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Supporting Information

Saccharine salts of biologically active hydrazone derivatives.

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Details of the DFT calculations

DFT computations with periodic boundary conditions (solid-state DFT calculations) were performed using the CRYSTAL14. The B3LYP functional was employed with an all-electron Gaussian-type localized orbital 6-31G(d,p) basis set. According to previous results,[S1] the B3LYP/6-31G** level of approximation provides reliable and consistent results in studying the various intermolecular (noncovalent) interactions in molecular crystals. The default CRYSTAL14 computation options are used to achieve an appropriate level of accuracy in evaluating the Coulomb and Hartree-Fock exchange series and the exchange-correlation contribution. Tolerance on energy controlling the self-consistent field convergence for geometry optimizations and frequencies computations is set to 1×10^{-9} and 1×10^{-10} hartree, respectively. The shrinking factor, reflecting the density of the k-points grid in the reciprocal space, was set at least to 3. The space groups and unit cell parameters of the considered cocrystal obtained in the single-crystal X-ray studies are fixed and structural relaxations are limited to the positional parameters of atoms. The atomic positions from experiment are used as the starting point in the solid-state DFT computations. All the optimized structures correspond to the minimum point on the potential energy surface.

References

S1 (a) J. Oddershede and S. Larsen, *J. Phys. Chem. A*, 2004, **108**, 1057; (b) H. Munshi and T. N. Guru Row, *J. Phys. Chem. A*, 2005, **109**, 659. (c) H. Munshi, T. S. Thakur, T. N. Guru Row and G. R. Desiraju, *Acta Cryst. B*, 2006, **62**, 118; (d) H. Munshi and T. N. Guru Row, *Acta Cryst. B*, 2006, **62**, 612; (e) M. V. Vener, A. V. Manaev, A. N. Egorova and V. G. Tsirelson, *J. Phys. Chem. A*, 2007, **111**, 1155.

Table S1. Characteristics of the intermolecular (noncovalent) interactions in the salts calculated by the solid-state DFT method coupled with the Bader analysis of the periodic wave-function*

