

The selectivity behaviour of 9,9'-bifluorenyl-9,9'-diol as a host compound for highly efficient separations of mixed pyridines

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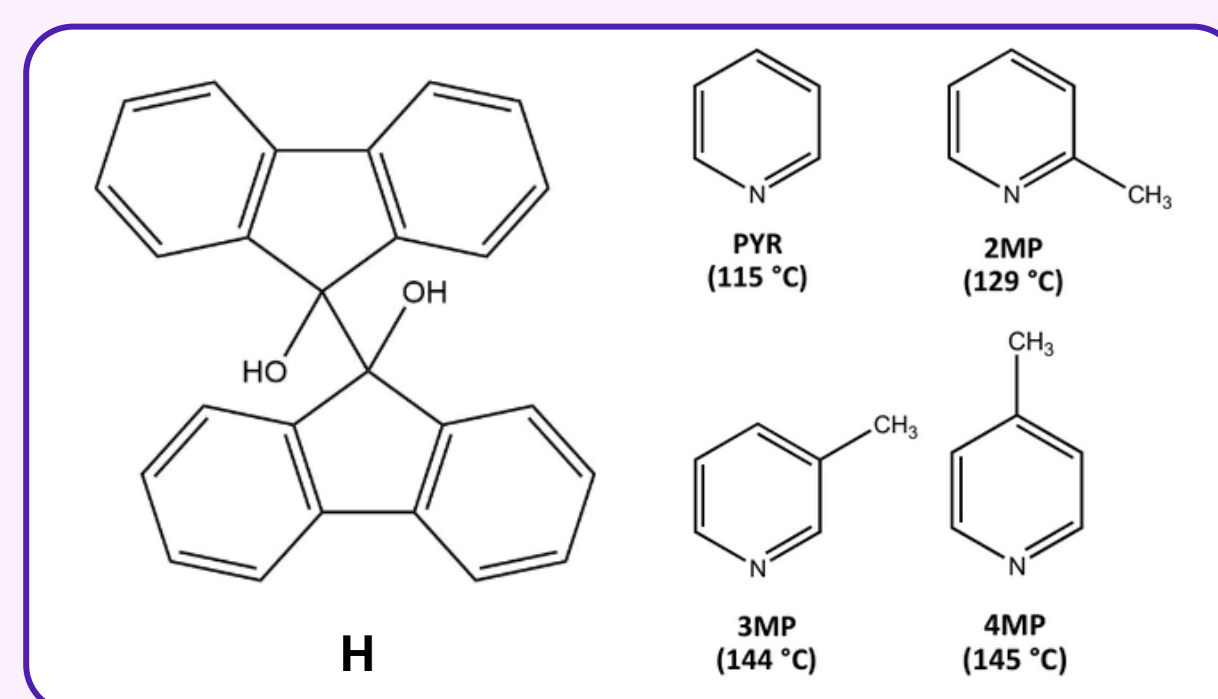
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INTRODUCTION

Isomer separation remains a significant challenge in the chemical industry due to their similar physiochemical properties, such as boiling points differing by as little as one degree. Conventional techniques such as fractional distillation and adsorption are resource-intensive, often yielding mixtures that require further purification.¹ Host–guest chemistry, a branch of supramolecular chemistry,^{2,3} presents an innovative alternative, overcoming many of the limitations associated with conventional methodologies. This approach leverages the structural attributes of both host and guest, whereby the host participates in noncovalent interactions (such as hydrogen bonding, $\pi\cdots\pi$ stacking and C–H $\cdots\pi$ close contacts) with specific guest molecules to obtain stable inclusion complexes. This non-destructive and recyclable separation strategy not only enhances efficiency but also aligns with green chemistry principles by minimizing solvent waste and energy consumption.

