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Host behaviour of related compounds, TETROL and DMT, in the presence of two different classes of aromatic guest compounds

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ABSTRACT

The host potential of two closely-related compounds, TETROL [(+)-(2R,3R)-1,1–4,4-tetraphenylbutane-1,2,3,4-tetraol] and DMT [(−)-(2R,3R)-2,3-dimethoxy-1,1,4,4-tetraphenylbutane-1,4-diol], were compared when recrystallized from two different classes of guests, namely toluene, ethylbenzene, cumene and aniline, *N*-methylaniline, *N*,*N*-dimethylaniline. TETROL formed complexes with only aniline and *N*-methylaniline (host:guest ratios, 2:3 and 2:4), while DMT included all six guests with a consistent ratio (2:1). Aniline competition experiments showed that TETROL preferred aniline (67%), followed by *N*-methyl- (29%) and *N*,*N*-dimethyl- (4%) aniline; surprisingly, this order was exactly reversed for DMT [*N*,*N*-dimethylaniline (62%) > *N*-methylaniline (32%) > aniline (6%)]. Crystal diffraction analyses revealed that TETROL formed stabilizing hydrogen bonds with guests, behaving as both donor and, for the first time, acceptor (in 2TETROL•4N-methylaniline). DMT did not form bonds of this type with any guests. Furthermore, the host packing was isostructural for all DMT complexes but was guest-dependent for TETROL. Thermal analyses showed that complex stabilities correlated precisely with the host preferences.

1. Introduction

Host-guest chemistry is a burgeoning field within supramolecular chemistry, and considerations of host-guest methodologies and their applicability to the chemical industry are becoming increasingly pertinent [1]. One promising application of host-guest chemistry is the separation of mixtures of positional isomers which typically have similar physical properties and, therefore, frequently do not respond favourably to traditional separation methods [2]. Consequently, the selective inclusion by host materials of a particular guest species from such mixtures is an attractive attribute that may be exploited to potentially address this challenge. For example, industrial processes relying on single isomers of each of the cresols, xylenes and methylanisoles, amongst others, would benefit considerably if a simple method existed for their purification, since such isomers are widely used as precursors to an array of valuable end-products.

Kuhn et al. [3] have reviewed chiral separations by capillary zone electrophoresis and micellar electrokinetic capillary chromatography, which often involve host-guest chemistry principles, and have illustrated the potential of such methods. In particular are mentioned the host materials cyclodextrin and chiral crown ethers for these applications. Additionally, host materials may have the ability to enclathrate drug actives and, in so doing, improve the transport, activity, resistance, solubility, and overall drug delivery of these actives into the human body [4]. Other plausible applications include the removal of hazardous materials from the environment, improving the taste and stability of food products, asymmetric synthesis, and gas storage [5–9].

We have recently reported on the host behaviour of (−)-(2R,3R)-2,3-dimethoxy-1,1,4,4-tetraphenylbutane-1,4-diol (DMT, Scheme 1) in the presence of various mixtures of xylenes [10] and anilines [11]. These investigations were prompted by the fact that each of the guests in both series are employed as building blocks for a wide variety of industrially-important products, and challenges have been encountered in their isolation and purification [12,13]. TETROL [(+)-(2R,3R)-1,1–4,4-tetraphenylbutane-1,2,3,4-tetraol, Scheme 1] is closely related to DMT in that its two secondary hydroxyl functionalities are further derivatized as methoxyl moieties. This subtle

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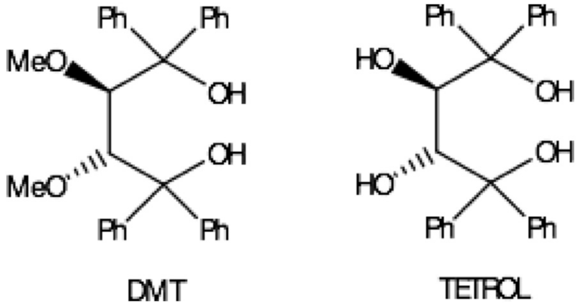

Scheme 1. Structures of related hosts DMT and TETROL.

change in host structure significantly changed the behaviour of the host when recrystallized under the same conditions in the presence of isomeric toluidine mixtures [14]: TETROL showed a marked increase in selectivity compared with DMT, but both host materials preferred the same guest (*p*-toluidine) in these competition experiments.

In the present work, we have investigated and compared the selective behaviour of TETROL and DMT when recrystallized from guest solvents comprising two different classes of aromatic compounds, namely the alkylated aromatics toluene, ethylbenzene and cumene, and the aminated aromatics aniline, *N*-methylaniline and *N*,*N*-dimethylaniline. Surprisingly, the preference order of DMT for the anilines [11] contrasted with that of TETROL; however, the extent of the selectivity for their preferred guests was comparable. These observations are distinctly different from the results obtained from the toluidine work, where TETROL was observed to be significantly more selective than DMT [14]. We employed single crystal diffraction analyses in order to ascertain the reasons for these differences, and thermal analyses to investigate the stabilities of all complexes formed, and report on these results here.

