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Anion binding *vs.* sulfonamide deprotonation in functionalised ureas†

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Supplementary information

Experimental Section

General remarks: All reactions were performed in oven-dried glassware under a slight positive pressure of nitrogen. ^{1}H-NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were determined on a Bruker AV300 spectrometer. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm), calibrated to the residual solvent peak set, with coupling constants reported in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and br = broad. Chemical shifts for ^{13}C NMR are reported in ppm, relative to the central line of a septet at δ = 39.52 ppm for deuterio-dimethylsulfoxide. Infrared (IR) spectra were recorded on a Mattson Satellite (ATR). FTIR are reported in wavenumbers (cm^{-1}). Elemental analysis were performed by Medac Ltd. All solvents and starting materials were purchased from commercial sources where available. NMR titrations were performed by adding aliquots of the putative anionic guest (as the TBA) salt (0.15 M) in a solution of the receptor (0.01M) in CD_3CN to a solution of the receptor (0.01M) – except in the case of the repeat of the fluoride titration with receptor **1** (presented at the end of the ESI).

***N*-(2-(3-phenylureido)phenyl)benzenesulfonamide (1)** To a solution of 1-(2-aminophenyl)-3-phenylurea (0.30 g, 1.32 mmol) in dry DMF (3 mL) and Et_3N (0.4 mL) a solution of benzenesulfonyl chloride (0.23 g, 1.32 mmol) in dry dichloromethane (10 mL) was added dropwise. The solution was stirred at room temperature under N_2 atmosphere for 16 h. After that time the solvent was removed

under reduced pressure and the residue was taken up in dichloromethane and washed with water (3 × 10 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product (a brown solid) was purified by flash chromatography on silica using a mixture of dichloromethane/ethylacetate (8/2 v/v) as eluent to afford a white solid (0.18 g, 0.49 mmol, 37% yield). M.p.= 63°C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.54 (s, 1H, NH sulfonamide), 9,50 (s, 1H, NH urea), 8.28 (s, 1H, NH urea), 8.01 (d, J = 8.3 Hz, 1H, ArH), 7.72-7.47 (m, 7H, ArH), 7.30 (t, J = 7.9Hz, 2H, ArH), 7.16 (t, J = 7.16 Hz, 1H, ArH), 6.99 (t, J = 7.53 Hz, 1H, ArH), 6.76 (t, J = 7.53 Hz, 1H, ArH), 6.44 (d, J = 7.53 Hz, 1H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6) = δ = 153.0 (CO), 140.2 (CH), 139.7 (C) 137.4(C), 133.4 (CH), 130.7 (C), 129.5 (CH), 129.3 (CH), 128.1 (CH), 127.6 (CH), 125.4 (C), 122.3 (CH), 121.4 (CH), 118.7 (CH); IR (film): ν = 1657, 1598, 1545, 1496, 1446, 1309, 1240, 1154, 1090, 750 cm^{-1}; LRMS (ES^-): m/z : 366.2 $[M\text{-H}]^-$; Elemental analysis for $C_{19}H_{17}N_3O_3S$ Calc (%): C = 62.11, H = 4.66, N = 11.44; Found (%): C = 62.09, H = 4.70, N = 11.49.

***N,N'*-(2,2'-carbonylbis(azanediyl)bis(2,1-phenylene))dibenzenesulfonamide (2)**

To a solution of 1,3-bis(2-aminophenyl)urea (0.20 g, 0.83 mmol) in dry DMF (3 mL) and Et_3N (0.2 mL) a solution of benzenesulfonyl chloride (0.29 g, 1.65 mmol) in dry dichloromethane (10 mL) was added dropwise. The solution was stirred at room temperature under N_2 atmosphere for 24 h. After that time the solvent was removed under reduced pressure and the residue was taken up in dichloromethane and washed with water (3 × 10 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product (a pale yellow solid) was purified by flash chromatography on silica using a mixture of dichloromethane/ethylacetate (8/2 v/v) as eluent to afford a white solid (0.17 g, 0.32

mmol, 39% yield). M.p.= 176°C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.52 (s, 2H, NH sulfonamide), 8.70 (s, 2H, NH urea), 7.74-7.70 (m, 6H, ArH), 7.65-7.52 (m, 6H, ArH), 7.17 (t, J = 8.28 Hz, 2H, ArH), 6.89 (t, J = 7.53 Hz, 2H, ArH), 6.73 (d, J = 7.17 Hz, 2H, ArH). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 153.8 (CO), 140.3 (C) 136.4 (C), 133.9 (CH), 130.1 (CH), 128.2 (C), 128.0 (CH), 127.7 (CH), 127.2 (CH), 123.9 (CH), 123.2 (CH); IR (film): ν = 3342, 1660, 1595, 1537, 1496, 1329, 1298, 1166, 1153, 1091, 732 cm^{-1}. LRMS (ES^-):m/z: 521 $[M-H]^-$; Elemental Analysis for $C_{25}H_{22}N_4O_5S_2$ Calc (%): C = 57.46, H = 4.24, N = 10.72; Found (%): C = 57.44, H = 4.26, N = 10.73.

