SUPPLEMENTARY MATERIALS TO:

The phase diagram of the API Benzocaine and its highly persistent, metastable crystalline polymorphs

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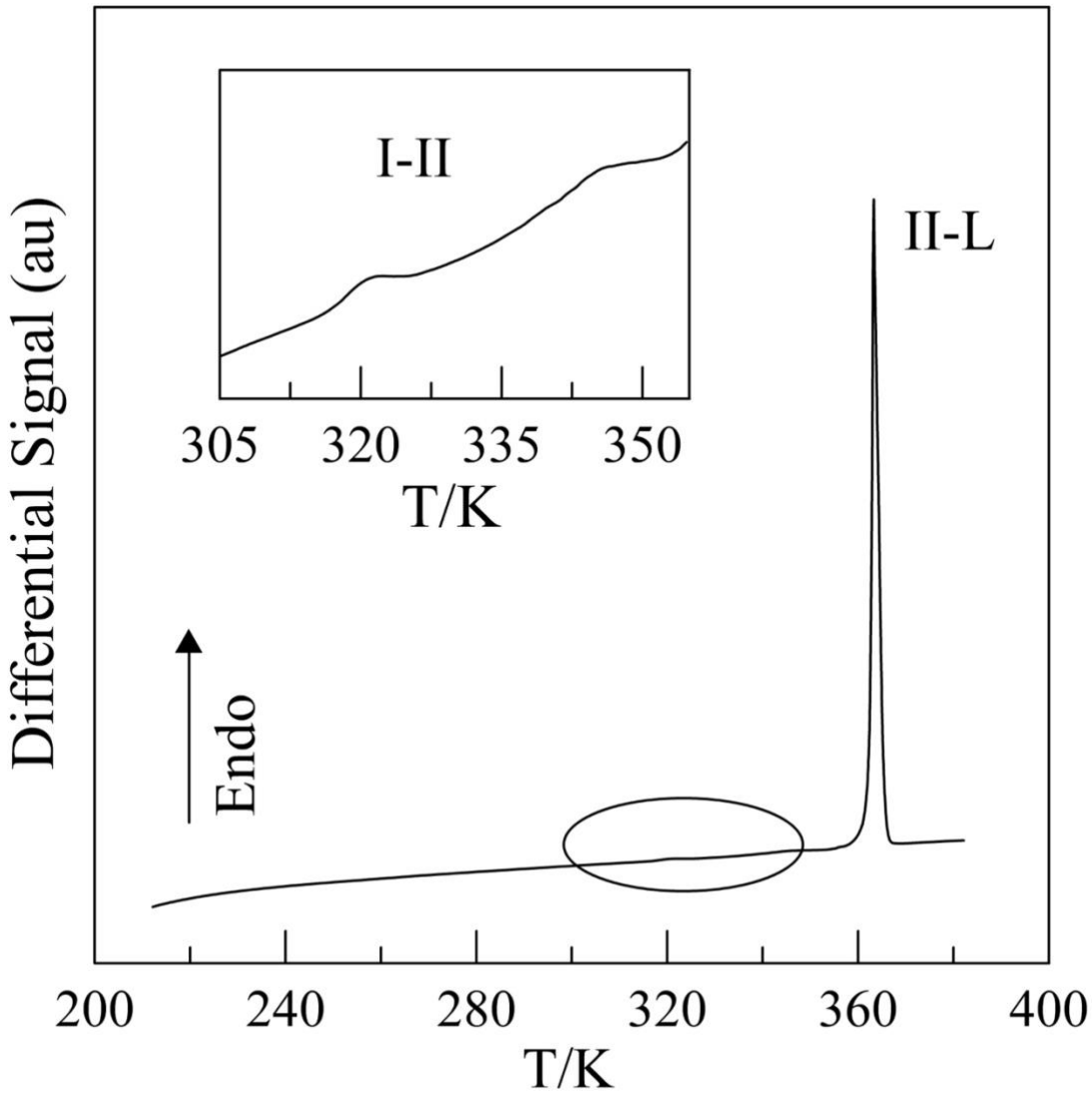

Figure S1. An example of the appearance of the I-II transition in a DSC measurement. Form I loaded into the capsule often leads to two small peaks after which the melting peak of form II is observed.

Table S1. Unit-cell parameters of form I ($P2_1/c$, $Z = 4$) as a function of temperature [a]

T /K	$a(\sigma)$ /Å	$b(\sigma)$ /Å	$c(\sigma)$ /Å	$\beta(\sigma)$ /°	$V(\sigma)$ /Å^3	V/Z /Å^3	v /cm^{3}g^{-1}
120	8.2001(4)	5.4400(4)	19.6206(12)	91.297(4)	874.90(9)	218.72	0.79736
170	8.2130(5)	5.4509(4)	19.6913(10)	91.449(4)	881.26(9)	220.31	0.80315
200	8.2243(6)	5.4641(4)	19.7493(12)	91.555(6)	887.17(11)	221.79	0.80855
225	8.2253(5)	5.4711(4)	19.7913(10)	91.594(5)	890.29(10)	222.57	0.81139
250	8.2419(5)	5.4839(4)	19.8494(11)	91.658(4)	896.77(10)	224.19	0.81729
275	8.2483(5)	5.4935(4)	19.9059(11)	91.696(4)	901.57(9)	225.39	0.82167
293	8.2562(5)	5.5028(3)	19.9572(10)	91.743(4)	906.27(9)	226.57	0.82595
310	8.2594(6)	5.5094(4)	19.9962(12)	91.745(5)	909.49(11)	227.37	0.82889
320	8.2638(5)	5.5155(4)	20.0254(12)	91.729(5)	912.32(11)	228.08	0.83147

