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Inclusion ability and selectivity of ethylenediamine derivatives for pyridine in the presence of methylpyridine isomers

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Abstract

The inclusion behaviour of compounds *N*,*N'*-bis(9-cyclohexyl-9-xanthenyl)ethylenediamine (OED) and *N*,*N'*-bis(9-cyclohexyl-9-thioxanthenyl)ethylenediamine (SED) was assessed in the presence of pyridine (PYR) and its three methylpyridine isomers (2MP, 3MP and 4MP). PYR, 3MP and 4MP were each enclathrated by OED when it was recrystallized independently from each guest solvent, but failed to include 2MP. The thio host derivative, SED, was less efficient, forming a complex only with PYR. When these guests were mixed in equimolar amounts and each host recrystallized from the mixture, OED constantly displayed a significantly enhanced preference for 4MP (near-complete in many instances), while complexation failed under these circumstances for SED, even when PYR was present in the guest mixture (despite PYR having been included in the single solvent experiment). A selectivity order of 4MP (92.8%) \gg PYR (6.0%) > 3MP (0.9%) > 2MP (0.3%) was noted for OED when it was recrystallized from the equimolar quaternary mixed solvent system. The selectivity of OED towards 4MP was investigated using single crystal diffraction (SCXRD) and thermal (TA) analyses: interestingly, only 4MP experienced a strong classical hydrogen bond with OED, in direct relation to the enhanced selectivity of OED for 4MP while, additionally, this complex displayed an increased thermal stability relative to the other two complexes with OED.

Keywords Host-guest chemistry · Supramolecular chemistry · Xanthenyl · Pyridine · Methylpyridine

Introduction

Host-guest chemistry forms part of the larger supramolecular chemistry field that can simply be defined as the complexation of two or more different compounds by means of non-covalent interactions. The aforementioned molecular compounds comprise host (H) molecules that crystallize and, in so doing, form cavities or channels in which suitable guest (G) compounds are trapped. Non-covalent forces such as hydrogen bonding, ion pairing, $\pi-\pi$, CH- π and van der Waals interactions are generally the forces responsible for this entrapment of the guest species [1–3]. The host compounds may be subdivided into two major groups based on

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Ulrich Senekal s214099601@mandela.ac.za whether they possess inter- (cavitands) or extra-molecular cavities (clathrands) [3].

Host-guest chemistry finds various applications in the chemical, biological and pharmaceutical fields such as the separation of enantiomers and other isomeric mixtures [3], modification of stationary phases for chromatography-assisted separations [4], storage of toxic ions, molecules and gases [3, 5], and increase in the water solubility, stability and bioavailability of drugs [2]. Some host compounds also display bioactivity, and an example is the calixarenes [6].

Pyridine (PYR) and the methylpyridine isomers (MPs, picolines, Scheme 1) are some of the main components found in the light oil fraction (up to a boiling point of 180 °C) of coal tar and may also be obtained through high temperature vapour phase processes involving acetaldehyde, ammonia and formaldehyde in the presence of a catalyst [7, 8]. These compounds are employed in the preparation of polyamides, herbicides, dyes, insecticides, resins and pharmaceuticals [9]. The challenge associated with the separation of the MP isomers from PYR (b.p. 116 °C) or from one another is as a result of their similar physical properties (boiling points, 2MP 129 °C, 3MP 144 °C, 4MP 145 °C),

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Scheme 1 Molecular structures of host compounds *N*,*N*'-bis(9-cyclohexyl-9-xanthenyl)ethylenediamine (OED) and *N*,*N*'-bis(9-cyclohexyl-9-thioxanthenyl)ethylenediamine (SED), and guests pyri-

dine (PYR), 2-methylpyridine (2MP), 3-methylpyridine (3MP) and 4-methylpyridine (4MP)

and so requires multiple fractional distillations or their syntheses from alternative precursors, which ensures that less conventional separation strategies become more alluring [8].

