Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Carboxylate binding in polar solvents using pyridylguanidinium salts.

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ELECTRONIC SUPPLEMENTARY INFORMATION

The synthesis and characterisation data of compounds **6** – **8**, **20**, **24**, **29** and **31**

NMR and ITC Titration data for all binding studies reported in tables 1 and 2 in manuscript

N-*1-Methyl-3-cyanobenzamide 6.*

$SOCl_2$ (1.44 cm^3, 20.4 mmol) was added to a solution of 3-cyanobenzoic acid **5** (1.5 g, 10.2 mmol) in CH_3OH (15 cm^3) at 4 ^oC, and the reaction stirred at reflux for 18 h. The solvent was removed *in vacuo* to yield a grey solid which was stirred in 40% $MeNH_2/H_2O$ (12 cm^3) and THF (6 cm^3) for 18 h. The solvent was removed *in vacuo*, and the residue dissolved in EtOAc (30 cm^3), washed with 1 M $KHSO_4$ (2 x 10 cm^3) and brine (10 cm^3), and dried ($MgSO_4$). Removal of the solvent *in vacuo* and purification by column chromatography (5% CH_3OH/CH_2Cl_2) gave amide **6** (895 mg, 5.59 mmol, 55%) as a white solid. mp 136-138 °C; ν_{max} (solid)/cm^{-1} 3288s, 3085w, 3066w, 2970w, 2943w, 2230m, 1742w, 1631s, 1553s; δ_H (400 MHz, $CDCl_3$) 3.02 (3 H, d, *J* 5, CH_3), 6.51 (1 H, br s, NH), 7.56 (1 H, t, *J* 8, Ar), 7.77 (1 H, dt, *J* 8 and 1, Ar), 8.01 (1 H, dt, *J* 8 and 1, Ar),8.06 (1 H, t, *J* 1, Ar); δ_C (75.5 MHz, $CDCl_3$) 27.0 (CH_3), 112.8 (C), 118.1 (C), 129.6 (CH), 130.7 (CH), 131.3 (CH),: 134.6 (CH), 135.7 (C), 166.2 (C); *m/z* (EI) 159 ($(M-H)^{+\bullet}$, 40%), 130 (80), 102 (100).

N-*1-Methyl-3-(aminomethyl)benzamide 7*

N-1-Methyl-3-cyanobenzamide **6** (756 mg, 4.73 mmol) and 10% Pd/C (cat.) in CH_3OH (10 cm^3) was stirred under a hydrogen atmosphere for 72 h. The solution was filtered, the solvent removed *in vacuo* and purified by column chromatography (4% NH_3 sat. CH_3OH/CH_2Cl_2) to give amine **7** (658 mg, 4.02 mmol, 85%) as a waxy solid. ν_{max} (solid)/cm^{-1} 3298w, 3072w, 2941w, 1629s, 1606s, 1580s, 1548s; δ_H (400 MHz, $CDCl_3$) 2.87 (3 H, d, *J* 5, CH_3), 3.84 (2 H, s, CH_2), 7.14 (1 H, br, NH), 7.39 (1 H, t, *J* 8, Ar), 7.48 (1 H, d, *J* 8, Ar), 7.63 (1 H, d, *J* 8, Ar), 7.77 (1 H, s, Ar); δ_C (75.5 MHz, $CDCl_3$) 25.2 (CH_3), 45.2 (CH_2), 124.4 (CH), 125.1 (CH), 127.8 (CH), 129.3 (CH), 134.5 (C), 144.1 (C),167.1 (C); *m/z* (EI) 165 ($(M+H)^+$, 100%); HRMS (ES) $C_9H_{13}N_2O$ $(M+H)^+$ requires 165.1022, found 165.1023.

N-*1-Methyl-3-(isothiocyanatomethyl)benzamide 8*

Amine **7** (86 mg, 0.43 mmol) was dissolved in CH_2Cl_2 (1 cm^3) at 4 ^oC and sat. K_2CO_3 (0.5 cm^3) was added. Thiophosgene (0.07 cm^3, 0.92 mmol) was added to the organic phase and the reaction was vigorously stirred at room temperature for 3 h. CH_2Cl_2 (8 cm^3) and H_2O (4 cm^3) were added and the phases separated. The organic phase was washed with H_2O (5 cm^3), 2 M HCl (2 x 5 cm^3) and brine (5 cm^3), dried ($MgSO_4$) and the solvent removed *in vacuo* to give isothiocyanate **8** (89 mg, 0.28 mmol, 67%) as a white solid. mp 98-100 °C; ν_{max} (solid)/cm^{-1} 3307m, 3083w, 2946w, 2182m, 2103m, 1636s, 1546s; δ_H (300 MHz, $CDCl_3$) 3.00 (3 H, d, *J* 5, CH_3), 4.73 (2 H, s, CH_2), 6.67 (1 H, br, NH), 7.41-7.45 (2 H, m, Ar), 7.71-7.74 (2 H, m, Ar); δ_C (100 MHz, $CDCl_3$) 27.0

(CH_3), 48.5 (CH_2), 125.7 (CH), 126.8 (CH), 129.4 (CH), 129.8 (CH), 133.4 (C), 135.0 (C), 135.6 (C), 167.7 (C); *m/z* (CI) 207 ($(M+H)^{+\bullet}$, 24%), 148 (100).

N-*2-Methyl-6-(aminomethyl)-2-pyridinecarboxamide 20*

Pyridyl ester **19**[10] (1.5 g, 4.84 mmol) was stirred in 40% $MeNH_2/H_2O$ (15 cm^3) for 18 h. The solvent was removed *in vacuo* and the resulting yellow oil purified by column chromatography (2-10% NH_3 sat. CH_3OH/CH_2Cl_2) to give amine **20** (304 mg, 1.84 mmol, 39%) as a waxy solid. mp 105-107 °C; ν_{max} (solid)/cm^{-1} 3285w, 3063w, 2926w, 1650s, 1589s, 1533s; δ_H (300 MHz, $CDCl_3$) 2.98 (3 H, d, *J* 5, CH_3), 3.96 (2 H, br, CH_2), 7.35 (1 H, d, *J* 8, pyr), 7.75 (1 H, t, *J* 8, pyr), 8.01 (1 H, d, *J* 8, pyr),8.08 (1 H, br, NH); δ_C (75.5 MHz, $CDCl_3$) 26.1 (CH_3), 47.5 (CH_2), 120.3 (CH), 121.1 (CH), 123.8 (CH), 137.9 (C), 149.4 (C), 160.6 (C); *m/z* (ES) 166 ($(M+H)^+$, 100%); HRMS (ES) $C_8H_{12}N_3O$ $(M+H)^+$ requires 166.0975, found 166.0975.

Benzyl* N-*[(3-[(methylamino)carbonyl]benzylamino)carbo thioyl]carbamate 24

CbzNCS (0.48 cm^3, 2.5 mmol) was added to a stirred solution of amine **7** (500 mg, 2.5 mmol) and DIPEA (1.36 cm^3, 7.5 mmol) in dry CH_3CN (15 cm^3), and the reaction was stirred for 18 h. The solvent was removed *in vacuo*, the crude was dissolved in EtOAc (60 cm^3), washed with 1% HCl (3 x 10 cm^3) and brine (10 cm^3), dried ($MgSO_4$) and the solvent removed *in vacuo* to yield thiourea **24** (884 mg, 2.5 mmol, 99%) as a yellow solid. Mp 147-149 °C; ν_{max} (solid)/cm^{-1} 3311w, 2969w, 1735s, 1647m, 1541s; δ_H (400 MHz, $CDCl_3$) 2.89 (3 H, d, *J* 4, CH_3), 4.98 (2 H, d, *J* 6, $ArCH_2NHC(S)$), 5.30 (2 H, s, OCH_2Ph), 7.44-7.59 (7 H, m, Ar), 7.82 (1 H, d, *J* 8, Ar), 7.89 (1 H, s, Ar), 8.52 (1 H, q, *J* 4, CH_3NH), 10.35 (1 H, t, *J* 6, $ArCH_2NHC(S)$),11.31 (1 H, s, CbzNH); δ_C (100 MHz, DMSO-d_6) 26.2 (CH_3), 47.7 (CH_2), 66.8 (CH_2), 125.7 (CH), 126.4 (CH), 127.9 (CH), 128.2 (CH), 128.3 (CH), 128.4 (CH), 130.1 (CH), 134.7 (C), 135.6 (C), 137.9 (C), 153.2 (C), 166.5 (C),179.9 (C); *m/z* (ES) 380 ($(M+Na)^+$, 100%); HRMS (ES) $C_{18}H_{19}N_3O_3SNa$ $(M+Na)^+$ requires 380.1039, found 380.1036.

