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Packing Polymorphism of a Conformationally Flexible Molecule (Aprepitant)

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Electronic Supporting Information

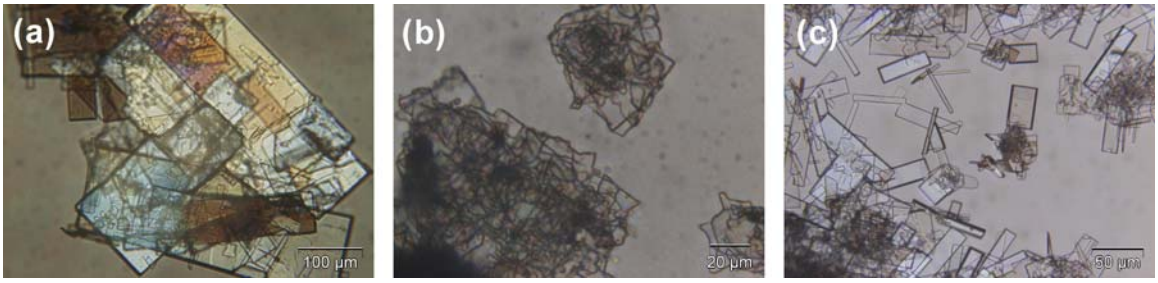

Figure S1. Light photomicrographs of aprepitant polymorphs at room temperature (a) form I°, (b) form II, and (c) mixture of the two polymorphs: rectangular plates form I°, irregular plates form II.

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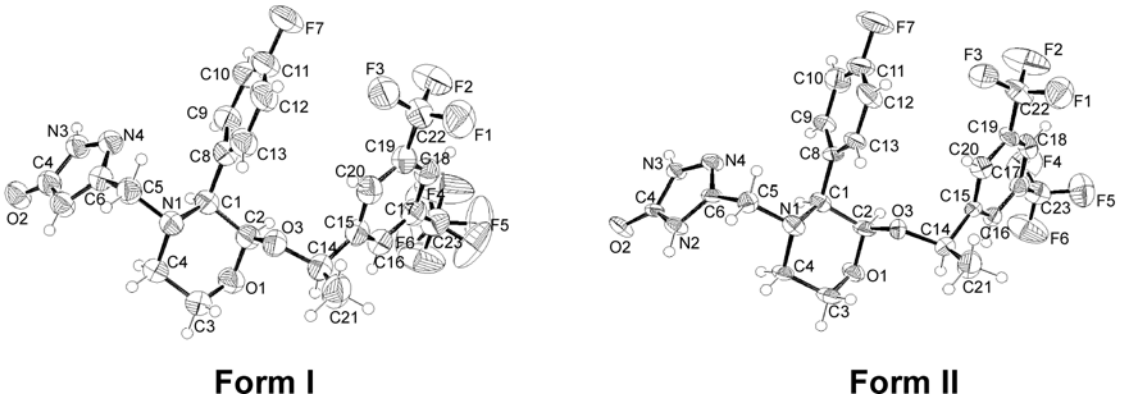

Figure S2. Thermal ellipsoide plots of aprepitant polymorphs (drawn at 50% probability level).