Interaction	Salt **I**				Salt **II**			
	D(X···A)/ Å (D(H···A)/ Å)	ρ_b/ a.u.	G_b/ a.u.	E_{int}/ kJ·mol^{-1}	D(X…A)/ Å (D(H···A)/ Å)	ρ_b/ a.u.	G_b/ a.u.	E_{int}/ kJ·mol^{-1}
Hydrogen bonds								
O2-H22···N2[a]**	2.681 (1.859)	0.038	0.027	**30.1**	1.842 (2.671)	0.038	0.026	**29.8**
N3-H3···O6[b]	2.589 (1.512)	0.071	0.051	**57.1**	3.579 (1.550)	0.072	0.052	**58.8**
N1-H21···O4[a]	3.074 (2.272)	0.017	0.013	**14.6**	3.030 (2.306)	0.019	0.014	**16.3**
C-H…O(N) contacts								
C7-H7···O5[a]	3.245 (2.363)	0.015	0.011	**12.6**	3.219 (2.320)	0.016	0.012	**13.5**
C4-H4···O4[a]	3.327 (2.454)	0.013	0.010	**11.7**	3.345 (2.395)	0.013	0.010	**10.8**
C1-H1···N4[b]	3.228 (2.554)	0.012	0.008	**9.4**	3.302 (2.521)	0.013	0.008	**9.5**
C7-H7···O4[a]	3.469 (2.711)	0.009	0.007	**8.2**	3.444 (2.734)	0.009	0.007	**8.0**
C12-H12···O5[c]	-	-	-	**-**	3.291 (2.660)	0.009	0.007	**8.2**
C14-H14B···O3[d]	3.298 (2.720)	0.009	0.007	**8.1**	-	-	-	**-**
C17-H17···O1[e]	3.202 (2.677)	0.009	0.007	**8.1**	3.049 (2.541)	0.013	0.010	**11.4**
C19-H19···O3[f]	3.733 (2.860)	0.009	0.007	**7.8**	-	-	-	**-**
C18-H18···O3[e]	3.320 (2.617)	0.009	0.007	**7.7**	-	-	-	**-**
C14-H14C···O2[g]	3.693 (2.759)	0.009	0.006	**7.0**	-	-	-	**-**
C18-H18···O1[e]	3.194 (2.644)	0.007	0.006	**6.8**	3.174 (2.609)	0.007	0.006	**6.7**
C13-H13···O5[a]	3.438 (2.596)	0.007	0.005	**6.1**	3.472 (2.609)	0.008	0.006	**6.7**
C14-H14B···O2[d]	3.508 (2.762)	0.007	0.005	**6.0**	-	-	-	**-**
C2-H2···O6[h]	3.757 (2.905)	0.006	0.005	**5.2**	3.769 (2.864)	0.005	0.004	**4.5**
C5-H5···O1[i]	3.654 (2.892)	0.005	0.004	**4.3**	3.502 (2.762)	0.007	0.005	**5.8**
C5-H5···O4[j]	3.572 (3.005)	0.005	0.003	**3.9**	3.445 (2.904)	0.006	0.005	**5.5**
C20-H20···O5[j]	3.557 (3.059)	0.004	0.003	**3.5**	3.510 (2.991)	0.005	0.004	**4.6**
C17-H17···O2[e]	-	-	-	**-**	3.225 (2.801)	0.005	0.005	**5.2**
C18-H18···O2[e]	-	-	-	**-**	3.907 (3.033)	0.005	0.004	**4.7**
***π*-stacking interactions**								
C4···O6[k]	3.124	0.009	0.007	**7.5**	3.114	0.009	0.006	**7.1**
C1···O1[j]	3.162	0.008	0.006	**6.8**	3.136	0.009	0.007	**7.4**
N1···N3[g]	3.212	0.008	0.006	**6.5**	3.186	0.008	0.006	**6.5**
C4···C7[j]	3.312	0.008	0.005	**5.3**	3.310	0.007	0.004	**4.7**
C1···N2[j]	3.402	0.006	0.004	**5.0**	3.353	0.006	0.004	**4.7**
C10···N1[g]	3.444	0.006	0.004	**5.0**	3.444	0.006	0.004	**4.2**
C12···N1[g]	3.619	0.007	0.004	**4.9**	-	-	-	**-**
C11···N2[g]	3.432	0.006	0.004	**4.8**	3.343	0.006	0.004	**4.1**
C17···N3[m]	3.366	0.006	0.004	**4.0**	3.298	0.007	0.004	**4.7**
C2···O4[k]	3.402	0.004	0.003	**3.5**	3.388	0.004	0.003	**3.5**
Other interactions								
H19···C12[f]	-	-	-	**-**	2.818	0.008	0.005	**6.0**
C12···O5[c]	3.190	0.006	0.005	**5.5**	-	-	-	**-**
H10···H18[l]	-	-	-	**-**	2.441	0.006	0.004	**5.0**
H13···H20[g]	2.456	0.006	0.004	**4.8**	2.525	0.004	0.003	**3.2**
C17···O2[e]	3.255	0.005	0.004	**4.8**	-	-	-	**-**
C19···N4[j]	-	-	-	**-**	3.422	0.006	0.004	**4.2**
C10···C10[d]	-	-	-	**-**	3.519	0.005	0.004	**4.1**
H14A···C15[c]	3.140	0.006	0.004	**4.1**	-	-	-	**-**
C18···O6[j]	-	-	-	**-**	3.363	0.005	0.003	**3.9**
H11···C19[c]	-	-	-	**-**	2.987	0.005	0.003	**3.7**
H12···H12[n]	2.784	0.004	0.003	**3.3**	-	-	-	**-**
H12···C15[c]	-	-	-	**-**	3.209	0.005	0.003	**3.2**
E_{latt}, kJ·mol^{-1}				**263.9**				**260.4**

