Solvent-free and catalysis-free approach to the solid state in situ growth of crystalline isoniazid hydrazones

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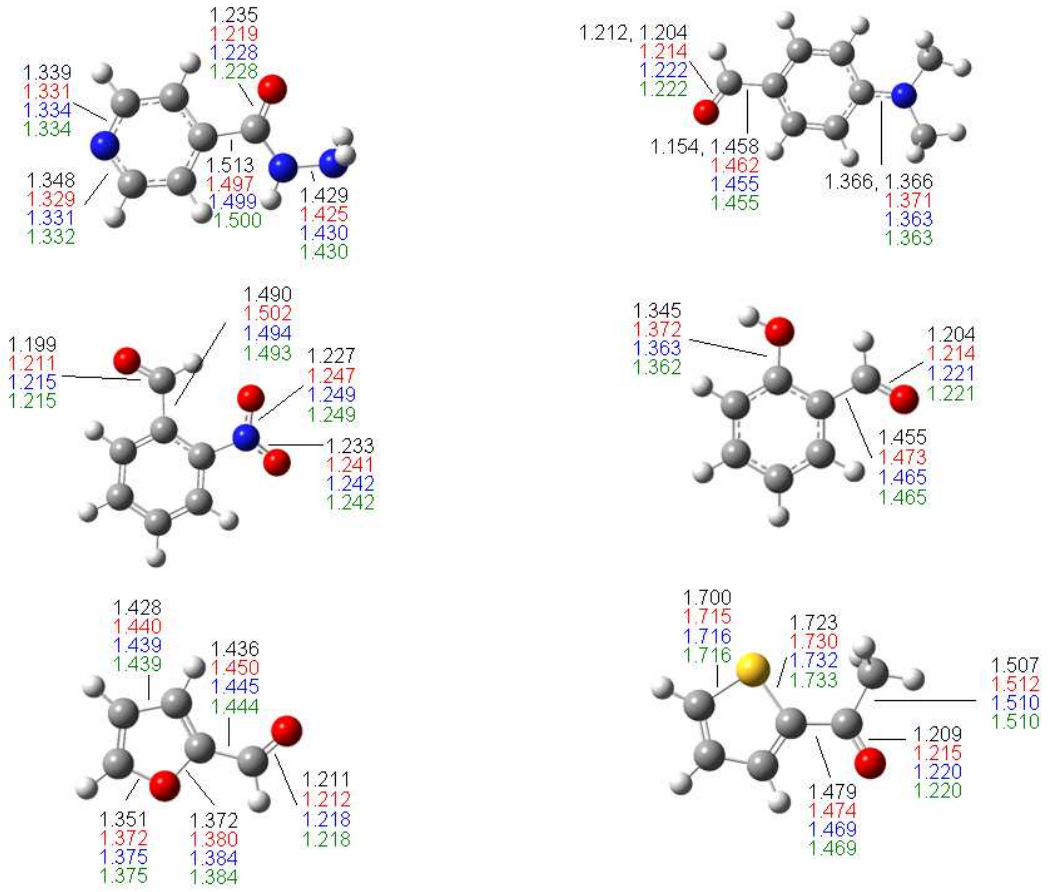

Fig.S1a The selected bond lengths (Å) of substrate molecules from the crystal structures[45-50] (black), for the gas-phase optimized structures (red) and implicit-solvent optimized molecule – methanol (blue) and water (green).