[a] (σ) standard deviation in the last digit

Table S2. Unit-cell parameters of form II ($P2_12_12_1$, $Z = 4$) as a function of temperature [a]

T /K	$a(\sigma)$ /Å	$b(\sigma)$ /Å	$c(\sigma)$ /Å	$V(\sigma)$ /Å^3	V/Z /Å^3	v /cm^{3}g^{-1}
250	8.2255(10)	5.2848(6)	20.8098(22)	904.61(18)	226.15	0.82444
260	8.2237(10)	5.283(6)	20.8289(21)	906.00(17)	226.50	0.82571
270	8.2306(8)	5.2964(5)	20.8431(19)	908.61(15)	227.15	0.82809
280	8.2332(9)	5.3015(5)	20.855(2)	910.28(16)	227.57	0.82961
290	8.2375(8)	5.3074(6)	20.8703(18)	912.43(15)	228.11	0.83156
300	8.2412(12)	5.3128(5)	20.888(3)	914.6(2)	228.64	0.83350
320	8.2497(10)	5.3244(6)	20.933(2)	919.46(18)	229.87	0.83797
330	8.2530(10)	5.3306(6)	20.961(2)	922.14(18)	230.53	0.84041
335	8.2501(15)	5.3315(10)	20.936(4)	920.9(3)	230.22	0.83928
340	8.2570(15)	5.3373(9)	20.966(3)	924.0(3)	230.99	0.84209
345	8.2671(6)	5.3464(4)	21.0205(12)	929.08(11)	232.27	0.84674
350	8.2610(10)	5.3427(6)	21.018(21)	927.64(18)	231.91	0.84543
355	8.2639(9)	5.3448(6)	21.040(2)	929.32(17)	232.33	0.84696

[a] (σ) standard deviation in the last digit(s)

Table S3. Unit-cell parameters of form III ($P2_1$, Z = 8) as a function of temperature [a]

T /K	$a(\sigma)$ /Å	$b(\sigma)$ /Å	$c(\sigma)$ /Å	$\gamma(\sigma)$ /°	$V(\sigma)$ /Å^3	V/Z /Å^3	v /cm^{3}g^{-1}
120	8.1908(9)	10.6294(11)	20.4674(19)	99.349(9)	1758.3(3)	219.79	0.80123
170	8.2021(10)	10.6653(11)	20.5263(19)	99.404(9)	1771.5(4)	221.43	0.80723
200	8.2090(10)	10.6900(10)	20.5656(18)	99.416(10)	1780.4(3)	222.55	0.81130
220	8.2173(10)	10.7125(11)	20.602(2)	99.414(9)	1789.1(4)	223.64	0.81526
230	8.2212(10)	10.7202(11)	20.622(3)	99.412(10)	1793.0(4)	224.13	0.81706
240	8.2228(10)	10.7290(11)	20.639(3)	99.388(10)	1796.4(4)	224.55	0.81860
250	8.2323(10)	10.7445(11)	20.668(3)	99.402(9)	1803.5(4)	225.44	0.82185
260	8.2313(19)	10.747(2)	20.698(3)	99.447(15)	1806.2(6)	225.77	0.82306
245	8.2284(10)	10.7392(12)	20.654(3)	99.399(9)	1800.6(4)	225.08	0.82051
255	8.2302(12)	10.7493(13)	20.680(3)	99.413(10)	1804.9(4)	225.61	0.82246

[a] (σ) standard deviation in the last digit(s)

Table S4. Heat capacity of benzocaine forms I, II, and III as a function of temperature obtained by adiabatic calorimetry.[a] Transition peaks are marked with yellow background.

Form I – form II (stable)		**Form III (metastable) – form II - melt**	
T /K	Cp /Jmol^{-1}K^{-1}	**T /K**	Cp /Jmol^{-1}K^{-1}
0	0 [b]	**0**	0 [c]
1.000	0.274 [b]	**1.000**	0.285 [c]
2.000	0.556 [b]	**2.000**	0.577 [c]
3.000	0.851 [b]	**3.000**	0.884 [c]
4.000	1.167 [b]	**4.000**	1.213 [c]
5.000	1.510 [b]	**5.000**	1.571 [c]
6.000	1.887 [b]	**6.000**	1.966 [c]
7.000	2.306 [b]	**7.000**	2.404 [c]
8.000	2.774 [b]	**8.000**	2.894 [c]
9.000	3.296 [b]	**9.000**	3.441 [c]
10.000	3.880 [b]	**10.000**	4.055 [c]
11.000	4.533 [b]	**11.000**	4.741 [c]
12.000	5.262 [b]	**11.382**	4.747
12.588	5.656	**13.512**	6.848
13.940	6.770	**15.210**	8.749
15.153	8.142	**16.671**	10.581
16.256	9.534	**17.975**	12.279
17.335	10.907	**19.168**	13.755
18.454	12.279	**20.279**	15.392
19.281	13.304	**21.327**	16.734
20.274	14.595	**22.336**	18.022
21.239	15.833	**23.313**	19.336
22.180	17.063	**24.266**	20.730
23.100	18.353	**25.230**	21.990
24.345	20.356	**26.231**	23.219

