CRYSTALLINE COMPLEXES OF N,N'-DITRITYLUREA (DTU) AND N-TRITYLUREA (NTU) HOSTS WITH MOLECULAR GUESTS

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ABSTRACT. *This paper reports crystalline complexes of the new hosts N,N'-ditritylurea (DTU) and N-tritylurea (NTU) with various uncharged molecular guests. The crystal structures of the following complexes were elucidated by single crystal X-ray diffraction analysis at 115°K: (I) 1:1 DTU-propanamide - space group C2/c, a=15.839Å, b=9.088Å, c=24.584Å, β=111.05°, Z=4; (II) 1:1 DTU-ethyl N-acetylglycinate - space group P1̄, a=9.010Å, b=10.800Å, c=19.810 Å, α=105.29°, β=94.33°, γ=93.03°, Z=2; (III) 2:1 NTU-N,N-dimethylformamide - space group Cc, a=29.614Å, b=8.906Å, c=16.127Å, β=121.04°, Z=4. The three crystal structures are stabilized mainly by a cooperative effect of hydrogen bonding between amide fragments displaced along the shortest axis of each crystal. This interaction occurs between host and guest in complexes I and II, and between host and host in complex III. The latter also represents a cage-type clathrate in which the guest molecules are accommodated in voids between the hydrophobic fragments of four neighboring NTU hosts. On the other hand, complexes of DTU are characterized by a more specific interaction between the two components, each guest molecule being inserted between two adjacent hosts (related by translation) and strongly bound to them via hydrogen bridges. These results illustrate a useful concept in the design of molecular species which can be potential hosts upon crystallization with neutral molecular guests.*
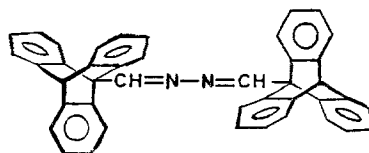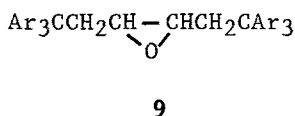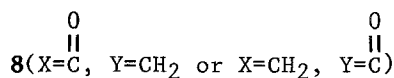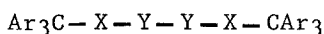
KEY WORDS. Host-guest complexation of molecular guests. Molecular design for hosts.

1. INTRODUCTION

In a recent communication [1] we proposed a new molecular design for hosts in crystalline host-guest complexes. Compounds with a long molecular axis, and with large, relatively rigid groups at each end are expected to function as hosts. Such molecules are most likely to pack well in a crystal when aligned (roughly) along the long molecular axis. The large end groups, however, act as "spacers" which prevent the hosts from packing closely. The voids thus created are expected to follow the long molecular axis of the host, and, if occupied by guest molecules, will result in channel-type complexes.

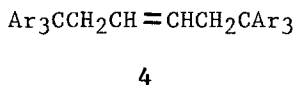This design for hosts was generalized from Toda's initial observations [2] that diacetylenic diols **1** form crystalline stoichiometric host-guest complexes with a variety of small molecules. X-ray structures [2,3] of these complexes showed that they are of the channel type and conform to our proposal. We have extended this design for hosts to structures of the type **2-10** [1].

$$Ar_2\underset{\underset{OH}{|}}{C} - C \equiv C - C \equiv C - \underset{\underset{OH}{|}}{C}Ar_2$$

1

$$Ar_3C - (C \equiv C)_n - CAr_3$$

2(n=2,3)

$$Ar_3C - CH = CHCH = CH - CAr_3$$

3

$$Ar_3CCH_2CH = CHCH_2CAr_3$$

4

$$Ar_3C - (CH_2)_n - CAr_3$$

5(n=4,6)

$$Ar_3C - CH = N - N = CH - CAr_3$$

6

$$Ar_3C - XCH_2CH_2X - CAr_3$$

7(X=O,NH)

$$Ar_3C - X - Y - Y - X - CAr_3$$
$$\overset{O}{\overset{\|}{}} \qquad\qquad\qquad \overset{O}{\overset{\|}{}}$$
8(X=C, Y=CH$_2$ or X=CH$_2$, Y=C)

