Supporting Information

Nucleation Behaviour of Racemic and Enantiopure Histidine

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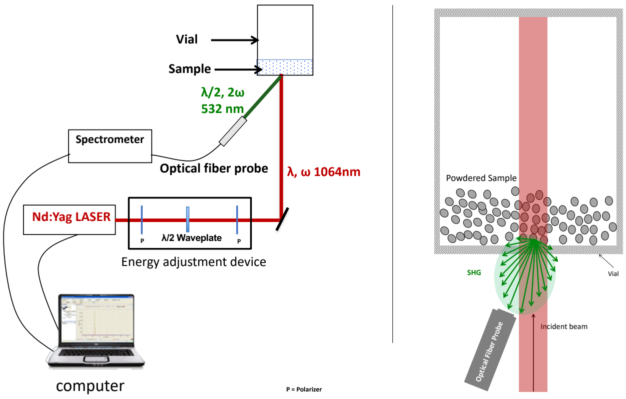

Figure S 1. Experimental setup Second Harmonic Generation Apparatus constituted of Nd:YAG Q-switched laser operating at 1064 nm.

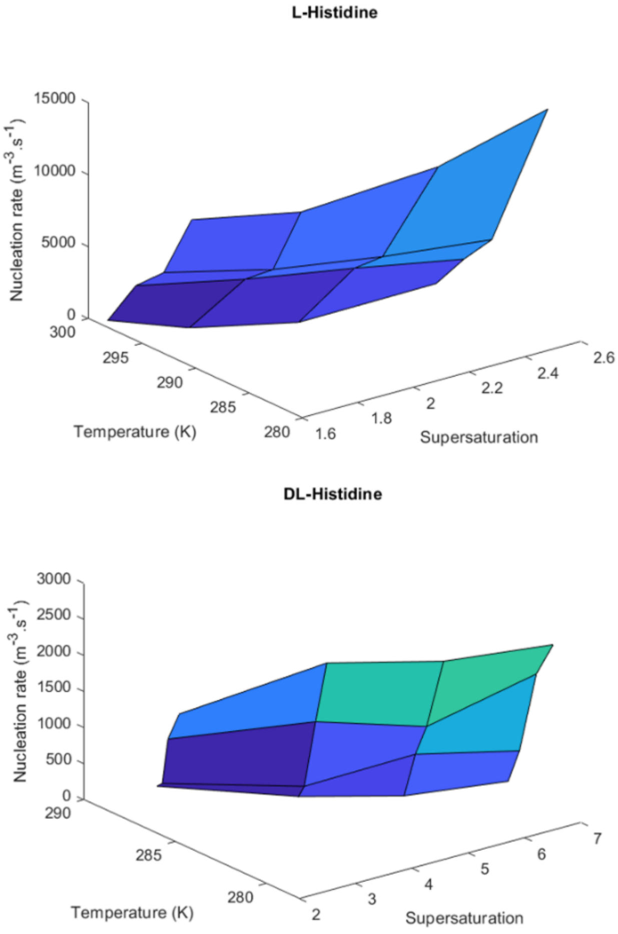

Figure S 2. Surface plot of relationships between the measured values (the lighter the colour, the higher the nucleation rate).

