



**HAL**  
open science

## Extending the hydrogen-bonding array in ortho-phenylenediamine based bis-ureas

Philip Alan Gale, Simon Brooks, Mark Light

► **To cite this version:**

Philip Alan Gale, Simon Brooks, Mark Light. Extending the hydrogen-bonding array in ortho-phenylenediamine based bis-ureas. *Supramolecular Chemistry*, 2007, 19 (01-02), pp.9-15. 10.1080/10610270600879076 . hal-00513484

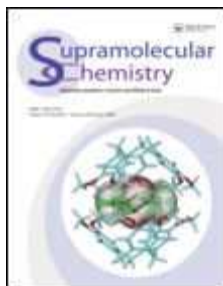
**HAL Id: hal-00513484**

**<https://hal.science/hal-00513484>**

Submitted on 1 Sep 2010

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



### Extending the hydrogen-bonding array in ortho-phenylenediamine based bis-ureas

Journal:	<i>Supramolecular Chemistry</i>
Manuscript ID:	GSCH-2006-0022.R1
Manuscript Type:	Special Issue Paper
Date Submitted by the Author:	08-Jun-2006
Complete List of Authors:	Gale, Philip; University of Southampton, School of Chemistry Brooks, Simon; University of Southampton Light, Mark; University of Southampton
Keywords:	Anion receptors, amides, ureas, crystallography
<p>Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.</p> <p>Figure4.cdx Figure5.cdx Structure of 1.cdx Scheme1.cdx Scheme2.cdx</p>	



1  
2  
3 FOR ISSC/ISMC SPECIAL ISSUE  
4  
5  
6  
7  
8

9 Extending the hydrogen-bonding array in *ortho*-phenylenediamine based  
10 bis-ureas  
11  
12

13  
14  
15  
16 Simon J. Brooks, Philip A. Gale\*, and Mark E. Light  
17

18  
19  
20 School of Chemistry, University of Southampton, Southampton, SO17 1BJ, UK.  
21  
22  
23

24  
25  
26 Abstract  
27

28 Two new *ortho*-phenylenediamine based bis-urea compounds have been synthesised  
29 with pendant amide groups. The stability constants of the new compounds with a  
30 variety of anionic guests have been measured by <sup>1</sup>H NMR titration techniques and  
31 compared to the parent bis-urea. The X-ray crystal structure of the acetate and  
32 benzoate complexes of a bis-amide functionalised system have been solved and reveal  
33 the receptor forming a dimer with two anions bound at the termini of the hydrogen  
34 bonded assembly.  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Keywords

Anion receptors, amides, urea, crystallography

Amides and urea groups have been employed in a wide variety of anion receptor systems over recent years.<sup>1</sup> We have been interested in the anion complexation properties of a variety of simple linear hydrogen bond donor molecules.<sup>2</sup> In 2000,

1  
2  
3 Reinhoudt and co-workers reported the anion binding ability of cyclic and acyclic  
4 receptors containing two *ortho*-phenylenediamine based bis-urea units with the  
5 receptor showing selectivity for dihydrogen phosphate anions in DMSO solution.<sup>3</sup>  
6  
7  
8 We have synthesised a variety of simple acyclic *ortho*-phenylenediamine systems e.g.  
9  
10  
11 **1** and demonstrated a general selectivity of these receptors for carboxylates in DMSO-  
12  
13 *d*<sub>6</sub>/0.5% water solution.<sup>4-6</sup> In this short paper we report the synthesis of two new bis-  
14  
15 urea compounds **2** and **3** (Schemes 1 and 2) that have appended amide groups. We  
16  
17 wished to ascertain whether the extra hydrogen bond donor groups in these receptors  
18  
19 would contribute to the stability of the oxo-anion complexes.  
20  
21  
22  
23  
24  
25  
26

27 **Insert structure of 1 here**

## 28 29 30 31 32 33 34 **Experimental**

35  
36  
37  
38 **Compound 6:** 1,1'-(1,2-Phenylene)bis(3-(2-aminophenyl)urea)

39  
40  
41  
42  
43 10% Pd/C (0.04 g, 0.1 mmol) and hydrazine monohydrate (1.4 mL) was added to a  
44 stirring suspension of compound **5** (1.33 g, 3.0 mmol) in EtOH (200 mL) and the  
45 reaction was heated to reflux for 16 hours under a nitrogen atmosphere. The reaction  
46 was then removed from reflux and allowed to cool to room temperature and the  
47 resulting white precipitate and Pd/C removed *via* filtration. The product was  
48 redissolved in a small volume of DMF (5 mL) and filtered to remove Pd/C. Removal  
49 of DMF under reduced pressure yielded a white precipitate in a green oil. The  
50 product was removed *via* filtration and washed with H<sub>2</sub>O (3 × 10 mL) followed by  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

methanol (3 × 10 mL) before drying under high vacuum affording the product as a white powder. Mass of product = 0.88 g. Yield = 78 %. <sup>1</sup>H NMR - 300 MHz (DMSO-*d*<sub>6</sub>) δ (ppm): 8.37 (s, 2H, urea NH), 8.29 (s, 2H, urea NH), 7.64 (dd, 2H, J = 5.6 & 3.4 Hz, ArH), 7.36 (d, 2H, J = 7.9 Hz, ArH), 7.02 (dd, 2H, J = 5.6 & 3.8 Hz, ArH), 6.82 (t, 2H, J = 7.1 Hz, ArH), 6.71 (d, 2H, J = 7.5 Hz, ArH), 6.55 (t, 2H, J = 7.5 Hz, ArH), 4.90 (bs, 4H, NH<sub>2</sub>). <sup>13</sup>C NMR – 75 MHz (DMSO-*d*<sub>6</sub>) δ (ppm): 153.7 (CO), 140.8 (C), 131.1 (CH), 124.5 (CH), 124.2 (C), 123.7 (C), 123.2 (CH), 116.4 (CH), 115.5 (CH). IR (cm<sup>-1</sup>): 3353, 3295, 1728, 1664, 1579, 1492, 1431, 1338, 1262, 1184, 1141. LRMS (ES<sup>+</sup>): 376.9 [M+H]<sup>+</sup>, 398.9 [M+Na]<sup>+</sup>, 439.9 [M+Na+MeCN]<sup>+</sup>, 753.1 [2M+H]<sup>+</sup>, 775.1 [2M+Na]<sup>+</sup>, 1129.2 [3M+Na]<sup>+</sup>, 1152.3 [3M+Na]<sup>+</sup>. HRMS (ES<sup>+</sup>): Calculated Mass = 377.1721. Observed Mass = 377.1721. Δ = 0.06 ppm.

**Compound 3:** *N,N'*-(2,2'-(1,2-Phenylenebis(azanediyl))bis(oxomethylene)bis(azanediyl))bis(2,1-phenylene))dibenzamide

Benzoyl chloride (0.74 mL, 6.4 mmol) in DMF (dry) was added dropwise over a 15 minute period and to a stirred solution of compound **6** (1.20 g, 3.2 mmol), triethylamine (0.76 mL, 7.1 mmol) and DMAP (0.01g, cat.) in anhydrous DMF (50 mL) under a nitrogen atmosphere. The reaction was stirred at room temperature for 18 hours before being filtered to remove precipitated triethylamine hydrochloride. The remaining DMF was removed *in vacuo* to give an oily brown residue that was redissolved in dichloromethane (50 mL). The solution was washed with water (3 × 50 mL) and the organic phase retained, dried over anhydrous MgSO<sub>4</sub> and filtered before the removal of solvent *in vacuo*. The resulting brown solid was washed with ethyl

1  
2  
3 acetate (10 mL), and then hot ethyl acetate (3 × 10 mL), giving a white solid, dried  
4  
5 under high vacuum. Mass of product = 0.55 g. Yield = 29 %. <sup>1</sup>H NMR 300 MHz  
6  
7 (DMSO-*d*<sub>6</sub>) δ (ppm): 10.02 (s, 2H, NH), 8.58 (s, 2H, NH), 8.44 (s, 2H, NH), 8.00  
8  
9 (app d, 4H, J = 7.0 Hz, ArH), 7.77 (dd, 2H, J = 8.0 & 1.0 Hz, ArH), 7.50 (m, 10H,  
10  
11 ArH), 7.20 (td, 2H, J = 7.9 & 1.1 Hz, ArH), 7.04 (m, 4H, ArH). <sup>13</sup>C NMR - 75 MHz  
12  
13 (DMSO-*d*<sub>6</sub>) δ (ppm): 165.6 (CO), 153.8 (CO), 134.2 (C), 133.9 (C), 131.1 (CH),  
14  
15 128.6 (C), 128.4 (CH), 127.7 (CH), 126.9 (CH), 126.1 (CH), 124.0 (CH), 123.0 (CH),  
16  
17 122.5 (CH). IR (cm<sup>-1</sup>): 3288, 3057, 1654, 1596, 1507, 1439, 1309, 1206, 757. LRMS  
18  
19 (ES): 619.3 [M+Cl]<sup>-</sup>, 697.2 [M+TFA-H]<sup>-</sup>, 1203.6 [2M+Cl]<sup>-</sup>, 1281.1 [2M+TFA-H]<sup>-</sup>.  
20  
21 Microanalysis for C<sub>34</sub>H<sub>28</sub>N<sub>6</sub>O<sub>4</sub>. Expected (%) C = 69.85 H = 4.83 N = 14.37. Found  
22  
23 (%) C = 69.54 H = 4.81 N = 14.38.  
24  
25  
26  
27  
28  
29  
30  
31

32 **Compound** **4:** diethyl 3,3'-(1,2-  
33 phenylenebis(azanediyl))bis(oxomethylene)bis(azanediyl)dibenzoate  
34  
35

36  
37 3-Ethylisocyanatobenzoate (2.16 mL, 13.1 mmol) was added dropwise to a stirring  
38  
39 solution of *ortho*-phenylenediamine (0.71 g, 6.5 mmol) in dry dichloromethane (150  
40  
41 mL). Within 5 minutes of addition the reaction mixture formed a viscous gel. At  
42  
43 this point MeOH (5 mL) was then added to dissolve the gel. The reaction was left at  
44  
45 room temperature for 16 hours, after which solvent was removed from reaction *via*  
46  
47 rotary evaporation. The product was recrystallized from boiling MeOH before  
48  
49 washing with Et<sub>2</sub>O (3 × 20 mL) and drying under high vacuum. The product was  
50  
51 isolated as a white solid. Mass of product = 2.74 g. Yield = 86 %. <sup>1</sup>H NMR 300  
52  
53 MHz (DMSO-*d*<sub>6</sub>) δ (ppm): 9.35 (s, 2H, NH), 8.15 (s, 2H, ArH), 8.07 (s, 2H, NH),  
54  
55 7.70 (m, 2H, ArH), 7.60 (m, 2H, ArH), 7.55 (m, 2H, ArH), 7.41 (t, 2H, J = 7.9 Hz,  
56  
57 ArH), 7.11 (dd, 2H, J = 6.0 & 3.8 Hz, ArH), 4.30 (q, 4H, J = 7.1 Hz, CH<sub>2</sub>), 1.31 (t,  
58  
59  
60

6H,  $J = 7.1$  Hz, CH<sub>3</sub>). <sup>13</sup>C NMR - 100 MHz (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm): 166.2 (CO), 153.7 (CO), 140.7 (C), 131.8 (C), 130.9 (C), 129.6 (CH), 124.7 (CH), 124.7 (CH), 123.1 (CH), 122.9 (CH), 119.0 (CH), 61.2 (CH<sub>2</sub>), 14.6 (CH<sub>3</sub>). IR (cm<sup>-1</sup>): 3351, 3245, 2980, 1724, 1652, 1559, 1458, 1280, 1251, 1217, 1103, 752. LRMS (ES): 491.3 [M+H]<sup>+</sup>, 513.3 [M+Na]<sup>+</sup>, 100.3 [2M+Na]<sup>+</sup>. Microanalysis for C<sub>26</sub>H<sub>26</sub>N<sub>4</sub>O<sub>6</sub>. Expected (%) C = 63.66 H = 5.34 N = 11.42. Found (%) C = 63.46 H = 5.34 N = 11.34.