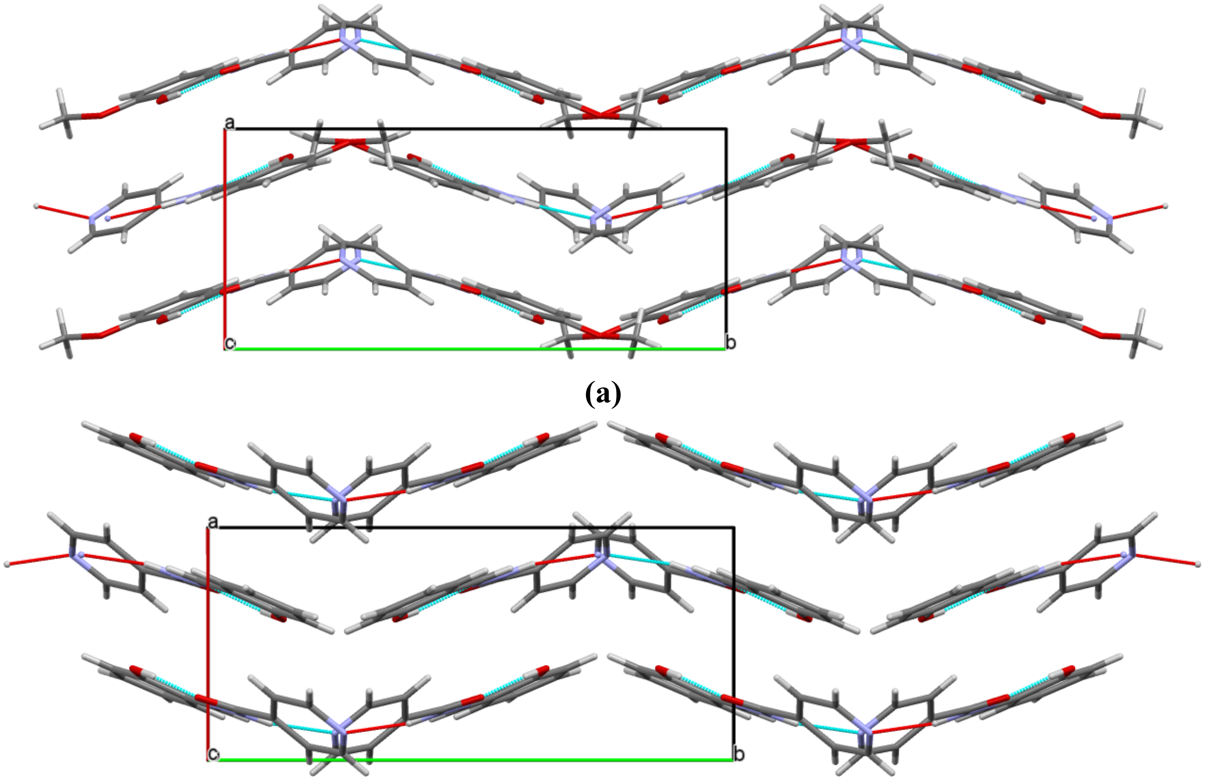
*The X…A and H…A distances, *D*(X…A) and *D*(H…A), where X, A = O, N and C; the electron density ρ_b and local electronic kinetic energy density G_b at the bond critical point; the energy of the intermolecular noncovalent interaction E_{int}.

**Intramolecular hydrogen bond. This energy did not count in E_{latt} calculation.

Symmetry codes: [a] (x, y, z); [b] (3/2+x, 1/2-y, 1/2+z); [c] (-x, -y, 1-z); [d] (-x, -y, 2-z); [e] (x, y, -1+z); [f] (1-x, -y, 1-z); [g] (-1+x, y, z); [h] (1+x, y, 1+z); [i] (1/2+x, 1/2-y, -1/2+z); [j] (1+x, y, z); [k] (1/2+x, 1/2-y, 1/2+z); [l] (-1+x, y, 1+z); [m] (-1/2+x, 1/2-y, -1/2+z); [n] (-1-x, -y, 1-z).