Researchers only recently considered the separation of PYR and its MP isomers through principles of host-guest chemistry. As examples, Bacsa et al. explored the wheeland-axle type host, 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol, and found it to possess clathration ability in the presence of each of PYR, 3MP and 4MP. PYR and 4MP were each shown to occupy channels in the host crystal, while two of the 3MP guests occupied a single cage. Additionally, this host displayed selectivity for 4MP when in the presence of 4MP/PYR mixtures, and (host)O-H...N(guest) hydrogen bonds were responsible for the stabilization of the complexes [10]. Nassimbeni et al. considered a host first designed and synthesized by Weber et al., 9,9'-(ethyne-1,2diyl)bis(fluoren-9-ol), containing two rigid hydroxyfluorenyl moieties connected by a spacer unit, for this purpose [11, 12]. This host formed inclusion compounds with all the MP guests, but distinctly favoured 4MP over the others. More recently, (+)-(2R,3R)-1,1,4,4-tetraphenylbutane-1,2,3,4tetraol (TETROL) was assessed for its possible application in the separation of these guest types [13]. This host compound possesses a rigid butane backbone, which adopts an anti conformation, as well as hydrogen bonding capabilities due to the presence of the four hydroxyl groups. Interestingly, TETROL displayed a similar tendency to form complexes with these solvents as 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol, and a selectivity order of 4MP > 3MP > PYR > 2MP was noted. The behaviour of racemic and optically pure $\alpha, \alpha, \alpha', \alpha'$ -tetraphenyl-2,2-dimethyl-1,3-dioxolane-4,5dimethanol (TADDOL), synthesized from the appropriate tartaric acid, has also been reported, and both hosts possess the ability to clathrate all four of these guests types [14]. Both also displayed a preference for 3MP (75% and 69%, respectively) when each was recrystallized from an equimolar mixture of the four solvents. In order to attempt to improve on these selectivities, host compound N,N'-bis(9phenyl-9-thioxanthenyl)ethylenediamine was employed in these experiments, but it only contained 47% of 3MP when recrystallized from the quaternary guest mixture [15].

In the present work, modified ethylenediamine-linked xanthenyl and thioxanthenyl host systems, *N*,*N*'-bis(9-cyclohexyl-9-xanthenyl)ethylenediamine (OED) and *N*,*N*'-bis(9-cyclohexyl-9-thioxanthenyl)ethylenediamine (SED), were employed in an attempt to improve on the very ordinary host selectivities in the presence of the title guest compounds reported before (Scheme 1), with exceptional findings. It has very recently been noted that these host compounds display preferential behaviour in the presence of xylenes and ethylbenzene [16], but their host ability in the presence of PYR and the MPs has not been reported to date. The successfully-formed complexes were analyzed by means of single crystal X-ray diffraction (SCXRD) and thermal analyses (TA) in

order to understand better the reasons for any preferential behaviour displayed by these host compounds.

Results and discussion

Synthesis of OED and SED

OED and SED were prepared very simply by considering a previous report [16]. A Grignard reaction was performed on xanthone 1 and thioxanthone 2 using cyclohexylmagnesium bromide followed by an acid workup to yield the respective alcohols 3 and 4 (Scheme 2). These were treated with perchloric acid to afford perchlorate salts 5 and 6 which were, in turn, added to ethylenediamine to afford the desired crystalline host compounds OED and SED, respectively.

Single solvent experiments

Table 1 summarizes the results of the experiments where hosts OED and SED were individually recrystallized from

 Table 1
 The H:G ratios of the complexes formed with OED and SED

Guest	OED	SED
PYR	1:1	1:1
2MP	_b	_ ^b
3MP	2:1	_b
4MP	1:2	_ ^b

^{a1}H-NMR spectroscopy was used to determine the host:guest (H:G) ratios, with CDCl₃ as solvent

^bNo inclusion occurred



Scheme 2 Synthetic route towards hosts OED and SED

each of the PYR and MP guest compounds. The results are strikingly contrasting in that OED formed inclusion compounds with each of PYR, 3- and 4-MP, but did not clath-rate 2-MP; host:guest (H:G) ratios varied (1:1, 2:1 and 1:2, respectively). SED, on the other hand, failed to form any complexes with each of the MPs and only clathrated PYR (H:G ratio 1:1).