**Compound 2: 3,3'-(1,2-Phenylenebis(azanediyl))bis(oxomethylene)bis(azanediyl)bis(*N*-phenylbenzamide)**

Aniline (0.40 mL, 4.1 mmol) was dissolved in dry dichloromethane (40 mL) and 2M trimethylaluminium in hexanes (2.03 mL, 4.06 mmol) added dropwise under a nitrogen atmosphere. Reagents were left stirring under nitrogen for 30 minutes at which time compound **4** (1.00 g, 2.03 mmol) was added to the reaction mixture. The reaction was heated at reflux for 5 days under a nitrogen atmosphere. The reaction was allowed to cool and 2M aqueous HCl solution was then added until reaction ceased bubbling resulting in the precipitation of the product. A further 20 mL of water was added and the mixture stirred for a further 15 minutes. The organic phase and precipitate were washed with water (3 × 50 mL). The organic phase containing the precipitate was then filtered and the white precipitate washed with Et<sub>2</sub>O (3 × 20 mL) before drying under high vacuum. Mass of product = 0.94 g. Yield = 94 %. <sup>1</sup>H NMR 300 MHz (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm): 10.22 (s, 2H, NH), 9.33 (s, 2H, NH), 8.15 (s, 2H, NH), 8.00 (s, 2H, ArH), 7.76 (m, 6H, ArH), 7.63 (m, 2H, ArH), 7.56 (m, 2H, ArH), 7.43 (t, 2H,  $J = 7.7$  Hz, ArH), 7.35 (t, 4H,  $J = 7.7$  Hz, ArH), 7.11 (m, 4H, ArH). <sup>13</sup>C NMR - 75 MHz (DMSO-*d*<sub>6</sub>)  $\delta$  (ppm): 165.6 (CO), 153.2 (CO), 140.1 (C), 139.2

(C), 135.8 (C), 131.3 (C), 128.8 (CH), 128.6 (CH), 124.2 (CH), 124.1 (CH), 123.6 (CH), 121.1 (CH), 120.8 (CH), 120.3 (CH), 117.6 (CH). IR (cm<sup>-1</sup>): 3351, 3250, 2980, 1724, 1648, 1555, 1462, 1280, 1217, 1103, 1026, 752. LRMS (ES): 619.1 [M+Cl]<sup>-</sup>, 696.9 [M+TFA-H]<sup>-</sup>, 1203.4 [2M+Cl]<sup>-</sup>, 1281.3 [2M+TFA-H]<sup>-</sup>, 1787.9 [3M+Cl]<sup>-</sup>. Microanalysis for C<sub>34</sub>H<sub>28</sub>N<sub>6</sub>O<sub>4</sub> + 0.4 CH<sub>2</sub>Cl<sub>2</sub>. Expected (%) C = 66.79 H = 4.69 N = 13.59. Found (%) C = 66.60 H = 4.90 N = 13.58.

#### X-ray crystallography

Cell dimensions and intensity data were recorded at 120K, using a Bruker Nonius KappaCCD area detector diffractometer mounted at the window of a rotating Mo anode ( $\lambda(\text{Mo-K}\alpha) = 0.71073\text{\AA}$ ). The crystal-to-detector distance was 30mm and  $\phi$  and  $\Omega$  scans were carried out to fill the asymmetric unit. Data collection and processing were carried out using the programs COLLECT<sup>8</sup>, and DENZO<sup>9</sup> and an empirical absorption correction was applied using SADABS.<sup>10</sup>

The structures were solved via direct methods<sup>11</sup> and refined by full matrix least squares on  $F^2$ . Non-hydrogen atoms were refined anisotropically and hydrogen atoms were treated using a riding model. The number of observed reflections was less than 50% and this is a contributing factor to the slightly high R-factors.

Crystal data for compound **3**: C<sub>34</sub>H<sub>28</sub>N<sub>6</sub>O<sub>4</sub>, Mr = 584.62, T = 120(2) K, monoclinic, space group  $P2_1/c$ ,  $a = 9.2368(5)$ ,  $b = 27.4133(16)$ ,  $c = 11.6115(7)$  Å,  $\beta = 96.593(2)^\circ$ ,  $V = 2920.7(3)$  Å<sup>3</sup>,  $\rho_{\text{calc}} = 1.330$  g cm<sup>-3</sup>,  $\mu = 0.090$  mm<sup>-1</sup>, Z = 4, reflections collected: 26187, independent reflections: 6645 ( $R_{\text{int}} = 0.0420$ ), final R indices [ $I > 2\sigma I$ ]: R1 =



0.0415,  $wR2 = 0.0980$ ,  $R$  indices (all data):  $R1 = 0.0635$ .  $wR2 = 0.1085$ . CCDC 607431.

Compound **3** – tetrabutylammonium acetate complex:  $C_{52}H_{67}N_7O_6$ ,  $Mr = 886.13$ ,  $T = 120(2)$  K, triclinic, space group  $P-1$ ,  $a = 13.3008(4)$ ,  $b = 14.9187(4)$ ,  $c = 25.3629(7)$  Å,  $\alpha = 97.297(2)$ ,  $\beta = 96.686(1)$ ,  $\gamma = 97.262(2)^\circ$ ,  $V = 4906.9(2)$  Å<sup>3</sup>,  $\rho_{\text{calc}} = 1.199$  g cm<sup>-3</sup>,  $\mu = 0.079$  mm<sup>-1</sup>,  $Z = 4$ , reflections collected: 88632, independent reflections: 21661 ( $R_{\text{int}} = 0.1139$ ), final  $R$  indices [ $I > 2\sigma I$ ]:  $R1 = 0.0914$ ,  $wR2 = 0.1778$ ,  $R$  indices (all data):  $R1 = 0.1995$ .  $wR2 = 0.2171$ . CCDC 607429

Compound **3** – tetrabutylammonium benzoate complex:  $C_{57}H_{69}N_7O_6$ ,  $Mr = 948.19$ ,  $T = 120(2)$  K, triclinic, space group  $P-1$ ,  $a = 9.2831(3)$ ,  $b = 10.9968(6)$ ,  $c = 24.9522(13)$  Å,  $\alpha = 91.299(2)$ ,  $\beta = 92.310(3)$ ,  $\gamma = 97.775(3)^\circ$ ,  $V = 2520.7(2)$  Å<sup>3</sup>,  $\rho_{\text{calc}} = 1.249$  g cm<sup>-3</sup>,  $\mu = 0.082$  mm<sup>-1</sup>,  $Z = 2$ , reflections collected: 40028, independent reflections: 11395 ( $R_{\text{int}} = 0.1568$ ), final  $R$  indices [ $I > 2\sigma I$ ]:  $R1 = 0.0809$ ,  $wR2 = 0.1712$ ,  $R$  indices (all data):  $R1 = 0.2068$ .  $wR2 = 0.2162$ . CCDC 607430

## Results and Discussion

Compound **4** was synthesised by reaction of 3-ethylisocyanatobenzoate with *ortho*-phenylenediamine in dry dichloromethane. Reaction of this compound with the aluminium amide<sup>7</sup> species resulting from the reaction of aniline and trimethylaluminium afforded compound **2**. (Scheme 1).

### Scheme 1 (i) Aniline, $AlMe_3/CH_2Cl_2$ /hexane

Compound **5** was synthesised according to literature methods.<sup>5</sup> This compound was reduced by addition of Pd/C and hydrazine monohydrate in ethanol affording compound **6**. This was coupled to benzoyl chloride to afford the bis-amide **3**.

**Scheme 2** (i) Pd/C, hydrazine (ii) benzoyl chloride, Et<sub>3</sub>N, DMAP (cat), DMF.

Crystals of compound **3** were grown from a DMSO solution of the receptor. The structure of the receptor was elucidated by single crystal X-ray diffraction and is shown in Figure 1. The molecule forms chains along the *a*-axis via amide NH<sup>+</sup>amide O and urea NH<sup>+</sup>urea OC hydrogen bonds (Figure 2).

Figure 1 The X-ray crystal structure of compound **3**.

Figure 2 The hydrogen-bonded chain in crystals of compound **3** extending along the *a* axis in the solid-state

<sup>1</sup>H NMR titrations were performed with compounds **2** and **3** and a variety of putative anionic guests (as tetrabutylammonium salts) in DMSO-*d*<sub>6</sub>/0.5% water at 298K. The NMR titration curves for compound **2** are shown in Figure 3. Stability constants were determined using the EQNMR computer program (Table 1).<sup>12</sup> Compound **2** was found to have very similar affinities for anions as the parent compound **1** with the exception that dihydrogen phosphate is bound with a stability constant approximately three times more strongly by compound **2** than compound **1**. This may be due to the participation of the terminal amide groups in dihydrogen phosphate complexation but not in benzoate complexation. Proposed structures for these complexes are shown in Figure 4.

1  
2  
3 Figure 3  $^1\text{H}$  NMR titration curves of compound **2** (central urea NH) upon addition of  
4  
5 anions as tetrabutylammonium salts in  $\text{DMSO-d}_6/0.5\%$  water solution.  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For Peer Review Only

Anion	Stability constants K (M <sup>-1</sup> ) β (M <sup>-2</sup> )		
	<b>1</b>	<b>2<sup>a</sup></b>	<b>3</b>
Cl <sup>-</sup>	43	54	17
HSO <sub>4</sub> <sup>-</sup>	10	12	-
H <sub>2</sub> PO <sub>4</sub> <sup>-</sup>	732	2290	K <sub>1</sub> = 7780 K <sub>2</sub> = 24 β <sub>2</sub> = 185000
CH <sub>3</sub> CO <sub>2</sub> <sup>-</sup>	3210	3200	K <sub>1</sub> = 6010 K <sub>2</sub> = <10 β <sub>2</sub> = 55230
C <sub>6</sub> H <sub>5</sub> CO <sub>2</sub> <sup>-</sup>	1330	974	K <sub>1</sub> = 10110 K <sub>2</sub> = <10 β <sub>2</sub> = 16554

a Non-random residual errors in the fitting of the data for oxo-anions with compound **2** is evidence that leads us to suggest that other stoichiometries may be present in solution. However it was found that the most satisfactory fit that could be obtained was to a 1:1 binding model.

Table 1 Stability constants of compounds **1**, **2** and **3** with anionic guests added as tetrabutylammonium salts in DMSO-d<sub>6</sub>/0.5% water solution at 298K. Errors in fitting estimated < 15%.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

Figure 4 Proposed structures of the complexes of a) benzoate and b) dihydrogen phosphate with compound **2**.