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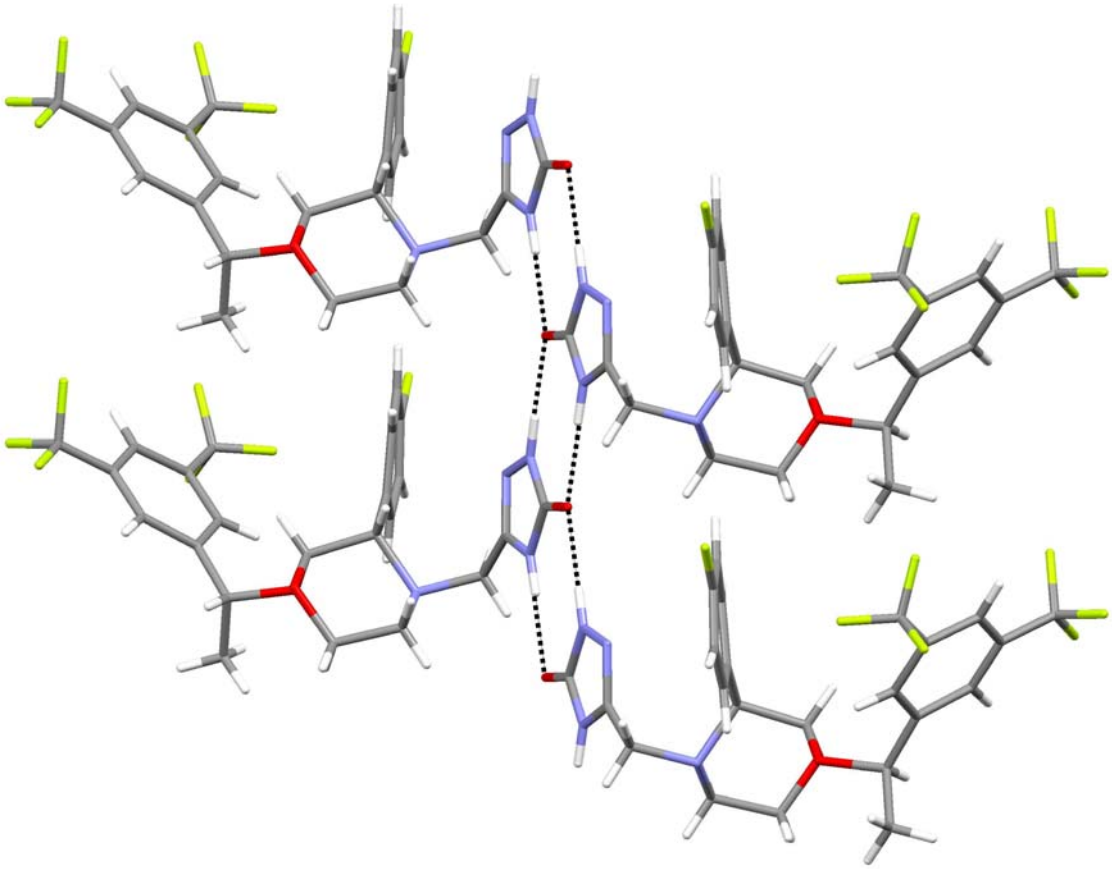

Figure S3. Ribbon formed by the strong hydrogen bonds of the aprepitant molecules along *a* in form I° and *b* in form II. 1D ribbon of form II shown.

