1-one	0.8 ± 0.05	106.9 ± 13.3	100.3 ± 7.3	79.2
175	57319-65-0		6-amino-1,3-dihydroisobenzofuran-1-one	0.04 ± 0.08	91.7 ± 12.2	105.9 ± 17	79.5
176	5580-34-7		2,3-dimethylbenzamide	0.06 ± 0.07	106.6 ± 12.1	**88.2 ± 12.4**	68.7
177	5580-33-6		3,4-dimethylbenzamide	-0.28 ± 0.08	29.9 ± 7.7	81.7 ± 16.8	64.2
178	769-92-6		4-(tert-butyl)aniline	-0.21 ± 0.06	**101.1 ± 6**	**108.9 ± 18.8**	87.6
179	5369-19-7		3-(tert-butyl)aniline	-0.37 ± 0.06	**92.3 ± 14.3**	99.3 ± 14.7	77.9
180	568577-84-4		N-(4-ethylbenzyl)-N-methylamine	0.14 ± 0.08	101.8 ± 4.4	**99.8 ± 1.1**	87
181	154471-65-5		1-methyl-3-(trifluoromethyl)-1H-pyrazole	0.11 ± 0.08	105.2 ± 8	114.9 ± 9.9	58.4
182	6272-26-0		6-hydroxy-2,3-dihydrobenzo[b]furan-3-one	0.92 ± 0.09	56.2 ± 7.7	**119.6 ± 2.4**	65.6
183	89-71-4		methyl 2-methylbenzoate	0.14 ± 0.08	99 ± 14.4	**114.2 ± 4.3**	51
184	1450-72-2		1-(2-hydroxy-5-methylphenyl)ethan-1-one	0.14 ± 0	**96.1 ± 4.8**	91.7 ± 11.6	53.1
185	99-36-5		methyl 3-methylbenzoate	0.14 ± 0.09	110.5 ± 12.7	105.5 ± 10.4	61.3
186	151155-53-2		2,3-Dihydrobenzo[b]furan-7-methanol	4.09 ± 0.09	33.8 ± 5.2	**86.5 ± 14.8**	41.8
187	66158-96-1		2,3-dihydro-1-benzofuran-2-ylmethanol	-0.04 ± 0.08	**66.8 ± 21.8**	94.3 ± 13.3	50.5
188	22977-34-0		N1-(3-pyridylmethyl)acetamide	0.05 ± 0.07	88.2 ± 7	104.2 ± 7.3	69.5
189	6788-68-7		3-[(2-furylmethyl)amino]propanenitrile	0.75 ± 0.08	**81.5 ± 19.2**	92.5 ± 7.2	84.4
190	39549-79-6		2-amino-4-methylbenzamide	1.52 ± 0.06	41.9 ± 11	**46.7 ± 23.7**	106.3

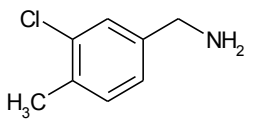
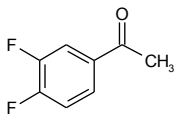
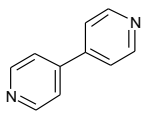
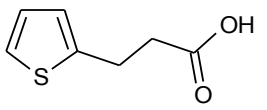
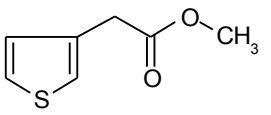
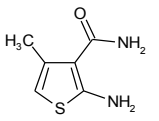
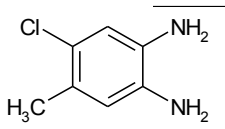
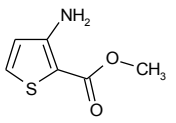
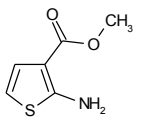
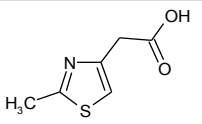
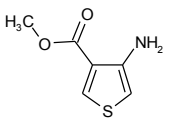
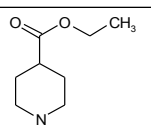
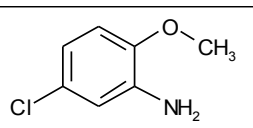
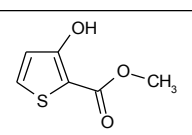
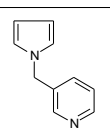
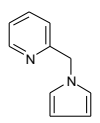
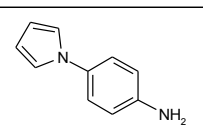
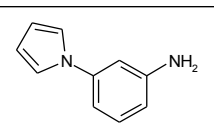
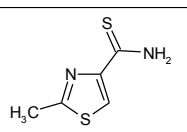
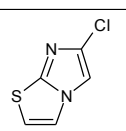
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

191	533-30-2		1,3-benzothiazol-6-amine	0.44 ± 0.11	47.7 ± 13.8	76.3 ± 15.1	38
192	17194-82-0		2-(4-hydroxyphenyl)acetamide	-0.02 ± 0.08	**107.7 ± 16.5**	96.9 ± 9.5	44.6
193	22013-33-8		2,3-dihydro-1,4-benzodioxin-6-amine	0.4 ± 0.09	29.5 ± 5.5	**79.9 ± 13.6**	44.7
194	4518-10-9		methyl 3-aminobenzoate	0.78 ± 0.06	89.8 ± 7	88.3 ± 9.2	38.9
195	22791-64-6		4,5-dihydro-1,3-benzodioxine-6-amine	1.16 ± 0.06	41.8 ± 8.8	**77.4 ± 10.5**	54.1
196	2305-36-4		2-amino-4-methylbenzoic acid	1.1 ± 0.06	87.4 ± 19.7	**97.4 ± 4.1**	36.7
198	88653-55-8		5-acetylthiophene-2-carbonitrile	0.24 ± 0.07	79.6 ± 18.5	93.3 ± 15.3	61.2
199	702-24-9		N-(4-methoxybenzyl)-N-methylamine	-0.11 ± 0.08	92.2 ± 16.8	95.1 ± 15.3	71
200	495-76-1		1,3-benzodioxol-5-ylmethanol	-0.07 ± 0.08	**84.2 ± 5.9**	85.2 ± 9.3	92.1
201	614-75-5		2-(2-hydroxyphenyl)acetic acid	0.65 ± 0.08	87.4 ± 8.7	94.1 ± 15.7	94.2
202	90-64-2		2-hydroxy-2-phenylacetic acid	0 ± 0.08	107.2 ± 16	96.7 ± 12.5	55.6
203	769-30-2		1,3-benzodioxol-4-ylmethanol	0.06 ± 0.08	74.8 ± 13.4	94.6 ± 14.1	60.8
204	699-83-2		1-(2,6-dihydroxyphenyl)ethan-1-one	2.35 ± 0.06	45.2 ± 9.7	36.3 ± 12.5	34.4
205	825-03-6		2-methylbicyclo[2.2.1]hept-5-ene-2-carboxylic acid	0.08 ± 0.08	**91.3 ± 1.8**	92.1 ± 17.2	53.8
206	16473-11-3		bicyclo[3.3.1]nonane-2,6-dione	-0.11 ± 0.08	93.2 ± 7.8	80.8 ± 7.6	42.1
207	25503-91-7		1-acetylpiperidine-4-carbonitrile	0.03 ± 0.07	96.5 ± 13.9	90 ± 2.9	65.3
208	6238-30-8		3-hydroxyquinuclidine-3-carbonitrile	-0.09 ± 0.07	101.6 ± 18	99.4 ± 11.2	61.8
209	768-95-6		adamantan-1-ol	-0.12 ± 0.07	101.4 ± 11.5	92.2 ± 6.7	76.1
210	6575-11-7		2-amino-6-chlorobenzonitrile	0.15 ± 0.08	93.5 ± 7.9	91.5 ± 10.8	89.2
211	3172-52-9		2,5-dichlorothiophene	0.02 ± 0.08	101.5 ± 10.9	99.6 ± 4.1	117.2

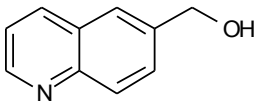
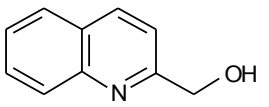
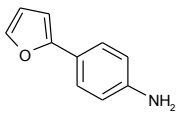
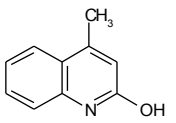
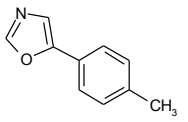
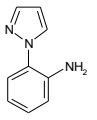
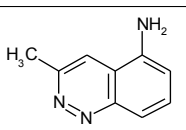
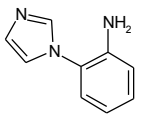
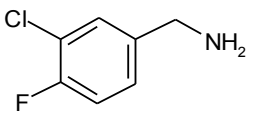
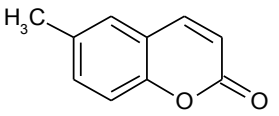
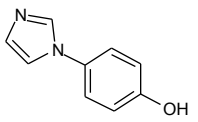
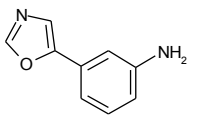
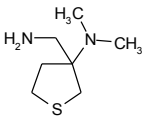
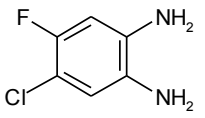
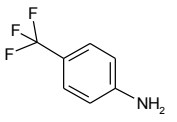
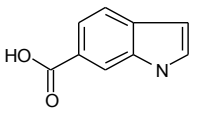
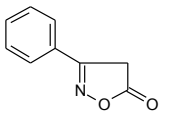
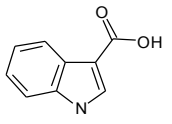
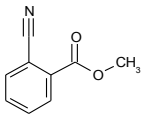
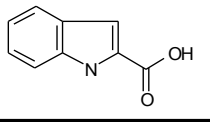
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

212	399-31-5		N1-(2-fluorophenyl)acetamide	-0.16 ± 0.08	97.3 ± 9.6	80.6 ± 6.6	65.4
213	2735-04-8		2,4-dimethoxyaniline		23.7 ± 5.8	14 ± 8.2	61.2
214	69687-80-5		methyl 2,5-dimethyl-1H-pyrrole-3-carboxylate	0.78 ± 0.06	35.1 ± 4.4	**74.8 ± 18**	64.4
215	164670-44-4		N-(4-pyridyl)thiourea	0.03 ± 0.08	118.6 ± 17	98.3 ± 16.5	59.6
216	118430-73-2		3-(tert-butyl)-1-methyl-1H-pyrazol-5-amine	0.15 ± 0.07	**97.5 ± 10.1**	80.1 ± 11.3	56.7
217	56004-83-2		2-(methylthio)benzylamine	-0.07 ± 0.07	**81.9 ± 10.4**	**27.1 ± 0.5**	70.3
218	13589-72-5		5-chloro-2-hydroxybenzonitrile	0.43 ± 0.07	**92.7 ± 13.6**	92 ± 11.8	67.7
219	405-50-5		2-(4-fluorophenyl)acetic acid	-1.9 ± 0.61	101.2 ± 18	94.3 ± 13.4	98.4
220	394-35-4		methyl 2-fluorobenzoate	-0.03 ± 0.1	108.4 ± 10.5	107.6 ± 17.6	99.5
221	349480-74-6		imidazo[2,1-b]thiazol-6-ylmethanol	0.09 ± 0.23	97.7 ± 7	106.6 ± 7.6	99.5
222	5122-77-0		4-hydroxy-1-methylbicyclo[2.2.2]octan-2-one	-0.11 ± 0.09	106.5 ± 8.6	101.8 ± 5.9	82.3
223	68283-19-2		(2-butyl-1H-imidazol-4-yl)methanol	-0.17 ± 0.14	100.4 ± 6.7	105.2 ± 13.7	139.3
224	90322-18-2		3-[(tetrahydrofuran-2-ylmethyl)amino]propanenitrile	0.21 ± 0.09	103.3 ± 15.4	96.5 ± 13.7	60
225	19155-86-3		5-chloro-2,1,3-benzoxadiazole	0.81 ± 0.19	95 ± 12.2	91.4 ± 15.1	68.9
226	38205-60-6		1-(2,4-dimethyl-1,3-thiazol-5-yl)ethan-1-one	0.37 ± 0.1	96.5 ± 10.9	85.8 ± 10.4	62
227	844891-03-8		1,3-dimethyl-1H-pyrazole-5-carbothioamide	0.57 ± 0.1	98.4 ± 13.7	106.7 ± 5.8	50.9
228	826-36-8		2,2,6,6-tetramethyltetrahydro-4(1H)-pyridinone	-0.07 ± 0.09	98.9 ± 16.8	101.3 ± 5.4	61.9
229	15679-11-5		4-(tert-butyl)-2-methyl-1,3-thiazole	0.23 ± 0.07	94.4 ± 6.3	107.5 ± 11.8	65.6
230	609-66-5		2-chlorobenzamide	-0.22 ± 0.07	96.7 ± 8.2	104.2 ± 8.8	92.9
231	104-11-0		N-(4-chlorobenzyl)-N-methylamine	-0.06 ± 0.07	86.3 ± 3.2	113.3 ± 3.7	106.6

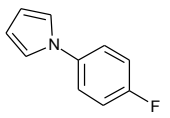
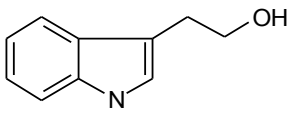
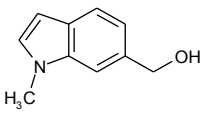
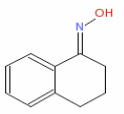
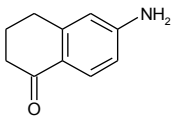
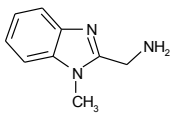
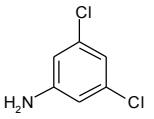
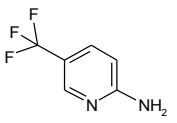
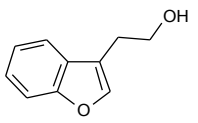
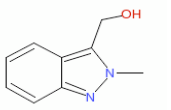
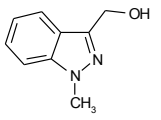
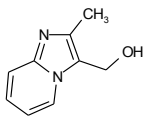
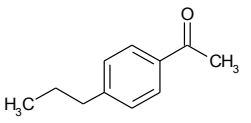
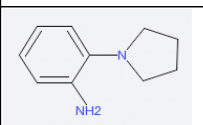
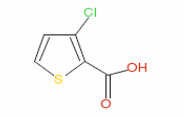
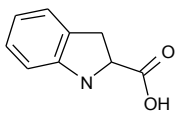
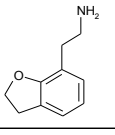
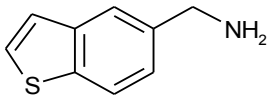
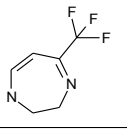
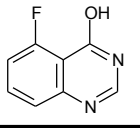
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