Competition experiments using equimolar guest mixtures

Equimolar competition experiments were employed in order to observe whether hosts OED and SED would display selectivity in the presence of mixtures of these guests. Surprisingly, binary, ternary and quaternary guest competition experiments with SED as the host resulted in only apohost crystallizing out, and none of these guests were included in this way. This was the case even where PYR was present (the only guest compound to form a complex with SED in the single solvent experiments). The obtained data are summarized in Table 2, and the preferred guest is indicated in bold italic text with percentage estimated standard deviations (% e.s.d.s) provided in parentheses.

OED displayed a significant preference for 4MP (76.9%, 96.8% and 94.8%, respectively) when it was recrystallized from PYR/4MP, 2MP/4MP and 3MP/4MP binary mixtures, while PYR/2MP and PYR/3MP experiments led to the favourable complexation of PYR (66.8% and 69.1%, respectively) (Table 2). In the absence of PYR and 4MP (2MP/3MP), 3MP was the favoured guest (66.6%), and by considering only these binary experiments, a host selectivity order of 4MP > PYR > 3MP > 2MP may be established.

The ternary equimolar experiment using 2MP/3MP/4MP showed that 4MP was, once more, favoured, with 96.5% of this guest being present in the mixed complex; only small amounts of the other two guests were present [3MP (1.9%) and 2MP (1.6%)]. A PYR/2MP/3MP mixture where two of the least preferred guests were present (2MP and 3MP) failed to form a complex, while the PYR/2MP/4MP and PYR/3MP/4MP, in which neither 2MP nor 3MP were present simultaneously, did indeed form inclusion compounds [PYR (20.3%), 2MP (5.0%), 4MP (74.7%) and PYR (13.8%), 3MP (2.8%), 4MP (83.4%)]. When all four guests were mixed in equimolar proportions and the host recrystallized from this mixture, the resulting complex contained 92.8% 4MP, which is a remarkable improvement on previous reports. The selectivity order of host OED was therefore $4MP(92.8\%) \gg PYR(6.0\%) > 3MP(0.9\%) > 2MP(0.3\%)$ for these guests, in direct correlation with observations made from the binary experiments. Notable is the observation that successfully-formed mixed complexes containing 4MP (the preferred guest) constantly adopted an overall H:G ratio that
 Table 2
 Results
 of
 competition
 experiments
 for
 host
 OED
 when
 recrystallized
 from equimolar mixtures of PYR, 2MP, 3MP and 4 MP
 AMP
 AMP

PYR	2MP	3MP	4MP	Guest ratios (% e.s.d.s) ^a	Overall H:G ratio
X	Х			66.8 :33.2 (1.4)	1:1
X		Х		69.1 :30.9 (0.3)	1:1
Х			X	23.1: 76.9 (1.6)	1:2
	Х	X		33.4: 66.6 (0.5)	2:1
	Х		X	3.2 :96.8 (0.7)	1:2
		Х	X	5.2 :94.8 (0.4)	1:2
Х	Х	Х		_b	_ ^b
Х	Х		X	20.3:5.0: 74.7 (2.9)(1.0)(3.9)	1:2
Х		Х	X	13.8:2.8: 83.4 (0.2)(0.7)(0.5)	1:2
	Х	Х	X	1.6:1.9: 96.5 (0.1)(0.0)(0.1)	1:2
Х	Х	Х	X	6.0:0.3:0.9: 92.8 (0.6)(0.0)(0.1)(0.7)	1:2

Guest:guest and overall H:G ratios were determined using GC-MS and ¹H-NMR spectroscopy, respectively

 $^{\mathrm{a}}\mathrm{The}~\%$ e.s.d.s obtained from triplicate data sets are displayed in parentheses

^bCrystals contained no guest solvent/s

corresponded with that of the OED 4MP complex from the single solvent experiment (Table 1, 1:2).

