Enantiospecific Formation of a Three-component Helical Structure by Spontaneous Self-assembly

Weimin Yue, Roger Bishop,* Marcia L. Scudder, and Donald C. Craig
School of Chemistry, The University of New South Wales, Sydney 2052, Australia

(Received March 5, 1998; CL-980162)

A toluene solution of the two racemic helical tubulands **1** and **2** yields crystals of the stoichiometric product $\mathbf{1\cdot 2_2}\cdot$toluene through molecular self-assembly involving simultaneous self-resolution of both diols. This composite helical tubulate structure contains parallel tubes with cross-sectional areas of 22.5 Å^2.

The generation of chirally pure substances, for example by design of new enantiospecific reactions or through efficient procedures which permit enantiomeric resolution, is a major object of contemporary chemistry.[1] Spontaneous self-resolution provides an extremely simple method for those 5-10% of cases[2,3] where crystallisation of a racemic solution yields a mixture of pure (+)- and pure (-)-crystals (a conglomerate). Seeding the solution can lead to preferential precipitation of that specific enantiomer even on an industrial scale.[3,4] We report here on a remarkable example involving two simultaneous self-resolutions whereby a five-component solution spontaneously affords stoichiometric three-component crystals with specific chirality.

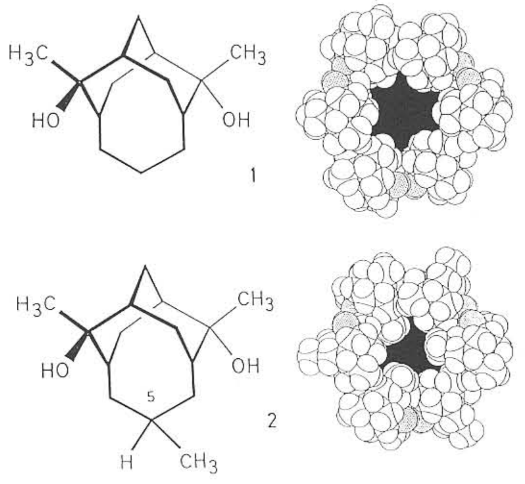

Figure 1. The molecular structures of typical helical tubuland diols **1** and **2** showing a projection view in the *ab* plane of just one host tube. Oxygen atoms are stippled and the unobstructed canal cross-sectional areas are coloured black.

For some time we have been investigating a family of diol host molecules called the helical tubulands, such as **1** and **2** (Figure 1), which crystallise with a hydrogen bonded network lattice containing parallel helical tubes which enclose guest molecules.[5] The intermolecular core is a series of OH···OH···OH spines which surround threefold screw axes. This motif may be retained, but the alicyclic skeleton modified,[6] allowing deliberate design of further compounds with similar lattice packing in the chiral space group $P3_121$ or its enantiomorph $P3_221$. Crystal growth permits incorporation of only one enantiomer in the host-guest structure, and hence a conglomerate is produced each time one of these racemic diols crystallises.

The tubes of diol **1** have a star-shaped cross-section (*ca.* 32 Å^2) and the resulting inclusion compounds can contain molecules as wide as ferrocene or as long as the biologically significant terpene squalene.[7] Similarly, diol **2** also forms chiral inclusion compounds but its propeller-shaped tube is much smaller (*ca.* 18 Å^2) due to the protruding C5-methyl groups.[8]

When a mixture of **1** and **2** was recrystallised from toluene, needle-like crystals (morphologically similar to previous helical tubulates) were produced. ^{1}H NMR spectroscopy showed the presence of both diols plus toluene in an individual crystal (rather than comprising a mixture). A single crystal X-ray structure determination confirmed formation of a mixed diol lattice structure.[9] When the toluene guest was omitted from the refinement R rose from 0.038 to 0.058. Recalculation of the final residual assuming that the host was just pure **1** or pure **2** resulted in increases to 0.063 or 0.050 respectively.

The two host diols **1** and **2** form a microporous hydrogen bonded lattice which tightly encloses the toluene guests within parallel tubes of a new and composite cross-section (22.5 Å^2). In this stoichiometric material, $\mathbf{1\cdot 2_2}\cdot$toluene, one guest is present per unit cell with adjacent toluene molecules related simply by unit cell translation along the tubes (Figures 2 & 3).

Formation of $\mathbf{1\cdot 2_2}\cdot$toluene is a startling example of molecular self-assembly. It involves specific, stoichiometric, and chiral combination of three components from a solution of five. The toluene molecules must exert a major templating role. All reasonable hydrogen bonds and attractive dispersion forces could be involved during the aggregation but such interactions involve

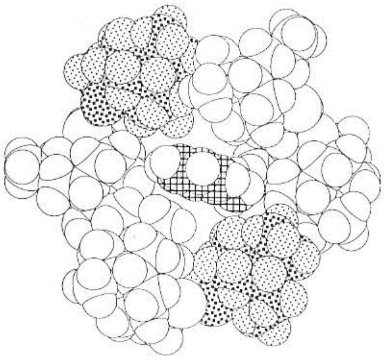

Figure 2. Projection view in the *ab* plane of just one tube of composite cross-section in solid $\mathbf{1\cdot 2_2}\cdot$toluene showing the template molecule surrounded tightly by the diols. Carbon atoms of toluene are crosshatched, carbons of **1** are stippled (C and O heavily, and H lightly), while all atoms of **2** (and the toluene hydrogens) are left white.

