Supporting Information for: Revisiting the Thermodynamic Stability of Indomethacin Polymorphs with Low-Frequency Vibrational Spectroscopy and Quantum Mechanical Simulations

Michael T. Ruggiero[1,2], Joshua J. Sutton[3], Sara J. Fraser-Miller[3], Adam J. Zaczek[4], Timothy M. Korter[4], Keith C. Gordon[3], and J. Axel Zeitler*[1]

[1]*Department of Chemical Engineering and Biotechnology, University of Cambridge, Philippa Fawcett Drive, Cambridge, CB3 0AS, United Kingdom*

[2]*Present Address: Department of Chemistry, University of Vermont, 82 University Place, Burlington, Vermont, 05054, United States of America*

[3]*The Dodd-Walls Centre for Photonic and Quantum Technologies, Dpartment of Chemistry, University of Otago, P.O. Box 56, Dunedin, New Zealand*

[4]*Department of Chemistry, Syracuse University, 1-014 Center for Science and Technology, Syracuse, New York, 13244, United States of America*

**jaz22@cam.ac.uk*

Visualization of Terahertz Vibrational Modes

All of the vibrational modes and instructions for visualizing are available for download from https://doi.org/10.17863/CAM.26383

1. Gamma Mode Assignment

Wavenumber (cm^{-1})	IR/Raman Active	Irreducible Representation	Mode Type	Principal Axis
25.03	Raman	Ag	Rotation	a
34.10	Raman	Ag	Rotation	bc
36.54	IR	Au	Rotation	bc
38.08	IR	Au	Rotation	ac
45.18	Raman	Ag	Rotation	ba
47.56	IR	Au	Translation	ab
48.16	Raman	Ag	Rotation + Torsion	ab
52.21	IR	Au	Rotation + Torsion	ac
57.19	IR	Au	Rotation + Torsion	ac
59.01	Raman	Ag	Rotation + Torsion	bc
68.98	Raman	Ag	Rotation + Torsion	ac
69.70	Raman	Ag	Rotation + Torsion	ac
71.80	IR	Au	Rotation + Torsion	a
74.74	Raman	Ag	Rotation + Torsion	a
81.52	Raman	Ag	Torsion of Ring	b
82.97	IR	Au	Torsion + Methyl Rotation	ab
86.99	IR	Au	Ring Torsion	abc
94.69	IR	Au	Torsion of Amide	a
96.47	IR	Au	Phenyl Torsion	a
96.99	Raman	Ag	Torsion of Amide	a
110.19	IR	Au	Indole-Carboxylic Torsion	abc
121.59	Raman	Ag	Indole-Torsion	abc
126.04	IR	Au	Carbonyl Torsion	abc
127.07	Raman	Ag	Carbonyl Torsion	abc
134.27	Raman	Ag	Carboxylic Torsion	abc
138.12	Raman	Ag	Indole Torsion	abc
140.39	IR	Au	Complex Torsion	abc
143.59	IR	Au	Complex Torsion	bc
148.89	IR	Au	Complex Torsion	bc

2. Alpha Mode Assignment

Wavenumber (cm^{-1})	Irreducible Representation	Mode Type	Principal Axis
10.67	A	Rotation	a
18.36	A	Rotation	a
20.16	B	Translation	b
21.56	A	Rotation	ac
26.06	B	Rotation	a
28.62	A	Rotation	c
29.38	A	Rotation	c
30.47	B	Rotation	ac
32.62	B	Rotation	b
35.90	B	Rotation	a
36.17	A	Rotation	c
39.32	A	Rotation	b
39.50	B	Rotation	bc
41.77	B	Rotation	ac
42.12	A	Rotation	a
43.69	B	Rotation	ac
43.93	A	Rotation	a
46.04	B	Rotation + Torsion	a
48.04	A	Rotation + Torsion	c
48.08	B	Rotation + Torsion	ac
49.09	B	Rotation + Torsion	bc
49.82	A	Rotation + Torsion	c
51.97	B	Rotation + Torsion	c
52.78	A	Rotation + Torsion	abc
55.12	B	Rotation + Torsion	b
55.77	B	Rotation + Torsion	ac
56.02	A	Rotation + Torsion	abc
59.09	A	Rotation + Torsion	a
60.47	B	Rotation + Torsion	b
61.48	A	Rotation + Torsion	bc
63.25	B	Rotation + Torsion	a
64.44	A	Rotation + Torsion	a
67.05	B	Rotation + Torsion	ac
68.23	A	Rotation + Torsion	a
70.57	B	Rotation + Torsion	bc
72.00	A	Rotation + Torsion	abc