$$Ar_3CCH_2CH \underset{\diagdown O \diagup}{-} CHCH_2CAr_3$$

9
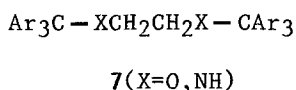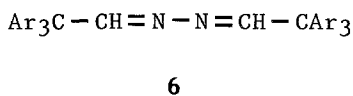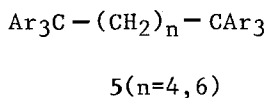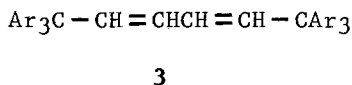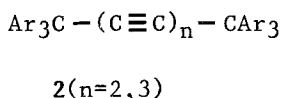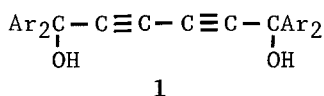
10

Each of these hosts formed stoichiometric complexes with a number of small molecules, such as benzene, toluene, xylenes, and chloroform. In most of these hosts Ar=phenyl, but substituted phenyls (including 4'-biphenylyl) have also been used and example **10** shows that the rigid 1-triptycyl group may also function as the 'spacer' [4]. The long molecular axis can be linear, as in **1** and **2** or 'bent' as in **3-10**. The double bonds or rings in **3**, **4**, **6**, **9**, and **10** have *trans* geometry, and in **5** and **7**, the methylene chains are extended and

staggered.

     With the idea in mind of including in the long molecular axis
functionality which could form hydrogen bonds with guest molecules
and add this strengthening feature to that of overall molecular shape,
we were led to prepare N,N'-ditritylurea (DTU) **11** and examine its
capacity to act as a host in crystalline complexes. The amide groups
in DTU would be expected to add rigidity to the long molecular axis,
and the hydrogen bonding feature would be expected to favor
complexation with polar guests [5]. We were pleased to find that
DTU does function as a host for a wide variety of guests, and report

$$(C_6H_5)_3CNHCNHC(C_6H_5)_3 \qquad (C_6H_5)_3CNHCNH_2$$

with the two $\overset{O}{\overset{\|}{}}$ groups shown above each carbonyl.

11 (DTU)   **12 (NTU)**
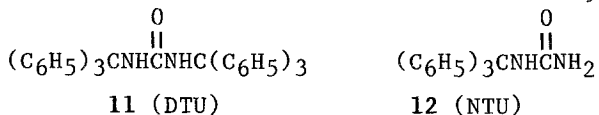
here on the structures of some of these complexes. At the same time
we also prepared N-tritylurea (NTU) **12**, and found that it too can
form complexes, though the one we have examined in detail so far
has a very different type of host-guest interaction from the complexes
of DTU.

     DTU contains two component moieties which have a famous history
in the field of inclusion compounds, urea [6] and triphenylmethane
[7]. It is perhaps therefore somewhat surprising that the capacity
of DTU to function as a host has not been previously studied. As
described below, however, the complexes formed by DTU are unique
and entirely different from those formed by either of its component
moieties.

2.   SYNTHESIS AND EXPERIMENTAL PROCEDURES

DTU and NTU were prepared by the reaction of trityl isocyanate with
tritylamine or ammonia, respectively, according to literature
procedures [8].

     DTU complexes were prepared by dissolving the host in hot ethyl
acetate, then adding five equivalents of the guest and allowing the
solution to gradually cool. The formation of a complex was established
by determining the solution NMR spectrum of the resulting crystals,
and the host/guest ratio was measured by NMR integration and confirmed
by elemental analysis.

     NTU complexes were prepared similarly, but using hot ethanol
as the solvent and adding ten equivalents of guest.

