Selective inclusion of phenylenediamine isomers by 1,1-bis(4-hydroxyphenyl)cyclohexane †

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The title host compound includes *para*- and *ortho*-phenylenediamine. The structures of the clathrates are stabilized by a network of hydrogen bonds. Competition experiments in solution and suspension show that the *para*-isomer is preferentially enclathrated. The inclusion compounds can also be formed by solid–solid reactions.

Introduction

The separation of close isomers by clathrate formation is industrially important because it is simple, efficient and is not energy intensive. The process relies on molecular recognition between host and guest molecules, and typically consists of dissolving an appropriate host compound in a mixture of two or more guests, allowing the formation of a crystalline inclusion compound which is enriched with respect to a particular guest. The inclusion compound is filtered and the enriched guest released by gentle warming, so that the host compound can be recycled. Depending on the selectivity of the process, separation of the targeted guest of >90% is usually achieved in at least three cycles.

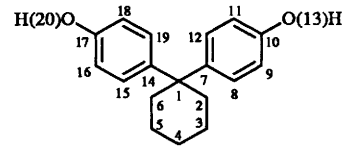
We have used a number of diol host compounds for isomer separation. These molecules typically consist of rigid, bulky groups, in order to provide suitable cavities in the crystal structure which will accommodate a guest. In addition, the hydroxy function can engage in hydrogen bonding, giving rise to 'coordinatoclathrates'.[2]

We have studied the inclusion compounds formed between 1,1,2,2-tetraphenylethane-1,2-diol and isomers of lutidine, and have shown that 3,5-lutidine is preferentially included over 2,6-lutidine.[3] The use of cholic acid as a selective host has also been demonstrated and the structures of its inclusion compounds with aniline and nitrobenzene have been elucidated. The latter guest is preferentially enclathrated and the competition was monitored by differential scanning calorimetry.[4] We have also studied the selective inclusion of phenol derivatives by tetraalkylammonium salts. In this study we demonstrated the viability of solid–solid reactions for the formation of inclusion compounds.[5]

The host compound 1,1-bis(4-hydroxyphenyl)cyclohexane forms inclusion compounds with a variety of guests, and its structures with water and ethanol have been elucidated.[6] The separation of phenol and cresols has been studied in detail, and the observed selectivity has been related to the topological complementarities occurring in the crystal structures.[7] This has also been carried out for cyclohexanol and cyclohexanone.[8]

In this work we present the results of the competition experiments carried out between this host and the isomers of phenylenediamine, and discuss the selectivity in terms of the interactions derived from the crystal structures.

† Complexation with diol host compounds. Part 21. For Part 20 of this series, see ref. 1.



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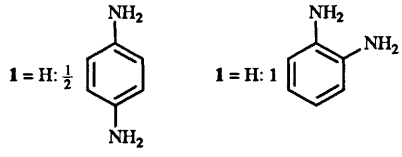

Scheme 1

Experimental

The inclusion compounds **1** and **2** were obtained by dissolving stoichiometric quantities of the host compound (**H**) and the phenylenediamine (PDA) in a minimum of ethyl acetate. Suitable crystals were obtained by slow evaporation over a period of 5 days. Preliminary cell dimensions and space group symmetry were determined photographically and subsequently refined by standard procedures on a CAD4 diffractometer. The intensities were collected with the ω–2θ scan mode and crystal stabilities were monitored by periodic reference reflections. The intensities were corrected for Lorentz and polarization effects, and the important crystal data and experimental details are given in Table 1. Both structures were solved by direct methods using SHELX-86,[9] and refined using full-matrix least-squares using SHELX-93,[10] refining on F^2.‡ The numbering scheme used is shown in Scheme 1.

In the final model, the aromatic and methylene hydrogens were geometrically constrained [d(C–H) = 1.00 Å] and assigned common isotropic temperature factors. The amino hydrogens were all independently located in difference electron density maps, and refined with a simple bond length constraint.[11]

‡ Crystallographic data has been deposited under the Cambridge Crystallographic Data Deposition Scheme. For details of the scheme see 'Instructions for Authors (1995)', *J. Chem. Soc., Perkin Trans. 2*, 1995, issue 1.