233	67952-93-6		3-chloro-4-methylbenzylamine	0.11 ± 0.08	27.7 ± 4.2	**91.7 ± 12.6**	163.3
234	369-33-5		1-(3,4-difluorophenyl)ethan-1-one	0.14 ± 0.08	98.7 ± 6.5	**90.3 ± 14**	73.9
235	553-26-4		4,4'-dipyridyl	0.2 ± 0.07	95 ± 4.3	63.7 ± 17.4	54.8
237	5928-51-8		3-(2-thienyl)propanoic acid	0.22 ± 0.07	**85.3 ± 11.8**	113 ± 7.8	70.9
238	58414-52-1		methyl 2-(3-thienyl)acetate	0.39 ± 0.07	**103.4 ± 4**	**111.2 ± 9.9**	64.7
239	4651-97-2		2-amino-4-methylthiophene-3-carboxamide	2.05 ± 0.05	22.9 ± 7	**95.8 ± 9.3**	69.8
240	63155-04-4		4-chloro-5-methylbenzene-1,2-diamine		28.9 ± 7.8	12.1 ± 8.7	14.7
241	22288-78-4		methyl 3-aminothiophene-2-carboxylate	0.38 ± 0.09	**81.2 ± 4.1**	94.5 ± 13	107.8
242	4651-81-4		methyl 2-aminothiophene-3-carboxylate	0.34 ± 0.08	**74 ± 4.7**	**37 ± 6.1**	80.5
243	13797-62-1		2-(2-methyl-1,3-thiazol-4-yl)acetic acid	-0.23 ± 0.07	97.4 ± 8.3	**99.5 ± 1.1**	113.1
244	69363-85-5		methyl 4-aminothiophene-3-carboxylate	0.61 ± 0.11	39.5 ± 14.5	**78.7 ± 17.9**	90.3
245	1126-09-6		ethyl piperidine-4-carboxylate	-0.04 ± 0.08	93.2 ± 7.2	**97.8 ± 3.2**	99
246	95-03-4		5-chloro-2-methoxyaniline	-0.25 ± 0.06	85.4 ± 17.2	112.6 ± 16.7	113
247	5118-06-9		methyl 3-hydroxythiophene-2-carboxylate	0.2 ± 0.07	88.6 ± 3.7	95.4 ± 6.1	108.7
248	80866-95-1		3-(1H-pyrrol-1-ylmethyl)pyridine	0 ± 0.08	72.1 ± 13.2	91.3 ± 11.9	86.6
249	78210-51-2		2-(1H-pyrrol-1-ylmethyl)pyridine	-0.36 ± 0.08	**79.2 ± 9.3**	93.1 ± 19.9	83.6
250	52768-17-9		4-(1H-pyrrol-1-yl)aniline	-0.4 ± 0.08	32.4 ± 12.8	107.2 ± 16.6	89.1
251	89353-42-4		3-(1H-pyrrol-1-yl)aniline	0.15 ± 0.05	29.2 ± 8.7	**80.5 ± 3.4**	79.8
252	174223-29-1		2-methyl-1,3-thiazole-4-carbothioamide	0.7 ± 0.07	92.9 ± 6.6	90.3 ± 10.7	101.7
253	23576-81-0		6-chloroimidazo[2,1-b][1,3]thiazole	-0.15 ± 0.08	52.8 ± 5.5	**82.1 ± 0**	85.1

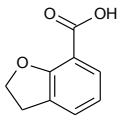
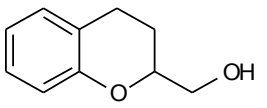
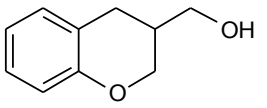
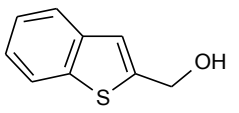
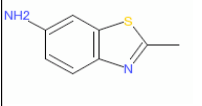
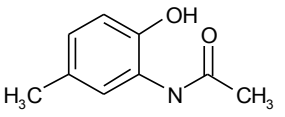
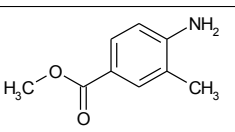
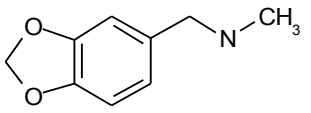
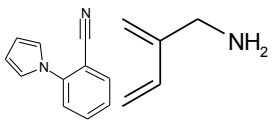
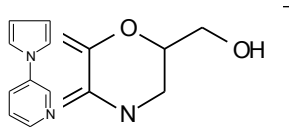
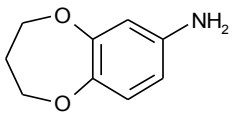
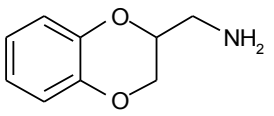
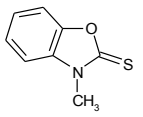
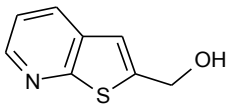
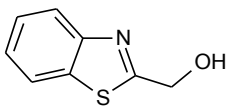
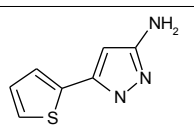
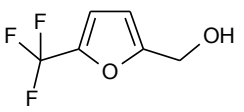
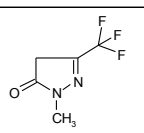
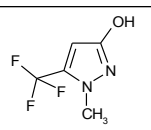
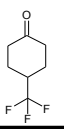
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

255	100516-88-9		6-quinolinylmethanol	-0.09 ± 0.08	48.1 ± 12	**89.6 ± 6.8**	84
256	1780-17-2		2-quinolinylmethanol	2.2 ± 0.06	21.7 ± 6	99.2 ± 19.5	119.1
257	59147-02-3		4-(2-furyl)aniline	0.83 ± 0.04	29.3 ± 8.5	**17 ± 12.7**	75.7
258	607-66-9		4-methyl-2-quinolinol	0.17 ± 0.06	92.9 ± 6.8	92.7 ± 13.6	90.7
259	143659-19-2		5-(4-methylphenyl)-1,3-oxazole	-0.39 ± 0.08	**90.2 ± 12.5**	88.4 ± 2.5	88.1
260	54705-91-8		2-(1H-pyrazol-1-yl)aniline	-0.06 ± 0.07	**80.8 ± 0.7**	98.1 ± 5.6	97.3
261	300690-74-8		3-methylcinnolin-5-amine	1.83 ± 0.11	21.7 ± 8.5	**62.5 ± 14.7**	74.1
262	26286-54-4		2-(1H-imidazol-1-yl)aniline	0.62 ± 0.08	72.4 ± 20	66.5 ± 16.1	76
264	72235-56-4		3-chloro-4-fluorobenzylamine	-0.34 ± 0.07	29 ± 5.5	**47.5 ± 13.5**	88.4
265	92-48-8		6-methyl-2H-chromen-2-one	-0.11 ± 0.07	91.1 ± 18.7	95.8 ± 17.2	63.8
266	10041-02-8		4-(1H-imidazol-1-yl)phenol	-0.1 ± 0.06	**81.3 ± 12.5**	83 ± 19.8	107.9
267	157837-31-5		3-(1,3-oxazol-5-yl)aniline	0.13 ± 0.09	**71.1 ± 9.8**	75 ± 15.2	79.8
268	176445-79-7		3-(aminomethyl)-N,N-dimethyltetrahydro-3-thiophenamine	0.32 ± 0.07	57.8 ± 19.5	88.4 ± 17.9	87.3
269	139512-70-2		4-chloro-5-fluorobenzene-1,2-diamine	-0.92 ± 0.08	25.1 ± 10.1	23.4 ± 14.8	50.4
270	455-14-1		4-(trifluoromethyl)aniline	-4.73 ± 0.19	25.8 ± 6.6	21.8 ± 14.5	103.6
271	1670-82-2		1H-indole-6-carboxylic acid	0.06 ± 0.08	**90.5 ± 2.4**	**110.8 ± 16.2**	75.6
272	1076-59-1		3-phenyl-4,5-dihydroisoxazol-5-one	3.56 ± 0.06	**60.1 ± 21**	**89.4 ± 3.9**	61.5
273	771-50-6		1H-indole-3-carboxylic acid	0.01 ± 0.05	88.6 ± 8.8	**85.4 ± 12.2**	61.8
274	6587-24-2		methyl 2-cyanobenzoate	-0.45 ± 0.07	91.2 ± 14.9	91 ± 19.6	64
275	1477-50-5		1H-indole-2-carboxylic acid	-0.26 ± 0.08	83 ± 15.6	89.7 ± 16.4	67.3

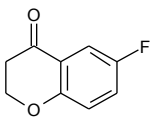
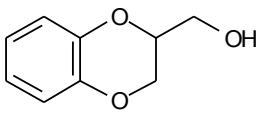
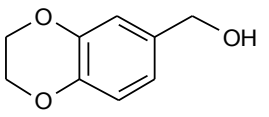
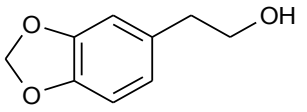
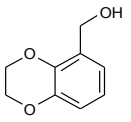
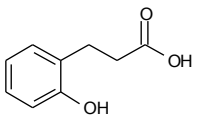
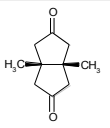
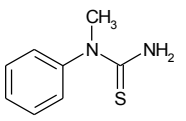
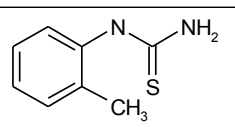
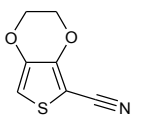
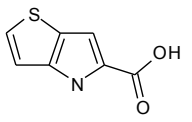
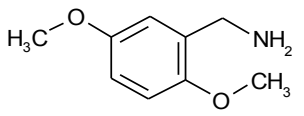
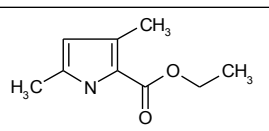
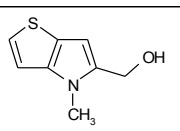
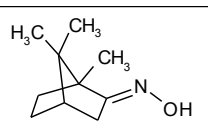
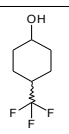
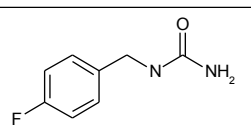
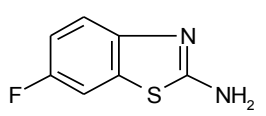
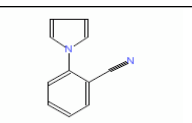
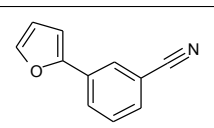
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

276	81329-31-9		1-(4-fluorophenyl)-1H-pyrrole	0.75 ± 0.08	**45.2 ± 16**	**103.9 ± 16.6**	70.2
277	526-55-6		2-(1H-indol-3-yl)ethan-1-ol	1.12 ± 0.06	31.4 ± 8.9	**66.3 ± 1.7**	59.9
278	199590-00-6		(1-methyl-1H-indol-6-yl)methanol	#VALUE!	28.8 ± 10.8	18.2 ± 10.4	47.8
279	3349-64-2		1,2,3,4-tetrahydronaphthalen-1-one oxime	0.76 ± 0.08	18.8 ± 5.8	19.9 ± 19.7	16.9
280	3470-53-9		6-amino-1,2,3,4-tetrahydronaphthalen-1-one	0.82 ± 0.09	**42.8 ± 6.8**	40.5 ± 19.2	87.3
281	20028-40-4		(1-methyl-1H-benzimidazol-2-yl)methylamine	0.7 ± 0.04	27.3 ± 7.7	47.6 ± 19.8	53.8
282	626-43-7		3,5-dichloroaniline	-0.76 ± 0.06	**78.4 ± 11.9**	86.4 ± 8.5	66.5
283	74784-70-6		5-(trifluoromethyl)pyridin-2-amine	-0.64 ± 0.08	99.7 ± 14.7	92.7 ± 5.3	63.6
284	75611-06-2		2-benzo[b]furan-3-ylethanol	-0.19 ± 0.07	68.3 ± 14.3	58.7 ± 17.4	63.3
285	58536-48-4		(2-methyl-2H-indazol-3-yl)methanol	0.29 ± 0.07	70.7 ± 13.2	73.4 ± 10.6	67.6
286	1578-96-7		(1-methyl-1H-indazol-3-yl)methanol	-0.31 ± 0.07	**65.3 ± 18**	**90.9 ± 3.1**	73.2
287	30489-44-2		(2-methylimidazo[1,2-a]pyridin-3-yl)methanol	-0.44 ± 0.08	84.7 ± 18.1	76.2 ± 14	79.7
288	2932-65-2		1-(4-propylphenyl)ethan-1-one	0.22 ± 0.08	**33.5 ± 0.5**	72.2 ± 17.1	90.6
289	21627-58-7		2-pyrrolidin-1-ylaniline		20.1 ± 5.4	11.4 ± 9.5	23.8
290	59337-89-2		3-chlorothiophene-2-carboxylic acid	-0.21 ± 0.08	**93.3 ± 13.4**	86.9 ± 14.3	117.3
292	78348-24-0		indoline-2-carboxylic acid	1.54 ± 0.11	32.9 ± 9.3	37.6 ± 25	78.3
293	850375-00-7		2,3-Dihydrobenzo[b]furan-7-ethylamine	-3.7 ± 0.06	31.2 ± 11.9	**10.8 ± 0.1**	19.8
294	56540-52-4		1-benzothiophen-5-ylmethylamine	-0.66 ± 0.07	49.4 ± 20	**98.5 ± 13.1**	70.6
295	177545-13-0		5-(trifluoromethyl)-2,3-dihydro-1H-1,4-diazepine	-0.26 ± 0.07	**94.6 ± 14.4**	75.2 ± 18.7	72.1
296	436-72-6		5-fluoroquinazolin-4-ol	-0.28 ± 0.08	80.2 ± 9.5	**92.7 ± 1.9**	63.7

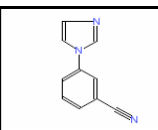
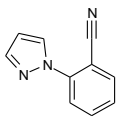
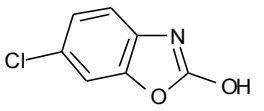
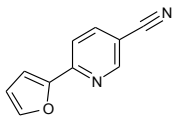
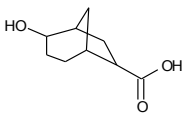
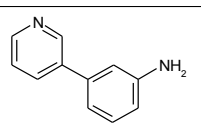
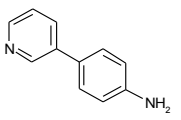
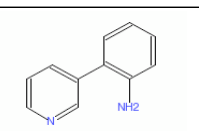
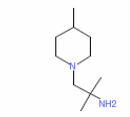
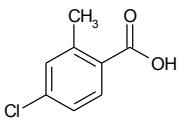
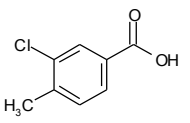
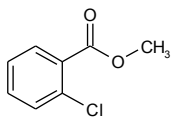
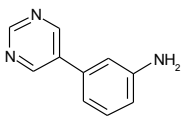
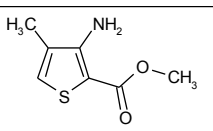
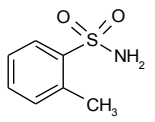
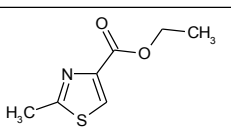
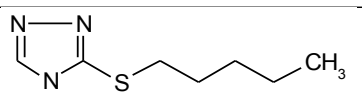
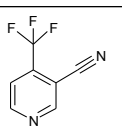
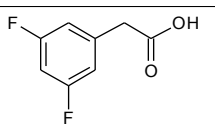
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