Compound **3** exhibits a higher affinity for oxo-anions than compound **2** and also a propensity to form 1:2 receptor:anion complexes albeit with low  $K_2$  values. Unfortunately for solubility reasons studies were limited to DMSO- $d_6$ /0.5% water solutions and so low variable temperature NMR experiments could not be performed to help elucidate the structure of the complex in solution. Figure 5 shows possible structures for solution state complexes with benzoate. The high  $K_1$  values lead us to suggest that complex a) predominates in solution at lower anion concentrations.

Figure 5 Possible binding modes of benzoate to compound **3** in a) and b) 1:1 stoichiometry and c) and d) 1:2 stoichiometry.

Crystals of the acetate and benzoate complexes of compound **3** were obtained by slow evaporation of an acetonitrile solution of the receptor in the presence of the excess tetrabutylammonium anion salt. The structures were elucidated by X-ray crystallography (Figures 6 and 7) and reveal that both complexes adopt a similar arrangement in the solid-state which can be regarded as a dimer formed by complexes

of type b) in Figure 5. The anions are bound at the ends of the dimer with the NH and OC group which are not involved in intramolecular hydrogen bonding in Figure 5b forming a cyclic hydrogen bonding array with another receptor. Hydrogen bonding interactions in the two complexes are tabulated in Tables 2 (acetate) and 3 (benzoate).

Figure 6 The X-ray crystal structure of the tetrabutylammonium acetate complex of receptor **3** (counter cation and non-acidic hydrogen atoms omitted for clarity) showing one of the dimers present in the unit cell binding two acetate anions.

Figure 7 The X-ray crystal structure of the tetrabutylammonium benzoate complex of receptor **3** (counter cation and non-acidic hydrogen atoms omitted for clarity) the dimers present in the unit cell binding two benzoate anions.

**Table 2.** Hydrogen bonds lengths and angles in the acetate complex of compound **3**. [Å and °]

<i>D</i> –H... <i>A</i>	<i>d</i> ( <i>D</i> –H)	<i>d</i> (H... <i>A</i> )	<i>d</i> ( <i>D</i> ... <i>A</i> )	∠( <i>DHA</i> )
N101–H101...O102	0.88	1.92	2.683(3)	143.7
N203–H203...O203	0.88	2.01	2.738(4)	139.8
N103–H103...O103	0.88	2.01	2.737(4)	138.8
N104–H104...O502	0.88	2.05	2.780(3)	139.8
N105–H105...O501	0.88	1.97	2.837(4)	167.8
N106–H106...O501	0.88	2.13	2.954(4)	156.5
N201–H201...O202	0.88	1.92	2.682(3)	143.8
N102–H102...O101 <sup>i</sup>	0.88	2.06	2.897(3)	158.9
N202–H202...O201 <sup>ii</sup>	0.88	2.10	2.924(4)	155.0
N204–H204...O602 <sup>iii</sup>	0.88	2.05	2.803(4)	143.5
N205–H205...O601 <sup>iii</sup>	0.88	1.89	2.750(3)	165.1
N206–H206...O601 <sup>iii</sup>	0.88	2.12	2.953(4)	158.5

Symmetry transformations used to generate equivalent atoms:

(i)  $-x, -y+1, -z$  (ii)  $-x+1, -y+2, -z$  (iii)  $x, y+1, z$

**Table 3.** Hydrogen bonds lengths and angles in the benzoate complex of compound **3**. [ $\text{\AA}$  and  $^\circ$ ]

$D-H\cdots A$	$d(D-H)$	$d(H\cdots A)$	$d(D\cdots A)$	$\angle(DHA)$
N1-H91...O2	0.88	1.94	2.698(4)	142.6
N2-H92...O1 <sup>i</sup>	0.88	2.22	3.030(4)	152.4
N3-H93...O3	0.88	1.98	2.709(4)	139.8
N4-H94...O6	0.88	1.99	2.761(4)	145.4
N5-H95...O5	0.88	1.97	2.830(4)	165.3
N6-H96...O5	0.88	2.18	3.016(4)	159.1

Symmetry transformations used to generate equivalent atoms:

(i)  $-x, -y, -z$

## Conclusion

Extending the hydrogen bond donor array has in the case of compound **3** resulted in a receptor with an enhanced affinity for anionic guests. X-ray crystallography has shown that in the solid-state carboxylate complexes of compound **3** dimerize with each anion bound by two urea and one amide hydrogen bond. We are continuing to investigate the anion binding properties of simple linear amidoureas and macrocyclic systems. These results will be published shortly.

## Acknowledgements

We would like thank the EPSRC for a DTA studentship (SJB) and for use of the crystallographic facilities at the University of Southampton.

## References

1. Sessler, J.L.; Gale, P.A.; Cho, W.S. *Anion Receptor Chemistry (Monographs in Supramolecular Chemistry)* Ed. Stoddart, J.F.; Royal Society of Chemistry, Cambridge UK, 2006; Schmidtchen, F.P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609; Antonisse, M.M.G.; Reinhoudt, D.N. *Chem. Commun.* **1998**, 443; Pascal Jr., R.A.; Spergel, J.; van Engen, D. *Tetrahedron Lett.* **1986**, *27*, 4099; Valiyaveetil, S.; Engbersen, J.F.J.; Verboom, W.; Reinhoudt, D.N. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 900; Beer, P.D. *Acc. Chem. Rec.* **1998**, *31*, 71; Kavallieratos, K.; Bertao, C.M.; Crabtree, R.H. *J. Org. Chem.* **1999**, *64*, 1675; Bondy, C.R.; Gale, P.A.; Loeb, S.J. *Chem. Commun.* **2001**, 729; Choi, K.; Hamilton, A.D. *J. Am. Chem. Soc.* **2001**, *123*, 2456; Hossain, Md.A.; Llinares, J.M.; Powell, D.; Bowman-James, K. *Inorg. Chem.* **2001**, *40*, 2936; Smith, P.J.; Reddington, M.V.; Wilcox, C.S. *Tetrahedron Lett.* **1992**, *33*, 6085; Hughes, M.P.; Smith, B.D. *J. Org. Chem.* **1997**, *62*, 4492; Pernía, G.J.; Kilburn, J.D.; Essex, J.W.; Mortishire-Smith, R.J.; Rowley, M. *J. Am. Chem. Soc.* **1996**, *118*, 10220.
2. Gale, P.A. *Acc. Chem. Res.* in press; Gale, P.A. *Chem. Commun.* **2005**, 3761.
3. Snellink-Ruël, B.H.M.; Antonisse, M.M.G.; Engbersen, J.F.J.; Timmerman P.; Reinhoudt, D.N. *Eur. J. Org. Chem.* **2000**, 165.
4. Brooks, S.J.; Gale, P.A.; Light, M.E.; *Chem. Commun.* **2005**, 4696.
5. Brooks, S.J.; Edwards, P.R.; Gale, P.A.; Light, M.E. *New. J. Chem.* **2006**, *30*, 65.
6. Brooks, S.J.; Gale, P.A.; Light, M.E.; *CrystEngComm* **2005**, *7*, 586.
7. Basha, A.; Lipton, M.; Weinreb, S. M. *Tetrahedron Lett.* **1977**, *48*, 4171.
8. COLLECT data collection software, Nonius B.V., 1998.



- 1  
2  
3 9. Otwinowski, Z.; Minor, W. *Methods in Enzymology*, Volume 276:  
4  
5 Macromolecular Crystallography, Part A, Eds., Carter Jr., C.W.; Sweet, R.M.  
6  
7 Academic Press. **1997**, pp.307.  
8  
9
- 10 10. Sheldrick, G. M. SADABS - Bruker Nonius area detector scaling and  
11  
12 absorption correction - V2.10.  
13  
14
- 15 11. SHELX97: Programs for Crystal Structure Analysis (Release 97-2). Sheldrick,  
16  
17 G.M. Institut für Anorganische Chemie der Universität, Tammanstrasse 4, D-  
18  
19 3400 Göttingen, Germany, 1998.  
20  
21
- 22 12. Hynes, M.J. *J. Chem. Soc. Dalton Trans.*, **1993**, 311.  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

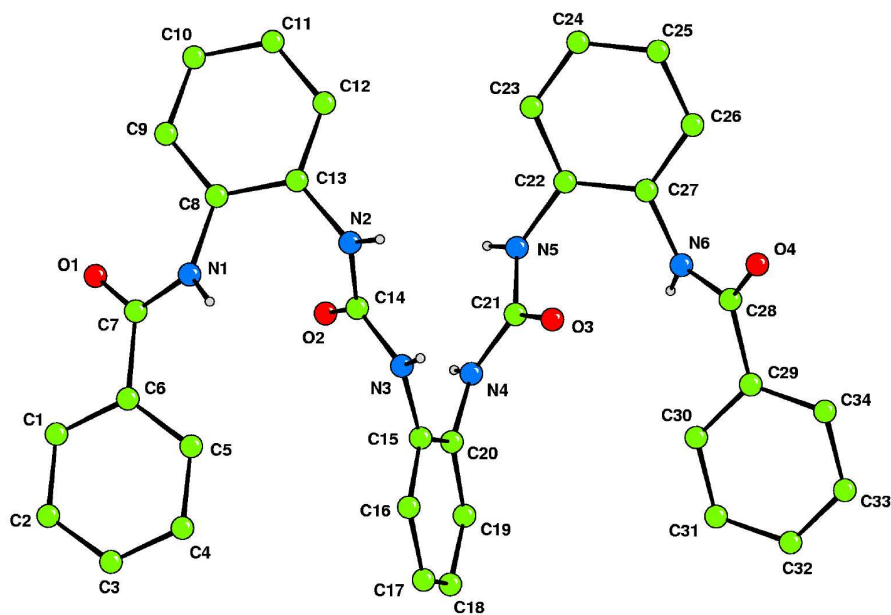


Figure 1 The X-ray crystal structure of compound 3.  
146x101mm (300 x 300 DPI)

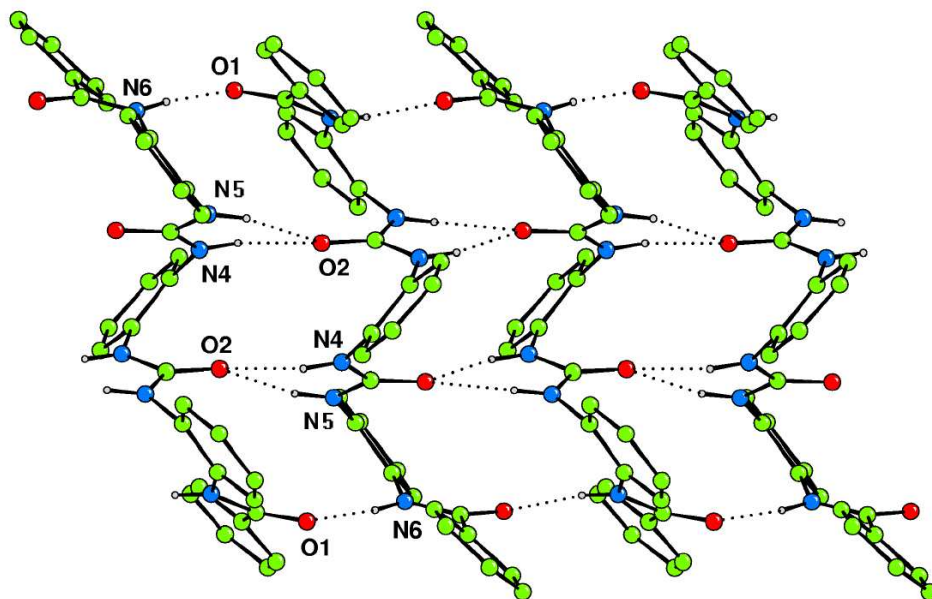


Figure 2 The hydrogen-bonded chain in crystals of compound 3 extending along the a axis in the solid-state  
98x60mm (300 x 300 DPI)