     X-ray diffraction data were measured initially at room temperature
on an CAD4 diffractometer equipped with a graphite monochromator,
using MoKα (λ=0.7107Å) radiation and the ω-2θ scan technique. After it
was realized that some of the guest components are disordered in

the crystal lattice, additional data sets were collected at $ca.$ 115°K on a Syntex $P\bar{1}$ automated diffractometer, using CuKα (λ = 1.5418Å) radiation. The results reported below are based on the low-temperature measurements, and refer to the following inclusion complexes of DTU and NTU:

I.   DTU - propanamide (1:1) $C_{39}H_{32}N_2O.C_3H_7NO$
II.   DTU - ethyl N-acetylglycinate (1:1), $C_{39}H_{32}N_2O.C_6H_{11}NO$
III.   NTU - N,N-dimethylformamide (2:1) $(C_{20}H_{18}N_2O)_2.C_3H_7NO$

The unit-cell constants and pertinent details of the experimental conditions are summarized in Table 1. All analyzed crystals remained

Table 1. Summary of Crystal Data and Experimental Parameters at 115°K.

compound	I	II	III
formula weight	617.8	689.8	677.8
space group	$C\,2/c$	$P\bar{1}$	Cc
Z	4.0	2.0	4.0
a, Å	15.839(2)	9.010(3)	29.614(8)
b, Å	9.088(1)	10.800(3)	8.906(3)
c, Å	24.584(3)	19.810(9)	16.127(4)
α, deg.	90.0	105.29(3)	90.0
β, deg.	111.05(1)	94.33(3)	121.04(2)
γ, deg.	90.0	93.03(2)	90.0
V, Å^3	3302.6	1848.8	3644.3
d_c, g.cm^{-3}	1.242	1.239	1.235
2θ limits, deg.	0-150.0	0-150.0	0-150.0
no. of unique data	2634.0	4946.0	2476.0
data with I⩾3σ$_I$	2419.0	4377.0	2209.0
refined parameters	236.0	478.0	503.0
R	0.070	0.084	0.069
R_w	0.093	0.119	0.082

stable during the entire period (in fact, the same crystals were used for both room and low temperature studies), and no reduction or significant fluctuation in the intensity of standard reflections was observed. The data sets were not corrected for absorption or extinction effects.

The three crystal structures were solved by a combination of direct methods (MULTAN80) and fourier techniques. The amide hydrogen atoms were found directly from electron density difference maps at an intermediate stage of the refinement; the remaining hydrogens were introduced in calculated positions. The hydrogen atoms were assigned isotropic temperature factors (U=0.05), but their parameters were not refined. Least-squares refinement calculations were based on observations above the threshold of 3σ of the measured intensity.

The initial refinement of structure I was carried out in the noncentric space group Cc in order to construct a suitable model of the disordered propanamide, using a geometrically constrained framework for this species. From four possible orientations of the nearly planar and asymmetric propanamide only two turned out to be consistent with the results obtained from difference electron-density calculations. These two orientations were found to be equally occupied and related to each other by a rotation about a C_2 symmetry axis extending along the C=O bond of DTU. Consequently, the final structural model was refined successfully in space group $C2/c$, all geometric constraints imposed on the propanamide structure being removed at final stages of the calculations.

The refinement of structure II proceeded smoothly; the results indicated, however, a few excessively large parameters of thermal motion. These were associated primarily with the ethyl residue of the guest species and a peripheral fragment of one of the phenyl rings, exhibiting a gradual increase with the distance from the center of the hydrogen bonded complex (see below). Inspection of the intermolecular arrangement in the crystal provided a reasonable explanation; the above fragments are positioned in loosely packed sections of the crystal which correspond to very wide potential energy wells of the nonbonding van der Waals interactions. We tend to conclude, therefore, that the large temperature factors in question (Table 6) should preferably be interpreted as representing a broad "wagging" thermal motion rather than a statically disordered structure.

In the crystal structure of compound III only one of the methyls of the guest moiety is characterized by large parameters of thermal motion, indicative of its disordered location; positions of all the remaining atoms were determined with relatively high precision.

The final atomic coordinates along with the anisotropic thermal parameters for the three complexes are summarized in Tables 2-7 (supplementary material). Molecular dimensions obtained for the various molecules are in good agreement with common values found in related compounds, and are of little interest in the context of the discussion that follows.