297	35700-40-4		2,3-dihydrobenzo[b]furan-7-carboxylic acid	-0.25 ± 0.08	**101.8 ± 16**	78.8 ± 7.5	74.9
299	83278-86-8		3,4-dihydro-2H-chromen-2-ylmethanol	-0.6 ± 0.08	66.4 ± 16.2	85.1 ± 14.7	80.3
300	76727-28-1		3,4-dihydro-2H-chromen-3-ylmethanol	-0.43 ± 0.08	73.2 ± 12.1	90 ± 16.3	112.9
301	17890-56-1		1-benzothiophen-2-ylmethanol	0.01 ± 0.05	68.5 ± 7.6	90.7 ± 4.5	71
302	2941-62-0		2-methyl-1,3-benzothiazol-6-ylamine	-0.01 ± 0.08	58 ± 4.6	71.9 ± 12.4	62.3
303	6375-17-3		N1-(2-hydroxy-5-methylphenyl)acetamide	0.15 ± 0.07	**82.9 ± 18.1**	95.3 ± 9.8	45
304	18595-14-7		methyl 4-amino-3-methylbenzoate	-0.44 ± 0.08	87 ± 11.8	100.5 ± 8.9	63.4
305	15205-27-3		N-(1,3-benzodioxol-5-ylmethyl)-N-methylamine	1.12 ± 0.05	49.3 ± 11.2	56.8 ± 29.4	58.3
306	17413-10-4		2,3-dihydro-1,4-benzodioxin-6-ylmethylamine	-0.14 ± 0.06	29.2 ± 8	**109.2 ± 5.6**	72.7
307	82756-74-9		3,4-dihydro-2H-1,4-benzoxazin-2-ylmethanol	0.56 ± 0.06	**76.9 ± 15.1**	81 ± 17.2	70.8
308	175136-34-2		3,4-dihydro-2H-1,5-benzodioxepin-7-amine	-0.38 ± 0.08	**110.4 ± 16.6**	**98.7 ± 6.1**	82.8
309	4442-59-5		2,3-dihydro-1,4-benzodioxin-2-ylmethylamine	-0.06 ± 0.07	24.7 ± 6.9	12.3 ± 8.8	68.9
310	13673-63-7		3-methyl-1,3-benzoxazole-2(3H)-thione	-0.38 ± 0.07	91.4 ± 3.7	102.6 ± 14.3	104.3
311	131337-81-0		thieno[2,3-b]pyridin-2-ylmethanol	0.8 ± 0.08	70.8 ± 9	92 ± 11.8	77.5
312	37859-42-0		1,3-benzothiazol-2-ylmethanol	-0.44 ± 0.09	73.2 ± 12.2	80.7 ± 16.2	64.4
313	96799-03-0		5-thien-2-yl-1H-pyrazol-3-amine	0.69 ± 0.08	52.4 ± 7	100.8 ± 18.9	81.7
314	65865-28-3		[5-(trifluoromethyl)-2-furyl]methanol	-0.28 ± 0.08	99.1 ± 0.6	113.8 ± 8.2	76.9
315	1481-02-3		1-methyl-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-5-one	0.09 ± 0.08	103.3 ± 15.9	**109.2 ± 4.4**	88.3
316	119022-51-4		1-methyl-5-(trifluoromethyl)-1H-pyrazol-3-ol	-0.59 ± 0.08	91.7 ± 8.2	111.8 ± 17.2	95.3
317	75091-99-5		4-(trifluoromethyl)cyclohexan-1-one	-0.33 ± 0.08	106 ± 12.4	110.7 ± 7.2	90.5

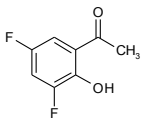
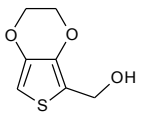
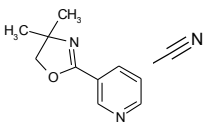
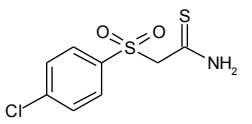
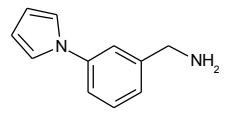
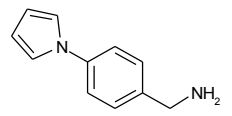
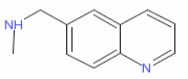
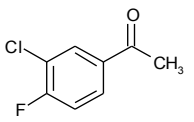
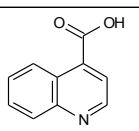
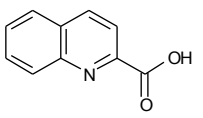
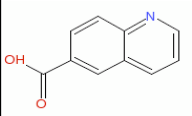
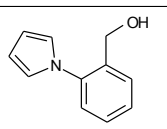
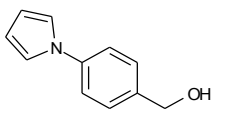
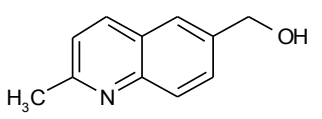
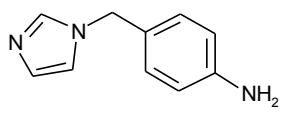
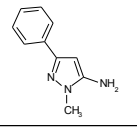
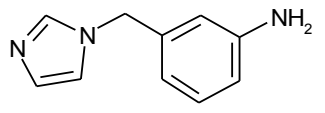
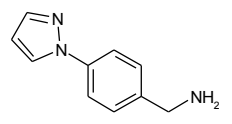
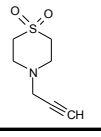
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

318	66892-34-0		6-fluorochroman-4-one	-0.19 ± 0.07	88.6 ± 12.2	104.4 ± 16.4	99
319	3663-82-9		2,3-dihydro-1,4-benzodioxin-2-ylmethanol	-0.54 ± 0.08	77.2 ± 5.4	102.6 ± 5.1	86.4
320	39270-39-8		2,3-dihydro-1,4-benzodioxin-6-ylmethanol	-0.73 ± 0.08	83.1 ± 11.5	111.9 ± 16.4	78.8
321	6006-82-2		2-(1,3-benzodioxol-5-yl)ethanol	-0.17 ± 0.08	35.2 ± 14.9	**109.4 ± 5.9**	138.3
322	274910-19-9		2,3-dihydro-1,4-benzodioxin-5-ylmethanol	-0.16 ± 0.07	90.8 ± 4.4	100.4 ± 14.9	96.4
323	495-78-3		3-(2-hydroxyphenyl)propanoic acid	1.23 ± 0.07	111.4 ± 8.6	113.1 ± 2.8	109.5
324	21170-10-5		3a,6a-dimethylperhydropentalene-2,5-dione	-0.05 ± 0.06	88.2 ± 0.7	103.2 ± 21.9	94.2
325	4104-75-0		N-methyl-N-phenylthiourea	-0.82 ± 0.06	24 ± 5.4	33.9 ± 11.6	82.7
326	614-78-8		N-(2-methylphenyl)thiourea	-0.03 ± 0.07	**90.2 ± 6.3**	111.4 ± 8.5	124.7
327	859851-02-8		2,3-dihydrothieno[3,4-b][1,4]dioxine-5-carbonitrile	0.12 ± 0.06	89.7 ± 4.3	115.5 ± 14.4	121.1
328	39793-31-2		4H-thieno[3,2-b]pyrrole-5-carboxylic acid	2.29 ± 0.1	**51.6 ± 13.3**	105.9 ± 6.9	136.2
329	3275-95-4		2,5-dimethoxybenzylamine	0.97 ± 0.05	24.1 ± 3.4	**26 ± 9**	155.7
330	2199-44-2		ethyl 3,5-dimethyl-1H-pyrrole-2-carboxylate	0.61 ± 0.06	90.7 ± 1.7	122.4 ± 12.3	155.7
331	121933-59-3		(4-methyl-4H-thieno[3,2-b]pyrrol-5-yl)methanol	1.54 ± 0.07	31 ± 7.1	**93.6 ± 14.9**	120.9
332	13559-66-5		1,7,7-trimethylbicyclo[2.2.1]heptan-2-one oxime	-0.76 ± 0.07	106.5 ± 18.9	110.6 ± 8.3	93.9
333	30129-18-1		4-(trifluoromethyl)cyclohexan-1-ol	0.47 ± 0.04	99.1 ± 5.6	109.7 ± 4.4	113.6
334	76523-24-5		N-(4-fluorobenzyl)urea	-0.33 ± 0.07	92.1 ± 14	**112.4 ± 4.7**	91.8
335	348-40-3		6-fluoro-1,3-benzothiazol-2-amine	-4.93 ± 2.59	37.7 ± 12	70.6 ± 6.1	113.2
336	33265-71-3		2-(1H-pyrrol-1-yl)benzonitrile		33.1 ± 13	68.5 ± 16.3	134.2
338	112598-77-3		3-(2-furyl)benzonitrile		35.6 ± 7.3	18.5 ± 15.2	57.8

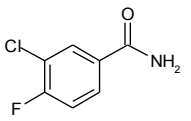
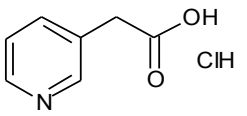
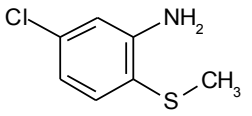
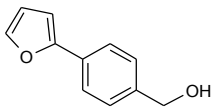
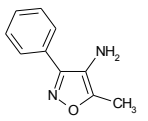
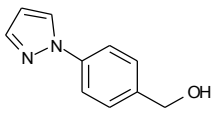
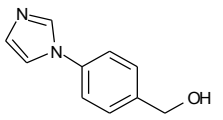
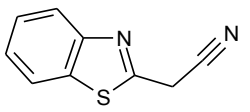
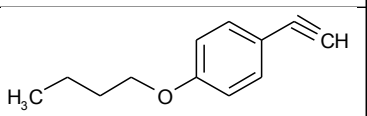
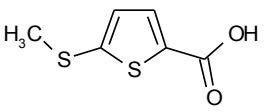
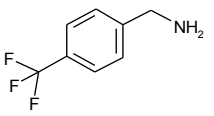
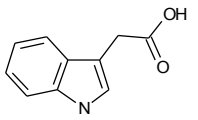
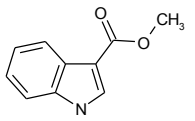
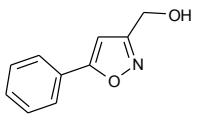
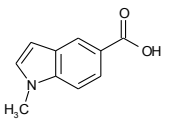
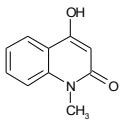
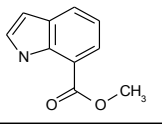
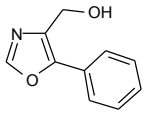
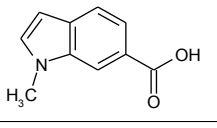
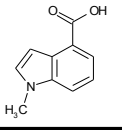
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

339	25699-85-8		3-(1H-imidazol-1-yl)benzonitrile	0.39 ± 0.06	72.1 ± 7.8	89.8 ± 5.8	134.7
340	25775-03-5		2-(1H-pyrazol-1-yl)benzonitrile	0.18 ± 0.06	78.8 ± 10.1	104.1 ± 16.5	134
342	19932-84-4		6-chloro-1,3-benzoxazol-2-ol	-0.61 ± 0.06	**111.3 ± 3.1**	94.3 ± 6.5	73.9
343	14099-81-1		1,2,3,4-tetrahydroisoquinoline hydrochloride	0.37 ± 0.06	**67 ± 10.6**	83.5 ± 7.8	86.3
344	619334-28-0		6-(2-furyl)nicotinonitrile	-0.23 ± 0.17	40.4 ± 13.9	48.9 ± 5	103.6
345	257932-29-9		2-hydroxybicyclo[3.2.1]octane-6-carboxylic acid	-0.22 ± 0.07	81.9 ± 2.6	87.4 ± 13	127
346	57976-57-5		3-pyridin-3-ylaniline		35.6 ± 9.3	73.9 ± 6.1	98.5
347	82261-42-5		4-pyridin-3-ylaniline	-0.88 ± 0.08	26.4 ± 5.2	79.3 ± 2.8	113.3
348	177202-83-4		2-pyridin-3-ylaniline	-0.23 ± 0.06	22.2 ± 5.6	18.2 ± 10	85.3
349	690632-11-2		2-methyl-1-(4-methylpiperidino)-2-propanamine	0.53 ± 0.06	103.1 ± 7.3	108.4 ± 7.2	144.1
350	7499-07-2		4-chloro-2-methylbenzoic acid	1.05 ± 0.07	**84.2 ± 12.3**	108.5 ± 9.9	159.9
351	5162-82-3		3-chloro-4-methylbenzoic acid	-0.41 ± 0.07	38 ± 12.2	88.2 ± 17.9	112.1
352	610-96-8		methyl 2-chlorobenzoate	-0.51 ± 0.41	93.2 ± 9.2	95.8 ± 19	76.4
353	69491-59-4		3-pyrimidin-5-ylaniline	0.44 ± 0.06	**69.2 ± 4.2**	78.7 ± 10	56.4
354	85006-31-1		methyl 3-amino-4-methylthiophene-2-carboxylate	-0.64 ± 0.07	81.3 ± 9.1	72.8 ± 8.6	32.3
355	88-19-7		2-methylbenzene-1-sulfonamide	-0.76 ± 0.06	98.8 ± 16	89.1 ± 16.6	87.9
356	6436-59-5		ethyl 2-methyl-1,3-thiazole-4-carboxylate	0.28 ± 0.08	101.4 ± 3.7	106.3 ± 5.3	79.8
357	71705-07-2		3-(pentylthio)-4H-1,2,4-triazole	-1.1 ± 0.07	23.8 ± 4.9	64.5 ± 8.6	45.3
358	13600-43-6		4-(trifluoromethyl)nicotinonitrile	-0.04 ± 0.08	111.9 ± 7.2	103.3 ± 1.7	129.4
359	105184-38-1		2-(3,5-difluorophenyl)acetic acid	0.13 ± 0.06	95.2 ± 10.8	107.5 ± 13.6	128.3

