Supplementary Material (ESI) for CrystEngComm

Searching for novel crystal forms by *in situ* high-pressure crystallisation: the example of gabapentin heptahydrate

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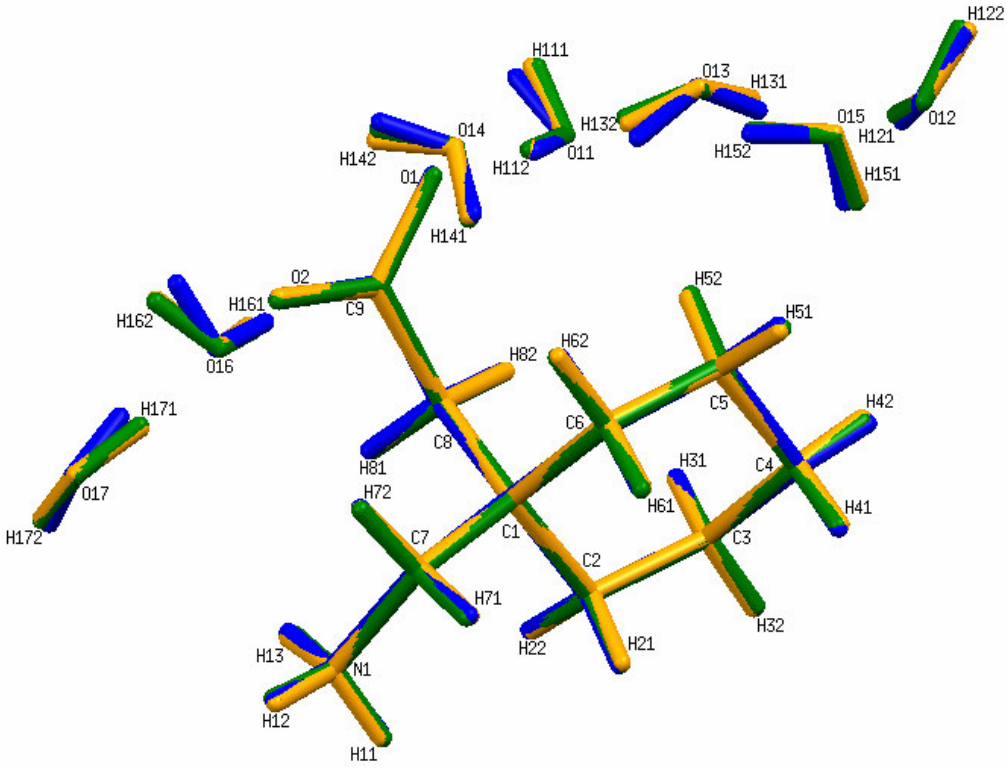
Electronic Supplementary Information

Contents:

Structural overlay of gabapentin heptahydrate, dataset 1, 2 and 1+2

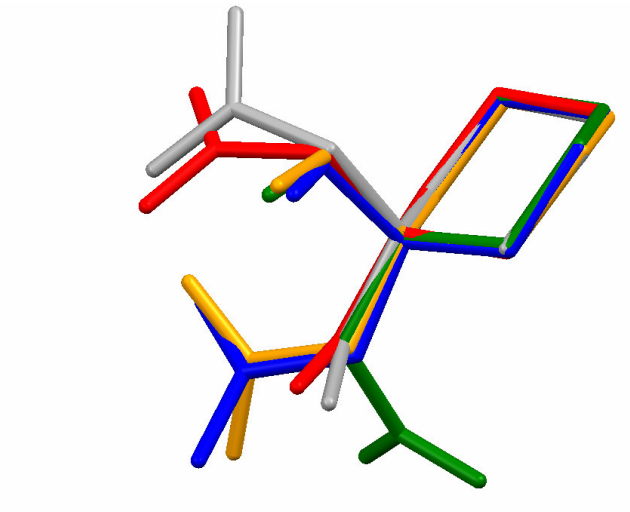


Colouring Scheme:

Dataset 1: blue
Dataset 2: orange
Dataset 1+2: green

Data completeness for dataset 1: 33% to 0.9 Å
Data completeness for dataset 2: 36% to 0.81 Å
Data completeness for combined dataset: 52% to 0.81 Å

Structural overlay of gabapentin zwitterions
H-atoms have been omitted for clarity



Colouring Scheme:

- Aminomethyl group in equatorial position:
β-gabapentin: red
Gabapentin heptahydrate: light grey

- Aminomethyl group in axial position:
α-gabapentin: blue
γ-gabapentin: orange
Gabapentin monohydrate (form I and II have the same conformation): green

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CSD searches for "heptahydrate" structures:
Define four CSD subsets:
1- CSD subset of 167 216 structures: “organic-only structures” for which 3D-coordinates had been determined and had an *R*-factor below 10%, no errors, and were not polymeric (CSD version 5.30, Nov. 2008 +1 update).
2- CSD subset of 141 384 structures: as in 1, but excluding disordered structures (*i.e.* disorder in either solvent or solute).
3- CSD subset of 376 547 structures: as in 1, but including organometallic structures.
4- CSD subset of 297 290 structures: as in 2, but including organometallic structures.

