Supporting information

Molecular salts of L-carnosine: Combining a natural antioxidant and geroprotector with"Generally Regarded As Safe" (GRAS) organic systems.

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S1: RAMAN spectra

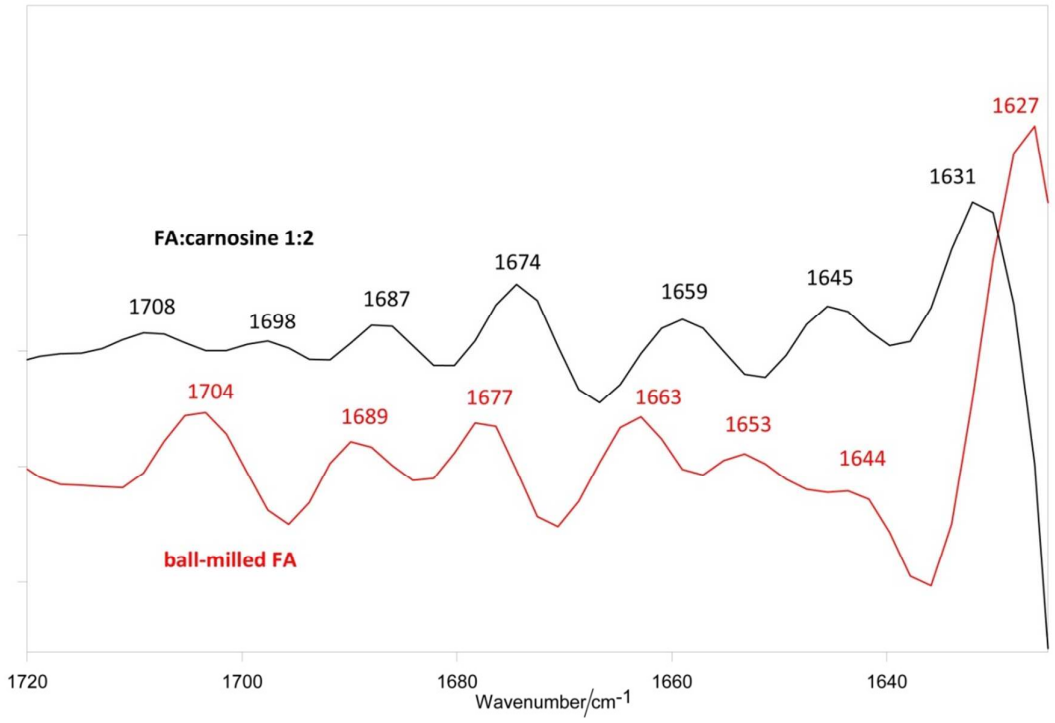

Figure SI 1. Fourth derivative Raman spectra in the C=O stretching range for the co-crystal and ball-milled folic acid dihydrate (FA).

Table SI-1. Wavenumbers (cm^{-1}) and assignments for the main Raman bands of crystalline and ball-milled folic acid dihydrate, L-carnosine and $[L\text{-}Hcar]_2[fol]$. Assignments have been given according to the literature.[14,23-27]

crystalline folic acid dihydrate	ball-milled folic acid dihydrate	L-carnosine	$[L\text{-}Hcar]_2[fol]$	Assignments
		3121 s	3140 vw, br	imidazole CH antisymmetric stretching[24]
2964 s		2971 vs	2970 sh	Aliphatic CH stretching
2929 s	2924 vw, br	2933 vs	2927 w, br	Aliphatic CH stretching
1710 vw	1702 w			C=O stretching of Glu in folic acid[14]
1664 w	1687-1677 w	1664 w	1684-1675 m	pteridine ring C=O stretching of folic acid;[14] Amide I of carnosine[23]
		1645 w		Amide I[23]
1637 ms				C=O stretching and NH_2 scissoring;[14] Amide I[26]
1606 vs	1598 vs		1608 vs	C=C benzene stretching + H_2O + NH_2 scissoring of folic acid[14]
1570 s	1565 vs	1570 m	1571 m	pteridine ring C=N stretching of folic acid;[24]

				imidazole C4=C5 stretching, tautomer I[25]
1521 m	1529 ms		1520 m	COO^- antisymmetric stretching of deprotonated Glu in folic acid;[23] pyrazine ring quadrant stretching of folic acid[24,27]
1485 w	1506 m		1478 m	pyrazine ring quadrant stretching of folic acid;[14] NH bending of positively charged imidazole group;[23]
		1431 m	1435 w	CH_2 bending, imidazole NH bending, tautomer II[23]
			1398 sh	COO^- symmetric stretching of deprotonated Glu in folic acid[23]
1357 s	1343 m		1352-1344 m	pteridine C=N stretching + CH_2 wagging, pteridine ring breathing of folic acid[14]
1291 m	1292 m	1289 vs	1300 ms	CH wagging mainly of Glu in folic acid;[14] imidazole ring breathing, tautomer I[23,25]
		1278 s	1270 sh	imidazole ring breathing, tautomer II[23]
1193 m	1210 m		1191 m	CH + CH_2 + NH wagging of folic acid[14]
1179 sh	1175 m		1182 m	CH + CH_2 + NH wagging of folic acid;[14] NH bending + NCN stretching of positively charged imidazole group[23]
		989 s	995 w	imidazole CH bending (at 990 and 1000 cm^{-1} in tautomers I[25] and II,[23] respectively)
973 w	968 vw, br		970 w	pyrazine ring out-of-plane bending of folic acid[24]
858 w	881-860 vw, br	860 mw	895-867 w	benzene ring breathing of folic acid;[26] NH_3^+ and imidazole ring deformation[23]

s = strong, m = medium, w = weak, br = broad, v = very, Glu = glutamic acid.

S2: Tables of structural data

Table SI 2. Structural data for the carnosine salts described in the present work.

	[Hcar][Hfum]·H_2O	[Hcar][Hsuc]·H_2O	[Hcar][Hglu]	[Hcar][Hadi]	[Hcar][Haze]	[Hcar][Hmal]·H_2O	[Hcar][gly]	[Hcar][sal]·H_2O
Formula	$C_{13}H_{20}N_4O_8$	$C_{13}H_{22}N_4O_8$	$C_{14}H_{24}N_4O_7$	$C_{15}H_{24}N_4O_7$	$C_{18}H_{30}N_4O_7$	$C_{13}H_{20}N_4O_8$	$C_{11}H_{18}N_4O_8$	$C_{18}H_{22}N_4O_7$
Fw (g mol^{-1})	360.30	362.32	376.35	372.37	414.45	360.30	302.28	382.35
Crystal system	Triclinic	Triclinic	Monoclinic	Monoclinic	Monoclinic	Triclinic	Monoclinic	Monoclinic
Space group	P1	P1	$P2_1$	$P2_1$	$P2_1$	P1	$P2_1$	$P2_1$
Z, Z'	1, 1	1, 1	4, 2	4,2	4, 2	2, 2	2, 1	2, 1
a (Å)	10.529(4)	10.963(7)	5.408(9)	5.44	5.5124(2)	17.305(4)	10.371(6)	12.081(1)
b (Å)	9.264(1)	10.451(4)	38.816(3)	42.18	49.775(2)	8.892(7	14.187(1)	10.523(6)
c (Å)	4.847(3)	4.844(1)	8.163(1)	8.04	7.6956(2)	5.735(1)	4.689(1)	7.186(8)
α (°)	91.895(4)	62.238(2)	90.0	90.0	90.0	75.625(1)	90.0	90.0
β (°)	98.208(6)	106.807(4)	90.369(18)	90.04	95.955(3)	102.491(7)	100.753(5)	90.183(1)
γ (°)	115.851(4)	120.892(2)	90.0	90.0	90.0	98.592(5)	90.0	90.0
V ($Å^3$)	418.74(16)	420.65(15)	1713.83(15)	1843.47	2100.1(1)	830.431(19)	677.84(17)	913.71(15)
R_wp	4.73	6.27	3.83	-	-	5.02	6.42	3.32
D_{calc} (g/cm^3)	-	-	-	-	1.311	-	-	-
μ (mm^{-1})	-	-	-	-	0.101	-	-	-
F(000)	-	-	-	-	888	-	-	-
θ range/deg	-	-	-	-	3.274<θ<29.392	-	-	-
reflns collected	-	-	-	-	9913	-	-	-
Indep reflns	-	-	-	-	7369	-	-	-
refined params	-	-	-	-	572	-	-	-
R1[on F_0^2, I>2σ(I)]	-	-	-	-	0.0547	-	-	-
wR_2 (all data)	-	-	-	-	0.1197	-	-	-

S2: Rietveld refinements

Legenda: Experimental (blue), calculated (red), and difference (grey) powder patterns. Peak positions are marked in blue.