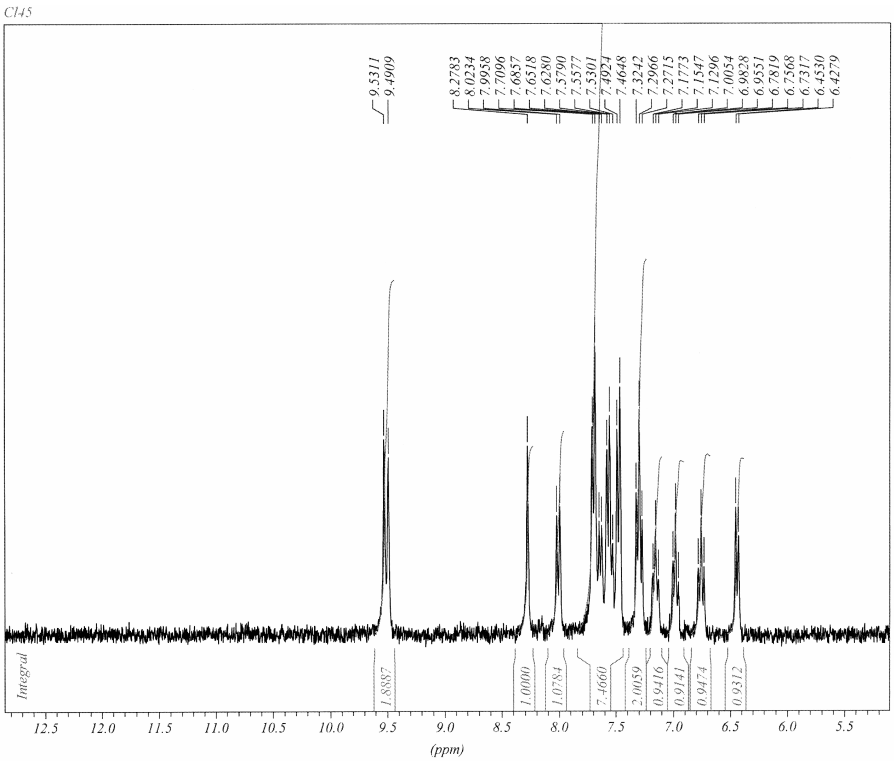


Figure S1 ^{1}H NMR spectrum of compound **1** in DMSO-d$_6$.

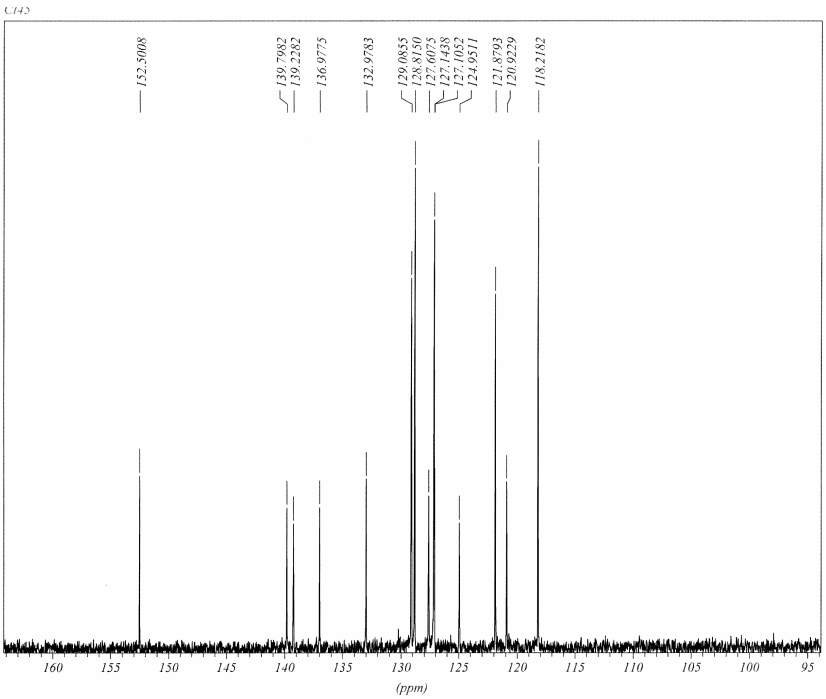


Figure S2 ^{13}C NMR spectrum of compound **1** in DMSO-d$_6$.

