Electronic Supplementary Material (ESI) for CrystEngComm.

Novel Co-crystals of the Nutraceutical Sinapic Acid

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Supporting Information

List of co-formers used for the co-crystallization of Sinapic Acid

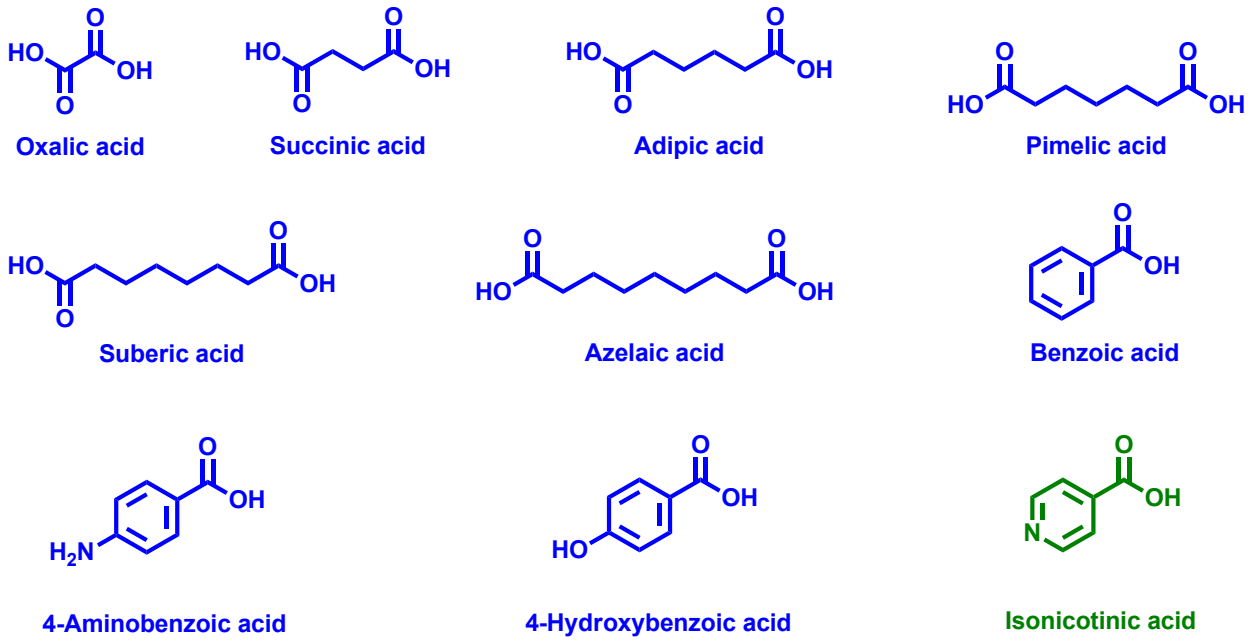


Figure 1. Carboxylic acids used as co-formers (blue – failed; green – success).

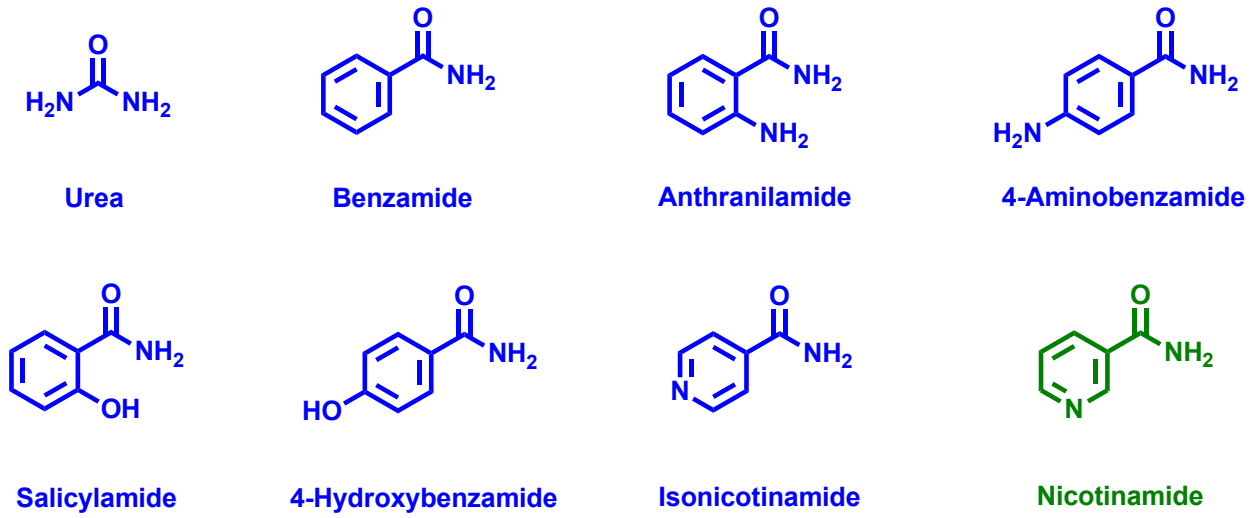
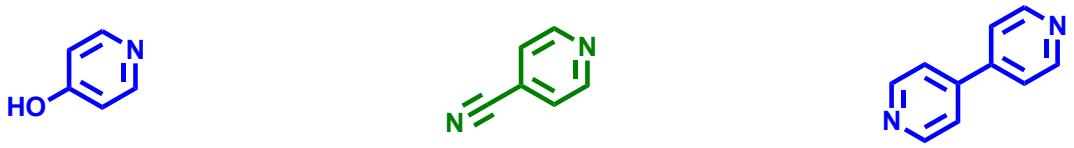
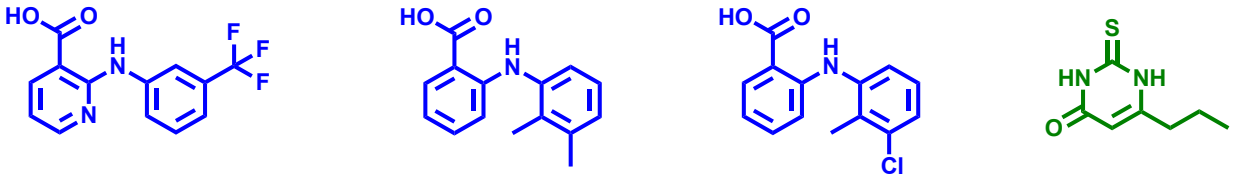


Figure 2. Amides used as co-formers (blue – failed; green – success).



4-Hydroxypyridine | 4-Pyridinecarbonitrile | 4,4'-Bipyridyl

Figure 3. Pyridines used as co-formers (blue – failed; green – success).



Niflumic acid | Mefenamic acid | Tolfenamic acid | 6-Propyl-2-thiouracil

Figure 4. Model active pharmaceutical ingredients (APIs) used as co-formers (blue – failed; green – success).

Single crystal XRD data for Sinapic Acid (SA)

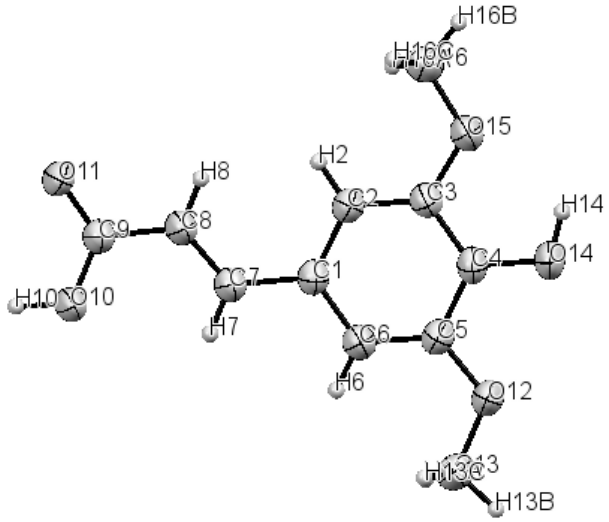


Figure 5. ORTEP diagram of the structure of **SA**.

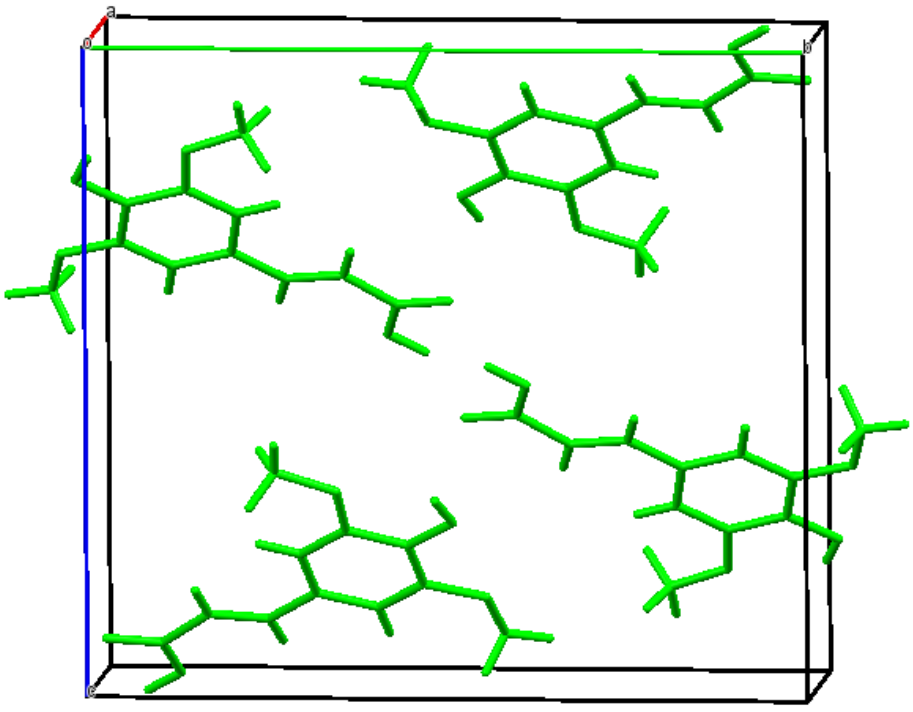


Figure 6. Crystal packing diagram of the structure of **SA**.

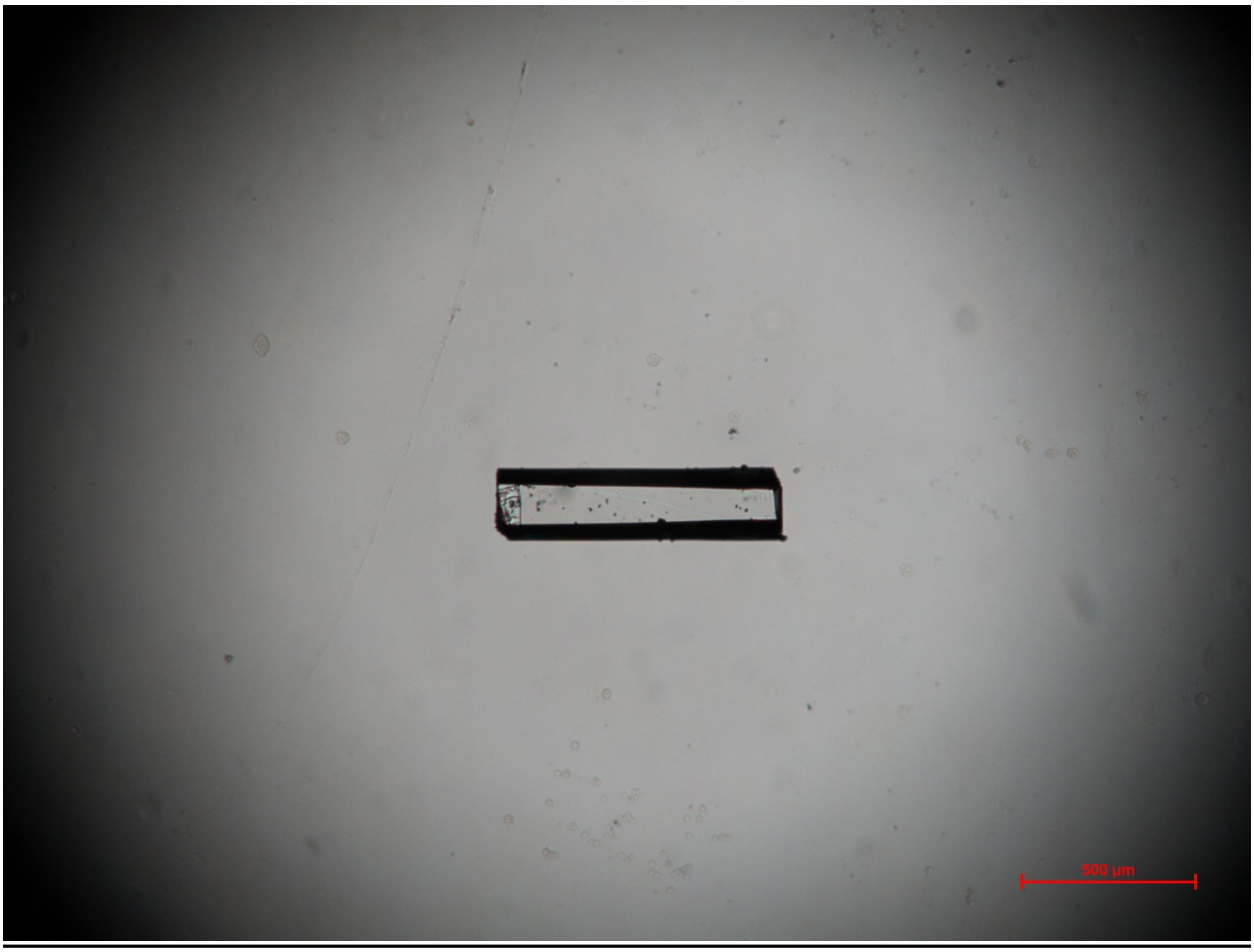


Figure 7. Photograph of **SA** crystal.

Sinapic Acid + Isonicotinic Acid (SA.INC)

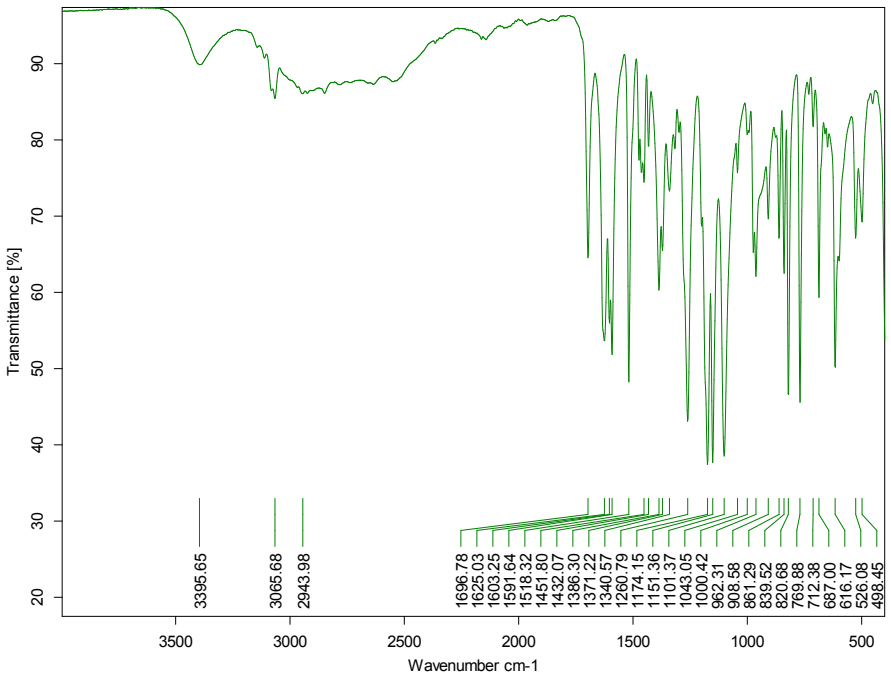


Figure 8. IR spectrum of **SA.INC**.

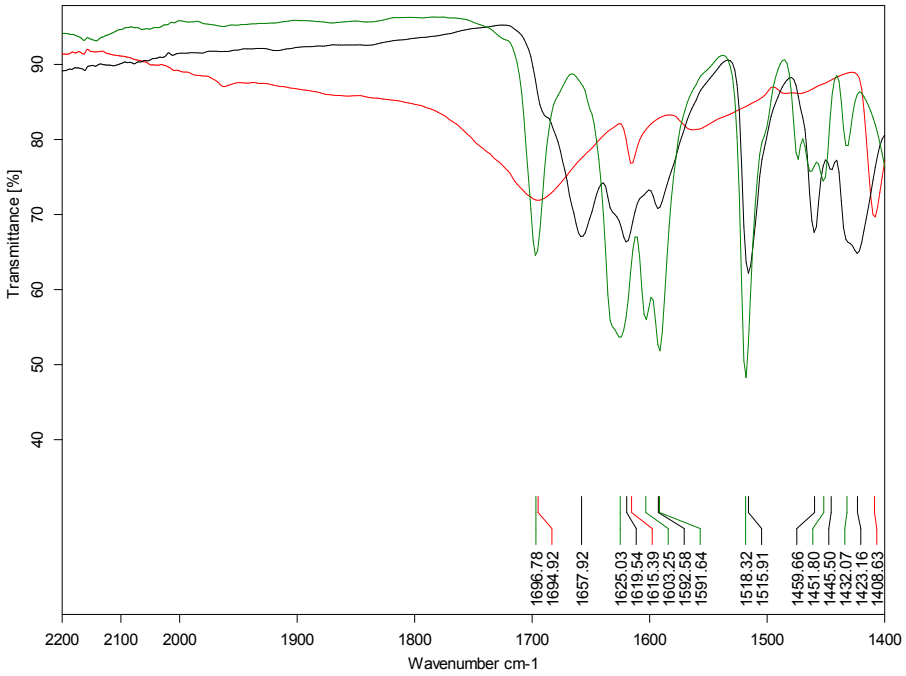


Figure 9. Expanded view of the IR spectrum of **SA.INC** (green) compared with **SA** (black) and **INC** (red).