CSD subset	*Number of hits*	*Number of unique hits*	*Number of unique hits, with no disorder reported for water molecules*	*Refcodes in file*
1	64	60	48	Search1.gcd
2	40	36	36	Search2.gcd
3	351	338	244	Search3.gcd
4	211	204	204	Search4.gcd

Comparison with study by van de Streek and Motherwell, *CrystEngComm*, 2007, **9**, 55–64:
CSD subset :100 864 "organic-only structures".
- of 5232"hydrates-only"structures, eleven are heptahydrates: `BACMIB10, CEHDIC, CPMIAL10, DAVHUD, FOYYUN, MEGXIF, SAQZUF02, TYRPXL10, WUNMUN, YUJJAO, ZEKBAS`
- of 364 "hydrates-of anhydrates" structures, one is heptahydrate: `DAFNOO`

Mercury Materials Module using "Motif Search" and "Crystal Packing Feature" tools and a "medium" level of geometrical similarity. H-atoms were not included in the searches

CSD searches for "L4(6)6(8)" motif:

CSD subset	*Refcodes*	*r.m.s.*
1	BULMEA02	0.439
	BUMLEA03	0.433
	HEKXAW	0.21
	RABCEY	0.44
2	HEKXAW	0.21
	RABCEY	0.44
3	BULMEA02	0.439
	BUMLEA03	0.433
	DUJRUV	0.21
	HEKXAW	0.44
	NARYOU	0.571
	RABCEY	0.352
	SALYUZ	0.222
	TMAMOH04	0.623
	VINKIN	0.626
	WIFGOH	0.396
4	DUJRUV	0.21
	HEKXAW	0.44
	NARYOU	0.571
	RABCEY	0.352
	SALYUZ	0.222
	VINKIN	0.626
	WIFGOH	0.396

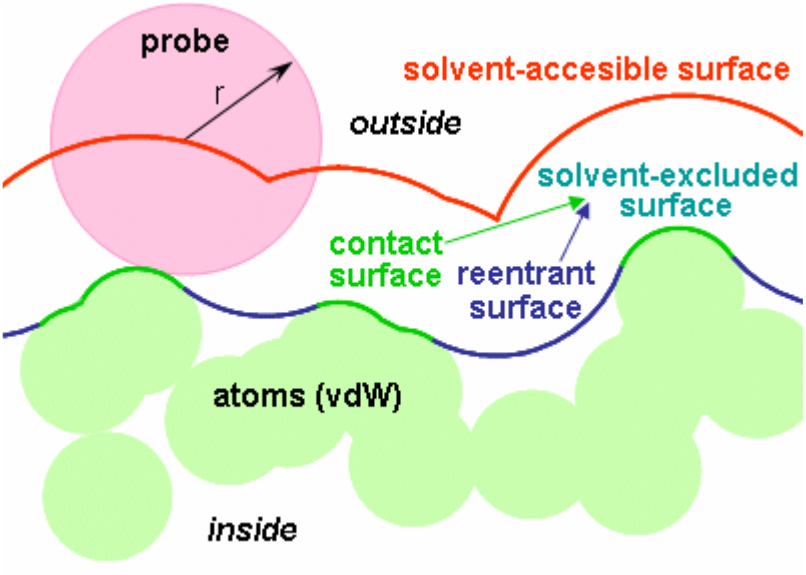
CSD searches for "R4D2" motif

This motif is more common than the "L4(6)6(8)" one; only the results from the search within the CSD subset **2** are reported below.

CSD subset	*Refcodes*	*r.m.s.*
2	DUDPOH	0.232
	EFAMIH	0.342
	FAJVOB	0.22
	FAVRID	0.357
	GADROT	0.461
	GIGQOD	0.482
	ISUSUK	0.44
	KOYTIB	0.282
	LOHQAA	0.254
	MUSJUV	0.437
	NASRII	0.1
	ODORUV	0.269
	RAJKES	0.195
	REPLIH	0.452
	SOYRAZ	0.145
	ZIWHUI	0.467
	ZZZSSY02	0.329

Further criterion used for the CSD searches: O...O distance less than the sum of the vdW radii.

Surfaces definitions



Reproduced from http://jmol.sourceforge.net/docs/surface/
Based on http://geometry.molmovdb.org/3v/ and
http://www.netsci.org/Science/Compchem/feature14.html

Note: The solvent-excluded surface is also known as the Connolly surface.
The surfaces detailed above are drawn *around* a molecule of interest. Similarly, these surfaces can also be applied to void space determination ("inside" becomes "outside"), so that:

Surface calculation for	*Volume inside the surface*
Molecule →	Solvent-accessible surface > Solvent-excluded surface
Void →	Solvent-accessible surface < Solvent-excluded surface

Molecular volume calculations

A positive molecular volume change of 30% was calculated for gabapentin heptahydrate (T = 298 K), with respect to the α-anhydrous form (T = 153 K). Molecular volume calculations were based on equations 1 and 2 as detailed on p. 58 in the paper by van de Streek and Motherwell (J. van de Streek and S. Motherwell, *CrystEngComm*, 2007, **9**, 55–64). Hofmann's molecular volume of water (21.55 Å^3, see D. W. M. Hofmann, *Acta Crystallogr., Sect. B: Struct. Sci.*, 2002, **58**, 489.) was used in the calculations.