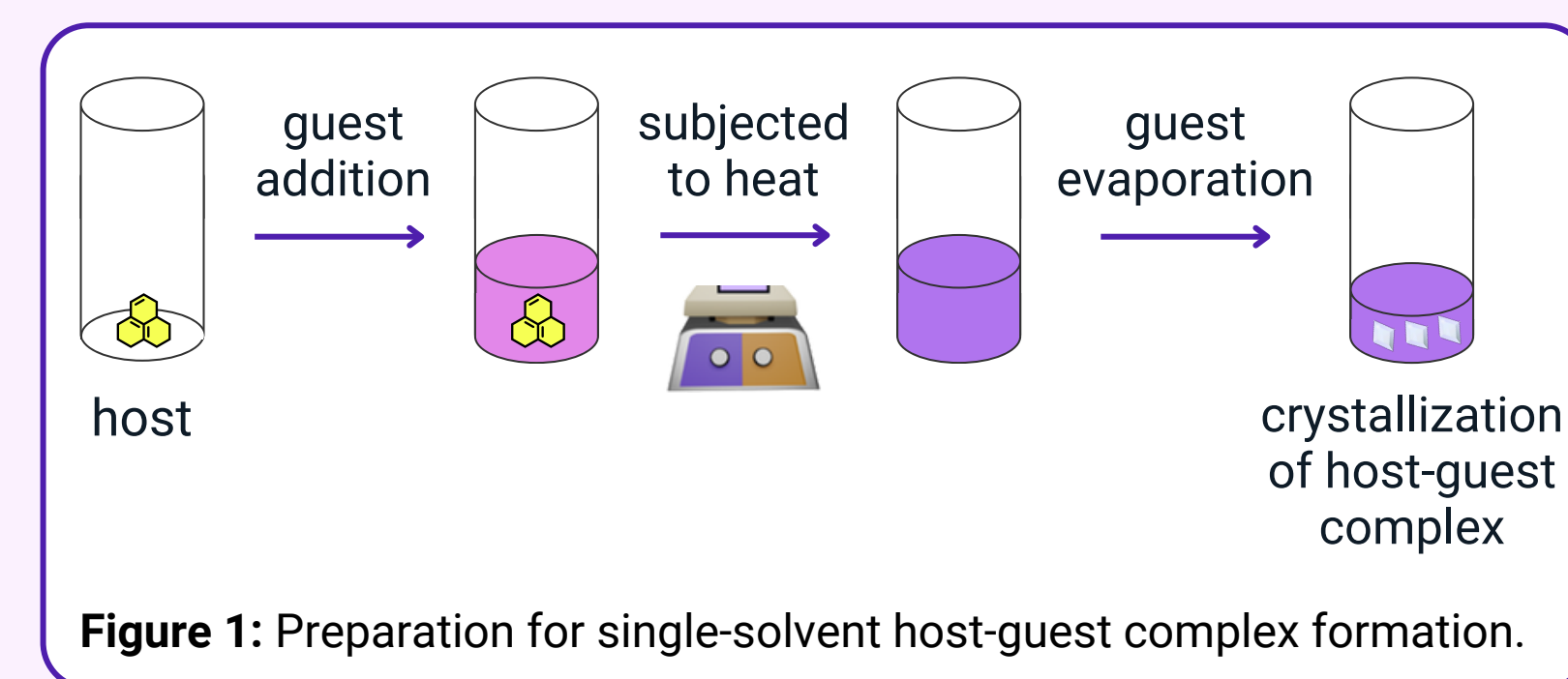
In the current investigation, the potential of 9,9'-bifluorenyl-9,9'-diol (**H**) to behave as a selective host compound for the separation of pyridine (PYR) and its methylated derivatives, 2-, 3-, and 4-methylpyridine (2MP, 3MP, and 4MP) through supramolecular host-guest strategies was assessed. All of the inclusion complexes were examined using single crystal X-ray diffraction (SCXRD) experiments, while Hirshfeld surfaces and thermoanalytical analyses were also considered.



METHODOLOGY

Synthesis of 9,9'-bifluorenyl-9,9'-diol (H): **H** was prepared through pinacol coupling of fluorenone with magnesium and iodine under reflux, affording a satisfactory yield of 93%.⁴

Single-solvent experiments: **H** was dissolved in each liquid pyridyl guest solvent with gentle heating, then left open under ambient conditions to promote crystal growth (Figure 1). Crystals were collected via vacuum filtration, washed with petroleum ether, and dissolved in CDCl₃ for ¹H-NMR spectroscopic analysis. Thus, host-to-guest (H:G) ratios of successfully formed complexes were determined.



