Molecular Solids Formed by the Self-Organisation of Dialcohols into Hydrogen-Bonded Ladders

Vi T. Nguyen,[a] Paul D. Ahn,[a] Roger Bishop,*[a] Marcia L. Scudder,[a] and Donald C. Craig[a]

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The ability of certain dialcohols to form solid-state structures containing unidirectional hydrogen-bonded ladders has been investigated. Two double-stranded structures, staircase-ladders and step-ladders, have been identified. In each, dialcohol molecules are hydrogen-bonded into linear strands with two parallel strands cross-linked through additional hydrogen bonding. Staircase-ladders are made up of $(O–H)_n$ chains of hydrogen bonds, with the molecules in the two strands out of phase with each other. Step-ladders are formed from $(O–H)_4$ cycles of hydrogen bonds, with the molecules of the two strands in phase. Sixteen examples of staircase-ladder structures and twelve cases of step-ladder structures were identified by use of the Cambridge Structural Database. A further three examples, all shown to be staircase-ladders by single-crystal X-ray analysis, were synthesised. Distinct structural preferences in ladder formation can be identified. Nearly all staircase-ladders contain only one type of enantiomer, with the dialcohol building blocks arranged around a twofold screw axis. This type of ladder is thus favoured for enantiomerically pure compounds. The preferred step-ladder construction contains (+)-enantiomers in one strand and (–)-enantiomers in the other, giving two repeating centres of symmetry along the ladder axis. There are, however, many exceptions to this norm. These two ladder types are compared with each other and with those formed by organic molecules containing other hydrogen-bonding functionalities.

Introduction

The factors involved in the self-organisation of molecules from solution to produce crystalline structures of a specific type constitute an area of intense current interest.[1] Crystal engineering[2] aims to uncover and determine the role of weak intermolecular forces involved in such processes, its ultimate aim being the prediction and control of such phenomena.[3] In this paper we report the ability of certain dialcohols to form double-stranded ladders in the solid state and analyse the characteristics of these unidirectional structures. Preferred ladder construction modes are identified, new examples are synthesised, and their ladder structures are analysed using X-ray crystallography.

Some common unidirectional molecular structures are shown diagrammatically in Figure 1. The simplest type (a) consists of a linear, covalently bonded polymeric chain, while its supramolecular equivalent is a ribbon structure (b) in which individual molecules are linked into chains through one or more types of weak intermolecular forces. A variant, the tape structure (c), involves planar building blocks joined by multiple links. It should be noted that the latter two structures may involve one or more types of building block, and that a wide range of supramolecular synthons is available for their construction. Over recent years there has been considerable activity in the deliberate design of new ribbons[4] and tapes.[5]

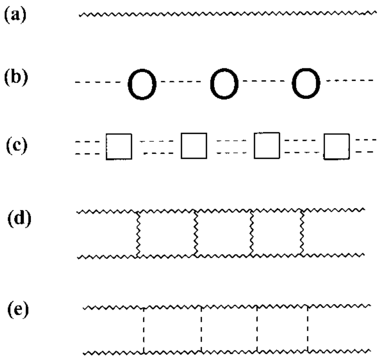

Figure 1. Schematic representations of some unidirectional molecular structures: (a) linear polymer, (b) ribbon with molecules linked by weak intermolecular forces, (c) tape with planar molecules linked by weak forces, (d) crosslinked polymer ladder structure, and (e) double-stranded ladder linked by weak intermolecular forces

Unidirectional structures can also result from double-stranded arrangements that create molecular ladders. Fully covalent examples (d) in which two chains are cross-linked at intervals are well known in the polymer field. Structures of this type are common in high-temperature plastics, membranes and elastomers. Two separate covalent strands may also be joined by intermolecular forces to form a ladder structure (e), as in DNA, some proteins and molecular duplexes.[6] Alternatively, as with the materials discussed in this paper, the entire ladder may be formed through the action of weak intermolecular forces.

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[a] School of Chemistry, The University of New South Wales,
Sydney 2052, NSW, Australia
Fax: (internat.) + 61-2/9385-6141
E-mail: r.bishop@unsw.edu.au

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Results and Discussion

Molecular Ladders

Although the hydroxy group is capable of many different hydrogen-bonding arrangements, it is well known that simple monoalcohol and dialcohol crystal structures frequently involve linear chains, helices or cycles of hydroxy groups. These outcomes are driven by energetically preferred factors such as attainment of co-operative hydrogen bonding and participation by each hydroxy group in two hydrogen bonds (one donor and one acceptor).[7,8] Organic dialcohols, however, can also form molecular ladders consisting of two strands of molecules joined by weak forces (the uprights), which are cross-linked by further weak forces (the rungs). Occasional examples of this structural arrangement have been noted previously but the extent of the phenomenon has not been explored. In fact, an appreciable number of dialcohols form ladder structures. This paper presents the first detailed description and examination of this supramolecular behaviour.

There are actually two distinct types of double-stranded ladders (Figure 2), which we term staircase-ladders and step-ladders. In both types, each dialcohol hydroxy group is fully hydrogen-bonded, participating in one donor and one acceptor bond. The staircase-ladders have the dialcohol molecules of the two strands staggered with respect to each other, and the hydroxy groups form zigzag hydrogen-bonded chains $(O-H)_n$ along the ladder direction. In contrast, the molecules of the strands forming the step-ladders are directly opposite each other and the hydrogen bonding comprises a series of $(O-H)_4$ cycles. Thus, in their simplest form, the two structures are related by translation of one strand relative to the other, with concomitant rearrangement of the hydrogen bonding.

In both cases, the polar hydroxy groups occupy the central rung region of the ladder, while the uprights are formed from the nonpolar hydrocarbon groups. The staircase description has been chosen here because the most common arrangement is for all the molecules to surround a twofold screw axis, while the step-ladder description reflects the geometry of the common household ladder.

A literature survey was carried out using the Cambridge Structural Database (CSD)[9] to identify examples of ladder formation. This search was restricted to compounds containing C, H and two hydroxy groups only. No further substituents were considered and no assumptions were made regarding the symmetry of the ladders or the chirality of their components.