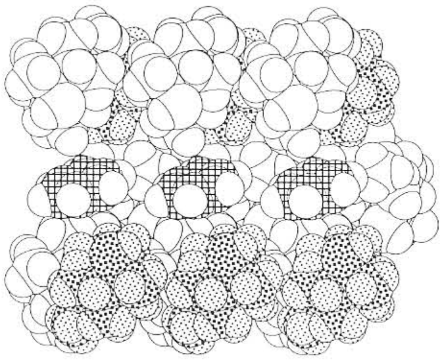

Figure 3. Side view of the host-guest arrangement within one tube of **1**·**2**$_2$·toluene, with the front column of diol molecules **2** removed to provide this cut-away diagram.

only weak forces and are rapidly reversible. Any 'mistakes' are rejected, and only those combinations leading to the most efficient product are retained, ultimately yielding the stoichiometric and chirally pure product of best fit.

Molecules participating in recognition and assembly processes can be regarded as being programmed information carriers.[10] Powerful supramolecular information is incorporated within their molecular structures, even though its potential expression may not be immediately apparent.[11] Therefore we speculate that formation of this remarkable three-component structure may have significance beyond these preliminary observations. First, it seems probable that other combinations of known helical tubulands should assemble similarly in the presence of appropriate guest templates.

More importantly, however, this outcome involves a highly specific self-assembly from a five-component 'molecular soup'. Extrapolation suggests that even apparently simple molecules of low molecular weight may have had the inherent ability to generate helical and chiral aggregates from primordial chemical mixtures. The molecular recognition factors underpinning the formation of aggregates like **1**·**2**$_2$·toluene therefore could provide important clues towards modelling prebiotic chemistry.

This work was supported financially by the Australian Research Council.

References and Notes

1 For example, see: R.E. Gawley and J. Aubé, Principles of Asymmetric Synthesis, Pergamon, Oxford (1996); G. Helmchen, R.W. Hoffmann J. Mulzer, and E. Schaumann, Stereoselective Synthesis: Houben-Weyl Methods of Organic Chemistry, Thieme, Stuttgart (1996), Vol. 1-10.

2 J. Jacques, A. Collet, and S.H. Wilen, Enantiomers, Racemates, and Resolutions, Wiley, New York (1981); A. Collet, in Comprehensive Supramolecular Chemistry, ed by D.N. Reinhoudt, Pergamon, Oxford (1996), Vol. 10, Chap. 5, pp. 113-149.

3 A. Collet, The Homochiral versus Heterochiral Packing Dilemma, in: Problems and Wonders of Chiral Molecules, ed by M. Simonyi, Akadémiai Kiadó, Budapest (1990), pp. 91-109.

4 A. Collet, M.-J. Brienne, and J. Jacques, *Chem. Rev.*, **80**, 218 (1980).

5 R. Bishop, in Comprehensive Supramolecular Chemistry, ed by D.D. MacNicol, F. Toda, and R. Bishop, Pergamon, Oxford (1996), Vol. 6, Chap. 4, pp. 85-115.

6 R. Bishop, I.G. Dance, S.C. Hawkins, and M.L. Scudder, *J. Incl. Phenom.*, **5**, 229 (1987); R. Bishop, D.C. Craig, M.L. Scudder, A.P. Marchand, and Z. Liu, *J. Chem. Soc., Perkin Trans. 2*, **1995**, 1295.

7 A.T. Ung, R. Bishop, D.C. Craig, I.G. Dance, A.D. Rae, and M.L. Scudder, *J. Incl. Phenom.*, **15**, 385 (1993).

8 W. Yue, R. Bishop, M.L. Scudder, and D.C. Craig, *J. Chem. Soc., Perkin Trans. 1*, **1997**, 2937.

9 X-ray crystal structure analysis: Enraf-Nonius CAD4 diffractometer, CuK$_\alpha$ radiation, $2\theta_{max.}$ 140°, $T = 294$ K, $(C_{14}H_{24}O_2)\cdot(C_{15}H_{26}O_2)_2\cdot(C_7H_8)$, $M = 793.23$, trigonal, $P3_121$ or $P3_221$, $a = 13.765(2)$, $c = 7.007(1)$ Å, $V = 1149.8(2)$ Å^3, $Z = 1$, $D_{calc.} = 1.15$ g cm^{-3}, $\mu = 5.31$ cm^{-1}. The final R was 0.038 for 1199 independent observed reflections and 111 variables $[I/\sigma(I) > 3]$. Although no distinction between the enantiomorphic space groups could be made, molecules of **1** and **2** in the crystal have the same handedness. Atomic coordinates, bond lengths and angles, thermal parameters, and details of solution and refinement, are available from The Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, United Kingdom, on quoting the full journal citation.

10 J.-M. Lehn, *Angew. Chem., Int. Ed. Engl.*, **29**, 1304 (1990).

11 M. Miyata, in Comprehensive Supramolecular Chemistry, ed by D.D. MacNicol, F. Toda, and R. Bishop, Pergamon, Oxford (1996), Vol. 6, Chap. 6, pp.147-176; see especially p.153.