2. Results and discussion

2.1. *Synthesis of DMT and TETROL*

Both host materials were prepared from naturally-occurring (+)-diethyl L-tartrate using published methods [10,15].

2.2. *Assessment of the inclusion ability of DMT and TETROL with the alkylated and aminated aromatic guests*

2.2.1. *Single-solvent recrystallizations*

Single solvent experiments were performed by dissolving each host individually in an excess of the six aromatic guest solvents, and the vessels left open under ambient conditions until crystallization occurred. The resulting solids were collected by vacuum filtration, washed with petroleum ether (b.p. 40–60 °C), and analysed by means of ^{1}H NMR spectroscopy using $CDCl_3$ as the solvent. Where inclusion complex formation occurred, the H:G ratios were determined from appropriate host and guest compound resonance integrals. Table 1 summarises these results.

It is clear from this table that TETROL is significantly more discriminating than DMT, including only aniline and *N*-methylaniline from the list of six possible guests, and showed no affinity at all for the alkylated benzenes. DMT, on the other hand, formed complexes with all six solvents. Furthermore, H:G ratios in the case of complexes with TETROL were guest-dependent with aniline and *N*-methylaniline being included with 2:3 and 2:4 H:G ratios, respectively. In contrast, DMT favoured the 2:1 ratio in every instance.

Table 1
Host:guest (H:G) ratios of complexes obtained when TETROL and DMT were recrystallized individually from the six aromatic guests species.

Guest	TETROL	DMT
Toluene	[a]	2:1
Ethylbenzene	[a]	2:1
Cumene	[a]	2:1
Aniline	2:3	2:1[b]
N-Methylaniline	2:4[c]	2:1[b]
N,*N*-Dimethylaniline	[a]	2:1[b]

[a] These guests were not clathrated.
[b] These results were published on a prior occasion and are inserted here for ease of comparison [11].
[c] Subsequent diffraction analyses showed the asymmetric unit to contain two host and four guest molecules.

2.2.2. *Equimolar mixed-solvent recrystallizations*

We subsequently conducted competition experiments using various combinations of the three alkylated and, independently, the three aminated aromatics in order to determine the effect of the availability of multiple guests on the inclusion behaviour of the host. In each case, the host was recrystallized from equimolar combinations of the guest solvent. The equimolar condition was maintained by storing the vessels at 0 °C after dissolution of the host. Where crystals formed, these were processed as in the single-solvent experiments. Table 2 (aminated aromatics) and 3 (alkylated aromatics) summarise the data obtained. Note that since none of the alkylated aromatics were included by TETROL, competition studies for this class of compounds and this host were disregarded.

These data reveal that TETROL has a distinct preference for including aniline whenever this compound was present in the recrystallizing mixture (Table 2). From the aniline/*N*-methylaniline and aniline/*N*,*N*-dimethylaniline binary mixtures, TETROL extracted 68 and 95% aniline, respectively. An *N*-methylaniline/*N*,*N*-dimethylaniline experiment, on the other hand, failed to furnish crystals and when aniline was also added, a host preference order of aniline (67%) > *N*-methylaniline (29%) > *N*,*N*-dimethylaniline (4%) was noted. In contrast to TETROL, DMT afforded a host selectivity order of *N*,*N*-dimethylaniline (62%) > *N*-methylaniline (32%) > aniline (6%) [11]. Furthermore, it is noteworthy that the extent of these host selectivities are comparable (62, 32, 6 *versus* 67, 29, 4) though for different guests. The selectivity of DMT in the aniline series appears to correlate with increasing polarity of the aniline guest compound, while the opposite is true for TETROL.[1]

In the case of the alkyl benzenes, binary competition experiments showed that DMT selected toluene (67%) and ethylbenzene (63%) in preference to cumene (33 and 37%, respectively, Table 3). When the host was recrystallized from an equimolar toluene/ethylbenzene mixture, toluene was only marginally preferred (51% *vs* 49%). A ternary competition experiment comprising all three alkyl aromatics resulted in poor selectivity with an order ethylbenzene (39%) > toluene (35%) > cumene (26%) being obtained. On the face of it, the inclusion selectivity displayed by DMT seems to correlate with the polarities of the guest compounds insofar as it exhibited higher selectivity in a ternary mixture of the three anilines (Table 2), while the inclusion selectivity was poor in a ternary mixture of the relatively non-polar alkyl benzene guests.

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[1] The dipole values for aniline, *N*-methylaniline and *N*,*N*-dimethylaniline, computed at the ωB97X-D/6-31G* level, are 1.69, 1.73 and 1.79, while those for toluene, ethylbenzene and cumene are 0.33, 0.29 and 0.27 Debye, respectively.