Table 1 Details of crystals, data collections and final refinements

Parameter	1	2
Molecular formula	$C_{18}H_{20}O_2 \cdot \frac{1}{2}C_6H_6N_2$	$C_{18}H_{20}O_2 \cdot C_6H_6N_2$
Molecular weight/(g mol^{-1})	322.41	376.48
Space group	$P2_1/c$	$C2/c$
a/Å	6.362(2)	21.080(2)
b/Å	26.610(3)	6.202(8)
c/Å	10.509(2)	32.132(2)
β/°	106.77(2)	101.88(6)
V/Å^3	1703.4(6)	4110.9(7)
Z	4	8
D_c/g cm^{-3}	1.257	1.217
D_m/g cm^{-3}	1.245	1.207
μ(Mo-Kα)/cm^{-1}	0.80	0.77
F(000)	692	1616
Data collection (20 °C)		
Crystal size/mm	0.3 × 0.2 × 0.3	0.4 × 0.5 × 0.5
Range scanned, θ(°)	1–25	1–25
Range of indices	h: ± 7; k: 0, 31; l: 0, 12	h: ± 24; k: 0, 7; l: 0, 38
Crystal decay (%)	3.0	7.0
No. reflections collected	3254	4049
No. reflections observed [$I_{rel} > 2\sigma(I_{rel})$]	2091	2722
No. parameters	236	279
R	0.0406	0.0479
R_w	0.1021	0.1334
w	$1/[\sigma^2(F_o^2) + (0.0773 \times P)^2 + (1.75 \times P)]$ $P = [\mathrm{Max}(F_o^2, 0) + 2 \times F_c^2]/3$	$1/[\sigma^2(F_o^2) + (0.1062 \times P)^2 + (3.37 \times P)]$ $P = [\mathrm{Max}(F_o^2, 0) + 2 \times F_c^2]/3$
S	0.850	0.977
Max. shift/esd)	0.024	0.420
$\Delta\rho$ excursions/e Å^{-3}	0.161; −0.202	0.281; −0.285

Competition experiments

We carried out competition experiments between the *p*-PDA and *o*-PDA guests by dissolving 0.0268 g (0.1 mmol) of host **H** in 3 cm^3 ethyl acetate in 11 tubes. To these we added a mixture of the two guests (total 0.054 g = 0.5 mmol), varying their mole fraction from 0 to 1. The ratio of **H** to combined guest was 1:5. The solutions were filtered through Millex micropore filters and sealed. The inclusion compounds were allowed to crystallise, filtered, dried and redissolved in ethyl acetate. The relative amounts of the two isomers were anlysed by GC using a Carlo Erba Fractovap 4200 instrument equipped with a BP255 capillary column (0.25 mm diameter, 25 m length) and a Spectra-Physics SP4290 integrator.

We repeated the competition experiments with the host in water suspension, shaken for 1 h with varying proportions of the dissolved guests. The molar ratio of the host:combined guests was again 1:5. The solid was filtered, dried and the relative proportions of the two guests analysed as before. The experiment was repeated with the *p*-PDA–*m*-PDA and *m*-PDA–*o*-PDA pairs of isomers.

Solid–solid reactions

We have carried out the synthesis of the host–guest compounds by grinding stoichiometric quantities of **H** with *p*-PDA and *o*-PDA. The powders were ground in a stainless steel tube containing a steel ball and shaken vigorously for 15 min in a Wigglebug (Grindex) apparatus. The resulting compounds were analysed by X-ray powder diffractometry.

Results and discussion

For **1**, the space group is $P2_1/c$ and the unit cell contains four host molecules, located at general positions, while the two *p*-PDA guest molecules are located on centres of inversion. The details of the hydrogen bonding are shown in Fig. 1(*a*) which clearly displays the cyclic scheme linking O(20), O(13) and N(21). Thus each *p*-PDA guest is stabilized by four hydrogen bonds.