3.   DTU COMPLEXES

No complex was formed when DTU was crystallized from pure ethyl acetate, hence the choice of this solvent for preparing complexes [9]. DTU formed 1:1 complexes with the following guests: methylene chloride, acetone, allyl alcohol, diethyl ether, methyl n-propyl ether, diethylamine, methyl n-propylamine, toluene, dimethylformamide, propanamide, 2-methylpropanamide, 2,2-dimethylpropanamide, benzamide, ethyl N-acetylglycinate, ethyl N-acetyl-L-alaninate, ethyl N-acetyl-L-methioninate and diethyl N-acetyl-L-aspartate. DTU also formed 1:2 complexes with methanol, ethanol, 1-propanol and 1-butanol, and a 2:1 complex with N,N,N',N'-tetramethylsuccinamide. Each of these complexes, on heating, becomes cloudy at some definite temperature (in the temperature range 125-230°C, and then melts sharply at 257-258°C, the melting point of uncomplexed DTU. We report here on the X-ray structures of the DTU complexes with propanamide and with ethyl N-acetylglycinate; structures of other complexes will be reported separately.

The molecular packing of the propanamide inclusion complex viewed down the shortest dimension of the unit-cell is shown in Figure la. The entire structure has a two-fold rotational symmetry, with the C=O bonds of DTU hosts coinciding with crystallographic two-fold axes and the propanamide guests being orientationally disordered about them. A characteristically unique association between the two components provides the main driving force for the formation of the crystalline inclusion compound. This can be appreciated by inspecting the intermolecular arrangement along the b axis, which reveals continuous chains of alternating host and guest moieties held together by an extensive network of hydrogen bonds between the amide fragments (Figure lb).
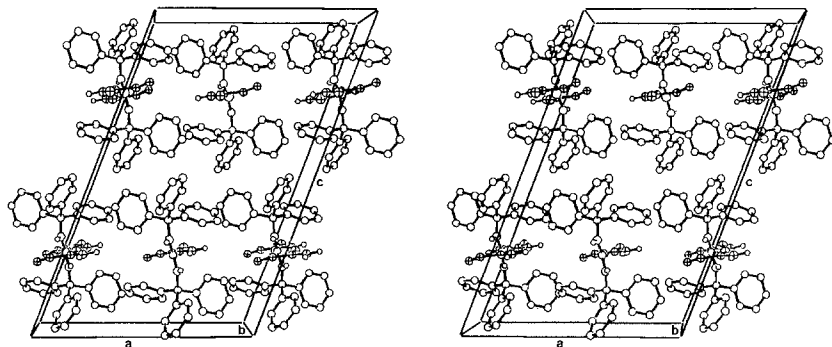

Figure la: Stereoview of the crystal structure of 1:1 DTU-propanamide; for clarity, only one orientation of the disordered guest is shown at each site.
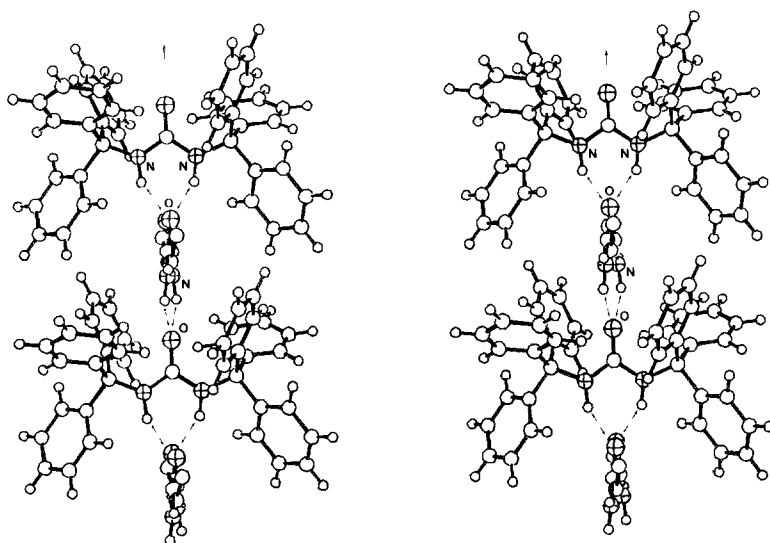
Figure 1b: Stereoview of the hydrogen-bonding association between DTU (the molecules shown are related by translation along *b*) and the orientationally disordered guest.