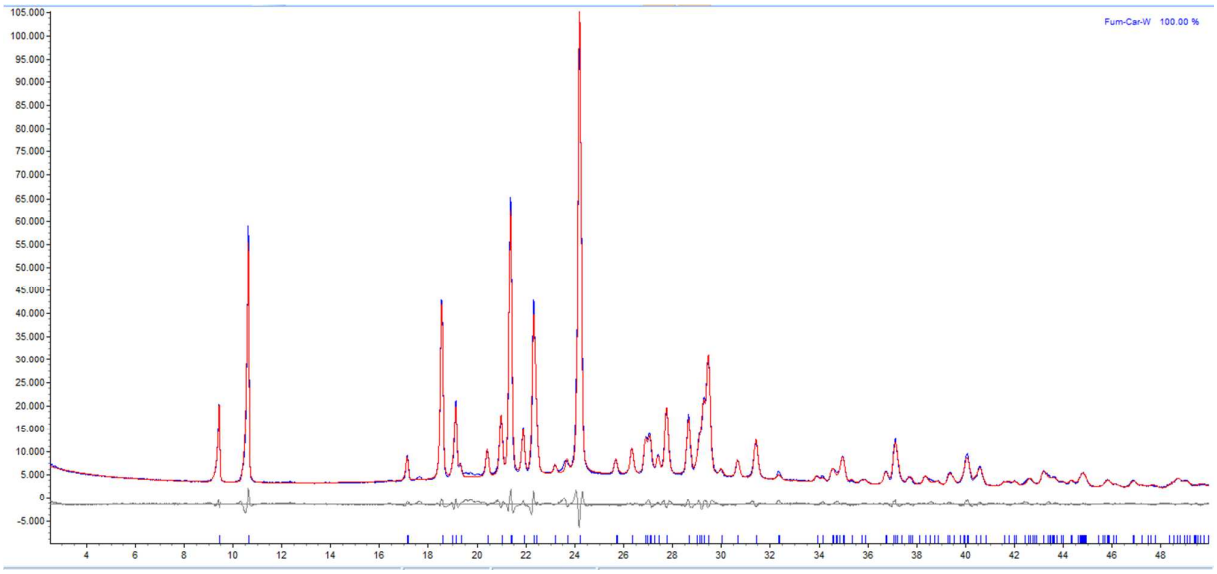

Figure SI 2 [L-Hcar][Hfum]·H_2O

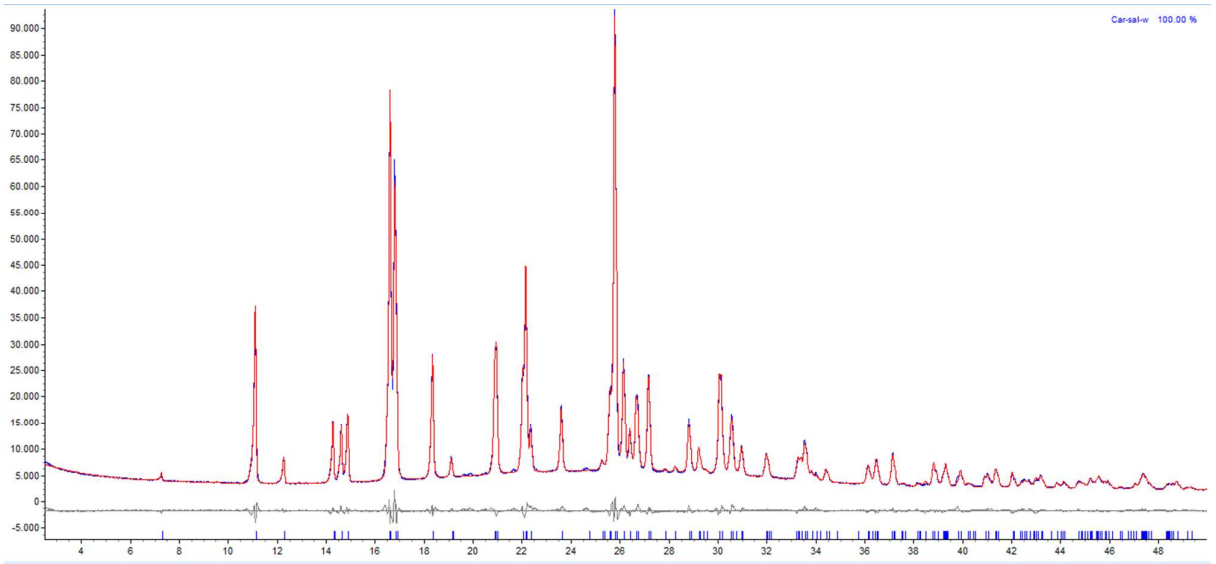

Figure SI 3 [L-Hcar][sal]·H_2O

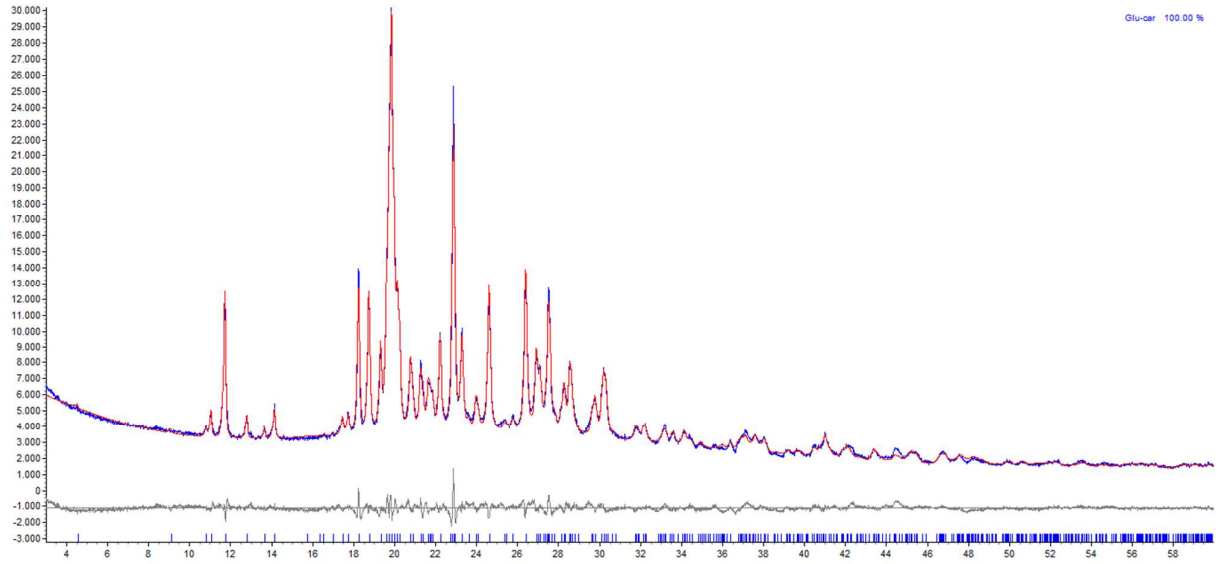

Figure SI 4 [L-Hcar][Hglu]

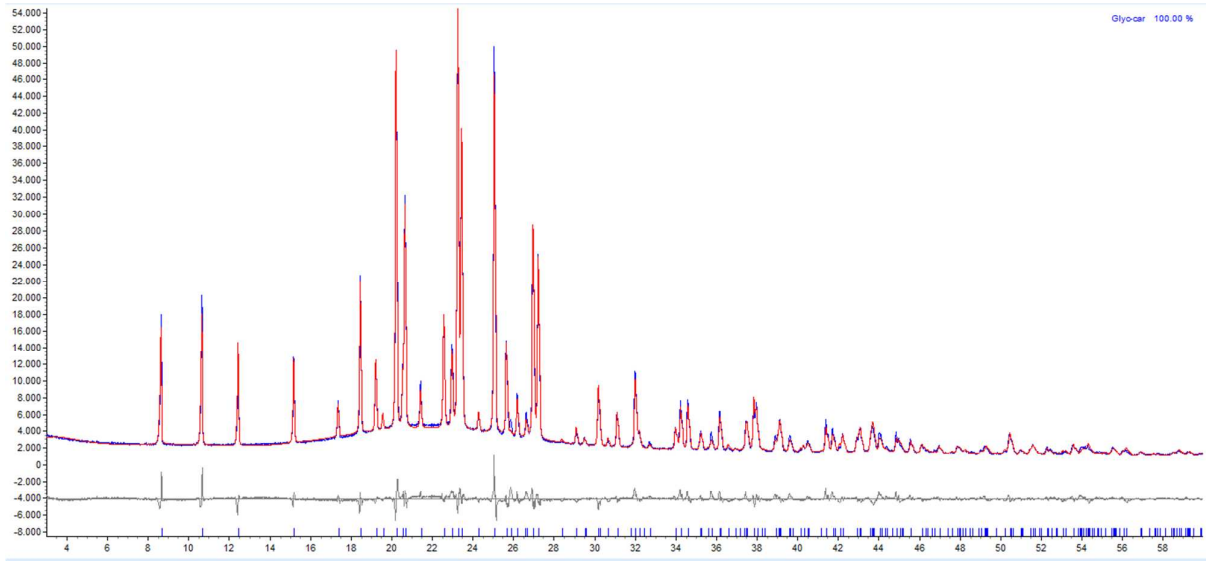

Figure SI 5 [L-Hcar][gly]