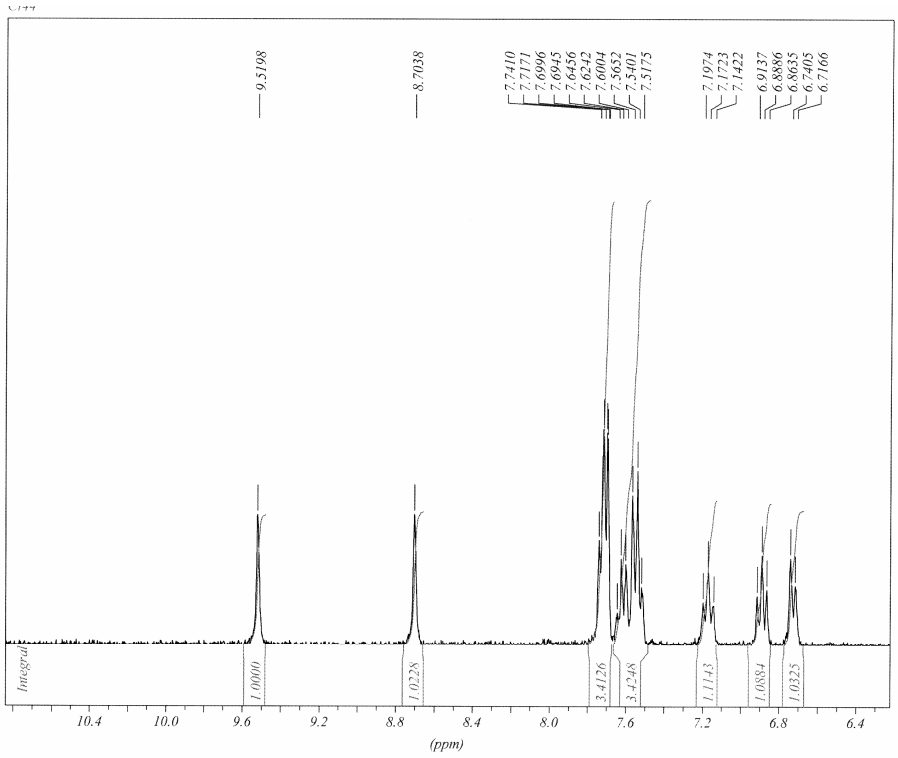


Figure S3 ^{1}H NMR spectrum of compound **2** in DMSO-d_6.

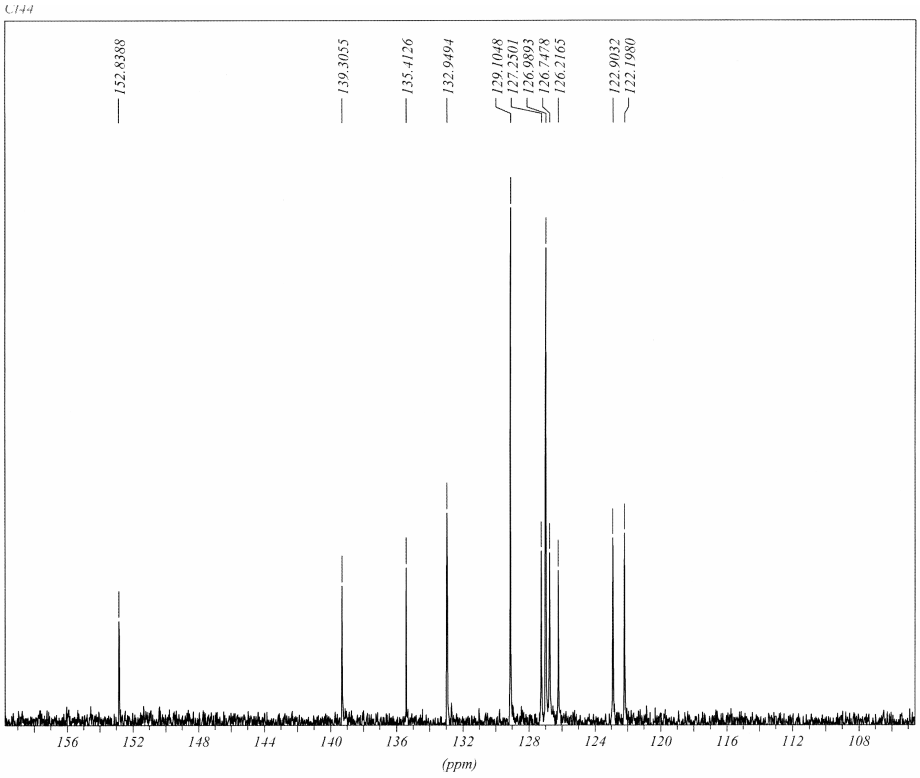


Figure S4 ^{13}C NMR spectrum of compound **2** in DMSO-d_6.