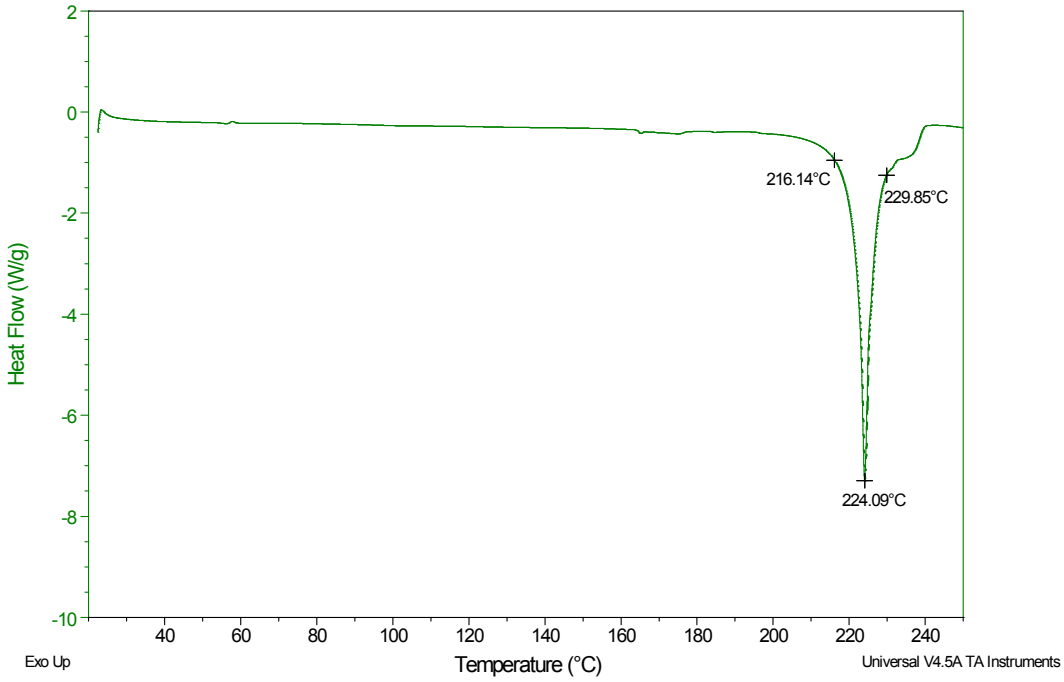


Figure 10. DSC spectrum of **SA.INC**.

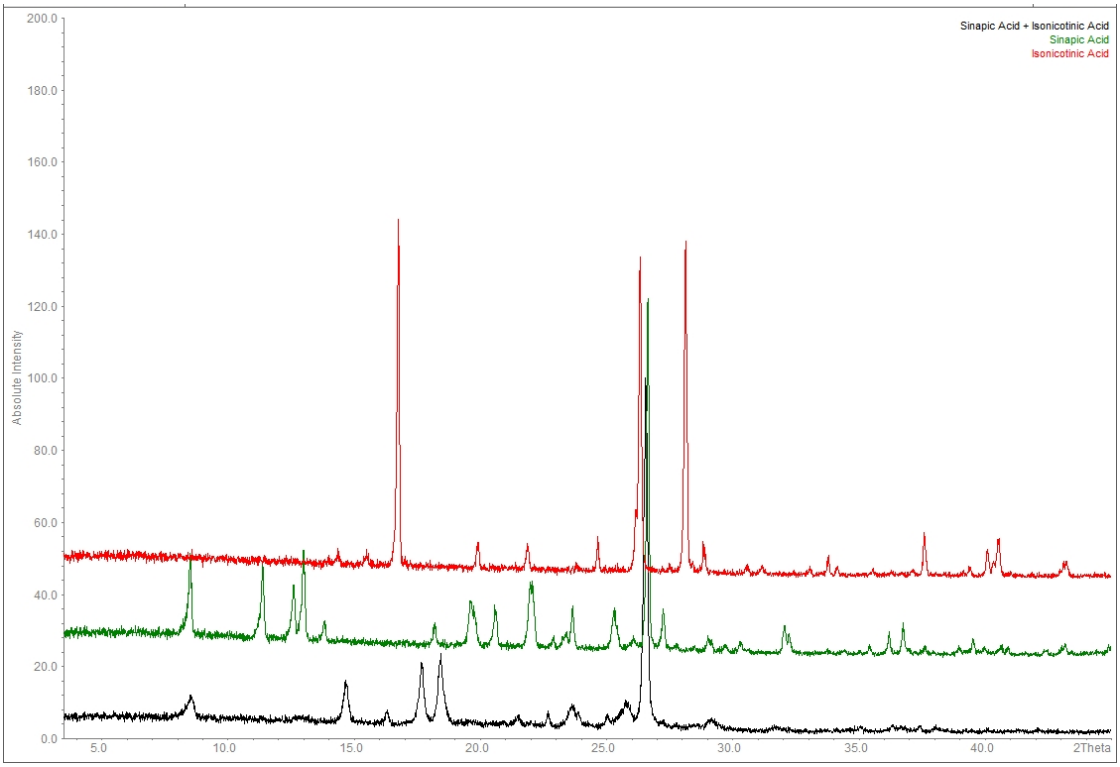


Figure 7. PXRD pattern of **SA.INC**.

Sinapic Acid + Nicotinamide (SA.NIA)

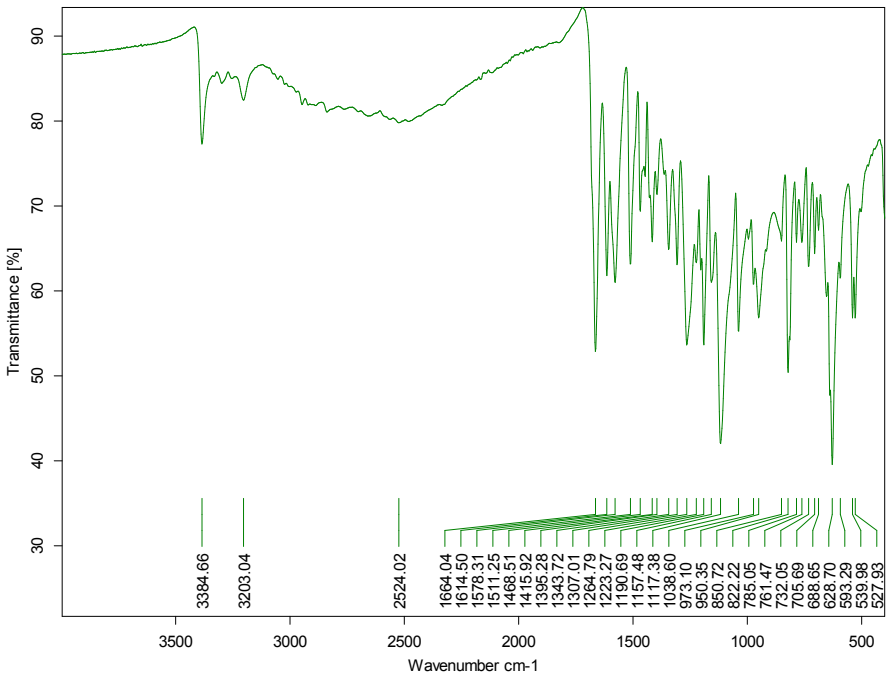


Figure 8. IR spectrum of **SA.NIA**.

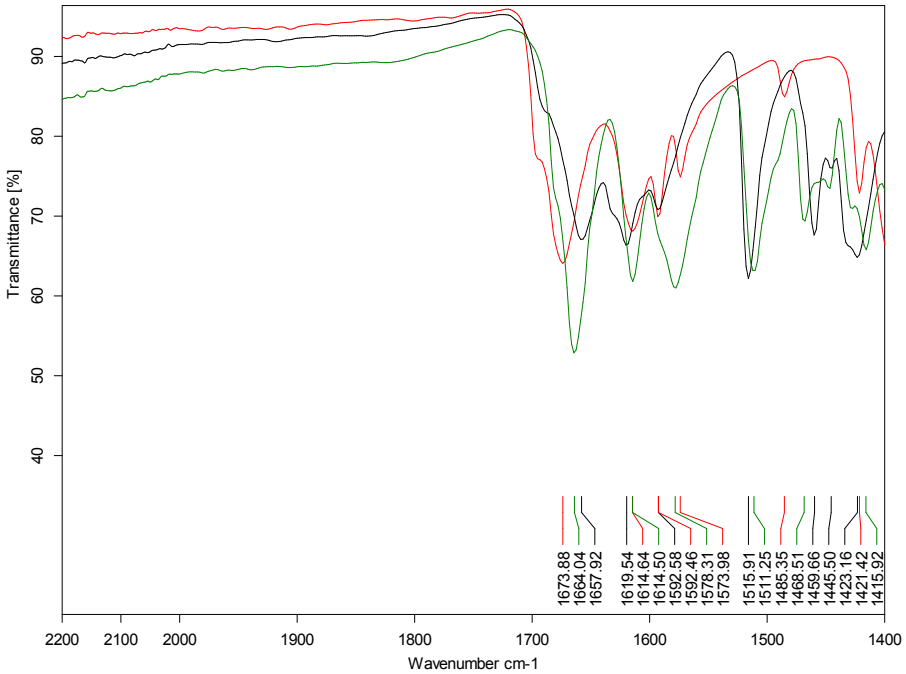


Figure 13. Expanded view of the IR spectrum of **SA.NIA** (green) compared with **SA** (black) and **NIA** (red).

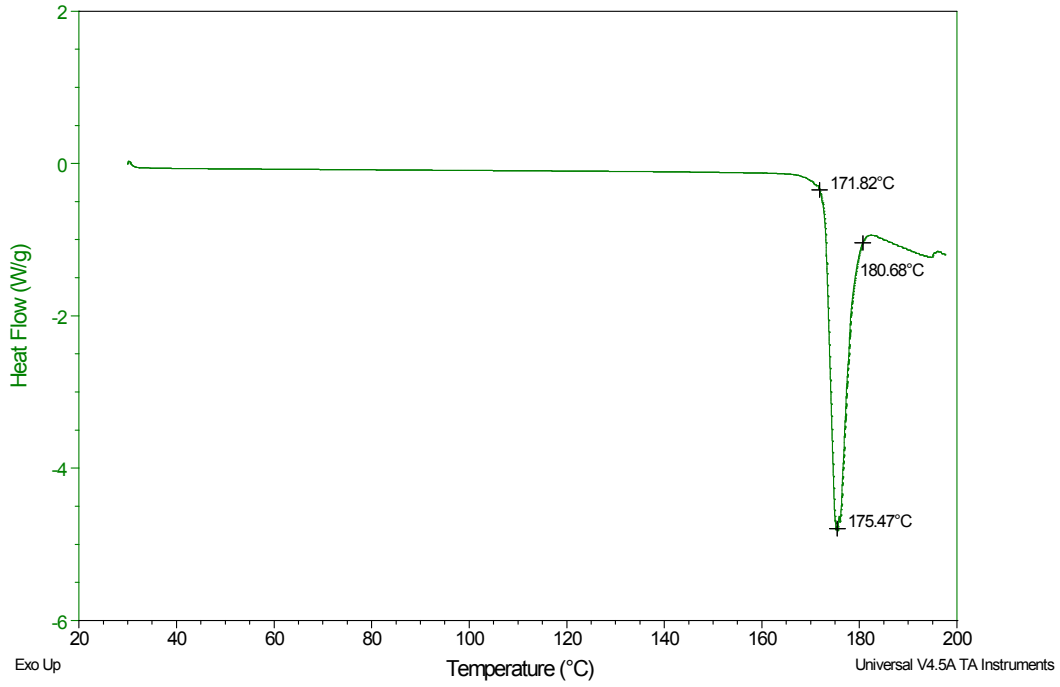


Figure 14. DSC spectrum of **SA.NIA**.

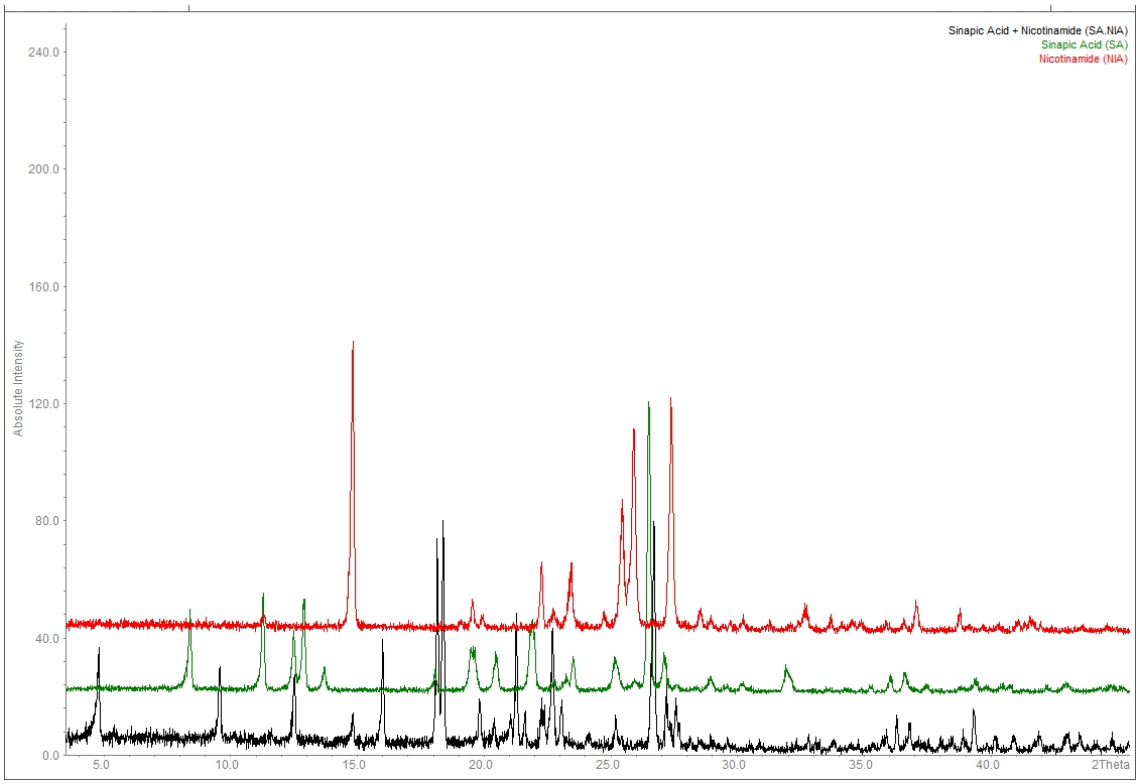


Figure 15. PXRD pattern of **SA.NIA**.

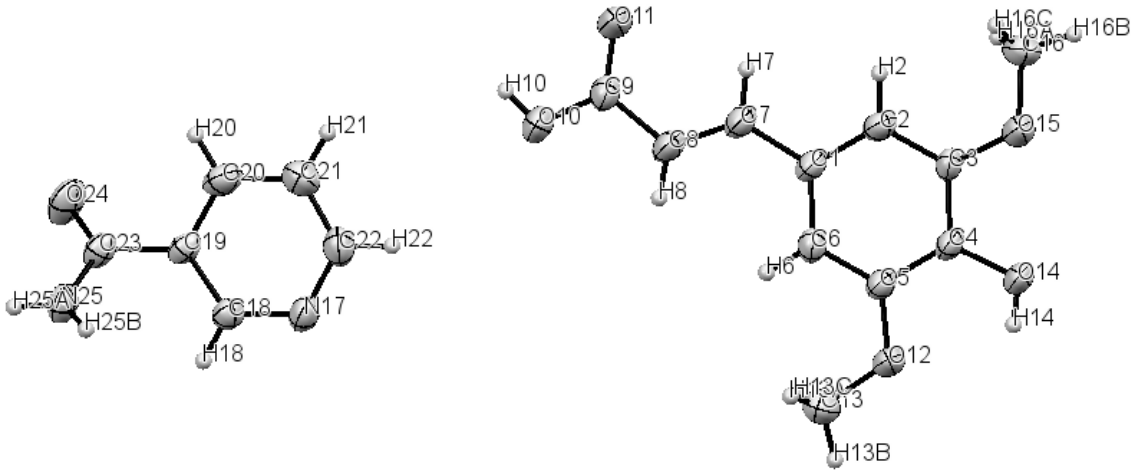


Figure 16. ORTEP diagram of the structure of **SA.NIA**.

