



Helical Aromatic Urea and Guanidine

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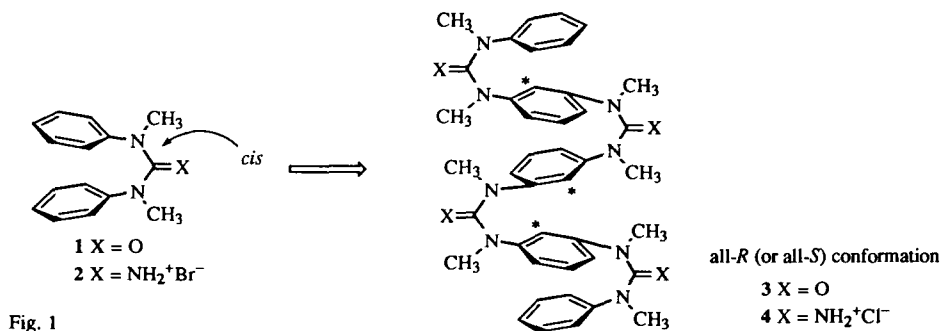
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Abstract: *N,N'*-Dimethyl-*N,N'*-dipheylurea (**1**) and *N,N'*-Dimethyl-*N,N'*-diphenylguanidinium bromide (**2**) each have folded structures with the two phenyl groups located face-to-face. Oligomeric compounds **3** and **4**, having five benzene rings connected at the *meta* positions by *cis*-urea or guanidino groups, form aromatic layered helices in the crystal state. The crystals are racemic with a 1 : 1 enantiomer ratio. They exhibit stacked (**3**) or zigzag chain (**4**) packing, reflecting displaced parallel structure for the terminal phenyl groups of neighboring molecules of **3** and tilted T-shaped structure for those of **4**, respectively. © 1997 Elsevier Science Ltd.

Helicity is a significant structural feature of biological macromolecules, as in double-stranded DNA¹ and α -helix structure of proteins,² and is also important in materials and polymer science.³ Various intramolecular and intermolecular helical structures have been reported, based on rigid helicene skeletons⁴ or supramolecular assembly by hydrogen bond networks⁵ or metal coordinations (helicates).⁶ Here, we describe a new type of molecular helices of multi-decked aromatics based on the *cis* conformational preference of *N*-methylated urea and guanidino groups.

We reported previously that *N,N'*-dimethyl-*N,N'*-diphenylurea (**1**) and *N,N'*-dimethyl-*N,N'*-diphenylguanidinium bromide (**2**) have folded structures with the two phenyl groups located in a face-to-face position, both in the crystal and in solution (Fig. 1).⁷ These conformations may be related to the alteration to *cis* conformation of the amide bond caused by *N*-methylation.⁸ Although the origin of the *cis* preference of these *N*-methylated bonds is not clear, these aromatic folded structures led us to consider the construction of oligomeric aromatic layers which might have helical structures. Thus, a tetraurea **3** and a tetraguanidinium salt **4** (Fig. 1), having five benzene rings connected at the *meta* positions, were designed, and synthesized by



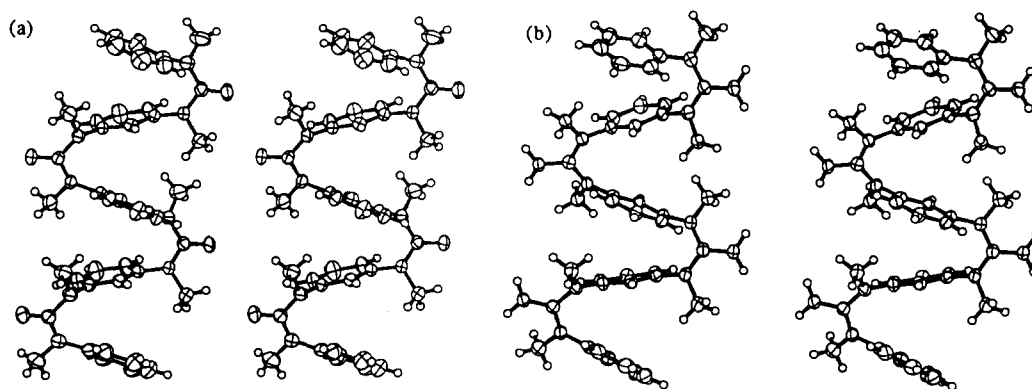


Fig. 2 ORTEP Stereoview of **3** (a), and **4** (b). The counteranions and 2 molecules of H₂O were omitted in the structure of **4**.

means of sequential condensations and functional group transformations using standard methods. Compound **4** was expected to be hydrophilic properties in layered aromatics, and was confirmed to be freely soluble in water.