Along each such chain the C=O and the N—H groups of all molecules point in opposite directions, thus providing geometrical and functional complementary relationships for an effective interaction between the complex constituents. The functional groups of the guest are disordered above and below the mean plane defined by urea fragments translated along *b*, thus providing an additional stabilizing contribution to this structure (by increasing the entropy of the system). The geometry of the hydrogen bonding between host and guest is described by the following parameters: NH(host)···O(guest) = 2.868(5)Å, H···O = 1.95Å, N—H···O = 149°; NH_2(guest)···O(host) = 2.907(9)Å, H···O = 2.03Å, N—H···O = 149°. The spatial arrangement of the hydrogen-bonded aggregates referred to above is stabilized by van der Waals forces. They are closely stacked one on top of the other along the *a* axis of the unit-cell. Side-packing of these chains along *c* appears considerably less efficient due to the steric hindrance provided by the large trityl end-groups, which results in a relatively low density of the crystals (Table 1).

The crystal structure of the DTU complex with ethyl N-acetylglycinate is characterized by an entirely different space symmetry, $P\bar{1}$ vs. *C2/c*. Nevertheless, the main features of the intermolecular association are very similar to those described above. The DTU molecules are lined up along the *a* axis of the crystal, with their urea moieties being nearly coplanar (Figure 2a); the translation between adjacent units is 9.01Å as compared to 9.09Å in the previous example. Along this direction the guest species are included between the DTU hosts in an alternating manner, an arrangement evidently

stabilized by hydrogen bonding. Figure 2b indicates that each guest interacts simultaneously with two host molecules approaching from opposite sides. Thus, the guest NH function donates its proton to
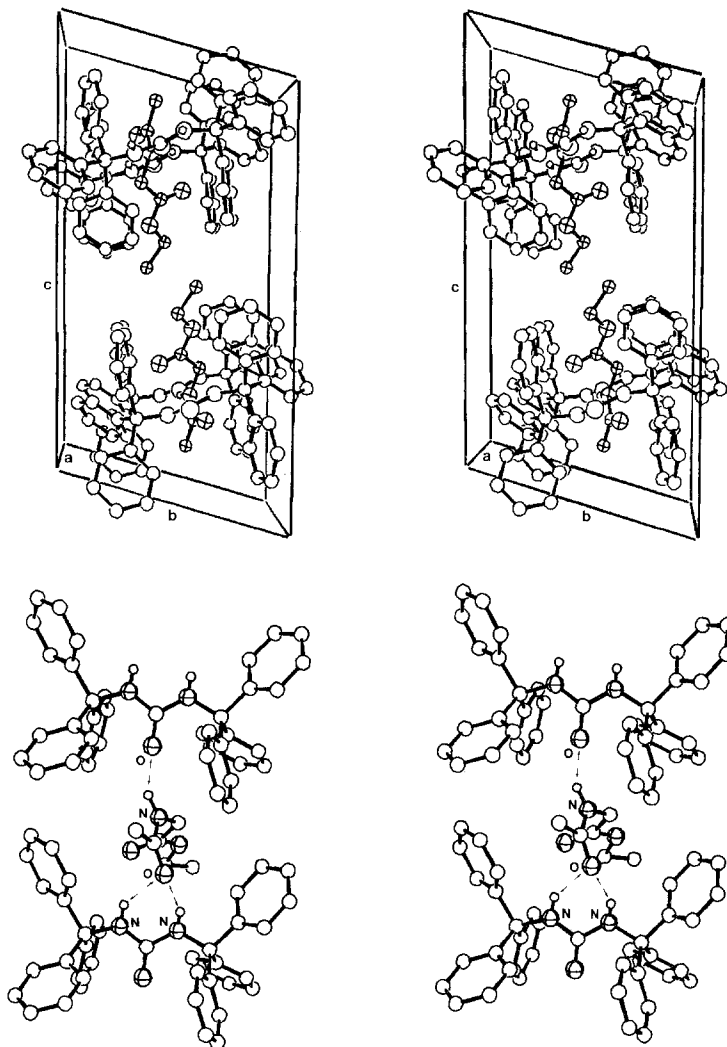

Figure 2. Stereoviews of (a) the crystal structure of 1:1 DTU-ethyl N-acetylglycinate, and (b) the hydrogen-bonding association of the guest to two adjacent hosts related by translation along a.