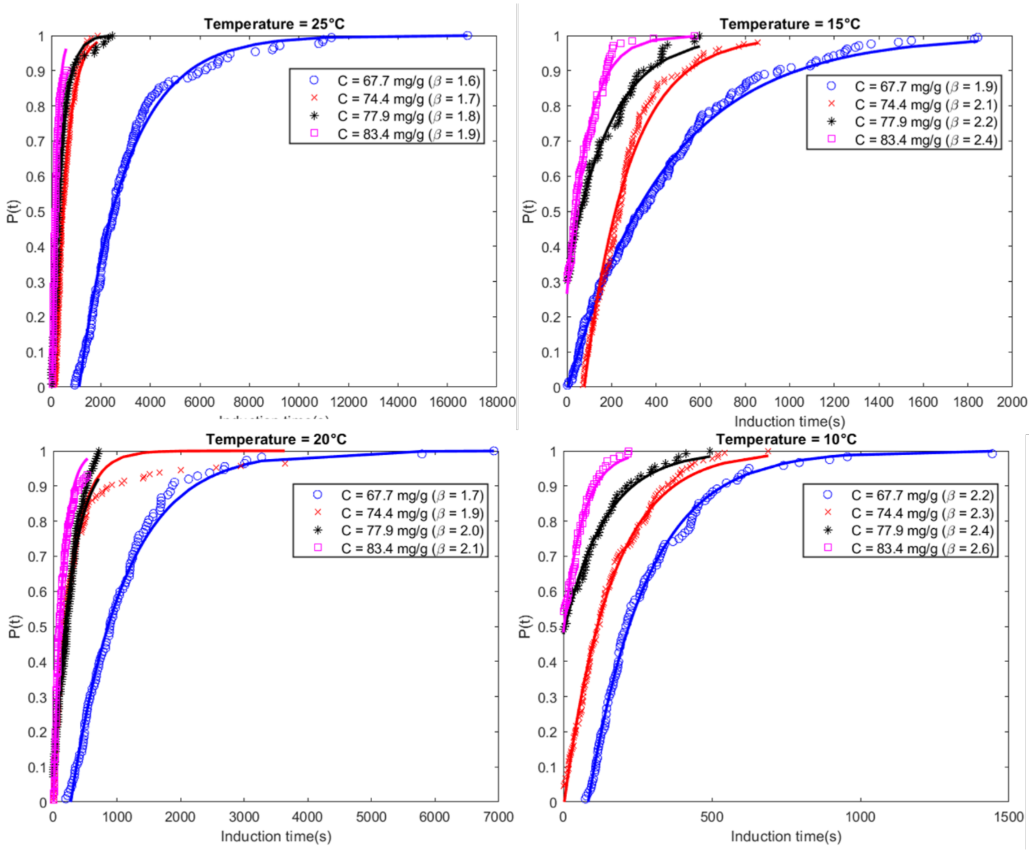

Figure S 3. Experimentally obtained probability distribution P(t) of the induction time for L-histidine at T = 25, 20, 15 and 10 °C and C_0 = 67.7, 74.4, 77.9 and 83.4 mg/g. The solid lines are fits of equation 1 to the experimental data.