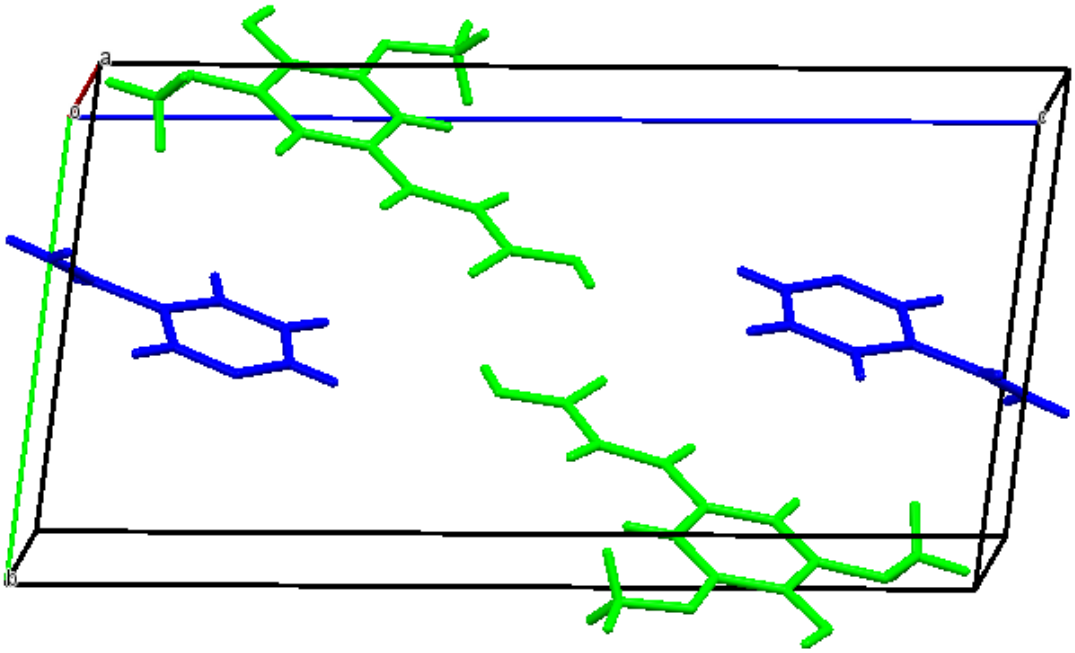


Figure 17. Crystal packing diagram of the structure of **SA.NIA**.

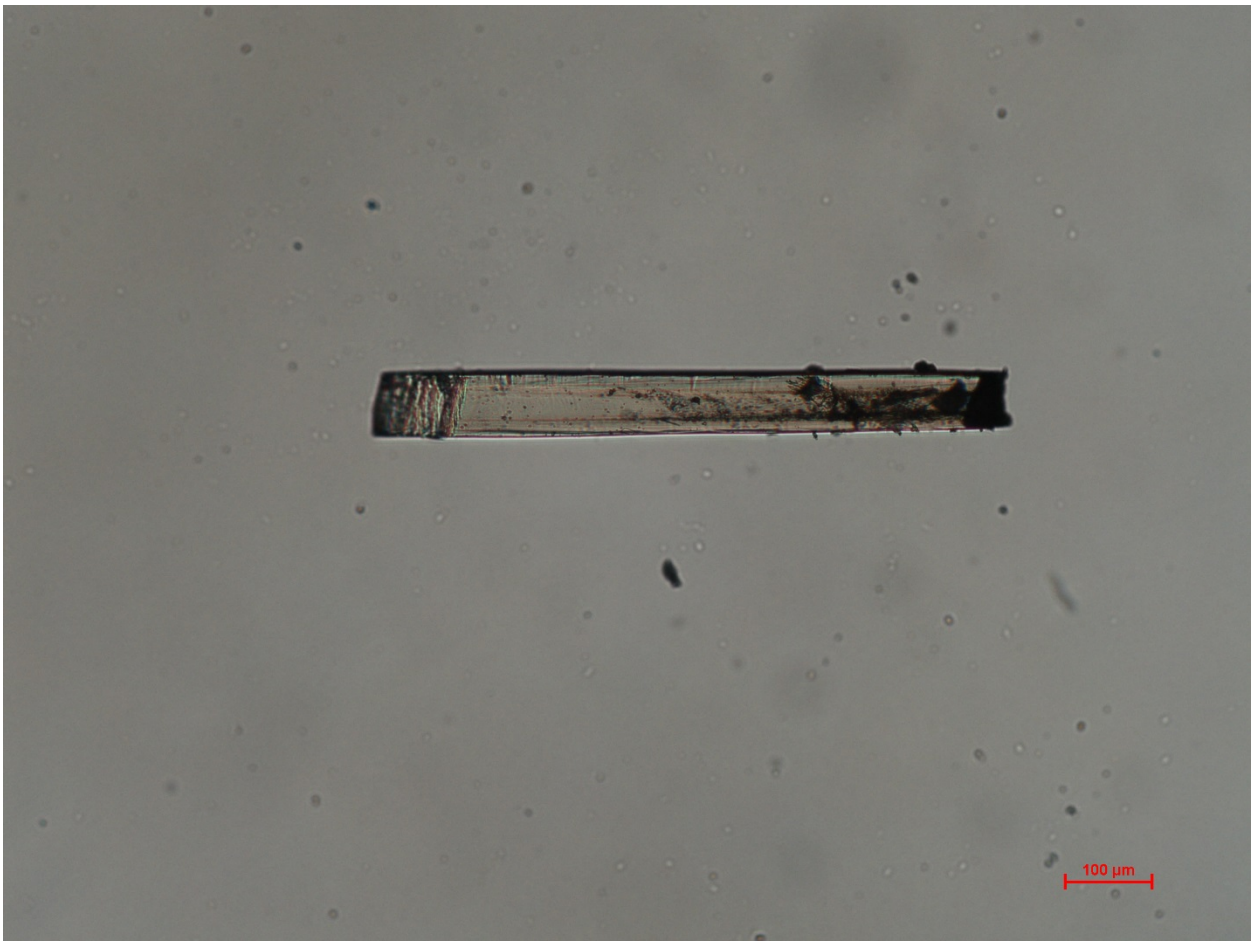


Figure 18. Photograph of **SA.NIA** crystal.

Sinapic Acid + 4-Pyridinecarbonitrile (SA.PYC)

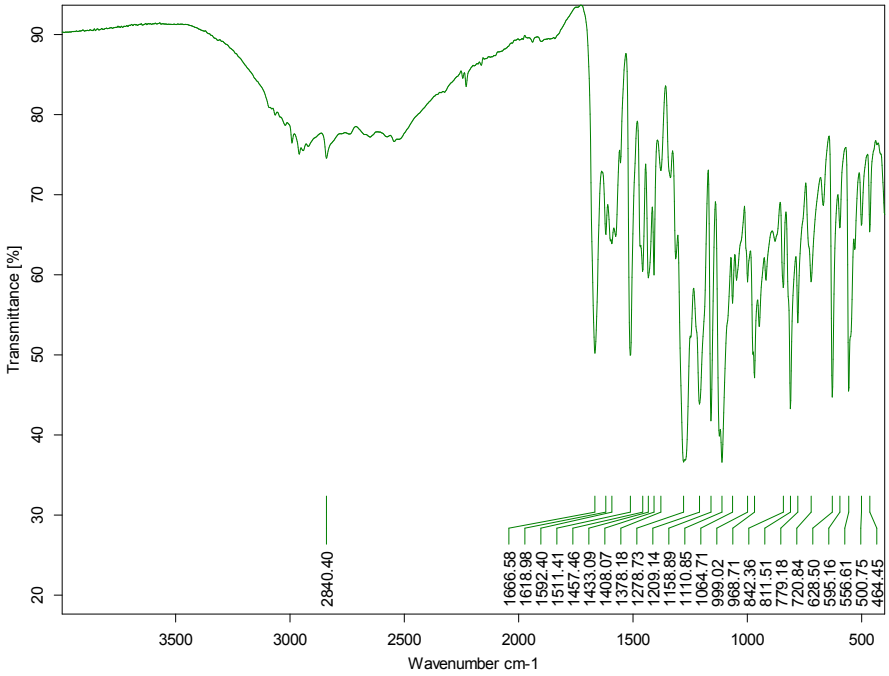


Figure 19. IR spectrum of **SA.PYC**.

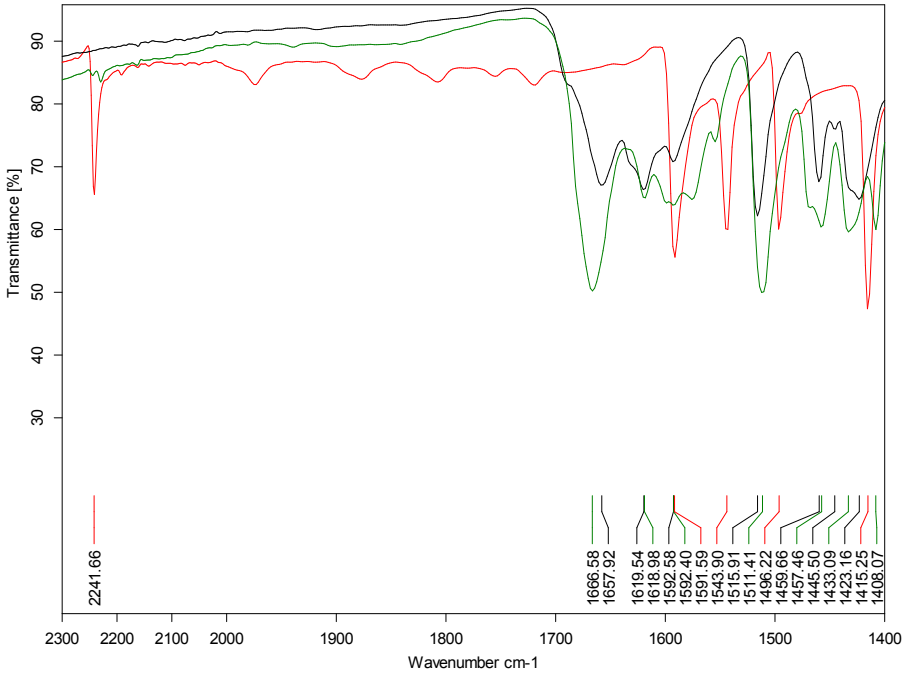


Figure 20. Expanded view of the IR spectrum of **SA.PYC** (green) compared with **SA** (black) and **PYC** (red).

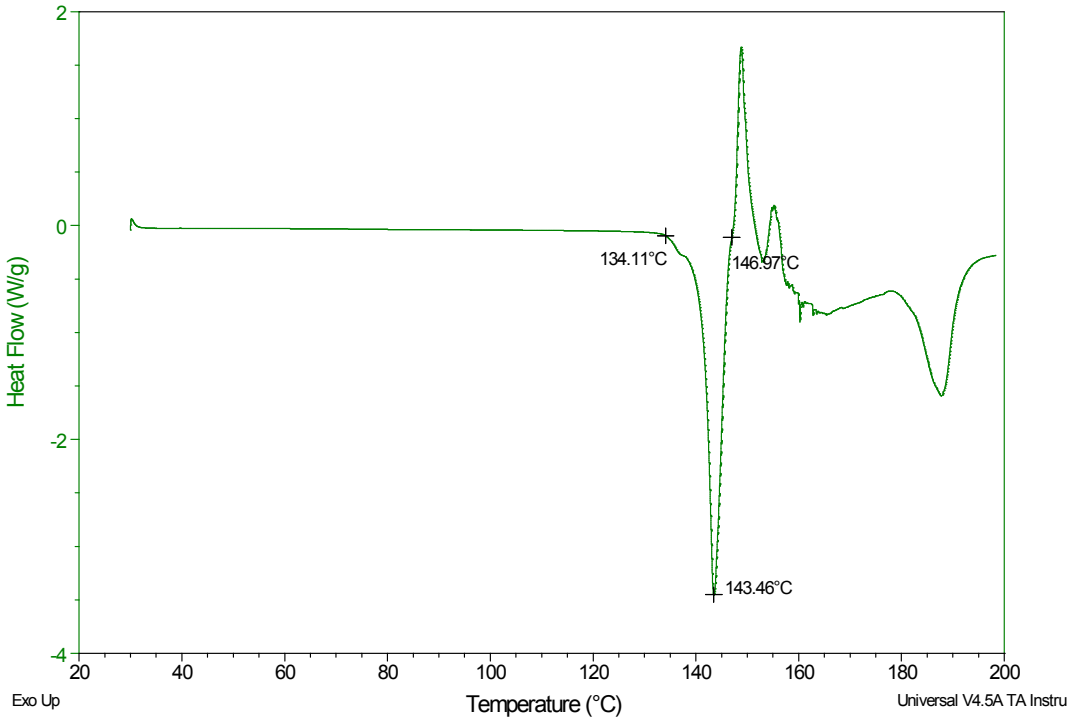


Figure 21. DSC spectrum of **SA.PYC**.

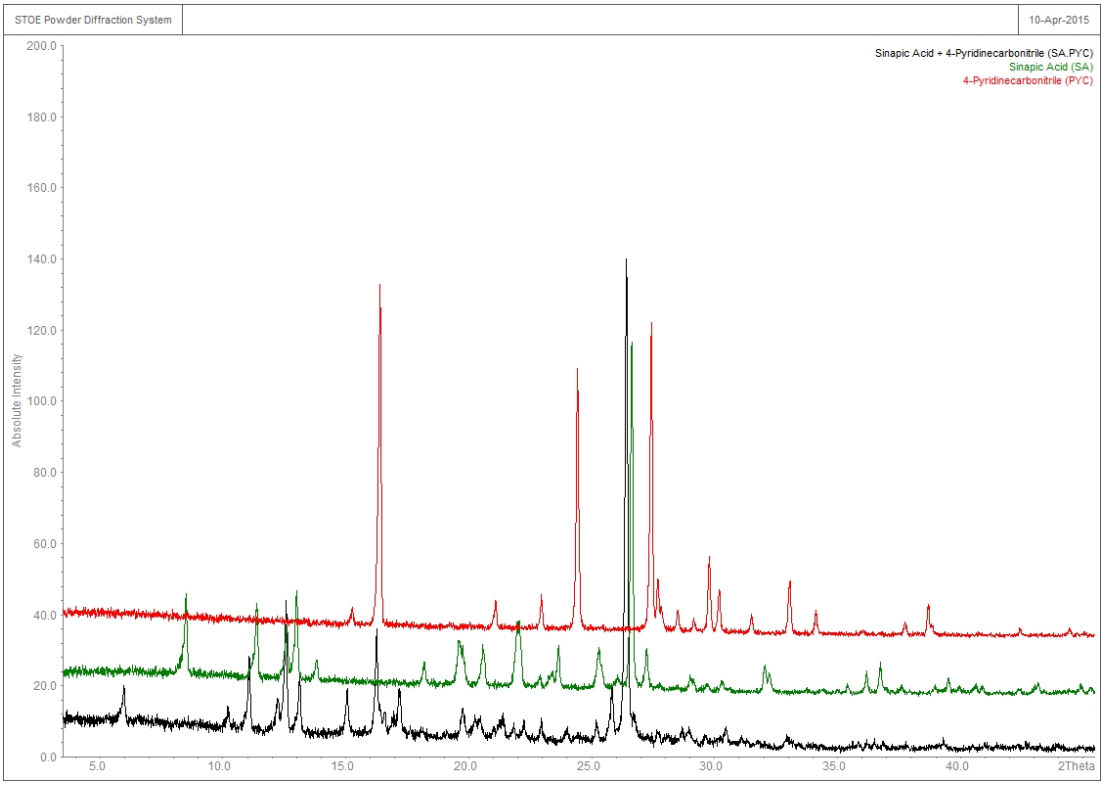


Figure 22. PXRD pattern of **SA.PYC**.

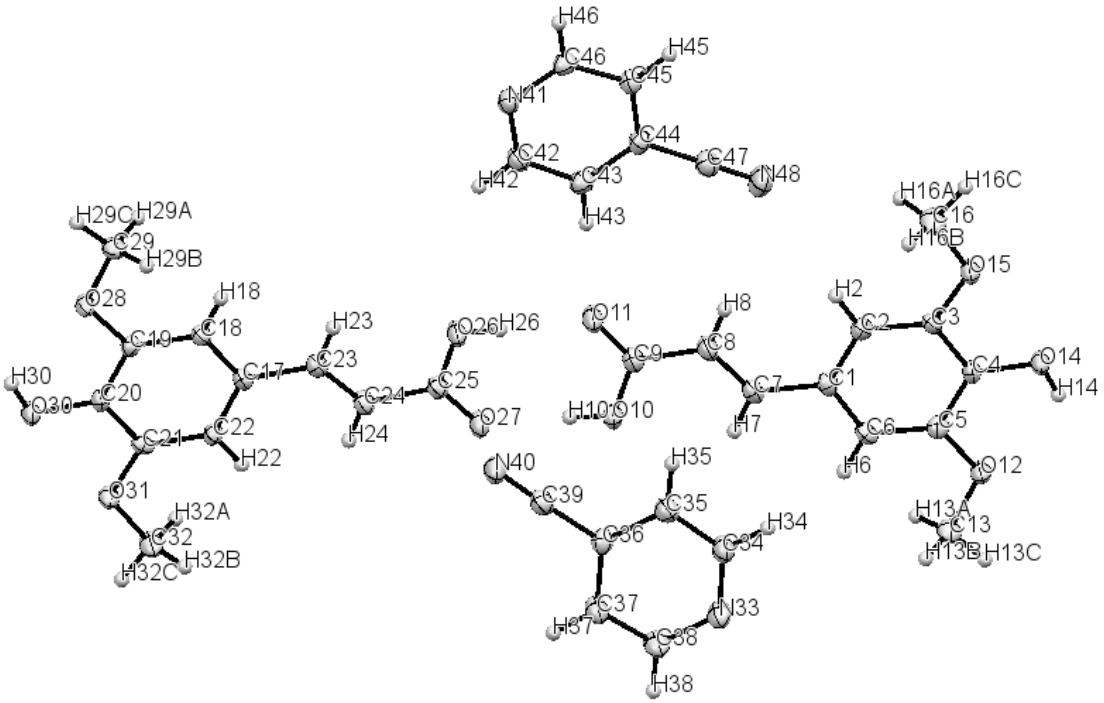


Figure 23. ORTEP diagram of the structure of **SA.PYC**.