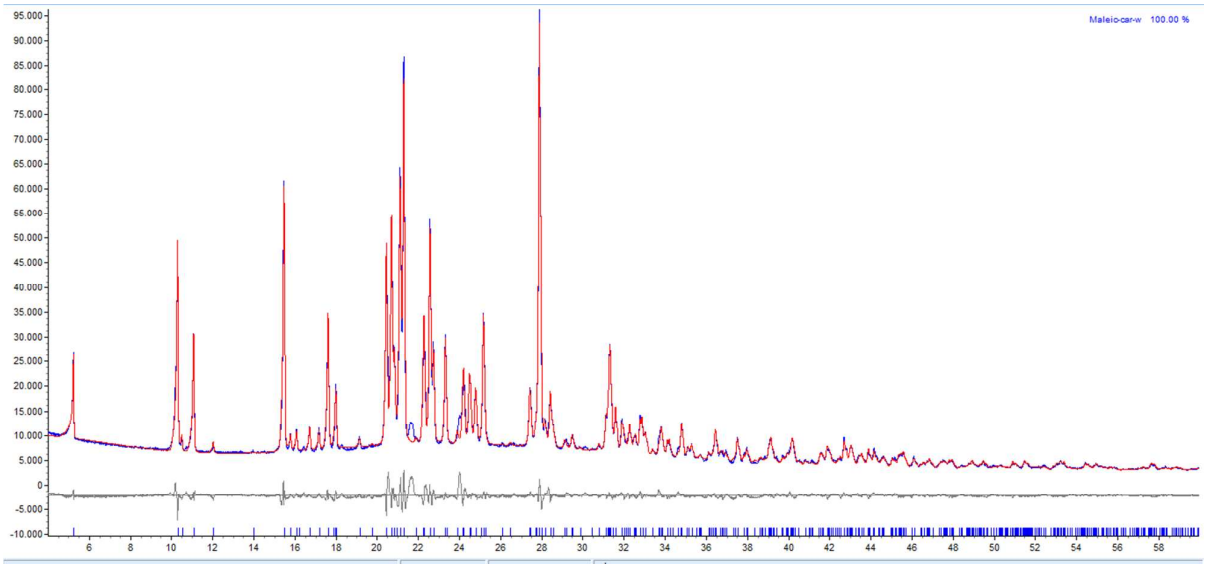

Figure SI 6 [L-Hcar][Hmal]·H_2O

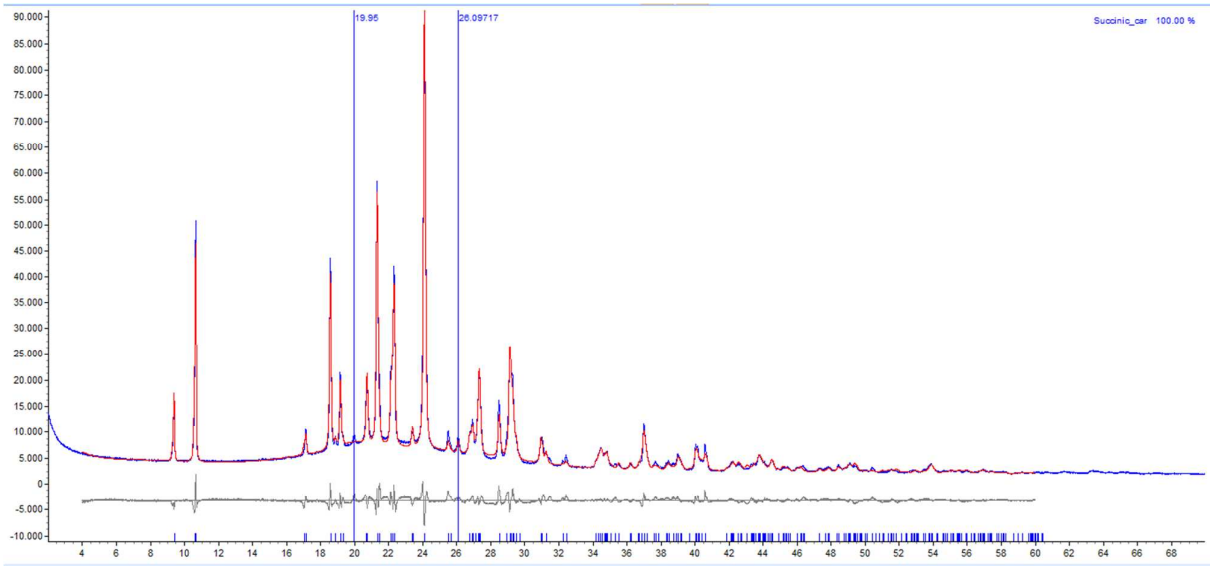

Figure SI 7 [L-Hcar][Hsuc]·H_2O

S3: TGA and DSC measurements

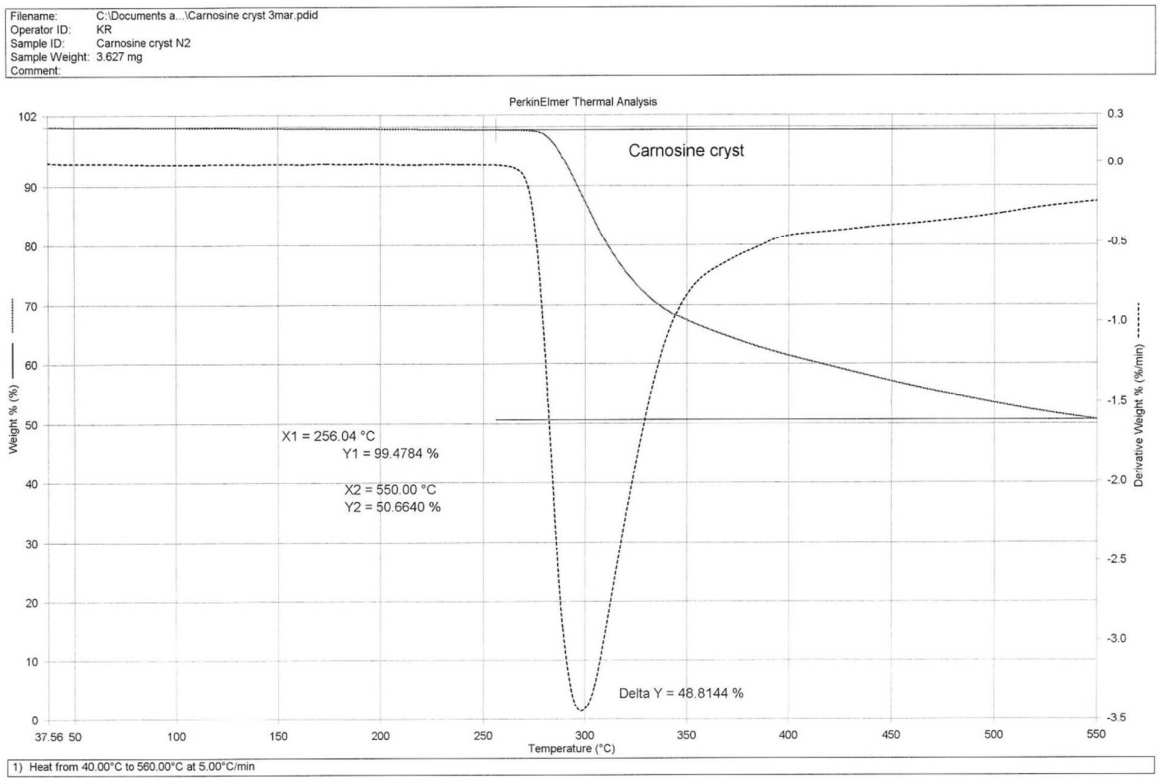

Figure SI 8 TGA of L-carnosine

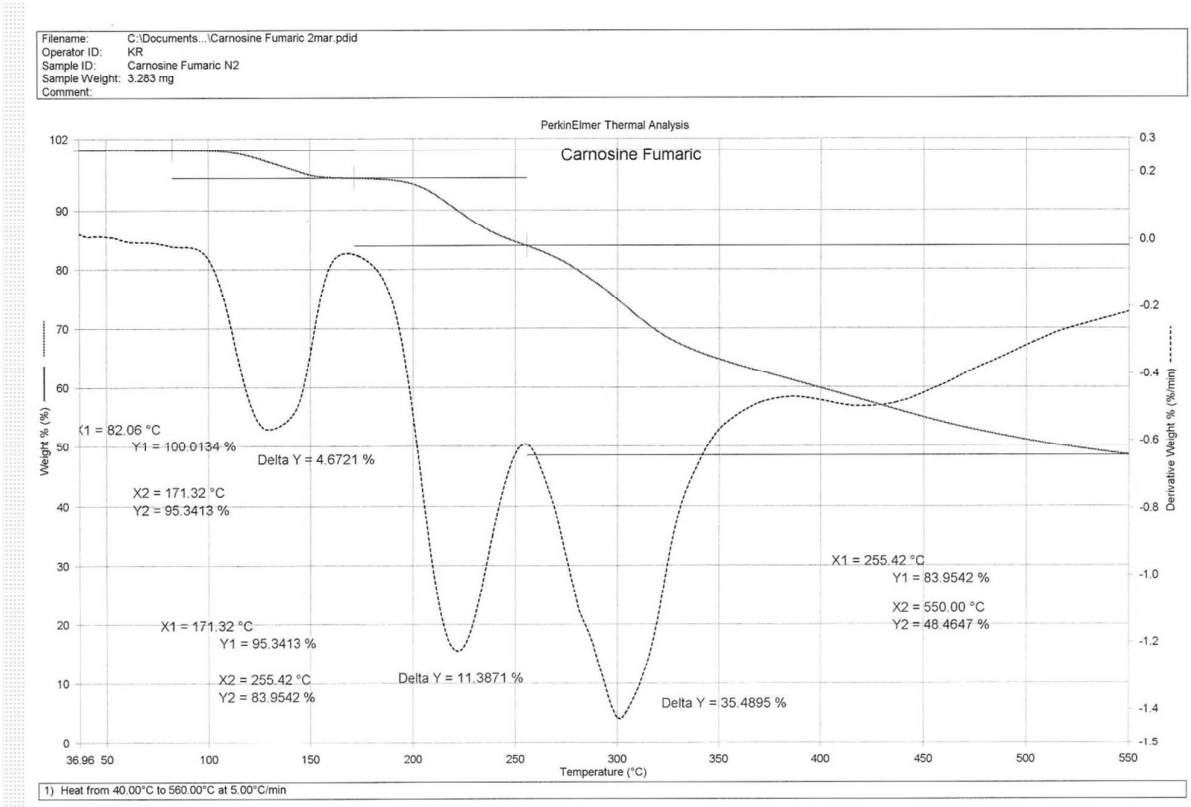

Figure SI 9 TGA of [L-Hcar][Hfum]·H_2O

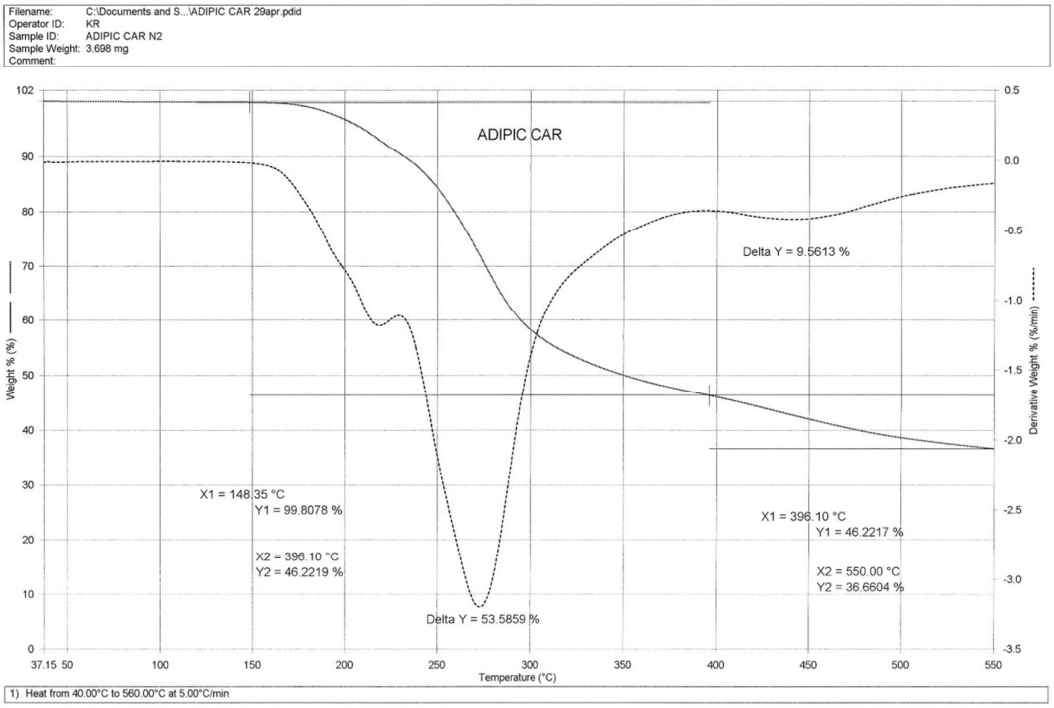

Figure SI 10 TGA of the salt obtained by reaction of carnosine with adipic acid.

