Four complementary hydrogen bonds between sulfamides and ureas link adjacent hydrogen-bonded ribbons to form sheets in the solid-state; this interaction is investigated in solution using model urea and sulfamide compounds.

We recently reported a series of achiral glycoluril monomers that form chiral hydrogen-bonded ribbons in the solid-state.1 The ribbons propagate by hydrogen-bonding between adjacent glycoluril monomers,2-4 wherein the urea protons donate intermolecular hydrogen bonds to adjacent carbonyl oxygen atoms.5 Isaacs and coworkers recently reported similar hydrogen-bonded chiral ribbons in a related syn-protected glycoluril monomer,6 and Grossman and coworkers have reported analogous monomers that form rosettes or ribbons in the solid-state depending on the crystallization conditions.6 Here we report a new glycoluril monomer (1) affixed with an additional sulfamide hydrogen-bonding motif (Fig. 1). The new functionality serves to bridge adjacent ribbons via specific sulfamide–glycoluril hydrogen bonds. These complementary hydrogen-bonding interactions between ureas and sulfamides provide an unanticipated driving force for forming higher order two-dimensional sheets over one-dimensional ribbons.8,9

Urea and sulfamide functionalities discriminate against homodimerization in solution by forming a strong hydrogen-bonded heterodimer (2-3, Fig. 3); this recognition motif has been used to assemble discrete capsules in solution and in the solid-state.7,10,11 Monomer 1 was prepared to investigate the propensity for the urea and sulfamide functionalities to interact in the solid-state and form discrete tetrameric capsules; however, capsule formation was never observed. Rather, an unusual two-dimensional network of hydrogen bonds that maintains the programmed head-to-tail specificity between glycoluril and sulfamide is observed.

Compound 1 is readily prepared by alkylation of 1,6-bis(p-methoxybenzyl)-7,8-di-p-tolylglycoluril with an o-dibromomethyl-aryl-sulfamide followed by deprotection (see experimental section). Slow evaporation of a 1,2-dichloroethane–methanol mixture of urea and sulfamide exhibits very different behavior. Fitting the dilution curve to a 1 : 1 isotherm gives a binding constant of 50 M⁻¹ for the heterodimer. A Job plot one-dimensional ribbon in the solid-state coincident with the 2₁ crystallographic screw axis (highlighted in orange in Fig. 2). Interestingly, one sulfonyle oxygen and both sulfamide protons of 1 (shown in green in Fig. 2) form intermolecular hydrogen bonds with glycoluril amide protons and carbonyl oxygens: the sulfamide oxygen bisects the curved surface of an adjacent glycoluril monomer and accepts two hydrogen bonds from the syn-ureido glycoluril protons. The sulfamide protons also donate two hydrogen bonds to two different glycoluril carbonyl oxygens along the ribbon. This specific hydrogen-bonding between glycolurils and sulfamides bridges adjacent ribbons to create two-dimensional sheets without disrupting the one-dimensional ribbon motif. We have previously reported qualitative results on the recognition between ureas and sulfamides in solution.2 To gain quantitative insight into this interaction, model compounds were prepared to determine the association constant of these urea–sulfamide heterodimers (Fig. 3). Each monomer self-associates (2-3, 3-3) with a modest homodimerization affinity in CD₂Cl₂ of Kₚ = 1.1 and 0.7 M⁻¹, respectively. An equimolar mixture of urea 2 and sulfamide 3 exhibits very different behavior. Fitting the dilution curve to a 1 : 1 isotherm gives a binding constant of 50 M⁻¹ for the heterodimer. A Job plot

Fig. 1 Crystal structure of glycoluril monomer 1 used in this study.

Fig. 2 (top) ChemDraw representation of the two-dimensional sheet network observed in the solid-state structure of 1 (Ar = 4-tolyl), (bottom) Wireframe representation of the sheet: the one-dimensional glycoluril ribbon structure is shown in orange, the sulfamide participation tethering adjacent ribbons is highlighted in green (some phenyl rings and hydrogen atoms are omitted for clarity). One molecule of 1,2-dichloroethane (omitted) resides on the concave surface of the monomer and fills the remaining space in the lattice.
confirms that the binding takes place in a 1 : 1 stoichiometry.13

This selective hydrogen-bonding between 2 and 3 arises from a complementary electrostatic attraction. The most acidic (and therefore the most electropositive) hydrogen bond donor in the system belongs to the sulfamide proton (pK 〈 6.5).14 The most electronegative hydrogen bond acceptor belongs to the carbonyl of the urea. This results in a complementary donor–acceptor hydrogen-bonding pair with a significant preference for heterodimerization over homodimerization—almost two orders of magnitude higher affinity.

The use of specific, complementary interactions (such as hydrogen-bonding) between different functional groups is an important tenet of crystal engineering.15,16 We have shown that a solid-state structure exhibits an additional dimension of ordering that uses a complementary hydrogen-bonding interaction observed in solution. Due to the ready availability of sulfamides and ureas, their complementary hydrogen-bonding preferences suggest application in the formation of engineered solids.