72.99	B	Rotation + Torsion	ac
74.54	A	Rotation + Torsion	abc
76.13	A	Rotation + Torsion	ac
76.99	B	Rotation + Torsion	bc
77.66	B	Rotation + Torsion	a
78.09	A	Rotation + Torsion	abc
81.92	A	Rotation + Torsion	b
82.04	B	Rotation + Torsion	bc
83.49	B	Complex Torsion	abc
85.88	A	Complex Torsion	abc
88.34	B	Complex Torsion	bc
88.98	A	Rotation + Torsion	abc
90.42	A	Rotation + Torsion	abc
90.94	B	Rotation + Torsion	abc
99.55	B	Rotation + Torsion	bc
100.45	A	Carboxylic Torsion	abc
106.30	B	Chlorophenyl Torsion	b
106.34	A	Chlorophenyl Torsion	b
109.74	A	Chlorophenyl Torsion	b
110.96	B	Chlorophenyl Torsion	b
112.87	B	Indole-Amide Torsion	ac
113.08	A	Indole-Amide Torsion	ac
114.83	A	Indole Torsion	ac
115.43	B	Indole Torsion	abc
115.99	B	Indole Torsion	bc
118.17	A	Indole Torsion	abc
119.95	A	Indole Torsion	abc
120.64	B	Indole-Carboxylic Torsion	ac
122.28	A	Indole-Carboxylic Torsion	abc
125.48	B	Indole-Carboxylic Torsion	abc
126.97	A	Ester Torsion	c
128.36	B	Indole Torsion	ab
129.38	A	Indole Torsion	ab
130.71	B	Ester-Ring Torsion	c
132.12	B	Ester-Ring Torsion	abc
132.13	A	Ester-Ring Torsion	abc
134.55	B	Ester-Ring-Indole Torsion	ac
136.14	A	Indole-Chlorophenyl Torsion	b
139.14	B	Chlorophenyl Torsion	ac
140.45	B	Chlorophenyl Torsion	ac
140.53	A	Complex Torsion	b

142.27	A	Complex Torsion	ab
146.13	B	Complex Torsion	ab
147.09	A	Complex Torsion	a
147.89	A	Complex Torsion	bc
149.34	B	Complex Torsion	abc

2. Comparison of Temperature-Dependent THz-TDS Data

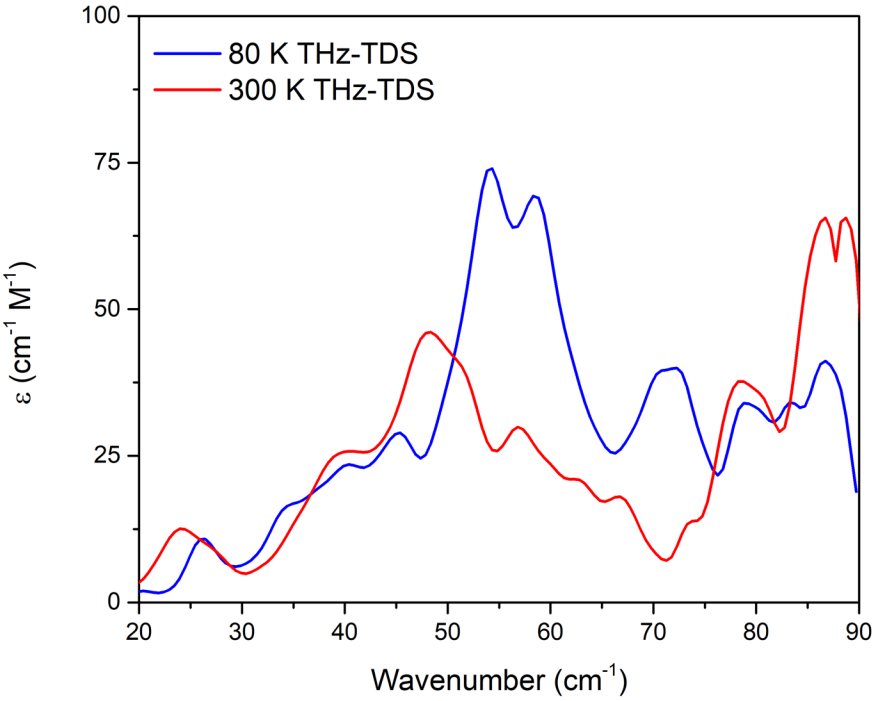

Figure S1. THz-TDS spectra of alpha indomethacin at 80 K (blue) and 300 K (red)