This survey identified 28 examples of ladder structures formed by dialcohols: 16 staircase-ladders **1**−**16**[10−24] and twelve step-ladders **15**[23] and **20**−**30**.[25−35] In addition, we report here three new ladder structures (**17**−**19**) from our synthetic program, all of which are staircase-ladders. Thus, of the 31 currently known examples, 61% are staircase-ladders (Table 1) and 39% are step-ladders (Table 2). As can be seen from the compounds **1**−**30** illustrated in Figures 3 and 4, a very wide range of molecular skeletons can participate in ladder formation and the alcohol groups may be primary, secondary or tertiary.

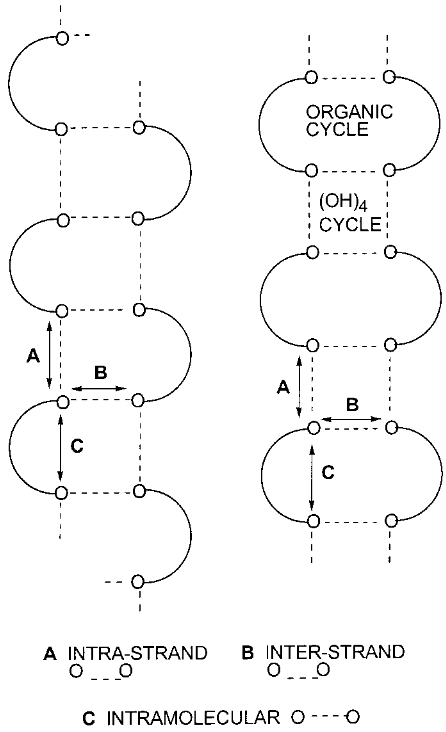


Figure 2. Schematic staircase-ladder (left) and step-ladder (right) structures; dialcohol molecules are represented as curved rods linking two hydroxy groups (O) and hydrogen bonds as dashed lines

Synthesis of New Ladder-Forming Dialcohols

In order to demonstrate control of this assembly mode, new examples of ladder-forming alcohols were synthesised. To achieve this required compounds in which the hydroxy groups protrude from one face of the molecule but remain relatively remote from each other, the other face being hydrocarbon in nature. Prediction is also assisted by analogy with known examples such as the cage compound **27**[32] and the bicyclo[3.3.1]nonane derivative **15**,[23] so here we targeted their analogues compound **17** and compounds **18** and **19**, respectively.

Treatment of diketone **31** with methylmagnesium chloride is known to give only the *anti*,*syn*- (36%) and *anti*,*anti*-diol (62%) isomers.[36] It was therefore necessary to prepare the required *syn*,*syn* isomer **17** by a different route (Scheme 1). Wittig reaction gave the diene **32**, which was epoxidised, and then reduced with lithium aluminium hydride. Diol **17** was isolated from the resulting mixture of three isomers by chromatography.

Diols **18** and **19** were both accessible from the diketone **33**,[37] by use of lithium aluminium hydride or methyllithium, respectively (Scheme 2). In each case the reagent attacks the more exposed upper face of the V-shaped molecule to yield the required *endo*,*endo*-diol as the major product. The structures of crystalline compounds **17**−**19** were determined by X-ray methods and all were found to be new

Table 1. Characteristics of hydrogen-bonded staircase-ladders formed by dialcohols in the solid state

Structure and ref.	Ref. code and molecular formula	Initial compd. composition	Final crystal composition	Space group	Enant. pure ladder	Ladder symmetry	Intramolecular O···O [Å]	Intrastrand *O*H···*O*H [Å]	Interstrand *O*H···*O*H [Å]
1[10]	CAPSID $C_{15}H_{24}O_2$	enant. pure	enant. pure	$P2_12_12_1$	yes	2_1 screw	4.17	2.84	2.80
2[11]	DHOMEN $C_{10}H_{18}O_2$	enant. pure	enant. pure	$P2_12_12_1$	yes	2_1 screw	5.24	2.81	2.84
3[12]	EABCEP $C_{10}H_{16}O_2$	racemic	enant. pure conglomerate	$P2_1$	yes	2_1 screw	3.60	2.82	2.72
4[13]	FEPKUG $C_{15}H_{28}O_2$	enant. pure	enant. pure	$P2_12_12_1$	yes	2_1 screw	3.92	2.83	2.74
5[14]	GEKTUL $C_{10}H_{18}O_2$	enant. pure	enant. pure	$C2$	yes	2_1 screw	4.76	2.69	2.73
6[15]	GIGYAW $C_9H_{20}O_2$	racemic	racemic	$C2/c$	yes	2_1 screw	3.47	2.77	2.72
7[15]	GIGYEA $C_{15}H_{16}O_2$	racemic	enant. pure conglomerate	$P2_1$	yes	2_1 screw	3.49	2.79	2.73
8[16]	JOFKOE $C_{10}H_{18}O_2$	enant. pure	enant. pure	$C2$	yes	2_1 screw	5.18	2.76	2.84
9[17]	KOTDUS $C_{10}H_{18}O_2$	racemic	racemic	$Pna2_1$	yes	2_1 screw	5.19	2.75	2.84
10[18]	LEPZAH $C_{16}H_{30}O_2$	enant. pure	enant. pure	$P2_12_12_1$	yes	2_1 screw	5.18	2.73	2.70
11[19]	NEZFON $C_{15}H_{26}O_2$	enant. pure	enant. pure	$P2_12_12_1$	yes	2_1 screw	4.93	2.72	2.72
12[20]	PUFJIJ $C_6H_{14}O_2$	enant. pure	enant. pure	$P2_1$	yes	2_1 screw	4.65	2.72	2.73
13[21]	QADVOG $C_{15}H_{26}O_2$	enant. pure	enant. pure	$P2_12_12_1$	yes	2_1 screw	4.58	2.71	2.71
14[22]	TOHBEX $C_{15}H_{22}O_2$	achiral (*meso*)	achiral	$I2/a$	n/a	2_1 screw	5.39	2.98	2.85
15[23]	VIRBUT[a] $C_{11}H_{16}O_2$	racemic	racemic	$C2/c$	yes	2_1 screw	5.17	2.82	2.78
16[24]	WAGWEG $C_{12}H_{16}O_2$	racemic	racemic	$P2_1/c$	yes	2_1 screw	3.62	2.73	2.69
17	– $C_{14}H_{20}O_2$	racemic	enant. pure conglomerate	$P2_12_12_1$	yes	2_1 screw	4.70	2.75	2.75
18	– $C_{11}H_{16}O_2$	racemic	racemic	$P2_1/c$	yes	2_1 screw	5.40	2.83	2.83
19	– $C_{13}H_{20}O_2$	racemic	racemic	$P\bar{1}$ $X = 2$	no	translation only	5.14 5.17	2.86 2.88	2.84 2.84

[a] VIRBUT contains both types of ladder; *X* is the number of independent molecules present in the asymmetric unit (where greater than one); *N/a* not applicable.

examples of staircase-ladders. Numerical details of their solution and refinement are listed in Table 3.