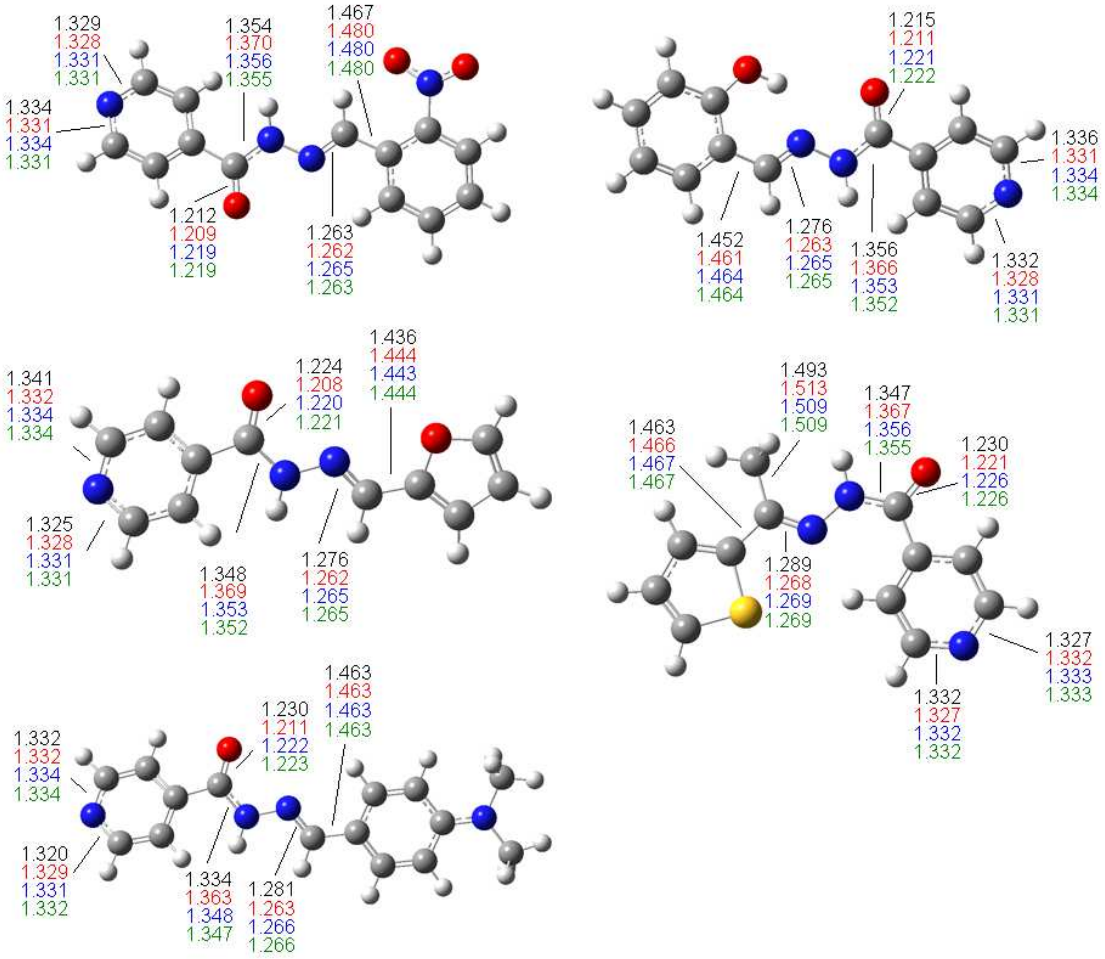

Fig.S1b The selected bond lengths (Å) of hydrazone molecules from the crystal structures[41-44] (black), for the gas-phase optimized structures (red) and implicit-solvent optimized molecule – methanol (blue) and water (green).