Figure SI 11 TGA of [L-Hcar][Haze]

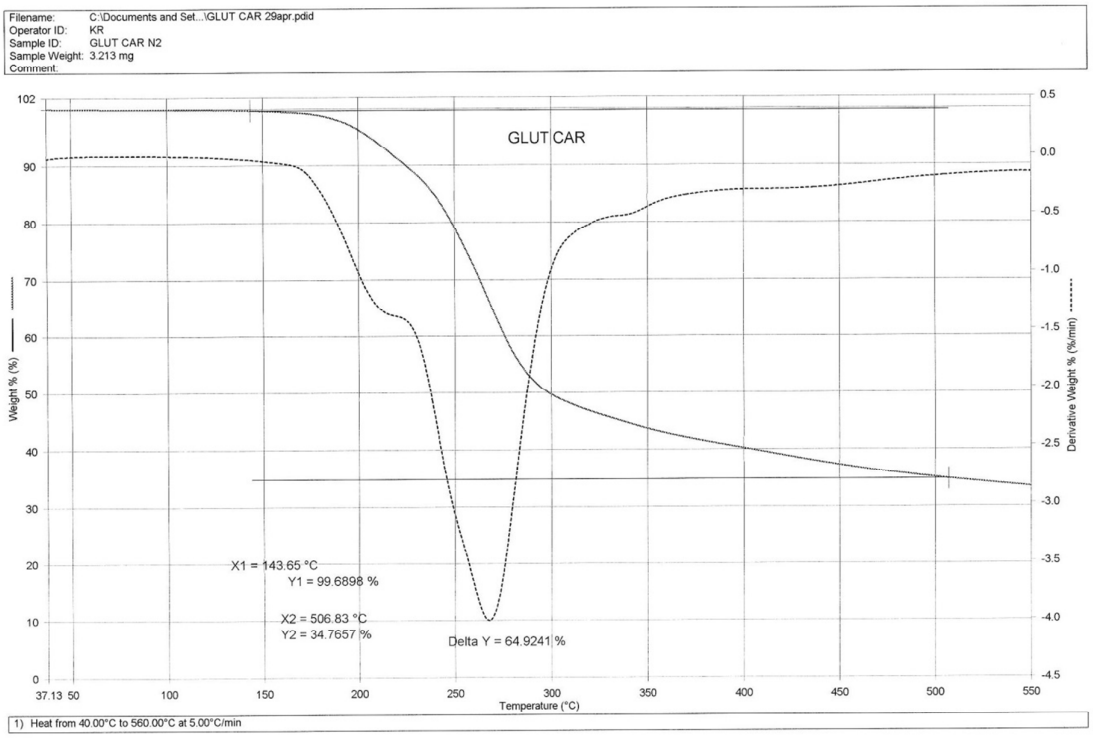

Figure SI 12 TGA of [L-Hcar][Hglu]

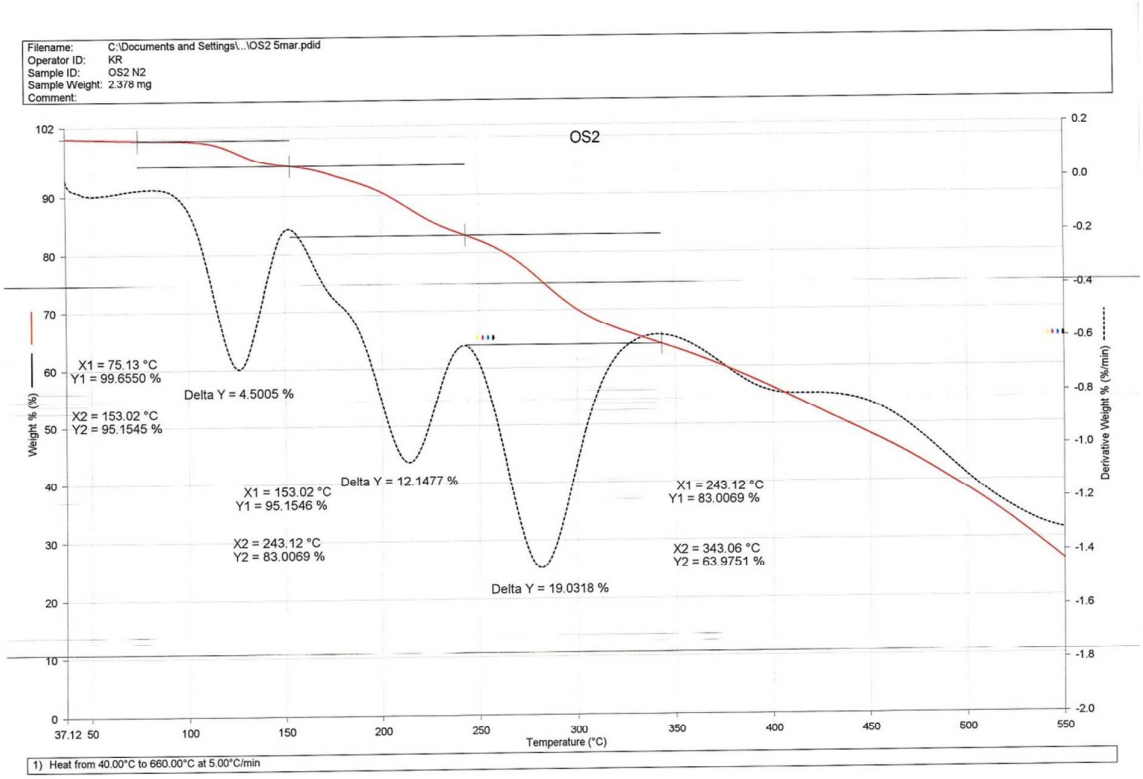

Figure SI 13 TGA of [L-Hcar][Hmal]·H_2O

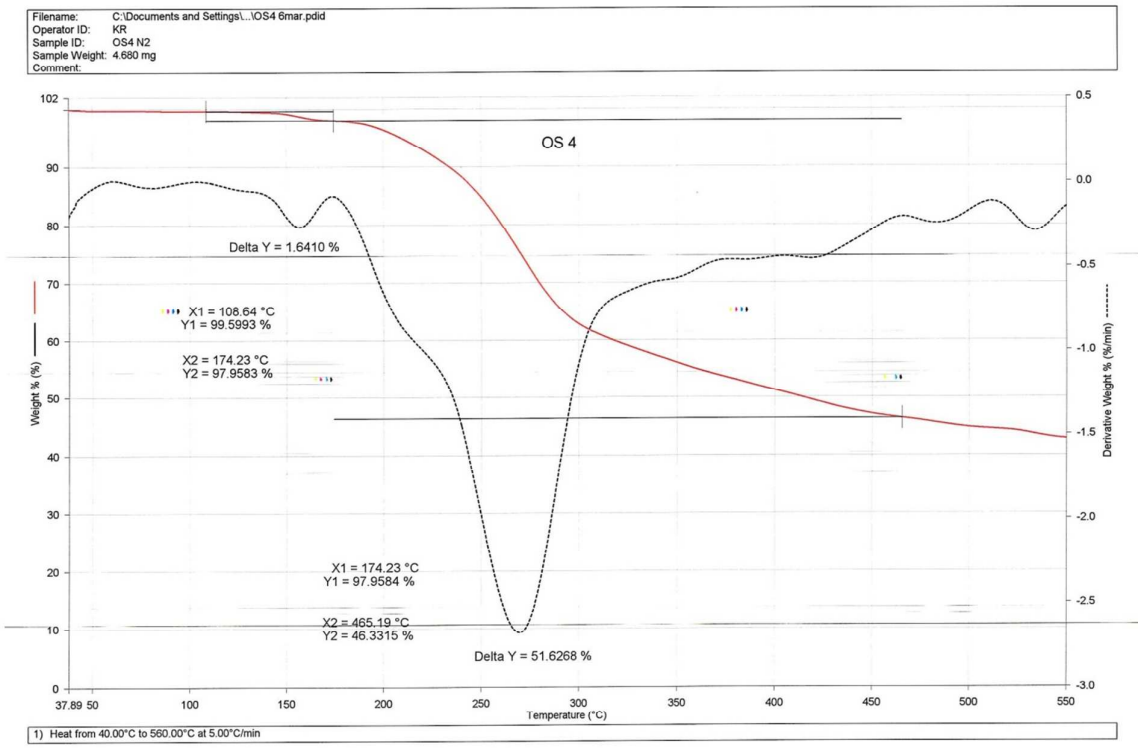

Figure SI 14 TGA of the salt obtained by reaction of carnosine with pimelic acid.