Ladder Dimensions

Analysis of all 31 ladder structures showed that intrastrand *O*H···*O*H hydrogen-bonding distances ranged over 2.69−2.98 Å for the staircase-ladders (Table 1) and 2.68−2.89 Å for the step-ladders (Table 2). The corresponding interstrand values were 2.69−2.85 Å and 2.69−2.88 Å, respectively. These values are unexceptional and lie within normal hydroxy group hydrogen-bonding parameters.

For the staircase-ladders, the intramolecular O···O separation distances lay in the 3.47−5.39 Å range, while the corresponding range observed for the step-ladders was 2.72−6.43 Å. The smaller range for the staircase-ladders is expected because the intramolecular O···O separations and intrastrand hydrogen-bonding O···O distances must be sufficiently compatible to permit formation of the zigzag hydrogen-bonded chain (see Figure 2). In contrast, both shorter and longer intramolecular O···O separation values were noted for the step-ladders. In principle, almost any distance should be possible here, since the partners from opposite strands are positioned opposite each other.

Structures of the Staircase-Ladders

Our literature survey identified 16 examples of dialcohols (**1**−**16**[10−24]) that formed double-stranded staircase-ladders. One of these compounds was achiral, nine were enantiomerically pure, and six were racemic. In their crystals, however, the molecules of each ladder surrounded a 2_1 screw axis. Hence the dialcohols in these ladders were either achiral (one case) or enantiomerically pure (fifteen cases). Of the six racemic dialcohols, two underwent spontaneous self-resolution to give a mixture of crystals containing either pure (+)-ladders or pure (−)-ladders (a conglomerate), while the remaining four produced crystals containing

Table 2. Characteristics of hydrogen-bonded step-ladders formed by dialcohols in the solid state

Structure and ref.	Ref. code and molecular formula	Initial compd. composition	Final crystal composition	Space group	Enant. pure ladder	Enant. pure strand	$(O-H)_4$ cycle	Organic cycle	Intramol. O···O [Å]	Intrastrand *OH*···*OH* [Å]	Interstrand *OH*···*OH* [Å]
15[23]	VIRBUT[a] $C_{11}H_{16}O_2$	racemic	racemic	*C*2/*c*	yes	yes	twofold axis along ladder	twofold axis along ladder	5.20	2.80	2.69, 2.87
20[25]	DXTHBP $C_{20}H_{16}O_2$	racemic	racemic	*P*2$_1$/*c*	no	yes	centrosym.	centrosym.	2.88	2.72	2.71
21[26]	HMMCHX $C_8H_{16}O_2$	racemic	racemic	*P*$\bar{1}$	no	yes	centrosym.	centrosym.	3.55	2.76	2.75
22[27]	MBZAOX10 $C_{20}H_{18}O_2$	racemic	racemic	*P*2$_1$/*a* *X* = 2	no	yes	no sym.	no sym.	2.83, 2.78	2.75, 2.71	2.69, 2.88
23[28]	NEPGCL02 $C_5H_{12}O_2$	achiral	achiral	*P*2$_1$/*c*	n/a	n/a	centrosym.	centrosym.	3.39	2.68	2.73
24[29]	QACXAT $C_{14}H_{22}O_2$	racemic	racemic	*P*2$_1$/*c*	no	yes	centrosym.	centrosym.	3.26	2.82	2.77
25[30]	SIVXEA $C_{18}H_{20}O_2$	achiral (*meso*)	achiral	*P*$\bar{1}$ *X* = 2	n/a	n/a	centrosym. centrosym.	no sym. no sym.	5.26 5.28	2.89 2.85	2.85 2.84
26[31]	VAHXAD $C_{10}H_{16}O_2$	racemic	racemic	*P*$\bar{1}$	no	yes	centrosym.	centrosym.	4.31	2.71	2.80
27[32]	WALDES $C_{13}H_{18}O_2$	racemic	racemic	*P*2$_1$/*c*	no	yes	centrosym.	centrosym.	4.76	2.77	2.80
28[33]	YAFLAS $C_{14}H_{24}O_2$	racemic	racemic	*C*2/*c*	no	no	centrosym.	twofold axis perp. to ladder	6.43	2.82	2.75
29[34]	YAVNAK $C_{12}H_{20}O_2$	racemic	racemic	*Cc* *X* = 2	no	yes	no sym.	no sym.	4.60, 4.60	2.70, 2.72	2.71, 2.74
30[35]	ZIVCEM $C_{18}H_{18}O_2$	racemic	racemic	*P*$\bar{1}$ *X* = 2	no	no	no sym.	centrosym.	2.72	2.78, 2.78	2.73, 2.72

[a] VIRBUT contains both types of ladder; *X* is the number of independent molecules present in the asymmetric unit (where greater than one); *N*/*a* not applicable.