Benzyl* N-*[(6-[(methylamino)carbonyl]-2-pyridylmethyl) amino]carbothioyl carbamate 29

Amine **20** (100 mg, 0.52 mmol) was dissolved in dry CH_2Cl_2 (1 cm^3) under N_2. CbzNCS (85 mg, 0.52 mmol) in dry CH_2Cl_2 (7 cm^3) was added and the reaction stirred for 4 h. Hexane (10 cm^3) was added and the solid precipitate was isolated by filtration and purified by column chromatography (1-2% CH_3OH/CH_2Cl_2) to give thiourea **29** (95 mg, 0.26 mmol, 51%) as a white solid. mp 193-195 °C; ν_{max} (solid)/cm^{-1} 3368w, 3323w, 3273w, 1700s, 1657s, 1530s, 1504s; δ_H (300 MHz, 1:1 $CD_3OD/CDCl_3$) 2.70 (3 H, s, CH_3), 4.62 (2 H, s, $CH_2NHC(S)$), 4.95 (2 H, s, $PhCH_2$), 7.18 (1 H, d, *J*

7.5, Ar),7.72 (1 H, d, *J* 7.5, Ar), 7.61 (1 H, t, *J* 7.5, Ar); δ_C (100 MHz, DMSO) 26.1 (CH_3), 49.1 (CH_2), 79.5 (C),120.5 (CH), 124.4 (CH), 128.1 (CH), 128.5 (CH), 128.7 (CH), 135.9 (CH), 138.9 (C), 148.9 (C), 154.0 (C), 154.6 (C), 164.1 (C),167.2 (CH_2); *m/z* (ES) 381 ($(M+Na)^+$, 100%); HRMS (ES) $C_{17}H_{18}N_4O_3SNa$ $(M+Na)^+$ requires 381.0992, found 381.0991.

Benzyl {[3-(benzylamino)-3-oxopropyl]amino}carbonothioyl carbamate 31

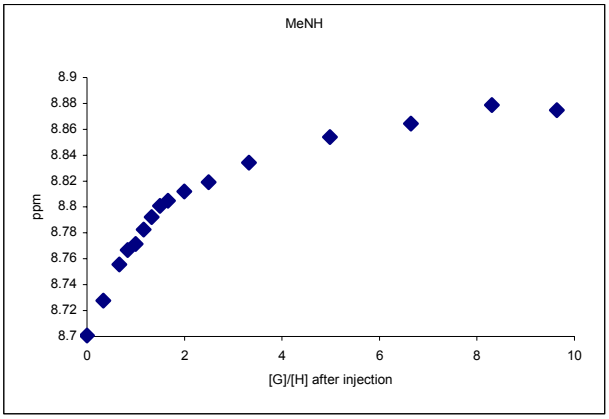
CbzNCS (0.300 cm^3, 1.55 mmol) in CH_2Cl_2 (2 cm^3) was added to amine **15** (500 mg, 1.69 mmol) and dry TEA (0.475 cm^3, 3.39 mmol) in dry CH_2Cl_2 (8 cm^3) and dry DMF (0.5 cm^3) and the mixture was stirred for 24 h. The solvent was removed *in vacuo* and purification by column chromatography (50% EtOAc/petroleum ether) gave thiourea **31** (384 mg, 1.01 mmol, 65%) as a white solid. Mp 144-146 °C; (Found: C, 61.82; H, 5.77; N, 11.05 $C_{19}H_{21}N_3O_3S$ requires C, 61.44; H, 5.78; N, 11.31%); ν_{max} (solid)/cm^{-1} 3290w, 3168w, 3018w, 2969w, 1737s, 1707s, 1634s, 1520s; δ_H (400 MHz, CD_3CN) 2.55 (2 H, t, *J* 6, $NHCH_2CH_2$), 3.88 (2 H, dt, *J* 6 and 6, $NHCH_2CH_2$), 4.34 (2 H, d, *J* 6, $NHCH_2Ph$), 5.17 (2 H, s, CH_2O), 6.94 (1 H, br, $NHCH_2Ph$), 7.21-7.41 (10 H, m, Ar), 8.91 (1 H, br, CbzNH), 10.06 (1 H, br, $NHCH_2CH_2$); δ_C (100 MHz, CD_3CN) 34.6 (CH_2), 42.4 (CH_2), 43.6 (CH_2), 68.6 (CH_2), 128.0 (CH), 128.3 (CH), 129.0 (CH), 129.4 (2 x CH), 129.6 (CH), 136.6 (C), 140.3 (C), 153.9 (C), 172.0 (C), 180.5 (C); *m/z* (ES) ESMS: m/z (%): 394 ($(M+Na)^+$, 100); HRMS (ES) for $C_{19}H_{21}N_3O_3S$ $(M+Na)^+$ requires 394.1196, found 394.1198.

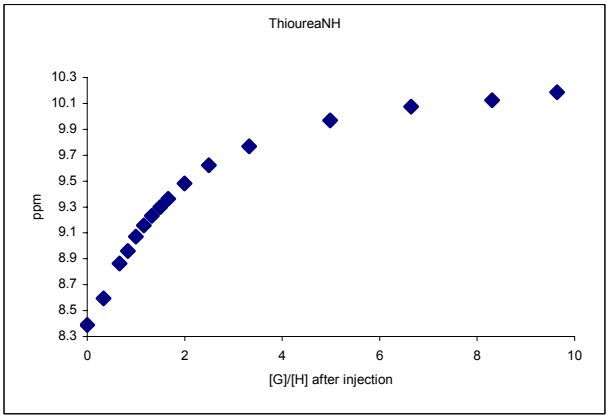
_N_1-Methyl-3-([(benzylamino)carbothioyl]aminomethyl)benzamide 9 and TBA acetate in DMSO

NMR data

[Host]/mM	3.2	Starting volume/µL	600
[Guest]/mM	31.9	K_a(average)/M^{-1}	260

Volume added /µL	MeN*H*	Thiourea-N*H*
0	8.7008	8.3901
20	8.7278	8.5944
40	8.7556	8.8637
50	8.7668	8.9598
60	8.7715	9.0718
70	8.7826	9.1568
80	8.7922	9.2330
90	8.8009	9.2990
100	8.8048	9.3641
120	8.8120	9.4817
150	8.8192	9.6215
200	8.8343	9.7692
300	8.8541	9.9686
400	8.8645	10.0743
500	8.8788	10.1243
580	8.8748	10.1855
K_a	310 M^{-1}	210 M^{-1}



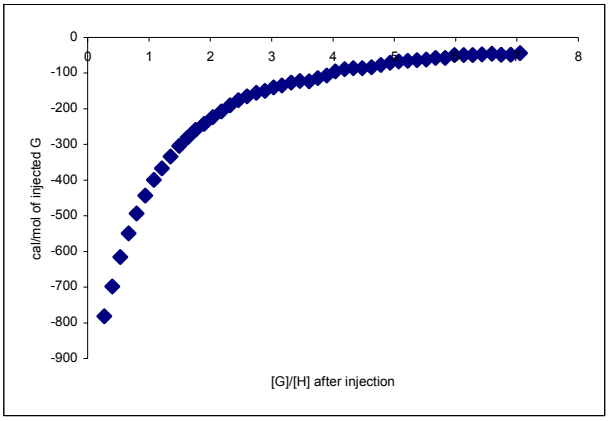


ITC data

[Host]/mM	1.95	ΔH/kJmol^{-1}	-6.87
[Guest]/mM	78.0	$T\Delta S$/kJmol^{-1}	8.49
K_a/M^{-1}	440	ΔG/kJmol^{-1}	-15.3