25.827	22.352	**27.255**	24.409
27.341	24.167	**28.277**	25.652
28.876	26.485	**29.245**	27.405
30.536	28.701	**31.224**	29.330
32.202	30.525	**32.239**	30.692
33.776	32.760	**33.355**	32.257
35.371	34.752	**34.524**	33.851
36.991	36.714	**35.673**	35.300
38.636	38.810	**36.876**	36.741
40.308	40.883	**38.195**	38.352
41.906	42.762	**39.620**	40.110
43.462	44.561	**41.143**	41.950
45.005	46.206	**42.694**	43.772
46.524	47.900	**44.212**	45.401
48.026	49.468	**45.706**	47.001
49.514	51.158	**47.181**	48.603
50.986	52.706	**48.680**	50.230
52.437	54.260	**50.199**	51.908
53.870	55.640	**51.691**	53.123
55.289	57.021	**53.158**	55.164
56.695	58.060	**54.609**	56.204
58.090	60.128	**56.046**	57.622
59.476	60.805	**57.469**	59.005
60.857	62.227	**58.881**	60.309
62.233	63.559	**60.283**	61.617
63.604	64.795	**61.678**	62.912
64.972	66.083	**63.068**	63.951
66.337	67.371	**64.451**	65.861
67.701	68.516	**65.832**	66.622
69.065	69.658	**67.211**	67.104
70.680	70.975	**68.529**	69.104
72.028	72.067	**69.907**	70.406
73.378	72.873	**71.284**	71.227
74.731	74.676	**72.663**	72.423
76.087	75.296	**74.043**	73.480
77.448	76.377	**75.424**	74.530
78.812	76.644	**76.808**	75.670
80.181	78.252	**78.195**	76.818
81.554	79.527	**79.585**	77.754
82.932	80.274	**80.978**	78.831
84.316	81.611	**82.377**	79.958
85.705	83.011	**83.779**	80.981
87.100	83.825	**85.187**	82.113

88.504	84.646	**86.599**	83.044
90.077	86.099	**87.600**	83.828
91.654	87.202	**89.161**	85.089
93.234	88.252	**90.725**	86.081
94.819	89.437	**92.292**	87.543
96.407	90.639	**93.863**	88.555
98.001	91.844	**95.439**	89.707
99.600	92.975	**97.020**	90.846
101.205	94.338	**98.606**	92.027
102.815	95.367	**100.198**	92.976
104.432	96.535	**101.796**	94.339
106.055	97.617	**103.399**	95.369
107.686	98.746	**105.010**	96.650
109.323	99.910	**106.628**	97.799
110.968	101.234	**108.252**	98.996
112.621	102.190	**109.885**	100.247
114.281	103.421	**111.525**	101.212
115.951	104.256	**113.172**	102.323
117.628	105.528	**114.829**	103.455
119.314	106.809	**116.493**	104.482
121.008	107.623	**118.166**	105.601
122.712	108.910	**119.848**	106.897
124.425	110.003	**121.539**	107.821
126.147	111.178	**123.238**	109.022
127.879	112.335	**124.947**	110.102
129.620	113.338	**126.666**	111.302
131.371	114.208	**128.394**	112.438
133.132	115.714	**130.132**	113.526
134.902	117.052	**131.880**	115.000
136.683	118.219	**133.637**	115.956
138.474	118.707	**135.405**	117.075
140.275	120.343	**137.182**	118.265
142.087	121.613	**138.971**	119.158
143.909	122.912	**140.770**	120.541
145.741	124.434	**142.579**	121.740
147.586	125.335	**144.398**	123.011
149.439	126.982	**146.229**	124.283
151.304	127.530	**148.070**	125.831
153.180	128.682	**149.922**	126.466
155.066	130.424	**151.785**	127.846
156.965	131.287	**153.659**	128.890
158.874	132.606	**155.544**	129.832
160.794	133.631	**157.440**	131.084

162.726	134.875	**159.280**	132.767
164.669	136.019	**161.199**	133.705
166.624	137.874	**163.129**	134.720
168.590	138.878	**165.070**	136.180
170.567	140.138	**167.024**	136.503
172.555	141.925	**168.982**	138.527
174.556	143.043	**170.947**	140.028
176.577	144.191	**172.933**	141.278
178.624	145.208	**174.939**	142.381
180.690	147.046	**176.965**	143.623
182.777	147.561	**179.011**	145.058
184.883	149.615	**181.077**	146.240
187.008	151.038	**183.162**	147.522
189.153	152.160	**185.267**	149.349
191.317	153.694	**187.392**	149.584
193.503	155.046	**189.537**	151.756
195.705	156.620	**191.700**	153.108
197.928	158.142	**193.883**	154.713
200.169	159.873	**196.086**	156.118
202.432	160.958	**198.308**	157.479
204.712	162.960	**200.549**	159.306
207.011	164.760	**202.810**	160.905
209.330	165.289	**205.090**	161.248
211.669	168.344	**207.391**	164.085
214.025	169.577	**209.708**	165.366
216.401	171.843	**212.046**	166.999
218.797	173.051	**214.402**	168.727
221.210	174.634	**216.777**	170.532
223.642	176.325	**219.172**	171.619
226.094	176.777	**221.587**	174.468
228.564	180.441	**224.019**	175.482
231.052	182.043	**226.469**	177.238
233.558	184.642	**228.939**	179.002
236.085	184.439	**231.426**	181.817
238.629	187.259	**233.936**	182.946
241.190	189.245	**236.461**	184.675
243.770	192.210	**239.005**	186.341
246.372	193.224	**241.567**	188.367
248.988	195.119	**244.148**	190.231
251.623	196.947	**246.746**	193.533
254.277	196.949	**249.367**	193.623
256.950	201.468	**251.669**	195.901
259.638	203.188	**253.651**	197.227