Equimolar guest crystallization experiments: **H** was dissolved in equimolar binary, ternary and quaternary guest mixtures. These glass vials were sealed and stored at 4 °C for crystallization. Overall H:G and guest-to-guest (G:G) ratios were determined using ¹H-NMR spectroscopy and gas chromatography (GC), respectively. These experiments were performed in duplicate, with percentage estimated deviations (% e.s.d.s) reported.

Binary guest competition experiments with varied guest concentrations: **H** was dissolved in binary pyridyl mixtures of Guest A and Guest B prepared at defined molar ratios of 20:80, 40:60, 60:40 and 80:20. The guests were quantified by GC analyses and selectivity profiles were constructed following the selectivity model of Pivovar *et al.*⁵

RESULTS & DISCUSSION

- Crystallization of **H** from the four pyridyl guest solvents afforded inclusion complexes with each of PYR, 3MP and 4MP (H:G ratios were 1:1 for all).
- H/2MP experiment did not crystallize and a gel resulted after repeated attempts.

- According to Table 1, **H** demonstrated an overwhelming affinity for 4MP in binary solvent experiments, followed by 3MP and PYR.

- 3MP was mostly favoured from ternary experiments.

- 4MP was favoured in presence of 3MP but only in absence of PYR. Thus, when PYR was present, 3MP was preferred.

- Trend was also observed in quaternary guest solutions, since PYR was present, 3MP was preferentially incorporated over 4MP (86.9%) (remarkably, no 4MP was measured in the complex).

Table 1: Results from **H** crystallization experiments in equimolar mixed pyridines.^a

PYR	2MP	3MP	4MP	Guest ratios (% e.s.d.s)	Overall H:G ratio
X	X			75.1:24.9 (2.2)	1:1
X		X		8.4:91.6 (1.0)	1:1
X			X	5.4:94.6 (3.3)	1:1
	X	X		1.7:98.3 (0.2)	1:1
	X		X	0.7:99.3 (0.4)	1:1
		X	X	0:100 (0.0)	1:1
X	X	X		8.2:2.4:89.4 (0.7)(0.6)(1.3)	1:1
X	X		X	68.1:31.4:0.5 (0.7)(0.7)(0.0)	1:1
X		X	X	6.5:93.5:0.0 (0.2)(0.2)(0.0)	1:1
	X	X	X	2.3:0.0:97.7 (0.3)(0.0)(0.3)	1:1
X	X	X	X	11.2:1.9:86.9:0.0 (1.1)(0.2)(0.9)(0.0)	1:1

^aG:G and overall H:G ratios were obtained using GC and ¹H-NMR spectroscopy, respectively.

Table 2: Calculated *K*-values for **H** in the binary pyridyl solutions.^a

Guest % (original solution)	<i>K</i> -values (in favour of)					
	PYR/2MP	3MP/PYR	4MP/PYR	3MP/2MP	4MP/2MP	4MP/3MP
20	3.4 (PYR)	8.9 (3MP)	18.4 (PYR)	13.3 (3MP)	2.8 (4MP)	∞ (4MP)
40	3.1 (PYR)	10.1 (3MP)	48.2 (PYR)	26.7 (3MP)	126.7 (4MP)	∞ (4MP)
50	3.0 (PYR)	10.9 (3MP)	17.5 (4MP)	57.9 (3MP)	134.0 (4MP)	∞ (4MP)
60	4.7 (PYR)	12.9 (3MP)	49.2 (4MP)	117.7 (3MP)	122.1 (4MP)	∞ (4MP)
80	3.1 (PYR)	84.8 (3MP)	25.5 (4MP)	23.6 (3MP)	33.7 (4MP)	∞ (4MP)

^aThe selectivity coefficient (*K*) for the data points from selectivity profiles provides a quantitative measure of the host preference and was calculated using Pivovar's equation.⁵

SCXRD analysis of the successful inclusion complexes revealed that in each case, the guest species were located in wide-open, continuous and unidirectional channels within the complex (Figure 2).

Each pyridyl guest molecule engaged in classical (host)O–H $\cdots$ N(guest) hydrogen bonding with **H** (Table 3). While less preferred PYR experienced a statistically shorter hydrogen bond with **H** than favoured 4MP, these bond distances were similar when comparing PYR and 3MP, and 3MP and 4MP.