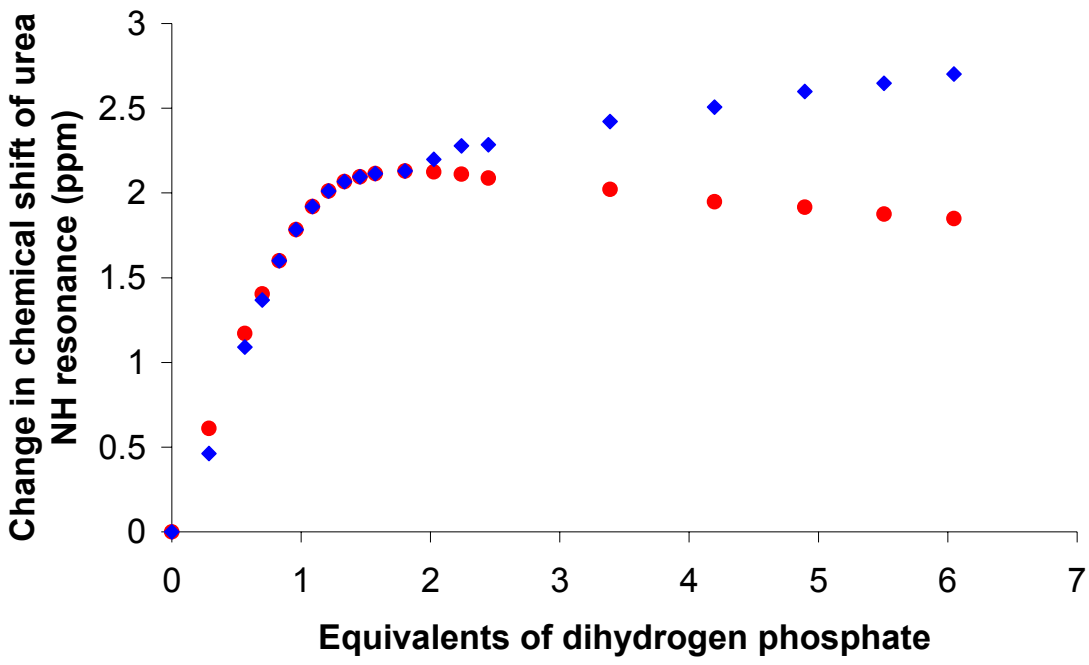


Figure S5 Shifts of the urea NH groups of compound **1** upon addition of tetrabutylammonium dihydrogen phosphate in CD_3CN.

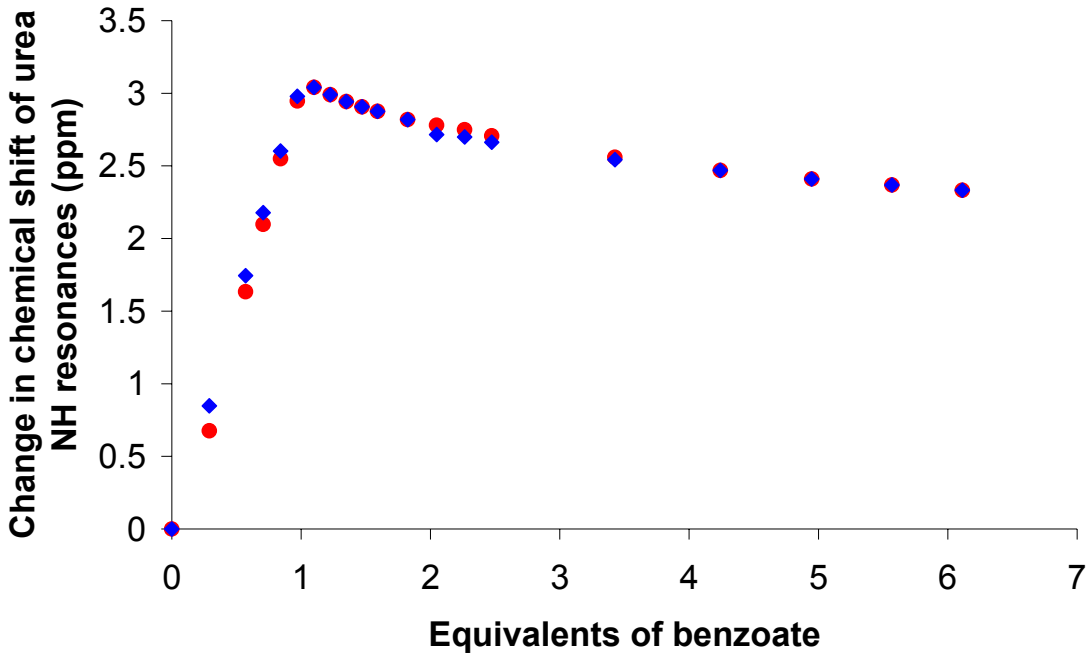


Figure S6 Shifts of the urea NH groups of compound **1** upon addition of tetrabutylammonium benzoate in CD_3CN.

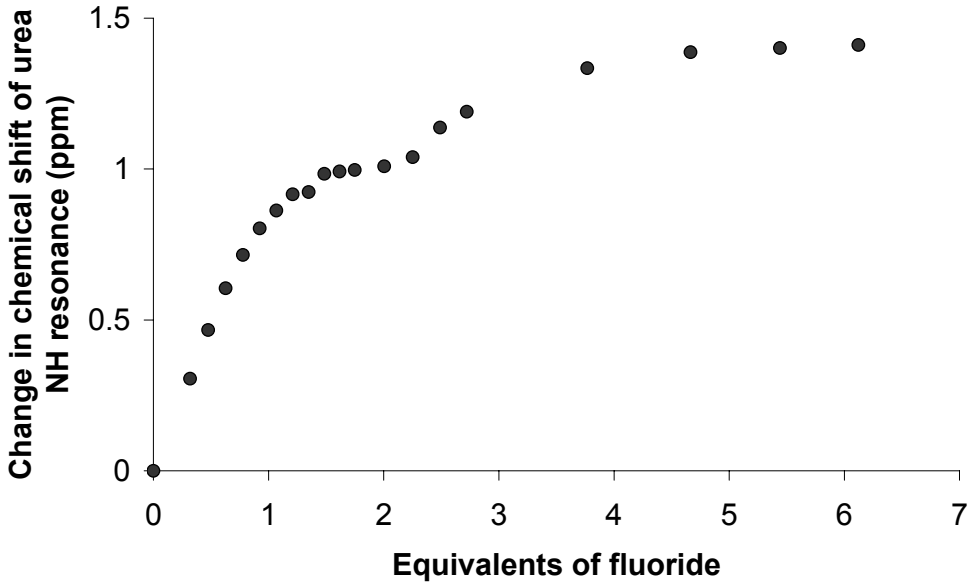


Figure S7 Shifts of the urea NH groups of compound **2** upon addition of tetrabutylammonium fluoride in CD_3CN. Upon addition of fluoride to compound **2** both the urea NH groups behave in an equivalent fashion presumably due to exchange between the sulfonamide NHs. As there are now two sulfonamide NH groups, 4 equivs. of fluoride are required to deprotonate them and generate 2 HF_2^- ions. As both urea NH groups are adjacent to a deprotonated sulfonamide they reach a plateau at 4 equivs. F^-

