N,N'-bis(9(4-chlorophenyl)-9H-thioxanthen-9-yl)butane-1,4-diamine as a host compound for organic heterocyclic solvents

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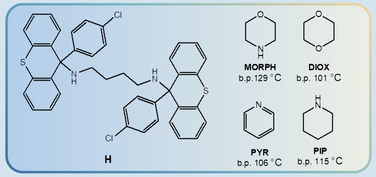
INTRODUCTION

Aromatic heterocyclic compounds have numerous pharmacological and industrial applications; however, their release as pollutants can harm ecosystems. Due to their high-water solubility, industrial effluents can contaminate water systems, with studies detecting traces of these compounds in agricultural crops. [1] Host-guest chemistry, a key area of supramolecular chemistry, involves the selective binding of smaller guest molecules by host molecules through non-covalent interactions.[2] Unlike conventional separation methods, it follows green chemistry principles as it is non-destructive, recyclable and less energy intensive, allowing selective separation of organic heterocyclic compounds despite their similar physiochemical properties.[3]

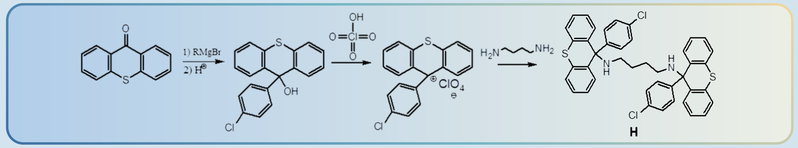
N,N'-Bis(9(4-chlorophenyl)-9H-thioxanthen-9-yl)butane-1,4-diamine (**H**) was synthesised and evaluated for its selectivity toward the organic heterocyclic solvents morpholine (MORPH), 1,4-dioxane (DIOX), pyridine (PYR) and piperidine (PIP) (Scheme 1). The resulting inclusion complexes were analysed using single crystal X-ray diffraction (SCXRD) and thermal analysis. In addition, selectivity competition experiments were performed using equimolar and non-equimolar guest mixtures to determine the host's preference for different guest species.



Scheme 1. Host compound and organic heterocyclic guest species.

EXPERIMENTAL

Synthesis of *N,N'*-bis(9(4-chlorophenyl)-9H-thioxanthen-9-yl)butane-1,4-diamine (H): H was synthesised through a multistep procedure involving a Grignard addition reaction to thioxanthone, conversion of the resultant alcohol intermediate into a perchlorate salt and subsequent linkage via 1,4-diaminobutane (Scheme 2).[4]



Scheme 2. General synthesis of host compound.

Single solvent experiments: H was crystallised in the guest species MORPH, DIOX, PYR and PIP. The crystals were isolated, and inclusion complex formation was confirmed using ^{1}H-NMR spectroscopy, which was also used to determine the H:G ratio (Fig. 1).

Figure 1. Experimental single solvent host-guest complex formation.

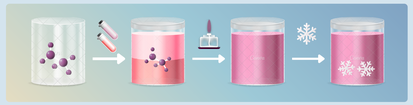


Figure 2. Experimental binary equimolar solvent complex formation.

Equimolar guest competition experiments: The selectivity of **H** dissolved in guest mixtures of equal molar ratios was investigated. Overall H:G ratios of the resulting crystals were determined using ^{1}H-NMR spectroscopy. All experiments were performed in duplicate, and percentage estimated standard deviations (% e.s.d.s) were calculated (Fig. 2).

Binary guest competition experiments in non-equimolar guest mixtures: The selectivity of **H** in binary guest mixtures of varying molar ratios was investigated. The resulting crystals were analysed using ^{1}H-NMR spectroscopy, and selectivity plots were constructed following the equation established by Pivovar et al (Fig.3). [5]

Figure 3. Experimental binary non-equimolar solvent complex formation.

RESULTS AND DISCUSSION

- Single-solvent experiments yielded an inclusion complex with MORPH in a 1:2 H:G ratio.
- Crystals obtained from DIOX, PIP, and PYR were guest-free, indicating no inclusions occurred.

Table 1. Equimolar competition results of **H** in organic heterocyclic solvents

MORPH	DIOX	PIP	PYR	G:G ratio[a]	Overall H:G ratio[a]	% e.s.d[b]
X	x			73.2 : 26.8	1:3	1.2
X		x		76.2 : 23.8	1:3	2.9
X			x	81.9 : 18.1	1:3	1.5
	X	x		55.9 : 44.1	2:1	3.0
	x		X	46.9 : 53.1	7:1	0.6
		x	X	47.3 : 52.7	5:1	2.2
X	x	x		56.1 : 27.5 : 16.4	1:2	3.1 : 4.1 : 1.0
X	x		x	64.9 : 28.9 : 8.2	1:2	1.5 : 2.3 : 0.8
X		x	x	43.0 : 19.4 : 37.6	3:1	4.4 : 0.0 : 4.4
	x	x	X	31.6 : 23.7 : 44.7	4:1	0.5 : 1.8 : 2.3
X	x	x	x	55.9 : 21.7 : 16.5 : 5.9	2:3	1.4 : 1.35 : 0.6 : 0.5

[a] G:G ratio and overall H:G ratios were obtained using ^{1}H-NMR spectroscopy, [b] duplicate experiments calculated % e.s.d values

In the equimolar experiments, MORPH was preferentially included in all mixtures in which it was present, indicating high selectivity among guest species (Table 1). The highest selectivity was observed in the MORPH/PYR mixture in favour of MORPH (81.9%). When MORPH was absent, PYR was generally preferred; however, the PYR-containing mixtures exhibited low H:G ratios, indicating less effective inclusions.