Competition experiments using varied guest concentration mixtures

The host behaviour of OED was also investigated when it was recrystallized from binary guest 1:guest 2 (G1:G2) mixtures with varying amounts of each guest present (from approximately 20:80 to 80:20 G1:G2 mol%). The selectivity profiles so-obtained are presented in Fig. 1a–f, where the black dotted line represents an unselective host compound (K = 1) for comparative purposes. The average selectivity coefficient (K) was only calculated for the PYR/2MP mixture, whereas the highest selectivity coefficients for the remaining binary guest mixtures were calculated and provided herein.

Figure 1a represents the selectivity profile of host OED when recrystallized from various concentrations of PYR and 2MP in binary mixtures. At low concentrations of PYR in the mother liquor (<42%), OED displayed only a slight preference for this guest relative to 2MP: a complex with 24.6%



Fig. 1 OED selectivity profiles for the a PYR/2MP, b PYR/3MP, c PYR/4MP, d 2MP/3MP, e 2MP/4MP and f 3MP/4MP mixtures

PYR and 75.4% 2MP was isolated from a 16.0% PYR and 84.0% 2MP solution. However, as the concentration of PYR in the mother liquor increased, so did the presence of this guest in the crystal: when the mother liquor comprised 47.4 and 69.1% PYR, the amount of this guest in the resultant complexes was found to be 77.4% and 88.7%, respectively. It is clear that OED was selective for PYR over the entire concentration range evaluated (the averaged K value was calculated to be 2.4).

In contrast, the selectivity of OED when recrystallized from PYR/3MP mixtures was guest concentration dependent (Fig. 1b): a low concentration of PYR (13.6%) in the mother liquor afforded a mixed complex with a significant amount of 3MP (96.3%). The selectivity of the host was then altered when the PYR concentration in the mother liquor was approximately 23%: from this point on, the amount of PYR in the resultant complexes surpassed that present in the

mother liquors, and the most significant selection towards this guest was 98.5%, and was obtained from a 69.5:30.5 PYR:3MP solution (K = 28.3).

The selectivity profile of OED for the PYR/4MP competition experiment (Fig. 1c) also showed that the selectivity of this host depended on the concentration of the guests. PYR was initially preferred by OED (95.8%) when the mother liquor contained 30.1% of 4MP and 69.9% of PYR. The host preference then switched from PYR to 4MP when approximately 40% of 4MP was present in the mother liquor: a solution comprising 60.9% 4MP afforded a mixed crystalline complex with 88.7% of 4MP present (K=5.0).

From 2MP/3MP mixtures, OED remained rather unselective for either guest when low concentrations of 3MP (<43%) were present (Fig. 1d). The selectivity for 3MP was, however, enhanced as its concentration in the mother liquor





further increased: a mother liquor of 81.0% 3MP afforded crystals containing 89.6% 3MP and 10.4% 2MP (K = 2.0).

The selectivity profiles obtained from both the 2MP/4MP (Fig. 1e) and 3MP/4MP (Fig. 1f) mixtures showed that 2MP (83.2%) and 3MP (94.4%) were present in increased amounts in the formed complexes when the mother liquors contained high concentrations of 2MP (78.5%) and 3MP (81.2%), respectively. Yet again, an increased concentration of 4MP [43.2% for 2MP/4MP (K=23.5) and 38.2% for 3MP/4MP (K=26.3)] instigated a significant selectivity shift towards 4MP and yielded complexes containing 94.7 and 94.2% of this guest, respectively.