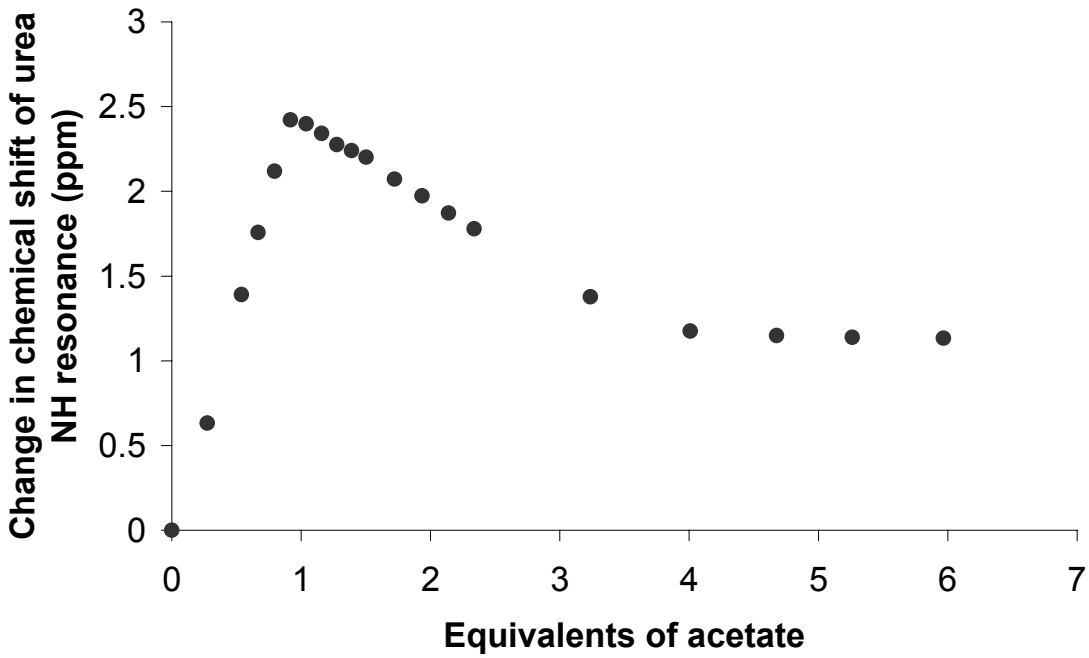


Figure S8 Shifts of the urea NH groups of compound **2** upon addition of tetrabutylammonium acetate in CD_3CN.

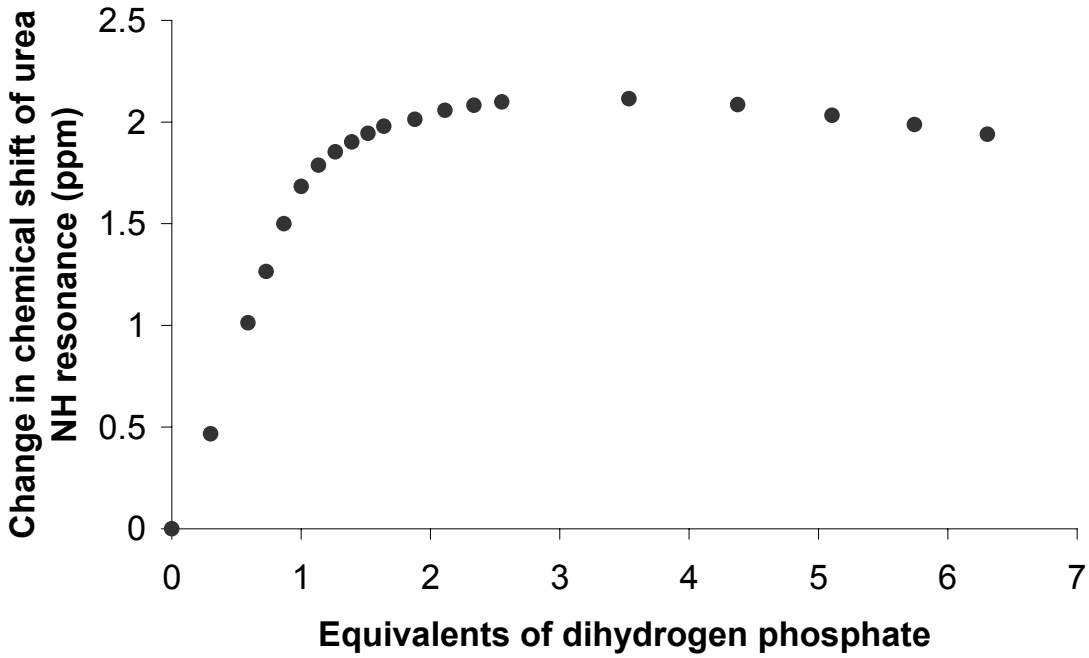


Figure S9 Shifts of the urea NH groups of compound **2** upon addition of tetrabutylammonium dihydrogen phosphate in CD_3CN.