The packing of the structure is shown in Fig. 1(*b*), viewed along [100]. The guest molecules lie in channels formed by opposing phenolic moieties of the host

For **2**, the space group is $C2/c$ and no crystallographic symmetry is imposed on either host or guest molecule. Fig. 2(*a*) again displays a cyclic hydrogen bonding scheme linking O(20), O(13) and N(21), but the other amine moiety, N(22), is not hydrogen bonded. The *ortho*-guest therefore is only stabilized by two hydrogen bonds. The hydrogen bonding details of both structures are given in Table 2. The packing diagram of **2** is shown in Fig. 2(*b*). The host and guest molecules form alternating layers parallel to the *ab* plane, similar to the arrangement between this host and phenol and the isomers of cresol.[7]

We have compared the host species conformation and the asymmetry parameters of the cyclohexane moiety of **1** and **2** with those found in previous determinations.[6–8] In all cases, the asymmetry parameters as defined by related endocyclic torsion angles,[12] have values below 5°, showing that the cyclohexane moiety is in an almost perfect chair conformation. The salient torsion angles of the host molecule in **1** and **2** and of other inclusion compunds with **H** are given in Table 3.§ The interesting parameters relating to the conformation of the phenyl rings are given by the two torsion angles C(6)–C(1)–C(7)–C(8) and C(6)–C(1)–C(14)–C(19). These values are similar for the structures of the ethanol, phenol and cresol inclusion com-

§ Tables of torsion angles, bond angles around C(1), and asymmetry parameters of inclusion compounds with **H** have been deposited. For details of the Supplementary Publications Scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1995, issue 1 [Supp. Pub. No. 57082 (3 pp.)].

Table 2 Hydrogen bond data for **1** and **2**

Compound	Donor	Acceptor	D–H/Å	D···A/Å	D–H···A(°)
1	O(20)	N(21)[a]	0.98(3)	2.742(0)	167(3)
	O(13)	O(20)[b]	0.93(3)	2.798(3)	168(3)
	N(21)	O(13)[c]	0.96(2)	3.144(3)	151(2)
2	O(13)	N(21)	0.95(2)	2.676(3)	171(3)
	O(20)	O(13)[d]	0.97(3)	2.675(3)	172(3)
	N(21)	O(20)[e]	0.98(2)	2.990(4)	164(3)

Symmetry code: (*a*) $1 - x, 1 - y, 1 - z$; (*b*) $x, y, z + 1$; (*c*) $1 - x, 1 - y, 2 - z$; (*d*) $x - \frac{1}{2}, y + \frac{1}{2}, z$; (*e*) $x + \frac{1}{2}, y + \frac{1}{2}, z$.

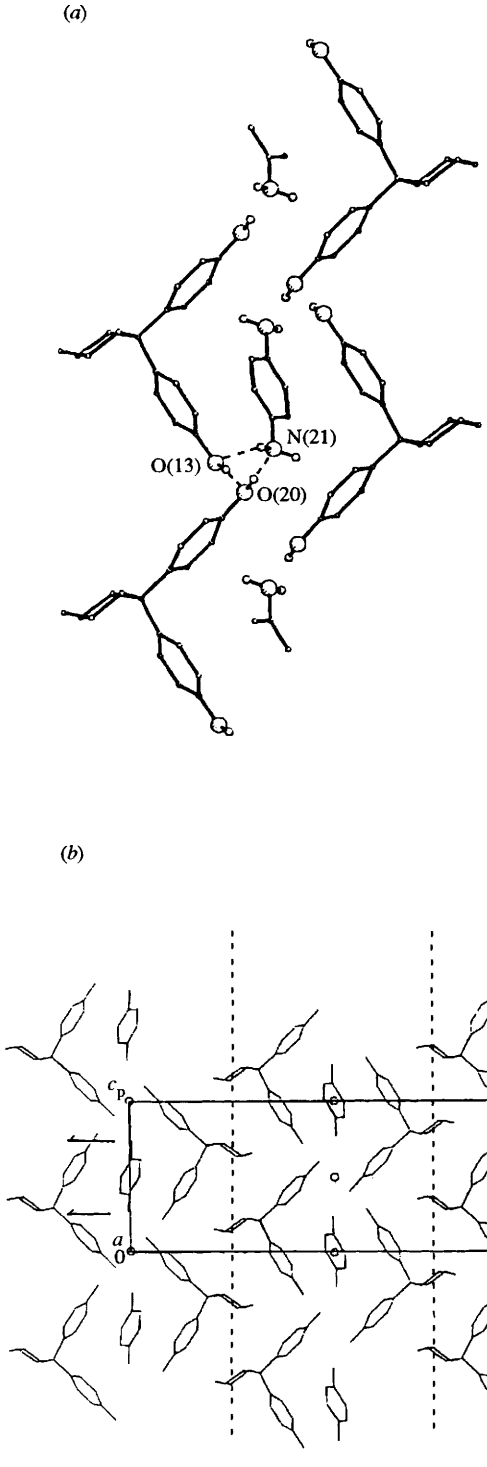

Fig. 1 (*a*) Hydrogen bonding scheme of compound **1**; (*b*) packing diagram of **1** viewed along [100]