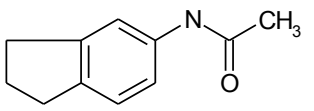
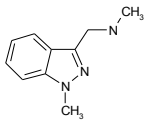
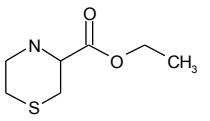
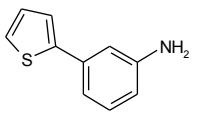
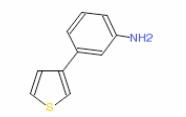
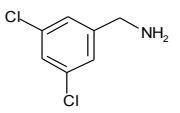
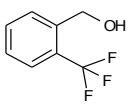
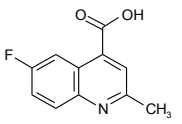
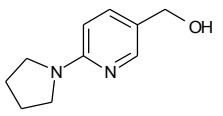
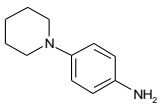
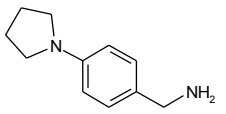
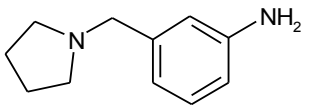
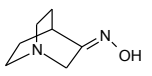
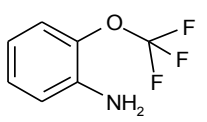
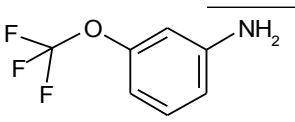
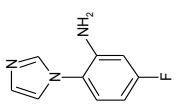
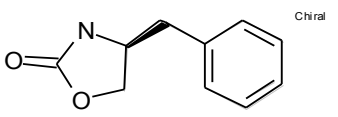
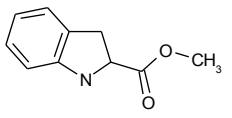
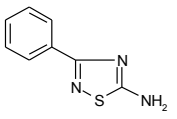
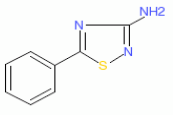
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

360	140675-42-9		1-(3,5-difluoro-2-hydroxyphenyl)ethan-1-one	1.29 ± 0.05	**98.4 ± 8.8**	103.5 ± 10	149.7
361	859851-01-7		2,3-dihydrothieno[3,4-b][1,4]dioxin-5-ylmethanol	-0.13 ± 0.08	**86.3 ± 8.1**	68.5 ± 12.9	93.7
362	175696-73-8		3-pyrrolidin-1-ylbenzonitrile	0.05 ± 0.07	**88.1 ± 5.6**	97.4 ± 19.9	63.3
363	39243-88-4		[2-(1H-pyrrol-1-yl)phenyl]methylamine	-0.09 ± 0.06	28.8 ± 7.9	42.6 ± 11.7	45.6
364	368869-95-8		3-(1H-pyrrol-1-yl)benzylamine	-0.1 ± 0.07	23.2 ± 4.2	29.5 ± 12.9	56.9
365	465514-27-6		4-(1H-pyrrol-1-yl)benzylamine	-0.51 ± 0.09	22.3 ± 5.1	**50.9 ± 11**	94.4
366	179873-36-0		N-methyl-N-(quinolin-6-ylmethyl)amine	-0.12 ± 0.06	41.5 ± 2.8	64.6 ± 11.4	74.6
367	2923-66-2		1-(3-chloro-4-fluorophenyl)ethan-1-one	-0.15 ± 0.07	101 ± 10.3	98.7 ± 6.5	58.8
368	486-74-8		quinoline-4-carboxylic acid	0.33 ± 0.08	96.3 ± 9.9	90.7 ± 7.5	90.3
369	93-10-7		2-quinolinecarboxylic acid	0.1 ± 0.67	**69.2 ± 10.7**	81.3 ± 14.1	152.1
370	10349-57-2		quinoline-6-carboxylic acid	0.57 ± 0.04	**107.3 ± 8.1**	109.3 ± 13.1	151.8
371	61034-86-4		[2-(1H-pyrrol-1-yl)phenyl]methanol	0.36 ± 0.07	38.3 ± 1.4	**88.5 ± 6.4**	87.3
372	143426-51-1		[4-(1H-pyrrol-1-yl)phenyl]methanol	3.12 ± 0.04	**37 ± 14**	**94.9 ± 19.4**	52.9
373	771573-27-4		[4-(2-furyl)phenyl]methylamine	0.48 ± 0.05	**50.5 ± 24.8**	**82.5 ± 14.3**	63.4
374	108166-02-5		(2-methyl-6-quinolinyl)methanol	0.1 ± 0.06	74.9 ± 15.6	53.2 ± 2.6	46.3
375	56643-85-7		4-(1H-imidazol-1-ylmethyl)aniline	-0.24 ± 0.08	96.3 ± 7.6	88 ± 18.8	90.7
376	10199-50-5		1-methyl-3-phenyl-1H-pyrazol-5-amine	-0.59 ± 0.06	62.2 ± 5.1	82.6 ± 4.6	64.7
377	120107-85-9		3-(1H-imidazol-1-ylmethyl)aniline	0.19 ± 0.07	93.8 ± 15.8	102.6 ± 12.6	62.4
378	368870-03-5		4-(1H-pyrazol-1-yl)benzylamine	0.19 ± 0.06	**46.3 ± 17.2**	100.7 ± 8.3	95.9
379	10442-03-2		4-(Prop-2-ynyl)thiomorpholine 1,1-dioxide	0.32 ± 0.08	102.9 ± 14.9	95.6 ± 12.9	154

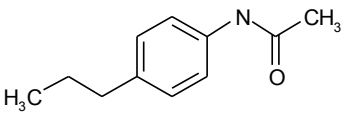
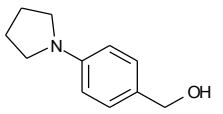
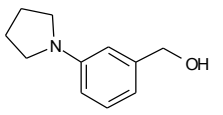
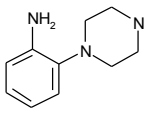
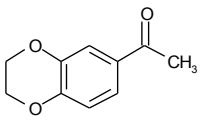
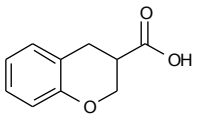
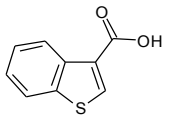
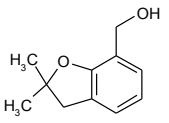
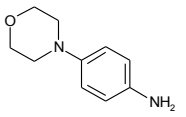
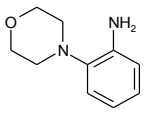
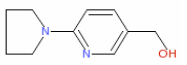
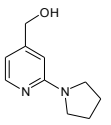
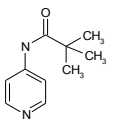
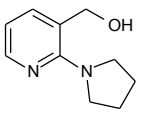
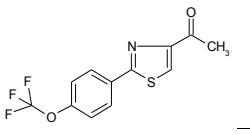
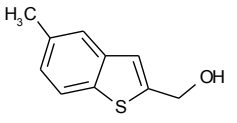
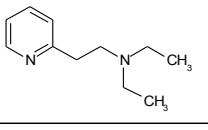
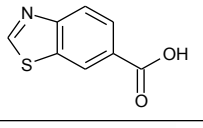
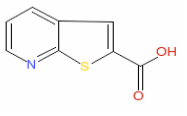
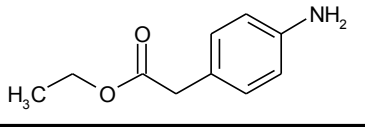
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

380	701-43-9		3-chloro-4-fluorobenzamide	0.31 ± 0.06	90.8 ± 9.6	92.2 ± 13.4	95.9
381	6419-36-9		pyridin-3-ylacetic acid hydrochloride	1.08 ± 0.05	**111.3 ± 15.5**	99.2 ± 9.9	105.4
382	16423-54-4		5-chloro-2-(methylthio)aniline	-0.75 ± 0.07	105 ± 13.7	109.8 ± 13.3	60.7
383	17920-85-3		[4-(2-furyl)phenyl]methanol	3.45 ± 0.09	33 ± 7.2	20 ± 10.6	89.6
384	21169-65-3		5-methyl-3-phenyl-4-isoxazolamine	-0.09 ± 0.07	**106.8 ± 7.1**	80.8 ± 13.4	75.5
385	143426-49-7		[4-(1H-pyrazol-1-yl)phenyl]methanol	-0.08 ± 0.07	78.3 ± 5	83.4 ± 12.4	117.5
386	86718-08-3		[4-(1H-imidazol-1-yl)phenyl]methanol	-0.75 ± 0.08	**87.6 ± 0.2**	102.8 ± 15.3	101.2
387	56278-50-3		2-(1,3-benzothiazol-2-yl)acetonitrile	1.29 ± 0.14	36 ± 8.3	86.4 ± 10.4	81
388	79887-15-3		1-butoxy-4-eth-1-ynylbenzene	-0.05 ± 0.07	100.2 ± 10.8	107.3 ± 8	114.5
389	20873-58-9		5-(methylthio)thiophene-2-carboxylic acid	0.43 ± 0.05	**85.6 ± 16.6**	104.2 ± 16.4	125.1
390	3300-51-4		4-(trifluoromethyl)benzylamine	0.38 ± 0.08	24 ± 4.6	**84.4 ± 6.8**	135.7
391	87-51-4		2-(1H-indol-3-yl)acetic acid	1.67 ± 0.08	38.8 ± 10.1	**42.6 ± 6.4**	133.7
392	942-24-5		methyl 1H-indole-3-carboxylate	0.22 ± 0.06	90.6 ± 14.9	109.9 ± 3.7	88.1
393	1619-37-0		(5-phenylisoxazol-3-yl)methanol	-0.58 ± 0.07	62.5 ± 6.9	64.8 ± 13.5	60
394	186129-25-9		1-methyl-1H-indole-5-carboxylic acid	0 ± 0.08	**111.3 ± 0.3**	95 ± 12.2	82
395	1677-46-9		4-hydroxy-1-methyl-1,2-dihydroquinolin-2-one	1.62 ± 0.03	54.3 ± 16.4	**93 ± 0.3**	174.4
396	93247-78-0		methyl 1H-indole-7-carboxylate	0.12 ± 0.11	35.3 ± 9.5	36.5 ± 11.9	164.1
397	352018-88-3		(5-phenyl-1,3-oxazol-4-yl)methanol	-0.06 ± 0.08	24.2 ± 6.1	18.2 ± 7.9	56.4
398	202745-73-1		1-methyl-1H-indole-6-carboxylic acid	-0.02 ± 0.08	**88.8 ± 14.9**	109.2 ± 10.3	101.4
399	90924-06-4		1-methyl-1H-indole-4-carboxylic acid	0.63 ± 0.07	77.4 ± 9.9	99.3 ± 14.2	123.2

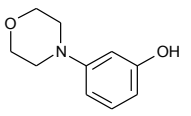
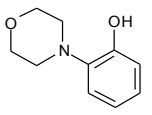
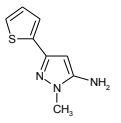
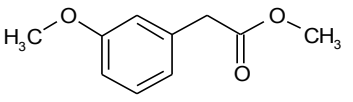
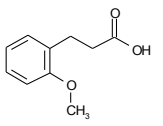
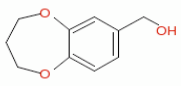
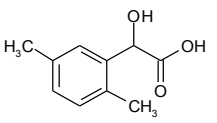
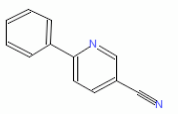
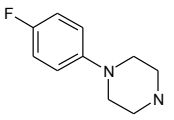
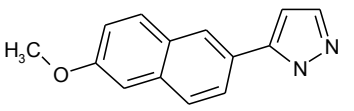
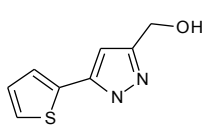
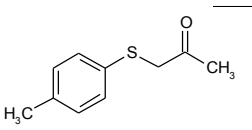
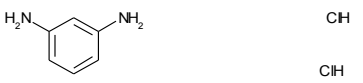
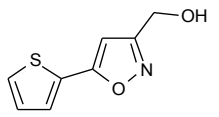
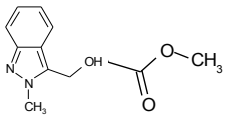
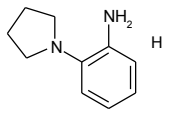
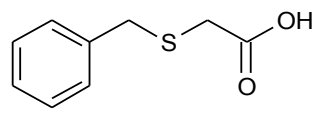
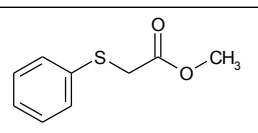
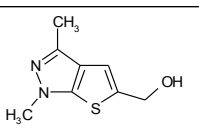
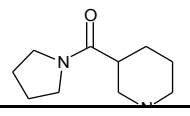
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

400	59856-06-3		N1-(2,3-dihydro-1H-inden-5-yl)acetamide	0.12 ± 0.07	**81.6 ± 17.2**	23.9 ± 13.6	99.3
401	124491-38-9		N-methyl-N-[(1-methyl-1H-indazol-3-yl)methyl]amine	-0.3 ± 0.07	**59.8 ± 8.8**	92.5 ± 7.4	91.7
402	58729-31-0		ethyl thiomorpholine-3-carboxylate	0.45 ± 0.08	**113.7 ± 12.9**	107.3 ± 18.3	95.2
403	92057-12-0		3-(2-thienyl)aniline	0.04 ± 0.04	32 ± 5.9	49.1 ± 15.7	52.3
404	161886-96-0		3-thien-3-ylaniline	0.17 ± 0.05	39.3 ± 5.7	89.4 ± 17.7	83.3
405	39989-43-0		3,5-dichlorobenzylamine	-0.53 ± 0.08	30.8 ± 5.6	**77.7 ± 13.9**	84.1
407	346-06-5		[2-(trifluoromethyl)phenyl]methanol	-0.43 ± 0.08	101.4 ± 9.7	103.7 ± 13.9	90.2
409	29427-69-8		3-oxoindane-1-carboxylic acid	0.03 ± 0.07	118.6 ± 18.3	106.7 ± 10.9	92
410	64175-51-5		benzo[b]furan-3-ylacetic acid	0.8 ± 0.07	55.1 ± 19.3	54.1 ± 10.3	97.4
413	2359-60-6		4-piperidinoaniline	#VALUE!	26 ± 4.8	11.6 ± 5.1	53.2
414	114365-04-7		[4-(1-pyrrolidinyl)phenyl]methanamine	0.14 ± 0.07	31.2 ± 6.3	68 ± 13.7	96.8
415	183365-31-3		3-(pyrrolidin-1-ylmethyl)aniline	0.34 ± 0.06	47.4 ± 18.4	**57.8 ± 4.5**	107.4
416	76883-37-9		quinuclidin-3-one oxime hydrochloride	-0.24 ± 0.08	109.1 ± 15	107.2 ± 9.6	109.3
418	1535-75-7		2-(trifluoromethoxy)aniline	0.14 ± 0.07	**86.8 ± 2.2**	**99.1 ± 14.1**	97.9
419	1535-73-5		3-(trifluoromethoxy)aniline	-0.13 ± 0.08	104.2 ± 2.1	104.9 ± 11.1	85
420	251649-52-2		5-fluoro-2-(1H-imidazol-1-yl)aniline	0.36 ± 0.07	77.6 ± 18.8	98.2 ± 10.9	100.1
421	90719-32-7		(S)-4-BENZYL-2-OXAZOLIDINONE	-0.54 ± 0.08	79.1 ± 9.8	86 ± 5.1	80.2
422	96056-64-3		methyl 2-indolinecarboxylate	-0.42 ± 0.1	32.3 ± 8.4	11.1 ± 5.7	40.1
423	17467-15-1		3-phenyl-1,2,4-thiadiazol-5-amine	-0.1 ± 0.08	59.6 ± 12.3	82.7 ± 3.9	52.7
424	27182-54-3		5-phenyl-1,2,4-thiadiazol-3-amine	-1.96 ± 0.19	**106.8 ± 4.7**	62.2 ± 15.4	60.1