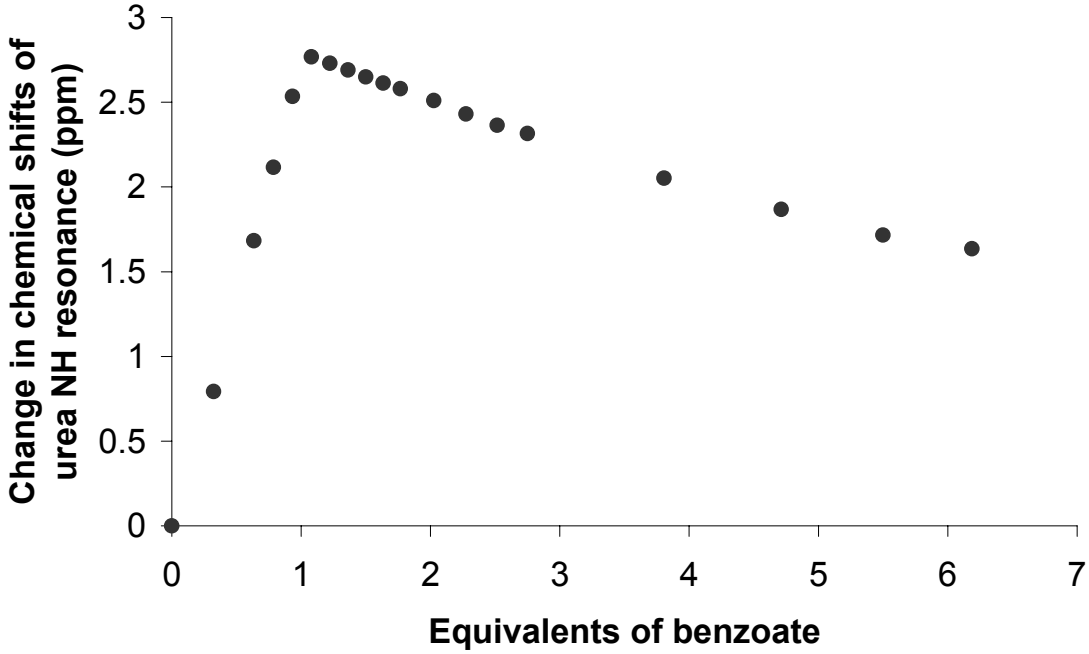


Figure S10 Shifts of the urea NH groups of compound **2** upon addition of tetrabutylammonium benzoate in CD_3CN.

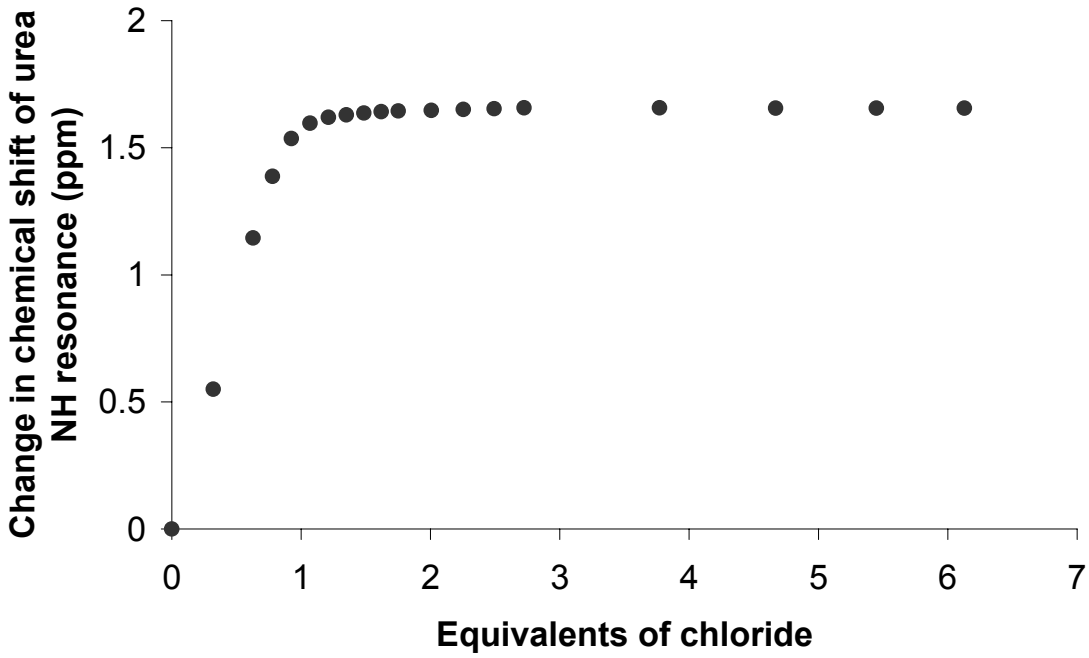


Figure S11 Shifts of the urea NH groups of compound **2** upon addition of tetrabutylammonium chloride in CD_3CN.