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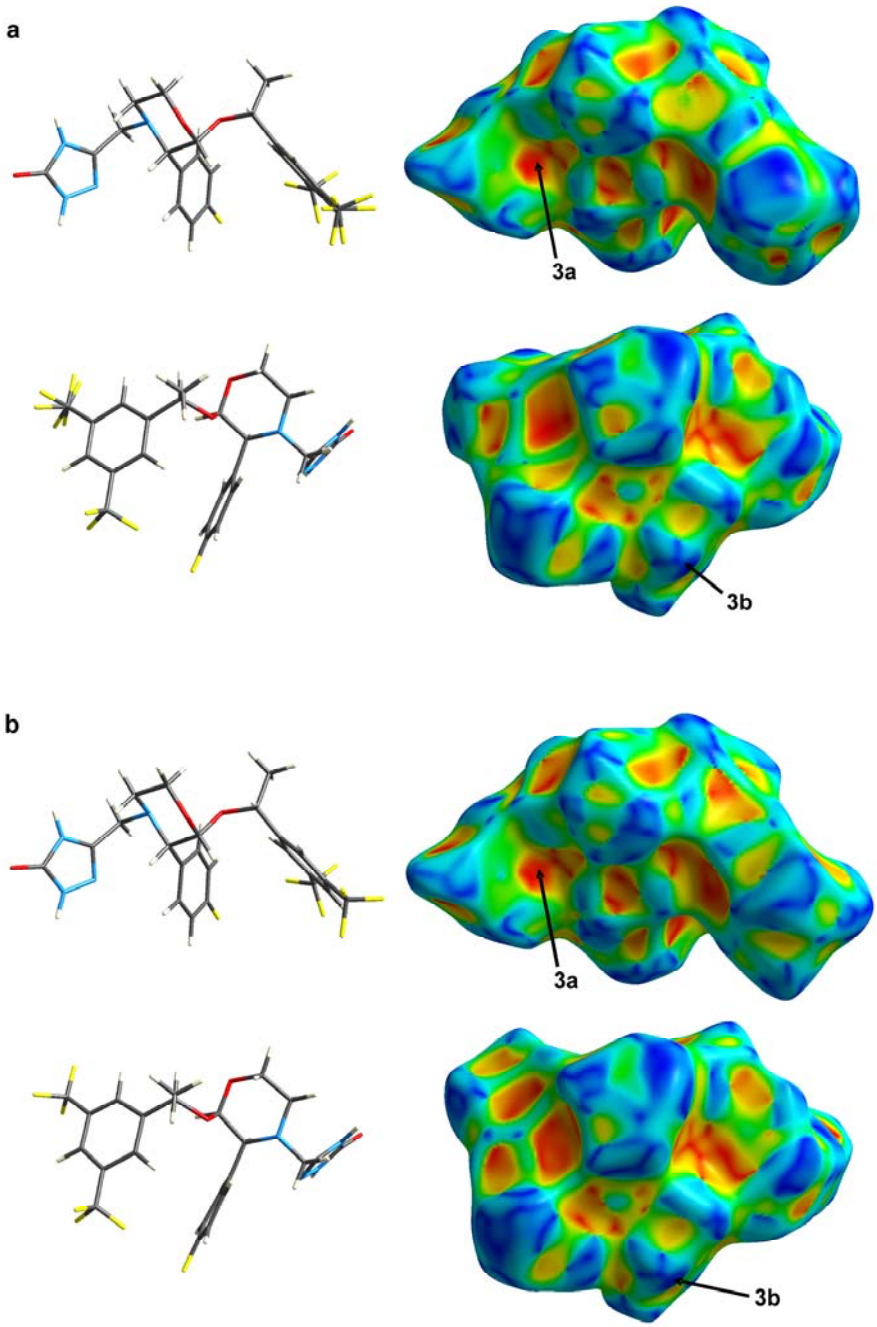

Figure S4. Hirshfeld surfaces for aprepitant polymorphs form I° (a) and form II (b). Shape index is mapped between -1.0 (red) and 1.0 (blue). Label: 3a C-H···π acceptor and 3b C-H···π donor.