Single crystal X-ray diffractometry analyses

The crystallographic data for the OED-PYR, 2OED·3MP, OED·2(4MP) and SED·PYR complexes are provided in Table 3. In the case of 2OED·3MP, the guest is disordered around an inversion point and the nitrogen hydrogens of the host are disordered over two positions. Furthermore, the OED·PYR complex has the host nitrogen hydrogens and the PYR guest disordered over two orientations, while one PYR guest experiences disorder in the SED·PYR complex. Finally, 4MP in its complex with OED, on the other hand, displays no disorder. The three inclusion compounds with OED all crystallized in the triclinic crystal system and P-1

space group, while SED·PYR adopted the monoclinic crystal system and $P2_1$ space group.

Figure 3a–d represents the calculated voids after guest removal for the four complexes using Mercury software [17]; the voids represent the empty spaces in the crystal that were able to hold a spherical probe with a radius of 1.2 Å. Host OED accommodates the PYR, 3MP and 4MP guests in discrete cavities, one guest in each in the former two, and two in the latter. The complex that resulted from SED and PYR showed that four of the guests occupy a single convoluted c-shaped cavity in the crystal structure of SED.

The more significant non-covalent interactions that were present in the four complexes are provided in Table 4. Intermolecular (host)CH···π(host) interactions ranging between 2.63 and 3.00 Å (86°–164°) in each which are responsible for the stabilization of the host geometry. These also experienced numerous weak (host) π ···π(guest) contacts while one (guest) π ···π(guest) interaction could also be identified in each of OED·2(4MP) and SED·PYR [5.845(1) Å and 5.521(3) Å, respectively] owing to the proximity of the guests in these instances. However, these are very weak indeed. C–H···π interactions were also evident between host and guest in both OED·PYR and SED·PYR ranging between 2.74 and 2.97 Å with angles of 144°–162°. These two complexes also experienced other strong short contacts between the hosts and guest. The former comprised two (host)C–H···H–C(guest)

	OED•PYR	20ED•3MP	OED•2(4MP)	SED•PYR
Chemical formula	$C_{40}H_{44}N_2O_2 \bullet C_5H_5N$	$2C_{40}H_{44}N_2O_2 \bullet C_6H_7N$	$C_{40}H_{44}N_2O_2\bullet 2C_6H_7N$	$C_{40}H_{44}N_2S_2 \bullet C_5H_5N$
Formula weight	663.87	1262.67	771.02	695.99
Crystal system	Triclinic	Triclinic	Triclinic	Monoclinic
Space group	P - 1	P - 1	P - 1	<i>P</i> 2 ₁
μ (Mo-K α)/mm ⁻¹	0.075	0.074	0.073	0.179
a/Å	9.3676(3)	9.3229(6)	9.7502(6)	10.2878(6)
b/Å	14.0406(4)	13.6496(9)	9.8653(5)	26.2000(14)
c/Å	14.0621(4)	14.4164(9)	12.4309(7)	27.6768(15)
alpha/°	89.754(2)	97.746(3)	67.588(2)	90
beta/°	78.014(2)	98.307(3)	81.443(2)	91.794(2)
gamma/°	80.324(2)	105.408(3)	73.729(2)	90
<i>V</i> /Å ³	1782.58(9)	1721.0(2)	1059.93(11)	7456.4(7)
Z	2	1	1	8
$D(calc)/g cm^{-3}$	1.237	1.218	1.208	1.240
F(000)	712	678	414	2976
Temp./K	200	200	200	200
Restraints	0	0	0	35
Nref	8878	8602	5266	33,252
Npar	428	467	267	1769
R	0.0579	0.0426	0.0414	0.0514
wR2	0.1561	0.1153	0.1171	0.1346
S	1.04	1.02	1.04	1.03
θ min–max/°	1.5, 28.4	1.9, 28.4	2.2, 28.3	0.7, 28.4
Tot. data	38,781	77,376	26,341	106,179
Unique data	8878	8602	5266	33,252
Observed data [I > 2.0 sigma(I)]	6185	7346	4158	26,420
R _{int}	0.032	0.025	0.021	0.026
Dffrn measured fraction θ full	1.000	0.998	1.000	1.000
Min. resd. dens. (e/Å ³)	-0.88	-0.28	-0.17	-0.68
Max. resd. dens. (e/Å ³)	0.86	0.33	0.30	1.30