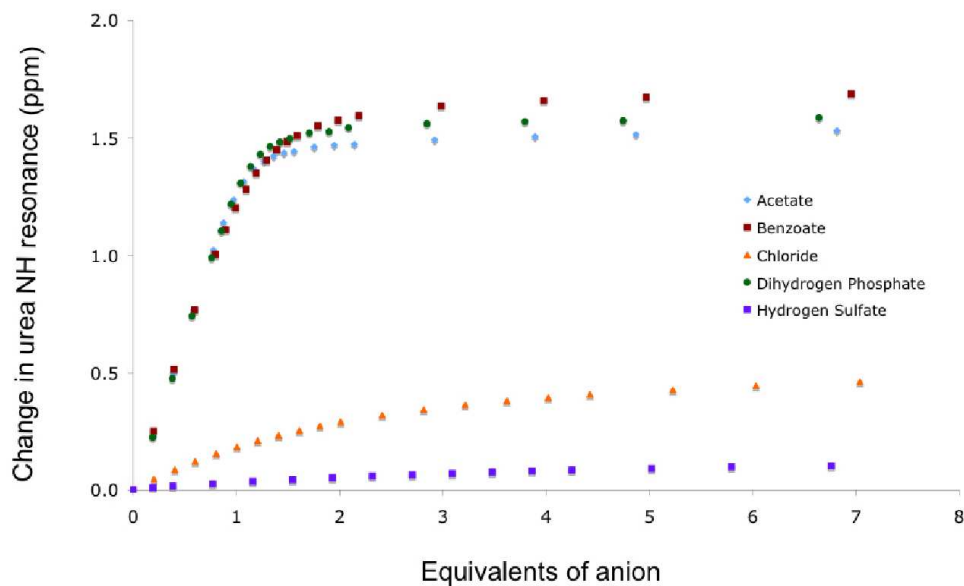


Figure 3  $^1\text{H}$  NMR titration curves of compound 2 (central urea NH) upon addition of anions as tetrabutylammonium salts in  $\text{DMSO-d}_6/0.5\%$  water solution.  
111x68mm (300 x 300 DPI)

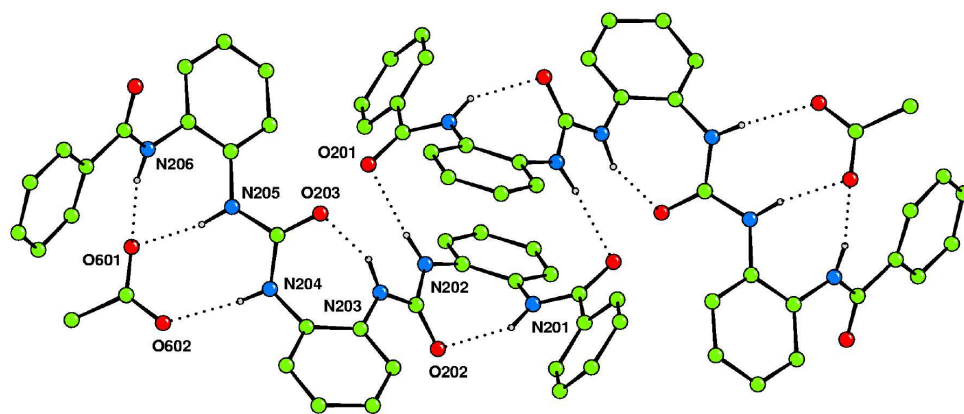


Figure 6 The X-ray crystal structure of the tetrabutylammonium acetate complex of receptor 3 (counter cation and non-acidic hydrogen atoms omitted for clarity) showing one of the dimers present in the unit cell binding two acetate anions.  
156x67mm (300 x 300 DPI)

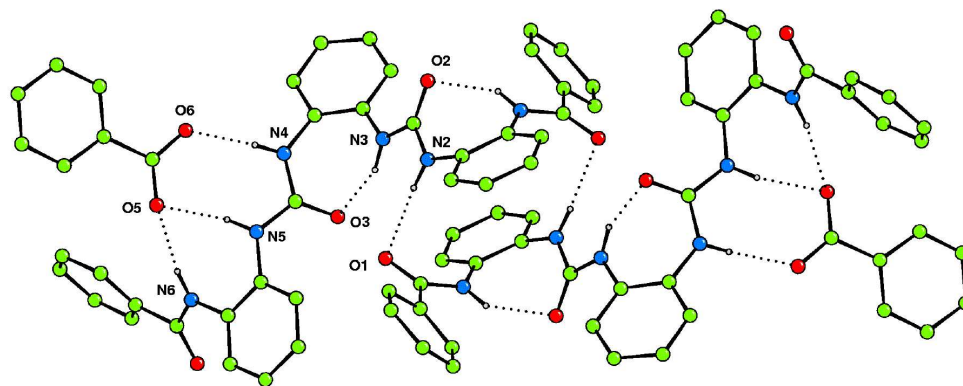


Figure 7 The X-ray crystal structure of the tetrabutylammonium benzoate complex of receptor 3 (counter cation and non-acidic hydrogen atoms omitted for clarity) the dimers present in the unit cell binding two benzoate anions.  
156x61mm (300 x 300 DPI)

Extending the hydrogen-bonding array in *ortho*-phenylenediamine based  
bis-ureas

Simon J. Brooks, Philip A. Gale\*, and Mark E. Light

School of Chemistry, University of Southampton, Southampton, SO17 1BJ, UK.