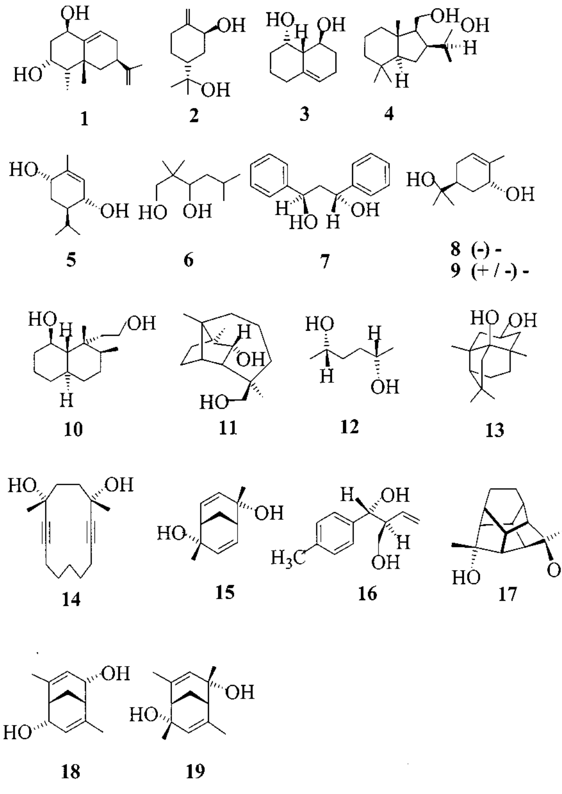


Figure 3. Structures of dialcohols that form hydrogen-bonded staircase-ladders

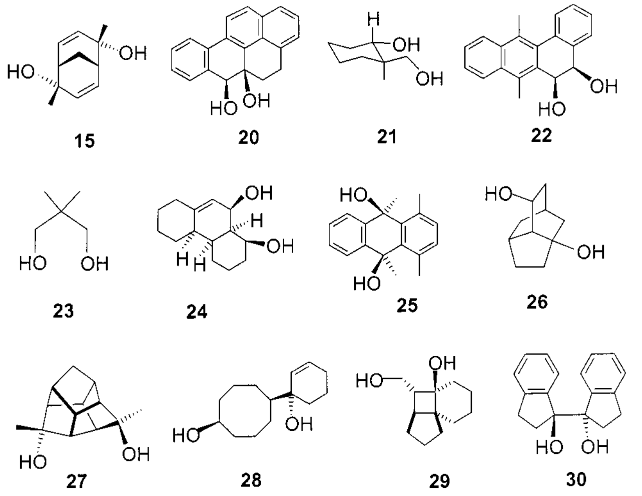
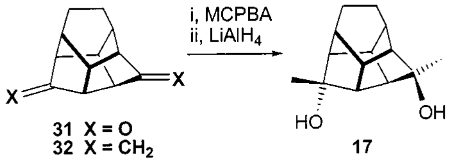


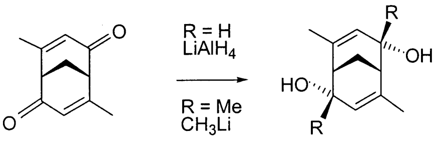
Figure 4. Structures of dialcohols that form hydrogen-bonded step-ladders



Scheme 1

both (+)- and (−)-ladders. Hence, resolution processes to create chiral ladders took place even when racemic dialcohols were allowed to crystallise − despite several other options being theoretically possible (such as enantiomers alternating along the hydrogen-bonded chain, or the use of blocks of alternating enantiomers).

Our three new racemic dialcohols **17−19** all crystallised as staircase-ladders, but here the pattern of behaviour was



33

18 R = H
19 R = Me

Scheme 2

rather different. Only two cases (**17** and **18**) had ladders with 2_1 symmetry, and these typical staircase-ladder arrangements are illustrated in Figure 5a and b. One compound (**17**) underwent self-resolution to yield a conglomerate, while the other (**18**) formed crystals containing both (+)- and (−)-ladders.

The remaining diol **19** proved to have a ladder arrangement not observed previously. Its structure (Figure 5c) contains two independent molecules (A, B) in its asymmetric unit of the centrosymmetric $P\bar{1}$ space group. Its staircase-ladders contain both enantiomers, but there is still considerable ordering present in the structure. Each ladder is constructed from one strand of A molecules (all of one handedness) and one strand of B molecules (all of opposite handedness). Hence, there are equal numbers of A-(+)-/B-(−)- and A-(−)-/B-(+)-ladders in the crystal. The only symmetry along any strand is translation.

Our analysis of the staircase-ladder structures reveals striking preferences for enantiomer ordering during the self-organisation process. In particular, eight out of the nine racemic compounds (89%) gave enantiomerically pure 2_1 ladders on crystallisation. The one achiral compound and the nine enantiomerically pure compounds also gave 2_1 ladders. Hence, no fewer than 18 out of 19 (95%) of the recorded staircase-ladders have 2_1 symmetry. We shall see in the next section that no enantiomerically pure dialcohol forming a step-ladder structure has been reported.

Structures of the Step-Ladders

Dialcohol step-ladder structures are characterised by two regions, termed the $(O-H)_4$ cycle and the organic cycle (see Figure 2). The hydrogen bonding synthon is a cyclic arrangement of four hydroxy groups, a motif first encountered in pentaerythritol in 1937[38] and commonly observed in solid-state structures of dialcohols.[39,40]

There are considerable differences in enantiomer ordering and symmetry between the staircase-ladders and step-ladders. Of the twelve dialcohol compounds that form step-ladders, two are achiral and ten are racemic, but none are enantiomerically pure materials either before or after crystallisation. If the two achiral cases are discounted, nine out of ten examples (90%) have ladders containing both enanti-

Table 3. Numerical details of the solution and refinement of the crystal structures

Compound	**17**	**18**	**19**
Empirical formula	$C_{14}H_{20}O_2$	$C_{11}H_{16}O_2$	$C_{13}H_{20}O_2$
Formula mass	220.3	180.2	208.3
Space group	$P2_12_12_1$	$P2_1/c$	$P\bar{1}$
a [Å]	7.4302(7)	8.170(4)	7.803(4)
b [Å]	11.980(2)	7.622(2)	10.290(7)
c [Å]	12.979(2)	16.017(6)	15.663(10)
α[°]	90	90	107.42(4)
β [°]	90	104.58(2)	91.65(4)
γ [°]	90	90	102.12(4)
V [Å^3]	1155.3(2)	965.3(6)	1168(1)
T [°C]	21(1)	21(1)	21(1)
Z	4	4	4
$D_{\mathrm{calcd.}}$ [g cm^{-3}]	1.27	1.24	1.18
Radiation, λ [Å]	Cu-K_α, 1.5418	Cu-K_α, 1.5418	Cu-K_α, 1.5418
μ [mm^{-1}]	0.615	0.631	0.580
Scan mode	$\theta/2\theta$	$\theta/2\theta$	$\theta/2\theta$
$2\theta_{\mathrm{max.}}$ [°]	140	140	120
No. of intensity measurements	1280	1821	3461
Criterion for observed reflection	$I/\sigma(I) > 3$	$I/\sigma(I) > 3$	$I/\sigma(I) > 3$
No. of indep. obsd. reflections	1181	1441	2174
No. of reflections (m) and	1181	1441	2174
variables (n) in final refinement	146	119	272
$R = \Sigma^m\lvert\Delta F\rvert/\Sigma^m\lvert F_o\rvert$	0.035	0.039	0.041
$R_w = [\Sigma^m w\lvert\Delta F\rvert^2/\Sigma^m w\lvert F_o\rvert^2]^{1/2}$	0.054	0.076	0.059
$s = [\Sigma^m w\lvert\Delta F\rvert^2/(m-n)]^{1/2}$	1.59	1.69	1.49
Crystal decay	none	none	none
Max./min. transmission coefficients	−/−	−/−	0.96/0.92
R for multiple measurements	−	0.020	−
Largest peak in final diff. map [e Å^{-3}]	0.17	0.21	0.26