Table 3 Crystallographic data for OED·PYR, 2OED·3MP, OED·2(4MP) and SED·PYR

The unit cells for the OED·PYR, 20ED·3MP, OED·2(4MP) and SED·PYR complexes are presented in Fig. 2a-d

interactions (2.15, 2.16 Å and 116°, 151°), while the latter experienced one (host)C–H···H–C(host) (2.18 Å and 140°), and one favourable (guest)C–H···C–S(host) contact (2.69 Å and 175°). Most remarkably, however, is the observation that only the OED·2(4MP) complex experiences a particularly stabilizing classical (host)N–H···N–C(guest) hydrogen bond measuring 3.304(2) Å (D···A) [170.9(14)°] which correlates with the significant preference of OED for 4MP in the competition experiments. The stereoview provided in Fig. 4 illustrates this important interaction more clearly.

Thermal analyses

The successfully formed complexes of hosts OED and SED were subjected to thermogravimetric analysis (TG)

and differential scanning calorimetry (DSC) and the resultant traces, together with the derivative of the TG (DTG), are displayed in Fig. 5a–d. The complexes were heated at 10 °C min⁻¹ from 45 to 260 °C and the thermal data from these are summarized in Table 5.

The expected guest mass losses correlate reasonably well with those obtained in these experiments upon removal of all of the guest through heating [OED·PYR 13.2, 11.9, 2OED·3MP 7.6, 7.4, OED·2(4MP) 24.2, 24.2 and SED·PYR 10.7, 11.4%]. Figure 5a, b and d show a convoluted guest release process for the OED·PYR, 2OED·3MP and SED·PYR complexes, respectively, while 4MP is released in a clear single step from the crystals of OED.

For complexes formed by OED, both T_{on} (the onset temperature of the guest release process estimated from the

Fig. 3 The calculated voids in **a** OED·PYR, **b** 2OED·3MP, **c** OED·2(4MP) and **d** SED·PYR; host compounds are represented in a wireframe style and the voids in a dark yellow colour



Table 4 A summary of the significant host-host and host-guest interactions in OED-PYR, 2OED-3MP, OED-2(4MP) and SED-PYR

Interactions	OED•PYR	20ED•3MP	OED●2(4MP)	SED•PYR
$(host)\pi\cdots\pi(guest)$	4.832(1)–5.969(1) Å [7—major guest, 6—minor guest]	5.042(1)–5.692(2) Å [4]	4.950(1)—5.953(1) Å [7]	4.990(3)-5.928(4) Å [18-major guest, 5-minor guest]
C-H··· π (host 1)CH··· π (guest 1) (guest 1) <i>p</i> -ArH··· π (host 1) (guest 2 <i>d</i> 1) <i>o</i> -ArH··· π (host 1) (guest 2 <i>d</i> 1) <i>m</i> -ArH··· π (host 2) (guest 2 <i>d</i> 2) <i>o</i> -ArH··· π (host 2)	2.74–2.91 Å, 144–154°	None	None	2.87 Å, 156° 2.92 Å, 162° 2.80 Å, 153° 2.97 Å, 149°
Hydrogen bonding (host 1)N-H…N-C(guest 1)	None	None	3.304(2) Å, 170.9(14)°, ≪	None
$\begin{array}{l} (host 1)m - ArH \cdots H - C(guest 1d2) \\ (host 1)C - H \cdots H - C(guest 1d2) \\ (host 1)m - ArH \cdots H - C(host 2) \\ (guest 1)p - ArH \cdots C - S(host 2) \end{array}$	2.15 Å, 116°, ≪ 2.16 Å, 151°, ≪	None	None	2.18 Å, 140°, ≪ 2.69 Å, 175°, ≪

The host and guest in each complex are given each a different number because of the different chemical environments they find themselves in, with respect to each other

The major host and guest are indicated by a 'd1' while the minor host and guest are indicated by a 'd2' after the appropriate number

≪ Denotes contacts than this sum minus 0.2 Å. The number of □…□ interactions are provided in square brackets



Fig.4 Stereoview illustrating the hydrogen bond (blue line) between OED and 4MP

DTG and indicative of relative thermal stabilities) [17] and the T_p (obtained from the peak on the DTG trace that represents guest loss) values are greater for the complex containing the preferred 4MP guest (77.0 and 98.7 °C) relative to these temperatures for the remaining two complexes. This too is in accordance with the enhanced selectivity of OED for 4MP in the competition experiments.