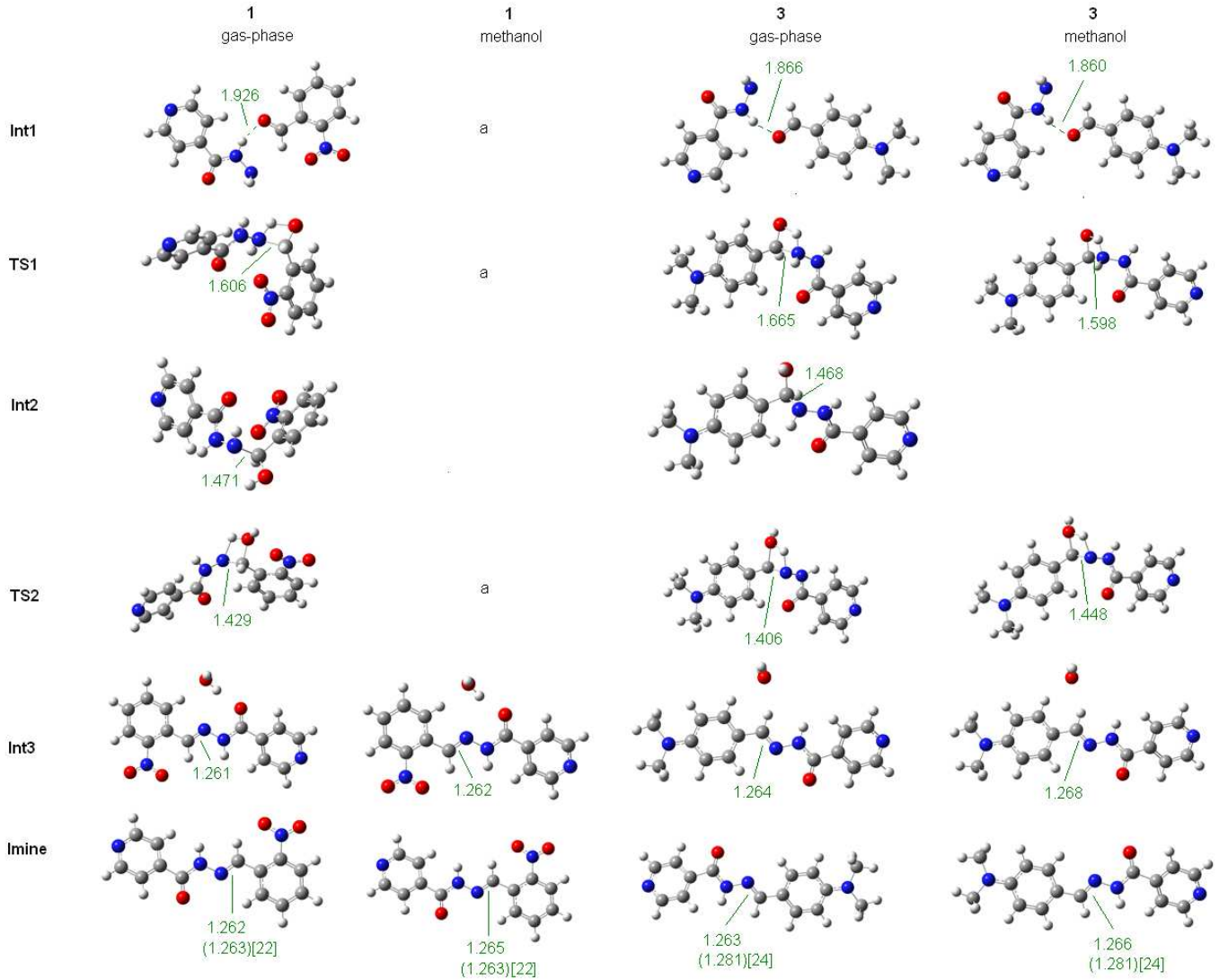

Fig. S2a The optimized structures of intermediates (Int), transition structures (TS), substrate and product molecules for **1** and **3**. The imine bond length is in Å.

a – an energy minimum could not be found.