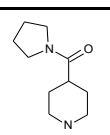
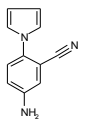
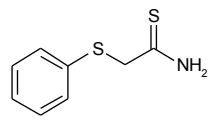
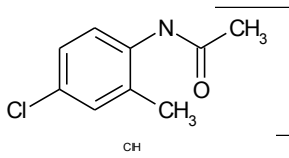
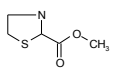
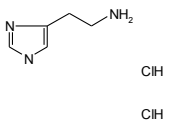
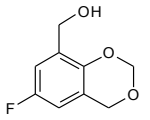
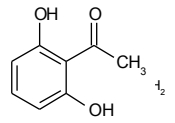
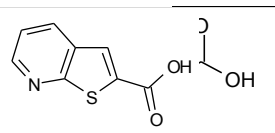
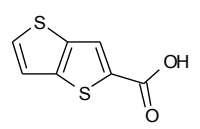
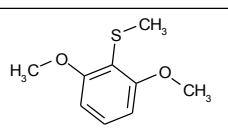
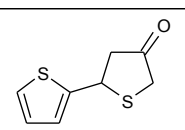
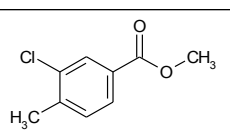
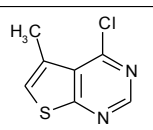
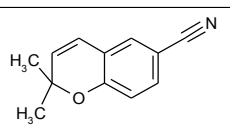
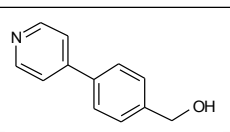
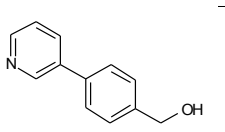
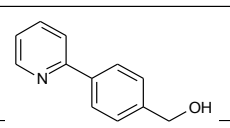
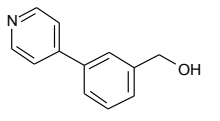
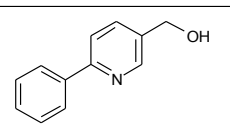
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

426	20330-99-8		N1-(4-propylphenyl)acetamide	-2.28 ± 0.07	**104.3 ± 11.3**	89.8 ± 10.8	71.7
427	676245-12-8		[4-(1-pyrrolidinyl)phenyl]methanol	0.35 ± 0.06	27.3 ± 5.7	59.8 ± 14.4	64.2
428	859850-72-9		(3-pyrrolidin-1-ylphenyl)methanol	0.44 ± 0.07	37.2 ± 16.5	**12.6 ± 5.6**	81.2
429	13339-02-1		2-piperazin-1-ylaniline	-0.13 ± 0.07	40.2 ± 13.4	**78.5 ± 7.7**	54.3
430	2879-20-1		1-(2,3-dihydro-1,4-benzodioxin-6-yl)ethan-1-one	0.13 ± 0.08	**90.9 ± 7.7**	91.1 ± 12.8	101.8
431	115822-57-6		3-chromanecarboxylic acid	-0.1 ± 0.07	95.2 ± 14.3	102.3 ± 5.9	95.8
432	5381-25-9		1-benzothiophene-3-carboxylic acid	-0.41 ± 0.08	83.1 ± 17.9	88.5 ± 12.2	55.1
434	38002-89-0		(2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl)methanol	-0.23 ± 0.06	30 ± 6.2	80.2 ± 12	51.1
435	2524-67-6		4-morpholinoaniline	-6.78 ± 0.07	21.3 ± 3.7	10.2 ± 6.9	33.5
436	5585-33-1		2-morpholinoaniline	-0.36 ± 0.07	**83 ± 6.1**	79.1 ± 5.8	56.4
437	690632-01-0		[6-(1-pyrrolidinyl)-3-pyridinyl]methanol	-0.2 ± 0.08	29.4 ± 4.1	9.3 ± 4.8	44.3
438	906352-65-6		(2-pyrrolidin-1-ylpyrid-4-yl)methanol	-0.24 ± 0.08	**73.4 ± 14**	102.6 ± 14.9	71.9
439	70298-89-4		2,2-dimethyl-N-(4-pyridinyl)propanamide	-0.24 ± 0.07	61 ± 18.6	54.6 ± 4.5	65
440	690632-85-0		[2-(1-pyrrolidinyl)-3-pyridinyl]methanol	0.78 ± 0.08	44.3 ± 11.8	**74.6 ± 7.5**	94
441	159724-40-0		3-morpholin-4-ylaniline	0.27 ± 0.08	52.6 ± 19.5	77.7 ± 16.7	85
442	22962-49-8		5-Methylbenzo[b]thiophene-2-methanol	-0.17 ± 0.07	**30.5 ± 6**	71.3 ± 3.5	53.7
443	25877-30-9		N,N-diethyl-N-[2-(2-pyridyl)ethyl]amine	-0.31 ± 0.07	**98.7 ± 8.7**	90.9 ± 9.8	49.2
444	3622-35-3		1,3-benzothiazole-6-carboxylic acid	0.73 ± 0.06	111.5 ± 19.8	92 ± 9.7	63.5
445	59944-76-2		thieno[2,3-b]pyridine-2-carboxylic acid	0.61 ± 0.08	97 ± 18.5	88 ± 8.1	45.2
446	5438-70-0		ethyl 2-(4-aminophenyl)acetate	-0.6 ± 0.07	**110.8 ± 15.4**	80.1 ± 14.8	63.2

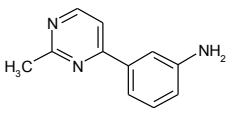
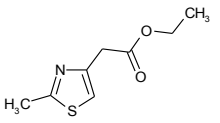
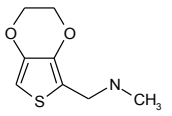
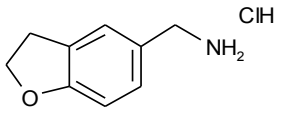
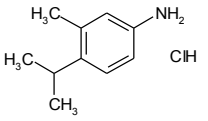
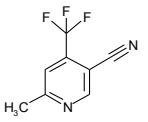
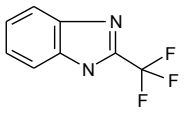
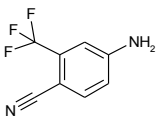
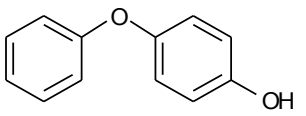
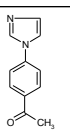
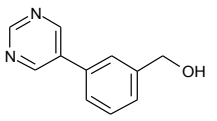
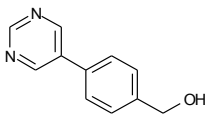
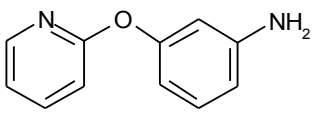
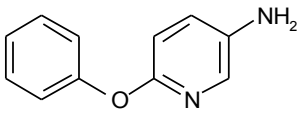
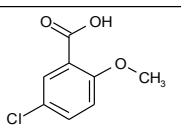
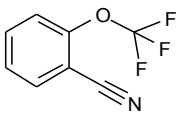
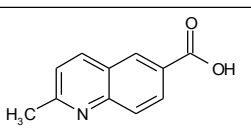
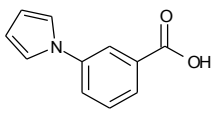
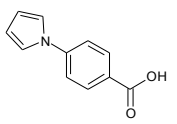
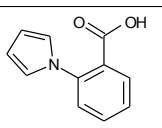
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

447	27292-49-5		3-morpholinophenol	-0.1 ± 0.08	**70.4 ± 22.1**	77.8 ± 11.8	62.8
448	41536-44-1		2-morpholinophenol	-0.04 ± 0.08	101 ± 18.8	93.3 ± 6.7	71.1
450	118430-78-7		1-methyl-3-(2-thienyl)-1H-pyrazol-5-amine	1.1 ± 0.06	55.3 ± 16.7	89.3 ± 5.5	90.7
451	18927-05-4		methyl 2-(3-methoxyphenyl)acetate	-0.68 ± 0.08	**50.7 ± 17.1**	100.7 ± 9.6	93.2
452	6342-77-4		3-(2-methoxyphenyl)propanoic acid	-0.61 ± 0.08	49.2 ± 15	97.3 ± 7.2	61.6
453	62823-14-7		3,4-dihydro-2H-1,5-benzodioxepin-7-ylmethanol	-0.59 ± 0.08	**111.4 ± 1.5**	86.6 ± 3.2	51.6
454	5766-40-5		2-(2,5-dimethylphenyl)-2-hydroxyacetic acid	0.02 ± 0.06	**98.7 ± 11.9**	96.8 ± 12.7	60.8
456	39065-54-8		6-phenylnicotinonitrile	-1.66 ± 0.17	31.1 ± 4.1	33.9 ± 6.9	67.1
457	2252-63-3		1-(4-fluorophenyl)piperazine	-0.57 ± 0.08	32.3 ± 5.6	12.7 ± 10.1	74.7
458	868755-65-1		[5-(2-furyl)thien-2-yl]methanol	0.6 ± 0.02	71.4 ± 18	94 ± 12.5	73.6
459	852228-02-5		(5-thien-2-yl-1H-pyrazol-3-yl)methanol		**41.2 ± 2.9**	**27.8 ± 10.9**	85
460	1200-13-1		1-[(4-methylphenyl)thio]acetone	0.46 ± 0.07	34.1 ± 5.3	97 ± 2.5	96.9
461	541-69-5		benzene-1,3-diamine dihydrochloride	-0.49 ± 0.08	97.3 ± 16.9	105.6 ± 10.7	91.8
462	194491-44-6		[5-(2-thienyl)-3-isoxazolyl]methanol	-0.72 ± 0.08	**80.7 ± 24**	75.6 ± 5.9	76.2
463	118465-49-9		methyl 6H-thieno[2,3-b]pyrrole-5-carboxylate	-0.89 ± 0.09	**85.3 ± 19.7**	101.3 ± 11	59.7
464	841222-62-6		4-methyl-4H-thieno[3,2-b]pyrrole-5-carboxylic acid		**82 ± 5.9**	93.5 ± 4.2	89.4
465	103-46-8		2-(benzylthio)acetic acid	-0.33 ± 0.08	**110.7 ± 12.3**	99 ± 9.3	67.9
466	17277-58-6		methyl 2-(phenylthio)acetate	-0.65 ± 0.08	93.8 ± 5.2	101.8 ± 4.8	84.7
467	423769-75-9		(1,3-dimethyl-1H-thieno[2,3-c]pyrazol-5-yl)methanol	0.35 ± 0.09	65.6 ± 13.2	67.5 ± 16.4	70.7
468	35090-94-9		3-piperidinyl(1-pyrrolidinyl)methanone	-0.03 ± 0.08	93.4 ± 18.6	**109.8 ± 13.3**	80.7

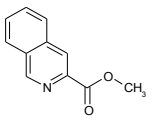
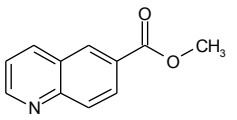
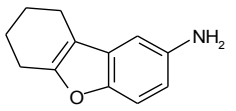
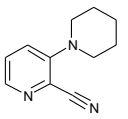
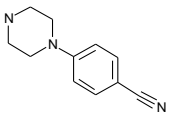
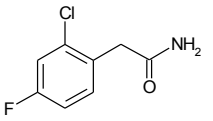
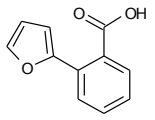
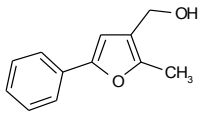
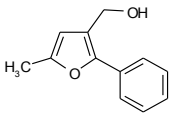
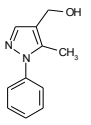
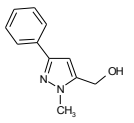
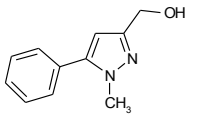
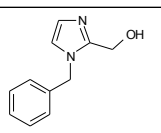
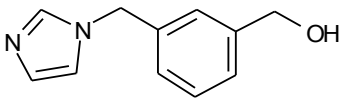
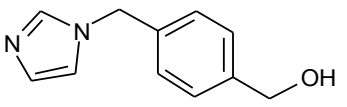
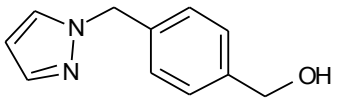
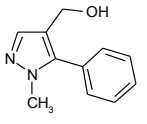
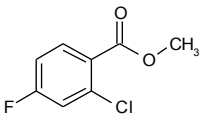
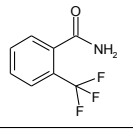
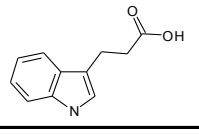
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

469	35090-95-0		4-piperidinyl(1-pyrrolidinyl)methanone	-0.35 ± 0.07	99.9 ± 7.5	99.5 ± 8.7	86.1
471	106981-51-5		5-amino-2-(1H-pyrrol-1-yl)benzonitrile	0.1 ± 0.08	42.4 ± 15.4	89.3 ± 18.8	81.4
472	59865-82-6		2-(phenylthio)ethanethioamide	-3.57 ± 0.04	43 ± 11	76.5 ± 11.2	86
473	5202-86-8		4-chloro-2-methylacetanilide	-0.4 ± 0.07	**86 ± 1**	108.7 ± 11.9	76.1
474	33305-08-7		methyl 1,3-thiazolane-2-carboxylate hydrochloride	2.81 ± 0.1	86.7 ± 16.4	108.2 ± 15.9	87
475	56-92-8		2-(1H-imidazol-4-yl)ethylamine dihydrochloride	-0.03 ± 0.08	**118.7 ± 4.4**	95.9 ± 6.6	80.3
476	306934-89-4		(6-fluoro-4H-1,3-benzodioxin-8-yl)methanol	0.01 ± 0.07	33.3 ± 4.3	102.6 ± 9.4	78.9
477	14742-32-6		2-amino-5-phenyl-3-furonitrile	0.04 ± 0.1	**93.4 ± 0.3**	98.3 ± 18.6	97.4
478	4653-08-1		4-oxo-4-(2-thienyl)butanoic acid	2.58 ± 0.05	**103.8 ± 13.1**	105.8 ± 9.3	92.3
479	1723-27-9		thieno[3,2-b]thiophene-2-carboxylic acid	0.21 ± 0.07	**91.9 ± 9**	108.9 ± 11.4	102.5
481	33617-67-3		1,3-dimethoxy-2-(methylthio)benzene	0.07 ± 0.08	**82.6 ± 6.8**	104.2 ± 17.6	102.7
482	108372-48-1		5-(2-thienyl)tetrahydrothiophen-3-one	-1.99 ± 0.06	40.9 ± 5.9	**115.5 ± 6.7**	111.9
484	56525-63-4		methyl 3-chloro-4-methylbenzoate	0.1 ± 0.07	98.3 ± 14	112.3 ± 12	119.6
486	43088-67-1		4-chloro-5-methylthieno[2,3-d]pyrimidine	0.24 ± 0.07	125.4 ± 5	100.7 ± 12.2	110.6
487	33143-29-2		2,2-dimethyl-2H-chromene-6-carbonitrile	0 ± 0.07	80.4 ± 8.8	112.5 ± 14.6	108
488	217192-22-8		(4-pyrid-4-ylphenyl)methanol	-0.35 ± 0.07	89.5 ± 10.5	65.5 ± 17.5	133.3
489	217189-04-3		(4-pyrid-3-ylphenyl)methanol	-0.57 ± 0.08	82.7 ± 13.7	66.4 ± 18.8	131
490	98061-39-3		(4-pyrid-2-ylphenyl)methanol	-0.25 ± 0.08	77 ± 4.4	102.2 ± 13.5	117.6
491	85553-55-5		(3-pyrid-4-ylphenyl)methanol	-0.2 ± 0.07	**53.1 ± 10.8**	34.4 ± 13.8	66.8
492	4634-09-7		(6-phenyl-3-pyridinyl)methanol	-0.18 ± 0.08	59.3 ± 3.2	**78.6 ± 15.6**	81.3