262.345	204.906	**255.641**	198.931
265.070	207.168	**257.641**	200.612
267.814	207.126	**259.648**	202.643
270.576	212.165	**261.663**	206.527
273.352	215.573	**263.681**	218.256
276.147	216.279	**265.695**	238.330
278.960	218.560	**267.664**	353.318
281.791	220.905	**269.632**	251.630
284.638	225.065	**271.673**	213.196
287.508	224.720	**273.740**	215.803
290.391	228.455	**275.815**	215.157
291.471	230.283	**278.731**	221.728
294.408	232.735	**280.841**	220.199
297.396	235.423	**282.967**	223.502
300.413	234.870	**285.113**	225.344
303.457	241.403	**287.278**	227.454
306.518	244.248	**289.400**	229.619
309.601	253.014	**292.211**	232.245
312.702	264.798	**295.047**	235.225
315.816	276.471	**297.909**	237.553
318.915	333.731	**300.796**	238.982
321.998	334.508	**303.708**	242.781
325.127	276.204	**306.645**	246.056
328.308	266.738	**309.605**	249.168
331.500	271.201	**312.590**	252.397
334.699	274.121	**315.599**	255.699
337.907	278.116	**318.633**	258.480
341.122	282.803	**321.691**	261.323
344.342	290.261	**324.772**	264.222
		327.878	267.234
		331.400	270.478
		334.214	273.477
		337.037	276.667
		339.869	280.254
		342.708	285.663
		345.552	294.049
		348.396	307.854
		351.230	335.052
		354.026	398.251
		356.714	576.973
		359.084	1228.500
		360.753	3957.290
		361.611	12550.000

	362.028	21454.200
	363.391	892.051
	366.057	336.660
	368.989	336.885

[a] Uncertainty in last digit
[b] Data obtained by extrapolation with equation S1.
[c] Data obtained by extrapolation with equation S2.

EXTRAPOLATION TO 0K

Form I

$$C_{p,I} = 0.2732\ T + 1.147\times10^{-3}\ T^3 \qquad R^2 = 0.997 \qquad \text{(S1)}$$

Form II

$$C_{p,III} = 0.2837\ T + 1.217\times10^{-3}\ T^3 \qquad R^2 = 0.996 \qquad \text{(S2)}$$

Table S5. Temperature-pressure data of the I-II, I-*l*, and II-*l* equilibria

Transition I-II		**Fusion II-*l***		**Fusion I-*l***	
T /K	P /MPa	**T /K**	P /MPa	**T /K**	P /Mpa
332.15	27.5	**363.15**	8.3	**384.15**	144.5
334.15	31.5	**367.15**	32.1	**388.15**	174.8
338.15	41.0	**368.15**	37.7	**391.15**	185.3
341.65	50.5	**369.15**	46.7	**396.15**	212.4
344.15	51.5	**370.15**	55.3	**398.15**	227.8
351.15	63.1	**373.15**	67.4	**400.15**	244.8
358.15	83.6	**374.15**	86.4		
368.15	95.6	**378.15**	109.9		
376.15	110.9	**378.15**	97.7		

Table S6. Entropy (S), Enthalpy (H), and Gibbs free energy (G) of the stable form I and form II as obtained from the heat capacity measurements (Table S1). Transition peaks are marked with a yellow background.

Form I – form II (stable)			
Temperature /K	Entropy /J K^{-1} mol^{-1}	Enthalpy /J mol^{-1}	Gibbs free energy /J mol^{-1}
0	0 [a]	0 [a]	0 [a]
1.000	0.274421 [a]	0.137211 [a]	-0.13721 [a]
2.000	0.551137 [a]	0.552285 [a]	-0.549989 [a]
3.000	0.832442 [a]	1.25555 [a]	-1.241776 [a]
4.000	1.12063 [a]	2.26421 [a]	-2.21831 [a]
5.000	1.418 [a]	3.60236 [a]	-3.48764 [a]

6.000	1.72684 [a]	5.30098 [a]	-5.06006 [a]
7.000	2.04945 [a]	7.39793 [a]	-6.94822 [a]
8.000	2.38812 [a]	9.93797 [a]	-9.16699 [a]
9.000	2.74515 [a]	12.9727 [a]	-11.73365 [a]
10.000	3.12283 [a]	16.5607 [a]	-14.6676 [a]
11.000	3.52345 [a]	20.7673 [a]	-17.99065 [a]
12.000	3.94932 [a]	25.6647 [a]	-21.72714 [a]
12.588	4.21037	28.874	-24.125717
13.940	4.84353	37.2722	-30.245155
15.153	5.46522	46.3154	-36.496893
16.256	6.0863	56.0691	-42.87101
17.335	6.74286	67.0963	-49.791852
18.454	7.46772	80.0674	-57.741158
19.281	8.02866	90.6509	-64.152102
20.274	8.72892	104.501	-72.47087
21.239	9.43614	119.18	-81.234177
22.180	10.1489	134.654	-90.446572
23.100	10.8688	150.952	-100.11945
24.345	11.8846	175.049	-114.28396
25.827	13.1459	206.691	-132.82816
27.341	14.4708	241.912	-153.73704
28.877	15.854	280.793	-177.01503
30.536	17.3953	326.579	-204.6004
32.202	18.9686	375.93	-234.90255
33.776	20.478	425.724	-265.93888
35.371	22.0351	479.56	-299.83912
36.991	23.6352	537.453	-336.83668
38.636	25.2777	599.562	-377.05963
40.308	26.9661	666.206	-420.74895
41.906	28.5914	733.014	-465.12863
43.462	30.1829	800.949	-510.84813
45.005	31.766	870.971	-558.64195
46.524	33.3282	942.467	-608.09418
48.026	34.8747	1015.57	-659.30839
49.514	36.4103	1090.47	-712.35688
50.986	37.9313	1166.9	-767.06147
52.437	39.4319	1244.5	-823.18265
53.870	40.9137	1323.26	-880.7692
55.289	42.3778	1403.17	-939.84347
56.695	43.823	1484.09	-1000.4594
58.090	45.2592	1566.51	-1062.5924
59.476	46.6848	1650.31	-1126.3058