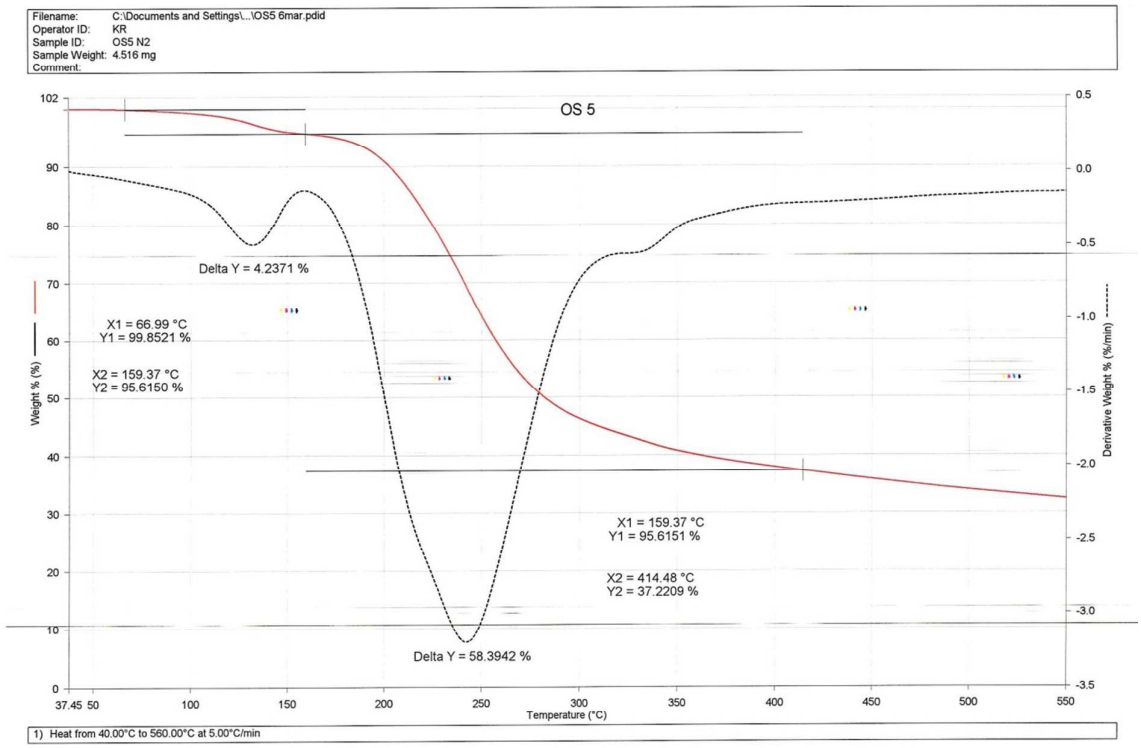

Figure SI 15 TGA of [L-Hcar][sal]·H_2O

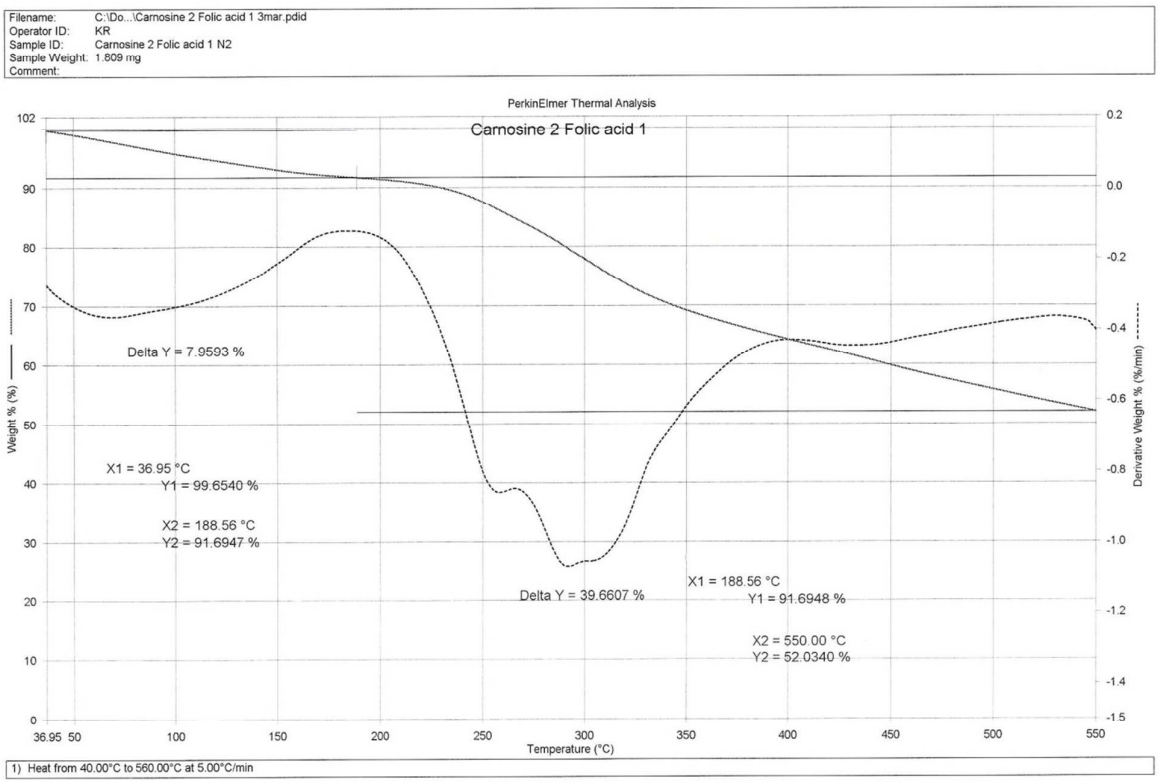

Figure SI 16 TGA of [L-Hcar]$_2$[fol]. From the shape of both the TGA trace and the derivative curve it can be inferred that the continuous loss of water, starting right at the beginning of the measurement, is due to adsorbed water, not to crystallization water.

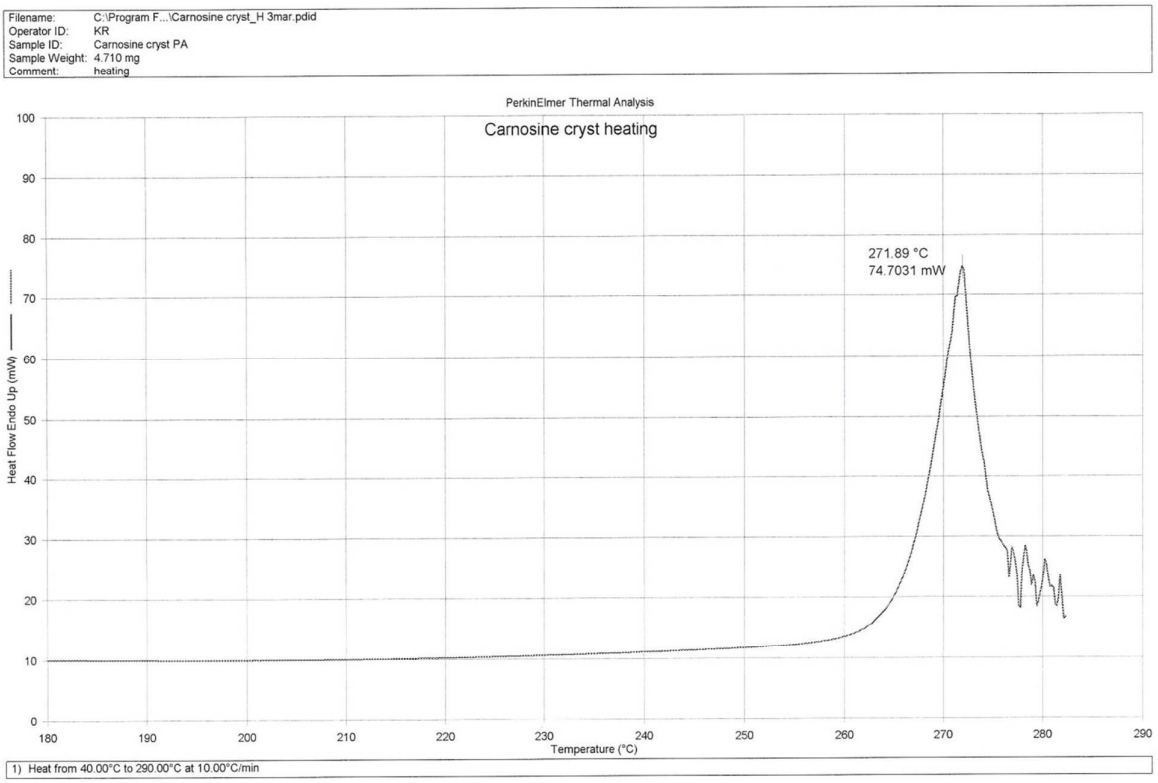

Figure SI 17 DSC of L-carnosine

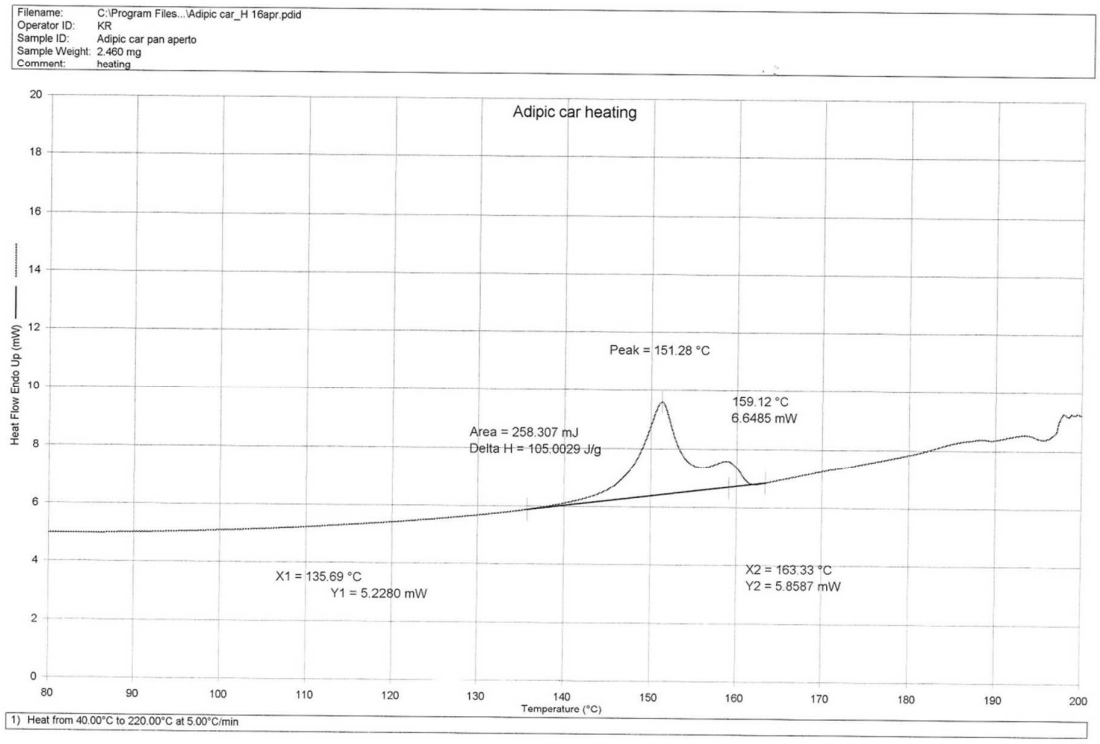

Figure SI 18 DSC of the salt obtained by carnosine – adipic acid interaction

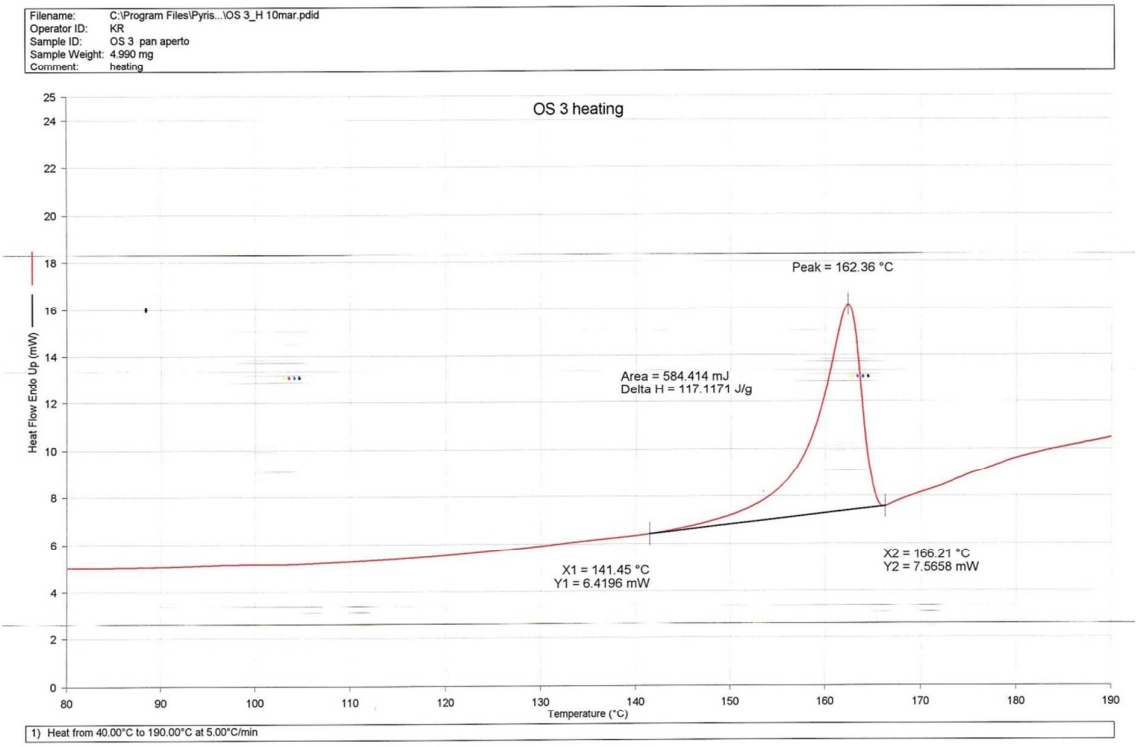

Figure SI 19 DSC of [L-Hcar][Haze]