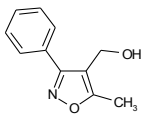
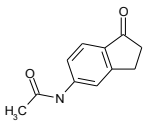
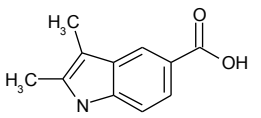
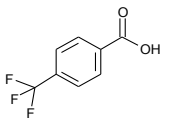
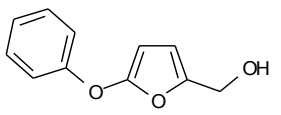
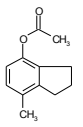
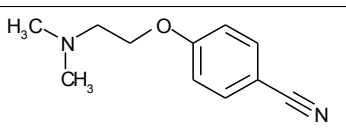
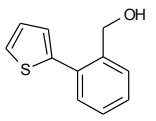
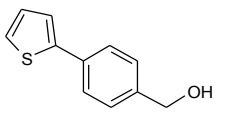
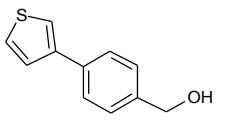
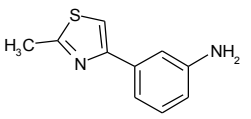
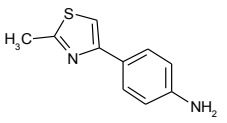
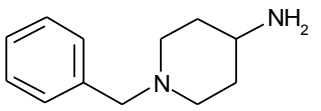
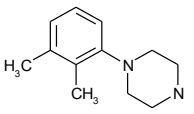
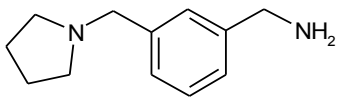
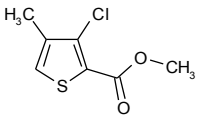
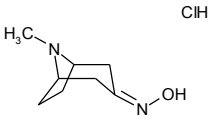
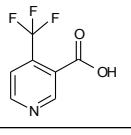
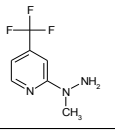
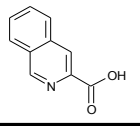
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

493	175201-90-8		3-(2-methylpyrimidin-4-yl)aniline	0.15 ± 0.07	72.2 ± 9.4	**65.9 ± 17**	92.6
494	37128-24-8		ethyl 2-(2-methyl-1,3-thiazol-4-yl)acetate	0.99 ± 0.08	107 ± 6.4	103 ± 17.9	119.5
495	859851-03-9		N-(2,3-dihydrothieno[3,4-b][1,4]dioxin-5-ylmethyl)-N-methylamine	-0.45 ± 0.07	28.2 ± 3.2	43.6 ± 17.7	96.9
496	55745-74-9		2,3-dihydrobenzo[b]furan-5-ylmethylamine hydrochloride	0.06 ± 0.08	75.4 ± 7.3	99.8 ± 15.5	96.7
497	4534-11-6		4-isopropyl-3-methylaniline hydrochloride	-0.21 ± 0.05	30.1 ± 9	**90.1 ± 2.1**	115.7
498	13600-49-2		6-methyl-4-(trifluoromethyl)nicotinonitrile	-0.1 ± 0.09	**102.8 ± 15.5**	102.9 ± 18.5	107.7
499	312-73-2		2-(trifluoromethyl)-1H-benzo[d]imidazole	-0.55 ± 0.07	**70.1 ± 5.1**	82 ± 14.1	116
500	654-70-6		4-amino-2-(trifluoromethyl)benzonitrile	-1.28 ± 0.14	27 ± 2.3	**51 ± 10.6**	72.8
502	831-82-3		4-phenoxyphenol	-3.59 ± 0.1	30.7 ± 4.5	39.6 ± 16.6	53.1
503	10041-06-2		1-[4-(1H-imidazol-1-yl)phenyl]-1-ethanone	-0.33 ± 0.07	60.7 ± 7.5	69.7 ± 7.3	94.5
504	852180-75-7		(3-pyrimidin-5-ylphenyl)methanol	-0.17 ± 0.07	87.8 ± 5.8	88.7 ± 9.9	88.2
505	198084-13-8		(4-pyrimidin-5-ylphenyl)methanol	-0.08 ± 0.08	**106.6 ± 3.1**	78.6 ± 20	85.3
506	86556-09-4		3-(pyridin-2-yloxy)aniline	0.23 ± 0.09	102.8 ± 5.4	99.2 ± 16.2	72.5
507	25194-67-6		6-phenoxy-3-pyridinamine	-0.22 ± 0.07	49.5 ± 6	**103.3 ± 15.4**	71.8
508	3438-16-2		5-chloro-2-methoxybenzoic acid	0.07 ± 0.07	**92.5 ± 12**	**78.4 ± 17.3**	101.2
509	63968-85-4		2-(trifluoromethoxy)benzonitrile	0.01 ± 0.08	114.1 ± 19.6	105.9 ± 16.9	110.4
510	635-80-3		2-methyl-6-quinolinecarboxylic acid	0.12 ± 0.08	91.2 ± 16.1	116.6 ± 10.8	126
511	61471-45-2		3-(1H-pyrrol-1-yl)benzoic acid	0.6 ± 0.08	46.2 ± 19.1	102.2 ± 12.3	73
512	22106-33-8		4-(1H-pyrrol-1-yl)benzoic acid	-4.93 ± 0.18	**42.1 ± 22.9**	97.5 ± 13.1	63.2
513	10333-68-3		2-(1H-pyrrol-1-yl)benzoic acid	3.14 ± 0.09	**104.3 ± 9.6**	**98.5 ± 6.5**	64.4

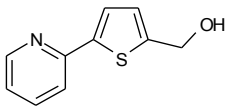
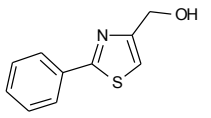
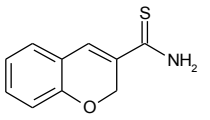
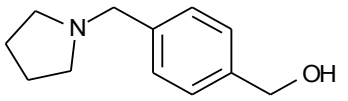
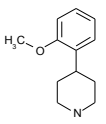
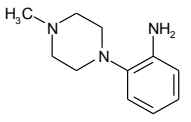
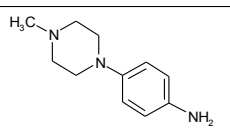
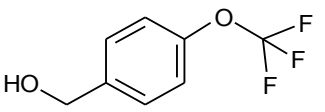
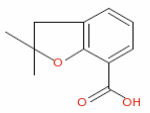
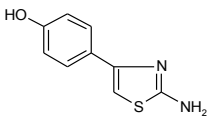
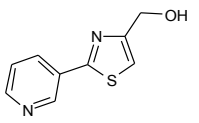
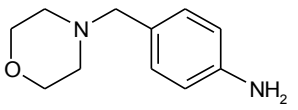
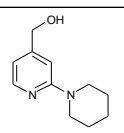
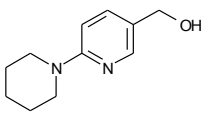
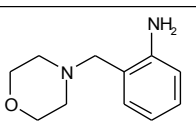
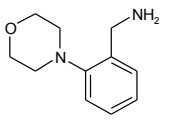
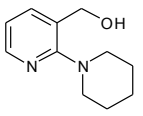
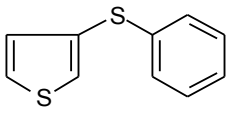
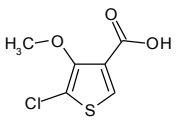
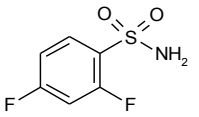
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

514	27104-73-0		methyl isoquinoline-3-carboxylate	-0.37 ± 0.07	56.8 ± 18.2	79.5 ± 14.3	65.3
515	38896-30-9		methyl quinoline-6-carboxylate	-0.1 ± 0.07	59.2 ± 1.4	**69.9 ± 8.1**	67.8
516	38084-44-5		6,7,8,9-tetrahydrodibenzo[b,d]furan-2-amine	0.2 ± 0.07	**36.8 ± 1.1**	**108 ± 5.2**	68.2
517	780802-33-7		3-piperidin-1-ylpyridine-2-carbonitrile	0.16 ± 0.07	32.2 ± 8.8	51.2 ± 17.9	54.7
518	68104-63-2		4-Piperazin-1-yl-benzonitrile	-0.26 ± 0.08	61.8 ± 2.1	92.1 ± 11	84.7
519	306937-35-9		2-(2-chloro-4-fluorophenyl)acetamide	-0.3 ± 0.08	105.2 ± 15.1	98.3 ± 15.4	102.4
520	331942-47-3		2-(2-furyl)benzoic acid	4.29 ± 0.07	35.4 ± 8.7	**73 ± 11.5**	123.9
521	111787-91-8		(2-methyl-5-phenyl-3-furyl)methanol	1.27 ± 0.07	35 ± 3.8	**41.5 ± 15**	57.1
522	183210-33-5		(5-methyl-2-phenyl-3-furyl)methanol	1.61 ± 0.06	45.4 ± 7.9	24.3 ± 17.4	27.1
523	153863-35-5		(5-methyl-1-phenyl-1H-pyrazol-4-yl)methanol	-0.01 ± 0.07	64.9 ± 10.9	75.9 ± 13.5	57.2
524	864068-97-3		(1-methyl-3-phenyl-1H-pyrazol-5-yl)methanol	-0.34 ± 0.08	**85.9 ± 17.5**	88.2 ± 10.3	60.7
525	124344-98-5		(1-methyl-5-phenyl-1H-pyrazol-3-yl)methanol	-0.44 ± 0.07	58 ± 13.5	64.8 ± 9.8	64.6
526	5376-10-3		(1-benzyl-1H-imidazol-2-yl)methanol	-0.13 ± 0.07	84.5 ± 7.1	81 ± 13.3	58
527	151055-79-7		[3-(1H-imidazol-1-ylmethyl)phenyl]methanol	-0.31 ± 0.07	78.7 ± 10.9	80.7 ± 17.6	69.2
528	103573-92-8		[4-(1H-imidazol-1-ylmethyl)phenyl]methanol	-0.2 ± 0.07	**78 ± 16**	90.8 ± 4.5	81.2
529	160388-55-6		[4-(1H-pyrazol-1-ylmethyl)phenyl]methanol	-0.19 ± 0.08	**78.1 ± 10.3**	85 ± 5.2	94
530	499785-47-6		(1-methyl-5-phenyl-1H-pyrazol-4-yl)methanol	-0.19 ± 0.09	66.6 ± 15.6	87.4 ± 6.2	109.5
531	85953-29-3		methyl 2-chloro-4-fluorobenzoate	0.25 ± 0.07	104 ± 17	84 ± 11.8	75.7
532	360-64-5		2-(trifluoromethyl)benzamide	0.43 ± 0.07	93.1 ± 13.1	88.3 ± 6.5	59.4
533	830-96-6		3-(1H-indol-3-yl)propanoic acid	0.73 ± 0.07	95.2 ± 14.2	94.9 ± 6	67.2

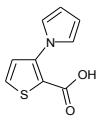
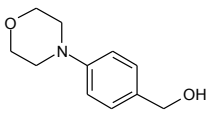
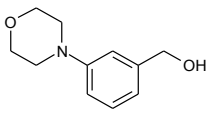
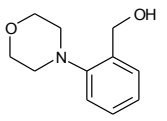
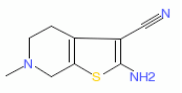
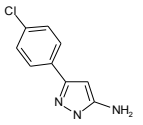
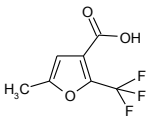
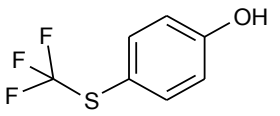
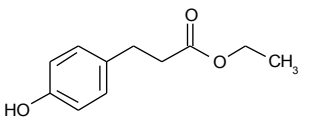
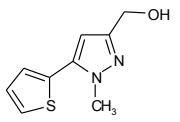
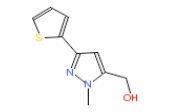
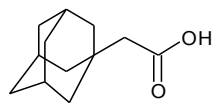
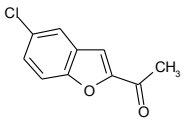
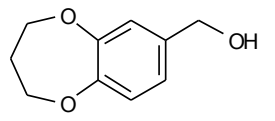
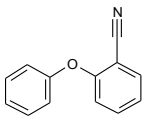
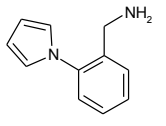
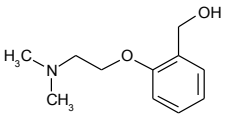
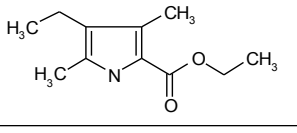
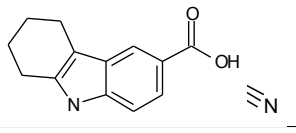
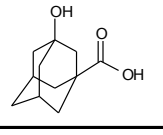
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