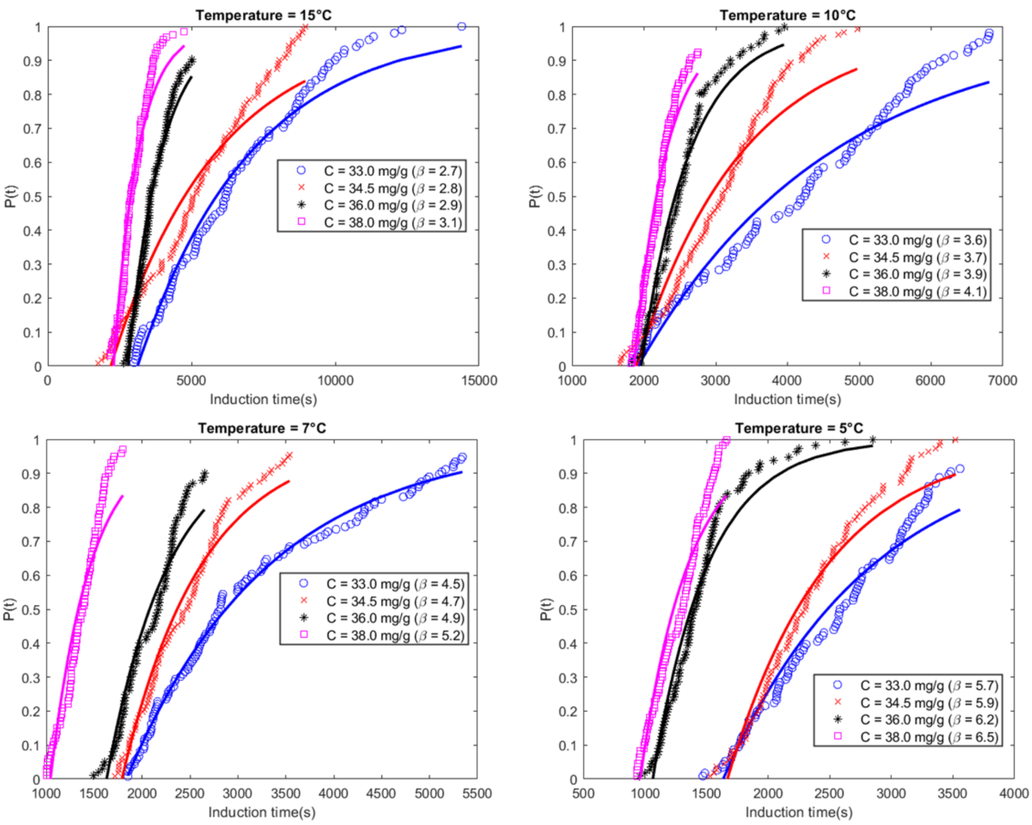

Figure S 4. Experimentally obtained probability distribution P(t) of the induction time for DL-histidine at T = 15, 10, 7 and 5 °C and C_0 = 33.0, 34.5, 36.0 and 38.0 mg/g. The solid lines are fits of equation 1 to the experimental data.

Table S 1. Estimated parameters for interface-transfer and volume-diffusion control for histidine.

a_I (J.mol^{-1}.K^{-1}.m^{-3})	b_I	a_D (J.mol^{-1}.K^{-1}.m^{-3})	b_D
4.5 x 10^{27}	2.2	5.5 x 10^{27}	5.5 x 10^{27}

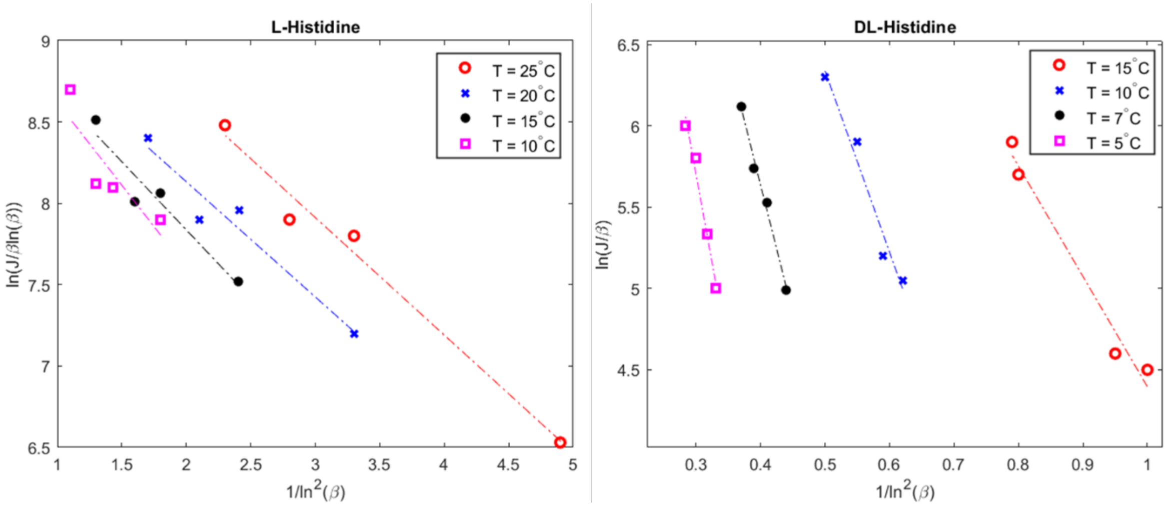

Figure S 5. Plot of ln(J/β lnβ) versus 1/ln²β and for four different temperatures. The experimental data are given by colored circles and the solid lines are the best fit to the experimental points.