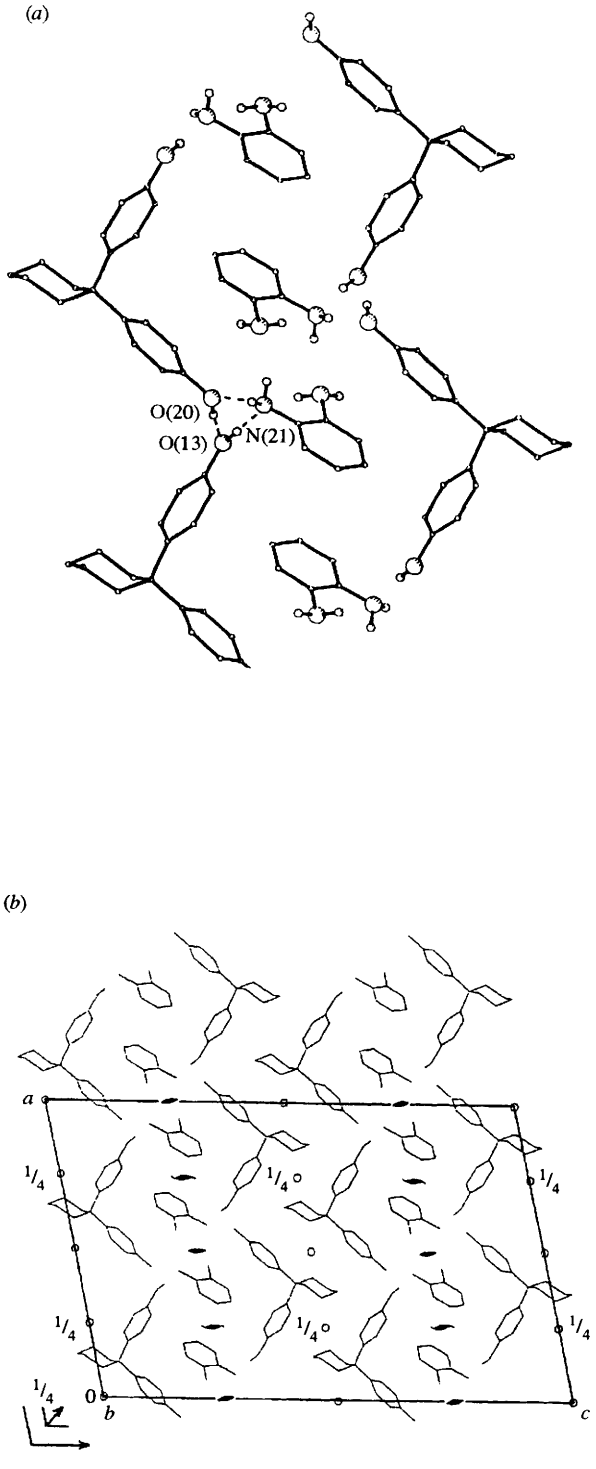

Fig. 2 (*a*) Hydrogen bonding scheme of compound **2**; (*b*) packing diagram of **2** viewed along [010]