Supplementary information

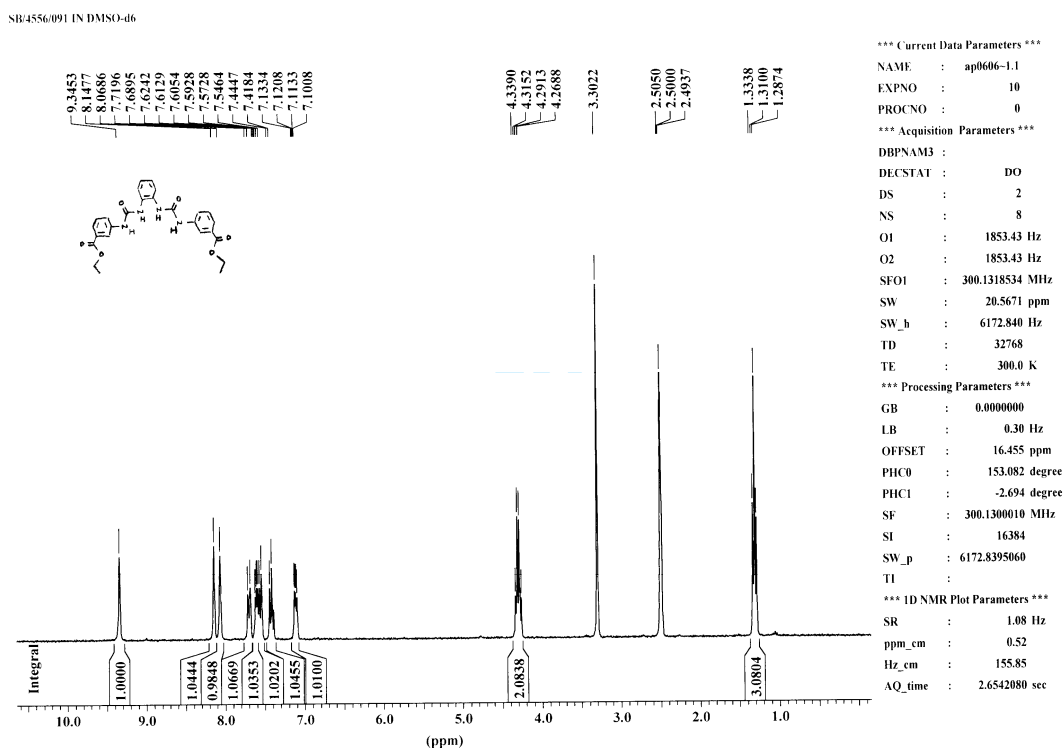


Figure S1  $^1\text{H}$  NMR of compound 4 in DMSO-d<sub>6</sub>

2

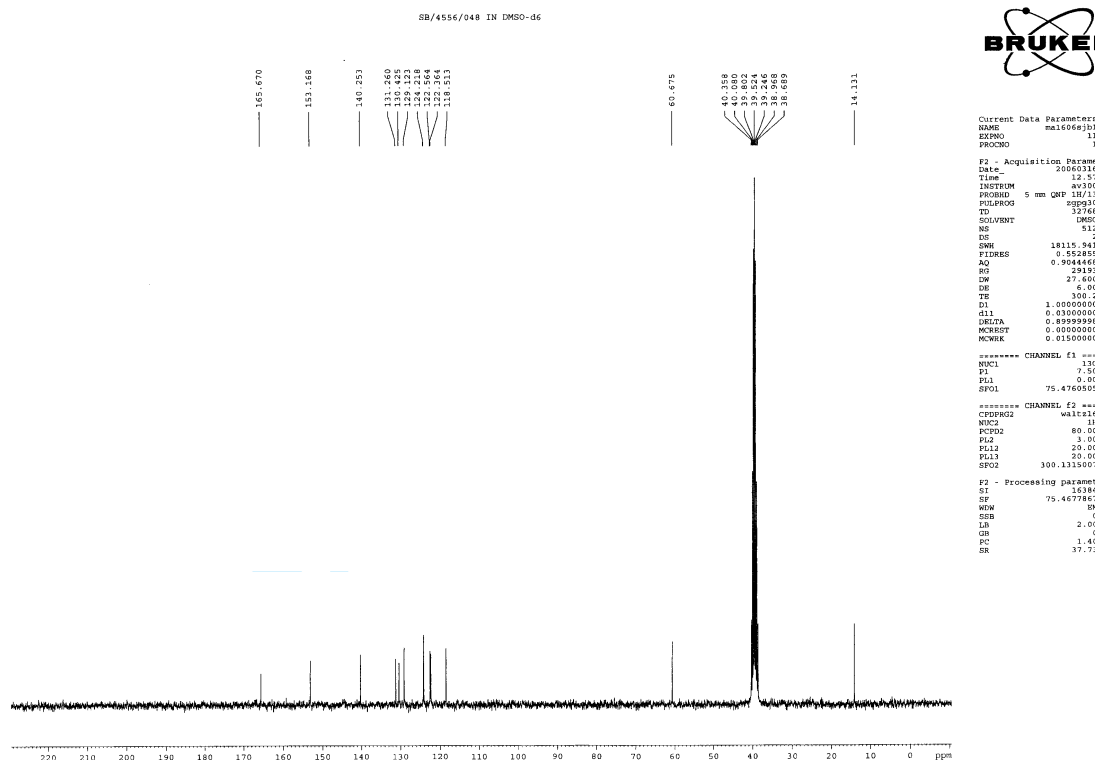
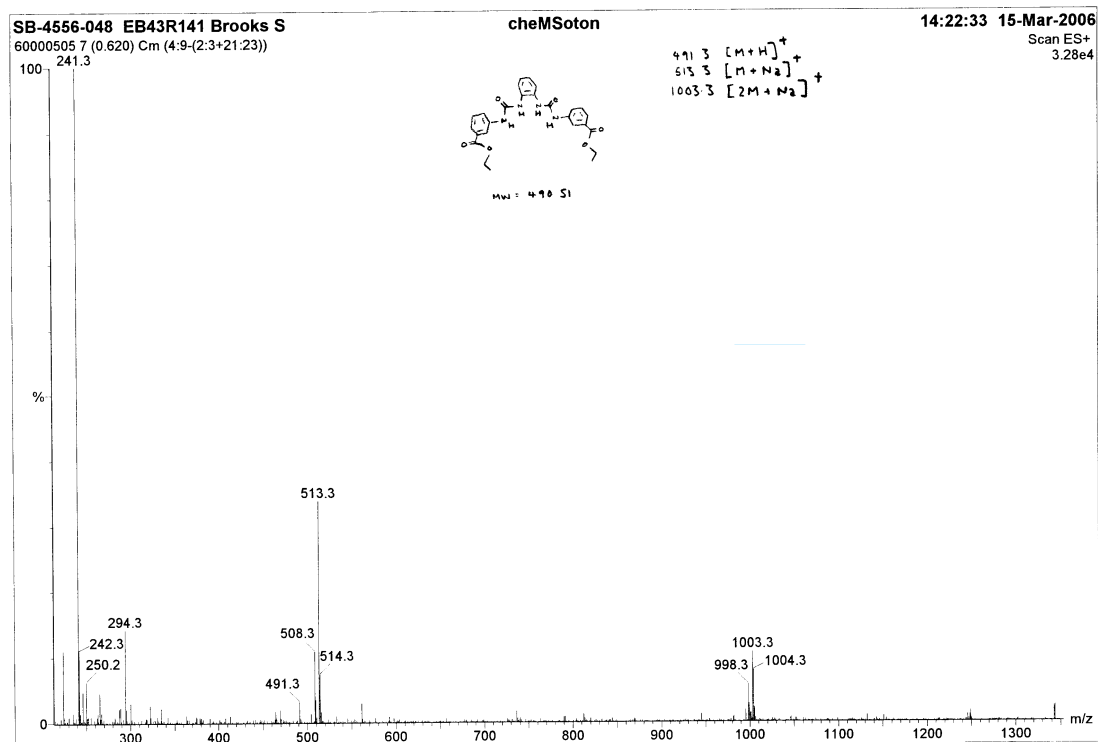
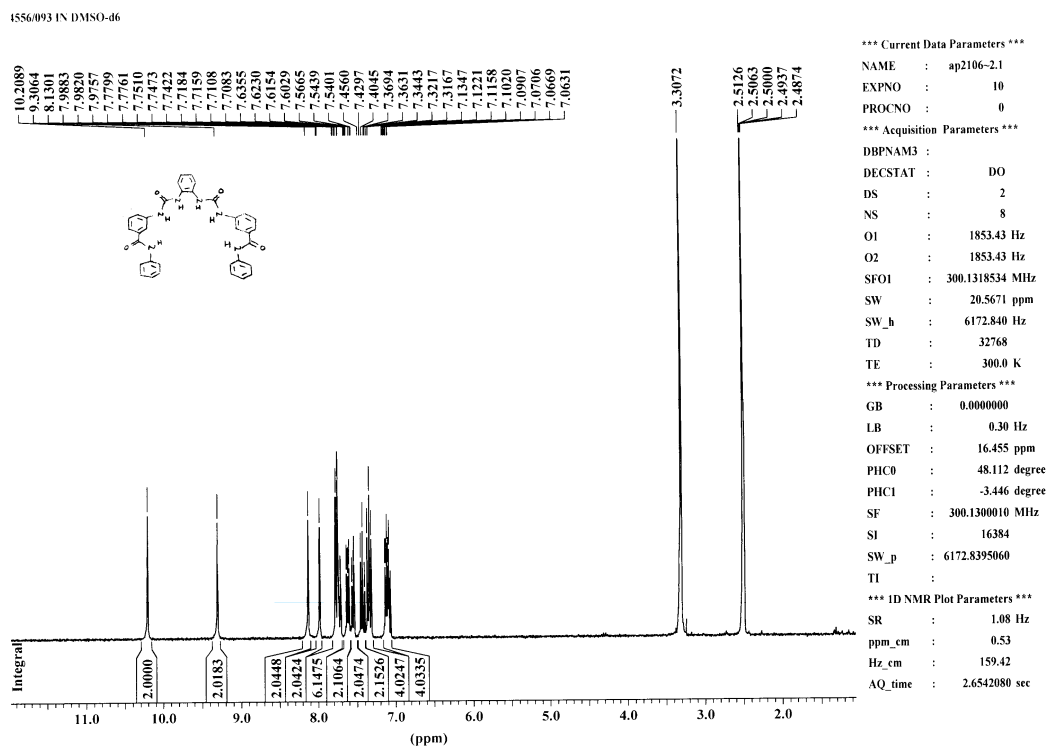
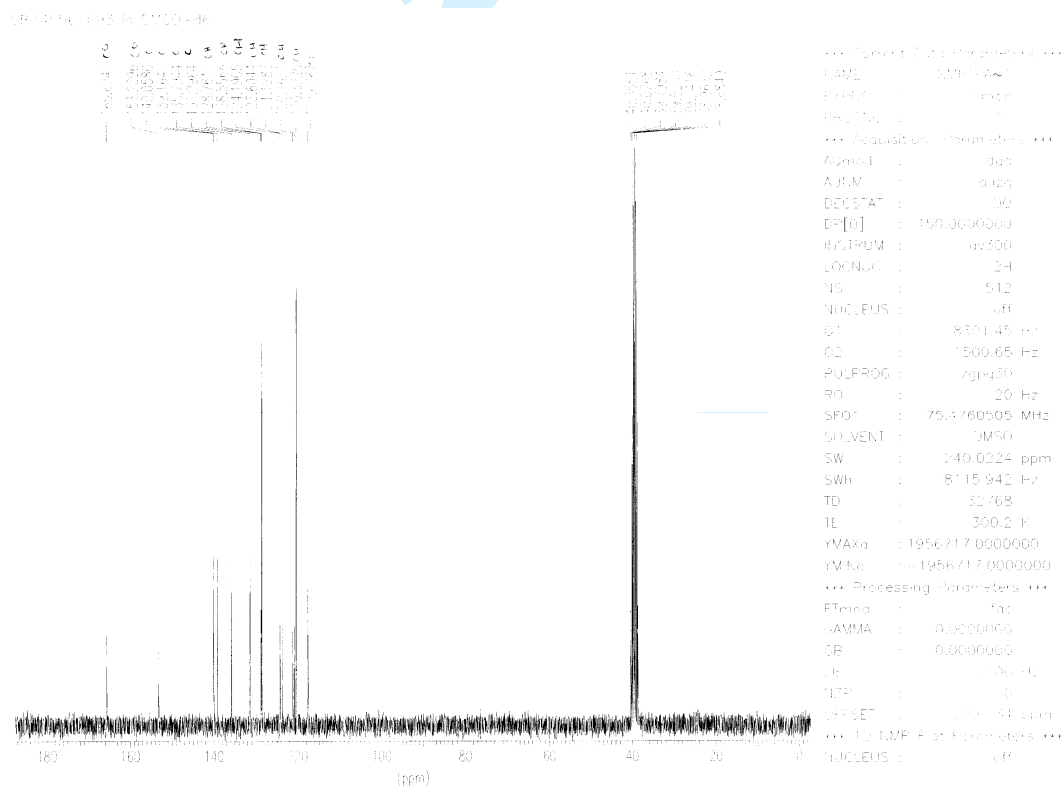
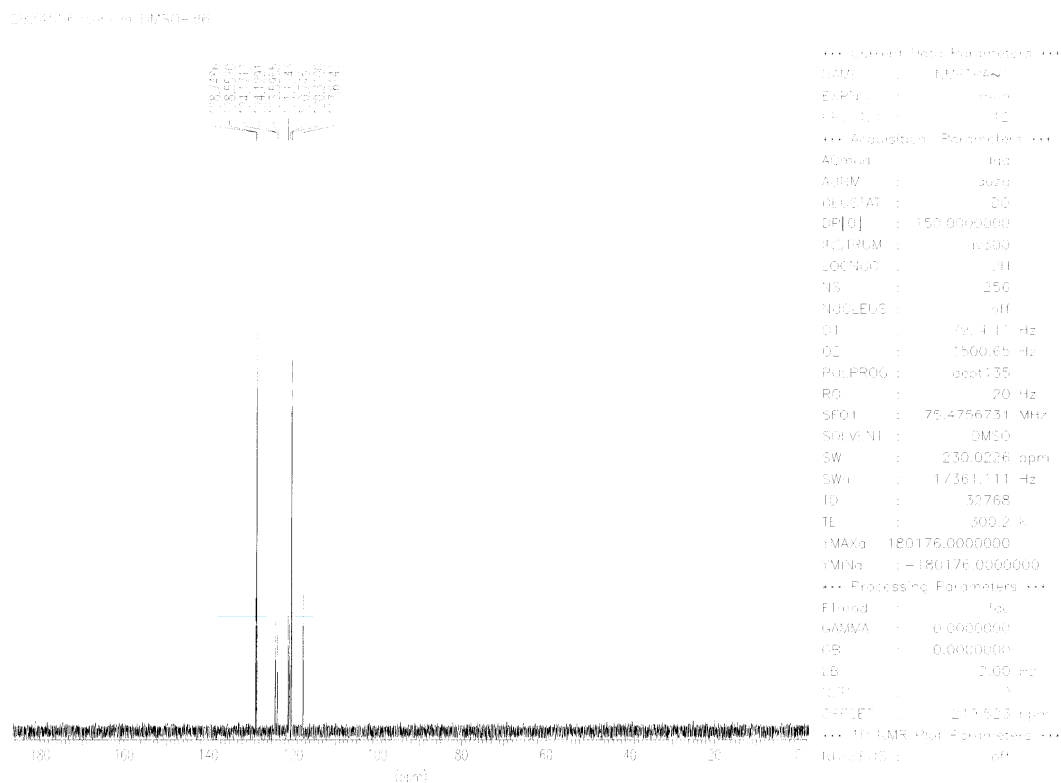
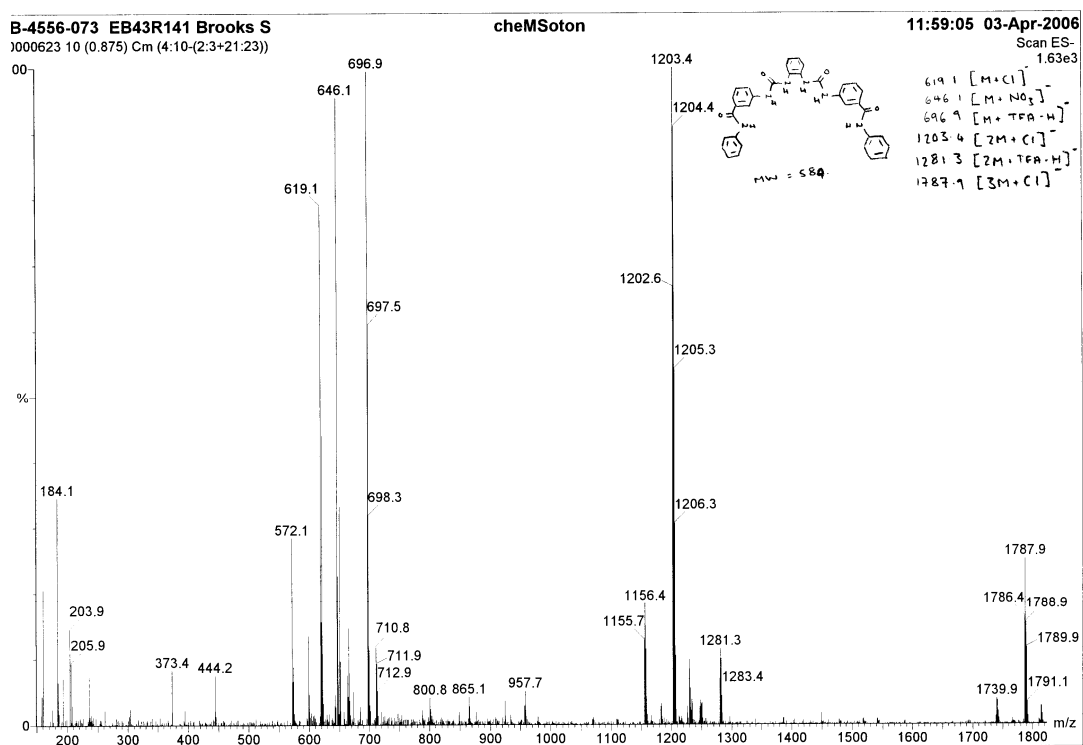
Figure S2 <sup>13</sup>C NMR of compound 4 in DMSO-d<sub>6</sub>