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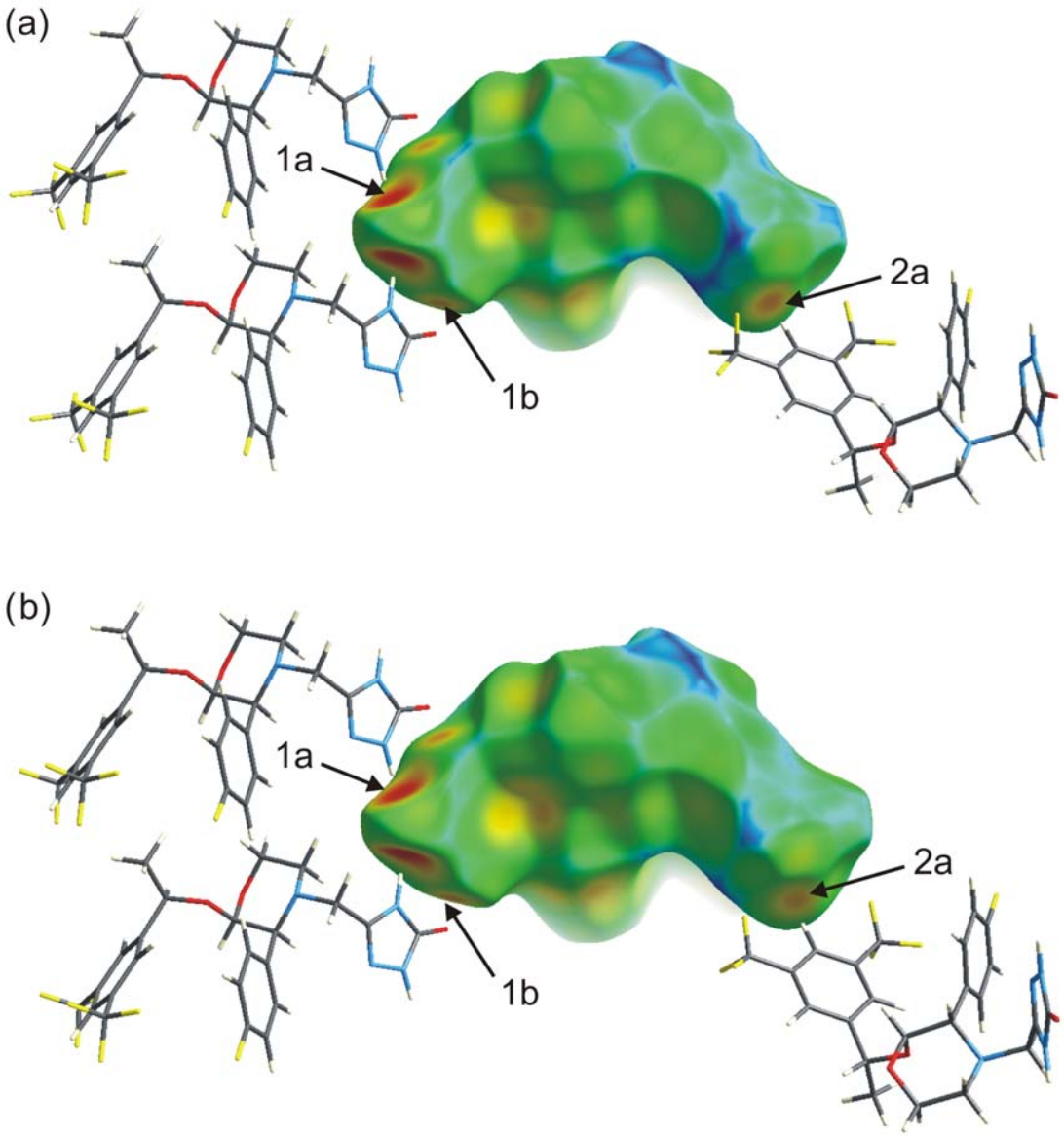

Figure S5. Hirshfeld surfaces of aprepitant modification I°, showing the two hypothetical "ordered" structures: (a) $-CF_3$ group involving the atoms F4, F5, and F6; (b) $-CF_3$ group involving the atoms F4A, F5A, and F6A. d_e Surfaces have been mapped between d_e 0.73 and 2.7 Å. 1a marks the acceptor, 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.

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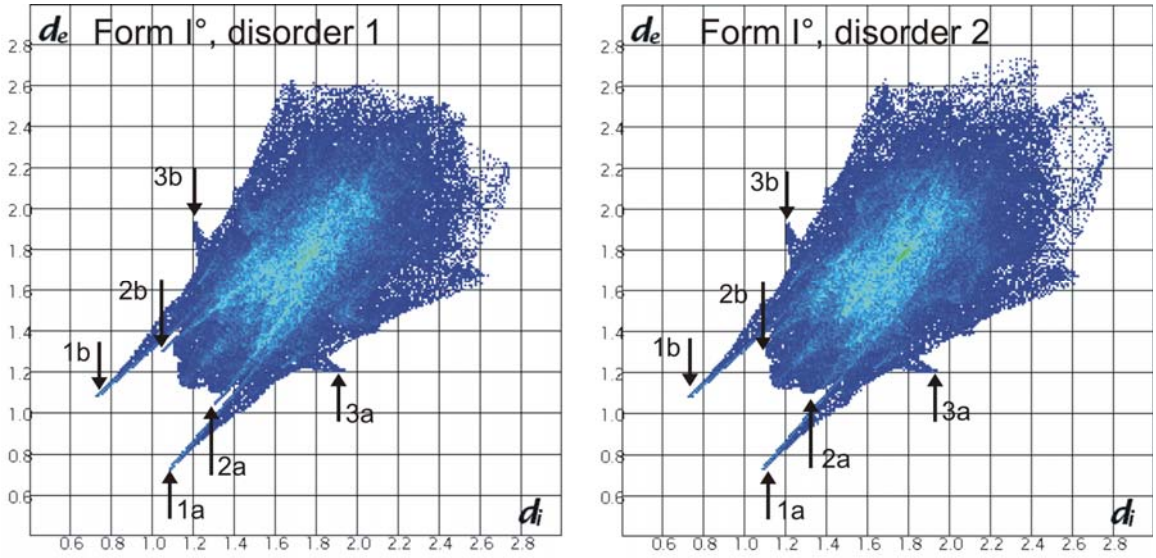

