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Supporting information for article:

Crystal structure of the orthorhombic pseudopolymorph for tacrine hydrochloride

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S1. Synthesis and crystallization

Tacrine was synthesized from 2-aminobenzonitrile according to a procedure described by Lee & Goehring (1992) but using $MgSO_4$ as desiccant instead of K_2CO_3. Tacrine (5.369 g) in 6N hydrochloric acid (45 ml) was stirred while slightly heated and decanted to a clean flask. Ethanol (25 ml) was added and the solution was divided over 60 test tubes. The tubes and flask with some remaining solution were covered with parafilm with a few holes and put in the fridge at 4°C. After 40 h crystals were harvested from the flask only.

S2. Single crystal X-ray diffraction

Diffraction data were collected at 100K on an Agilent SuperNova diffractometer using Mo-Kα radiation from a colourless crystal measuring 0.61 x 0.14 x 0.10 mm. Using Olex2 (Dolomanov *et al.*, 2009), the structure was solved with the ShelXS (Sheldrick, 2008) structure solution program using Direct Methods and refined with the ShelXL (Sheldrick, 2015) refinement package using full-matrix least-squares techniques. The 1,2,3,4-tetrahydroacridine ring is disordered over two positions (A and B) by rotation of 180° around the C4-N1 axis (occupancy factors 0.413(9) and 0.587(9) for A and B, respectively). The C-C distances of the phenyl and cyclohexene rings involved in the rotational disorder and the O-H distances were restrained. A planarity restraint was used for the phenyl ring of part A (C2, C3, C7, C8A, C9A, C10) for which the temperature factors were also restrained to have the same U_{ij} components. Rigid body restraints were used for all non-H atoms. The C-H hydrogens were placed at calculated positions and refined using in riding mode with C-H distances of 0.95 (aromatic) and 0.99 Å (methylene). The N-H and O-H hydrogens were located in a difference electron density map. All H atoms were refined with U_{iso}(H) values assigned as 1.2 times U_{eq} of the parent atoms.

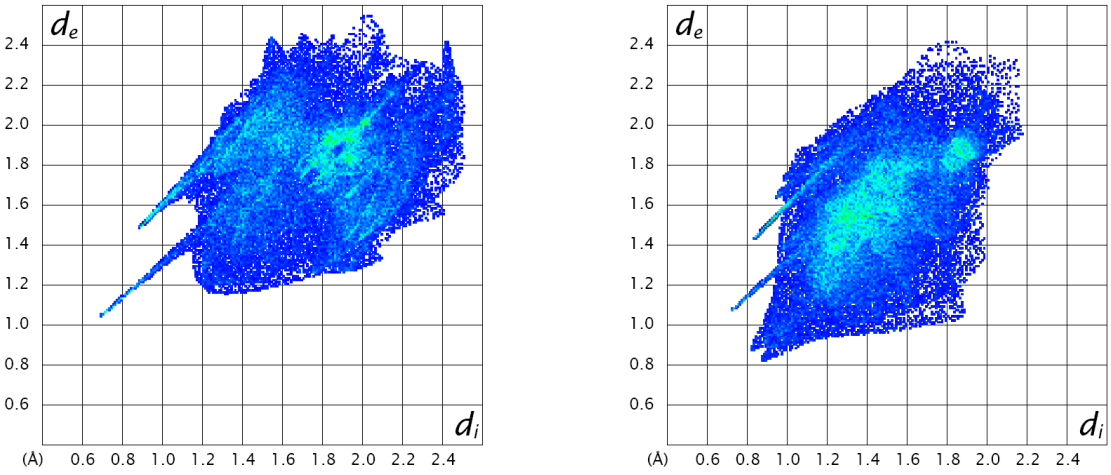
Table S1 Puckering parameters for cyclohexene rings in tacrine hydrochloride dihydrate

Ring atoms	Q (Å)	θ (°)	ϕ (°)	Ring conformation
C2,C3,C7,C8B,C9B,C10	0.484(6)	128.8(5)	31.0(6)	Half-chair
C5,C6,C12,C13A,C14A,C15	0.459(11)	50.9(9)	212.5(11)	Half-chair

Table S2 Simulated powder diffraction pattern for the orthorhombic pseudopolymorph of tacrine hydrochoride dihydrate (Cu-Kα radiation, simulated using Mercury, Macrae *et al.*, 2008)