[G]/[H] after injection	cal/mol of injected G
0.13	--
0.27	-781.41
0.40	-698.36
0.53	-615.29
0.67	-548.76
0.80	-493.96
0.94	-443.26
1.08	-398.98
1.21	-367.24
1.35	-333.39
1.49	-304.26
1.63	-280.81
1.76	-259.72
1.90	-242.64
2.04	-223.40
2.18	-207.33
2.32	-190.30
2.46	-175.59
2.60	-164.96
2.75	-155.46
2.89	-150.08
3.03	-140.34
3.17	-134.81
3.32	-126.95
3.46	-122.20
3.61	-122.75
3.75	-113.94
3.90	-106.49
4.04	-94.75
4.19	-88.91
4.33	-86.30
4.48	-85.77
4.63	-83.09
4.78	-77.36
4.93	-70.92
5.07	-67.20
5.22	-65.93
5.37	-63.66
5.52	-61.58
5.67	-57.44

5.83	-56.98
5.98	-48.93
6.13	-49.32
6.28	-49.68
6.43	-47.52
6.59	-45.78
6.74	-48.63
6.90	-48.32
7.05	-43.65
7.21	

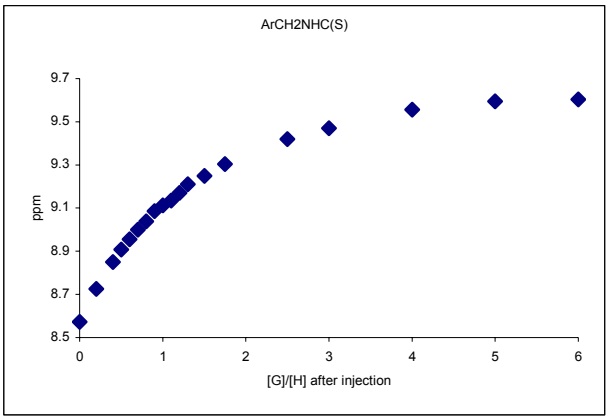


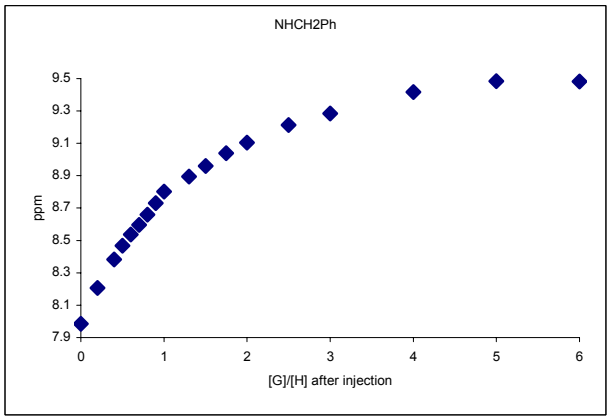
_N_1-Methyl-3-[([2-(benzylamino)-2-oxoethyl]aminocarbothioyl)amino]methyl benzamide 10 and TBA acetate in DMSO

NMR data

[Host]/mM	4.5	Starting volume/µL	600
[Guest]/mM	27.0	K_a(average)/M^{-1}	290

Volume added /µL	$ArCH_2NHC(S)$	$NHCH_2Ph$
0	8.5729	7.9847
20	8.7262	8.2059
40	8.8494	8.3823
50	8.9082	8.4681
60	8.9550	8.5364
70	9.0003	8.5968
80	9.0384	8.6603
90	9.0853	8.7302
100	9.1123	8.8025
110	9.1353	
120	9.1703	
130	9.2108	8.8949
150	9.2497	8.9598
175	9.3045	9.0392
200	-	9.1052
250	9.4197	9.2132
300	9.4706	9.2839
400	9.5564	9.4173
500	9.5945	9.4841
600	9.6032	9.4817
K_a	278 M^{-1}	293 M^{-1}



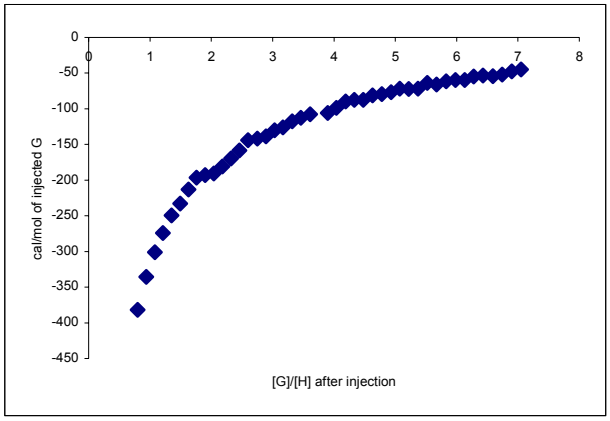


ITC data

[Host]/mM	1.96	ΔH/kJmol^{-1}	-6.32
[Guest]/mM	78.0	$T\Delta S$/kJmol^{-1}	7.15
K_a/M^{-1}	230	ΔG/kJmol^{-1}	-13.5

[G]/[H] after injection	cal/mol of injected G
0.13	783.99
0.27	1368.73
0.40	1271.58
0.54	1185.35
0.67	1112.47
0.81	1048.42
0.95	993.55
1.08	946.24
1.22	900.12
1.36	860.56
1.50	824.94
1.63	789.31
1.77	756.68
1.91	726.68
2.05	698.51
2.19	676.04
2.33	651.98
2.48	628.11
2.62	608.33
2.76	589.39
2.90	571.80
3.05	559.45
3.19	539.23
3.33	526.00
3.48	508.46
3.62	496.26
3.77	484.27
3.92	469.81
4.06	458.29
4.21	444.12
4.36	437.64
4.50	423.80
4.65	413.45
4.80	401.58
4.95	393.40
5.10	384.75
5.25	377.05
5.40	367.95
5.55	362.52
5.70	354.75

5.85	346.52
6.01	339.03
6.16	333.24
6.31	327.86
6.47	319.79
6.62	316.17
6.78	308.75
6.93	302.87
7.09	296.36
7.24	290.80

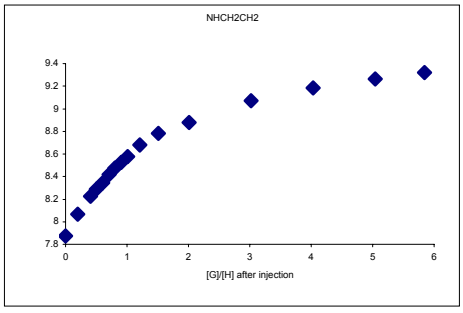


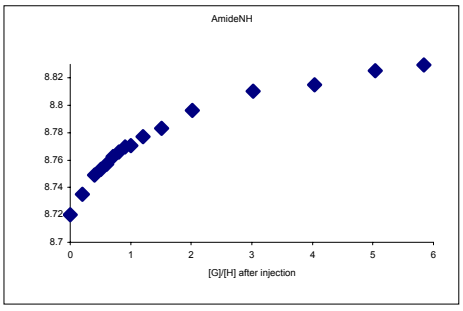
_N_1-Methyl-3-[([3-(benzylamino)-3-oxopropyl]aminocarbothioyl)amino]methyl benzamide 11 and TBA acetate in DMSO

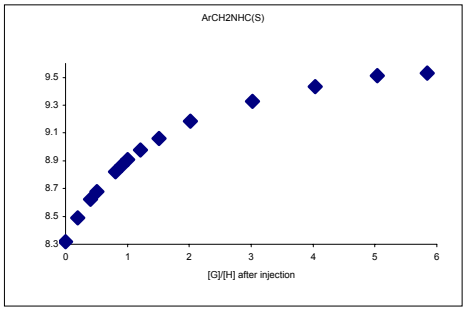
NMR data

[Host]/mM	4.3	Starting volume/µL	600
[Guest]/mM	26.0	K_a(average)/M^{-1}	200

Volume added /µL	Amide-N*H*	$ArCH_2NHC(S)$	$NHCH_2CH_2$
0	8.7199	8.3195	7.8747
20	8.7350	8.4903	8.0669
40	8.7493	8.6222	8.2242
50	8.7533	8.6794	8.2886
60	8.7572	-	8.3457
70	8.7628	-	8.4196
80	8.7660	8.8200	8.4736
90	8.7699	8.8684	8.5253
100	8.7707	8.9074	8.5793
120	8.7771	8.9796	8.6770
150	8.7834	9.0607	8.7834
200	8.7961	9.1830	8.8780
300	8.8104	9.3276	9.0726
400	8.8152	9.4340	9.1852
500	8.8255	9.5103	9.2664
580	8.8295	9.5325	9.3204
K_a	183 M^{-1}	197 M^{-1}	218 M^{-1}