534	18718-79-1		(5-methyl-3-phenyl-4-isoxazolyl)methanol	-0.6 ± 0.08	59.9 ± 18.3	78.8 ± 15.6	62.9
535	58161-35-6		N1-(1-oxo-2,3-dihydro-1H-inden-5-yl)acetamide	0.21 ± 0.07	97.5 ± 6.6	87.3 ± 4.6	76.5
537	14844-73-6		2,3-dimethyl-1H-indole-5-carboxylic acid	0.7 ± 0.08	**85.3 ± 0.3**	89.3 ± 2.4	74.5
539	455-24-3		4-(trifluoromethyl)benzoic acid	-0.18 ± 0.08	80 ± 13.8	92.4 ± 8.2	103.6
540	51551-74-7		(5-phenoxy-2-furyl)methanol		29.9 ± 2.8	13.7 ± 6.5	57.7
541	175136-12-6		7-methyl-2,3-dihydro-1H-inden-4-yl acetate	0.01 ± 0.07	**45.5 ± 23.2**	79.8 ± 6.6	93.1
542	24197-95-3		4-[2-(dimethylamino)ethoxy]benzonitrile	-0.18 ± 0.09	79.7 ± 7.3	91.6 ± 9.5	69.7
543	773872-97-2		(2-thien-2-ylphenyl)methanol	-0.61 ± 0.07	30.9 ± 1.2	73.9 ± 3.7	56.5
544	81443-44-9		(4-thien-2-ylphenyl)methanol	0.16 ± 0.08	71.6 ± 7	74.7 ± 10.2	80
545	160278-20-6		(4-thien-3-ylphenyl)methanol	-0.55 ± 0.1	**60.7 ± 9.2**	84.3 ± 13.2	87.2
546	89250-34-0		3-(2-methyl-1,3-thiazol-4-yl)aniline	-0.35 ± 0.08	52.8 ± 15.6	68.5 ± 8.2	61.9
547	25021-49-2		4-(2-methyl-1,3-thiazol-4-yl)phenylamine	0.12 ± 0.07	47.6 ± 17.4	74.3 ± 11	63.2
548	50541-93-0		1-benzylpiperidin-4-amine	-0.23 ± 0.07	39.5 ± 10.8	39.5 ± 10	89.3
549	1013-22-5		1-(2,3-dimethylphenyl)piperazine	-0.73 ± 0.07	25.8 ± 3.4	10.1 ± 5.7	13.6
550	91271-78-2		[3-(1-pyrrolidinylmethyl)phenyl]methanamine	0.03 ± 0.07	51.6 ± 9	47.8 ± 11.7	108.7
551	175137-11-8		methyl 3-chloro-4-methylthiophene-2-carboxylate	-0.16 ± 0.07	108 ± 11.9	90.7 ± 10.3	104.9
552	212079-30-6		8-methyl-8-azabicyclo[3.2.1]octan-3-one oxime hydrochloride	0 ± 0.09	94.3 ± 14.4	103.5 ± 9.7	105.3
553	158063-66-2		4-(trifluoromethyl)nicotinic acid	0.28 ± 0.07	102.6 ± 10.9	102.4 ± 12.4	102.6
554	208720-09-6		2-(1-methylhydrazino)-4-(trifluoromethyl)pyridine	0.15 ± 0.08	**96.3 ± 4.3**	**95.6 ± 16.7**	96.1
555	6624-49-3		isoquinoline-3-carboxylic acid hydrate	0.5 ± 0.09	34.9 ± 11.7	92.1 ± 10.1	100.4

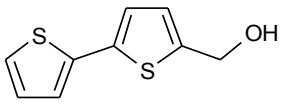
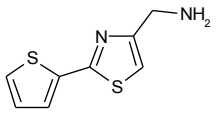
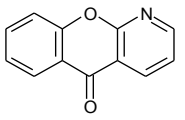
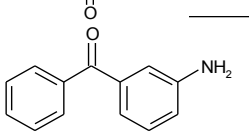
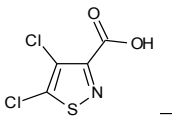
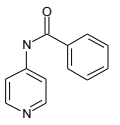
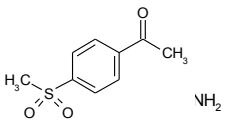
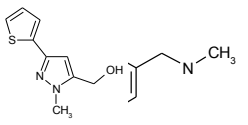
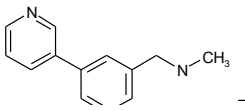
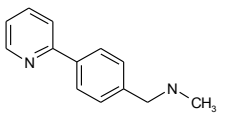
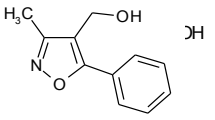
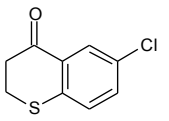
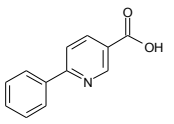
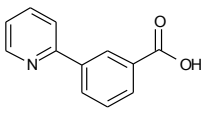
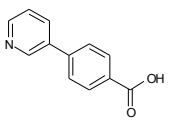
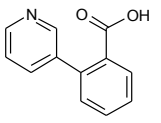
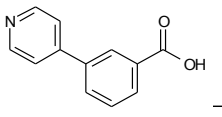
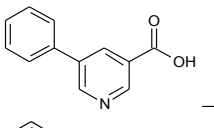
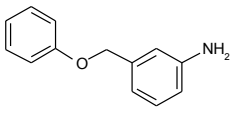
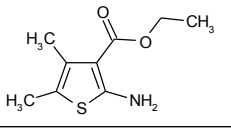
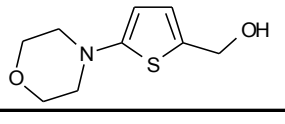
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

556	197899-76-6		[5-(2-pyridinyl)-2-thienyl]methanol	0.19 ± 0.08	**128.4 ± 2.4**	70.2 ± 11	93.9
557	23780-13-4		(2-phenyl-1,3-thiazol-4-yl)methanol	-0.18 ± 0.07	64.1 ± 11.9	58.1 ± 13.4	78.4
558	423768-57-4		2H-chromene-3-carbothioamide	0.05 ± 0.09	**41.2 ± 13.3**	80.8 ± 8.8	98.1
559	91271-60-2		[4-(pyrrolidin-1-ylmethyl)phenyl]methanol	0.05 ± 0.08	82.9 ± 2.2	91.7 ± 15.8	110
560	58333-75-8		4-(2-methoxyphenyl)piperidine	-0.37 ± 0.08	25 ± 2.7	20.2 ± 2.8	63.7
561	180605-36-1		2-(4-methylpiperazin-1-yl)aniline	0.46 ± 0.07	72.8 ± 18.6	**74.3 ± 11.7**	101.2
562	16153-81-4		4-(4-methylpiperazino)aniline	-5.28 ± 0.14	15.6 ± 6.1	8.2 ± 6.5	17.5
563	1736-74-9		[4-(trifluoromethoxy)phenyl]methanol	0.01 ± 0.07	111.5 ± 10.3	94.5 ± 8.3	92.9
564	42327-95-7		2,2-dimethyl-2,3-dihydro-1-benzofuran-7-carboxylic acid	0.35 ± 0.07	108.5 ± 16.1	91.1 ± 19	101.2
565	57634-55-6		4-(2-amino-1,3-thiazol-4-yl)phenol	-4.02 ± 0.08	**48.7 ± 19.3**	**57.7 ± 17.7**	61.6
566	138745-99-0		(2-pyridin-3-yl-1,3-thiazol-4-yl)methanol	0.29 ± 0.07	84.4 ± 17.3	88.4 ± 18.2	104
567	51013-67-3		4-(morpholinomethyl)aniline	0.61 ± 0.05	**108.5 ± 0.2**	90.1 ± 15.9	102.7
568	888070-04-0		(2-piperidinopyrid-4-yl)methanol	0.03 ± 0.07	59.3 ± 16.3	**94.5 ± 18.7**	103
569	690631-99-3		(Piperidino-3-pyridinyl)methanol	0.35 ± 0.07	31.1 ± 5.4	**89.2 ± 4.8**	106.4
570	95539-61-0		2-(morpholin-4-ylmethyl)aniline	0.35 ± 0.05	**123.3 ± 10.8**	93.2 ± 17.1	104.5
571	204078-48-8		2-morpholinobenzylamine	0.06 ± 0.07	**65.8 ± 9.1**	95 ± 17.5	70.9
572	690632-84-9		(2-piperidino-3-pyridinyl)methanol	1.25 ± 0.09	32.5 ± 9	**65.1 ± 5.7**	80.1
574	16718-11-9		3-(phenylthio)thiophene	0.11 ± 0.07	112.3 ± 15.2	98.8 ± 18.5	93.9
575	133659-14-0		5-chloro-4-methoxythiophene-3-carboxylic acid	1.07 ± 0.08	84.1 ± 4.5	90.5 ± 15.4	91.2
576			2,4-difluorobenzenesulfonamide	-6.33 ± 0.07	39.2 ± 8	10.7 ± 9.3	12.9

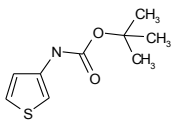
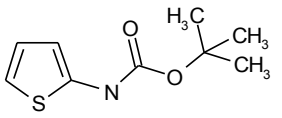
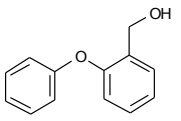
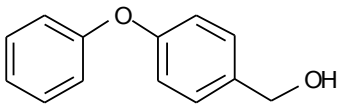
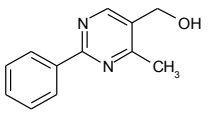
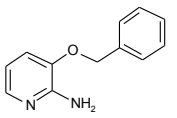
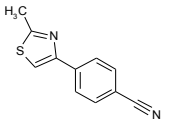
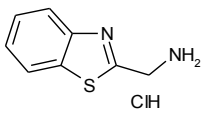
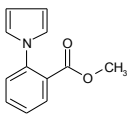
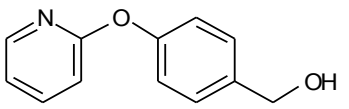
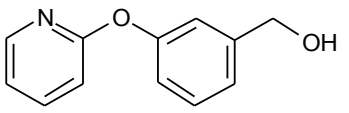
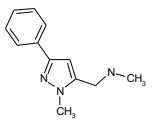
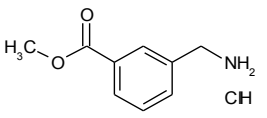
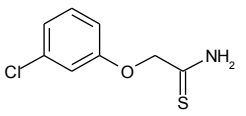
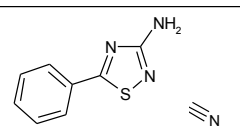
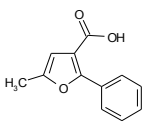
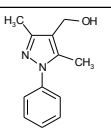
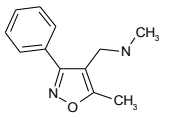
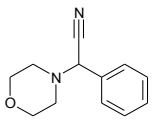
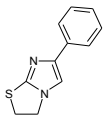
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

577	74772-17-1		3-(1H-pyrrol-1-yl)thiophene-2-carboxylic acid	2.78 ± 0.08	**32.2 ± 4.1**	**103.2 ± 2.8**	90.4
578	280556-71-0		(4-morpholin-4-yl-phenyl)-methanol	0.17 ± 0.08	**93 ± 7.9**	**42.3 ± 9**	75.4
579	145127-38-4		(3-morpholinophenyl)methanol	0.18 ± 0.08	69.7 ± 12.3	**100.1 ± 13.5**	100.8
580	465514-33-4		(2-morpholinophenyl)methanol	0.34 ± 0.06	**88.6 ± 0.9**	91.3 ± 16	122.7
581	37578-06-6		2-amino-6-methyl-4,5,6,7-tetrahydrothieno[2,3-c]pyridine-3-carbonitrile	1.39 ± 0.08	42.5 ± 18.5	**85.8 ± 12.8**	82.2
582	78583-81-0		3-(4-chlorophenyl)-1H-pyrazol-5-amine	0.01 ± 0.07	100.5 ± 19.6	90.4 ± 12.2	68.6
583	17515-74-1		5-methyl-2-(trifluoromethyl)-3-furoic acid	0.06 ± 0.07	98.2 ± 11.7	86.1 ± 15.8	59.6
584	461-84-7		4-[(trifluoromethyl)thio]phenol	-0.92 ± 0.07	**94.2 ± 17.2**	97.5 ± 15.9	68.4
585	23795-02-0		ethyl 3-(4-hydroxyphenyl)propanoate	-0.63 ± 0.08	**43.8 ± 15.9**	**63.1 ± 3.9**	61.7
586	879896-47-6		(1-methyl-5-thien-2-yl-1H-pyrazol-3-yl)methanol	-0.27 ± 0.07	71.4 ± 15.6	**82 ± 15.2**	63.4
587	879896-49-8		(1-methyl-3-thien-2-yl-1H-pyrazol-5-yl)methanol	0.36 ± 0.07	**61.3 ± 11.9**	**91.6 ± 8.8**	65.8
588	4942-47-6		2-(1-adamantyl)acetic acid	-0.39 ± 0.07	48.1 ± 17.5	95.4 ± 14.1	85.4
589	1646-32-8		1-(5-chlorobenzo[b]furan-2-yl)ethan-1-one	-0.01 ± 0.08	**81.4 ± 11.7**	**95.8 ± 12.5**	99.5
590	36157-40-1		1-(2,5-dichloro-3-thienyl)ethan-1-one	0.3 ± 0.07	**105.6 ± 10.2**	97.7 ± 13.9	129.7
591	6476-32-0		2-phenoxybenzonitrile	0.24 ± 0.06	**100.5 ± 1.9**	93 ± 2.5	58.3
592	690632-23-6		2,3-dihydro-1,4-benzodioxine-5-carbothioamide	0.18 ± 0.07	67.7 ± 17	54.3 ± 15.7	39.8
593	59115-26-3		{2-[2-(dimethylamino)ethoxy]phenyl}methanol	0.13 ± 0.06	**103.6 ± 18.7**	77.9 ± 13.5	59.2
594	2199-47-5		ethyl 4-ethyl-3,5-dimethyl-1H-pyrrole-2-carboxylate	0.17 ± 0.08	32.2 ± 12.3	**79.8 ± 6.6**	59.9
596	270260-33-8		4-(pyridin-2-yloxy)benzonitrile	0.68 ± 0.07	**89.3 ± 9**	**97.7 ± 11**	72.1
597	42711-75-1		3-hydroxyadamantane-1-carboxylic acid	0.29 ± 0.06	**105.8 ± 11**	75.2 ± 12.6	79.4

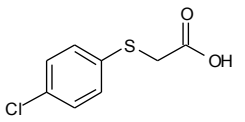
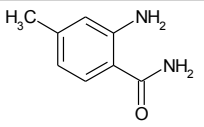
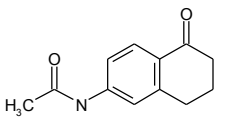
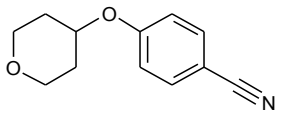
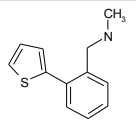
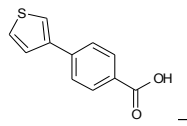
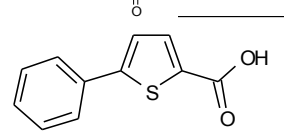
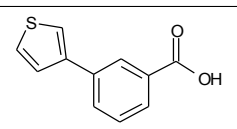
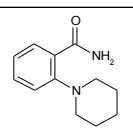
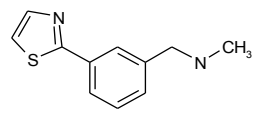
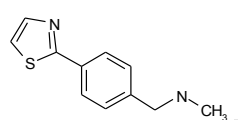
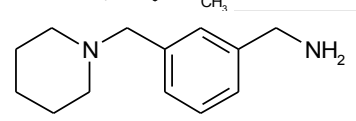
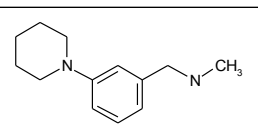
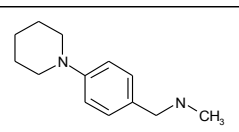
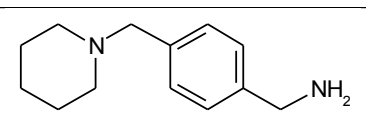
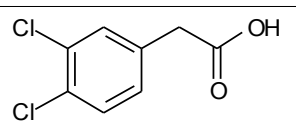
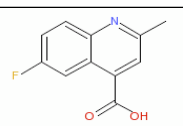
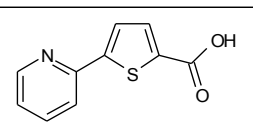
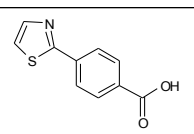
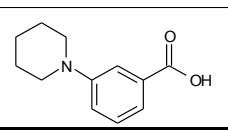
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