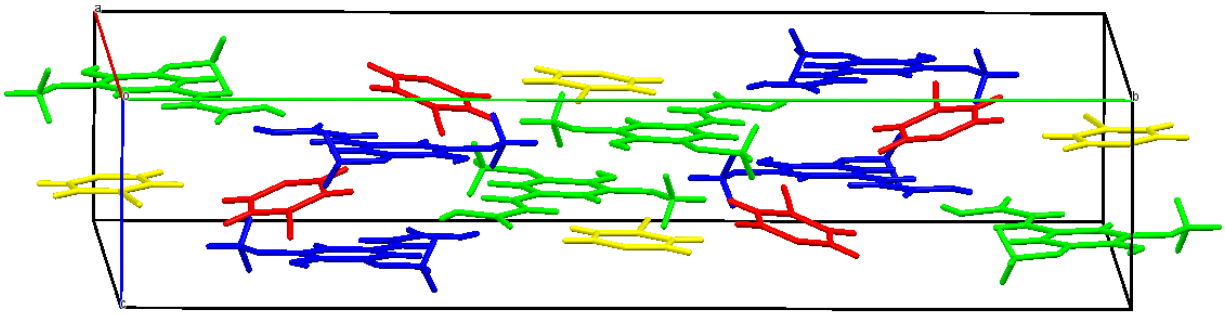


Figure 24. Crystal packing diagram of the structure of **SA.PYC**.

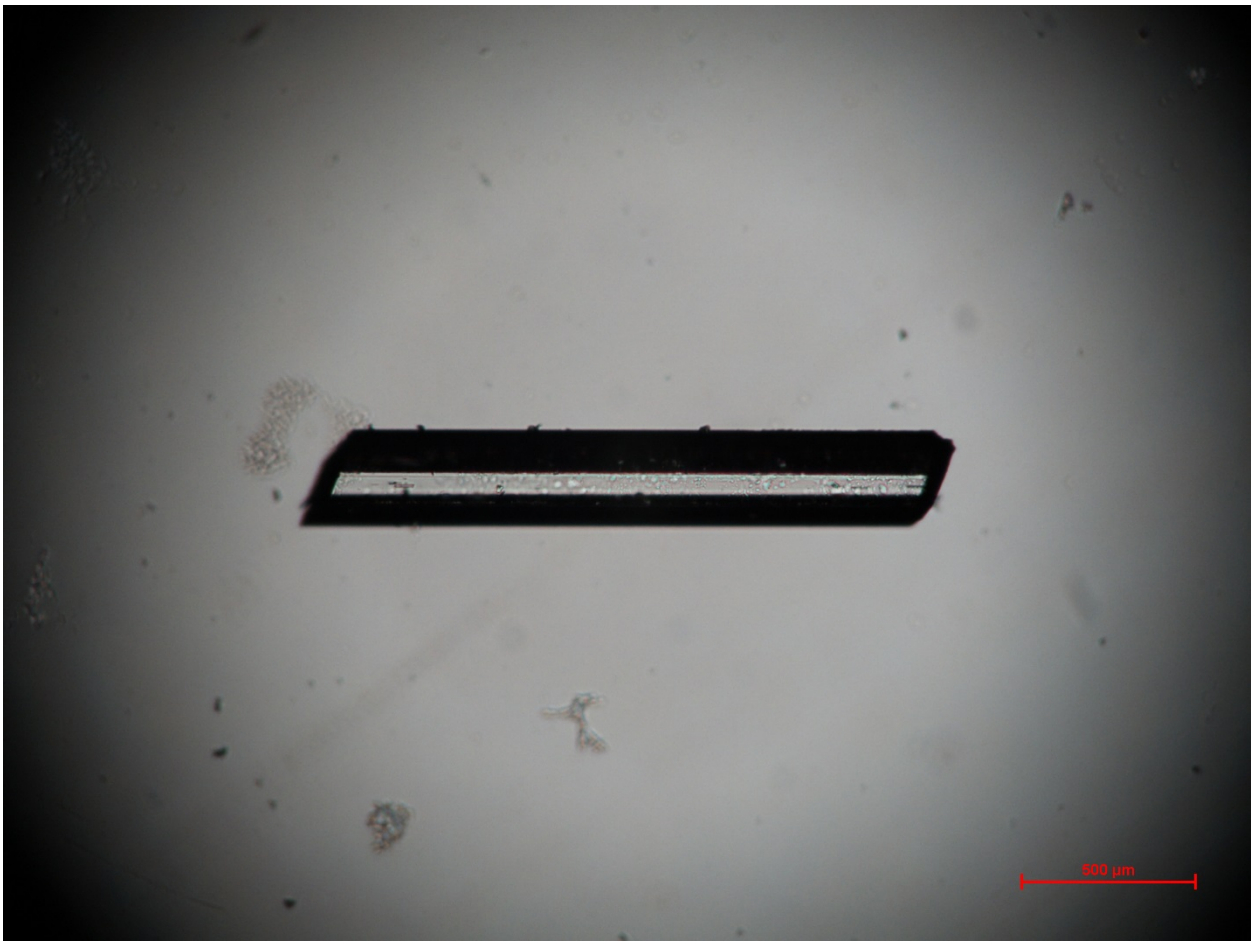


Figure 25. Photograph of **SA.PYC** crystal.

Sinapic Acid + 6-Propyl-2-Thiouracil + Acetonitrile (SA.PTU.2MeCN)

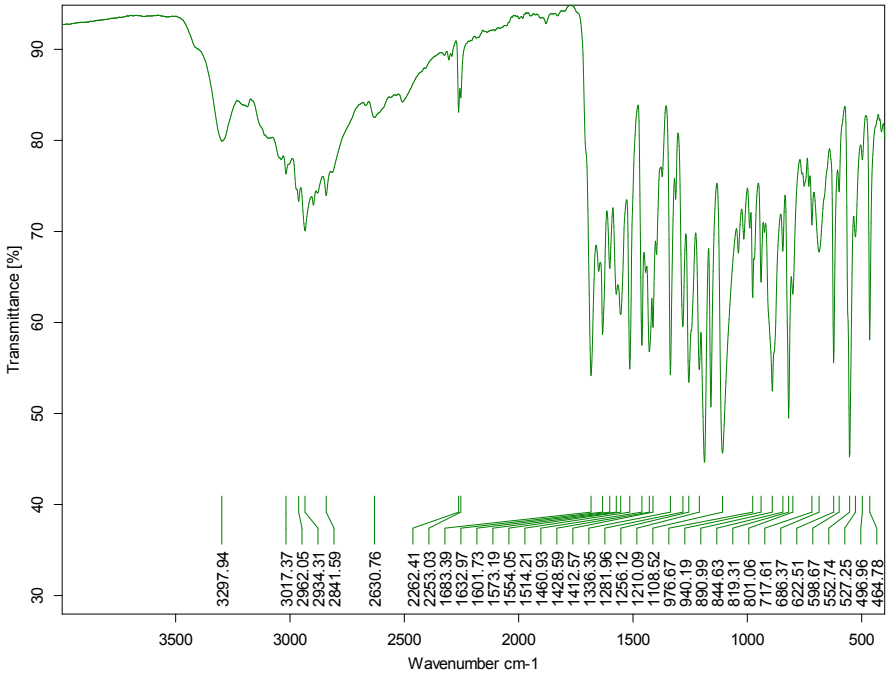


Figure 26. IR spectrum of **SA.PTU.2MeCN**.

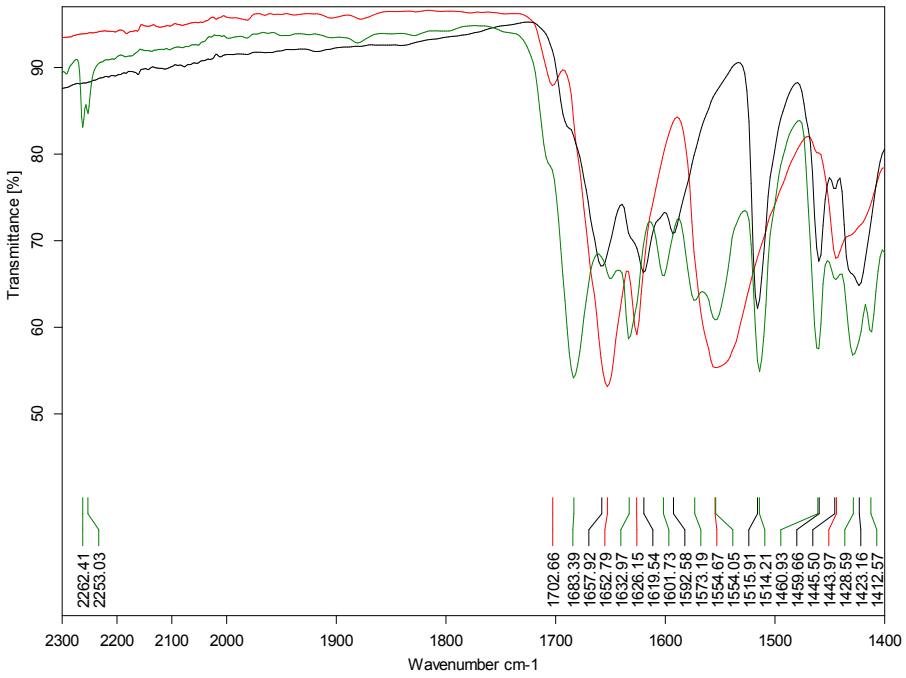


Figure 27. Expanded view of the IR spectrum of **SA.PTU.2MeCN** (green) compared with **SA** (black) and **PTU** (red).

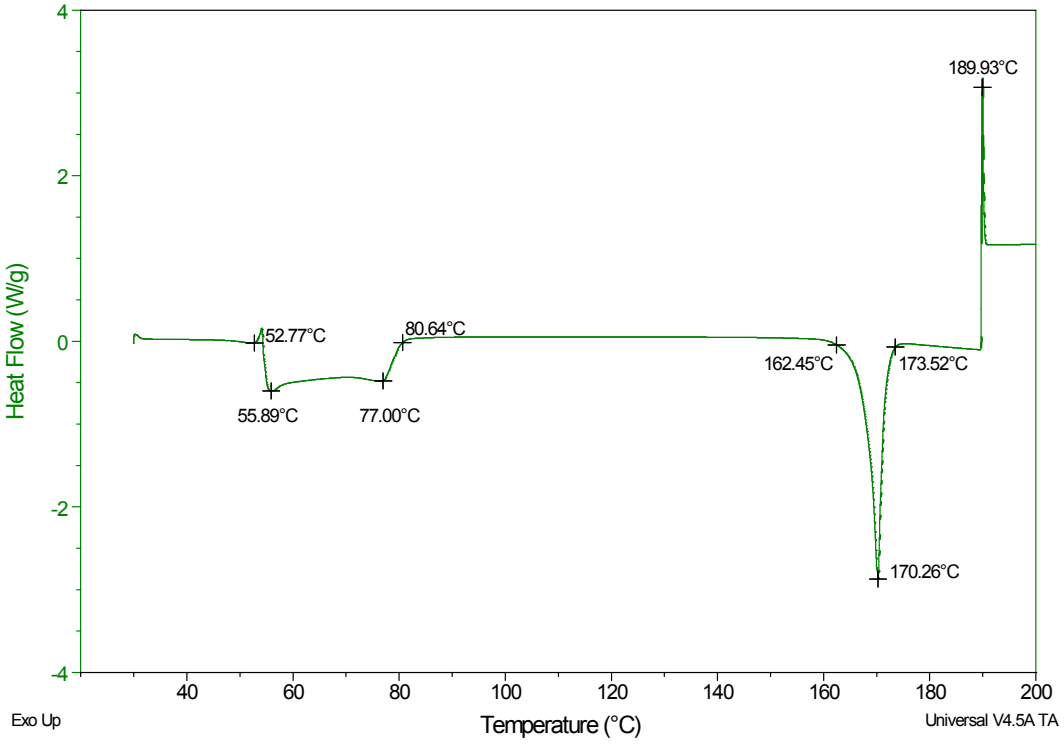


Figure 28. DSC spectrum of **SA.PTU.2MeCN**.

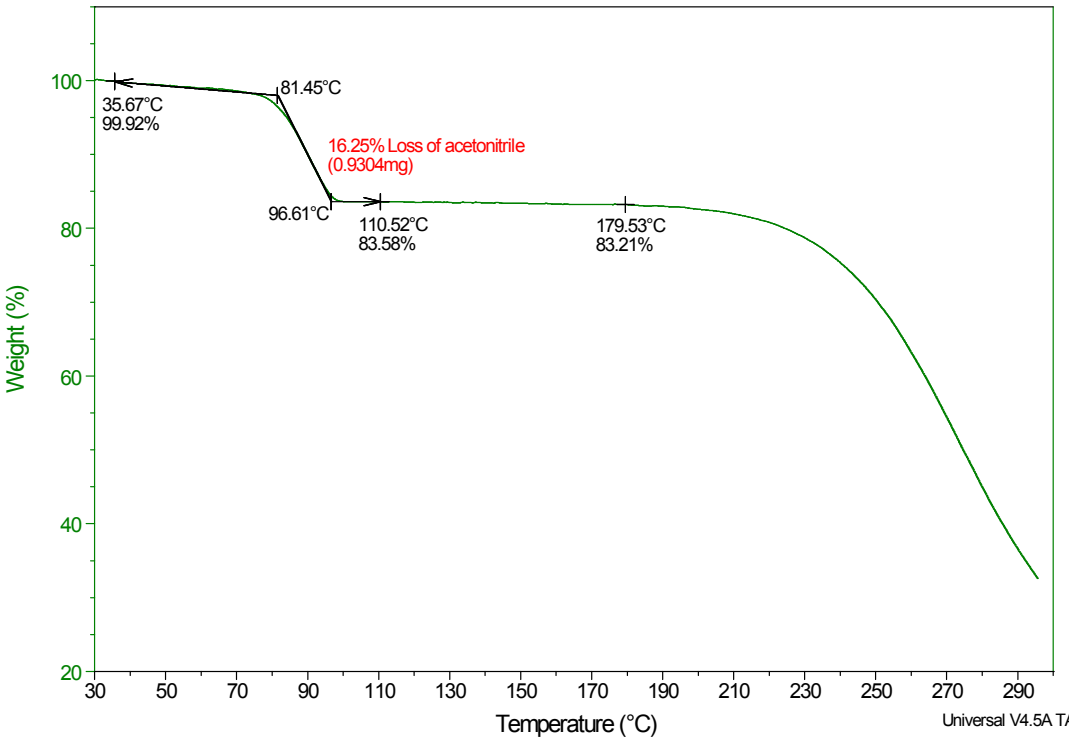


Figure 29. TGA spectrum of **SA.PTU.2MeCN**.

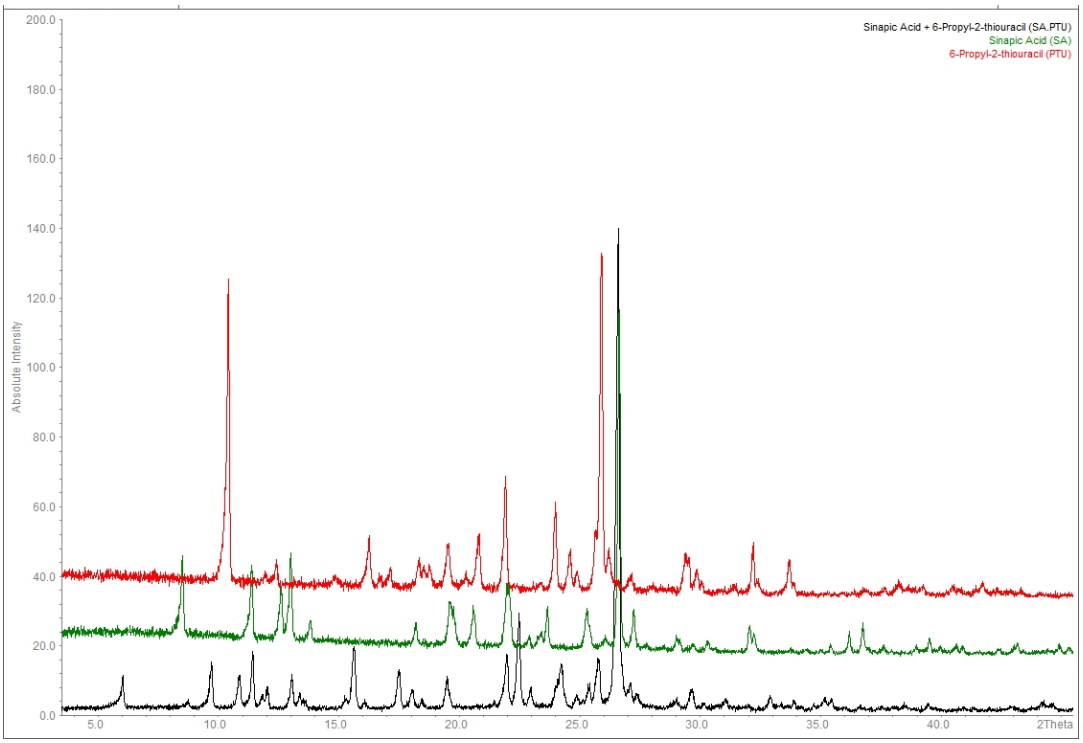


Figure 30. PXRD pattern of **SA.PTU.2MeCN**.