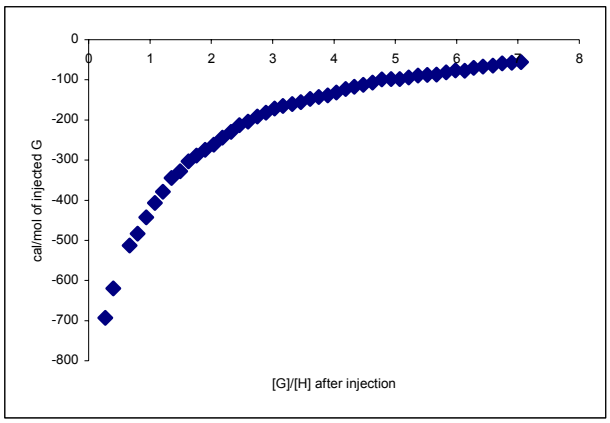


ITC data

[Host]/mM	1.95	ΔH/kJmol^{-1}	-8.67
[Guest]/mM	78.0	$T\Delta S$/kJmol^{-1}	5.19
K_a/M^{-1}	270	ΔG/kJmol^{-1}	-13.9

[G]/[H] after injection	cal/mol of injected G
0.14	--
0.27	-692.88
0.41	-619.70
0.55	--
0.69	-512.81
0.83	-483.13
0.97	-443.02
1.11	-406.63
1.25	-378.60
1.39	-344.55
1.53	-327.81
1.68	-303.30
1.82	-288.75
1.96	-274.67
2.11	-261.60
2.25	-244.19
2.39	-230.10
2.54	-213.23
2.68	-204.19
2.83	-191.17
2.98	-181.93
3.12	-171.88
3.27	-165.20
3.42	-160.51
3.57	-155.64
3.72	-147.81
3.87	-142.56
4.02	-139.18
4.17	-131.95
4.32	-122.69
4.47	-117.56
4.62	-112.44
4.77	-106.98
4.92	-99.11
5.08	-98.09
5.23	-97.72
5.38	-93.99
5.54	-89.19
5.69	-87.64

5.85	-86.69
6.00	-81.74
6.16	-76.64
6.32	-77.73
6.47	-70.25
6.63	-67.17
6.79	-64.72
6.95	-59.26
7.11	-57.58
7.27	-55.85
7.43	-55.24

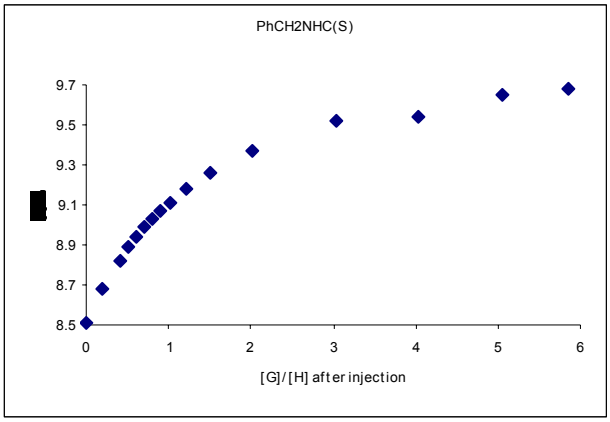


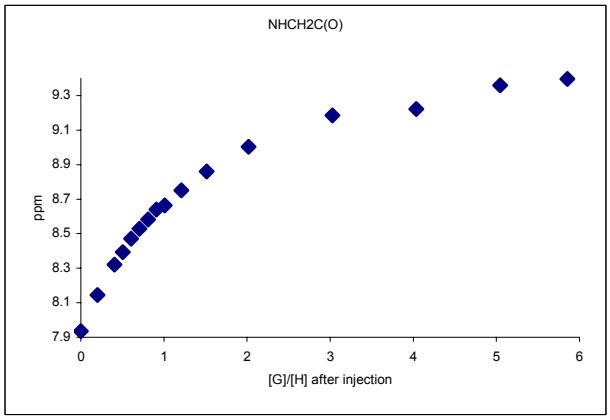
_N_1-Benzyl-2-[(benzylamino)carbothioyl]aminoacetamide 12 and TBA acetate in DMSO

NMR data

[Host]/mM	3.7	Starting volume/µL	600
[Guest]/mM	22.4	K_a(average)/M^{-1}	230

Volume added /µL	$PhCH_2NHC(S)$	$NHCH_2C(O)$
0	8.5110	7.9351
20	8.6826	8.1440
40	8.8240	8.3211
50	8.8859	8.3926
60	8.9360	8.4713
70	8.9900	8.5292
80	9.0265	8.5825
90	9.0742	8.6405
100	9.1052	8.6633
120	9.1774	8.7509
150	9.2577	8.8597
200	9.3689	9.0027
300	9.5150	9.1854
400	9.5421	9.2211
500	9.6549	9.3601
580	9.6787	9.3967
K_a	237 M^{-1}	225 M^{-1}



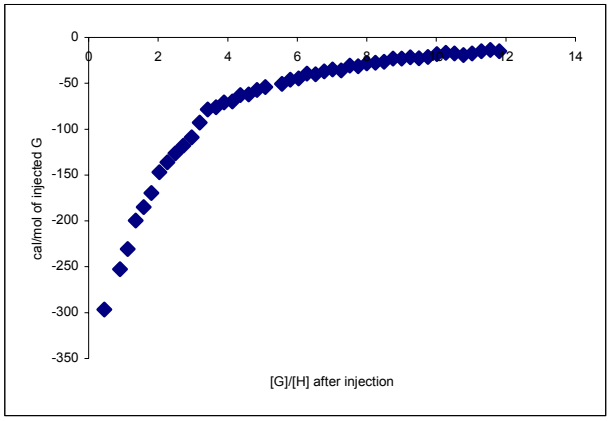


ITC data

[Host]/mM	1.20	ΔH/kJmol^{-1}	-4.76
[Guest]/mM	78.0	$T\Delta S$/kJmol^{-1}	9.92
K_a/M^{-1}	370	ΔG/kJmol^{-1}	-14.7

[G]/[H] after injection	cal/mol of injected G
0.22	--
0.45	-296.74
0.67	--
0.90	-252.58
1.12	-230.79
1.35	-199.77
1.58	-184.97
1.80	-169.56
2.03	-146.85
2.26	-135.95
2.49	-126.48
2.72	-117.78
2.96	-108.83
3.19	-92.78
3.42	-78.58
3.66	-76.18
3.89	-70.73
4.13	-69.66
4.36	-62.97
4.60	-62.04
4.84	-57.20
5.08	-54.20
5.32	--
5.56	-50.71
5.80	-46.02
6.04	-44.59
6.28	-39.47
6.53	-40.02
6.77	-36.84
7.01	-34.95
7.26	-36.09
7.51	-30.63
7.75	-31.54
8.00	-28.34
8.25	-27.74
8.50	-26.57
8.75	-23.18
9.00	-23.17
9.25	-21.74
9.50	-22.58

9.76	-21.22
10.01	-18.14
10.27	-16.83
10.52	-17.45
10.78	-19.16
11.03	-17.50
11.29	-15.02
11.55	-13.74
11.81	-15.05
12.07	-12.55