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Notes and references
† General X-ray diffraction experimental: Crystallographic data were collected using a Siemens SMART III diffractometer equipped with a CCD area detector using Cu-Kα radiation. Strategies for high-resolution data collection were determined in PROTEUM4 to collect batches of frames using omega scans of 0.3°.20 An empirical absorption correction was applied using SADABS.21 The structure solution was performed using SIR9222 and SHELXTL23 was used for all subsequent refinements using the software package WinGX.24 Details on the refinement of the structure and data collection as well as all listings of crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 203373 (1). See http://www.rsc.org/suppdata/cc/c6/305508e for crystallographic data in cif format.

Crystal data: Monomer 1. C34H34Cl2N8O5S; pale yellow plate crystals grown by slow evaporation of dichloroethane–methanol, crystal size 0.16 × 0.04 × 0.01 mm. FW = 615.52. T = −113 °C, monoclinic, space group P 21/c. a = 14.385(5), b = 11.273(7), c = 22.309(12) Å, β = 96.48(3); V = 2716(3) Å³. Z = 4, μ = 3.275 mm⁻¹. 4968 reflections measured (1832 unique, R(int) = 0.061); R1 = 0.078 (for 1456 reflections with I > 2σ(I), 232 parameters), wR2 = 0.24 (for all 1832 data), GOF = 1.13.

Synthetic experimental: 1. To a solution of 1,6-bis(4-methoxyphenyl)-7,8-di-p-tolyl-glycoluril24 (400 mg, 0.71 mmol) in anhydrous DMF (10 mL) was added a 60% dispersion of NaH (58 mg, 1.5 mmol) and stirring was continued under nitrogen for 30 min. A solution of the dibromomethyl sulfamide25 (400 mg, 0.71 mmol) in anhydrous DMF (2 mL) was quickly added via a pipet and the reaction was stirred under nitrogen for an additional 90 min. The solution was concentrated to dryness and chromatographed over silica (30–50% EtOAc : hexane) to yield the protected monotmer (PMB-Boc-J) as a white solid (75 mg, 11%). Deprotection was effected by treating a solution of PMB-Boc-J (79 mg, 0.083 mmol) with trifluoroacetic acid (2 mL) in a sealed tube heated at 70 °C for 23 h. The solution was concentrated to dryness and chromatographed (5% MeOH in CH2Cl2) to give 1 as a white solid (43 mg, 100%).17 H NMR (THF-d8, 600 MHz): δ 2.13 (s, 3H), 2.17 (s, 3H), 4.03 (t, 2H, J = 15.2 Hz), 4.64 (2H, J = 15.3 Hz), 6.81 (s, 2H), 6.84 (d, 2H, J = 8.2 Hz), 6.95 (d, 2H, J = 8.2 Hz), 7.00 (d, 2H, J = 8.2 Hz), 7.09 (d, 2H, J = 7.6 Hz), 7.16 (s, 2H), 9.58 (s, 2H).

1-Dodecyl-2-imidazolidinone (2). To a solution of 2-imidazolidinone (860 mg, 10 mmol) in dry DMF (12 mL) was added NaH (60% in mineral oil, 400 mg, 10 mmol). After stirring for 1 h, 1-bromodecane (2.50 g, 10 mmol) was added and stirring continued for 2 h at room temperature and for 40 min at 60 °C. Water and 1 M HCl were added and the mixture was extracted with CH2Cl2. The organic phase was washed with water, dried over Na2SO4, and evaporated. The residue was purified by flash chromatography (silica gel, 4 : 1 hexane–EtOAc) to give a white, waxy solid (770 mg, 34%).18 H NMR (DMSO-d6, 600 MHz): δ 0.85 (t, 3H, J = 15.2 Hz), 1.11–1.35 (m, 18H), 1.40 (m, 2H), 2.99 (t, 2H, J = 7.2 Hz), 3.15–3.34 (m, 4H), 6.21 (s, 1H).

1-Decybenzothiazolide-2,2-dioxide (3). To a solution of benzothiazolidone-2,2-dioxide (800 mg, 4.7 mmol) in dry DMF (5 mL) was added NaH (60% in mineral oil, 190 mg, 4.7 mmol). After 20 min, 1-bromodecane (1.0 g, 4.7 mmol) was added to the clear solution and stirred for 20 h. Water and 1 M HCl were added and the mixture was extracted with CHCl3. The organic phase was washed with water, dried over Na2SO4, and concentrated to dryness. The residue was purified by flash chromatography (silica gel, 4 : 1 hexane–EtOAc) to give a colorless, waxy solid (270 mg, 19%).19 H NMR (DMSO-d6, 300 MHz): δ 0.85 (t, 3H, J = 6.4 Hz), 1.15–1.40 (m, 14H), 1.69 (m, 2H), 3.62 (t, 2H, J = 7.3 Hz), 6.82–6.96 (m, 4H), 13.11 (s, 1H).

17. SMART. Area Detector Software Package, Madison, WI, USA, 1995.