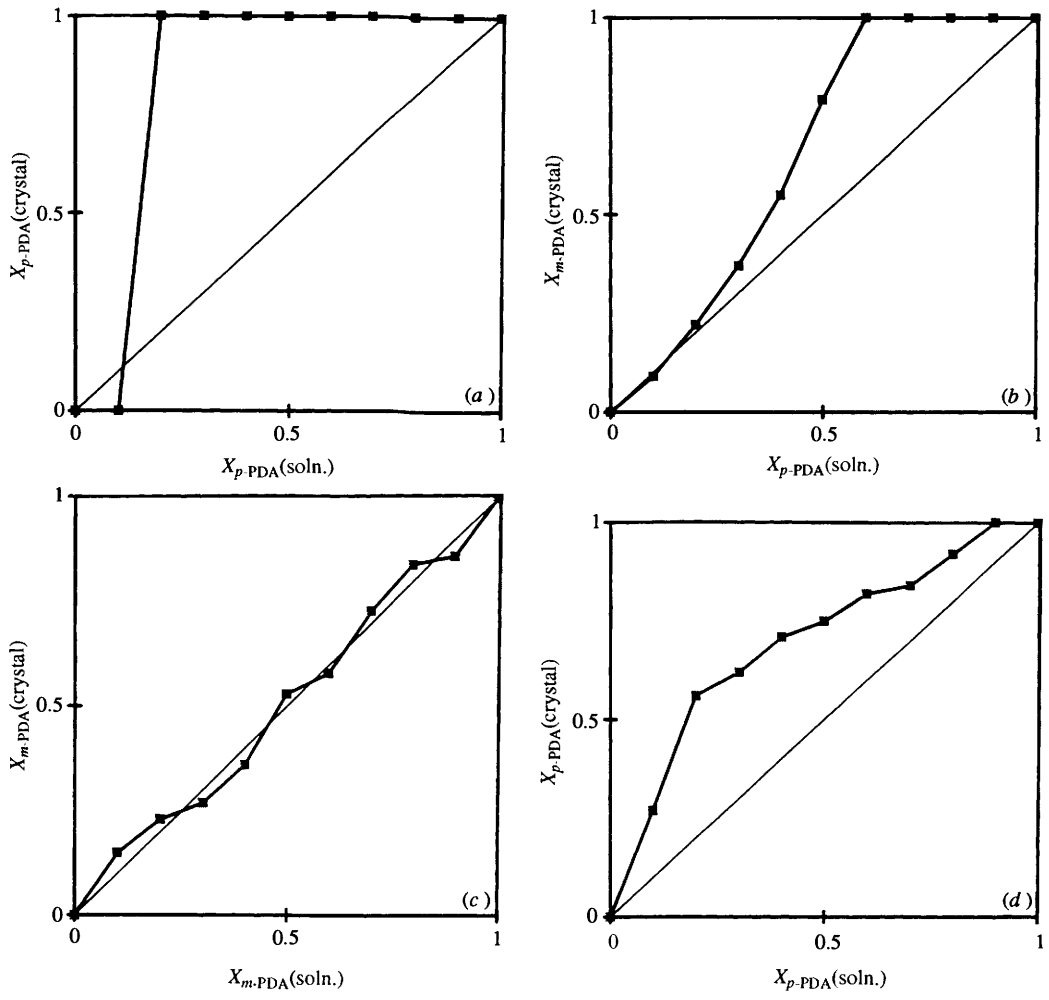

Fig. 3 Competition experiments of: (*a*) *o*-PDA *versus p*-PDA in solution: (*b*) *o*-PDA *versus p*-PDA in water suspension; (*c*) *o*-PDA *versus m*-PDA in water suspension: (*d*) *p*-PDA *versus m*-PDA in water suspension

Table 3

Torsion angle	1	2	H·H_2O	Average[a]
C(6)–C(1)–C(7)–C(8)	−20.2(1)	−13.0(1)	−38.2(1)	−48.6(1)
C(6)–C(1)–C(14)–C(19)	54.8(1)	69.3(1)	24.1(1)	−2.4(1)

[a] The average of the relevant torsion angles of H·EtOH; H·Phenol; H·Cresols.

pounds, but vary considerably for the structures where the guests are water and the phenylenediamines. This strongly suggests that the enclathrating abilities of this host compound lie in its torsional flexibility about the C–C bonds joining the phenyl moieties to the central atom C(1). This is reminiscent of the Werner clathrates, in which substituted pyridines, co-ordinated to a central metal atom, show torsional flexibility and thus enclathrate a variety of aromatic guests.[13]

The angles subtended at C(1) show a small variation around the tetrahedral value (range 106.1–112.8°), and the intra-molecular bond lengths in **1** and **2** are similar to those found in the related inclusion compounds.[6–8]

The results of the competition experiments are shown in Fig. 3. From the solution experiment of the *para- versus ortho*-isomers, the *p*-PDA is strongly favoured, giving 100% selectivity beyond $X_{p\text{-PDA}}$ of 0.1.

The suspension experiments were less dramatic, but the *para*-isomer is again favoured over both the *o* and *m*-PDA isomers. There is very little difference in selectivity between the *m*- and *o*-PDA isomers.