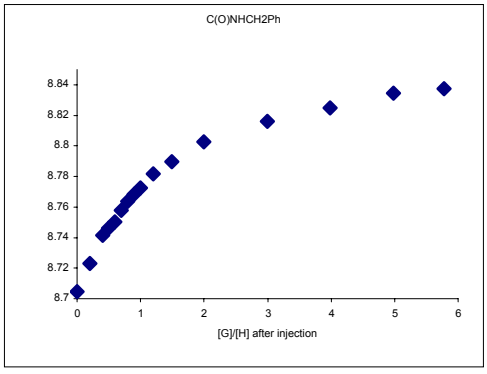


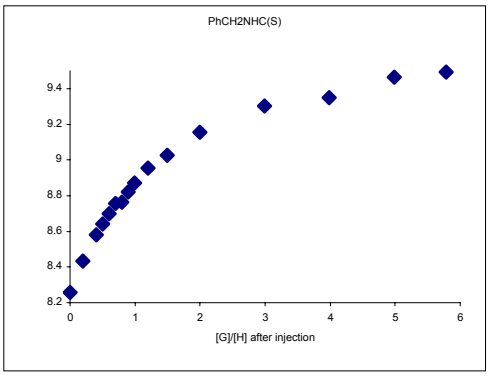
_N_1-Benzyl-3-[(benzylamino)carbothioyl]aminopropanamide 13 and TBA acetate in DMSO

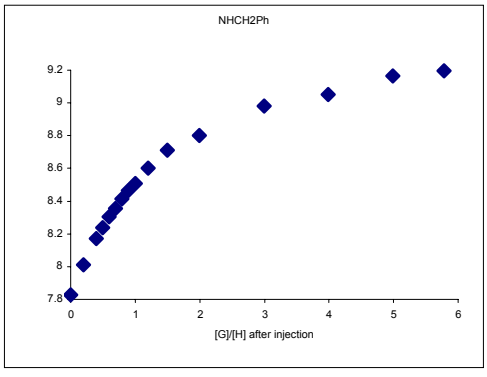
NMR data

[Host]/mM	5.1	Starting volume/µL	600
[Guest]/mM	30.5	K_a(average)/M^{-1}	230

Volume added /µL	C(O)N*H*CH_2Ph	PhCH_2N*H*C(S)	N*H*CH_2Ph
0	8.7048	8.256	7.8262
20	8.7231	8.4331	8.0121
40	8.7413	8.5817	8.1734
50	8.7461	8.6428	8.2385
60	8.7501	8.7000	8.3036
70	8.7580	8.758	8.3553
80	8.7636	8.7636	8.4149
90	8.7683	8.8200	8.4641
100	8.7723	8.8724	8.5094
120	8.7819	8.9542	8.6031
150	8.7898	9.0273	8.7112
200	8.8025	9.1544	8.8025
300	8.8160	9.3030	8.9804
400	8.8247	9.3498	9.0511
500	8.8343	9.4634	9.1631
580	8.8375	9.4944	9.1957
K_a	248 M^{-1}	209 M^{-1}	223 M^{-1}





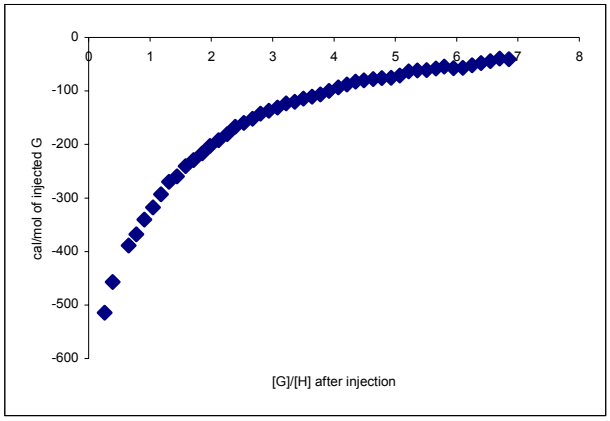


ITC data

[Host]/mM	1.99	ΔH/kJmol^{-1}	-6.60
[Guest]/mM	78.0	$T\Delta S$/kJmol^{-1}	7.14
K_a/M^{-1}	260	ΔG/kJmol^{-1}	-13.7

[G]/[H] after injection	cal/mol of injected G
0.13	--
0.26	-514.626
0.39	-457.022
0.52	--
0.65	-388.796
0.78	-367.690
0.91	-340.101
1.05	-317.501
1.18	-293.019
1.31	-269.580
1.44	-259.711
1.58	-240.249
1.71	-229.256
1.85	-216.499
1.98	-202.599
2.12	-191.810
2.26	-180.826
2.39	-166.754
2.53	-159.788
2.67	-152.072
2.80	-142.377
2.94	-136.889
3.08	-130.758
3.22	-123.222
3.36	-120.534
3.50	-114.131
3.64	-110.623
3.78	-106.402
3.92	-99.945
4.07	-93.314
4.21	-87.726
4.35	-82.775
4.49	-80.215
4.64	-77.777
4.78	-75.812
4.93	-75.506
5.07	-70.955
5.22	-63.429
5.36	-61.416
5.51	-60.885

5.66	-58.181
5.80	-54.218
5.95	-57.548
6.10	-56.781
6.25	-52.106
6.40	-47.927
6.55	-44.137
6.70	-39.558
6.85	-40.659
7.00	-38.701

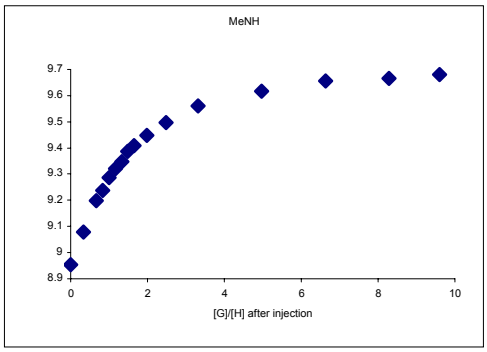


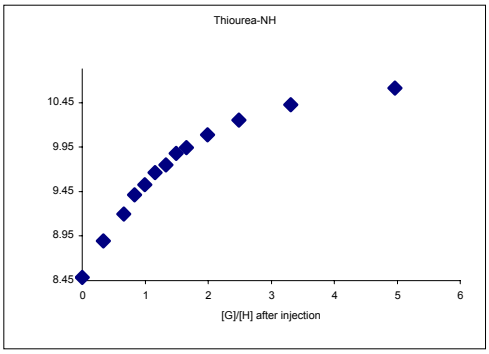
_N_2-Methyl-6-([(benzylamino)carbothioyl]aminomethyl)-2-pyridinecarboxamide 21 and TBA acetate in DMSO

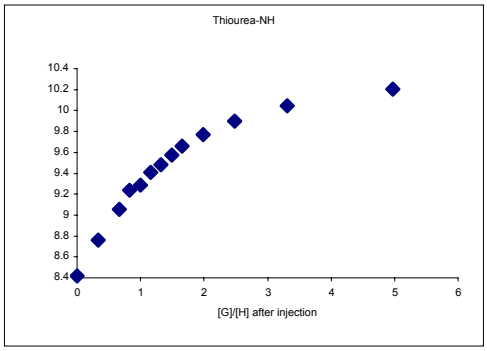
NMR data

[Host]/mM	3.2	Starting volume/µL	600
[Guest]/mM	31.8	K_a(average)/M^{-1}	370

Volume added /µL	MeN*H*	Thiourea-N*H*	Thiourea-N*H*
0	8.9539	8.4887	8.4196
20	9.0789	8.8931	8.7580
40	9.1973	9.1973	9.0519
50	9.2378	9.4142	9.2378
60	9.2855	9.5317	9.2855
70	9.3196	9.6668	9.4094
80	9.3474	9.7502	9.4801
90	9.3864	9.8804	9.5770
100	9.4078	9.9448	9.6572
120	9.4491	10.0917	9.7700
150	9.4968	10.2514	9.8955
200	9.5603	10.4301	10.0433
300	9.6159	10.6168	10.2061
400	9.6564	10.7384	10.3110
500	9.6660	10.7630	10.3277
580	9.6795	10.8257	10.3817
K_a	364 M^{-1}	368 M^{-1}	373 M^{-1}