Table S 2. Comparison of the parameters A and B obtained by regressing experimental data and those obtained theoretically.

	T (°C)	$B_{D\,(exp)}$	$A_{D\,(exp)}/ln\beta$	B_D (predicted)	$A_{D\,(predicted)}/ln\beta$
L-His	25	7.2 x 10^{-1}	2.4 x 10^4	7.2 x 10^1	2.7 x 10^{35}
	20	7.0 x 10^{-1}	1.4 x 10^4	7.0 x 10^1	2.1 x 10^{35}
	15	8.3 x 10^{-1}	1.5 x 10^4	10.8 x 10^1	1.6 x 10^{35}
	10	10.2 x 10^{-1}	1.6 x 10^4	11.7 x 10^1	1.2 x 10^{35}
DL-His	15	6.4	4.9 x 10^4	2.3 x 10^2	5.1 x 10^{34}
	10	11.3	12.2 x 10^4	2.7 x 10^2	3.2 x 10^{34}
	7	14.4	5.7 x 10^4	3.1 x 10^2	2.2 x 10^{34}
	5	20.7	8.2 x 10^4	3.5 x 10^2	1.6 x 10^{34}

Table S 3. ΔG(kJ.mol^{-1}) values for L-Histidine.*

T (°C) \ β	1.7	1.8	1.9	2.1	2.2	2.4
25	6.42	5.24	4.39	3.29	2.91	2.36
20	7.86	6.40	5.37	4.02	3.56	2.89
15	9.62	7.84	6.57	4.92	4.36	3.53
10	10.04	8.18	6.86	5.13	4.55	3.69

Table S 4. n (molecules) values for L-Histidine.*

β / T (°C)	1.7	1.8	1.9	2.1	2.2	2.4
25	9.77	7.19	5.52	3.57	2.98	2.18
20	12.16	8.94	6.87	4.45	3.71	2.71
15	15.14	11.14	8.55	5.54	4.61	3.37
10	16.07	11.83	9.08	5.88	4.90	3.58

Table S 5. ΔG(kJ.mol-1) values for DL-Histidine.*

β / T (°C)	2.6	2.7	2.8	2.9	3.1	3.6
15	17.79	16.46	15.32	14.32	12.69	9.90
10	28.72	26.58	24.73	23.13	20.48	15.98
7	40.09	37.10	34.53	32.29	28.59	22.31
5	55.17	51.05	47.51	44.43	39.35	30.70

Table S 6. n (molecules) values for DL-Histidine.*

β / T (°C)	2.6	2.7	2.8	2.9	3.1	3.6
15	15.54	13.84	12.42	11.24	9.36	6.45
10	25.54	22.74	20.42	18.46	15.39	10.60
7	36.04	32.08	28.80	26.05	21.71	14.96
5	49.95	44.47	39.92	36.10	30.09	20.73