Conclusions

N,*N*'-Bis(9-cyclohexyl-9-xanthenyl)ethylenediamine (OED) was demonstrated to be a highly effective host compound in the presence of PYR and the MPs, including each of PYR, 3MP and 4MP in single solvent experiments; however, it failed to form a complex with 2MP. This host, furthermore, displayed remarkable selectivity for 4MP when recrystallized from various equimolar mixtures containing this guest, and a selectivity order of 4MP (92.8%) \gg PYR (6.0%) > 3MP (0.9%) > 2MP (0.3%) was obtained from the corresponding quaternary guest solvent mixture. On the other hand, *N*,*N*'-bis(9-cyclohexyl-9-thioxanthenyl)ethylenediamine (SED) was rather ineffective in this regard, only including PYR, and only in the single solvent experiments. Surprisingly, this host did not form complexes when recrystallized from these solvent mixtures, even those where PYR was present.

The SCXRD analyses showed that only the OED·2(4MP) complex possessed a hydrogen bond between the host and guest, and this observation explains the high affinity of OED for 4MP. Thermal analyses also supported this host preference in that the complex that displayed increased T_{on} and T_p values was that containing the preferred 4MP guest.

Therefore, in this work, OED demonstrated that it is a superior host compound for the enclathration of 4MP from mixtures of these solvents, displaying near-complete selectivity for this guest (92.8%) when recrystallized from an equimolar quaternary mixture of the title guest solvents.

Experimental

General

All chemicals were purchased from Merck and used without further purification. ¹H-NMR spectra were obtained using a 400 MHz Bruker 400 Ultrashield Plus spectrometer, with CDCl₃ as the solvent, and analysed using Bruker TopSpin 3.2 data software.

SCXRD experiments were performed on the successfully formed complexes from the single solvent experiments for both hosts OED and SED. These diffraction data were obtained at 200 K using a Bruker Kappa Apex II diffractometer utilizing a graphite-monochromated Mo Ka radiation ($\lambda = 0.71073$ Å). The data were analyzed by means of APEXII data software while the SAINT program was used for data reduction and cell refinement [18]. The structures were solved with SHELXT-2018/2 [19] using a dual-space algorithm. SHELXL-2018/3 [20], with SHELXLE [21] as a graphical interface, was used to refine the structures by employing the least-squares procedure. All atoms, excluding hydrogen, were refined anisotropically. Absorption effects present in the data were corrected for using the numerical method implemented in SADABS [18]. The Mercury 3.10.1 software package [22] was used to construct figures displaying the unit cells as well as for calculating the voids present in the crystal after removal of the guest from the packing calculation. The complexes were deposited at the Cambridge Crystallographic Data Centre with CCDC numbers 1918458 (OED•PYR), 1918459 (2OED•3MP), 1918460 [OED•2(4MP)] and 1918461 (SED•PYR).

DSC and TG experiments were conducted on all four of the complexes. The thermal data were obtained using a Perkin Elmer Simultaneous Thermal Analyzer (STA) 6000 and analysed using Pyris Series data software. Samples were placed in a ceramic pan and an empty open ceramic pan was used as a reference in these experiments, which were conducted in high purity nitrogen gas, and samples were heated at 10 °C min⁻¹ from about 45 to 260 °C.