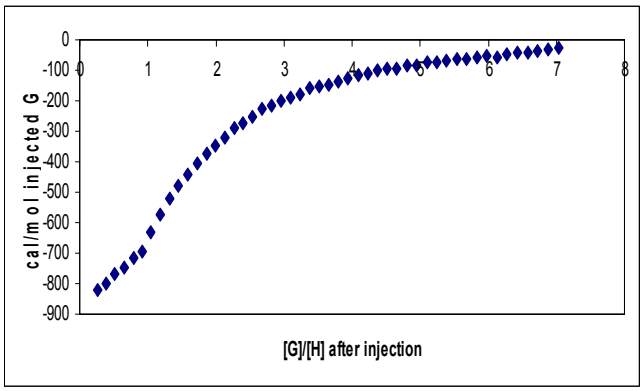




ITC data

[Host]/mM	2.06	ΔH/kJmol^{-1}	-9.7
[Guest]/mM	78.0	$T\Delta S$/kJmol^{-1}	5.0
K_a/M^{-1}	370	ΔG/kJmol^{-1}	-14.7

[G]/[H] after injection	cal/mol of injected G
0.10	--
0.26	-822.44
0.39	-800.75
0.52	-718.04
0.65	-745.96
0.79	-766.90
0.92	-696.91
1.05	-633.62
1.18	-574.20
1.32	-523.68
1.45	-479.94
1.59	-442.02
1.72	-407.56
1.86	-372.93
1.99	-347.24
2.13	-321.40
2.27	-290.81
2.40	-271.61
2.54	-250.14
2.68	-226.32
2.82	-214.25
2.96	-197.99
3.10	-189.47
3,24	-176.42
3,38	-160.32
3,52	-153.13
3,66	-146.35
3,80	-137.30
3,94	-125.42
4,09	-117.40
4,23	-108.60
4,37	-98.68
4,52	-96.92
4,66	-94.11
4,81	-85.20
4,95	-86.74
5,10	-73.64
5,24	-72.57
5,39	-69.21
5,54	-6199
5,68	-63.80
5,83	-57.68
5,98	-52.49
6,13	-56.34
6,28	-48.16
6,43	-43.12
6,58	-42.48
6,73	-36.81
6,89	-32.22
7,03	-28.60

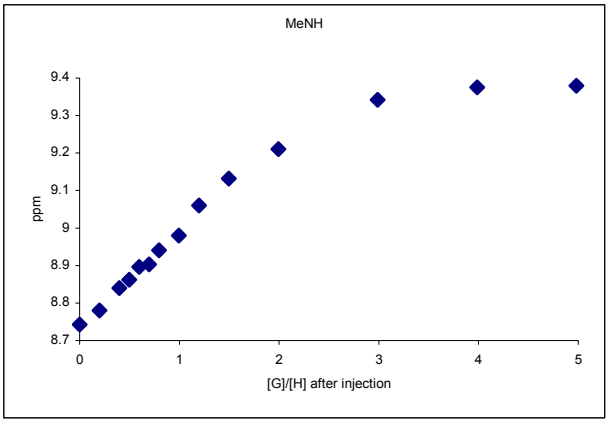


_N_2-Methyl-6-[([2-(benzylamino)-2-oxoethyl]aminocarbothioyl)amino]methyl-2-pyridinecarboxamide 22 and TBA acetate in DMSO

NMR data

[Host]/mM	4.5	Starting volume/µL	600
[Guest]/mM	26.9	K_a(average)/M^{-1}	950

Volume added /µL	MeN*H*
0	8.7429
20	8.7804
40	8.8398
50	8.8620
60	8.8962
70	8.9033
80	8.9407
100	8.9804
120	9.0606
150	9.1321
200	9.2107
300	9.3418
400	9.3752
500	9.3799
K_a	947 M^{-1}



ITC data

[Host]/mM	2.02	ΔH/kJmol^{-1}	-3.77
[Guest]/mM	78.0	$T\Delta S$/kJmol^{-1}	13.3
K_a/M^{-1}	980	ΔG/kJmol^{-1}	-17.1

[G]/[H] after injection	cal/mol of injected G
0.13	715.51
0.27	962.89
0.40	989.12
0.53	961.24
0.67	929.41
0.80	903.81
0.94	877.00
1.08	848.19
1.21	823.15
1.35	793.00
1.49	766.93
1.63	742.84
1.76	717.38
1.90	692.76
2.04	668.80
2.18	650.01
2.32	629.50
2.46	610.25
2.60	592.91
2.75	579.55
2.89	562.17
3.03	545.05
3.17	531.93
3.32	514.74
3.46	503.28
3.61	491.36
3.75	479.13
3.90	467.45
4.04	456.29
4.19	445.55
4.33	432.68
4.48	424.38
4.63	418.69
4.78	408.64
4.93	401.80
5.07	393.35
5.22	386.07

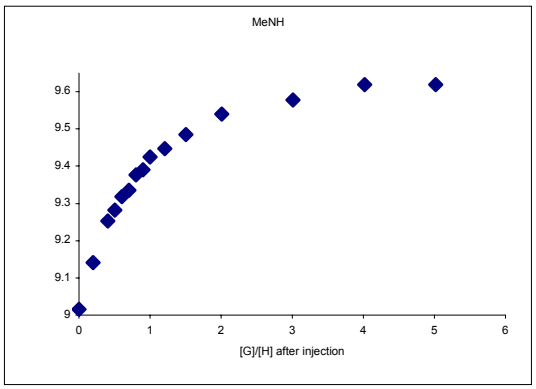
5.37	374.40
5.52	365.85
5.67	360.15
5.83	353.46
5.98	345.24
6.13	338.64
6.28	334.02
6.43	323.90
6.59	321.10
6.74	311.73
6.90	306.41
7.05	301.32
7.21	296.49

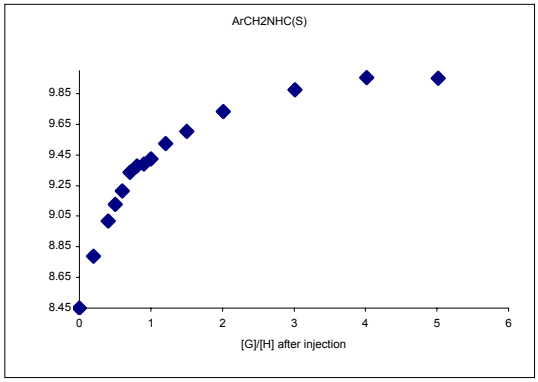
_N_2-Methyl-6-[([3-(benzylamino)-3-oxopropyl]aminocarbothioyl)amino]methyl-2-pyridinecarboxamide 23 and TBA acetate in DMSO

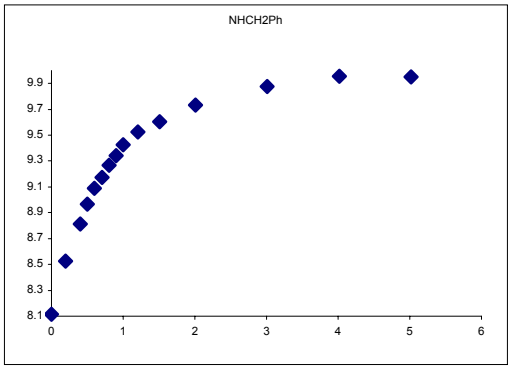
NMR data

[Host]/mM	4.3	Starting volume/µL	600
[Guest]/mM	25.9	K_a(average)/M^{-1}	1740

Volume added /µL	$ArCH_2NHC(S)$	$NHCH_2CH_2$
0	8.4514	8.1154
20	8.7866	8.5253
40	9.0202	8.8120
50	9.1266	8.9677
60	9.2156	9.0909
70	9.3355	9.1735
80	9.3760	9.2672
90	9.3903	9.3435
100	9.4245	9.4245
120	9.5230	9.5230
150	9.6040	9.6040
200	9.7311	9.7311
300	9.8749	9.8749
400	9.9551	9.9551
500	9.9511	9.9511
K_a	1430 M^{-1}	2050 M^{-1}







ITC data

[Host]/mM	1.95	ΔH/kJmol^{-1}	-4.31
[Guest]/mM	78.0	$T\Delta S$/kJmol^{-1}	14.8
K_a/M^{-1}	2.2 x 10^3	ΔG/kJmol^{-1}	-19.1