one host molecule [NH···O = 2.729(2)Å, H···O = 1.89Å and N—H···O = 153°], while the carbonyl group acts as proton acceptor from the two NH groups of another molecule [O···HN = 2.898(5) and 3.036(5)Å, O···H = 2.08 and 2.30Å, and O···H—N=150 and 138° respectively]. Correspondingly, every molecule of DTU is bound to two adjacent guests, thus forming a continuous array of hydrogen bonds along the a axis

of the crystal. As in the previous example, the alkyl residue of the guest is oriented in a direction roughly perpendicular to the plane of the urea fragment. In the present case, however, there is no disorder in the bonding region probably due to the elongated shape of the guest. The significance of the above described interaction between host and guest is even more emphasized by an observation that the ester part of the latter is not involved in any significant hydrogen bonding. Moreover, the long residues prevent an efficient stacking of the hydrogen-bonded chains along c, which is best reflected in a very broad wagging motion (in the ab plane) of several fragments located near the central section of the unit-cell.

4.   NTU COMPLEXES

The NTU complexes have not yet been investigated as fully as the DTU complexes, although as seen below their structures are also extremely interesting. NTU formed 2:1 complexes with N,N-dimethylformamide (DMF), N,N-dimethylacetamide and toluene. The X-ray structure of the DMF complex is described here.

An illustration of the crystal packing of this complex, given in Figure 3a, indicates an entirely different association between the two components than that observed for the complexes of DTU. It reveals a clathrate-type structure with the guest species being enclosed within lattice cavities formed by the trityl groups of four neighboring hosts. There is no structural evidence for any significant interaction between host and guest or between guest and guest other than through dispersion forces.
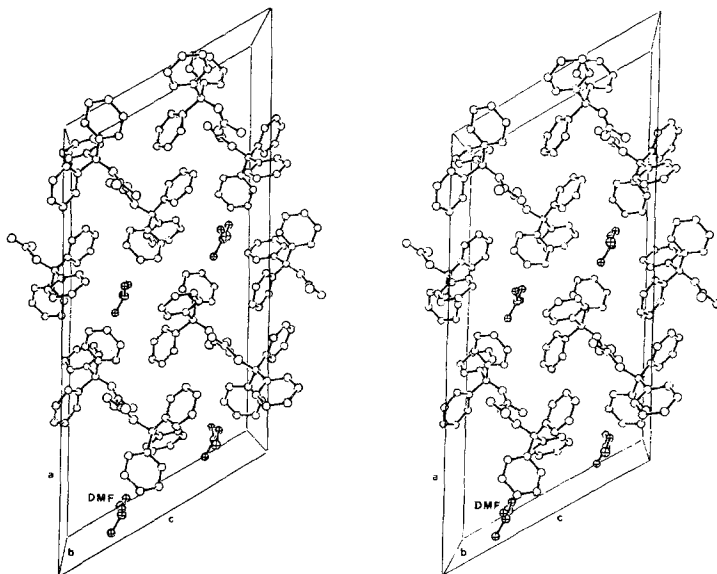

Figure 3*a*. Stereoview of the crystal structure of 2:1 NTU-DMF showing the lattice type inclusion.
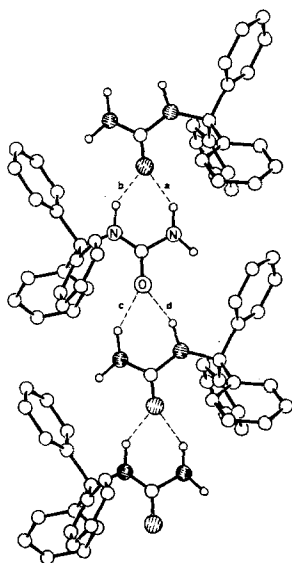
Figure 3*b*. Illustration of the layered arrangement and self-association of NTU molecules along the b axis of the crystal. The parameters of the hydrogen bonds shown are: *a*. 2.871(6)Å, 2.03Å, 143°; *b*. 2.839(5)Å, 1.92Å, 148°; *c*. 2.825(5)Å, 2.00Å, 139°; *d*. 2.778(5)Å, 1.88Å, 145°; for the N···O, H···O distances and the N—H···O angle respectively.