Table S2. Sums of the intermolecular interaction energies (kJ·mol^{-1}) between the different types of molecules calculated using by the solid-state DFT method coupled with the Bader analysis of the periodic wave-function

	API-API	**API-Saccharin**	**Saccharin-Saccharin**	**Total**
Salt **I**	67.0 (25.4%)	193.4 (73.3%)	3.5 (1.3%)	263.9
Salt **II**	41.5 (15.9%)	206.2 (79.2%)	12.7 (4.9%)	260.4



(a)

(b)

Fig. S1 Molecular packing projections for (**a**) vanillin isoniazid (CANCOK01) along c-axis and (**b**) salinazid (WEHFEU03) along c-axis.

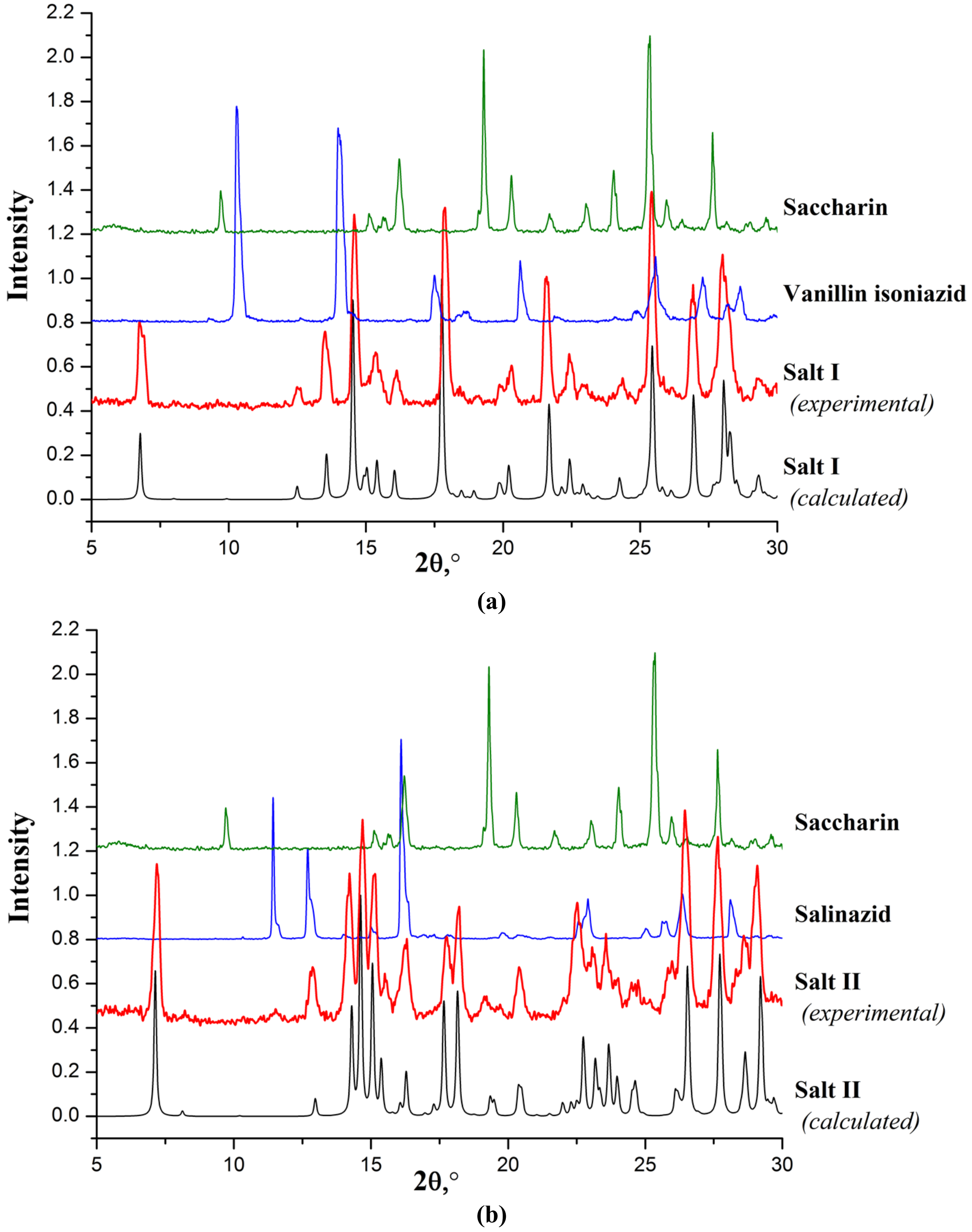
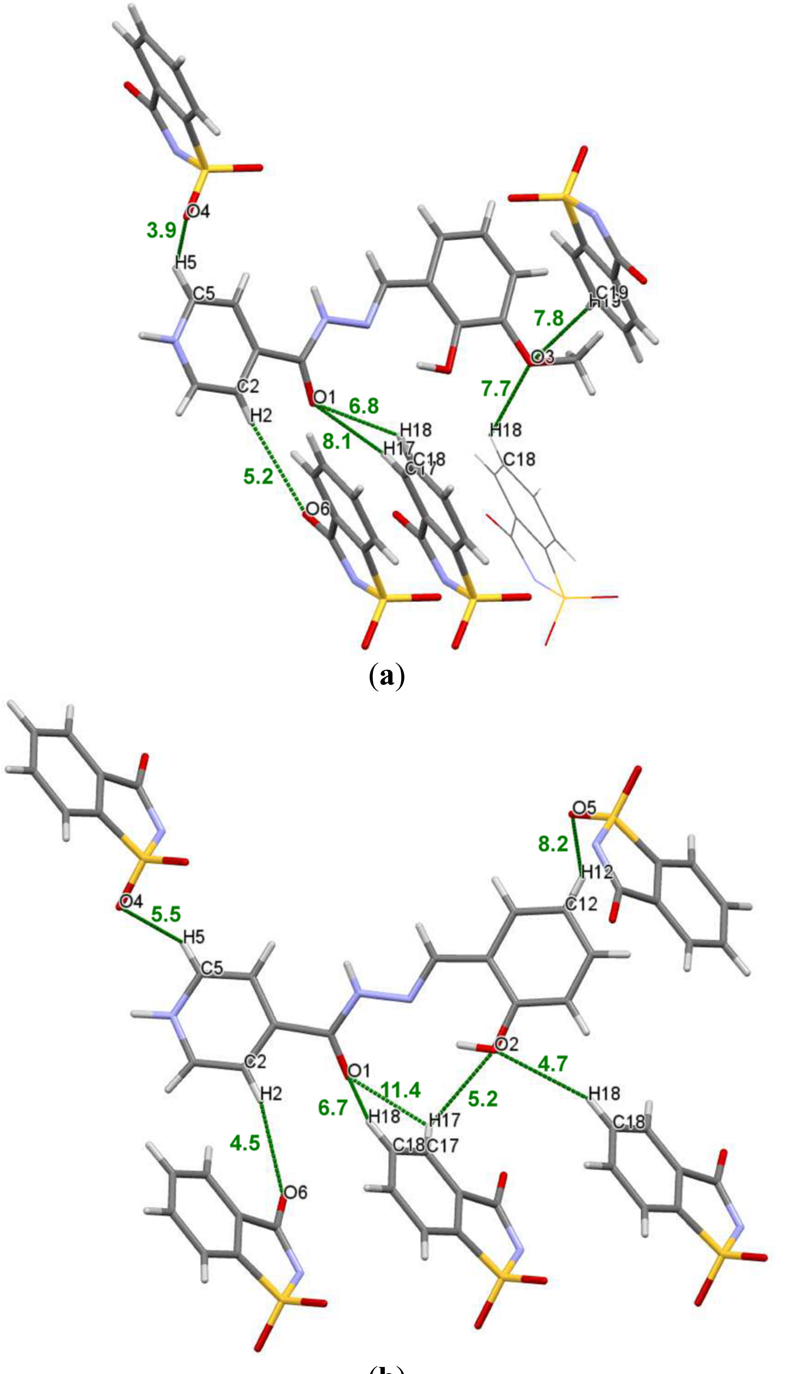


Fig. S2 Results of PXRD analysis of **(a)** salt **I** and its components, **(b)** salt **II** and its components.