Owing to instrument availability, two GC–MS methods were used to analyse the various PYR/MP experiments: (a) an Agilent 7890A gas chromatograph, fitted with an Agilent 5975C VL mass spectrometer, was equipped with an Agilent J&W DB-wax column. An initial temperature of 50 °C was held for 1 min, followed by a heating ramp of 0.5 °C min⁻¹ until 54 °C was attained, and this temperature was maintained for 5 min; (b) a Young Lin YL6500 gas chromatograph equipped with an Agilent J&W Cyclosil-B column was employed. The latter GC system was heated to an initial temperature of 50 °C and maintained here for 2 min. This was followed by a heating ramp of 30 °C min⁻¹ until 100 °C was reached, and this was followed by yet another



Fig. 5 Overlaid TG (red), DSC (blue) and DTG (green) traces obtained from thermal analyses on the **a** OED·PYR, **b** 2OED·3MP, **c** OED·2(4MP) and **d** SED·PYR complexes

Table 5 Thermal data for the OED·PYR, 2OED·3MP, OED·2(4MP) and SED·PYR complexes

Complex	$T_{on} (^{\circ}C)^{a}$	$T_p (^{\circ}C)^b$	Theoretical mass loss (%)	Observed loss (%) ^c
OED·PYR	67.7	78.9	11.9	13.2
		125.9		
		208.6		
20ED·3MP	76.7	95.2	7.4	7.6
		164.5		
		170.3		
		180.8		
		185.7		
		195.3		
		226.5		
OED·2(4MP)	77.0	98.7	24.2	24.2
SED·PYR	73.3	86.7	11.4	10.7
		214.1		

 $^{a}\text{Onset}$ temperature for guest release (T_{on}) is estimated from the DTG trace

^bDTG peak temperature (T_p) representing the temperature at which guest release is most rapid

^cObserved mass loss was calculated from the TG trace

temperature ramp of 1.5 °C min⁻¹ until 102 °C was attained. Finally, the temperature was ramped at 0.5 °C min⁻¹ to reach 103 °C.

Synthesis of host OED and SED

Host OED and SED were synthesized according to a previously published procedure [16].

Single solvent experiments

OED and SED (0.05 g) were each dissolved in an excess of the PYR and MP guest compounds (5 mmol) utilizing glass vials as vessels. Heat by means of a water-bath was applied to ensure that the host compounds dissolved completely in these solvents. The vials were left at room temperature and ambient atmospheric pressure until crystallization occurred. The crystals were collected by means of vacuum filtration, washed with petroleum ether (40–60 °C) and analysed using ¹H-NMR spectroscopy, with CDCl₃ as the solvent. H:G ratios were determined through integration of relevant host and guest signals on these spectra.

Competition experiments using equimolar mixtures

OED and SED (0.05 g) were each recrystallized from equimolar combinations of the PYR and MP guests (combined amount, 5 mmol) in glass vials. The vials were closed and stored in a cold-room at 0 °C. The crystals that formed were treated in the same manner as in the single solvent experiments. GC–MS was employed in order to determine the guest:guest ratios here (with dichloromethane as the solvent), while ¹H-NMR spectroscopy provided the overall H:G ratios.

Competition experiments using varied molar concentrations of binary guest mixtures

OED and SED (0.05 g) were independently recrystallized from binary mixtures of PYR and the MP isomers but the concentrations of these guests were varied (a total of 5 mmol was used). The molar guest 1:guest 2 ratios ranged from 20:80 to 80:20. Vials were treated as per the equimolar experiments and the crystals that formed as well as the solution from which they formed were analysed by means of GC–MS. The host selectivity profiles (Fig. 1a–f) were obtained by plotting the molar fraction of the guest in the crystal (Z) against that of the same guest in the solution (x). The selectivity coefficient for the resultant selectivity profiles was calculated using the equation $K_{A:B} = Z_A/Z_B x$ X_B/X_A , where $X_A + X_B = 1$ [23]. The mole fraction of guest A in the liquid mixture is given as X_A and the amount of the same guest present in the crystal as Z_A .

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Compliance with ethical standards

Conflict of interest There are no conflicts to declare.

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