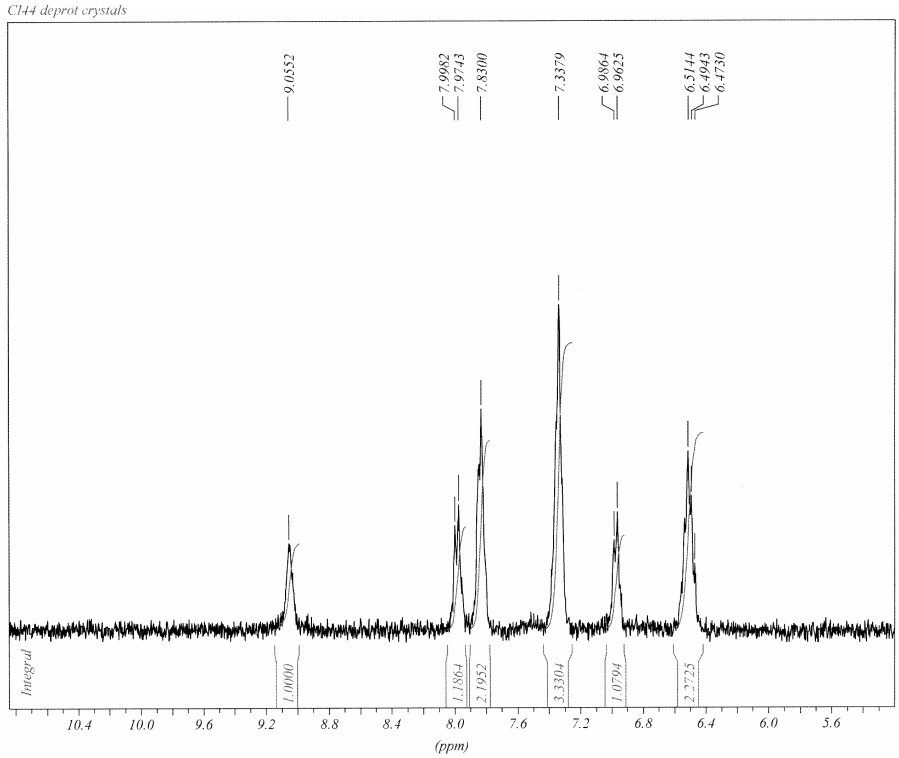
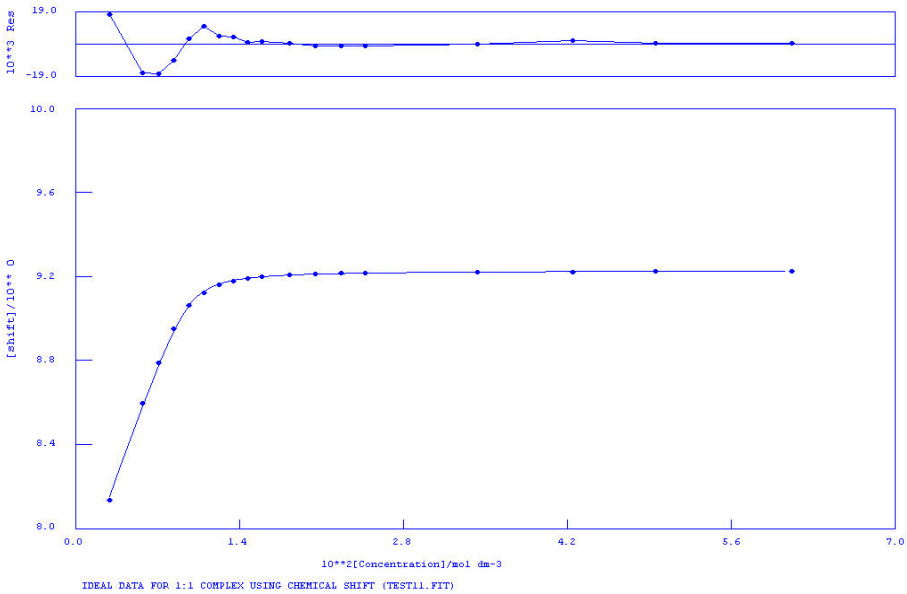


Figure S12 ^{1}H NMR spectrum of doubly deprotonated sulfonamide **2** in acetonitrile-d_3.