In the absence of specific interactions between the two components (at least partly due to the poor hydrogen-bonding capability of DMF) the host molecules make use of their hydrogen-bonding potential by associating with each other. Figure 3b shows the intermolecular interaction between hosts along the *b* axis. It also indicates that the host lattice can be best described as consisting of hydrogen bonded continuous chains of NTU molecules; in every chain the nearly coplanar urea residues are aligned in the same direction with an alternating arrangement of the trityl substituents on both sides. The geometric parameters of the H-bonds are within the range: NH···O from 2.778 to 2.871Å, H···O from 1.88 to 2.03Å, and N—H···O from 139 to 148°. Interestingly, the length of the translation vector between identical units is 8.91Å, in good agreement with previous observations in the heteromolecular chains involving DTU.

The hydrogen bonded assemblies of NTU are stacked along the *c* axis, forming a layered lattice of the host molecules parallel to the (100) plane. Adjacent layers are separated by about 14.8Å, their packing along the *a* direction inducing "cages" that are occupied by the guest moieties. In spite of the apparent weak interaction between NTU and DMF, this crystalline inclusion-type structure is very stable due to the strong associations within the host lattice and the clathrate nature of the guest inclusion in it.

5. CONCLUSIONS

This study provides an illustration of the remarkable capability
of DTU and NTU molecules to function as hosts for different types
of molecular guests. The three crystal structures presented above
exhibit an exceptional stability, being dominated by extensive arrays
of hydrogen bonds. The significance of these interactions is also
reflected in the consistent geometrical features which characterize
the bonding between the various amide moieties. As outlined at the
outset, DTU appears to be particularly well suited for the formation
of inclusion complexes due to its irregular shape which prevents
the molecules from packing closely, and due to its concave and polar
surface which provides attractive binding sites for guest molecules
with complementary features. The resulting solid complexes of DTU
with propanamide and ethyl N-acetylglycinate (some of the complexes
of DTU with other guest have similar structures) exhibit a directional
and specific interaction between the host and the guest, the two
components being strongly linked to each other. They may thus be
classified as representing an intermediate form between molecular-
inclusion and lattice-inclusion crystals [10]. NTU appears to complex,
preferably, with less polar guests. With only one trityl substituent
on urea, the packing arrangement of NTU molecules is optimized through
self-association and the formation of homomolecular hydrogen-bonded
aggregates in the crystal. The host-guest interactions are mainly
of a hydrophobic nature, with the guest molecules being accommodated
in apolar cage-type voids between host molecules (lattice inclusion).
In this respect the structural results for the NTU-N,N-dimethylfor-
mamide complex demonstrate the validity of the "spacers" concept
in the design of hosts which may exhibit inclusion behaviour upon
crystallization. Furthermore, the hydrogen bonding between NTU mole-
cules in this structure is associated with an alternating arrangement
of the large trityl end groups on both sides of the polar region.
Similar proximity between urea hosts substituted with two trityl
groups is unlikely for steric reasons, which leads to different types
of inclusion structures involving the DTU hosts.

Complexation of these hosts and their structural variations
with chiral guests is currently being explored in order to assess
their potential function as effective and specific synthetic receptors.

6. ACKNOWLEDGEMENTS

7.   SUPPLEMENTARY DATA

Supplementary data relating to this article (Tables of atomic position-
al and thermal parameters) are deposited with the British Library
as Supplementary Publication No. SUP 82022 (7 pages).

8.   NOTES AND REFERENCES

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4.   Other rigid end groups (such as 9-anthracenyl) work well; H.
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5.   There was already in the literature an indication that DTU might
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8.   H. Bredereck and E. Reif: *Chem. Ber.* **81**, 426 (1948).

9.   However, during an attempt to prepare a DTU complex with ethyl
      4-aminobenzoate in the usual way, the crystals which deposited
      were a 1:1 complex of DTU with ethyl acetate. Similarly, DTU
      does not form a complex when crystallized from pure tetrahydro-
      furan (THF). However, crystallization from THF containing 30%
      water gives a 1:1 DTU-THF complex that does not contain water.

10. A similar phenomenon has recently been also classified as 'coor-
     dination-assisted clathration'; E. Weber, I. Csoregh, B. Stensland
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