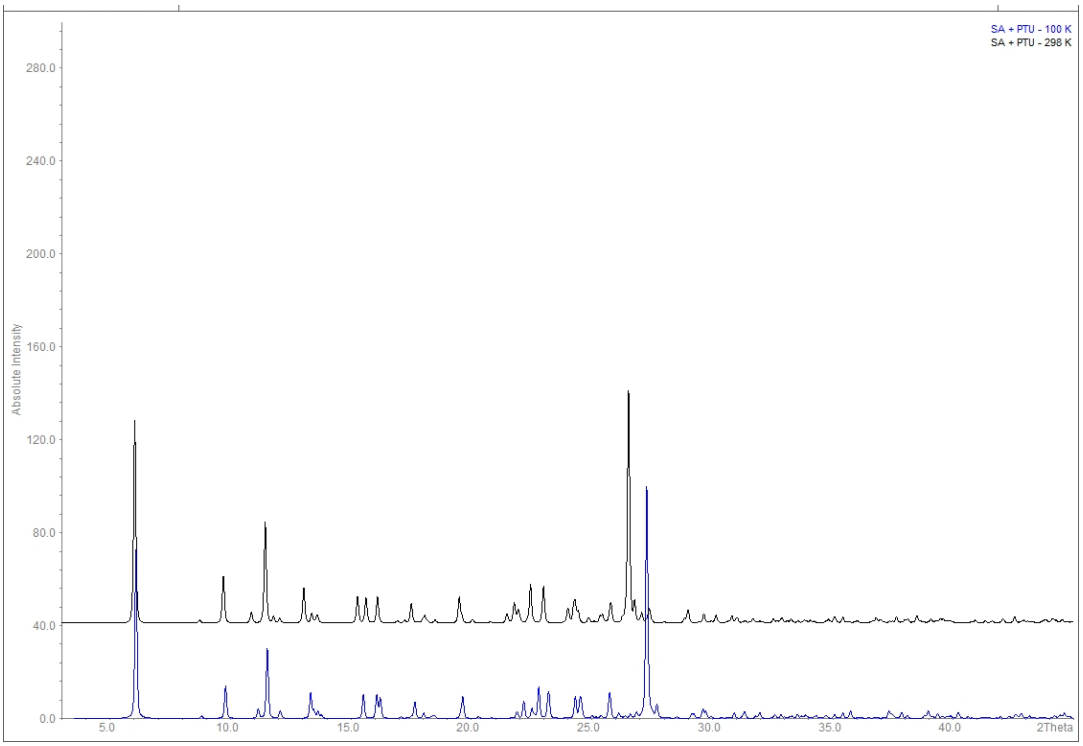


Figure 31. PXRD pattern overlay of **SA.PTU.2MeCN** single crystal data collected at 100 K (blue) and 298 K (black).

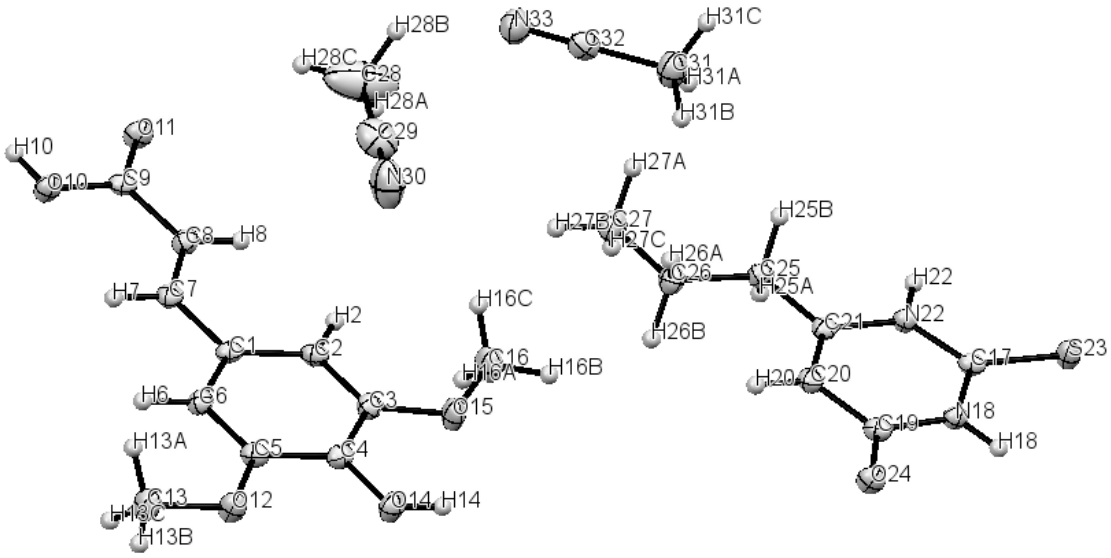


Figure 32. ORTEP diagram of the structure of **SA.PTU.2MeCN**.

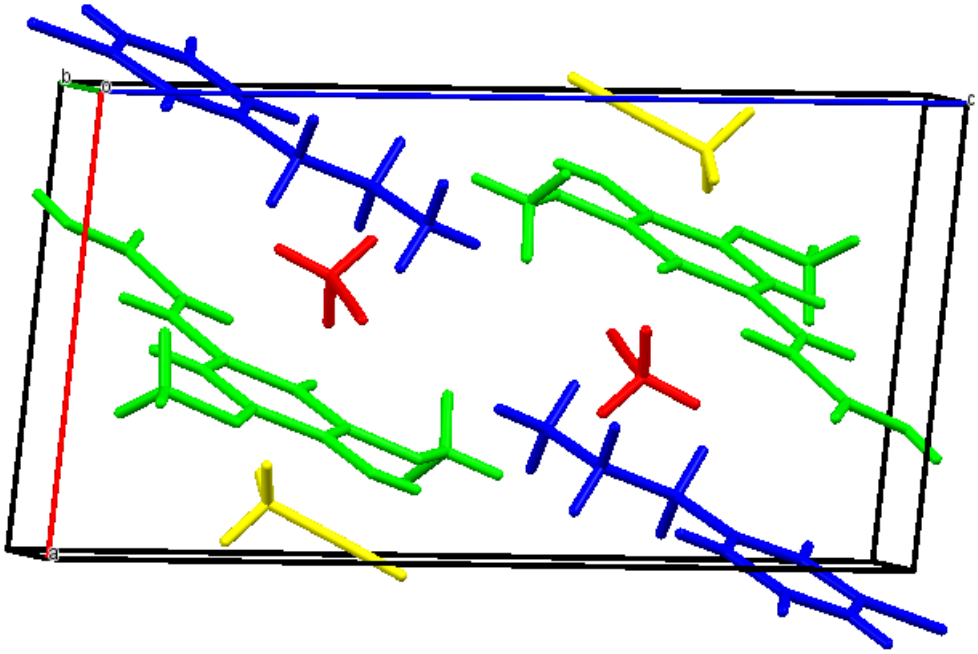


Figure 33. Crystal packing diagram of the structure of **SA.PTU.2MeCN**.

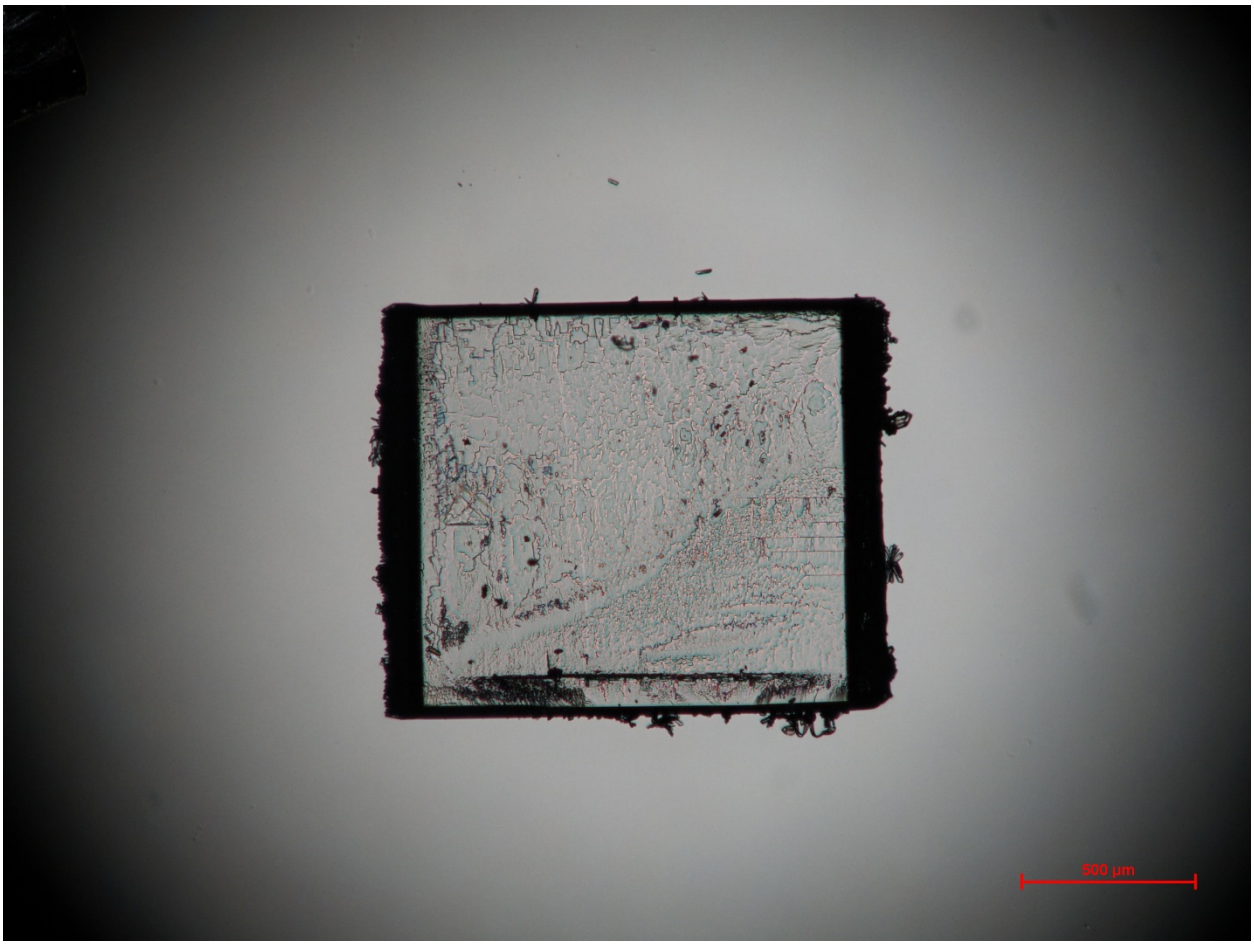


Figure 34. Photograph of **SA.PTU.2MeCN** crystal.

Desolvation experiments with SA.PTU.2MeCN

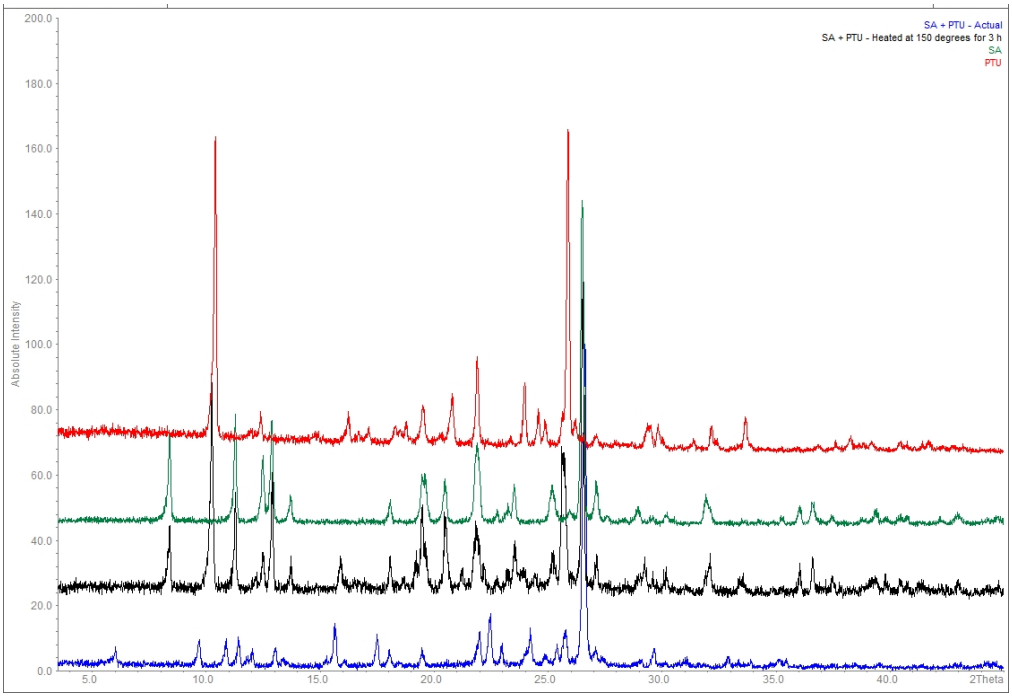


Figure 35. PXRD pattern of **SA.PTU.2MeCN** (blue) compared with desolvated sample (black), sinapic acid (green), and 6-propyl-2-thiouracil (red).

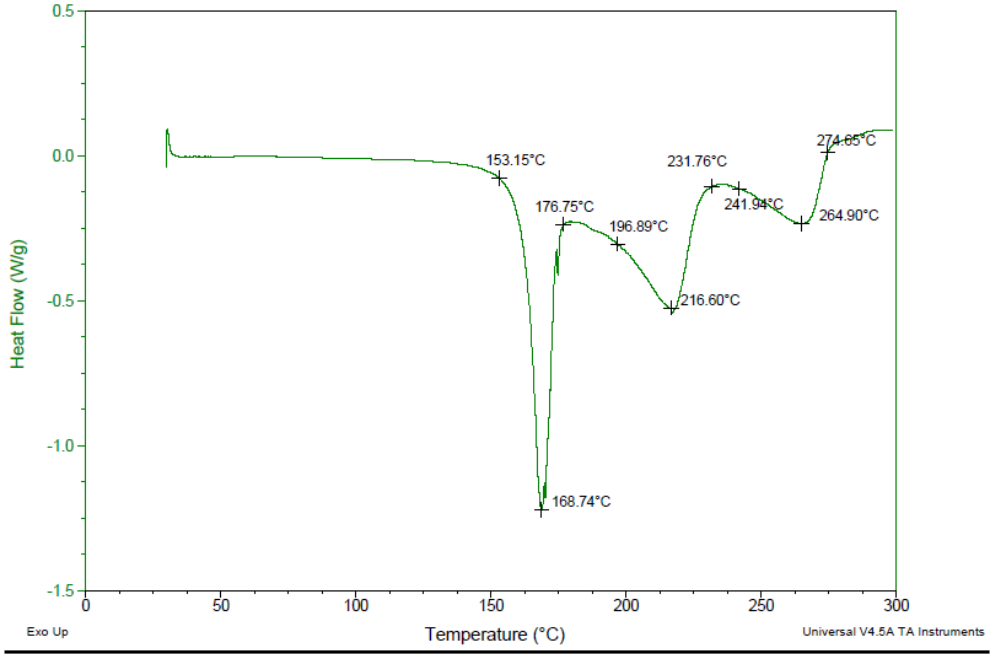


Figure 36. DSC spectrum of **SA.PTU.2MeCN** heated at 150 ºC for 3 h.

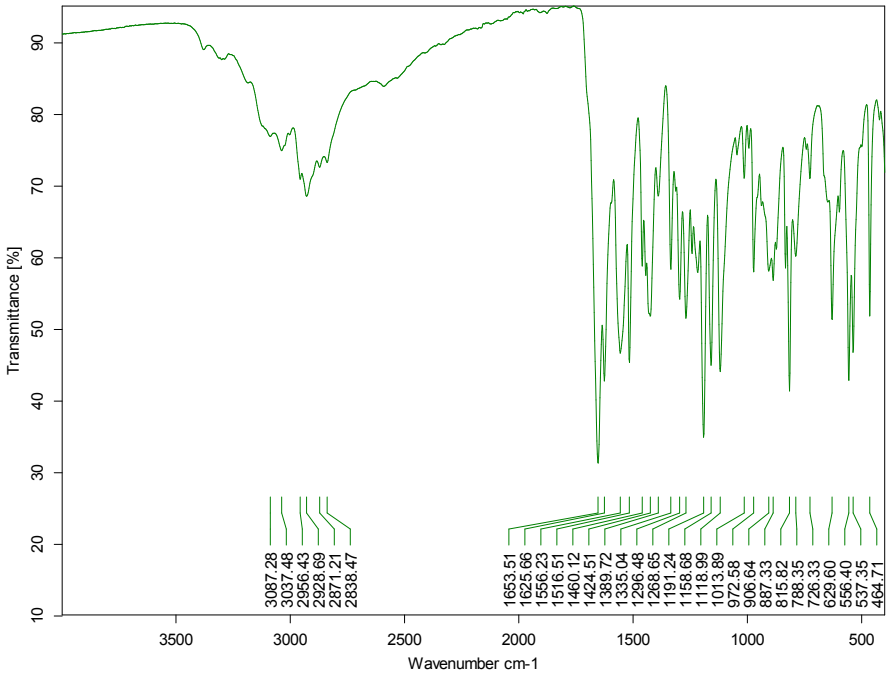


Figure 37. IR spectrum of a 1:1 dry grind mixture of **SA** with **PTU**.

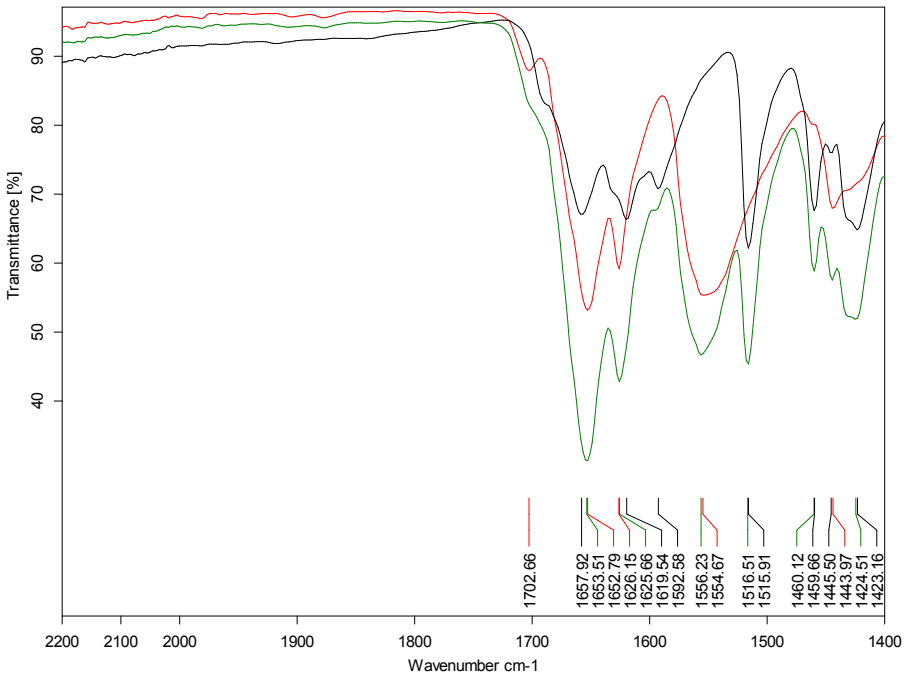


Figure 38. Expanded view of the IR spectrum of a 1:1 dry grind mixture of **SA** with **PTU** (green) compared with **SA** (black) and **PTU** (red).