The crystal structures of **3** (mp, 179.5–182.5 °C) and **4** (mp, 242–245 °C, dec.) are shown in Fig. 2.⁹ Both compounds have multi-layered aromatic structures with large dihedral angles (65 – 80°) between the benzene ring planes and the planes of the –N–C(=X)–N– groups (all-*cis*-conformations). Each pair of face-to-face aromatic rings is tilted; this should be at least partly due to repulsive interactions of their π electrons by analogy with the splayed-out structures of the conformationally restricted 1,8-diarylnaphthalenes.¹⁰ The stable conformations of the simple benzene dimer have also been calculated to be T-shaped or displaced parallel rather than parallel sandwich structure.¹¹ It is interesting to form the multi-layered aromatics with displaced parallel conformation linked by flexible urea or guanidine bonds in **3** and **4**. The dihedral angles between two neighboring benzene in a molecule ring planes are 30 – 40°, similar to those in the simple compounds **1** (35°) and **2** (31°), while the alternate benzene rings are nearly parallel (10 – 18°) in both compounds. Similarly, the planes of the alternate linking groups [–N–C(=X)–N– planes] in a molecule are nearly parallel; for example, the dihedral angles are 8.6° and 3.5° in the case of the guanidinium groups in **4**.

The orderly helical structures in both compounds arise from the same-directional conformations of the two substituents on the benzene rings. For example, the structure of **3** (Fig. 2a) has all-*R* (or all-*S*) chirality along the axes.¹² Although the oligomeric compounds **3** and **4** have no fixed chirality, well-ordered structures would be favored rather than diastereomeric broken helical conformations (*R*- and *S*-mixed conformations in a molecule) for steric reasons.

The crystals are racemic (space group, **3**: *P*2₁/*c*, **4**: *P*2₁/*c*), both enantiomeric helices existing in 1 : 1 ratio in the unit cell (*Z* = 2 and 4 for **3** and **4**, respectively). Interesting packing structures are seen in the crystals (Fig. 3). The helical molecules in **3** are ordered in the same direction with an alternate arrangement of all-*R* and all-*S* conformers in the crystal. The terminal phenyl groups of one molecule lie in parallel to those of neighboring molecules with the opposite helicity, the distance between two planes being 4.1 Å (Fig. 3c). Similarly, all of the urea bonds are arranged in a face-to-face parallel manner with respect to those of the opposite helical molecules with a 3.5 Å C...O distance (Fig. 3d). Unlike **3**, compound **4** formed double zigzag chains consisting of molecules arranged alternately in the reverse direction, each chain being composed of molecules with one helicity. In this case, the terminal phenyl groups of two neighboring molecules in one chain form tilted T-structures with a 4.9 Å C...C distance (Fig. 3e), like the stable conformer of benzene dimer deduced from calculation.¹¹ The difference in crystal packing may be caused by the electronic nature of the linking groups including counter anions of **4**. Both arrangements of aromatic layered helix are of

interest from the viewpoint of crystal engineering of aromatic layers which might have special electronic or magnetic properties.

The ^1H NMR spectra of **3** and **4** showed high-field chemical shifts of the aromatic proton signals, indicate that the layered structures are retained in solution. The observation of the signals of three protons (those on the carbons shown by asterisks in Fig. 1) ortho to two linking groups at particularly high field (6.04 ppm for **3** in CDCl_3 ; 6.18 and 6.22 ppm for **4** in D_2O) suggested that both compounds exist in solution in similar conformations to those observed in crystals.¹³ However, the enantiomeric conformers could not be distinguished in ^1H NMR spectra obtained in the presence of chiral reagents, such as (*R*)-binaphthol or (*R*)- α -methoxy- α -(trifluoromethyl)phenylacetic acid, at 183 K, probably due to the rapid equilibrium between the two helices and other conformations. Further detailed investigations on the conformational behavior in solution, as well as the separation of the two helices both in the crystal form and in solution, are in progress.