60.857	48.0971	1735.29	-1191.76
62.233	49.5027	1821.8	-1258.8867
63.604	50.9014	1909.8	-1327.7276
64.972	52.2936	1999.3	-1398.2936
66.337	53.6814	2090.42	-1470.6484
67.701	55.0644	2183.1	-1544.8315
69.065	56.4421	2277.31	-1620.858
70.680	58.067	2390.85	-1713.2965
72.028	59.4183	2487.27	-1792.4935
73.378	60.7647	2585.16	-1873.6565
74.731	62.1122	2684.95	-1956.763
76.087	63.4608	2786.64	-2041.9146
77.448	64.8048	2889.82	-2129.1692
78.813	66.1412	2994.23	-2218.5233
80.181	67.4743	3100.21	-2309.9334
81.554	68.8141	3208.56	-2403.5189
82.933	70.1531	3318.68	-2499.292
84.316	71.4924	3430.68	-2597.2803
85.705	72.8373	3545.01	-2697.5254
87.100	74.1842	3661.38	-2800.0861
88.504	75.5307	3779.61	-2905.144
90.077	77.035	3913.93	-3025.1594
91.654	78.5387	4050.57	-3147.816
93.234	80.0385	4189.21	-3273.1315
94.819	81.5355	4329.97	-3401.1283
96.408	83.0316	4473.02	-3531.849
98.001	84.5276	4618.43	-3665.3762
99.600	86.023	4766.19	-3801.7094
101.205	87.5198	4916.46	-3940.9814
102.815	89.017	5069.19	-4083.0929
104.432	90.5141	5224.33	-4228.2385
106.055	92.0116	5381.93	-4376.3602
107.686	93.5094	5542	-4527.6532
109.323	95.0084	5704.65	-4681.9533
110.968	96.5105	5870.1	-4839.4772
112.621	98.014	6038.18	-5000.2547
114.281	99.519	6208.93	-5164.2008
115.951	101.025	6382.24	-5331.7098
117.628	102.531	6558.15	-5502.3665
119.314	104.042	6737.15	-5676.5172
121.008	105.554	6918.86	-5854.0184
122.712	107.068	7103.32	-6035.2084

124.425	108.585	7290.78	-6219.9086
126.147	110.105	7481.23	-6408.1854
127.879	111.628	7674.74	-6600.137
129.620	113.154	7871.22	-6795.8015
131.371	114.681	8070.43	-6995.3277
133.132	116.212	8272.86	-7198.676
134.902	117.749	8478.91	-7405.6656
136.683	119.292	8688.4	-7616.7884
138.474	120.834	8900.59	-7831.7773
140.275	122.379	9115.9	-8050.8142
142.087	123.931	9335.05	-8273.934
143.909	125.489	9557.83	-8501.1665
145.741	127.054	9784.45	-8732.527
147.586	128.624	10014.7	-8968.4017
149.439	130.199	10248.6	-9208.2084
151.304	131.777	10485.9	-9452.4872
153.180	133.355	10726.2	-9701.1189
155.066	134.941	10970.6	-9954.1611
156.965	136.534	11219.1	-10211.959
158.874	138.129	11471	-10474.107
160.794	139.728	11726.6	-10740.824
162.726	141.331	11985.9	-11012.328
164.669	142.939	12249.1	-11288.522
166.624	144.555	12516.8	-11569.532
168.590	146.178	12788.8	-11855.349
170.567	147.804	13064.6	-12145.885
172.555	149.439	13345	-12441.447
174.557	151.082	13630.2	-12742.221
176.577	152.735	13920.5	-13048.988
178.624	154.403	14216.6	-13363.481
180.690	156.083	14518.5	-13684.137
182.777	157.775	14826	-14011.641
184.883	159.477	15138.9	-14345.686
187.008	161.195	15458.3	-14686.455
189.153	162.924	15783.5	-15034.063
191.317	164.664	16114.4	-15388.622
193.503	166.417	16451.8	-15750.389
195.705	168.181	16795.1	-16118.763
197.928	169.958	17144.8	-16494.647
200.169	171.749	17501.2	-16877.626
202.432	173.552	17864.2	-17268.278
204.712	175.366	18233.5	-17666.025

207.011	177.196	18610.2	-18071.321
209.330	179.034	18992.9	-18484.287
211.669	180.888	19383.1	-18905.282
214.025	182.758	19781.2	-19333.581
216.401	184.642	20186.7	-19770.013
218.797	186.541	20600	-20214.611
221.210	188.448	21019.5	-20667.082
223.642	190.367	21446.2	-21127.857
226.094	192.292	21879	-21597.067
228.564	194.232	22320.2	-22074.243
231.052	196.195	22771.1	-22560.147
233.558	198.172	23230.6	-23054.056
236.085	200.159	23697	-23557.538
238.629	202.15	24169.8	-24069.052
241.190	204.16	24651.9	-24589.45
243.770	206.189	25144	-25118.693
246.372	208.235	25645.4	-25657.873
248.988	210.287	26153.4	-26205.54
251.623	212.35	26669.9	-26762.244
254.277	214.416	27192.6	-27328.457
256.950	216.5	27725.1	-27904.575
259.638	218.605	28269	-28489.165
262.345	220.722	28821.4	-29083.913
265.070	222.85	29382.7	-29688.15
267.814	224.984	29951.1	-30302.765
270.576	227.135	30530.2	-30927.08
273.352	229.318	31123.9	-31560.634
276.147	231.514	31727.3	-32204.597
278.960	233.718	32339	-32858.973
281.791	235.936	32961	-33523.641
284.638	238.178	33595.9	-34198.61
287.508	240.435	34241.4	-34885.586
290.391	242.695	34894.5	-35581.944
292.949	244.719	35485	-36205.186
295.898	247.05	36171.3	-36930.301
298.899	249.426	36877.9	-37675.282
301.930	251.795	37589.7	-38434.764
304.983	254.224	38326.9	-39207.098
308.057	256.674	39077.7	-39992.522
311.149	259.2	39859.9	-40789.921
314.256	261.832	40682.7	-41599.577
317.376	264.563	41545.3	-42420.647

320.454	267.783	42572.4	-43239.733
323.542	270.991	43605.3	-44071.67
326.712	273.685	44481.1	-44935.074
329.905	276.279	45332.7	-45813.123
333.100	278.893	46199.1	-46700.158
336.303	281.516	47077.2	-47597.475
339.514	284.159	47970.3	-48505.659
342.732	286.827	48880.4	-49424.391
345.953	289.542	49815.2	-50352.724

[a] Data obtained by extrapolation, stable form *H* and *G* set to 0.