- Preferred guests 3MP and 4MP formed short contacts with the O–H $\cdots$ N angles significantly closer to linearity (174 vs. 168°), which may explain **H**'s affinity in competition experiments.

As per the criterion set by Nassimbeni and coworkers, $K \geq 10$ signifies high selectivity, making the host an ideal candidate for effective separations in a practical setting.⁶

- Table 2 demonstrates that **H** is a highly effective host compound for the separation of many binary pyridyl mixtures such as 3MP/PYR (excluding 20% 3MP), 4MP/PYR (all), 3MP/2MP (all), 4MP/2MP (excluding 20% 4MP) and 4MP/3MP (all).

Figure 2: Channel occupation of pyridine within **H** crystal.

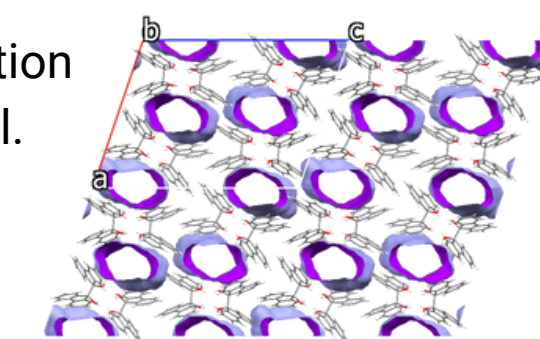


Table 3: Hydrogen bonding parameters in the pyridyl complexes with **H**.

Complex	H $\cdots$ N/Å	O $\cdots$ N/Å	O–H $\cdots$ N/°
H-PYR	1.87	2.7025(15)	168
H-3MP	1.87	2.7084(16)	174
H-4MP	1.88	2.7144(19)	174

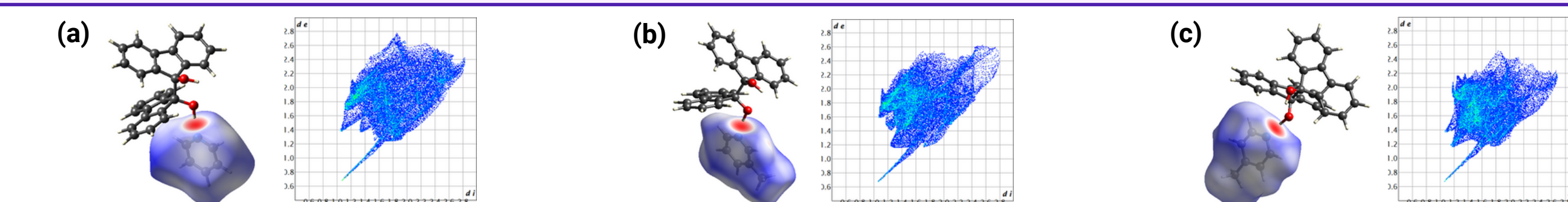


Figure 3: Three-dimensional Hirshfeld surfaces (left) and their corresponding fingerprint plots (right) for (a) **H**-PYR, (b) **H**-3MP and (c) **H**-4MP.

Figure 3 depicts the 3D Hirshfeld surfaces enveloping each pyridyl guest molecule, with red regions indicating areas of pronounced hydrogen bonding interactions.⁷ The adjacent fingerprint plots illustrate the distribution of all the intermolecular G $\cdots$ H interactions, while the bar graph in Figure 4 summarises the percentage of these interactions.

- The hydrogen atom contacts (%) between the host and guest species were greatest in the complex with 4MP (56.1%), followed by 3MP (43.6%), while in the PYR-containing inclusion complex these were only 38.7%.

This aligns with the fact that 3MP and 4MP were preferred in the guest competition experiments (note that the presence of methyl groups in 3MP/4MP accounts for their higher H $\cdots$ H contacts vs. PYR). Thus, it is expected that 3MP and 4MP would experience greater % of these interactions.