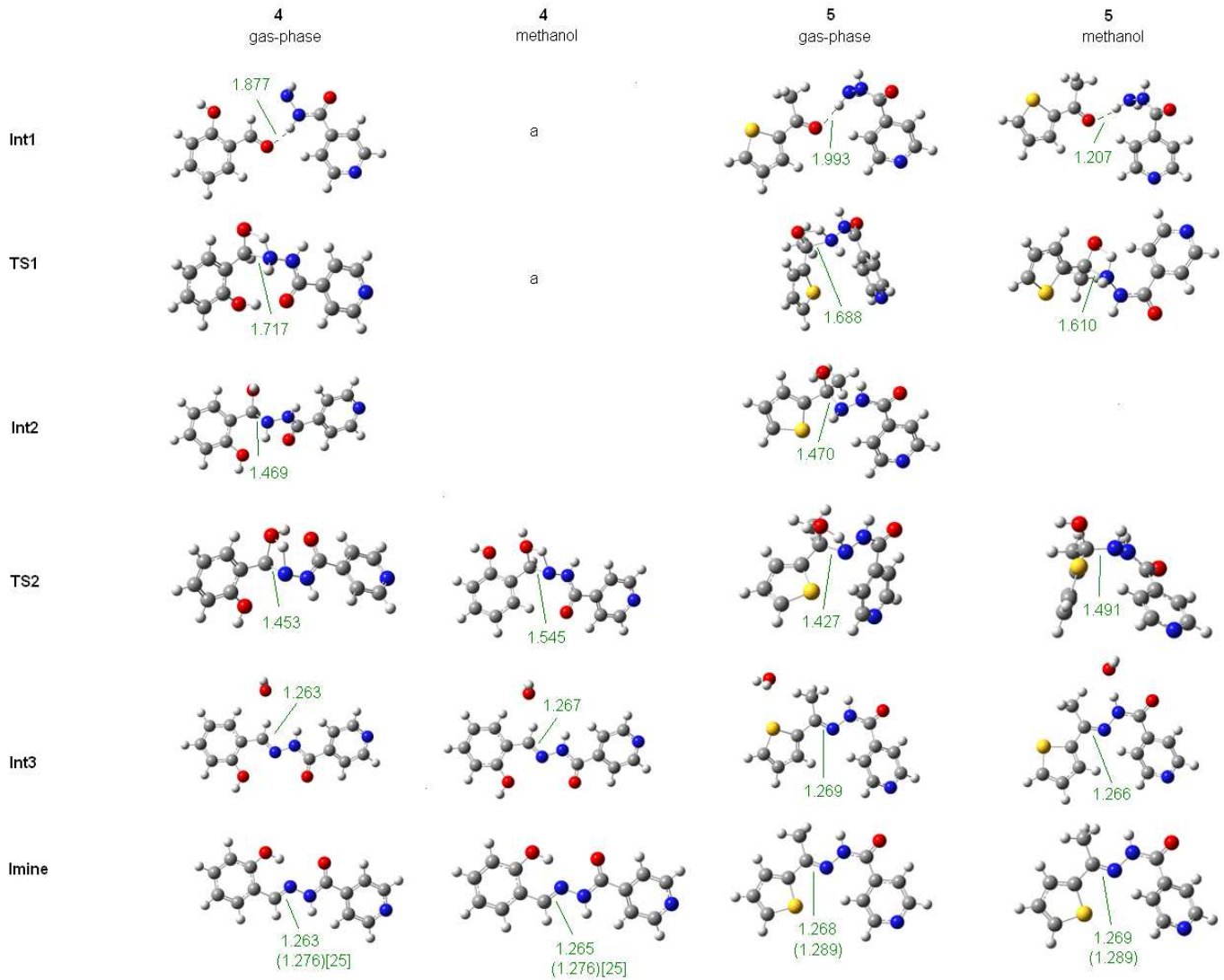

Fig. S2b The optimized structures of intermediates (Int), transition structures (TS), substrate and product molecules for **4** and **5**. The imine bond length is in Å.

a – an energy minimum could not be found.

Table S1
The calculated Gibbs free energy values (a.u.) for reactant and product molecules as well as for transition states and intermediates in the gas phase and in the presence of the methanol solvent as a polarizable continuum. The barrier heights (ΔE) are in kcal mol^{-1}.

Compound	**1**		**2**		**3**		**4**		**5**	
Gibbs free energy	gas-phase	methanol	gas-phase	methanol	gas-phase	methanol	gas-phase	methanol	gas-phase	methanol
S	-1021.028668	-1021.070021	-814.568895	-814.606396	-950.485761	-950.524701	-891.885915	-891.932943	-1176.441522	-1176.477478
Int1	-1021.022857	a	-814.555844	-814.590444	-950.481991	-950.510172	-891.880952	a	-1176.427021	-1176.457714
TS1	-1020.968268	a	-814.499667	-814.542158	-950.413067	-950.455786	-891.819392	a	-1176.36564	-1176.398874
Int2	-1021.026243		-814.565718		-950.477739		-891.881811		-1176.431195	
TS2	-1020.929954	a	-814.468110	-814.511769	-950.384137	-950.423737	-891.797933	-891.837842	-1176.342539	-1176.450842
Int3	-1021.030897	-1021.068501	-814.564604	a	-950.480415	-950.519979	-891.878221	-891.926998	-1176.431206	-1176.465889
P	-1021.037872	-1021.085016	-814.573829	-814.622414	-950.491018	-950.537023	-891.902510	-891.949282	-1176.446599	-1176.485645
$\Delta_1 E$ (TS1-S)	37.9		43.4	40.3	45.6	43.2	41.7		47.6	49.3
$\Delta_2 E$ (TS2-S)	61.9		63.2	59.4	63.8	63.4	55.2	59.7	62.1	16.7
Δ_1D ($\Delta_1 E$g - $\Delta_1 E$m)				3.1		2.4				-1.7
Δ_2D ($\Delta_2 E$g – $\Delta_2 E$m)				3.8		0.4		-4.5		45.4
$\Delta_1 E$ (TS1-Int1)	34.3		35.3	30.3	43.3	34.1	38.6		38.5	36.9
$\Delta_2 E$ (TS2-Int1)	58.3		55.1	49.4	61.4	54.2	52.1		53.0	4.3

a – an energy minimum could not be found.
S – a sum of isolated substrate molecules Gibbs free energy
P – a sum of isolated product molecules Gibbs free energy
ΔD – a difference between the barrier heights in gas-phase (g) and methanol (m)