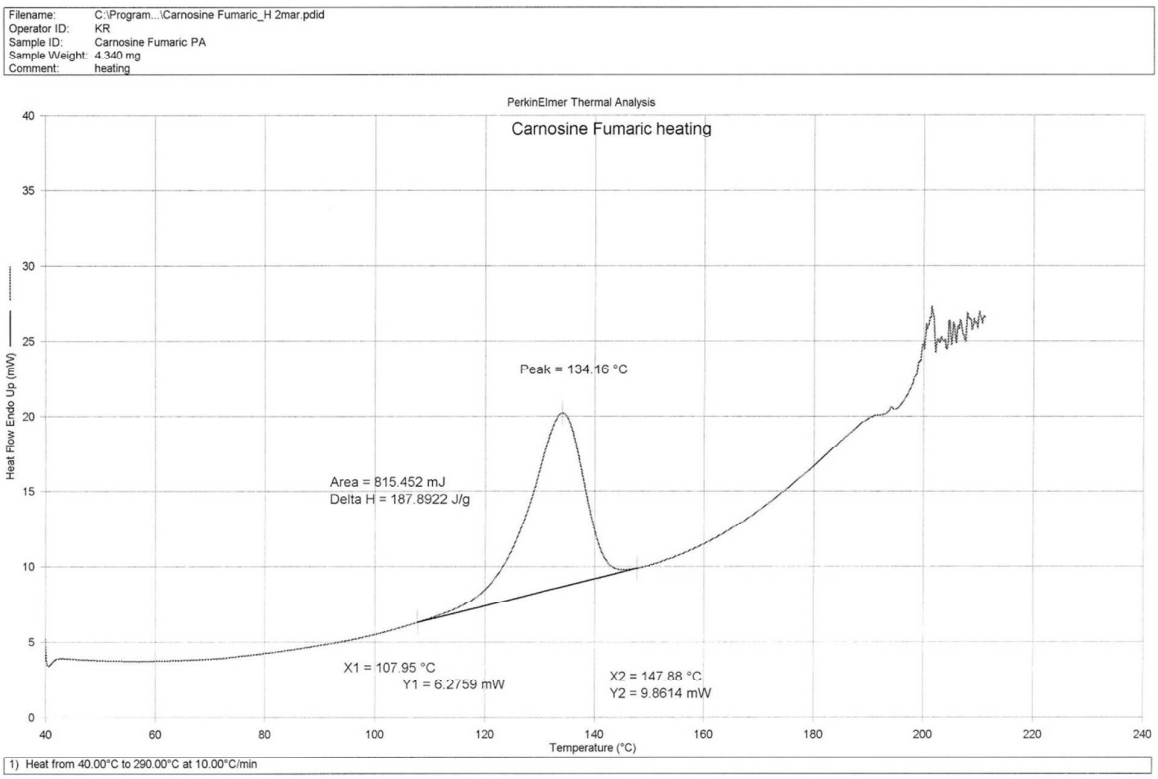

Figure SI 20 of [L-Hcar][Hfum]·H_2O

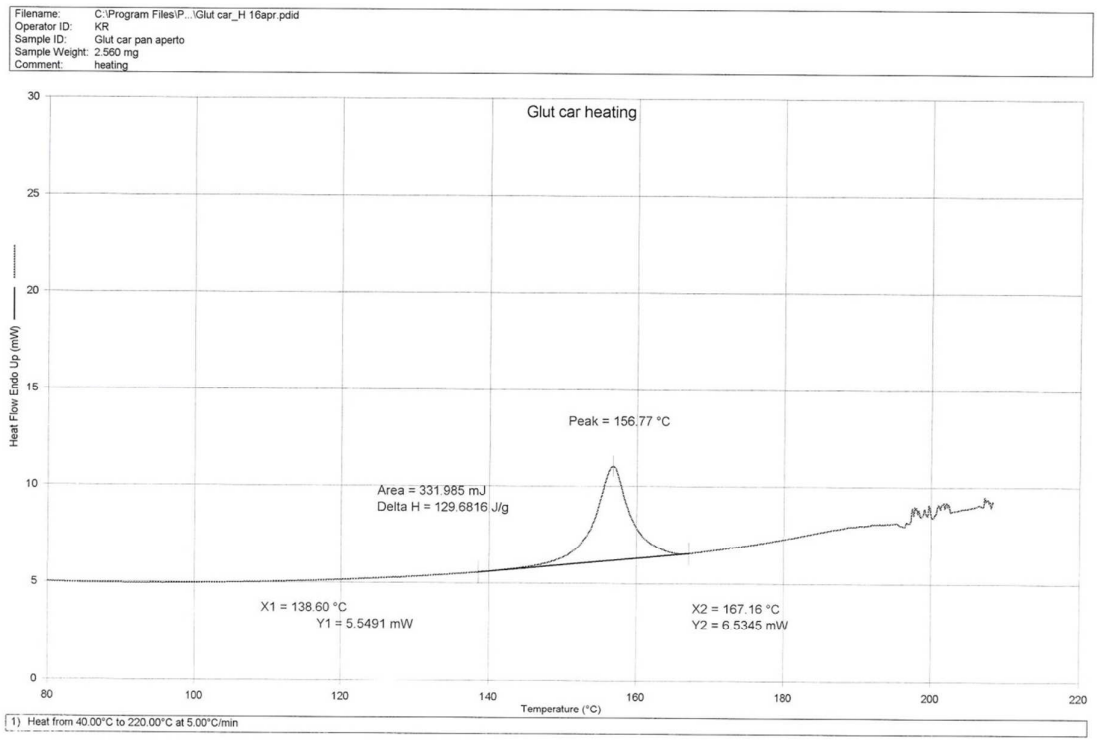

Figure SI 21 DSC of [L-Hcar][Hglu]

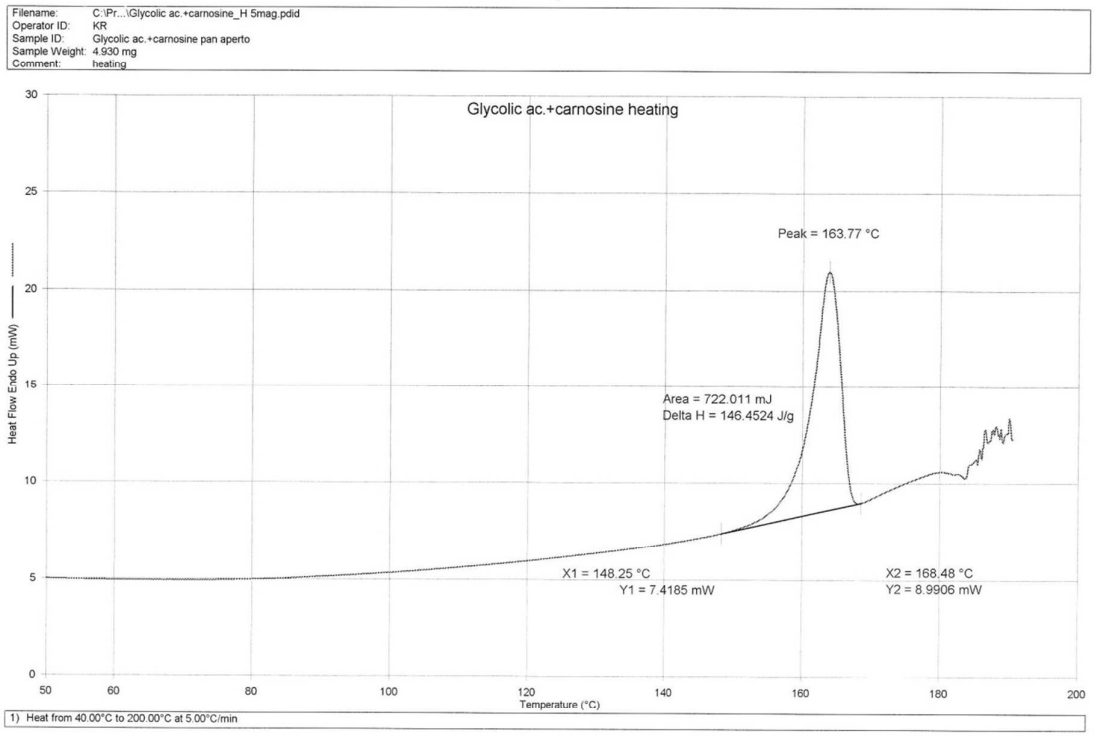

Figure SI 22 DSC of [L-Hcar][gly]

