Hydrophobic vs. hydrophilic: ionic competition in remacemide salt structures, Gareth R. Lewis,[a*] Gerry Steele,[a] Alastair J. Florence[b] and Norman Shankland[bc], [a]*AstraZeneca R&D Charnwood, Bakewell Road, Loughborough, Leicestershire LE11 5RH, UK,* [b]*Department of Pharmaceutical Sciences, University of Strathclyde, 27 Taylor Street, Glasgow G4 0NR, UK, and* [c]*CrystallografX Limited, 38 Queen Street, Glasgow G1 3DX, UK*. E-mail: gareth.r.lewis@astrazeneca.com

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Remacemide [2-Amino-N-(1-methyl-1,12-diphenylethyl)-acetamide] was developed as a potential antagonist for epilepsy, Parkinsonism and Huntingon's disease. This paper reports the crystal structure of remacemide **1** and six of its salts [**2** = chloride; **3** = nitrate; **4** = acetate; **5** = hemi-fumarate ($C_4H_3O_4^-$); **6** = naphthalene-2-sulphonate (napsilate, $C_{10}H_7O_3S^-$); **7** = 1-hydroxynaphthalene-2-carboxylate (xinafoate, $C_{11}H_7O_3^-$)], and an investigation of which H-bond motifs and hydrophobic interactions recur across the structural series.

The salts **2**-**7** are polarised into hydrophobic and hydrophilic regions, giving bilayer structures. Within these segregated regions, a range of intermolecular interactions between hydrophilic and hydrophobic components is observed. The molecules occupying the hydrophilic regions of these structures form multiple H-bonds, with the charged NH_3^+ group in **2**-**7** being very aggressive in forming contacts from each of the three protons. The majority of the H-bonds are discrete interactions, as shown by Graph Set Analysis. As most hydrophilic regions form layers, where the individual H-bonds extend to give more complex patterns, these are shown to be chain and ring motifs. Very few intermolecular interactions between the phenyl interactions are identified between the aromatic rings which constitute the hydrophobic regions of the crystal structures, indicating that the observed crystal structures of **1**-**7** result from dominating H-bonds.

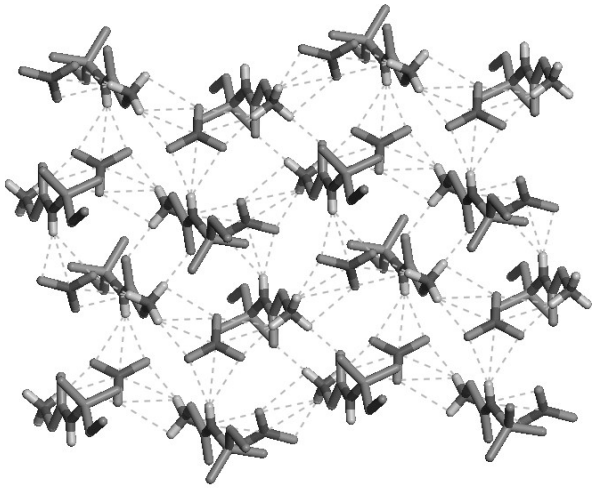

Figure. The network of H-bonds between remacemide cations and nitrate anions in the structure of **3**.