In conclusion, we present an efficient method for the construction of aromatic helices with multi-layered structures, contrasting with usual methods for obtaining layered structure which are based on conformational fixation^{10,14} as in cyclophanes,¹⁵ or special aromatic donor-acceptor interactions.¹⁶ The *cis* preference of *N*-methylated urea and guanidine bonds is general, regardless of the aromatic rings,¹⁷ and the resultant flexible helices show unique structural features. Considering the lipophilic or freely water-soluble character of **3** or **4**, respectively, this approach could be applied to develop aromatic architectures with various functions.

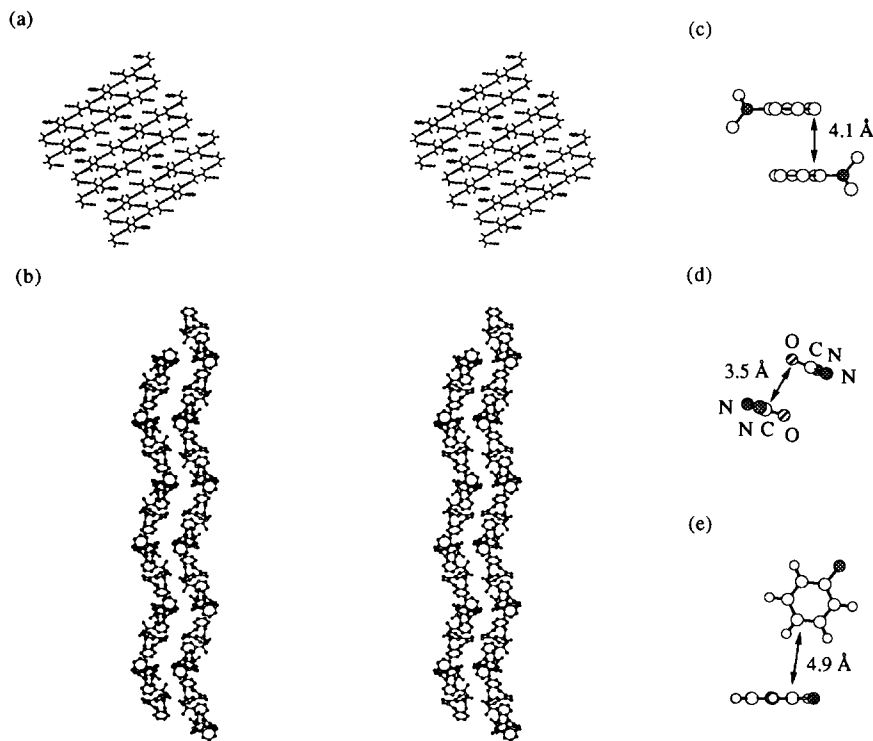


Fig. 3 Packing Structures (stereoviews) of **3** (a), and **4** (b). The intermolecular relationships of terminal phenyl rings (parallel, c), urea bonds (d) of **3**, and T-shaped terminal phenyl rings of **4** (e) are also shown.

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- 9 Crystal data for **3** (C₄₂H₄₆N₄O₄); monoclinic, space group *P2₁/c*, *a* = 15.818(2), *b* = 6.9823(2), *c* = 17.778(1) Å, β = 93.380(6)°, *V* = 1960.1(2) Å³, *Z* = 2, *D*_{calc} = 1.231 g·cm⁻³, λ (Cu K α 1) = 1.54178 Å, *T* = 296 K, *R* = 0.043 for 2328 reflections. Crystal data for **4** (C₄₂H₅₈N₁₂Cl₄O₂); monoclinic, *P2₁/c*, *a* = 11.647(2), *b* = 25.027(3), *c* = 15.866(2) Å, β = 93.52(1)°, *V* = 4616.1(9) Å³, *Z* = 4, *D*_{calc} = 1.302 g·cm⁻³, λ (Mo K α 1) = 0.71070 Å, *T* = 173 K, *R* = 0.066 for 4814 reflections. Further details of the crystal structure investigation are available on request from the Director of the Cambridge Crystallographic Data Center.
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(Received in Japan 24 March 1997; revised 6 May 1997; accepted 9 May 1997)