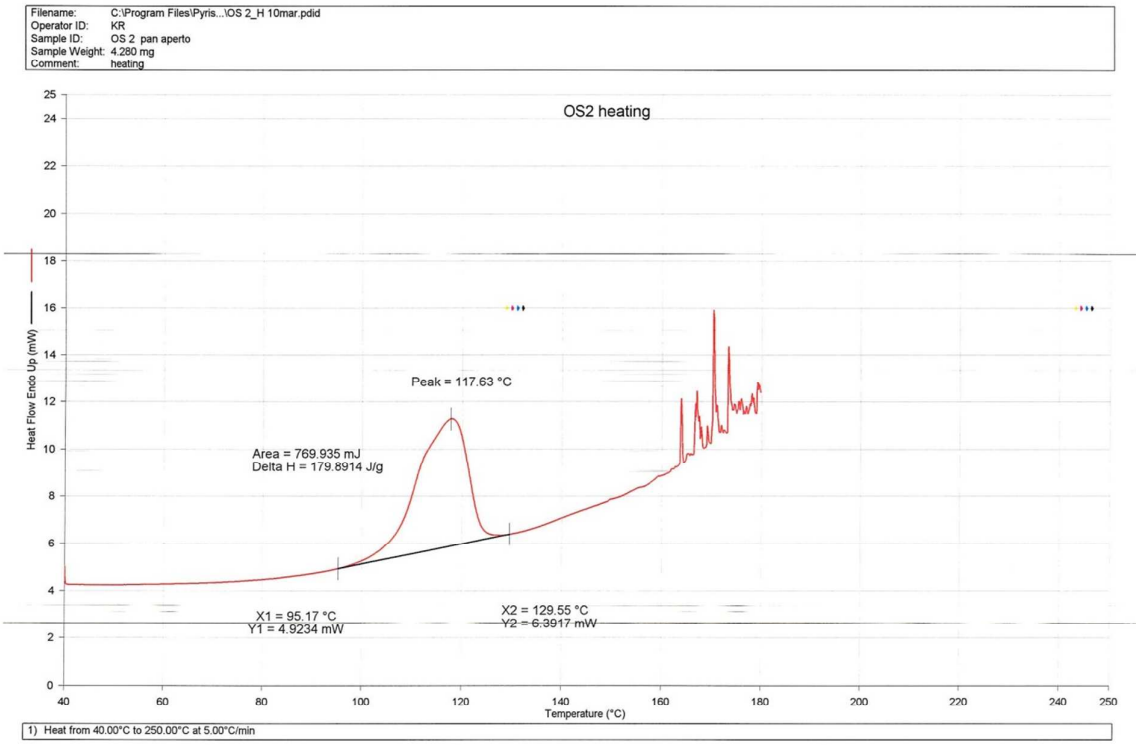

Figure SI 23 DSC of [L-Hcar][Hmal]·H_2O

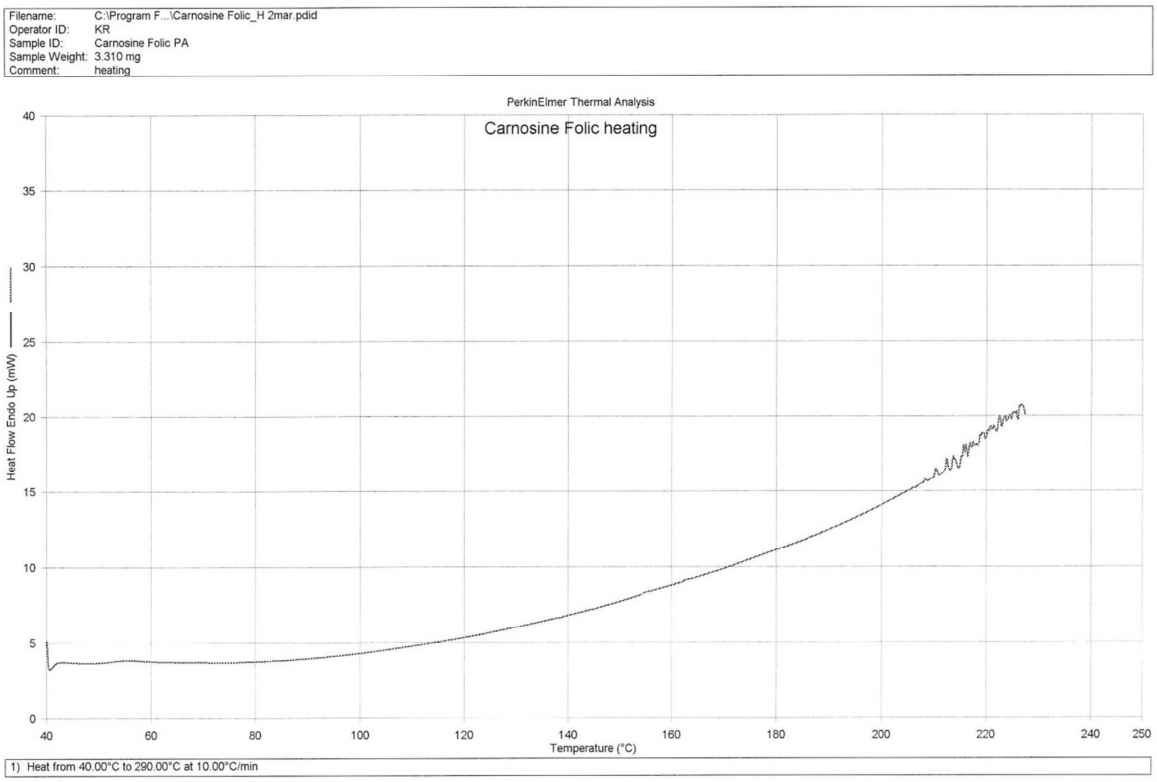

Figure SI 24 DSC of $[L\text{-}Hcar]_2[fol]$

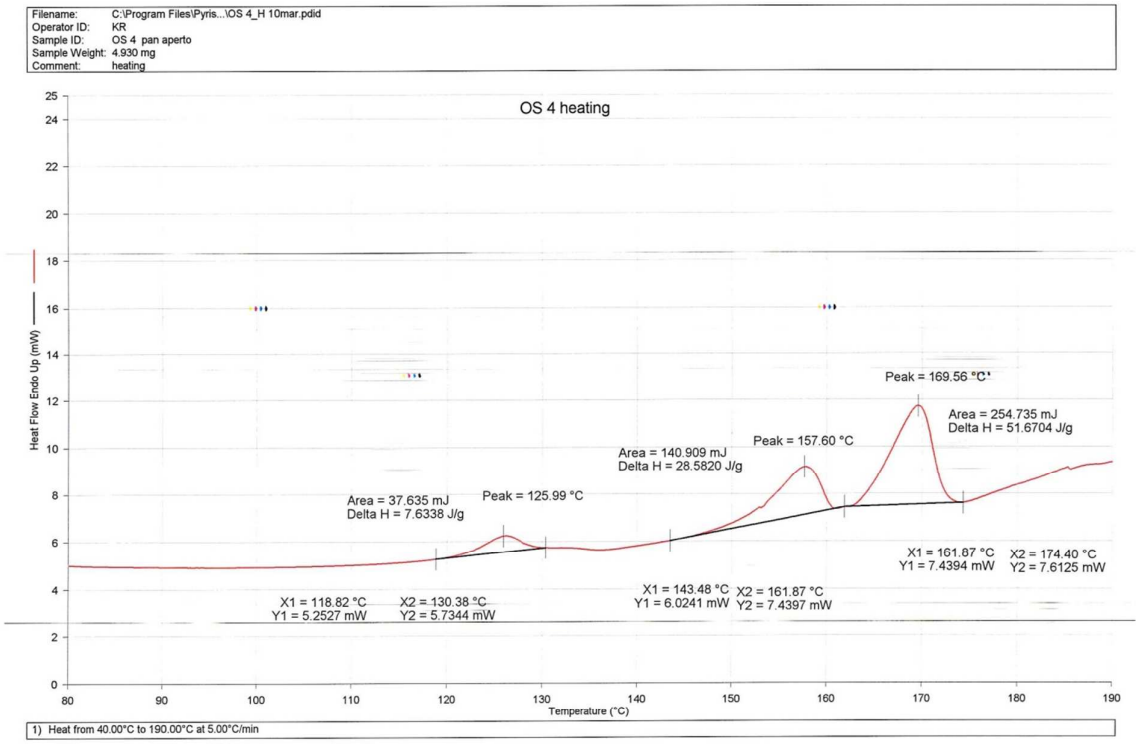

Figure SI 25 DSC of the salt TGA of the salt obtained by reaction of carnosine with pimelic acid.