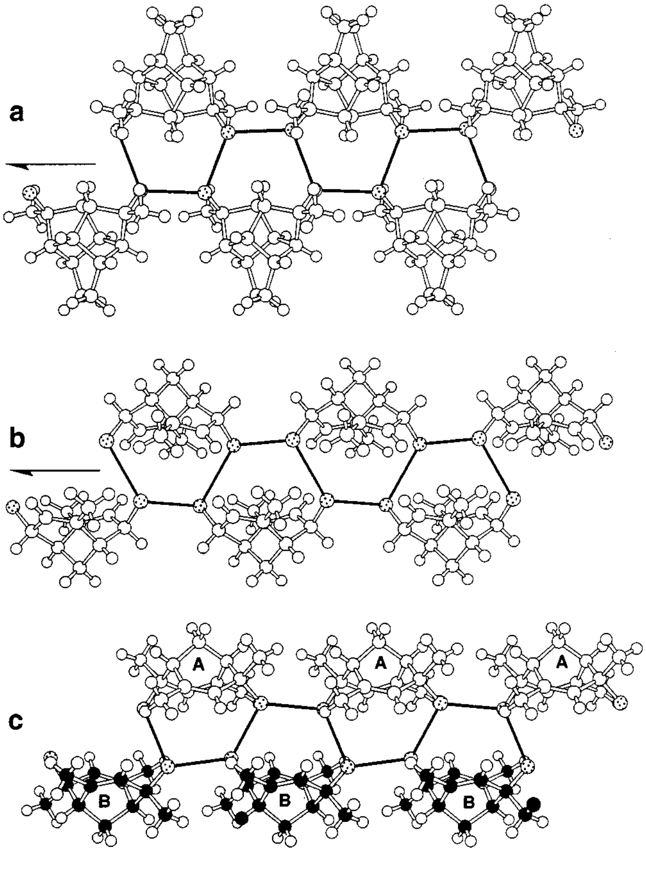


Figure 5. Examples of staircase-ladders formed by dialcohols; hydroxy hydrogen atoms are omitted, oxygen atoms are stippled, hydrogen bonds are indicated by solid black lines, and the opposite enantiomers are indicated by white and black carbon atoms: (a) **17** and (b) **18** illustrate the archetypal arrangement in which molecules of the same handedness surround a 2_1 axis; (c) solid dialcohol **19** contains ladders built from strands of crystallographically independent A and B molecules; the A strand comprises molecules all of one handedness, and the B strand contains molecules all of the opposite handedness

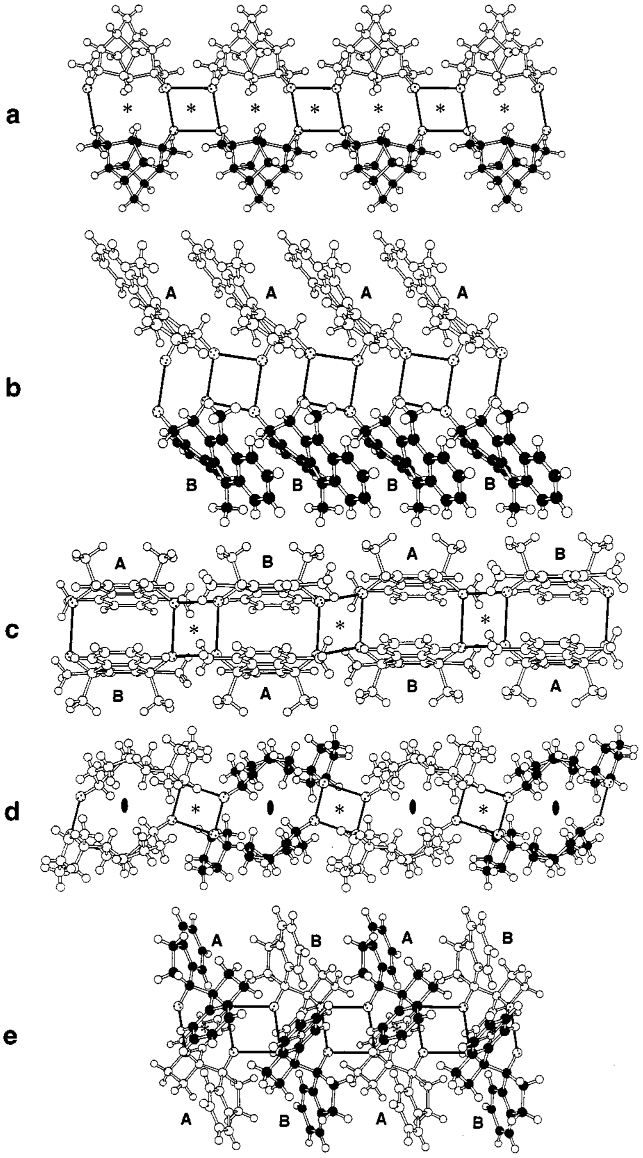


Figure 6. Examples of solid-state step-ladder structures formed by dialcohols; opposite enantiomers are coloured white and black, oxygen atoms are stippled, hydroxy hydrogen atoms are omitted, and hydrogen bonding is indicated by solid black lines; the symbols A and B indicate crystallographically independent molecules; centres of symmetry are designated by a star symbol and twofold rotation axes by ellipses: (a) the most common arrangement, illustrated by **27**, which has centres of symmetry at both the $(O-H)_4$ and organic cycle sites; diagrams (b)−(e) show the less typical variants of step-ladder construction: (b) **22**, (c) **25**, (d) **28**, and (e) **30**

omers, but eight out of ten (80%) have enantiomerically pure strands.

The favoured ladder arrangement, seen in six cases out of twelve (50%), has centres of symmetry at both the $(O-H)_4$ and organic cycle sites (as illustrated for **27** in Figure 6a). There is, however, considerably more variation amongst the step-ladder structures than in the staircase-ladders. Among the six examples without double centres of symmetry, five distinct symmetry alternatives are observed.