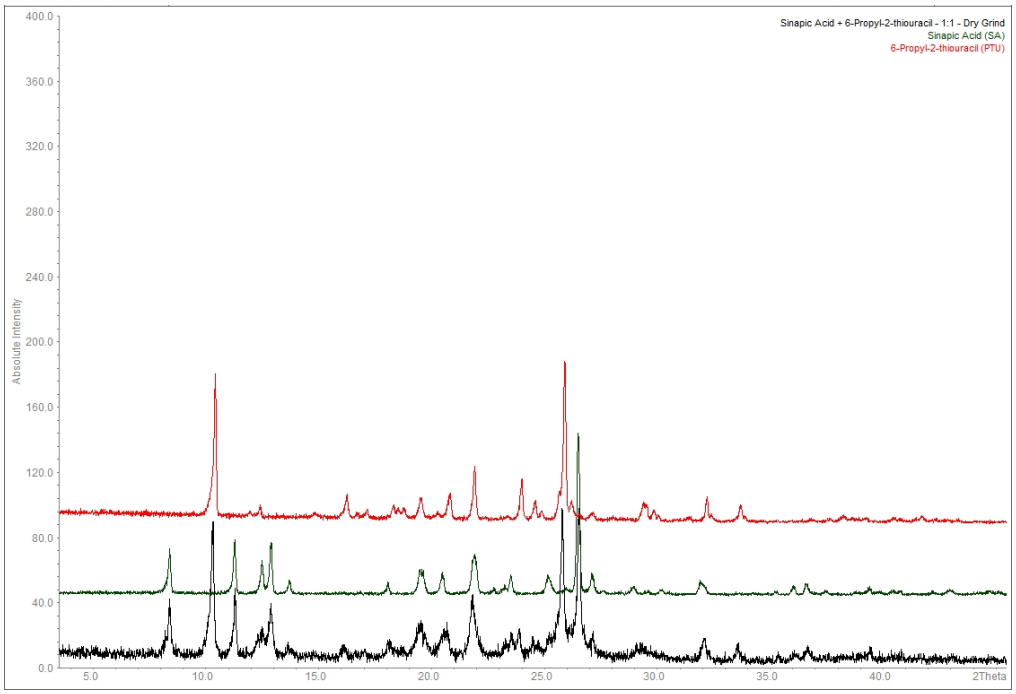


Figure 39. PXRD pattern of a 1:1 dry grind mixture of **SA** with **PTU** (black) compared with sinapic acid (green), and 6-propyl-2-thiouracil (red).

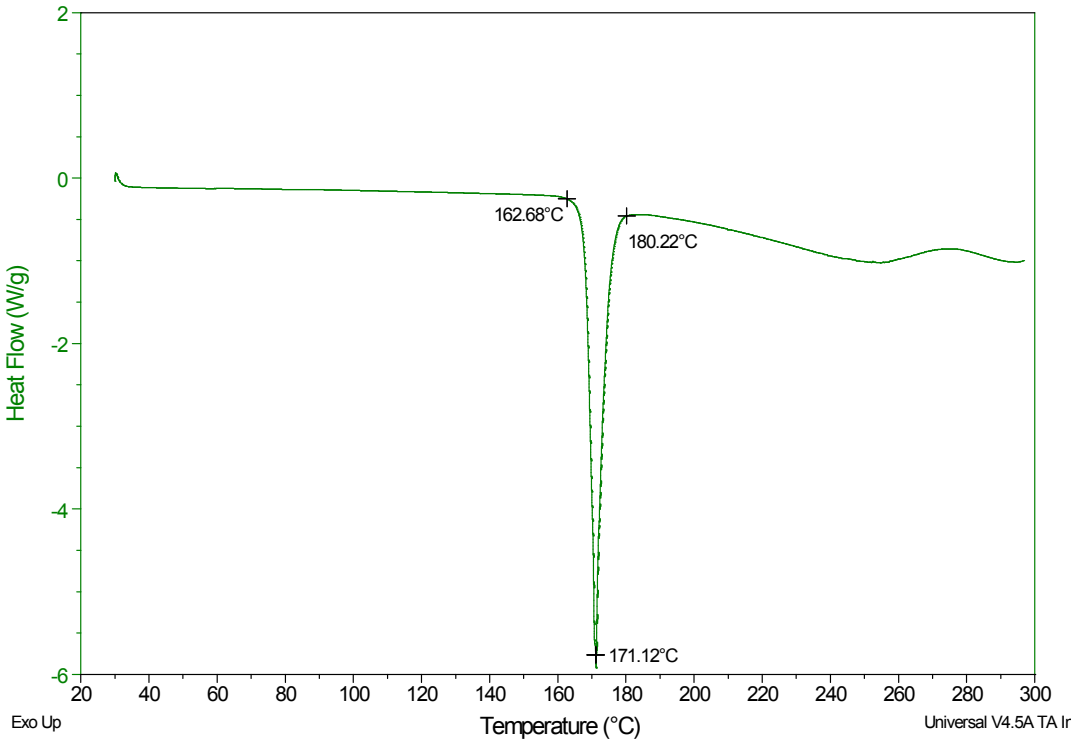


Figure 40. DSC spectrum of a 1:1 dry grind mixture of **SA** with **PTU**.

Table 1. Key hydrogen-bond parameters for the crystal structures.

Compound	Interaction	*d*(D-H)/Å	*d*(DH···A)/Å	*d*(D···A)/Å	*Angle*(D-H···A)/º
SA	O10-H10···O11	0.97(2)	1.68(2)	2.6410(15)	177.(2)
	O14-H14···O11	0.88(3)	2.07(3)	2.8594(17)	149.(2)
	O14-H14···O15	0.88(3)	2.16(2)	2.6561(17)	115.1(19)
SA.NIA	O10-H10···O11	0.82	1.81	2.626(3)	171.7
	O14-H14···N17	0.82	1.95	2.681(3)	148.6
	O14-H14···O12	0.82	2.28	2.714(3)	113.3
	N25-H25A···O15	0.856(10)	2.317(19)	3.059(3)	145.(3)
	N25-H25A···O14	0.856(10)	2.473(18)	3.228(3)	147.(2)
	N25-H25B···O24	0.848(10)	2.036(11)	2.879(3)	172.(3)
SA.PYC	O10-H10···O27	0.84	1.75	2.590(3)	176.4
	O14-H14···N41	0.84	1.89	2.635(3)	146.8
	O26-H26···O11	0.84	1.80	2.644(3)	178.9
	O30-H30···N33	0.84	1.99	2.771(3)	154.4
SA.PTU.2MeCN	N18-H18···O11	0.881(5)	1.935(7)	2.8013(18)	167.(2)
	N22-H22···S23	0.878(5)	2.452(6)	3.3199(14)	169.6(18)
	O10-H10···O24	0.842(5)	1.797(6)	2.6363(16)	174.(2)
	O14-H14···N33	0.839(5)	2.012(10)	2.820(2)	161.(2)

Stability of Sinapic Acid (SA)

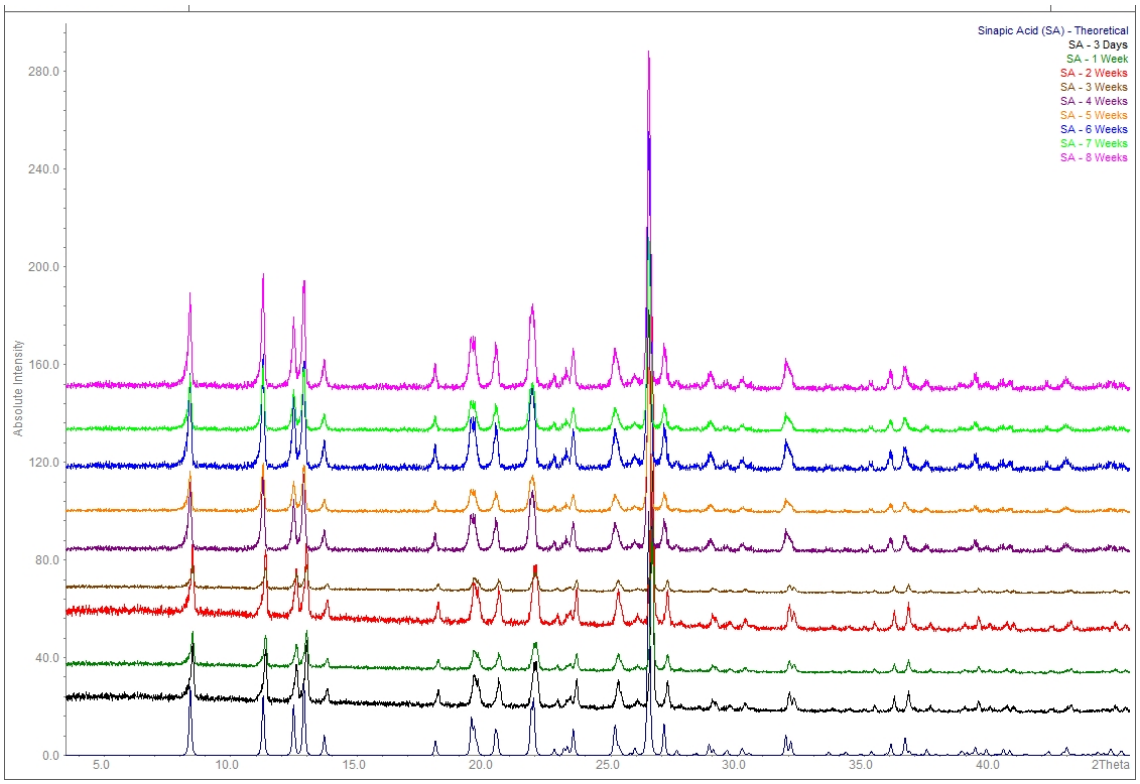


Figure 41. Stability of sinapic acid (**SA**) based on PXRD data.

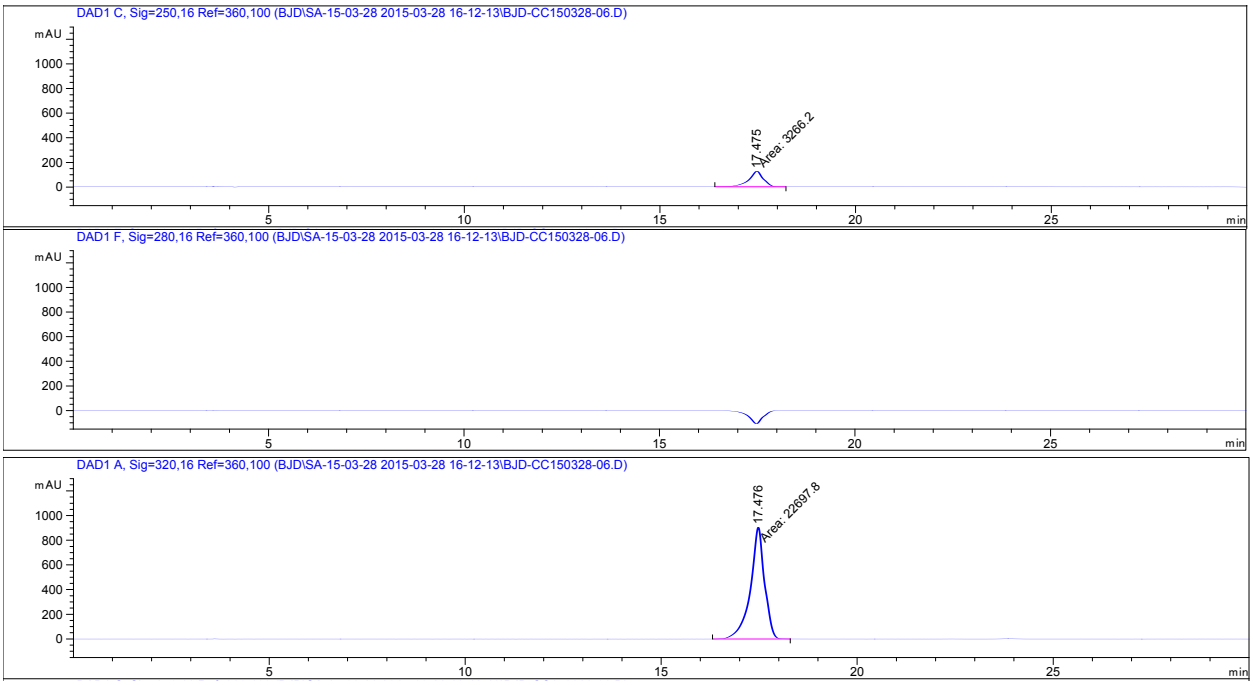


Figure 42. HPLC analysis of sinapic acid measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (**SA**).

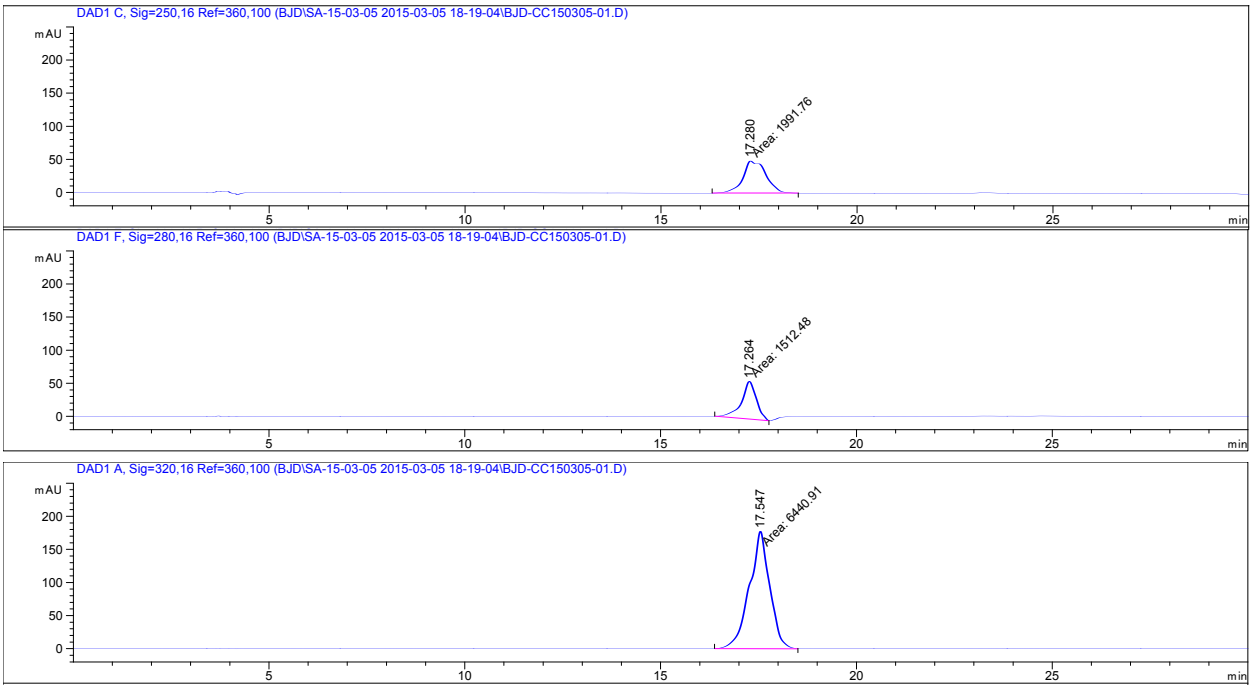


Figure 43. HPLC analysis of sinapic acid (**SA**) after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).