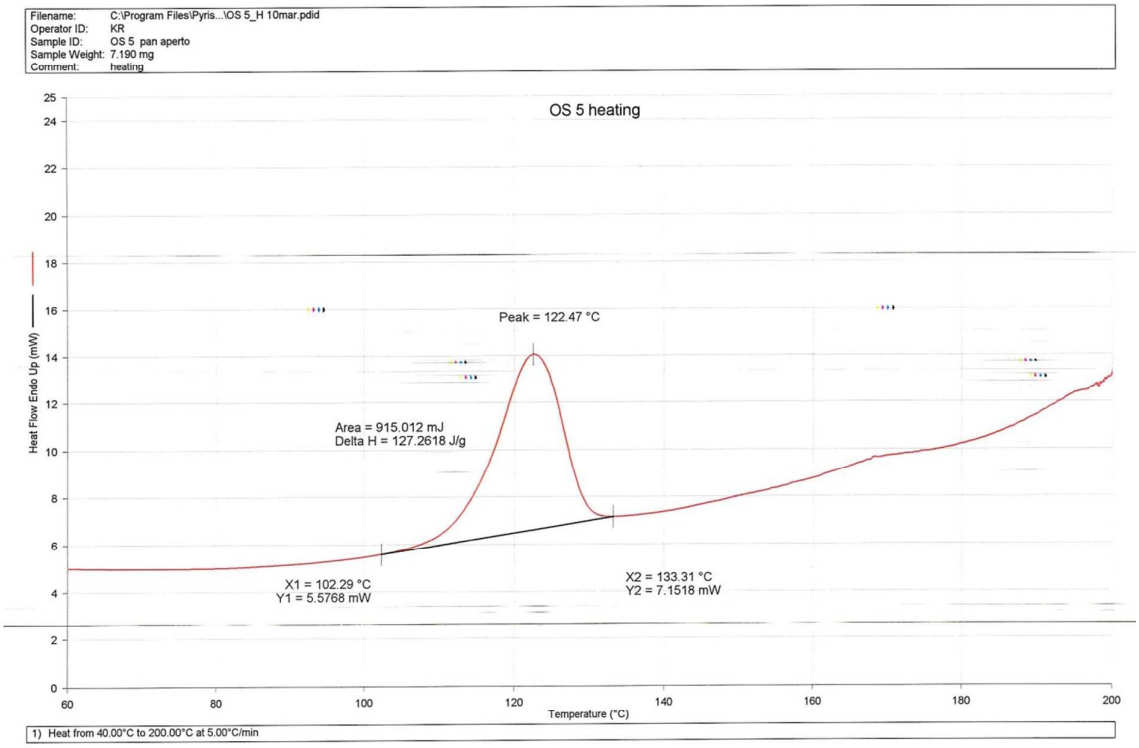

Figure SI 26 DSC of [L-Hcar][sal]·H_2O

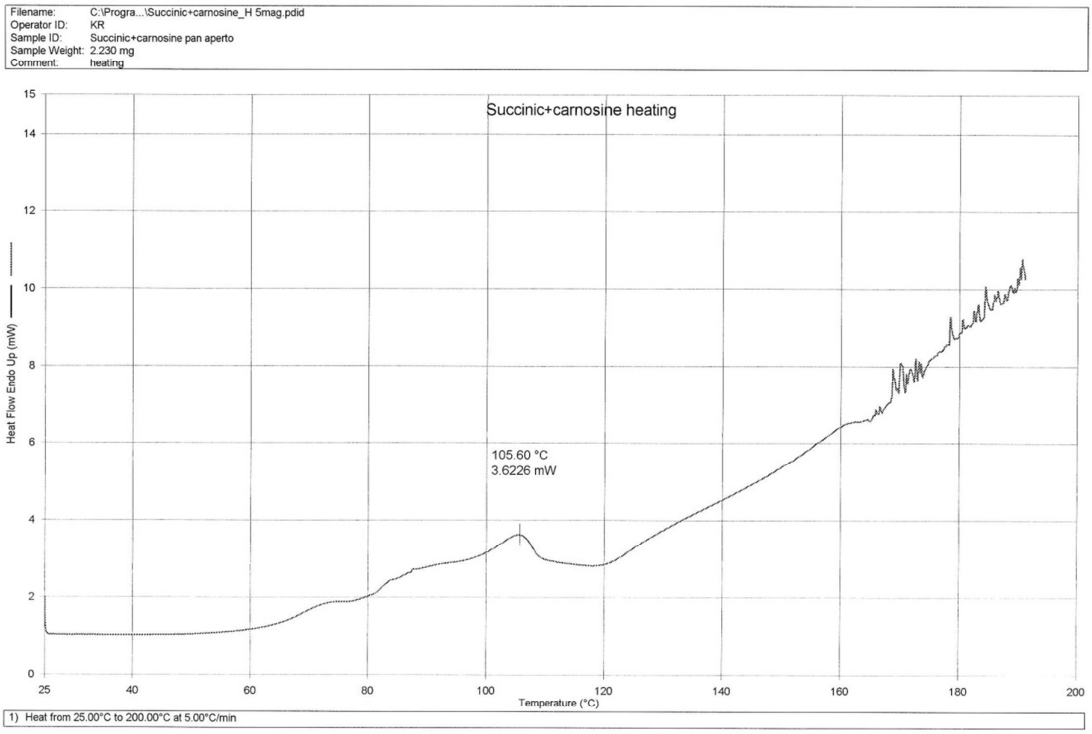

Figure SI 27 DSC of [L-Hcar][Hsuc]·H_2O

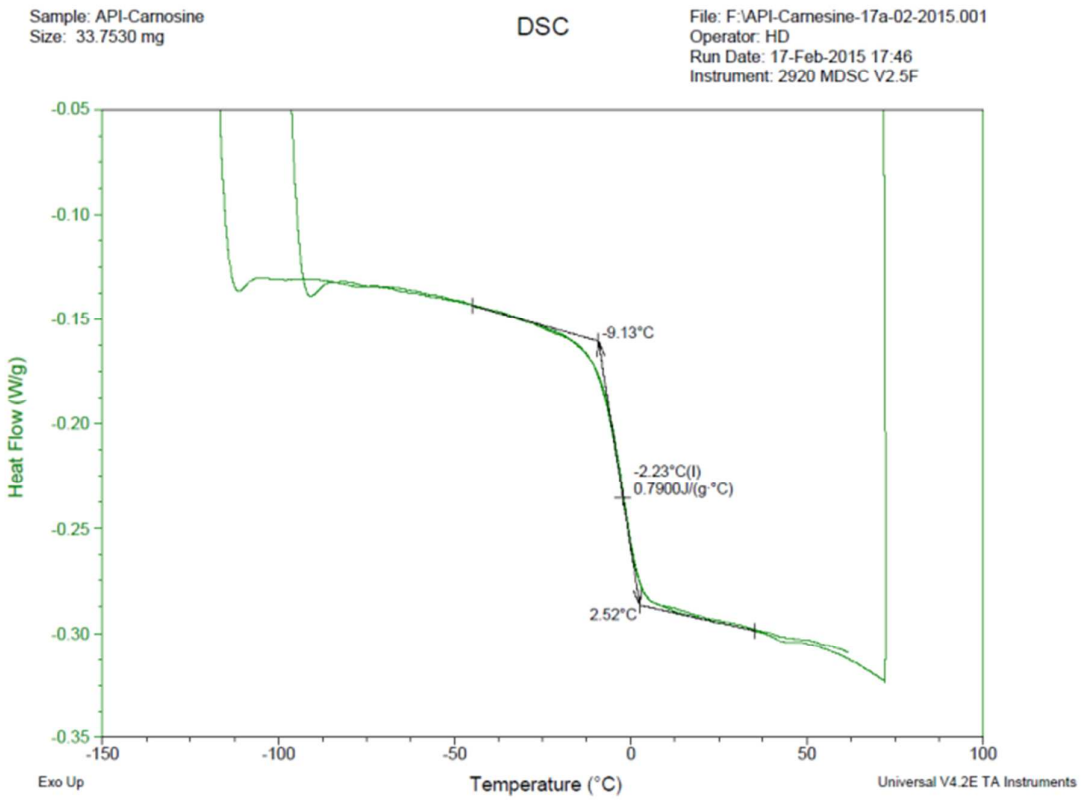

Figure SI 28. The glass transition observed at ca. 0°C for the thermally quenched sample of the salt obtained by reaction of L-carnosine with malic acid.

S4: XRPD: comparison between reagents and products

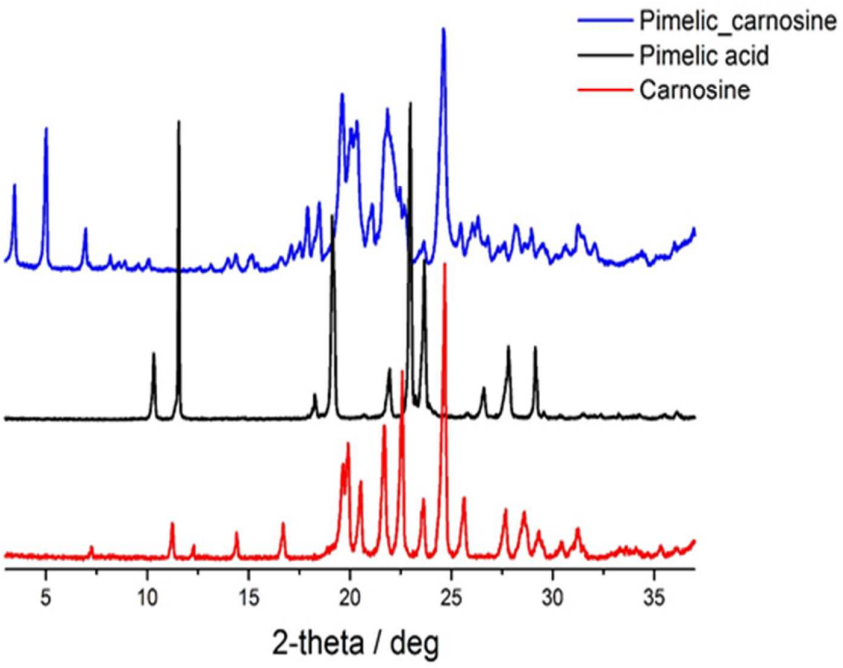

Figure SI 29. Comparison of the XRPD patterns for reagents and product of the reaction of L-carnosine with pimelic acid.

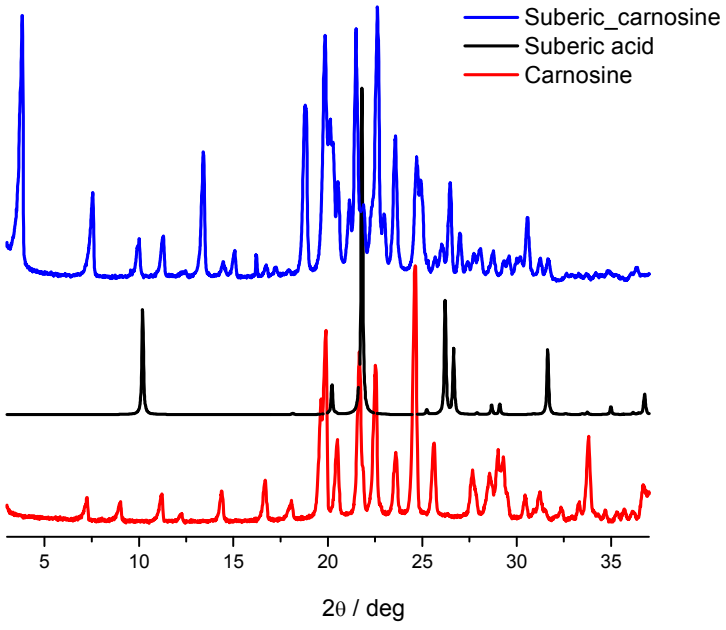

Figure SI 30. Comparison of the XRPD patterns for reagents and product of the reaction of L-carnosine with suberic acid.

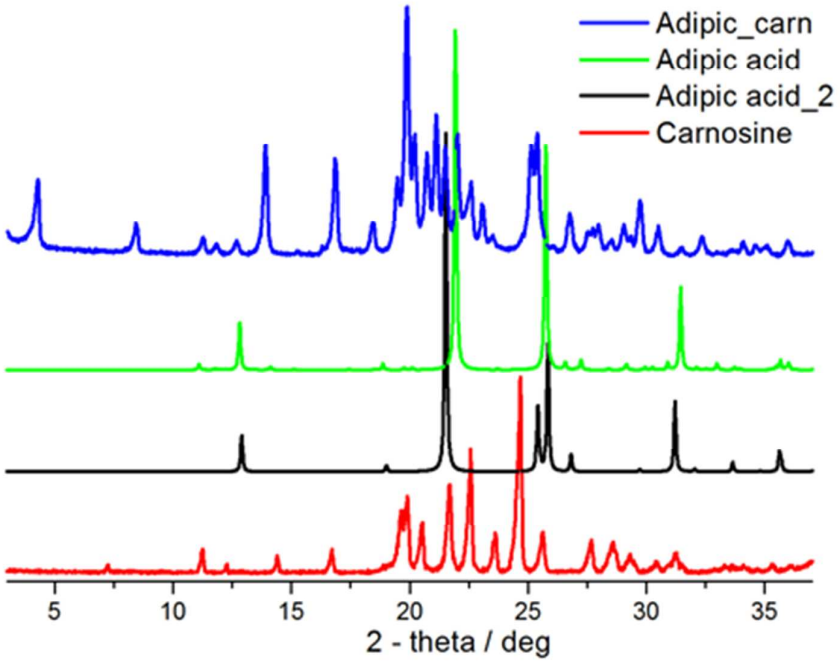

Figure SI 31. Comparison of the XRPD patterns for reagents and product of the reaction of L-carnosine with adipic acid.