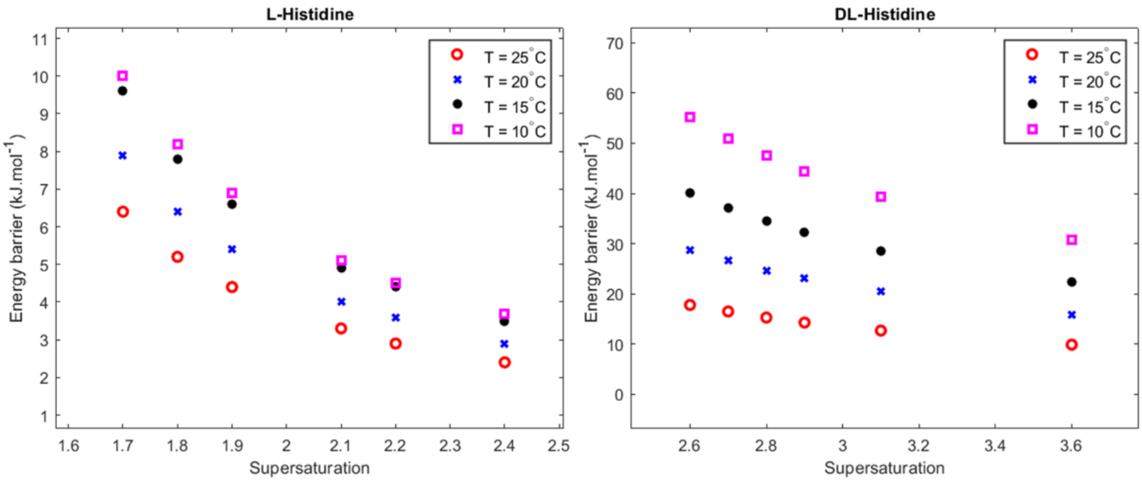

Figure S 6. ΔG(kJ.mol-1) values for L-Histidine (1.7 ≤ β ≤ 2.4) and DL-Histidine (2.6 ≤ β ≤ 3.6).*

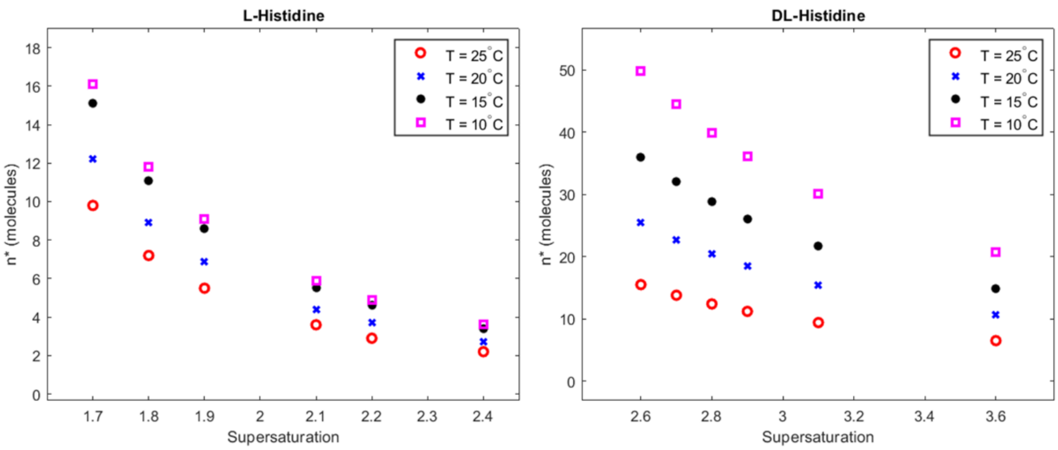

Figure S 7. n (molecules) values for L-Histidine (1.7 ≤ β ≤ 2.4) and DL-Histidine (2.6 ≤ β ≤ 3.6).*

