Packing Polymorphism of a Conformationally Flexible Molecule (Aprepitant)

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Electronic Supporting Information

Figure S1. Light photomicrographs of aprepitant polymorphs at room temperature (a) form I°, (b) form II, and (c) mixture of the two polymorphs: rectangular plates form I°, irregular plates form II.
Figure S2. Thermal ellipsoide plots of aprepitant polymorphs (drawn at 50% probability level).
**Figure S3.** Ribbon formed by the strong hydrogen bonds of the aprepitant molecules along $a$ in form I° and $b$ in form II. 1D ribbon of form II shown.
Figure S4. Hirshfeld surfaces for aprepitant polymorphs form I° (a) and form II (b). Shape index is mapped between -1.0 (red) and 1.0 (blue). Label: 3a C-H···π acceptor and 3b C-H···π donor.
**Figure S5.** Hirshfeld surfaces of aprepitant modification I°, showing the two hypothetical “ordered“ structures: (a) $-\text{CF}_3$ group involving the atoms F4, F5, and F6; (b) $-\text{CF}_3$ group involving the atoms F4A, F5A, and F6A. $d_e$ Surfaces have been mapped between $d_e$ 0.73 and 2.7 Å. 1a marks the acceptor, 1b the donor of the stronger (shorter) of the two N–H···O hydrogen bonds. The label 2a marks the fluorine atom (F4/ F4A) of the C–H···F interaction. The weak colour difference of spot 2a indicates that the disorder of the CF$_3$ group does not affect this interaction significantly.
Figure S6. 2D fingerprint plots for the two hypothetical “ordered“ structures of form I°: (a) –CF₃ group involving the atoms F4, F5, and F6; (b) –CF₃ group involving the atoms F4A, F5A, and F6A. $d_e$ and $d_i$ are the distances to the nearest atom centre exterior and interior to the surface. In the separated modelled fingerprint plots the C(18)-H···F(4) interaction appears as sharp spikes, whereas the C(18)-H···F(4A) is not distinguishable from the other C-H···F interactions (see Table 3).
Figure S7. Semi-schematic energy/temperature diagram of the aprepitant polymorphs I° and II. \(G\): Gibbs free energy, \(H\): enthalpy, \(\Delta_{\text{fus}}H\): enthalpy of fusion, liq: liquid phase (melt). The bold vertical arrows mark the experimentally measured enthalpies.