Table S7. Entropy (S), Enthalpy (H), and Gibbs free energy (G) of the metastable form III and form II as obtained from the heat capacity measurements (Table S1). Transition peaks are marked with a yellow background.

Form III (metastable) – form II (metastable, stable) – melt (stable)			
Temperature /K	Entropy /J K^{-1} mol^{-1}	Enthalpy /J mol^{-1}	Gibbs free energy /J mol^{-1}
0	0.015 [a]	197.4 [a]	197.4 [a]
1	0.300052 [a]	197.542526 [a]	197.242474 [a]
2	0.587537 [a]	197.973754 [a]	196.79868 [a]
3	0.879889 [a]	198.70463 [a]	196.064963 [a]
4	1.17954 [a]	199.75341 [a]	195.03525 [a]
5	1.48892 [a]	201.14564 [a]	193.70104 [a]
6	1.81047 [a]	202.91416 [a]	192.05134 [a]
7	2.14662 [a]	205.09912 [a]	190.07278 [a]
8	2.4998 [a]	207.748 [a]	187.7496 [a]
9	2.87244 [a]	210.9155 [a]	185.06354 [a]
10	3.26699 [a]	214.6636 [a]	181.9937 [a]
11	3.68586 [a]	219.0618 [a]	178.51734 [a]
11.3819	3.84777	220.8737	177.078767
13.5115	4.83979	233.2211	167.828277
15.2101	5.7622	246.4677	158.824062
16.6707	6.64781	260.5847	149.761054
17.9748	7.50827	275.49	140.530348
19.1681	8.34465	291.023	131.071914
20.2787	9.16526	307.208	121.348442
21.3266	9.9744	324.04	111.319961
22.3356	10.7775	341.574	100.852071
23.3134	11.5777	359.837	89.9214488
24.2656	12.3795	378.912	78.5160048
25.2296	13.2116	399.503	66.1796166
26.2313	14.0916	422.147	52.5060129
27.2547	15.0029	446.518	37.6184614

28.2766	15.9242	472.097	21.8147663
29.2449	16.8173	497.783	5.96274323
31.2241	18.6743	553.929	-29.159211
32.2395	19.6346	584.402	-48.607687
33.3552	20.7053	619.517	-71.112423
34.5241	21.8437	658.156	-95.978083
35.6734	22.9759	697.895	-121.73347
36.8756	24.1696	741.196	-150.0725
38.1945	25.489	790.719	-182.82061
39.6201	26.9265	846.646	-220.18462
41.1425	28.4733	909.11	-262.35275
42.6936	30.0593	975.592	-307.74773
44.2122	31.6175	1043.299	-354.58023
45.7058	33.1524	1112.308	-402.94896
47.1808	34.6705	1182.812	-452.96993
48.6805	36.2167	1256.92	-506.12706
50.199	37.7853	1334.47	-562.31427
51.6915	39.3237	1412.85	-619.85104
53.1583	40.8386	1492.27	-678.64055
54.6095	42.3383	1573.08	-738.99339
56.046	43.8159	1654.83	-800.87593
57.4689	45.2779	1737.81	-864.26111
58.8807	46.7257	1822.03	-929.21192
60.2831	48.1606	1907.53	-995.74027
61.6783	49.5851	1994.4	-1063.9247
63.0678	50.9982	2082.53	-1133.8143
64.4509	52.4062	2172.31	-1205.3168
65.8318	53.8103	2263.78	-1278.6489
67.2113	55.197	2356.02	-1353.8421
68.529	56.5192	2445.76	-1427.4443
69.907	57.9079	2541.88	-1506.2876
71.2838	59.289	2639.38	-1586.9652
72.6627	60.6651	2738.42	-1669.67
74.0427	62.0375	2839.09	-1754.334
75.4244	63.4057	2941.34	-1840.9969
76.8084	64.7713	3045.28	-1929.6999
78.1951	66.1355	3151.01	-2020.462
79.5853	67.4975	3258.46	-2113.3488
80.9784	68.856	3367.52	-2208.3287
82.3766	70.2151	3478.53	-2305.5512
83.7793	71.5737	3591.4	-2404.9945
85.1866	72.9321	3706.17	-2506.6676