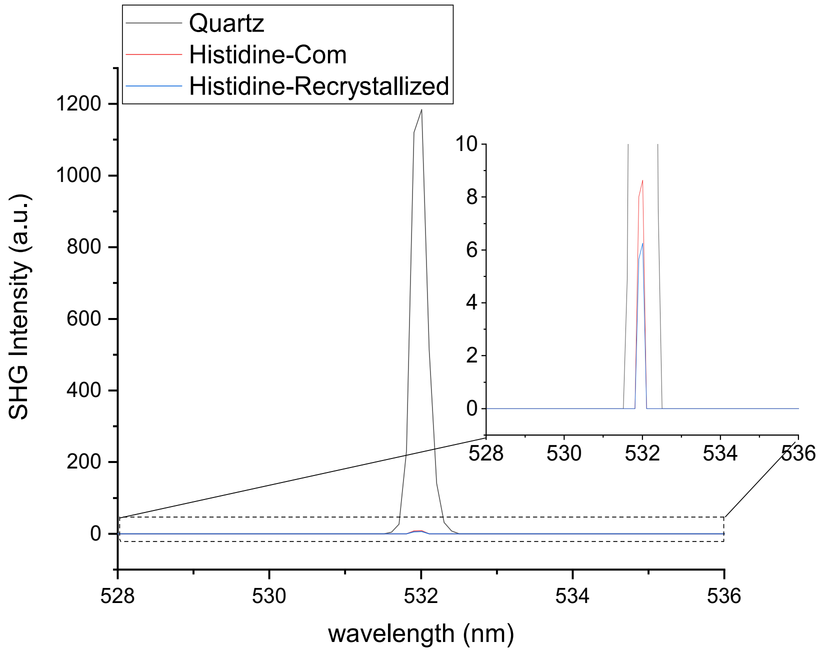

Figure S 8. SHG spectra obtained using Kurtz&Perry test. Samples give a signal at circa 0.5% of the signal of alpha-quartz (45µm).

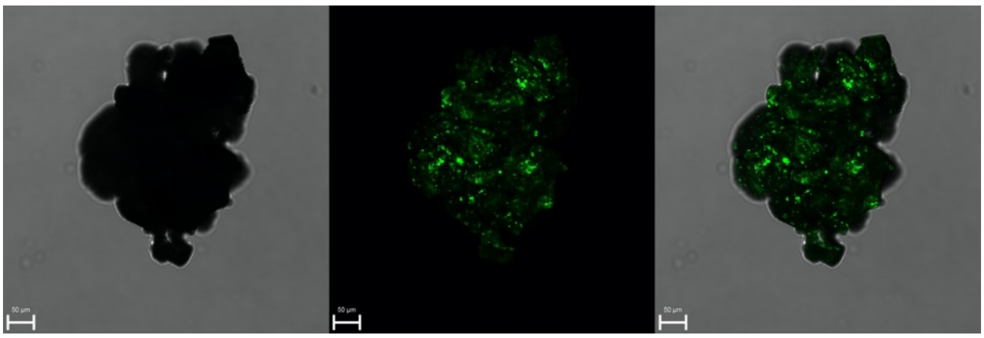

Figure S 9. Aggregate of racemic histidine obtained by precipitation (β = 15) in stagnant aqueous solution; left optical microscopy (bright field), middle SHG microscopy, right overlay of optical and SHG microscopy.