(**a**)

(**b**)

Fig. S3 Intermolecular C–H···O interactions between API and the neighboring saccharin molecules in the crystal of (**a**) salt **I** and (**b**) salt **II**. The interaction energies are given in kJ·mol^{-1}.

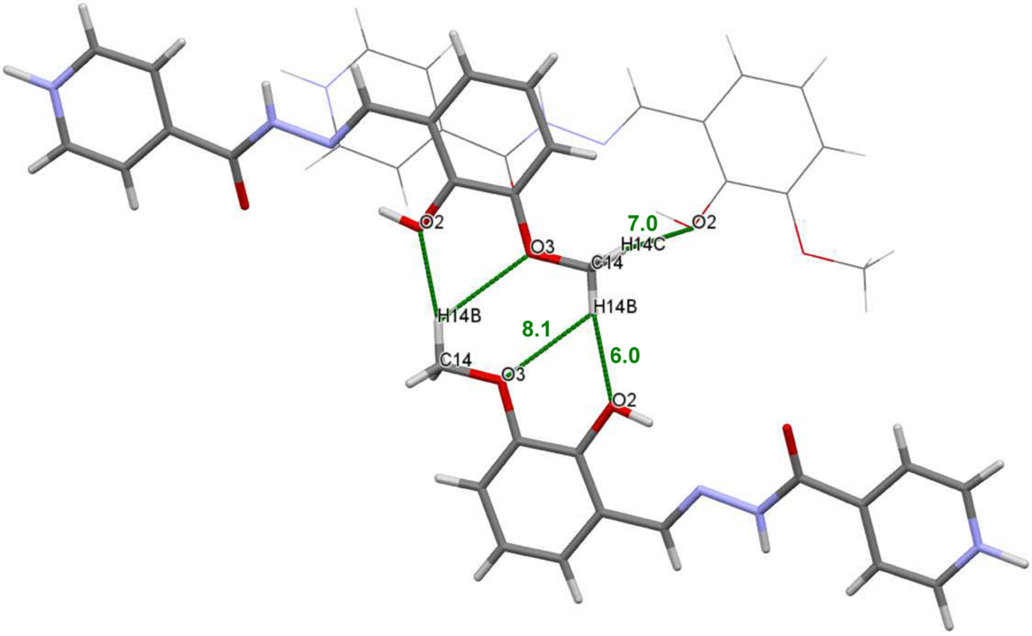


Fig. S4 Weak C–H···O interactions between the methoxy and hydroxy groups of the vanillin isoniazid molecules in the crystal of salt **I**. The interaction energies are given in kJ·mol^{-1}.