Dialcohols **22** (Figure 6b) and **29** each contain two independent molecules (A and B) in their asymmetric unit and have no symmetry at either type of cycle. One strand contains enantiomerically pure A, and the other enantiomerically pure B (but of opposite chirality). Compound **15**, discussed further below, has a twofold axis running along the centre of the ladder and is the only case in which the step-ladder structure is constructed from only one enantiomer.

A further three examples (25% of the step-ladder total) each have a centre of symmetry at just one of the two cycle locations. Dialcohol **25** (Figure 6c) has two independent molecules A and B, which alternate along each strand, and its ladder contains two different $(O-H)_4$ cycles, both of which are centrosymmetric. There is only one type of organic cycle; this has no symmetry, despite **25** being an achiral meso compound, as the opposing molecules are crystallographically distinct (A and B).

Of the ten racemic dialcohols, compounds **28** and **30** are the only two examples with strands containing both enantiomers. Diol **28** has enantiomers of alternating handedness running along each strand, with molecules of the same chirality opposite each other. The $(O-H)_4$ cycles each have a centre of symmetry and the organic cycles each have a twofold rotation axis perpendicular to the ladder direction (Figure 6d).

In contrast to this, **30** has enantiomers of alternating handedness running along each strand, but with molecules of different chirality opposite one another. This structure is further complicated in that it contains two crystallographically independent molecules of **30** (A and B) that alternate along each strand, with the same types situated opposite to each other. Each ladder hence contains four different molecules of **30**, as illustrated in Figure 6e. This complex structure has no symmetry at the $(O-H)_4$ cycles, but is centrosymmetric at the organic cycle sites.

The Choice of Ladder Motif and Inter-Ladder Packing

Molecular bulk or shape is a significant factor in determining which type of hydrogen-bonding motif (chain, helix or cycle) is adopted by alcohols.[7,8] This has been analysed in some detail for the monoalcohol case by Brock and Duncan. Relatively small molecules can be fully hydrogen-bonded and participate in cooperative hydrogen bonding if they aggregate into chains by means of translation, glide planes or 2_1 screw axes. Bulkier monoalcohols tend to aggregate around three-, four- or sixfold screw or rotation-inversion axes instead.[8]

Size can also influence which of the step- or staircase-ladder structures is adopted by dialcohols. The methano-bridged cage diol **27** thus forms the step-ladder structure, but its ethano analogue **17** switches to the staircase-ladder type. Similarly (as discussed further below), crystalline dialcohol **15** contains both step- and staircase-ladders, but its dimethylated analogue **19** forms staircase-ladders exclusively. These limited data suggest that bulkier molecules are accommodated more easily as the staircase-ladder motif.

Alternatively, some of the larger monoalcohols can retain their hydrogen-bonded chain motifs and reduce crowding through incorporation of more than one molecule in their asymmetric unit.[8] This phenomenon is also evident in the crystal structure of **19**, the only dialcohol staircase-ladder structure without a 2_1 axis. Here, both diol enantiomers are also present, which represents an additional means of fine-tuning the steric packing.

Four of the six step-ladder structures that lack double centres of symmetry also contain two different molecules (A and B) in their asymmetric units. For this type of molecular ladder, however, considerable variations in enantiomer arrangements and symmetry are also possible.

Since ladders of both types contain their polar hydroxy groups in the centres of the motifs, their exterior surfaces are hydrocarbon in nature. The ladders hence pack alongside each other, with only C−H dispersion forces between them. In projection, the ladders are packed either parallel or nonparallel to each other. Figure 7 illustrates the typical examples of **19** (parallel) and **17** (nonparallel).

The Unique Structure of Dialcohol 15

The solid-state structure of 2,6-dimethylbicyclo[3.3.1]nona-3,7-diene-2-*endo*,6-*endo*-diol (**15**)[23] is unique amongst ladder-forming dialcohols in containing both types of double-stranded ladder (Figure 8). The staircase-ladders are of the favoured type: In other words they contain only one type of enantiomer arranged around a 2_1 screw axis. Unusually, however, the step-ladders are also made up of chirally pure material, with the strands of **15**

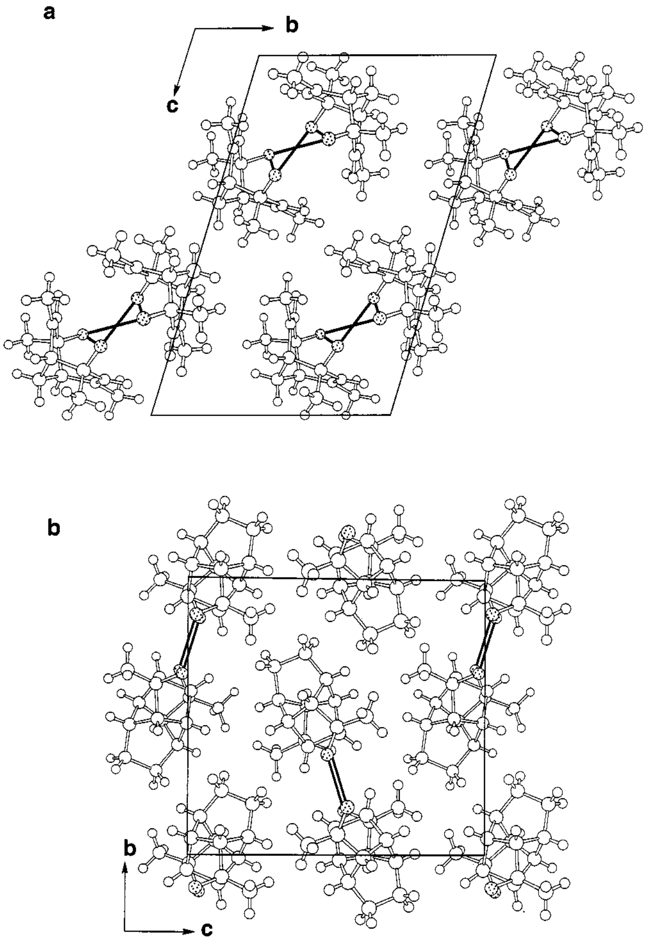


Figure 7. Typical solid-state packing modes of double-stranded ladders involving only hydrocarbon dispersion forces between the ladders: (a) **19**, (b) **17**