Figure S3 ES+ MS of compound 4

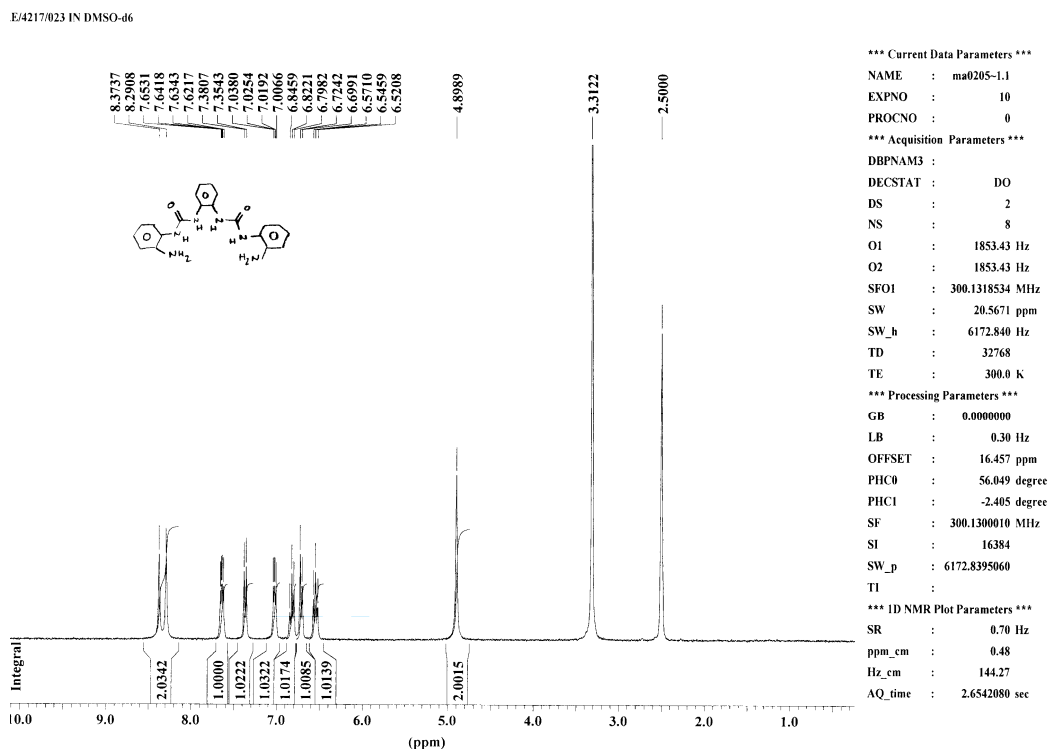
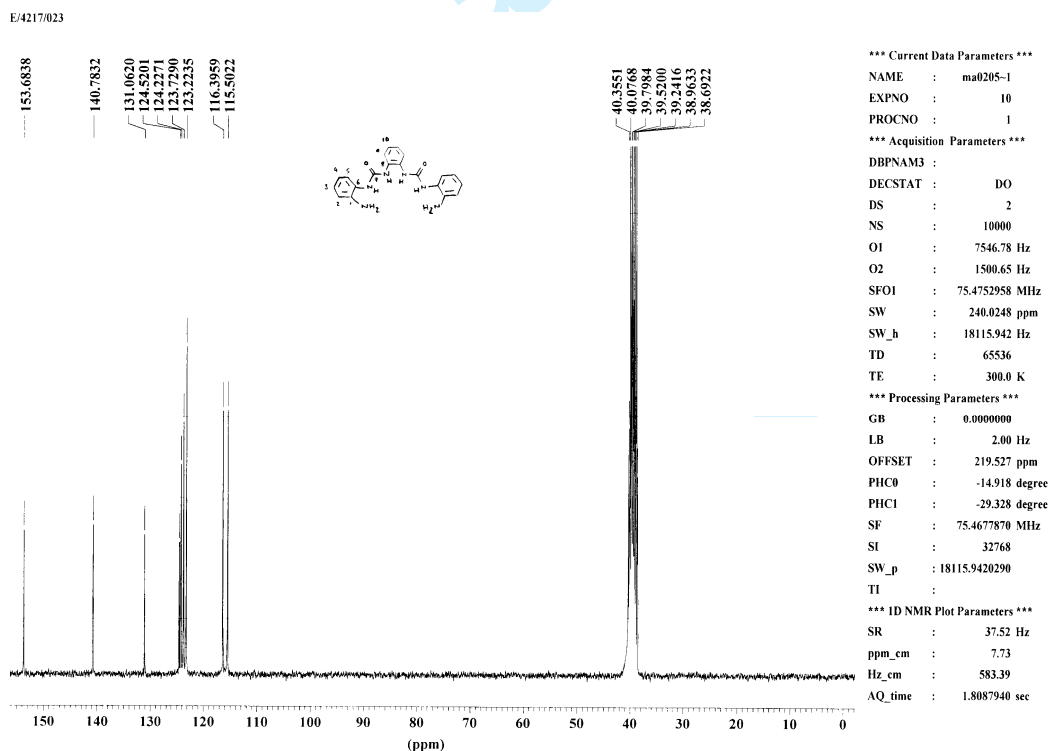


Figure S4  $^1\text{H}$  NMR of compound 2 in DMSO- $d_6$ .Figure S5  $^{13}\text{C}$  NMR of compound 2 in DMSO- $d_6$ .

4

Figure S6  $^{13}\text{C}$  DEPT NMR of compound **2** in  $\text{DMSO-d}_6$ .Figure S7 ES- MS of compound **2** in  $\text{DMSO-d}_6$ .

5

Figure S8 <sup>1</sup>H NMR of compound 6 in DMSO-d<sub>6</sub>Figure S9 <sup>13</sup>C NMR of compound 6 in DMSO-d<sub>6</sub>