Figure S6. 2D fingerprint plots for the two hypothetical "ordered" structures of form I°: (a) $-CF_3$ group involving the atoms F4, F5, and F6; (b) $-CF_3$ group involving the atoms F4A, F5A, and F6A. d_e and d_i are the distances to the nearest atom centre exterior and interior to the surface. In the 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 interatctions (see Table 3).

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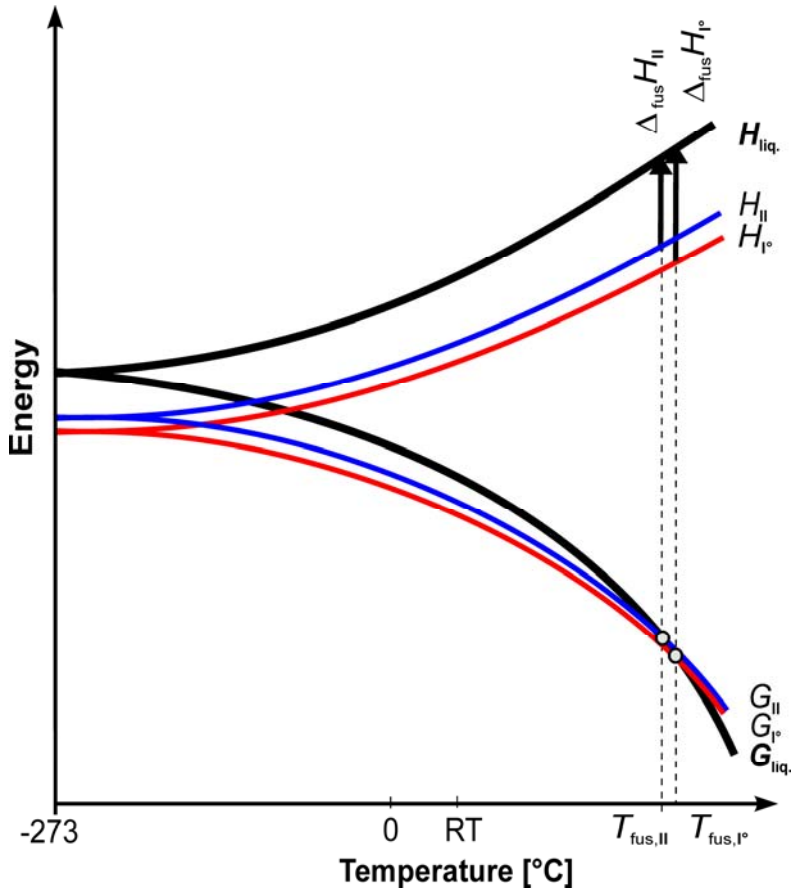

Figure S7. Semi-schematic energy/temperature diagram of the aprepitant polymorphs I° and II. *G*: Gibbs free energy, *H*: enthalpy, $\Delta_{fus}H$: enthalpy of fusion, liq: liquid phase (melt). The bold vertical arrows mark the experimentally measured enthalpies.