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Calculations by WinEQNMR Version 1.20 by Michael J. Hynes
Program run at 15:22:25   on 08/02/2007

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 FILE: TEST11.FIT
 IDEAL DATA: K1 = 63.091; DELTA M = 20.0; DELTA ML = 120.0
 File prepared by M. J. Hynes, October 22 2000

NO.  A   PARAMETER    DELTA     ERROR    CONDITION   DESCRIPTION
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   3  1  9.22791E+00 1.000E+00 3.312E-03 2.115E+00    SHIFT ML
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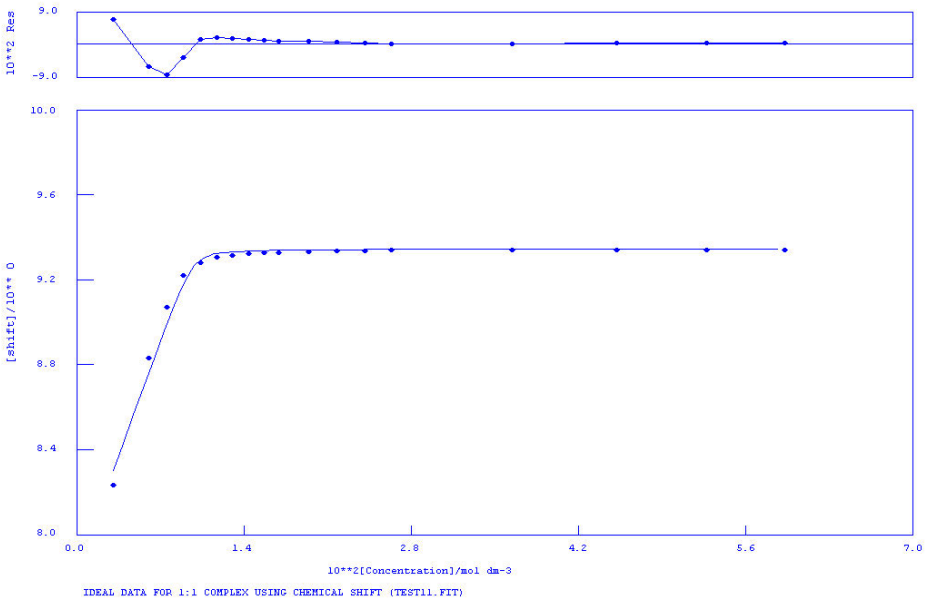
Figure S13 NMR titration of compound **1** *vs*. TBACl in CD_3CN.

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Calculations by WinEQNMR Version 1.20 by Michael J. Hynes
Program run at 10:10:20   on 08/29/2007

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 FILE: TEST11.FIT
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 File prepared by M. J. Hynes, October 22 2000

NO.  A   PARAMETER    DELTA      ERROR     CONDITION   DESCRIPTION
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   3  1  9.34449E+00 1.000E+00 9.384E-03 1.128E+00    SHIFT ML

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Figure S14 NMR titration of compound **2** *vs*. TBACl in CD_3CN.

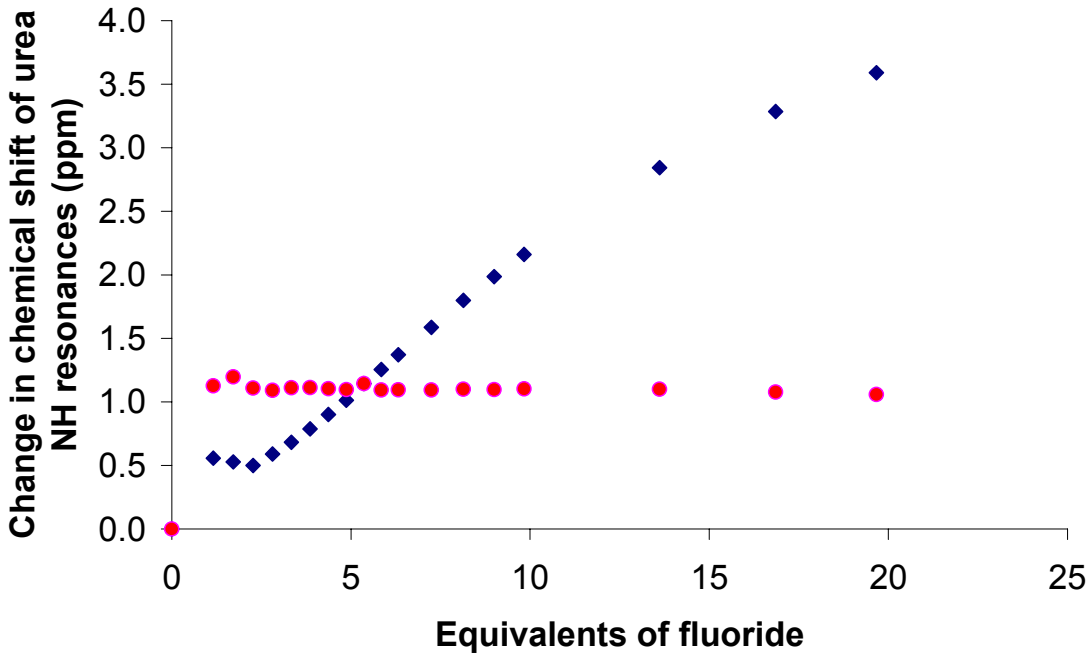

Figure S15 Shifts of the urea groups of compound **1** upon addition of aliquots of tetrabutylammonium fluoride (0.13 M) in a solution of the receptor (2.2 x 10^{-3}M) CD_3CN to a solution of receptor (2.2 x 10^{-3}M). The urea NH adjacent to the sulfonamide reaches a plateau upon deprotonation due to intramolecular hydrogen bonding. The other urea is free to bind to added aliquots of fluoride and continues to shift downfield as the fluoride concentration increases.