6

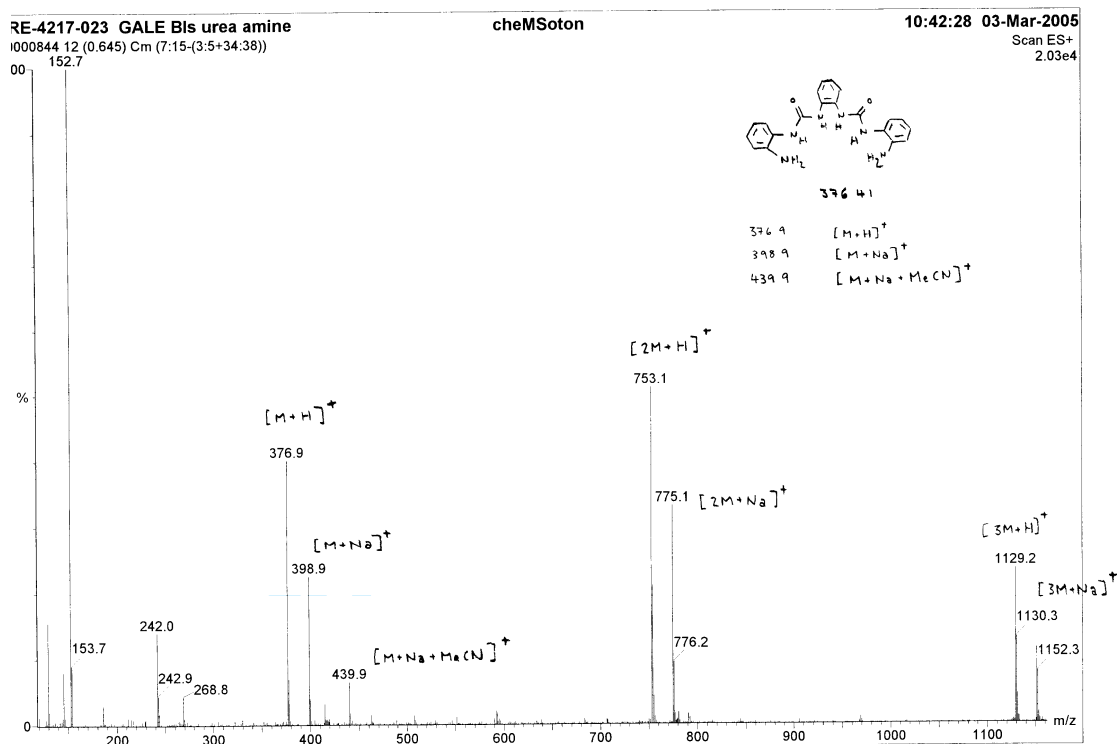
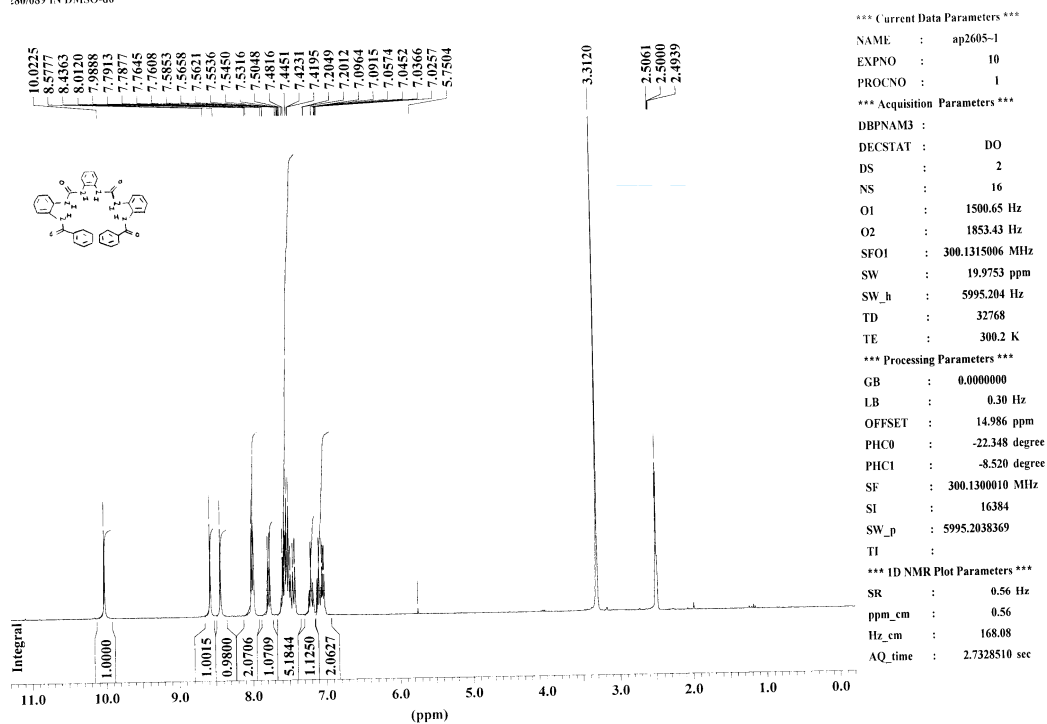
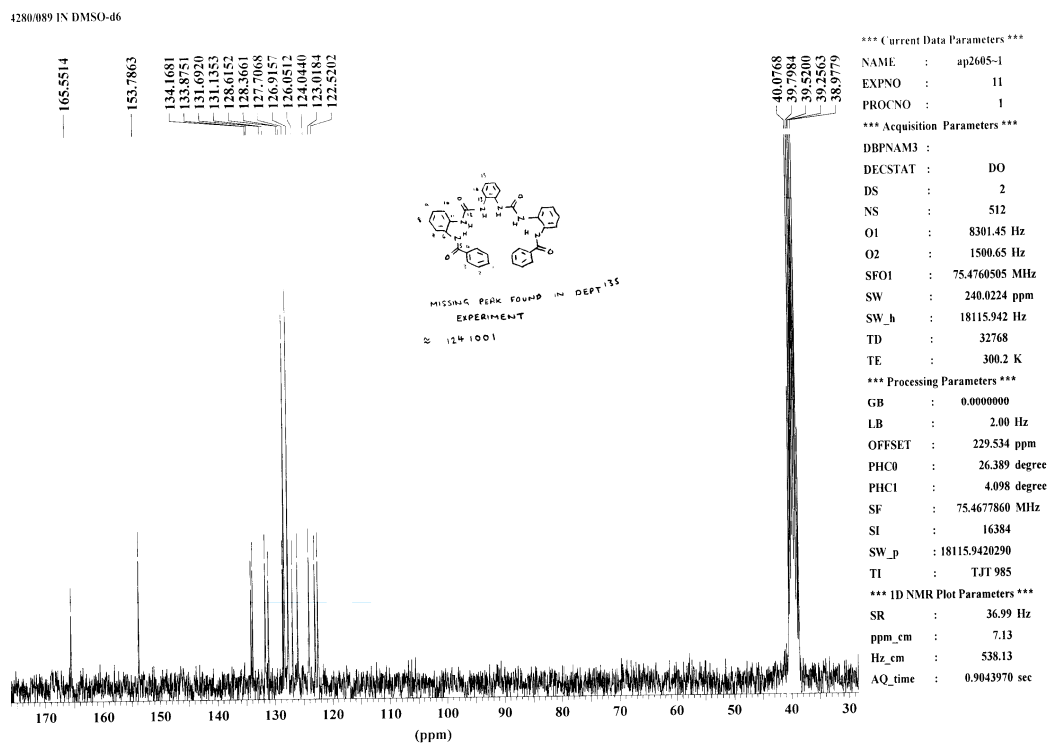
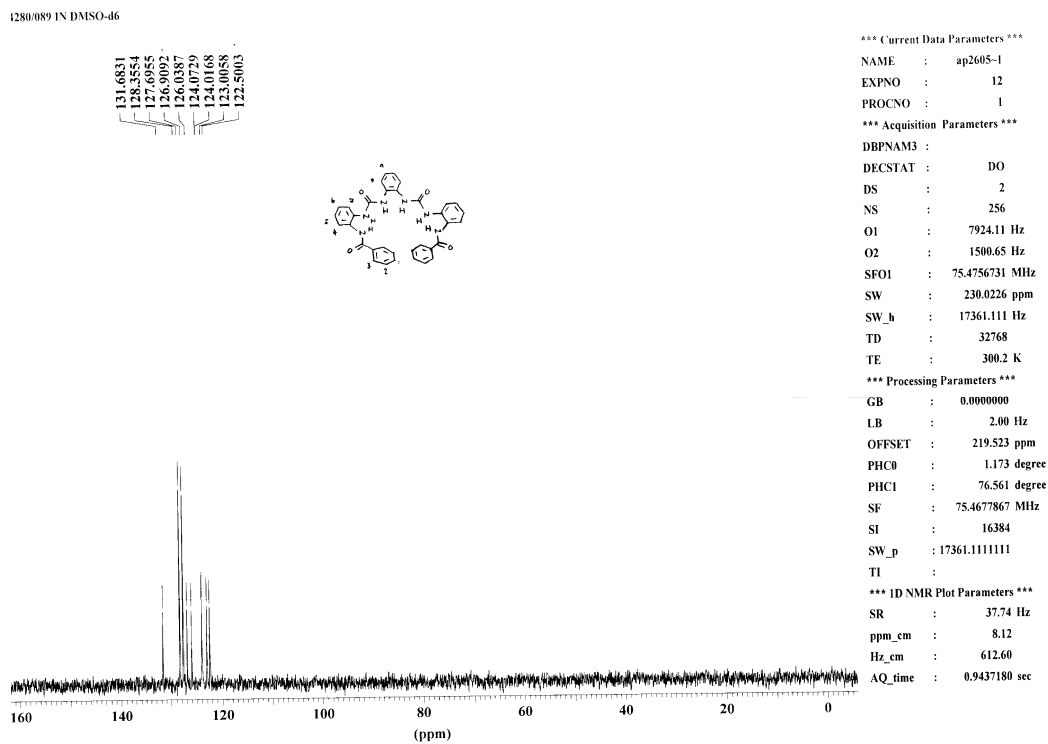
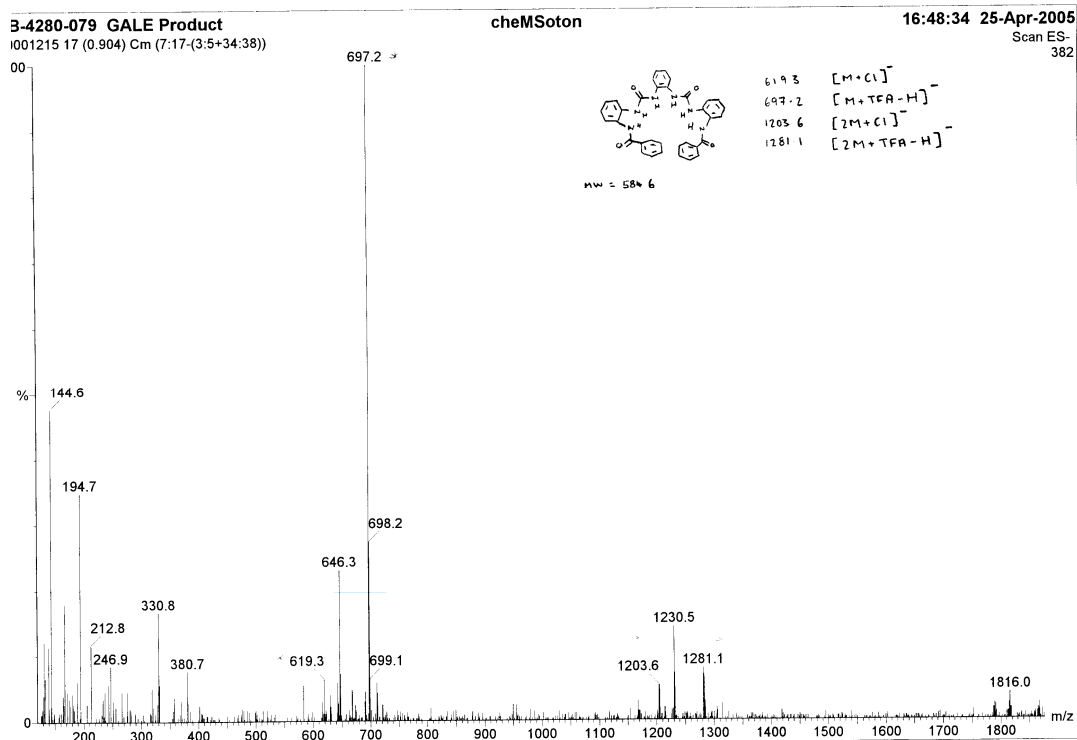
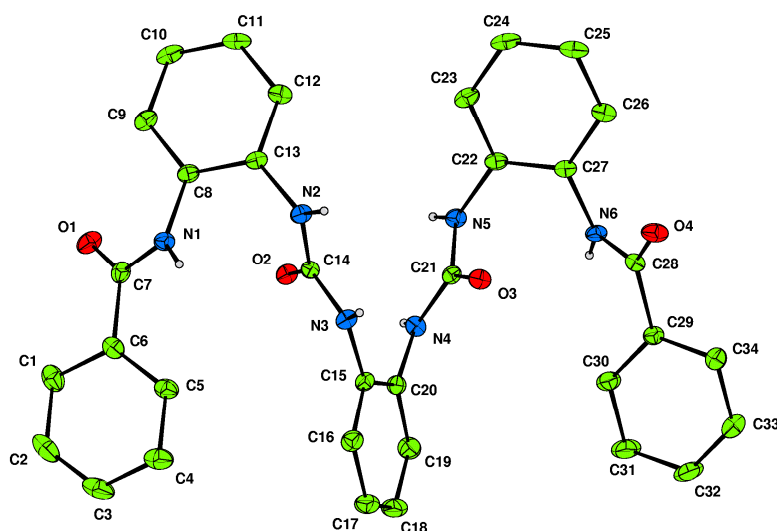


Figure S10 ES+ MS of compound 6

280/089 IN DMSO-d<sub>6</sub>Figure S11 <sup>1</sup>H NMR of compound 3 in DMSO-d<sub>6</sub>

Figure S12  $^{13}\text{C}$  NMR of compound **3** in DMSO-d<sub>6</sub>Figure S13  $^{13}\text{C}$  DEPT NMR of compound **3** in DMSO-d<sub>6</sub>

Figure S14 ES- MS of compound **3**Figure S15 The X-ray crystal structure of compound **3**. Thermal ellipsoids are drawn at the 35% probability level.