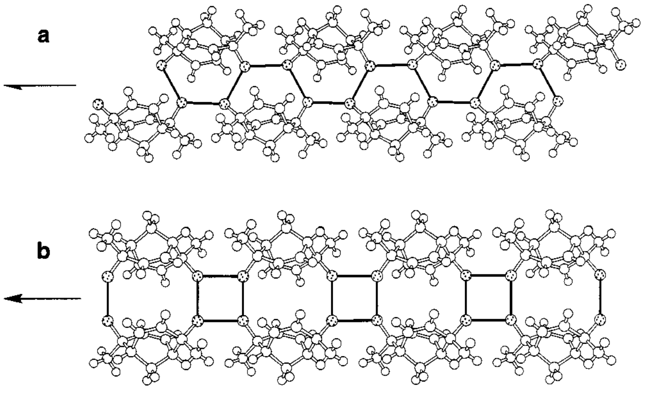


Figure 8. The two types of ladder structure present together in solid dialcohol **15**: (a) the chirally pure staircase-ladder and (b) the chirally pure step-ladder

molecules lying around a twofold axis. This is the only known example of a racemic dialcohol yielding an enantiomerically pure step-ladder.

The energies of the two ladder types are presumably similar, with the combination of weak hydrocarbon dispersion forces between such a mixture of ladder types representing the lowest energy arrangement. The enantiomer ordering is also remarkable in this example. Although each crystal is racemic in nature, every individual ladder present [(+)-step, (−)-step, (+)-staircase, and (−)-staircase] consists of chirally pure **15**.

Relationship with other Structures

The ability of dialcohols to self-organise into staircase-ladders and step-ladders has been demonstrated. Can these arrangements be extended, and how do they relate to other functional group compounds? The favoured arrangement of the double-stranded staircase-ladders is to have chirally pure molecules surrounding a 2_1 axis. In principle, therefore, larger dialcohols might be able to form doubly-stranded 3_1 or 4_1 staircase-ladders.

Over recent years, considerable interest has developed in metal coordination compounds that form double-stranded ladder structures. Silver, cadmium, cobalt and copper complexes have been studied most often.[41] A variety of hydrogen-bonded organic molecules, however, are also capable of producing double-stranded ladder structures and the examples in Figures 9 and 10 are representative of these.

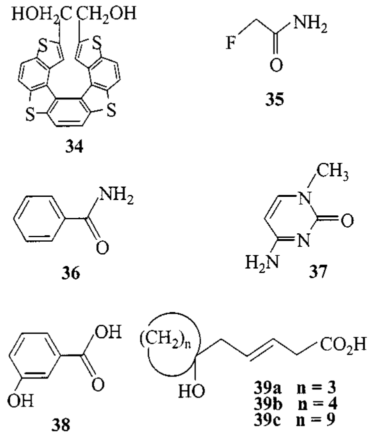


Figure 9. Structures of some molecules with alternative functionality that form double-stranded ladders in the solid state

Dialcohols containing additional functionality (beyond the limits of our CSD survey) can also form ladder structures. One example is the heterohelicene diol **34**, the (*PM*) form of which crystallises with a staircase-ladder of (*P*) molecules comprising one strand and (*M*) molecules the other. This arrangement is an exception to the normally preferred 2_1 symmetry and it is therefore unsurprising that pure (*P*)-**34** adopts a nonladder structure.[42]

Although amides exhibit many hydrogen-bonded packing modes, Leiserowitz and his colleagues have noted that many simple primary amides crystallise with double-stranded ladder structures.[43] Examples include fluoroacetamide **35**[44] (Figure 10a) and benzamide **36**.[45] The ladders formed are invariably step-ladders, which suggests that the dimeric interstrand amide motif is the predominant synthon here. Both the inter- and intrastrand hydrogen bonds are of the −C=O···H−N type, and both the interstrand cycles are centrosymmetric.

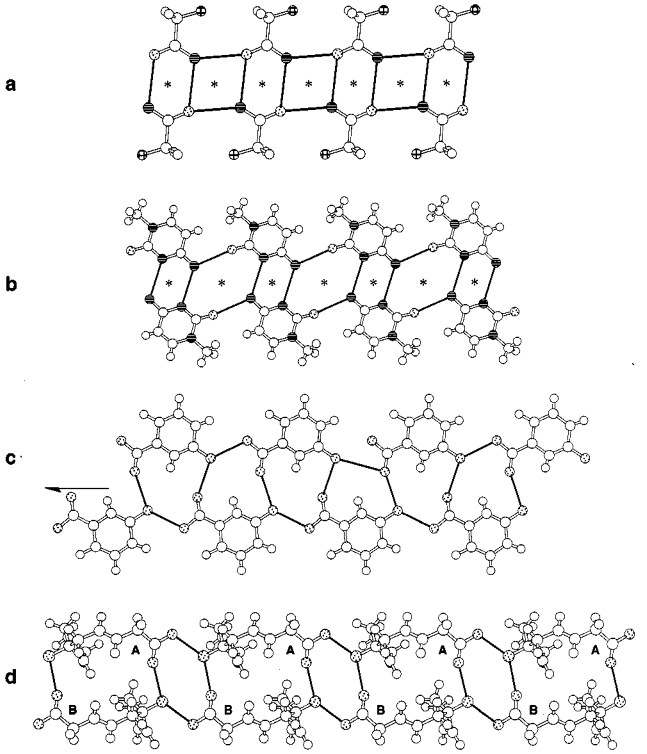


Figure 10. Examples of typical double-stranded ladders formed by functionalities other than dialcohols: (a) the step-ladder structure formed by fluoroacetamide **35** (FACETA),[44] (b) step-ladder formed by 1-methylcytosine (**37**) (METCYT01),[46] (c) staircase-ladder formed by 3-hydroxybenzoic acid (**38**) (BIDLOP01),[48] and (d) the step-ladder structure present in solid hydroxy acid **39b** (ZIZCOA);[49] atom coding: nitrogen (horizontal hatching), oxygen (stippling), fluorine (cross hatching); hydroxy hydrogen atoms are omitted and hydrogen bonds are shown as black lines; all four molecular examples are achiral

1-Methylcytosine (**37**) forms base pairs (interstrand N−H···N hydrogen bonds) that are linked to produce double strands (intrastrand C=O···H−N hydrogen bonds), yielding another step-ladder structure (Figure 10b).[46] Once again, both interstrand cycles are centrosymmetric.