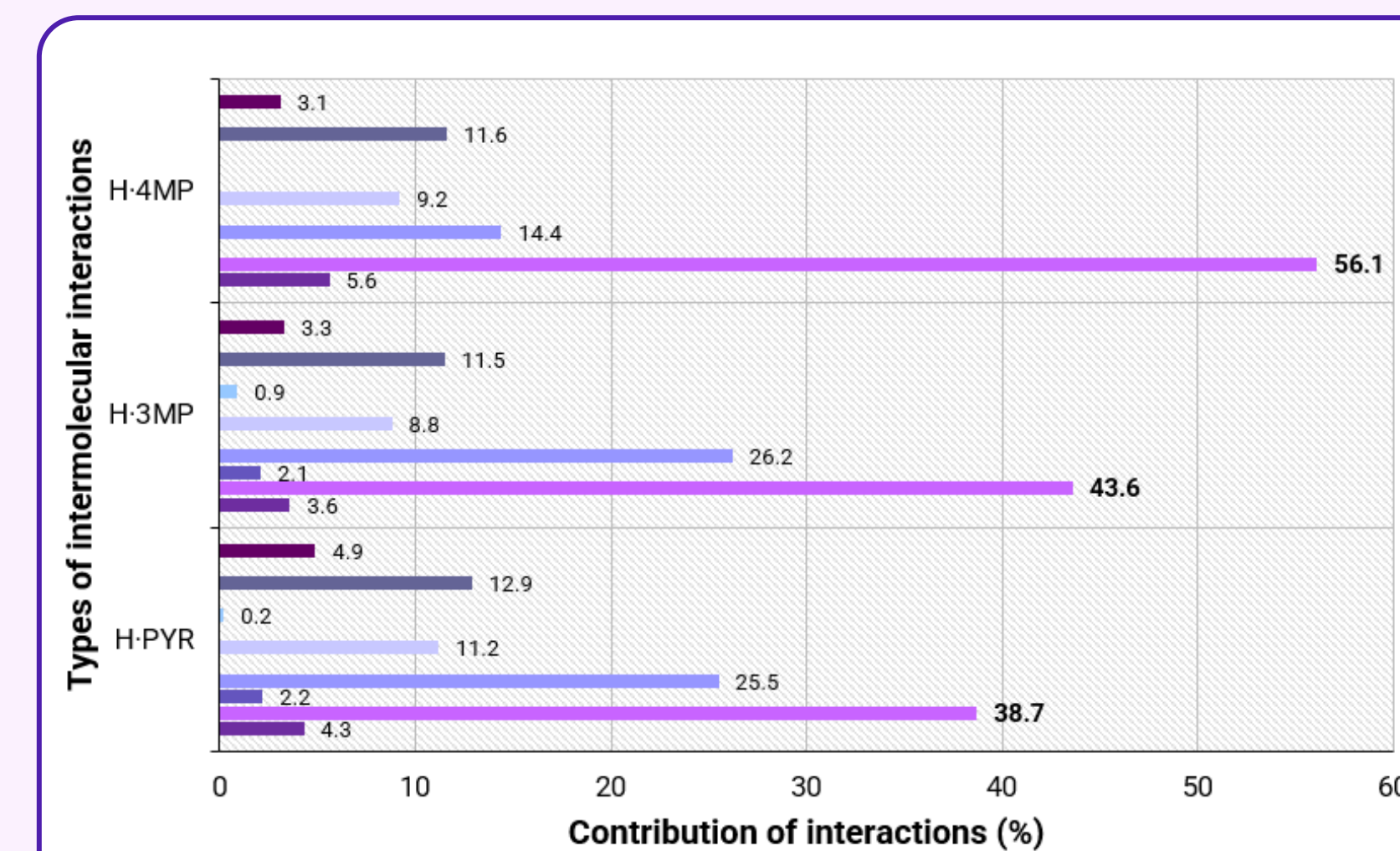


Figure 4: Quantification of G $\cdots$ H interactions in the three complexes.