[G]/[H] after injection	cal/mol of injected G
0.14	-639.52
0.27	-820.88
0.41	-818.21
0.55	-808.37
0.69	-800.23
0.83	-791.46
0.97	-780.77
1.11	-766.85
1.25	-750.47
1.39	-739.20
1.53	-729.74
1.68	-716.38
1.82	-695.91
1.96	-681.28
2.11	-674.62
2.25	-655.45
2.39	-636.97
2.54	-628.15
2.68	-609.90
2.83	-599.97
2.98	-587.93
3.12	-575.26
3.27	-563.55
3.42	-553.26
3.57	-541.80
3.72	-529.72
3.87	-523.22
4.02	-514.86
4.17	-508.76
4.32	-496.10
4.47	-484.09
4.62	-474.49
4.77	-463.85
4.92	-455.07
5.08	-448.81
5.23	-443.83
5.38	-429.97
5.54	-425.60
5.69	-419.74
5.85	-414.23

6.00	-404.08
6.16	-401.34
6.32	-394.21
6.47	-384.81
6.63	-379.08
6.79	-373.09
6.95	-365.56
7.11	-364.21
7.27	-359.39
7.43	-357.17

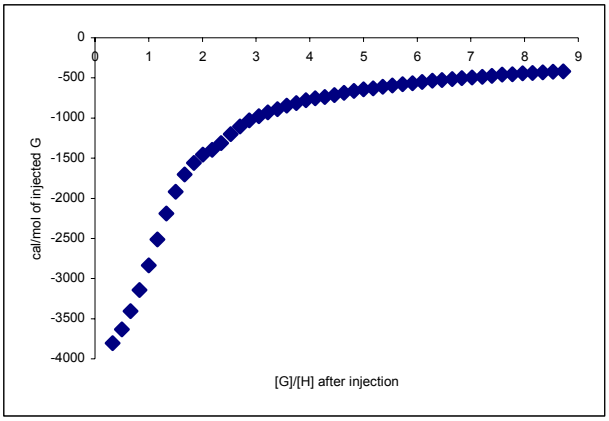
_N_1-Methyl-3-[(ammonio[2-(benzylamino)-2-oxoethyl]aminomethyl)amino]methylbenzamide hexafluorophosphate 27 and TBA acetate in DMSO

ITC data

[Host]/mM	1.00	[Guest]/mM	48.0
K_a^1/M^{-1}	6900	K_a^2/ M^{-1}	130
ΔH^1/kJmol^{-1}	-19.6	ΔH^2/kJmol^{-1}	-51.8
$T\Delta S^1$/kJmol^{-1}	2.3	$T\Delta S^2$/kJmol^{-1}	-39.7
ΔG^1/kJmol^{-1}	-21.9	ΔG^2/kJmol^{-1}	-12.0

[H]/[G] after injection	cal/mol of injected G
0.16	--
0.33	-3803.86
0.50	-3633.58
0.66	-3405.39
0.83	-3142.99
1.00	-2835.03
1.16	-2513.61
1.33	-2190.81
1.50	-1917.11
1.67	-1701.98
1.84	-1558.07
2.01	-1456.14
2.18	-1397.21
2.35	-1312.05
2.53	-1200.59
2.70	-1105.44
2.87	-1030.77
3.05	-978.23
3.22	-930.19
3.40	-891.16
3.57	-847.28
3.75	-811.61
3.93	-778.95
4.10	-752.83
4.28	-739.68
4.46	-714.24
4.64	-687.93
4.82	-663.37
5.00	-641.78
5.18	-629.93
5.36	-608.90
5.54	-593.49

5.73	-578.00
5.91	-566.14
6.09	-550.69
6.28	-533.86
6.46	-524.43
6.65	-512.88
6.83	-501.17
7.02	-493.70
7.21	-484.77
7.39	-472.75
7.58	-459.66
7.77	-453.58
7.96	-441.09
8.15	-438.13
8.34	-432.19
8.53	-424.01
8.72	-418.32
8.91	-408.89



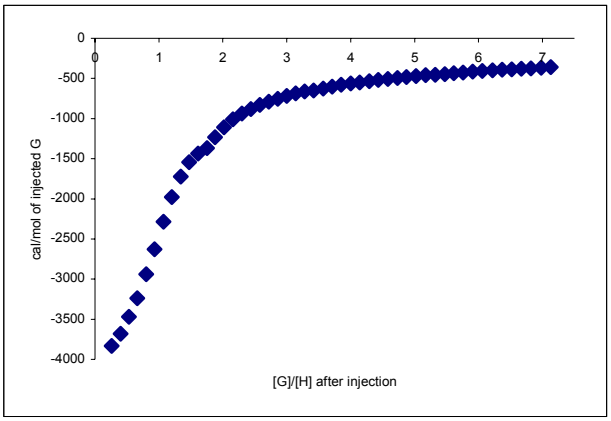
_N_1-Methyl-3-[(ammonio[3-(benzylamino)-3-oxopropyl]aminomethyl)amino]methyl benzamidehexafluorophosphate 28 and TBA acetate in DMSO

ITC data

[Host]/mM	1.25	[Guest]/mM	48.0
K_a^1/M^{-1}	5.3×10^3	K_a^2/ M^{-1}	70
ΔH^1/kJmol^{-1}	-19.4	ΔH^2/kJmol^{-1}	-43.8
$T\Delta S^1$/kJmol^{-1}	1.8	$T\Delta S^2$/kJmol^{-1}	-33.5
ΔG^1/kJmol^{-1}	-21.3	ΔG^2/kJmol^{-1}	-10.4

[H]/[G] after injection	cal/mol of injected G
0.13	--
0.26	-3833.02
0.40	-3679.64
0.53	-3468.25
0.66	-3238.77
0.80	-2939.42
0.93	-2628.23
1.07	-2287.00
1.20	-1976.70
1.34	-1722.09
1.47	-1544.85
1.61	-1436.82
1.75	-1368.01
1.88	-1232.94
2.02	-1108.07
2.16	-1009.39
2.30	-937.17
2.44	-881.18
2.58	-829.86
2.72	-790.22
2.86	-751.86
3.00	-718.03
3.14	-685.65
3.28	-663.54
3.42	-648.30
3.57	-626.64
3.71	-601.32
3.85	-579.90
4.00	-563.09
4.14	-549.27
4.29	-533.89

4.43	-520.15
4.58	-507.79
4.73	-494.01
4.87	-481.05
5.02	-470.80
5.17	-459.82
5.32	-453.51
5.47	-445.04
5.61	-434.55
5.76	-425.78
5.91	-415.71
6.06	-408.62
6.22	-398.35
6.37	-390.79
6.52	-385.44
6.67	-380.18
6.82	-373.69
6.98	-367.56
7.13	-359.50



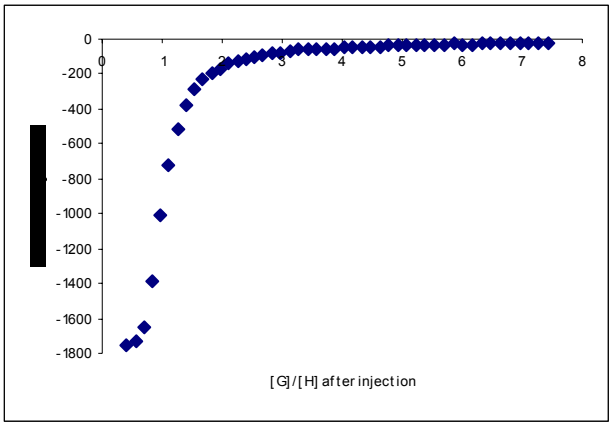
_N_2-Methyl-6-[(ammonio[3-(benzylamino)-3-oxopropyl]aminomethyl)amino]methyl-2-pyridinecarboxamide hexafluorophosphate 33 and TBA acetate in DMSO

ITC data

[Host]/mM	1.17	[Guest]/mM	48.0
K_a^1/M^{-1}	2.2×10^4	$\Delta H^1/kJmol^{-1}$	-8.0
$T\Delta S^1/kJmol^{-1}$	16.8	$\Delta G^1/kJmol^{-1}$	-24.8