The selectivity coefficient (K) provides a quantitative measure of host preference. According to Nassimbeni and coworkers, a K-value ≥ 10 is required for the separation of binary guest mixtures in industrial and practical applications. [6]

Table 2. Selectivity coefficients of **H** obtained from selectivity profiles

Binary mixture	K values (in favour of)			
	80:20	60:40	40:60	20:80
MORPH/DIOX	1.8 (MORPH)	1.6 (MORPH)	1.4 (MORPH)	2.3 (MORPH)
MORPH/PIP	4.3 (MORPH)	3.6 (MORPH)	3.4 (MORPH)	4.0 (MORPH)
MORPH/PYR	6.2 (MORPH)	8.5 (MORPH)	5.3 (MORPH)	3.0 (MORPH)
DIOX/PIP	1.0 (PIP)	1.0 (DIOX)	1.3 (DIOX)	1.4 (PIP)
DIOX/PYR	4.1 (DIOX)	3.1 (DIOX)	1.0 (PYR)	1.1 (DIOX)
PIP/PYR	3.0 (PYR)	2.6 (PYR)	2.2 (PYR)	1.8 (PYR)

The highest selectivity observed in this study was seen in the 60:40 MORPH/PYR mixture, which yielded a K-value of 8.5, in favour of MORPH (Table 2). Other MORPH/PYR mixtures also exhibited relatively high K-values. However, all K-values obtained were below the practical threshold of K = 10, indicating that the host cannot be applied in practical applications.

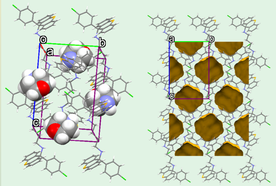


Figure 4. Unit cell and guest packing (left) and void (right) diagrams of **H**-MORPH.

SCXRD analysis of the **H**-MORPH complex revealed that it crystallises in the monoclinic crystal system with space group $P2_1/c$. The MORPH guest molecules exhibited some degree of disorder along the inversion point.

Figure 4 displays the unit cell (left) of the complex and the voids (right) generated upon the removal of the guest molecules. These voids, visualised using Mercury software, reveal discrete cavities within the host framework that accommodate guest molecules in a 1:1 H:G ratio.

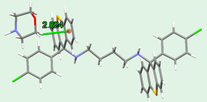


Figure 5. The (guest) C–H···π (host) interaction.

The significant (guest)C–H···π(host) interaction measured 2.82 Å (guest)H···π(host), 3.64(2) Å (guest)C···π(host) and 140° (guest)C–H···π(host)(Fig. 5).

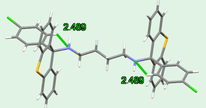


Figure 6. An intramolecular (host) C–H···N (host) interaction.

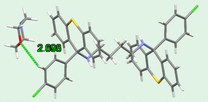


Figure 7. An intermolecular (host) C–H···O (guest) interaction.

Significant non-classical hydrogen bonding interactions occurred within the host molecule between N and H with a (host)H···N(host) distance of 2.49 Å, a (host)C···N(host) distance of 2.846(4) Å and (host)C–H···N(host) angle of 102°. Another non-classical hydrogen bonding interaction was between the host and guest molecules, involving atoms O and H, with a (host)C–H···O(guest) distance of 2.70 Å and (host)C–H···O(guest) angle of 145° (Fig. 6 and 7).

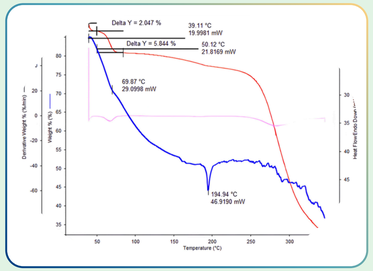


Figure 8. Overlay of thermal traces (TGA (red), DSC (blue) and dTG (pink)) of **H**-MORPH complex.

T_{on} is the temperature at which the guest is released from the inclusion crystal and, therefore, used as a measure of thermal stability. T_p corresponds to the melting temperature of the host compound.

Table 3. Thermal parameters of **H**-MORPH complex

Complex	T_{on}/ °C	T_p/ °C	Measured mass loss (%)	Expected mass loss (%)
H-MORPH	[a]	194.9	[a]	19.9

[a] Complex was unstable at ambient conditions.

For **H**-MORPH, T_{on} could not be determined, as the guest molecules escaped before thermal analysis via multistep guest liberation, indicating instability under ambient conditions (Fig. 8). Consequently, reliable mass loss (%) could not be measured, preventing the determination of guest content (Table 3).

- Water studies were conducted, and **H** was found to be unable to absorb MORPH from aqueous solutions.

CONCLUSION

H was successfully synthesised and evaluated as a host toward a series of organic heterocyclic solvents. Selective inclusion was observed exclusively for MORPH, yielding a 1:2 H:G complex, while DIOX, PIP and PYR produced only guest-free crystals, as confirmed by ^{1}H-NMR spectroscopy. Guest competition experiments demonstrated a preference for MORPH, with the highest selectivity observed in MORPH/PYR binary mixtures; however, the K-values demonstrate practical separation applications cannot be applied. SCXRD analysis revealed a 1:1 H:G ratio, in contrast to the 1:2 H:G ratio observed by ^{1}H-NMR spectroscopy, suggesting variability in guest occupancy between the single crystal analysed by SCXRD and the bulk sample analysed by NMR. Thermal analysis showcased a multistep guest release event and thermal instability of the inclusion complex under ambient conditions.

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