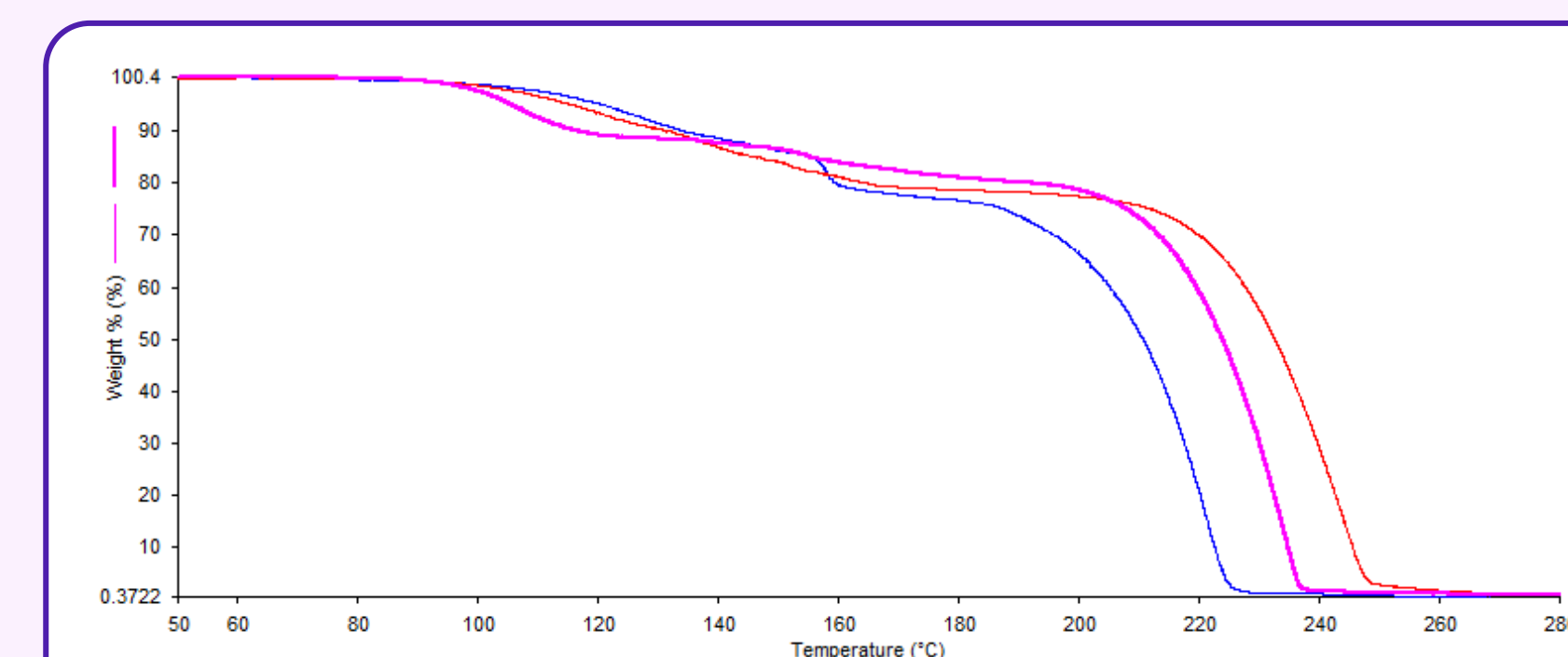


Figure 5: Overlay of TGA traces for complexes of **H** with PYR, 3MP and 4MP.

Thermal analyses were performed on each complex (thermogravimetric (TG), its derivative (DTG) and differential scanning calorimetry (DSC)). Results were obtained after heating each sample at a rate of 10 °C·min^{–1} over a temperature range of 50 to 280 °C. The mass losses observed during these experiments for the **H**-PYR, **H**-3MP and **H**-4MP complexes, agreed reasonably well with those that were calculated (Table 4).

- Onset temperatures for the complexes of **H** with 3MP and 4MP were higher (T_{on} 79.3 and 80.5 °C), indicative of greater relative thermal stabilities, compared with **H**-PYR (Table 4). This aligns with guest competition studies. Endotherm peak temperatures (T_p) representative of host melt, ranged between 188–191°C.⁴

CONCLUSION

Crystallization of **H** with PYR, 3MP, and 4MP yielded 1:1 complexes, while 2MP formed a gel. In guest competition experiments, **H** favoured 4MP in binary mixtures and 3MP in ternary/quaternary mixtures, with PYR influencing selectivity toward 3MP. **H** effectively separated many binary mixtures, exhibiting significant *K*-values. These findings, supported by SCXRD, Hirshfeld surface and thermoanalytical analyses confirm **H** as a highly effective host candidate for the separation of pyridyl guest mixtures for practical application.

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