86.5992	74.2902	3822.82	-2610.6519
87.5999	75.2489	3906.32	-2685.4761
89.1608	76.7405	4038.15	-2804.0944
90.7247	78.2286	4171.99	-2925.2763
92.2917	79.7152	4308.03	-3049.0213
93.8631	81.2017	4446.39	-3175.4533
95.4392	82.6859	4586.86	-3304.6161
97.02	84.1689	4729.57	-3436.4967
98.6061	85.6516	4874.6	-3571.1702
100.198	87.133	5021.86	-3708.6923
101.796	88.6145	5171.48	-3849.1216
103.399	90.0973	5323.62	-3992.3507
105.01	91.5813	5478.26	-4138.6923
106.628	93.0675	5635.52	-4288.0814
108.252	94.5555	5795.39	-4440.432
109.885	96.0462	5957.98	-4596.0567
111.525	97.5386	6123.2	-4754.7924
113.172	99.0311	6290.88	-4916.6676
114.829	100.526	6461.27	-5082.0301
116.493	102.022	6634.33	-5250.5188
118.166	103.52	6810.05	-5422.4943
119.848	105.021	6988.74	-5597.8168
121.539	106.525	7170.28	-5776.662
123.238	108.031	7354.55	-5958.9744
124.947	109.54	7541.81	-6144.8844
126.666	111.052	7732.04	-6334.4726
128.394	112.568	7925.36	-6527.6958
130.132	114.087	8121.69	-6724.6795
131.88	115.611	8321.42	-6925.3587
133.637	117.14	8524.36	-7129.8782
135.405	118.671	8730.32	-7338.3268
137.182	120.206	8939.52	-7550.5795
138.971	121.744	9151.81	-7767.0754
140.77	123.285	9367.41	-7987.4195
142.579	124.832	9586.57	-8211.8517
144.398	126.384	9809.24	-8440.3568
146.229	127.941	10035.56	-8673.1245
148.07	129.506	10265.8	-8910.1534
149.922	131.074	10499.4	-9151.4762
151.785	132.644	10736.3	-9397.0695
153.659	134.219	10976.9	-9647.0573
155.544	135.796	11220.7	-9901.553

157.44	137.377	11468.1	-10160.535
159.28	138.91	11710.8	-10414.785
161.199	140.506	11966.5	-10682.927
163.129	142.103	12225.5	-10955.62
165.07	143.706	12488.5	-11233.049
167.024	145.31	12754.9	-11515.357
168.982	146.912	13024.1	-11801.384
170.947	148.523	13297.8	-12091.761
172.933	150.147	13577.2	-12388.171
174.939	151.783	13861.7	-12691.066
176.965	153.43	14151.4	-13000.34
179.011	155.089	14446.7	-13315.937
181.077	156.76	14747.6	-13638.031
183.162	158.441	15053.8	-13966.57
185.267	160.138	15366.3	-14301.987
187.392	161.843	15684	-14644.083
189.537	163.557	16007.1	-14993.003
191.7	165.287	16336.8	-15348.718
193.883	167.03	16672.8	-15711.477
196.086	168.785	17015.1	-16081.276
198.308	170.552	17363.5	-16458.326
200.549	172.332	17718.6	-16842.41
202.81	174.127	18080.5	-17234.197
205.09	175.928	18447.9	-17633.174
207.391	177.743	18822.1	-18040.199
209.708	179.573	19203.8	-18454.095
212.046	181.415	19592.2	-18876.125
214.402	183.27	19987.8	-19305.655
216.777	185.139	20390.7	-19743.177
219.172	187.019	20800.4	-20188.928
221.587	188.915	21218.3	-20642.808
224.019	190.825	21643.8	-21104.626
226.469	192.743	22075.9	-21574.414
228.939	194.675	22515.8	-22052.9
231.426	196.625	22964.6	-22539.537
233.936	198.592	23422.3	-23035.518
236.461	200.565	23886.5	-23539.3
239.005	202.55	24358.3	-24052.163
241.567	204.548	24838.4	-24573.647
244.148	206.559	25326.9	-25104.067
246.746	208.591	25825.5	-25643.495
249.367	210.636	26332.9	-26192.767

250.682	211.652	26587.6	-26469.747
252.659	213.192	26974.9	-26889.978
254.645	214.736	27366.6	-27314.849
256.64	216.288	27763.4	-27744.752
258.643	217.848	28165.3	-28179.56
260.655	219.418	28572.9	-28619.499
262.673	221.011	28989.8	-29063.822
264.691	222.681	29430.3	-29511.357
266.702	224.485	29909.4	-29961.198
268.629	227.029	30590.6	-30395.973
270.643	228.908	31097	-30855.348
272.705	230.526	31536.6	-31328.993
274.775	232.158	31983.3	-31807.914
276.856	233.781	32431	-32292.673
278.731	235.267	32844	-32732.206
280.841	236.934	33310.3	-33230.481
282.967	238.607	33782	-33735.907
285.113	240.302	34263.5	-34249.724
287.278	242.016	34753.8	-34772.072
289.4	243.698	35238.8	-35287.401
292.211	245.929	35887.8	-35975.359
295.047	248.187	36550.7	-36676.13
297.909	250.469	37227.2	-37389.769
300.796	252.767	37915.1	-38116.203
303.708	255.088	38616.7	-38855.566
306.645	257.44	39334.3	-39608.389
309.605	259.818	40067.4	-40373.552
312.59	262.225	40815.9	-41153.013
315.599	264.659	41580.4	-41945.716
318.633	267.118	42360.3	-42752.31
321.691	269.6	43155.1	-43572.794
324.772	272.106	43964.9	-44407.51
327.878	274.635	44790.2	-45256.575
331.4	277.507	45737	-46228.82
332.804	278.654	46119.1	-46618.066
335.622	280.961	46889.9	-47406.793
338.45	283.282	47672.2	-48204.593
341.287	285.621	48467.1	-49011.634
344.129	287.99	49279.1	-49826.611
346.974	290.411	50115.7	-50649.366
349.817	292.923	50990.9	-51478.545
352.642	295.618	51937.3	-52310.023

355.411	298.733	53040	-53132.994
358.018	302.949	54544.1	-53917.095
360.15	310.245	57164.1	-54570.637
361.356	323.476	61937	-54952.993
361.866	341.18	68339.2	-55122.242
362.189	360.274	75251.7	-55235.58
364.594	366.179	77397.3	-56109.366
367.52	368.87	78382.5	-57184.602
370.458	371.552	79372.3	-58272.111

[a] Data obtained by extrapolation, metastable form H and G relative to stable form in Table XS2. S ≠ 0 at 0 K may be due to experimental error or the extrapolation of Cp to 0K.