[H]/[G] after injection	cal/mol of injected G
0.14	--
0.27	--
0.41	-1759.25
0.55	-1726.12
0.69	-1652.39
0.83	-1389.76
0.97	-1013.43
1.11	-719.70
1.25	-512.77
1.39	-382.22
1.53	-289.09
1.68	-227.40
1.82	-191.63
1.96	-168.05
2.11	-140.79
2.25	-125.74
2.39	-112.07
2.54	-99.00
2.68	-93.86
2.83	-78.51
2.98	-75.67
3.12	-69.38
3.27	-54.92
3.42	-61.13
3.57	-60.00
3.72	-57.71
3.87	-52.46
4.02	-49.37
4.17	-48.60
4.32	-47.69
4.47	-42.04
4.62	-41.44
4.77	-36.06
4.92	-36.09
5.08	-37.50
5.23	-35.82

5.38	-34.40
5.54	-28.81
5.69	-35.26
5.85	-28.43
6.00	-32.19
6.16	-31.92
6.32	-27.99
6.47	-23.07
6.63	-27.37
6.79	-28.21
6.95	-25.68
7.11	-26.57
7.27	-25.86
7.43	-23.99



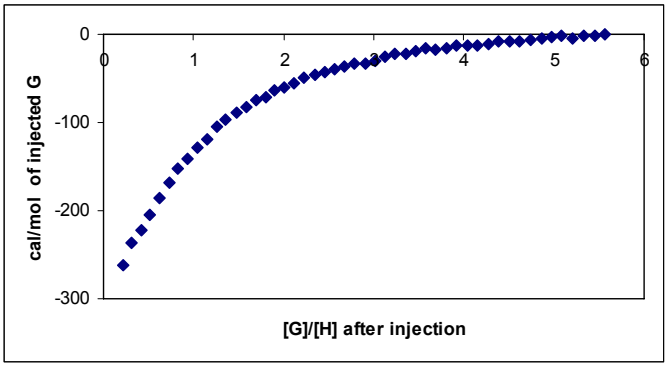
_N_2-Methyl-6-[(ammonio[3-(benzylamino)-3-oxopropyl]aminomethyl)amino]methyl-2-pyridinecarboxamide hexafluorophosphate 33 and TBA acetate in 10%H_2O/DMSO

ITC data

[Host]/mM	1.17	[Guest]/mM	48.0
K_a^1/M^{-1}	5.5×10^3	$\Delta H^1/kJmol^{-1}$	-1.90
$T\Delta S^1/kJmol^{-1}$	19.4	$\Delta G^1/kJmol^{-1}$	-21.3

[G]/[H] after injection	cal/mol of injected G
0.21	-262.03
0.31	-237.14
0.42	-222.56
0.52	-204.50
0.62	-185.53
0.73	-168.40
0.83	-151.72
0.94	-141.43
1.04	-128.26
1.15	-118.70
1.26	-105.15
1.36	-97.27
1.47	-88.34
1.58	-82.67
1.69	-74.87
1.80	-72.03
1.90	-64.05
2.01	-60.40
2.12	-56.14
2.23	-49.96
2.34	-45.51
2.45	-42.62
2.56	-39.69
2.68	-36.94
2.79	-33.83
2.9	-33.43
3.01	-29.46
3.12	-26.03
3.24	-22.34
3.35	-22.16
3.46	-19.45
3.58	-15.38
3.69	-17.00
3.81	-16.19
3.92	-13.18
4.04	-13.02
4.15	-13.06
4.27	-10.99
4.39	-8.21

4.50	-8.04
4.62	-7.16
4.74	-6.07
4.86	-5.32
4.97	-3.28
5.09	-1.38
5.21	-4.02
5.33	-1.44
5.45	-0.86
5.57	0



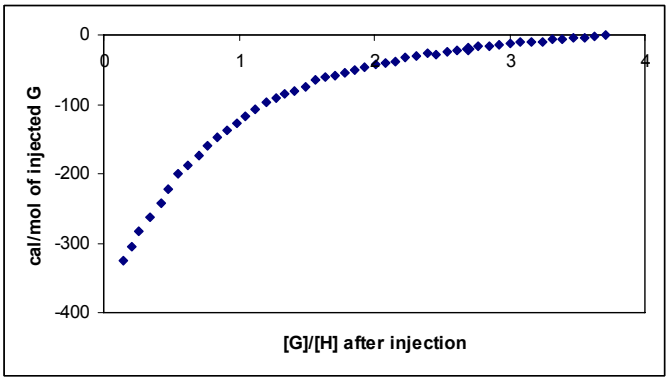
_N_2-Methyl-6-[(ammonio[3-(benzylamino)-3-oxopropyl]aminomethyl)amino]methyl-2-pyridinecarboxamide hexafluorophosphate 33 and TBA acetate in 30%H_2O/DMSO

ITC data

[Host]/mM	1.17	ΔH/kJmol^{-1}	-2.0
[Guest]/mM	48.0	$T\Delta S$/kJmol^{-1}	13.3
K_a/M^{-1}	480	ΔG/kJmol^{-1}	-15.3

[G]/[H] after injection	cal/mol of injected G
0,14	-324,771
0,21	-304,974
0,26	-282,438
0,34	-262,064
0,42	-241,52
0,48	-221,36
0,55	-200,97
0,62	-187,78
0,70	-173,09
0,77	-159,61
0,84	-147,53
0,91	-136,69
0,98	-127,00
1,05	-117,64
1,12	-107,57
1,20	-97,05
1,27	-91,63
1,34	-84,41
1,41	-81,05
1,49	-75,33
1,56	-65,15
1,64	-61,57
1,71	-58,27
1,78	-54,22
1,86	-50,07
1,93	-47,06
2,01	-43,30
2,08	-39,40
2,16	-38,32
2,23	-32,94
2,31	-30,04
2,39	-26,51
2,46	-27,37
2,54	-25,02
2,61	-21,60
2,69	-19,43
2,77	-17,12
2,85	-16,31
2,92	-13,53
3,00	-11,93

3,08	-10,90
3,16	-10,36
3,24	-10,34
3,32	-6,71
3,39	-6,26
3,47	-3,18
3,55	-3,17
3,63	-2,69
3,71	-0,93



Di(benzylamino)methylene]ammonium hexafluorophosphate and TBA acetate in DMSO

ITC data

[Host]/mM	1.00	[Guest]/mM	48.0
K_a^1/M^{-1}	3.1×10^3	K_a^2/ M^{-1}	30
$\Delta H^1/kJmol^{-1}$	-21.8	$\Delta H^2/kJmol^{-1}$	-46.4
$T\Delta S^1/kJmol^{-1}$	-1.8	$T\Delta S^2/kJmol^{-1}$	-37.6
$\Delta G^1/kJmol^{-1}$	-19.9	$\Delta G^2/kJmol^{-1}$	-8.9

[H]/[G] after injection	cal/mol of injected G
0.16	--
0.33	-3684.98
0.50	-3285.25
0.66	-2862.15
0.83	-2450.29
1.00	-2074.87
1.16	-1777.55
1.33	-1607.48
1.50	-1480.68
1.67	-1215.86
1.84	-1034.12
2.01	-901.01
2.18	-804.05
2.35	-728.03
2.53	-667.13
2.70	-612.91
2.87	-564.68
3.05	-524.42
3.22	-494.68
3.40	-461.81
3.57	-439.18
3.75	-418.27
3.93	-385.92
4.10	-383.46
4.28	-363.72
4.46	-351.42
4.64	-338.65
4.82	-323.22
5.00	-315.15
5.18	-313.16

5.36	-295.30
5.54	-282.85
5.73	-270.24
5.91	-267.53
6.09	-260.13
6.28	-253.02
6.46	-250.08
6.65	-238.91
6.83	-238.13
7.02	-227.74
7.21	-219.33
7.39	-215.67
7.58	-209.74
7.77	-201.00
7.96	-197.84
8.15	-193.41
8.34	-189.92
8.53	-186.48
8.72	-181.80
8.91	-178.29