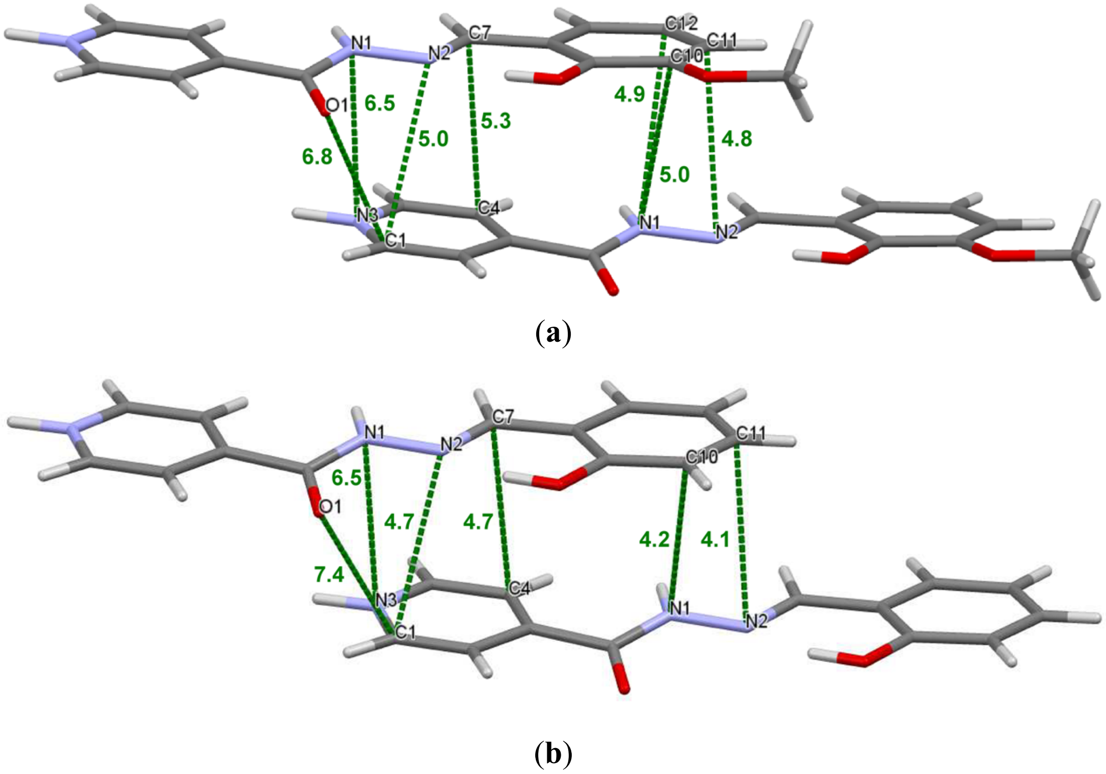
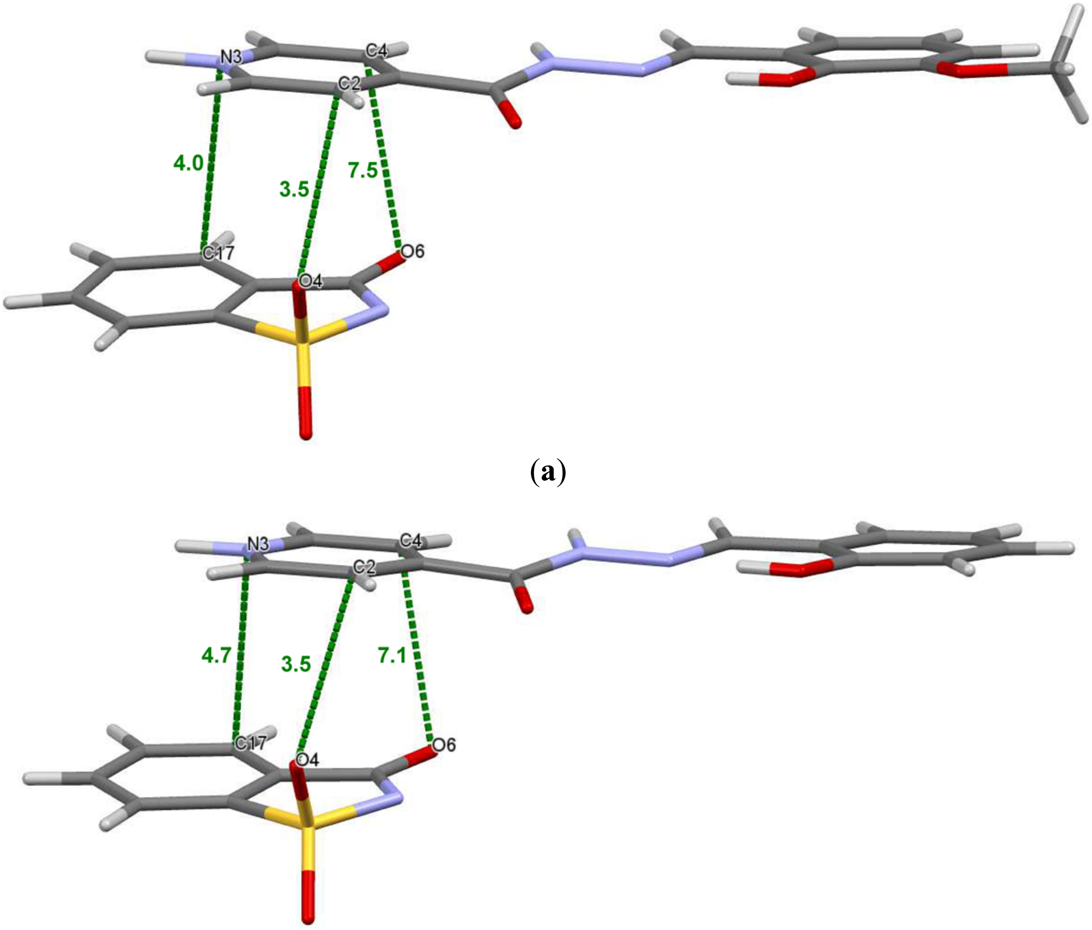