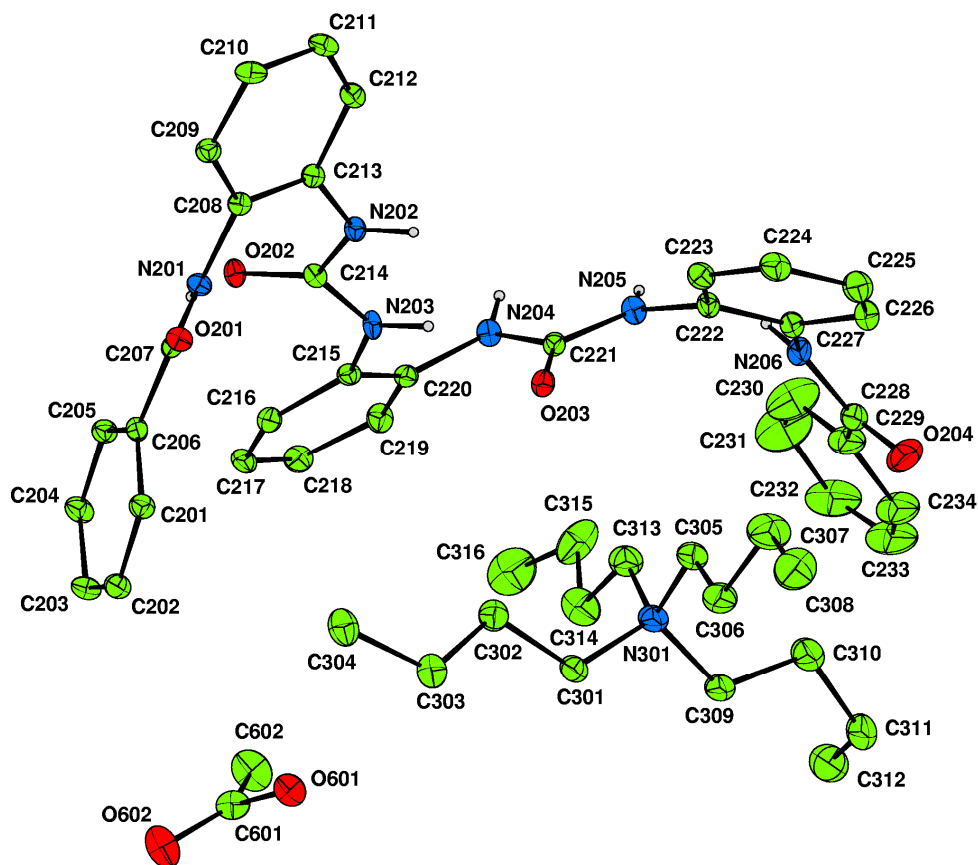


Figure S16 Half of the asymmetric unit (the other half is labelled in a similar fashion) in the TBA acetate complex of 3, thermal ellipsoids drawn at the 30% probability level.

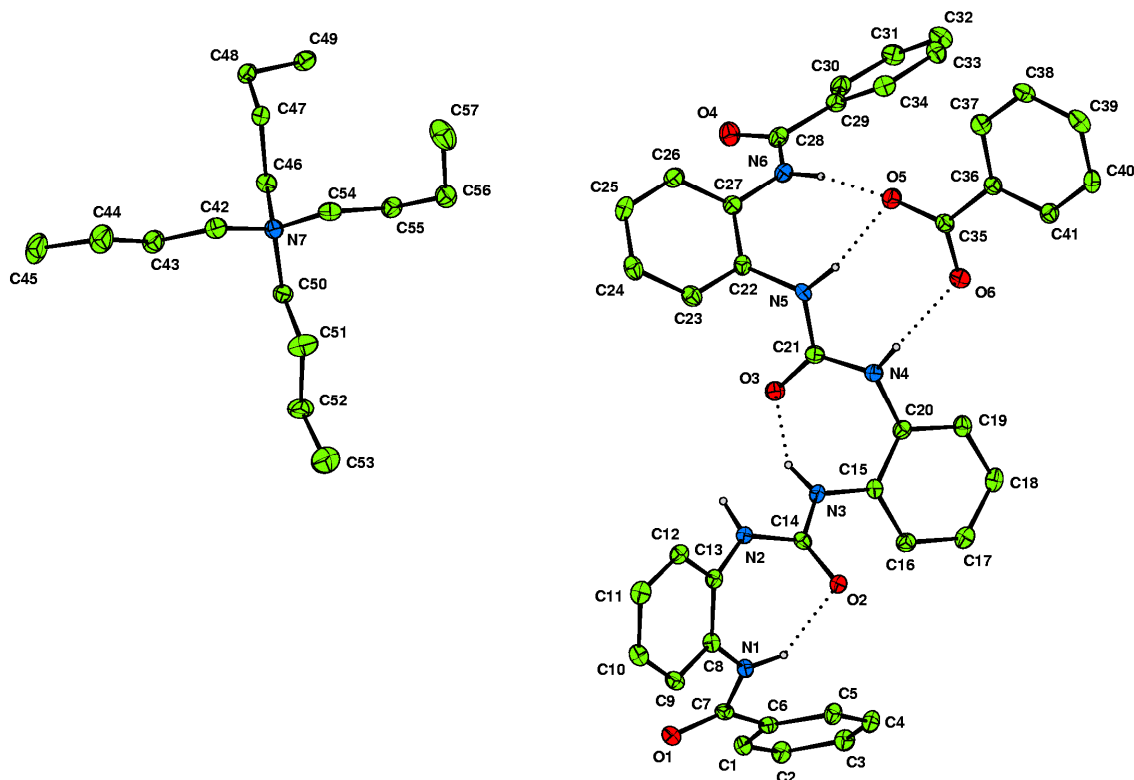


Figure S17 X-ray crystal structure of the TBA benzoate complex of **3**. Thermal ellipsoids drawn at the 30% probability level.



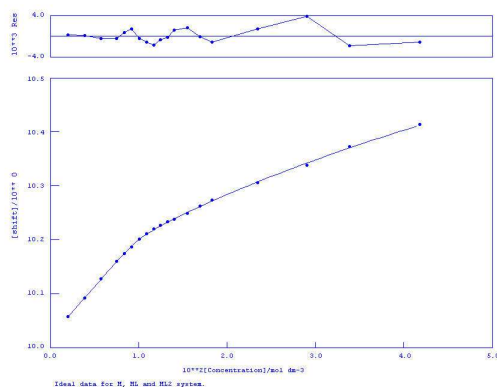
**Figure S18 Compound 3 in DMSO-*d*<sub>6</sub>/0.5% water.**

Acetate.

$$K_1 = 6008 \quad K_2 = <10$$

$$K_{12} = 55230$$

Error = 2.2 &amp; 3.2 %

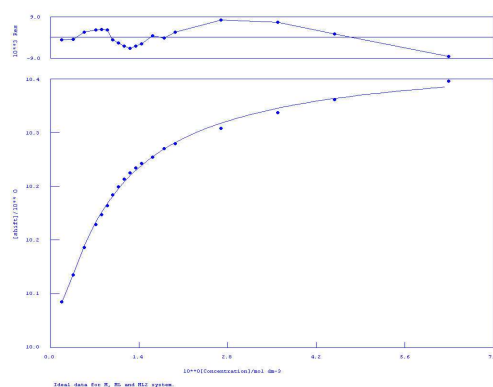


Benzoate.

$$K_1 = 10110 \quad K_2 = <10$$

$$K_{12} = 16554$$

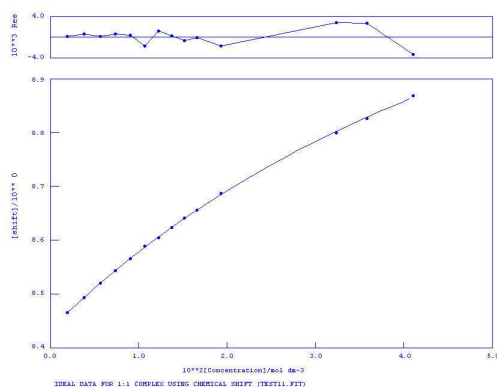
Error = 3.4 % &amp; 12.5 %



Chloride.

$$K_a = 17$$

Error = 4.7 %

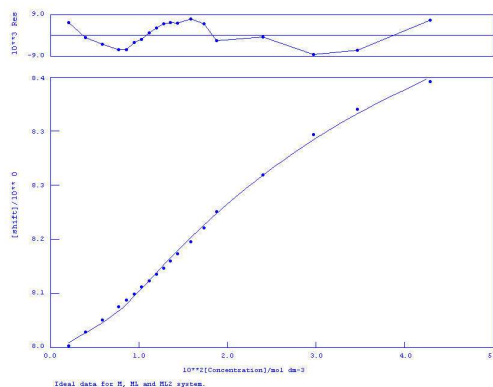


Dihydrogen Phosphate.

$$K_1 = 7777 \quad K_2 = 24$$

$$K_{12} = 185149$$

Error = 5.7 &amp; 4.0 %

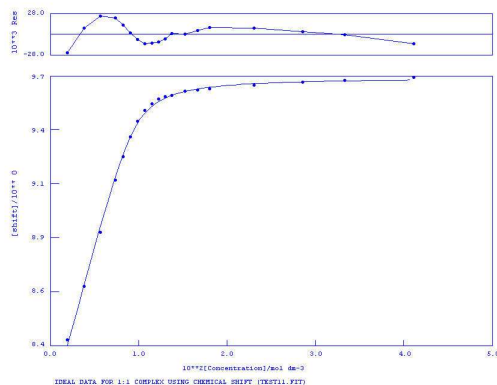


**Figure S19 Compound 2 in DMSO- $d_6$ /0.5% water.**

Acetate.

 $K_a = 3199$ 

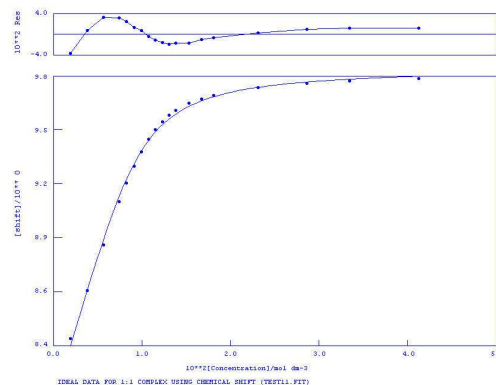
Error = 7.2 %



Benzoate.

 $K_a = 974$ 

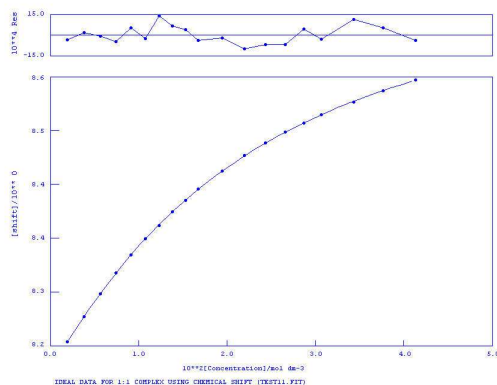
Error = 7.2 %



Chloride.

 $K_a = 52$ 

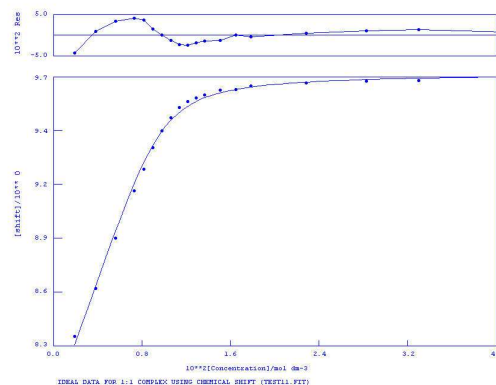
Error = 1.0 %



Dihydrogen Phosphate.

 $K_a = 2289$ 

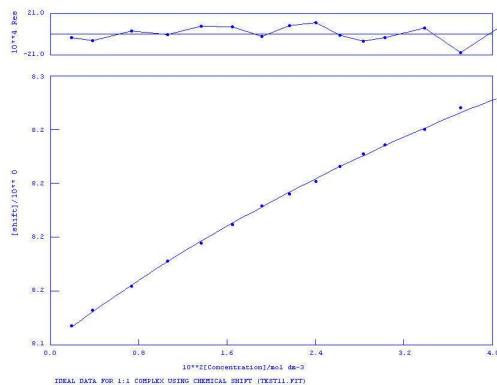
Error = 11.8 %



Hydrogen Sulfate.

 $K_a = 12$ 

Error = 10.8 %



1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For Peer Review Only