Stability of Sinapic Acid + Isonicotinic Acid (SA.INC)

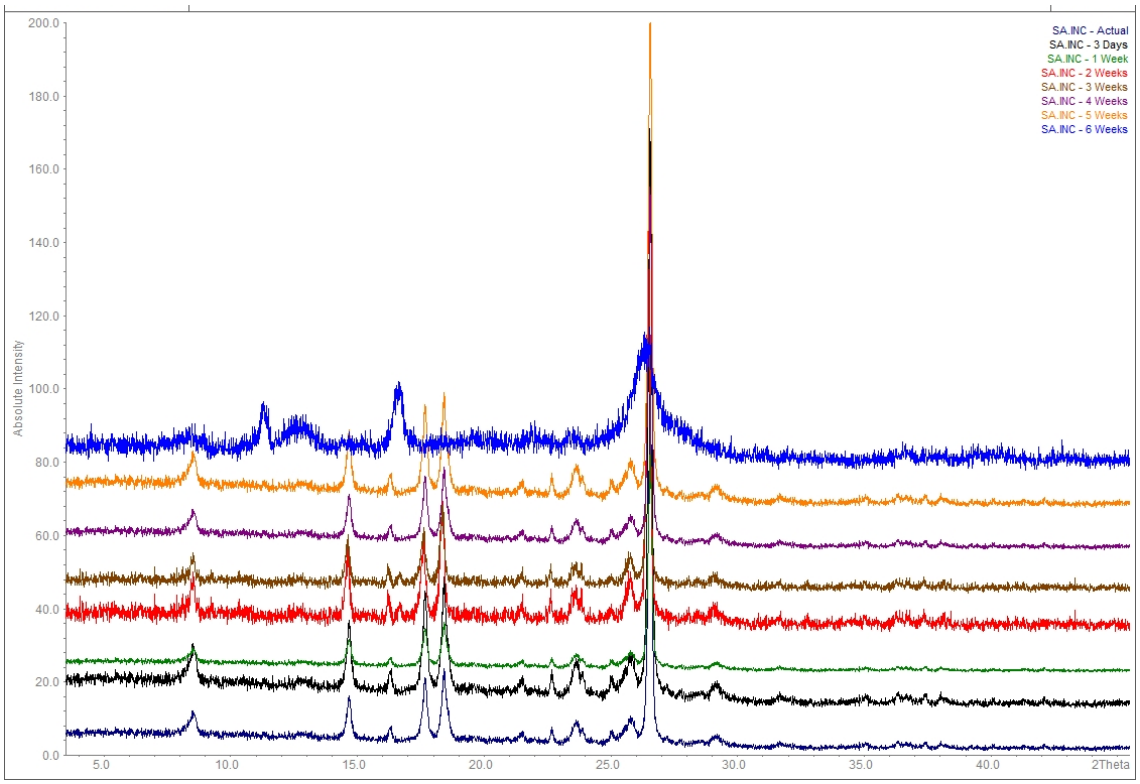


Figure 44. Stability of **SA.INC** based on PXRD data.

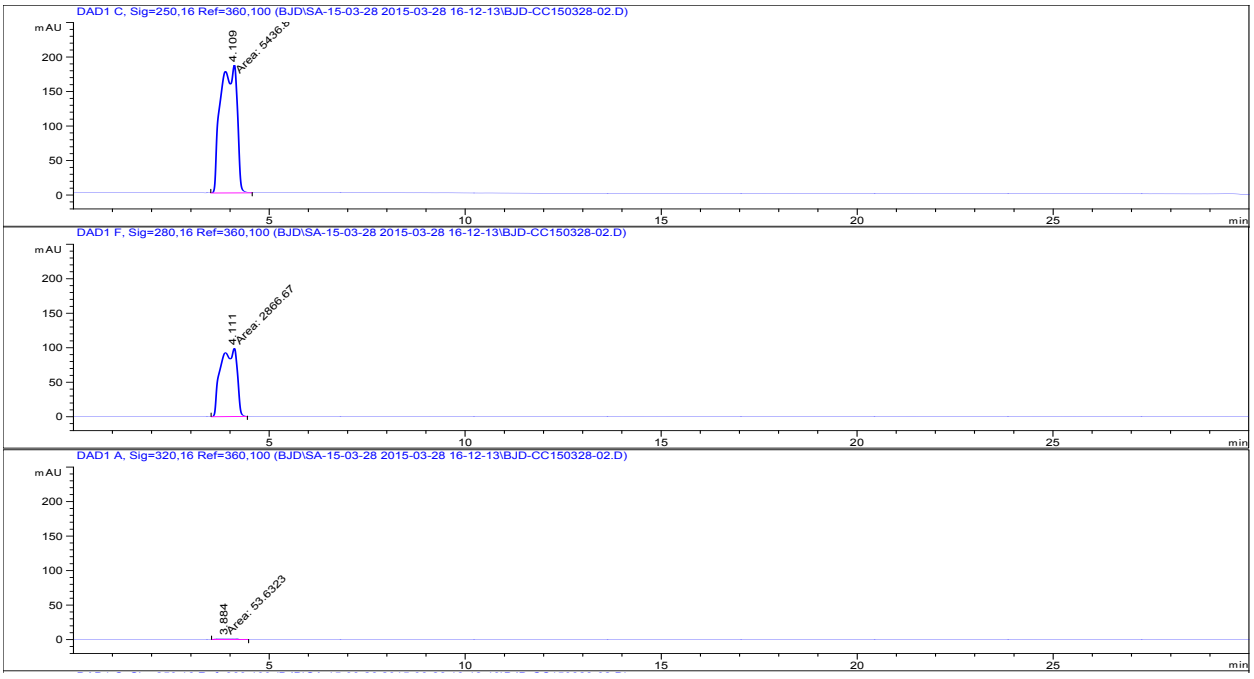


Figure 45. HPLC analysis of isonicotinic acid measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (**INC**).

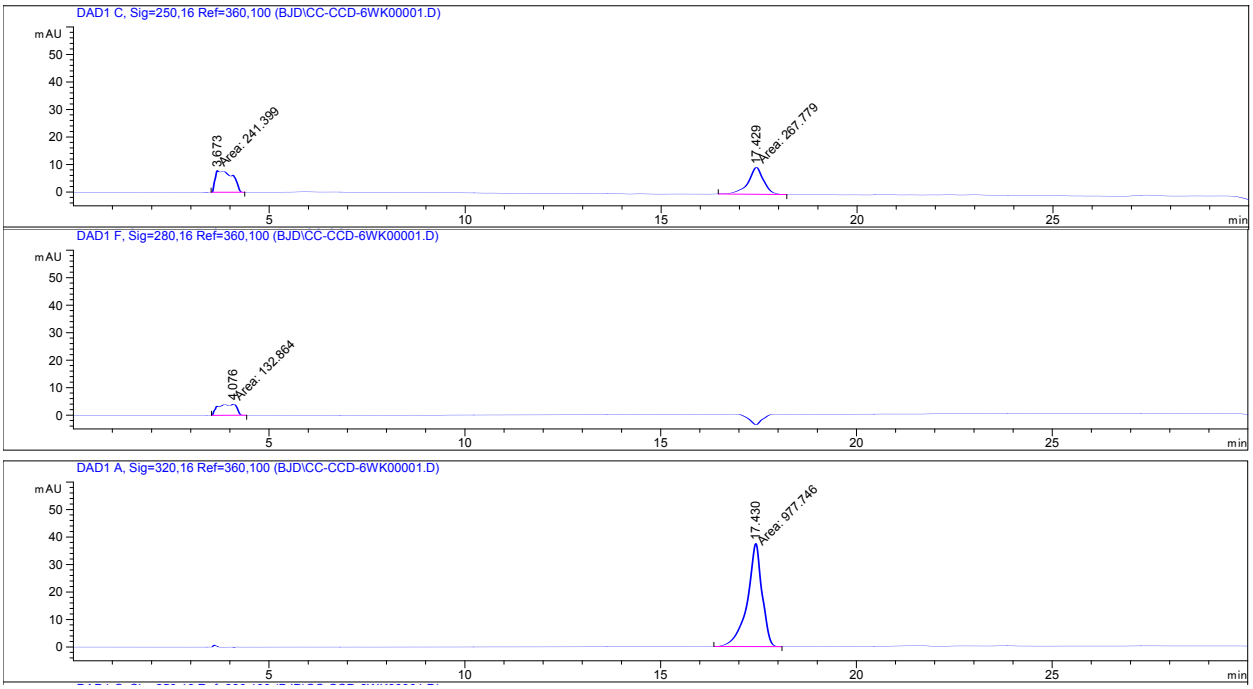


Figure 46. HPLC analysis of **SA.INC** after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).

Stability of Sinapic Acid + Nicotinamide (SA.NIA)

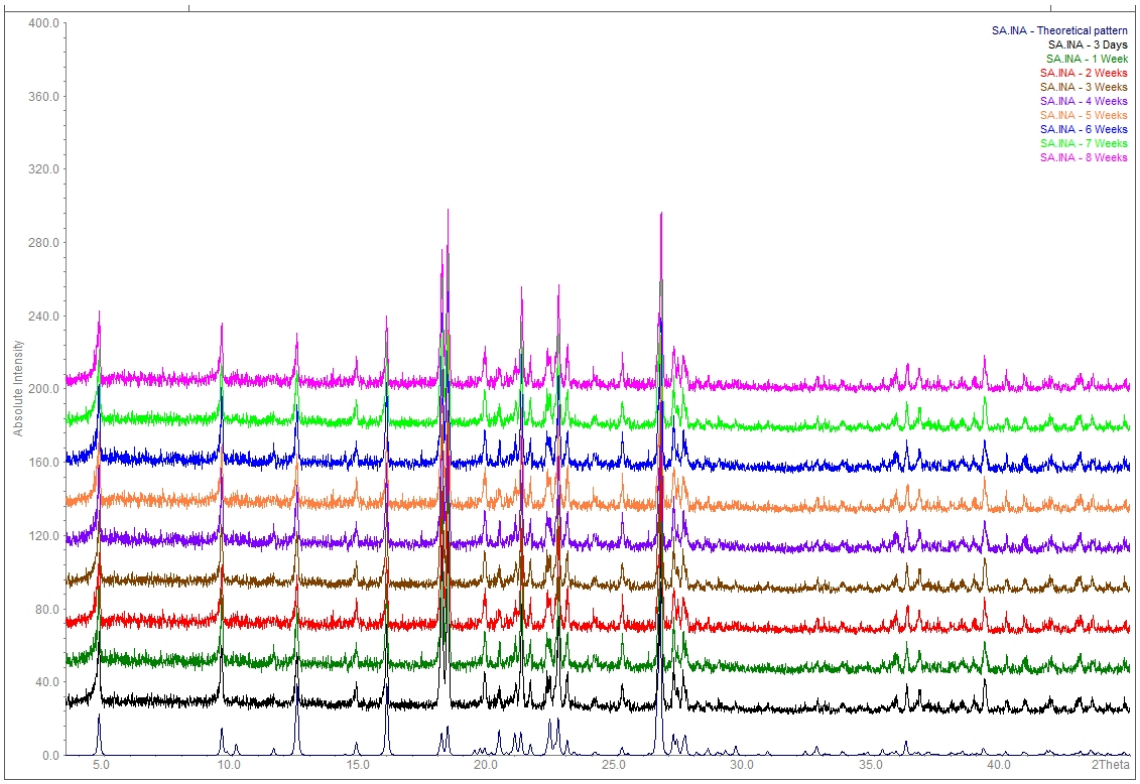


Figure 47. Stability of **SA.NIA** based on PXRD data.

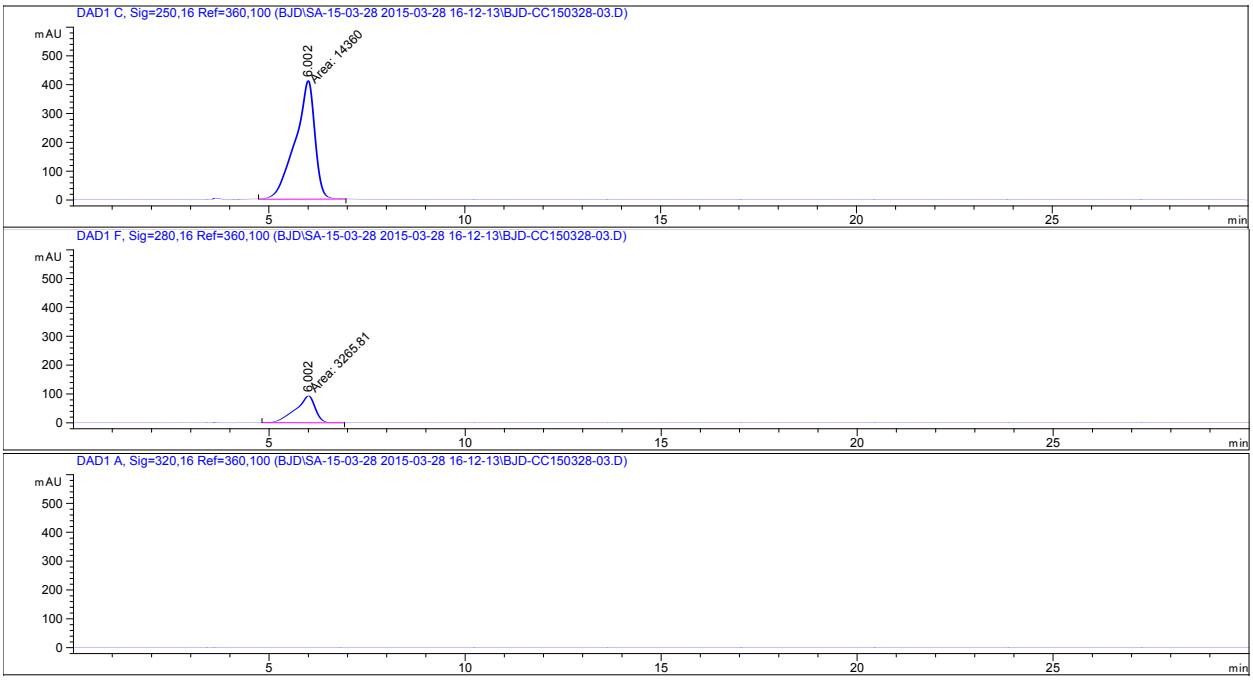


Figure 48. HPLC analysis of nicotinamide measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (**NIA**).

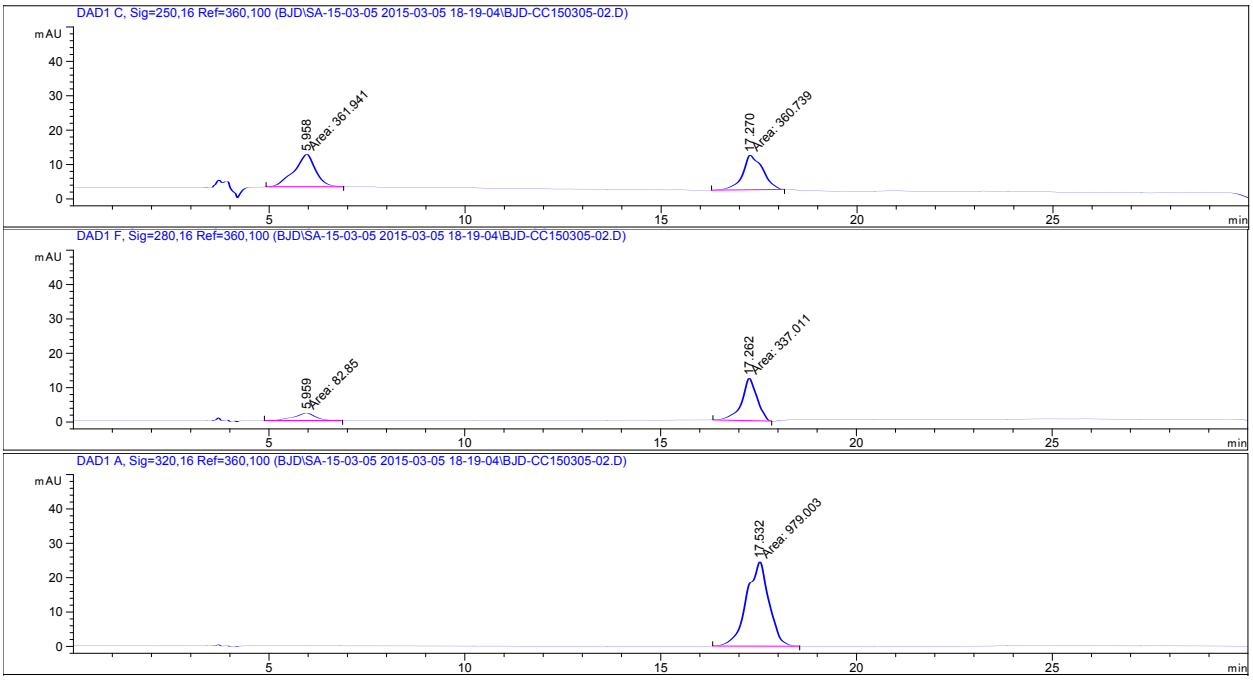


Figure 49. HPLC analysis of **SA.NIA** after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).

Stability of Sinapic Acid + 4-Pyridinecarbonitrile (SA.PYC)

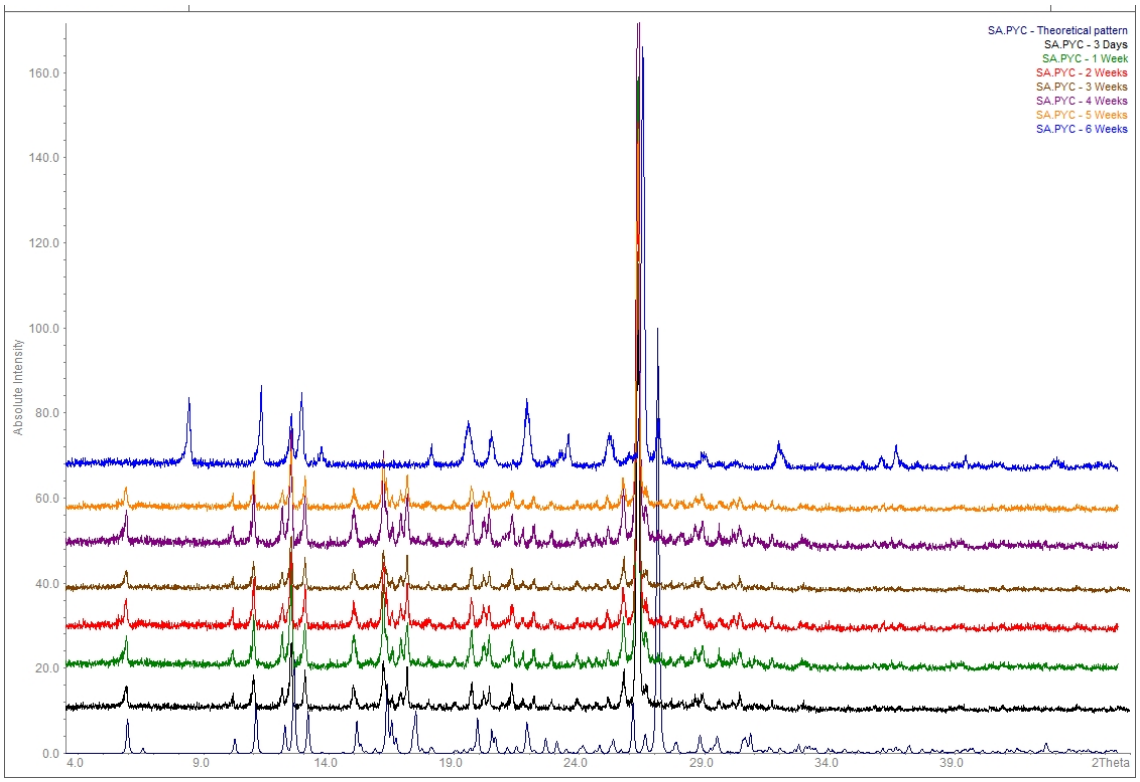


Figure 50. Stability of **SA.PYC** based on PXRD data.