Fig. S5 Weak π-stacking interactions between the API molecules in the crystal of (**a**) salt **I** and (**b**) salt **II**. The interaction energies are given in kJ·mol^{-1}.



(**a**)

(**b**)

Fig. S6 Weak π-stacking interactions between the API and saccharin molecules in the crystal of (**a**) salt **I** and (**b**) salt **II**. The interaction energies are given in kJ·mol^{-1}.

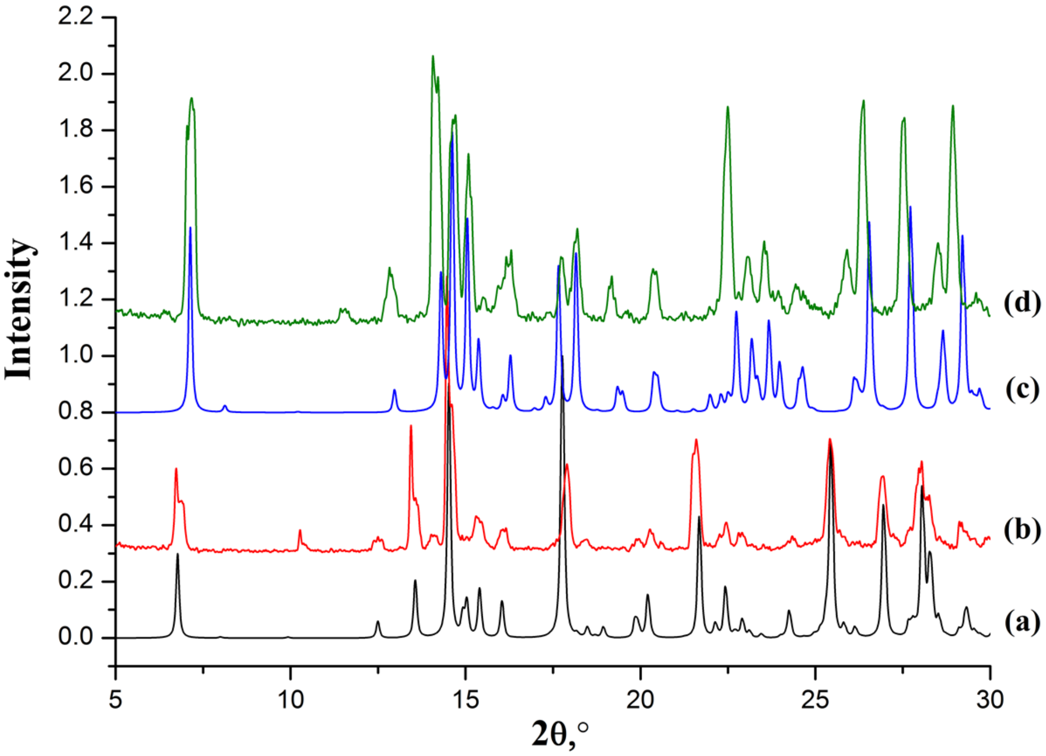


Fig. S7 PXRD analysis of: **(a)** simulated pattern of salt **I**, **(b)** residual material after solubility of salt **I** in water, **(c)** simulated pattern of salt **II**; **(d)** residual material after solubility of salt **II** in water.