h	k	l	d-spacing (Å)	F^2	multiplicity
0	0	2	10.3198	4368.55	2
1	0	2	8.93104	17941	4
2	0	0	8.9126	18024.3	2
2	0	2	6.74525	2983.27	4
1	1	0	6.73229	501.698	4
1	1	1	6.4004	387.849	8
1	1	2	5.63854	620.442	8
2	1	1	5.43505	229.44	8
0	0	4	5.1599	641.204	2
3	0	2	5.14923	12251	4
1	0	4	4.95642	2494.28	4
2	1	2	4.94498	342.507	8
1	1	3	4.81177	163.852	8
3	1	0	4.60085	1956.31	4
3	1	1	4.49063	148.52	8
2	0	4	4.46552	12563.8	4
4	0	0	4.4563	804.971	2
2	1	3	4.35887	763.232	8
3	1	2	4.20215	10008.9	8
1	1	4	4.09538	6673.37	8
4	0	2	4.09116	7571.71	4
3	0	4	3.8959	127.913	4
3	1	3	3.82447	394.054	8
2	1	4	3.80516	246.622	8
4	1	1	3.73666	5244.22	8
0	2	0	3.6354	84883.5	2
0	2	1	3.58029	24904.3	4
4	1	2	3.56547	10503.6	8
1	1	5	3.51908	2209.91	8
1	2	1	3.51018	54843.3	8
0	0	6	3.43993	2370.17	2
3	1	4	3.434	6122.26	8
0	2	2	3.42886	105699	4
1	0	6	3.37761	889.971	4
4	0	4	3.37262	3366	4
5	0	2	3.36964	23451.5	4
1	2	2	3.36713	135.317	8

2	2	0	3.36614	1781.49	4
2	1	5	3.32979	695.047	8
4	1	3	3.32596	3860.09	8
2	2	1	3.32225	9862.67	8
0	2	3	3.21425	6524.65	4
2	0	6	3.2092	5048.62	4
5	1	0	3.20096	1613.44	4
2	2	2	3.2002	3466.84	8
1	2	3	3.16324	1238.54	8
5	1	1	3.16315	1440.3	8
3	1	5	3.07252	13.971	8
3	2	1	3.06659	547.945	8
1	1	6	3.06322	8033.97	8
4	1	4	3.0595	4772.89	8
5	1	2	3.05727	1247.52	8
2	2	3	3.02363	1426.53	8
3	0	6	2.97701	6405.04	4



(a) (b)

Figure S1 The two dimensional fingerprint plots of tacrine hydrochloride monohydrate (a) and tacrine hydrochloride dihydrate (b).

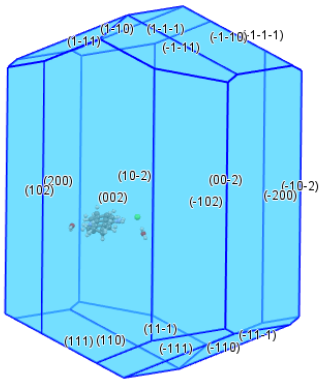


Figure S2 Simulated morphology for tacrine hydrochloride dihydrate using Mercury (Macrae *et al.*, 2008).

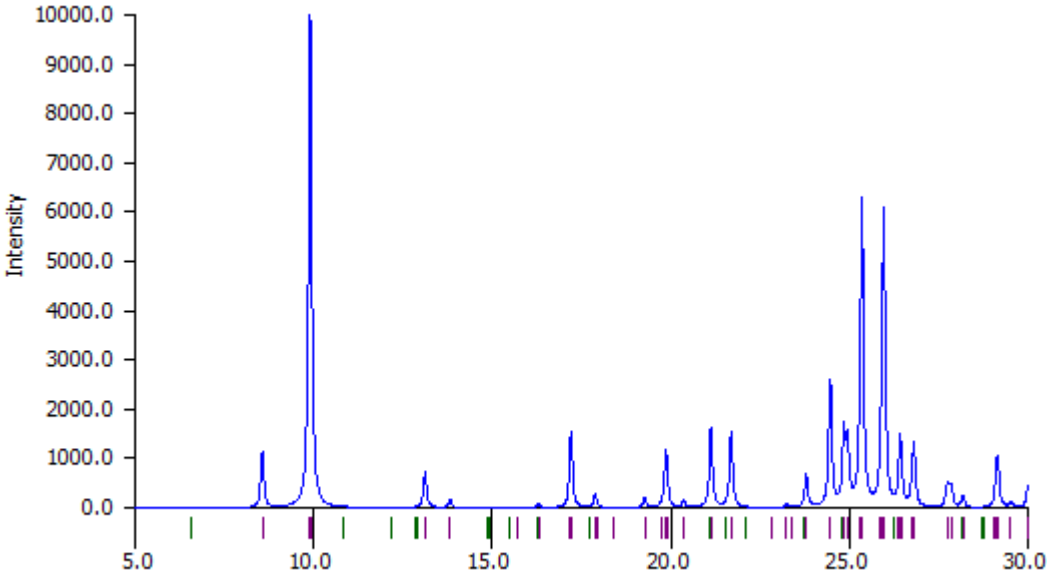


Figure S3 Simulated powder diffraction pattern for the orthorhombic pseudopolymorph of tacrine hydrochloride dihydrate (Cu-Kα radiation, simulated using Mercury, Macrae *et al.*, 2008).

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