598	3515-30-8		2,2'-bithien-5-ylmethanol	1.72 ± 0.06	55.3 ± 15.6	**78 ± 11.6**	86.3
599	321309-35-7		[2-(2-thienyl)-1,3-thiazol-4-yl]methylamine	0.41 ± 0.06	**35.2 ± 15.5**	**71.9 ± 7.1**	98.4
600	6537-46-8		5H-chromeno[2,3-b]pyridin-5-one	0.62 ± 0.05	**80.8 ± 9.9**	78.4 ± 11	126
601	2835-78-1		(3-aminophenyl)(phenyl)methanone	0.21 ± 0.06	97.7 ± 12.1	89.2 ± 6.6	63.8
602	131947-13-2		4,5-dichloroisothiazole-3-carboxylic acid	0.1 ± 0.07	31.7 ± 9.1	83.2 ± 12.5	68.2
603	5221-44-3		N1-(4-pyridyl)benzamide	0.32 ± 0.07	82.8 ± 5	79 ± 15.1	57.3
604	10297-73-1		1-[4-(methylsulfonyl)phenyl]ethan-1-one	0.18 ± 0.06	**108.6 ± 11.7**	83.1 ± 19.6	63.9
605	852180-67-7		N-methyl-N-(3-pyridin-4-ylbenzyl)amine	0.05 ± 0.07	37.4 ± 13.7	21.3 ± 13.8	36.2
606	852180-72-4		N-methyl-N-(3-pyridin-3-ylbenzyl)amine	0.07 ± 0.08	43.2 ± 12.9	**70.8 ± 5.8**	69.8
607	869901-08-6		N-methyl-N-(4-pyridin-2-ylbenzyl)amine	0.02 ± 0.06	32.8 ± 7.4	57.7 ± 17.1	71.5
608	306934-93-0		(5-chloro-1-benzothiophen-3-yl)methanol	-1.33 ± 0.1	**99 ± 26.1**	**78.3 ± 1**	63.8
609	13735-12-1		6-chloro-3,4-dihydro-2H-1-benzothiin-4-one	2.49 ± 0.04	**86.3 ± 6.6**	**74.5 ± 13.7**	104.8
610	29051-44-3		6-phenylnicotinic acid	0.46 ± 0.06	78.4 ± 13.4	82.3 ± 8.2	125.4
611	4467-07-6		3-pyrid-2-ylbenzoic acid	0.19 ± 0.07	98.5 ± 13.5	87 ± 12.6	73.9
612	4385-75-5		4-pyrid-3-ylbenzoic acid	-0.97 ± 0.06	40.1 ± 12.4	**77.2 ± 5.7**	74.2
613	134363-45-4		2-pyrid-3-ylbenzoic acid	0.14 ± 0.07	80.1 ± 7	80 ± 5.6	59.8
614	4385-78-8		3-pyrid-4-ylbenzoic acid	0.46 ± 0.12	41.6 ± 12.5	81.2 ± 15.9	66.3
615	10177-12-5		5-phenylnicotinic acid	1.28 ± 0.09	77.6 ± 10.5	80.4 ± 11.7	75.6
616	93189-16-3		3-(phenoxymethyl)aniline	-1.45 ± 0.08	35.4 ± 10.2	80.5 ± 17.9	57.5
617	4815-24-1		ethyl 2-amino-4,5-dimethylthiophene-3-carboxylate	1.47 ± 0.07	**100.4 ± 13.8**	69.1 ± 9.3	75.2
618	910036-90-7		(5-morpholinothien-2-yl)methanol	1.12 ± 0.11	29.7 ± 4.6	70.4 ± 13.2	76.3

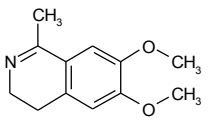
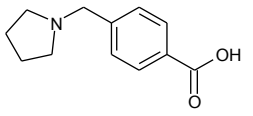
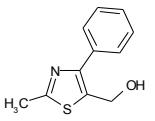
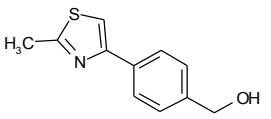
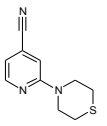
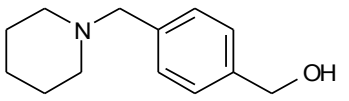
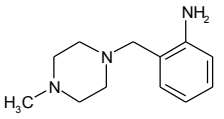
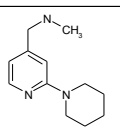
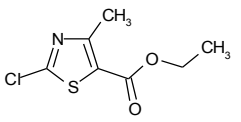
Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

619	19228-91-2		tert-butyl N-(3-thienyl)carbamate	0.21 ± 0.07	60.5 ± 3.8	80 ± 17.5	74.9
620	56267-50-6		tert-butyl N-(2-thienyl)carbamate	2.08 ± 0.1	40.1 ± 17.6	71.3 ± 13.6	109.4
621	13807-84-6		(2-phenoxyphenyl)methanol	-0.77 ± 0.08	45 ± 4.4	74.9 ± 14.8	73.7
622	2215-78-3		(4-phenoxyphenyl)methanol	-0.33 ± 0.07	84 ± 5.4	78.3 ± 15.4	70.7
623	342405-27-0		(4-methyl-2-phenyl-5-pyrimidinyl)methanol	-0.05 ± 0.07	61.8 ± 14.4	**66.5 ± 11.6**	85.4
624	24016-03-3		3-(benzyloxy)pyridin-2-amine	-0.32 ± 0.08	**70.4 ± 12.1**	**72.9 ± 14.8**	82.7
625	127406-79-5		4-(2-methyl-1,3-thiazol-4-yl)benzonitrile	1.06 ± 0.07	83.5 ± 5.3	**74.1 ± 7.1**	79.4
626	29198-41-2		1,3-benzothiazol-2-ylmethylamine hydrochloride	2.03 ± 0.08	52.9 ± 13.9	**95.1 ± 15.5**	85.7
628	10333-67-2		methyl 2-(1H-pyrrol-1-yl)benzoate	0.84 ± 0.08	**35.1 ± 9.3**	70.4 ± 14	85.1
629	194017-70-4		[4-(pyrid-2-yloxy)phenyl]methanol	-0.15 ± 0.07	82 ± 5.4	84.1 ± 9.9	96.1
630	869901-22-4		[3-(pyrid-2-yloxy)phenyl]methanol	-0.36 ± 0.07	**81.4 ± 5.7**	80 ± 1	98.3
631	864068-98-4		N-methyl-N-[(1-methyl-3-phenyl-1H-pyrazol-5-yl)methyl]amine	0.5 ± 0.08	31 ± 6.5	66.2 ± 16.3	100.2
632	17841-68-8		3-Aminomethylbenzoic acid methyl ester hydrochloride	0.22 ± 0.07	57.9 ± 14.5	44.8 ± 10.2	107.3
633	35370-95-7		2-(3-chlorophenoxy)ethanethioamide	-0.45 ± 0.14	**86.5 ± 6.5**	46.9 ± 11.1	90.3
634	680593-95-7		2-{[5-(trifluoromethyl)-2-pyridyl]oxy}acetonitrile	0.24 ± 0.09	**80.4 ± 15**	**73.3 ± 1.6**	87.2
635	64354-50-3		5-methyl-2-phenyl-3-furoic acid	0.38 ± 0.04	40.5 ± 7.4	17.7 ± 16.2	90.1
636	58789-53-0		(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)methanol	-0.18 ± 0.07	70.4 ± 15.2	73 ± 13.4	94.9
637	857283-57-9		N-methyl-N-[(5-methyl-3-phenylisoxazol-4-yl)methyl]amine	0.02 ± 0.07	66.1 ± 6.7	79.8 ± 7.5	112.6
638	15190-10-0		2-morpholino-2-phenylacetonitrile	-0.29 ± 0.09	**94.8 ± 10**	80.5 ± 8.2	89.8
639	4335-28-8		6-phenyl-2,3-dihydroimidazo[2,1-b][1,3]thiazole	-1.69 ± 0.03	31.1 ± 5.8	61 ± 9.8	109.1

Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

641	3405-88-7		2-[(4-chlorophenyl)thio]acetic acid	-0.53 ± 0.07	**129.4 ± 24.6**	105.2 ± 3.7	118.7
643	103788-65-4		2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethan-1-ol	-0.74 ± 0.07	28.1 ± 8.8	45.5 ± 7.7	104.4
644	88611-67-0		N1-(5-oxo-5,6,7,8-tetrahydronaphthalen-2-yl)acetamide	-0.13 ± 0.08	**104.2 ± 9.2**	99.2 ± 7.5	93.5
645	884507-34-0		4-(tetrahydropyran-4-yloxy)benzonitrile	0.18 ± 0.05	**121 ± 12.5**	77.4 ± 15.8	101.5
646	852180-66-6		N-methyl-N-(2-thien-2-ylbenzyl)amine	0.1 ± 0.05	27.9 ± 11	36.5 ± 9.5	66.9
648	29886-64-4		4-(3-thienyl)benzoic acid	0.25 ± 0.08	71.2 ± 17.9	105.3 ± 8.2	149.3
649	19163-24-7		5-phenylthiophene-2-carboxylic acid	-2.8 ± 0.08	**71.2 ± 14.3**	**121.8 ± 18.7**	140.7
650	20608-89-3		3-thien-3-ylbenzoic acid	-0.96 ± 0.07	**30.5 ± 9**	113.5 ± 15.9	165.2
651	3430-40-8		2-piperidinobenzamide	-1.33 ± 0.07	31.6 ± 9.7	82.4 ± 5.4	93.1
653	892501-89-2		N-methyl-3-(1,3-thiazol-2-yl)benzylamine	-0.96 ± 0.69	26.6 ± 6.5	**93.3 ± 2.7**	99.6
654	886851-31-6		N-methyl-4-(1,3-thiazol-2-yl)benzylamine	-0.49 ± 0.06	28.2 ± 6.4	66.2 ± 16.9	113.7
655	91271-80-6		3-piperidin-1-ylmethyl benzylamine	-0.13 ± 0.06	59.2 ± 10.9	73.7 ± 15.9	126.1
656	859850-65-0		N-methyl-N-(3-piperidin-1-ylbenzyl)amine	-0.36 ± 0.05	28.2 ± 9.7	27.4 ± 13.3	103.5
657	852180-55-3		N-methyl-N-(4-piperidin-1-ylbenzyl)amine	-0.79 ± 0.06	27.3 ± 8.2	40.9 ± 12	77.4
658	91271-81-7		[4-(piperidinomethyl)phenyl]methylamine	-0.23 ± 0.08	46.6 ± 16.8	**22.8 ± 5.5**	123.5
659	5807-30-7		2-(3,4-dichlorophenyl)acetic acid	-0.42 ± 0.07	**36.2 ± 19.3**	74 ± 17.1	106.4
660	716-03-0		6-fluoro-2-methyl-4-quinolinecarboxylic acid	0.5 ± 0.06	**115.1 ± 0.7**	103 ± 3.9	146.9
661	119082-97-2		5-(2-pyridyl)thiophene-2-carboxylic acid	0.91 ± 0.07	89.3 ± 17.6	95.3 ± 3.5	94.1
662	266369-49-7		4-(1,3-thiazol-2-yl)benzoic acid	0.36 ± 0.06	**116.4 ± 24**	102 ± 7.2	100.5
663	77940-94-4		3-piperidinobenzoic acid	1.23 ± 0.07	**78.6 ± 22.6**	**97.9 ± 1.5**	104.1

Supplementary Table 1: Screening the Maybridge Rule of Three Fragment Library: TbINO1 differential scanning fluorimetry and cytotoxicity studies against bloodstream form *T.brucei*, HeLa and A549 cells.

664	4721-98-6		6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline	-0.27 ± 0.07	48.8 ± 12	75.4 ± 2.2	77.7
665	159691-25-5		4-(pyrrolidin-1-ylmethyl)benzoic acid	-0.14 ± 0.07	**79.6 ± 19.9**	90.3 ± 6.3	103.9
666	857284-12-9		(2-methyl-4-phenyl-1,3-thiazol-5-yl)methanol	0.08 ± 0.05	**85.9 ± 17.4**	95.3 ± 5	113.4
667	857283-96-6		[4-(2-methyl-1,3-thiazol-4-yl)phenyl]methanol	0.4 ± 0.07	**41.7 ± 12.6**	76.7 ± 4.3	103.8
668	884507-30-6		2-thiomorpholinoisonicotinonitrile	1.06 ± 0.07	**106.2 ± 23.6**	80.3 ± 19.6	98.5
669	91271-62-4		[4-(piperidin-1-ylmethyl)phenyl]methanol	-0.3 ± 0.07	72.2 ± 11.3	93.2 ± 12.6	121
670	19577-84-5		2-[(4-methylpiperazin-1-yl)methyl]aniline	0.05 ± 0.07	**52.6 ± 17.6**	94.6 ± 8.5	120.8
671	879896-58-9		N-methyl-N-[(2-piperidin-1-ylpyridin-4-yl)methyl]amine	-0.49 ± 0.06	27.3 ± 6.8	54.8 ± 9.2	82.7
672	7238-62-2		ethyl 2-chloro-4-methyl-1,3-thiazole-5-carboxylate	-0.22 ± 0.07	87.2 ± 12.5	89.6 ± 12.5	60.5

[a] Arbitrary library number

[b] CAS numbers are unique identifiers assigned by the "Chemical Abstracts Service" to describe every chemical described in open access scientific literature.

[c] Tm shift in °C, observed for TbINO1 in the presence of compound (1mM), value is mean ± SD from the Boltzman curve fitting, see Experimental for details.

[d] Cytotoxicity studies, see Experimental for details, values are percentage of controls in the absence of compound, either mean ± SD (n=3) or mean ± SE (n=2), the latter being in bold.

[e] Cytotoxicity studies, see Experimental for details, values are percentage of controls in the absence of compound, (n=1).

[f] TbINO1 Tm in presence of DMSO (true control), shows slight plate to plate variation, value is mean ± SD. The positive controls, 5 mM glucose-6-phosphate and 4 mM 2-deoxy-glucose-6-phosphate had Tm values (mean ± SD) of 0.70 ± 0.28°C and 2.84 ± 0.47°C, respectively.