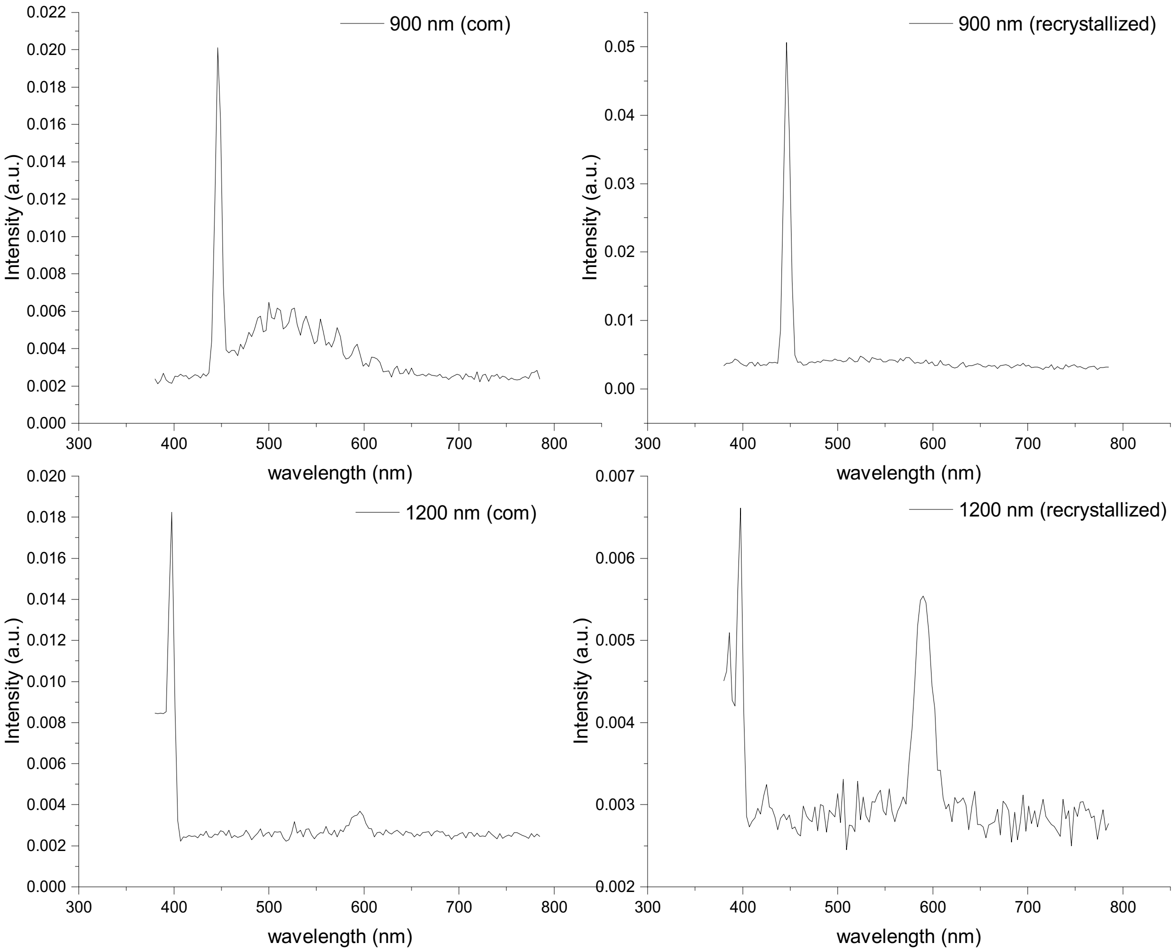

Figure S 10. SHG emission spectra obtained using SHG microscopy for excitation wavelength of 900nm and 1200 nm.

Theory:

According to CNT for homogeneous nucleation, the kinetic parameter *A* for volume-diffusion is given by:

$A_{D,hom} = (kT/\nu_0^2\gamma)^{1/2} Ds\ln\beta$ (S1)

υ_0 is the molecular volume defined as:

$\upsilon_0 = M/\rho_c N_A$ (S2)

Where M is the molar mass, ρ_c is the crystal density and N_A is Avogadro number (6.022×10^{-23} mol^{-1}).

The diffusion coefficient *D* is calculated using this equation:

$D = kT/6\pi r_0 \eta$ (S3)

In equation (S3), r_0 is the radius of the molecule calculated from the molecular volume (r_0 = 3.53 Å) and η is the dynamic viscosity given in (Pa·s) estimated using the following equation for pure water: $\eta = (0.001\theta + 0.246)/((0.05594\theta + 5.2842)\theta + 137.37)$ with θ the temperature in °C.

J for volume-diffusion control:

$$J = a_D\, T/\eta\, (\ln(\rho_c/Ms))^{0.5}\, s\beta\ln(\beta)\exp(-b_D(\ln^2(\rho_c/Ms))/(\ln^2\beta)) \quad \text{(S4)}$$

and a_I, a_D, b_I and b_D are given by:

$$a_I = (4\pi/3\nu_0)^{1/3}\,(0.514(\rho_c/M\,N_A)^{2/3})^{1/2}\, k\, N_A/6\pi r_0 \quad \text{(S5)}$$

$$a_D = (1/0.514\, \nu_0^2\, (\rho_{c\,N_A}/M)^{2/3})^{1/2}\, k\, N_A/6\,\pi\, r_0 \quad \text{(S6)}$$

$$b_I = b_D = 16\,\pi\, \nu_0^2/3\, (0.514)^3\, (\rho_{c\,N_A}/M)^2 \quad \text{(S7)}$$