The inclusion compounds are also formed by grinding the two solids. Fig. 4 compares the X-ray powder diffraction patterns of the crystals derived from solution, the solid–solid reaction and the pattern generated by the program Lazy Pulverix[14] employing the coordinates obtained from the single crystal study. The results are given for *o*-PDA, but similar results were obtained for *p*-PDA. Interestingly, we also carried out a competition experiment in the solid state by grinding **H**:*p*-PDA:*o*-PDA in the molar ratio $1:\frac{1}{2}:1$. We then placed the ground sample in a drying pistol at 160 °C under vacuum, and after 1 h part of the specimen had sublimed. This was analysed by GC and proved to be predominantly the *o*-PDA isomer (94% pure, 87% yield).

The structures of **1** and **2** are characterized by the hydrogen bonding occurring between host and guest. The important feature is that the *p*-PDA is stabilized by four hydrogen bonds per guest molecule, while the *o*-PDA is only stabilized by two. We suggest therefore that this gives the *para*-isomer the additional stability which allows it to be selected preferentially in the competition experiments.

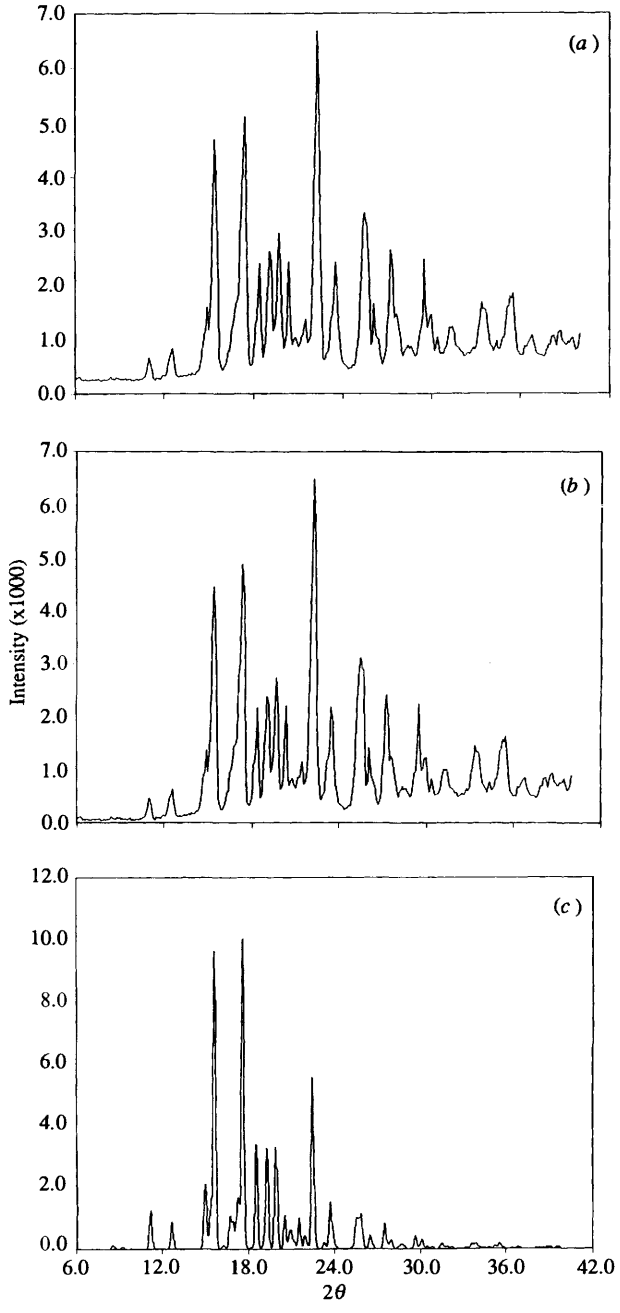

Fig. 4 (*a*) Experimental powder pattern: *o*-PDA + **H** from solution; (*b*) experimental powder pattern: *o*-PDA + **H** ground; (*c*) calculated powder pattern for compound **2**

The results provide evidence that the inclusion phenomenon is a useful tool for the molecular separation of similar molecules. The degree of interaction between the host and guest species in each of the complexes is an indication of the stability of the complexes. The preferential complexation of the host with *p*-PDA out of the mixture of isomers therefore agrees well with the structural features of the complex formed.

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