CLAUSIUS-CLAPEYRON EQUATION AND THE VAPOUR PRESSURES OF THE CONDENSED PHASES

The Clausius-Clapeyron equation can be written as:

$$\ln P = -\frac{\Delta H}{RT} + B \qquad \text{(S3)}$$

In this equation P is the vapour pressure of the condensed phase, ΔH is the enthalpy of vaporization in case of the liquid and the sublimation enthalpy in case of a solid, R is the gas constant, 8.314472 J K^{-1} mol^{-1}, T is the temperature in kelvin and B is a constant.
Using the boiling point and the enthalpy of vaporization of 583.85 K and 55160 kJ mol^{-1} obtained from ACD/Labs (ACDLabs *Advanced Chemistry Development (ACD/Labs) Software*, V11.02), the constant *B*vap can be calculated. It should be realised that at the boiling point the vapour pressure of the liquid is equal to the pressure in the atmosphere or 1×10^5 Pa. Since ΔH, R, and T are known in eq. S3, B can be obtained. The results can be found in Table S8. With these parameters the vapour pressure of the liquid can be calculated at the melting point of form II and because the liquid and form II are at equilibrium at the melting point, their vapour pressures must be the same (triple point II-*l*-*v*). Moreover, the enthalpy of vaporization is known, thus through thermodynamic cycling, the enthalpy of sublimation of form II should be the enthalpy of vaporization with the melting enthalpy added to it: $\Delta_{II\rightarrow v}H = \Delta_{l\rightarrow v}H + \Delta_{II\rightarrow l}H$ = 55160 + 22038 = 77198 J mol^{-1}. With this information B_{II} can be calculated. The same can be done for form I, using as enthalpy of sublimation $\Delta_{I\rightarrow v}H = \Delta_{l\rightarrow v}H + \Delta_{II\rightarrow l}H + \Delta_{I\rightarrow II}H$ = 77828 J mol^{-1}. The pressure at the fusion of form I can be calculated with the equation for the liquid leading to 83 Pa and with this information the constant B_I can be determined. In the same way the vapour pressure of form III can be obtained.

Table S8. Vapour pressure calculations [a]

Phase	Transition	Temperature /K	Pressure /Pa	ΔH /J mol^{-1}	B
Liquid (*l*)	boiling	583.85	1×10^5	55160	*22.88*
II	fusion II	362.0	*95*	77198	*30.20*
I	fusion I	359.5	*83*	77828	*30.46*
III	fusion III	358.3	*78*	77648	*30.42*

[a] italic values have been calculated using eq. S3 and R = 8.314472 J K^{-1} mol^{-1}

Once the vapour pressure data of each condensed phase is given by the Clausius-Clapeyron equation (eq. S3), it can be demonstrated which phase is the most stable by comparing the vapour pressures reflecting the vapour pressure equilibrium lines in Figure S2 and Figure 9. The phases in equilibrium will have the same vapour pressure, whether they are the most stable phases or not. In the case of the I-III-*v* triple point, because its temperature is very high, the vapour pressure for the solid phases is in the order of MPa. The most stable phase may appear to be the liquid phase with 0.3 MPa, however, it should not be forgotten that atmospheric pressure is 0.1 MPa, which implies that even the liquid is not stable anymore at this temperature. The pressures at the other triple points involving the vapour phase are very low in terms of MPa. The most stable phase always has the lowest vapour pressure.

Table S9. Vapour pressures of individual phases at triple points [a]

Triple point	P_I /Pa	P_{II} /Pa	P_{III} /Pa	P_l /Pa
II-*l*-*v* (1)	100	95	102	95
I-*l*-*v* (2)	83	79	86	83
III-*l*-*v* (3)	76	73	78	78
I-II-*v* (7)	2.4	2.4	2.5	6.8
III-II-*v* (8)	0.011	0.012	0.012	0.15
I-III-*v*	7.4×10^6	6.4×10^6	7.4×10^6	0.3×10^6

[a] The numbers in parentheses correspond to the triple points in Figure S2 below.

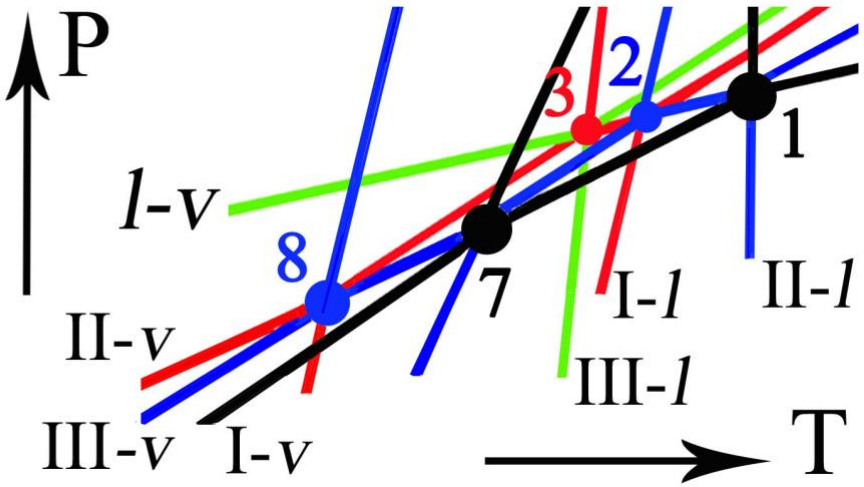

Figure S2. Schematic close-up of the melting and vapour equilibria in the pressure temperature phase diagram of benzocaine including the vapour equilibria. Solid black line, black circle: stable, blue line/circle: metastable, red line/circle: supermetastable, green line: hypermetastable.