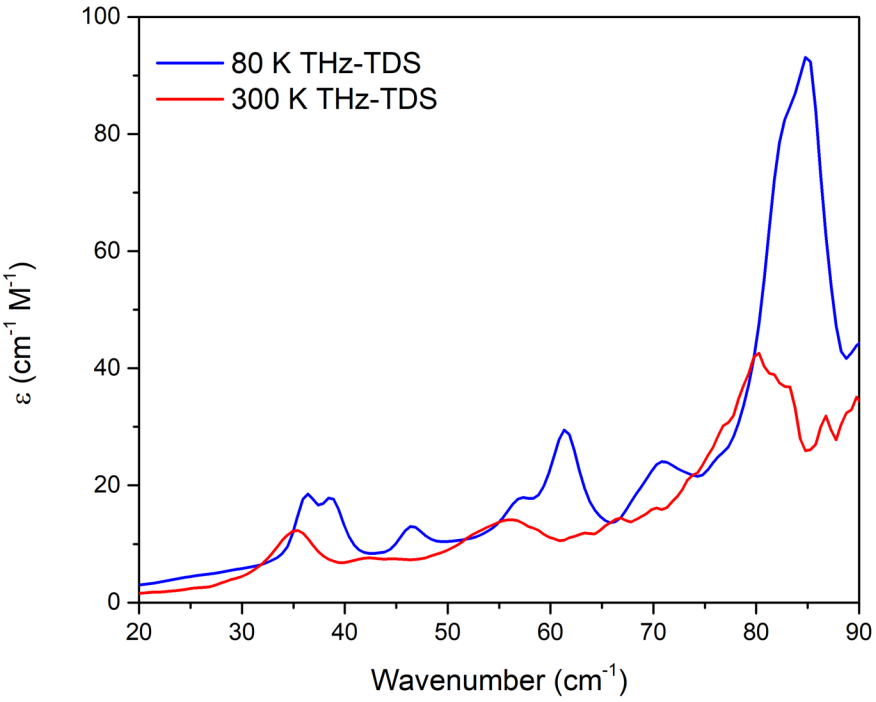

Figure S2. THz-TDS spectra of gamma indomethacin at 80 K (blue) and 300 K (red)

3. Relative Thermodynamic Stability of Indomethacin Polymorphs

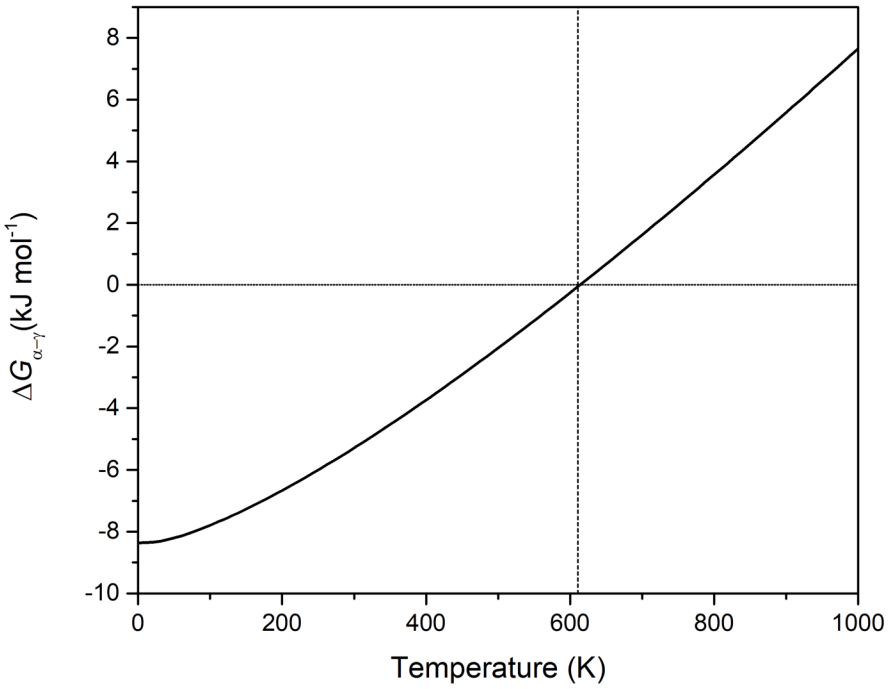

Figure S3. The difference in Gibbs free energy between the alpha and gamma polymorphs of indomethacin as a function of temperature. The stability ranking changes above 607 K, well above the melting point of both solids, indicating the system is monotropic.