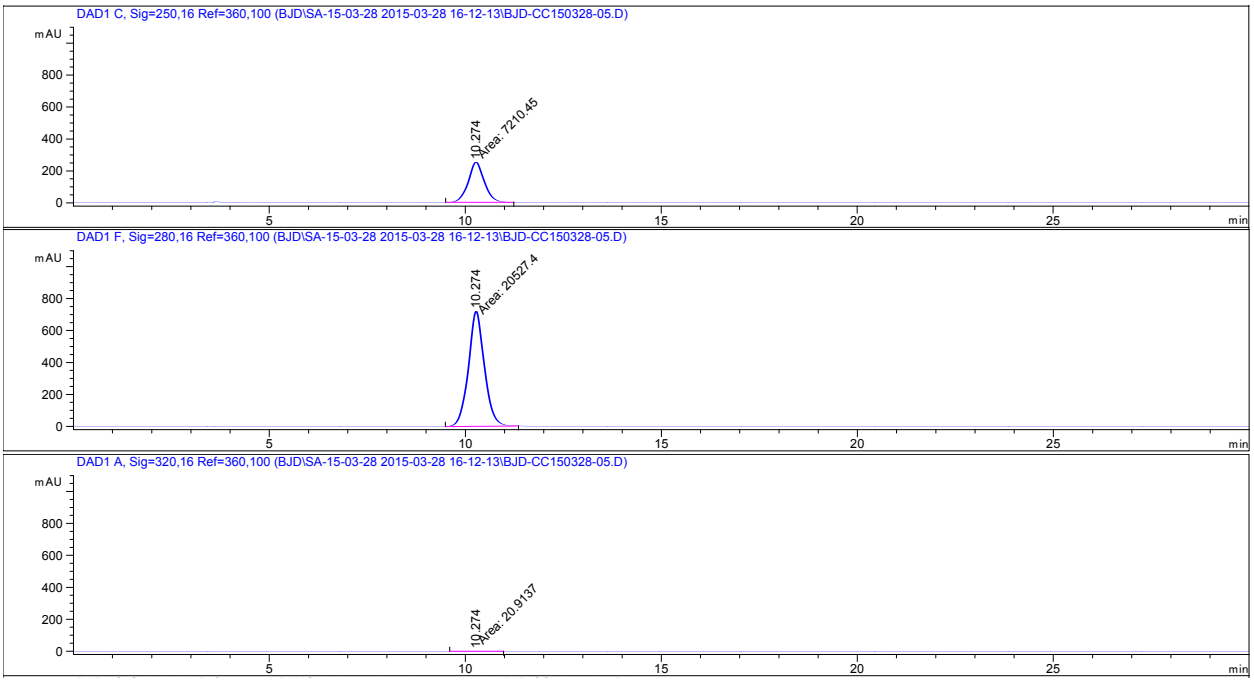


Figure 51. HPLC analysis of 4-pyridinecarbonitrile measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (**PYC**).

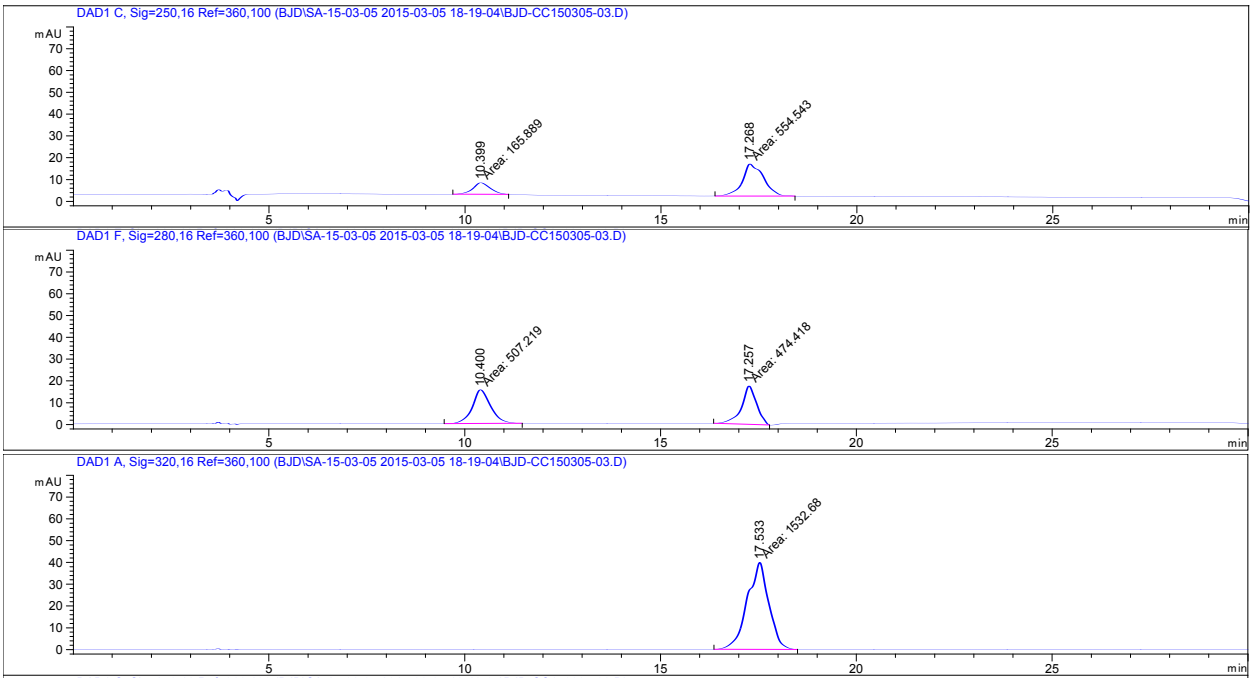


Figure 52. HPLC analysis of **SA.PYC** after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).

Stability of Sinapic Acid + 6-Propyl-2-Thiouracil + Acetonitile (SA.PTU.2MeCN)

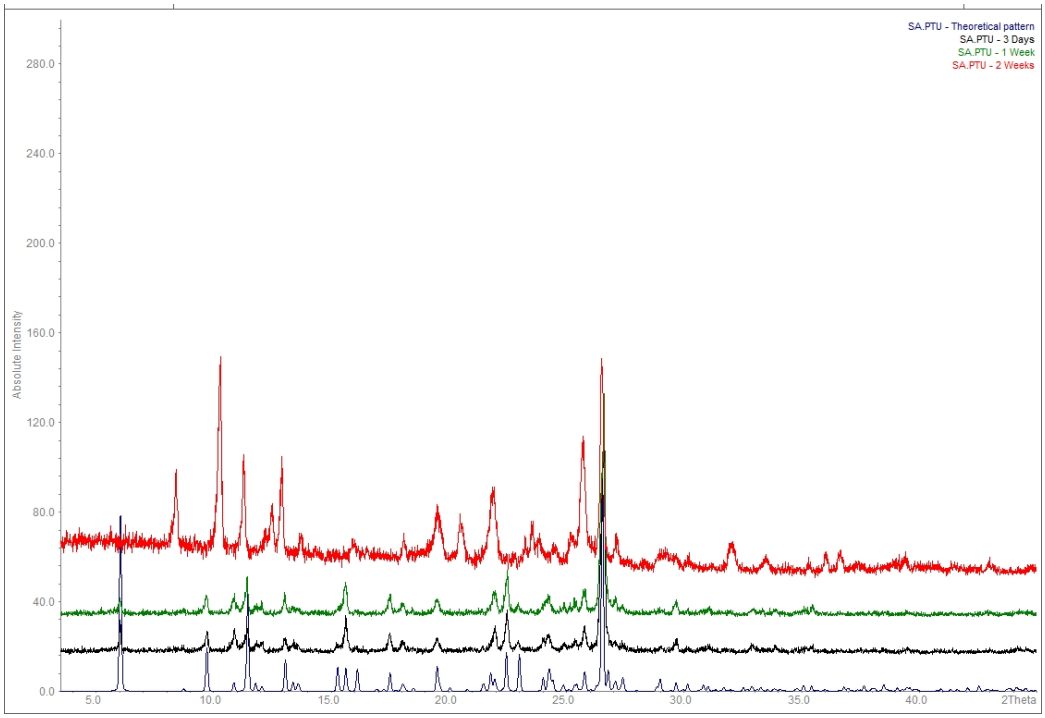


Figure 53. Stability of **SA.PTU.2MeCN** based on PXRD data.

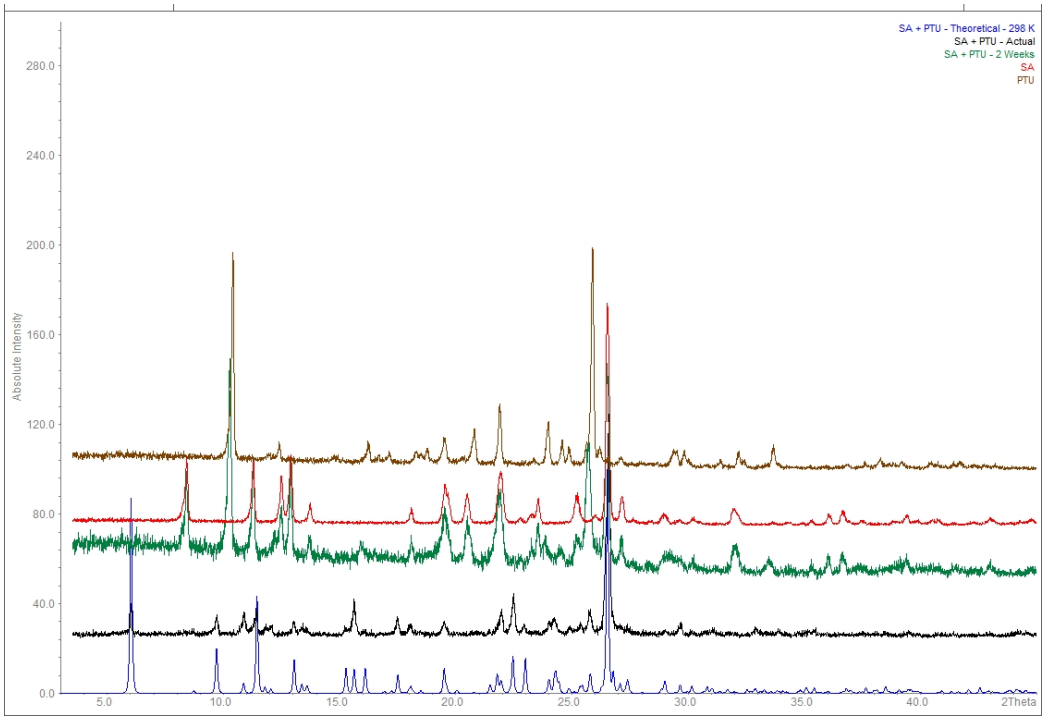


Figure 54. Comparison of **SA.PTU.2MeCN** PXRD theoretical pattern (blue) with actual (black), 2 week stability (green), sinapic acid (red), and 6-propyl-2-thiouracil (brown) spectra.

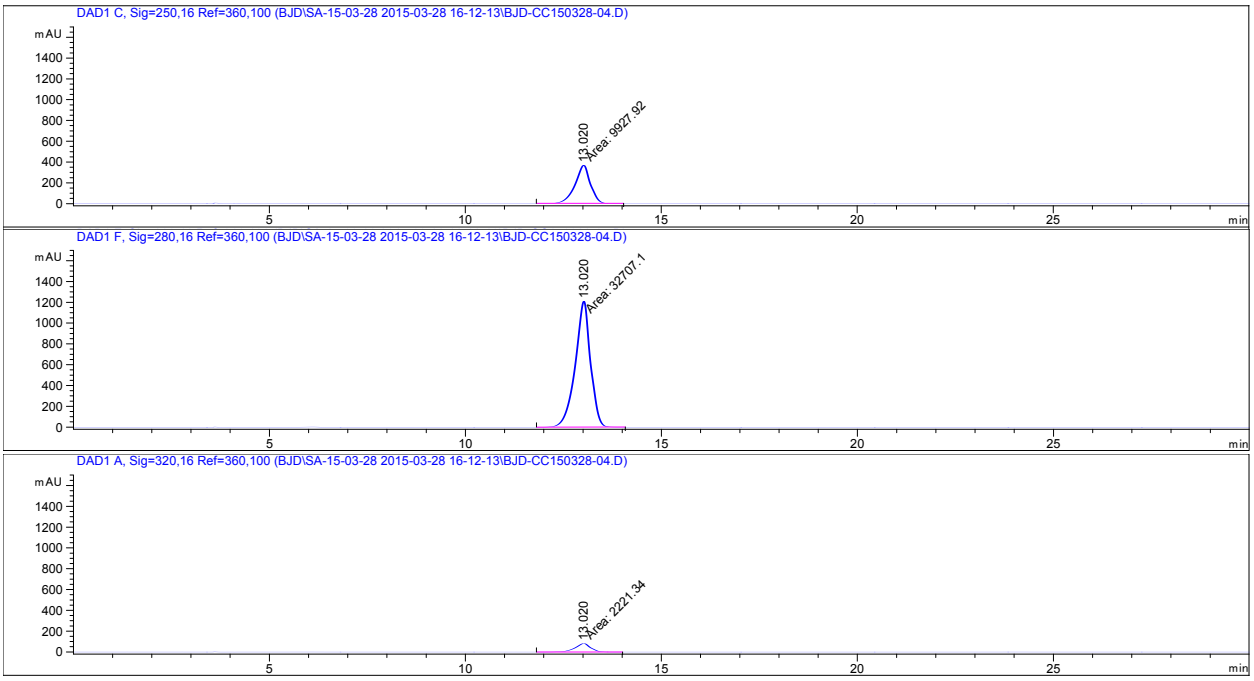


Figure 55. HPLC analysis of 6-propyl-2-thiouracil measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom) (**PTU**).

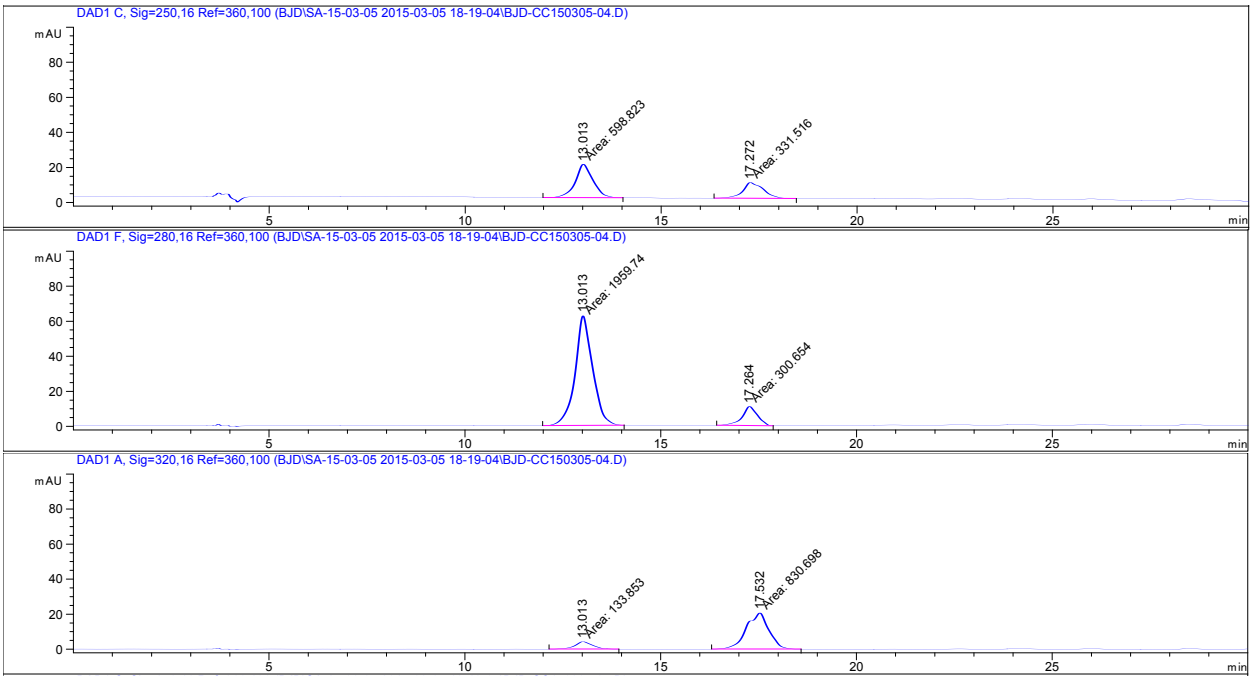


Figure 56. HPLC analysis of **SA.PTU.2MeCN** after 6 weeks at 40 °C and 75% RH, measured at 250 nm (top), 280 nm (middle) and 320 nm (bottom).