Nonchiral or racemic carboxylic acids usually form cyclic hydrogen-bonded pairs,[47] but an exception is the noncentrosymmetric phase II of 3-hydroxybenzoic acid (**38**), which has a staircase-ladder structure (Figure 10c).[48] The interstrand hydrogen bonding involves the −C=O···HO− motif, but the intrastrand hydrogen bonding is −CO−OH···O−. Parallel head-to-tail orientations are present in both strands of the ladder, resulting in 2_1 symmetry.

Other related examples have recently been reported.[49] While the cyclobutane derivative **39a** forms a layer structure, both the cyclopentane **39b** and the cyclodecane homologues **39c** form doubly stranded ladders. The latter forms a staircase-ladder with the hydroxy acid molecules arranged around a 2_1 screw axis.

In contrast, **39b** forms a step-ladder structure (Figure 10d) with antiparallel head-to-tail hydroxy acid molecules in the two strands. There are two independent molecules in the asymmetric unit, with the A molecules occupying one strand and the B molecules the other. Therefore, neither the organic cycle nor the hydrogen-bonded cycle have any symmetry in this case. (This arrangement is analogous to the structure of dialcohol **29**.) The switch from step- to staircase-ladders (**39b** to **39c**) once again correlates with increased molecular size of the building block.

Conclusions

Two distinct types of hydrogen-bonded doubly stranded ladders have been identified as being formed by dialcohol molecules in the solid state. The observed structural symmetries are remarkably consistent within these two families of compounds. For staircase ladders, the strongly preferred construction mode (18 out of 19 cases, 95%) comprises enantiomerically pure (or achiral) molecules arranged around a 2_1 axis.

The preferred dialcohol step-ladder construction mode (six out of twelve cases, 50%) contains (+)-enantiomers along one strand, (−)-enantiomers along the other, and two repeating centres of symmetry along the ladder direction. There is, however, a considerably greater extent of exception to and variation from the ideal situation in this case. Currently, no enantiomerically pure dialcohol compound is known to form a step-ladder structure, although there is one known case (**15**) of an enantiomerically pure step-ladder.

We have demonstrated by preparation and analysis of the new compounds **17−19** that a reasonable degree of prediction is possible for dialcohols on the basis of their molecular structure, but selection of the precise ladder type is not yet possible. Prediction of unidirectional hydrogen bonding may ultimately prove useful for development of future smectic phase materials.[50]

Experimental Section

^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded with a Bruker ACF300 instrument at 25 °C and are reported as chemical shifts (δ) relative to $SiMe_4$. The substitution of carbon atoms was determined by the DEPT procedure. Melting points were determined with a Kofler instrument and are uncorrected. Mass spectra (EI) were recorded with a VG Quattro triple quadrupole instrument by Dr. J. J. Brophy. IR spectra were recorded with a Perkin−Elmer 298 infrared spectrophotometer. Microanalyses were carried out at the University of New South Wales and the Australian National University. Petroleum ether refers to material with bp range 60−80 °C.

4,7-Dimethylenepentacyclo[6.4.0.0^{2,6}.0^{3,10}.0^{5,9}]dodecane (32): Potassium *tert*-butoxide (0.55 g, 2.88 mmol) was added to a stirred suspension of diketone **31**[34] (0.36 g, 1.89 mmol), tetrabutylammonium chloride (2.5 mg), hydroquinone (2.5 mg) and methyltriphenylphosphonium bromide (1.75 g, 4.89 mmol) in dry benzene (20 mL) under nitrogen. The mixture was heated briefly for 5 min at 80 °C, then left to stir at room temp. overnight. Petroleum ether (25 mL) was added to the mixture and stirring was continued for 10 min. The reaction mixture was filtered through a wad of silica under suction, the silica was washed with petroleum ether, and solvents were removed from the combined filtrate by fractional distillation. The residual light yellow oil was then purified by elution through a silica column with petroleum ether, followed by removal of solvent by distillation, to yield **32** as a white solid (0.26 g, 71%). M.p. 48−49 °C. ^{1}H NMR ($CDCl_3$): δ = 1.43−1.72 (m, 6 H), 2.09−2.18 (m, 2 H), 2.26−2.28 (m, 2 H), 2.43−2.45 (m, 2 H), 4.56 (br. s, 2 H), 4.60 (br. s, 2 H). ^{13}C NMR ($CDCl_3$): δ = 18.6 (CH_2), 37.2 (CH), 39.7 (CH), 42.9 (CH), 51.8 (CH), 96.2 (CH_2), 158.1 (C). IR (paraffin mull): ṽ = 3080 w, 1690 m, 1320 w, 1280 w, 1240 w, 1225 w, 1210 w, 1120 w, 1040 w, 880s, 780 m, 760 m, 720w cm^{-1}. MS: *m/z* (%) = 184 (42) [M^+], 183 (25), 169 (33), 155 (20), 142 (40), 128 (61), 115 (37), 104 (38), 93 (24), 92 (38), 91 (100), 79 (33), 78 (35), 77 (71), 65 (20), 51 (28). $C_{14}H_{16}$ (184.3): calcd. C 91.25, H 8.75; found C 91.11, H 8.78.

4,7-Dimethylpentacyclo[6.4.0.0^{2,6}.0^{3,10}.0^{5,9}]dodecane-4-*syn*,7-*syn*-diol (17): A solution of MCPBA (85%; 0.72 g, 4.17 mmol) in dichloromethane (8 mL) was added dropwise to a vigorously stirred mixture of the diene **32** (0.37 g, 1.96 mmol) and aq. sodium hydrogen carbonate solution (0.5 M; 5.5 mL, 2.73 mmol). The mixture was stirred for 1 h and satd. aq. sodium sulfide (5 mL) was then added. The mixture was extracted with dichloromethane, and the combined organic extracts were washed with water and dried (Na_2SO_4). Evaporation of solvent from the filtrate gave the crude bis(epoxide) (0.33 g) as a gum. This unpurified material (0.33 g) was dissolved in dry diethyl ether (20 mL), lithium aluminium hydride (0.30 g, 7.91 mmol) was added, and the mixture was stirred at room temp. overnight. The mixture was chilled in an external ice-bath, and wet diethyl ether was then added to destroy excess lithium aluminium hydride. Once vigorous reaction had subsided, water (10 mL) was added, followed by sulfuric acid (5 M; 20 mL). The mixture was then filtered and the solid residue was washed with methanol. The filtrate and washings were combined and most of the solvent was removed by evaporation under reduced pressure. Water (10 mL) was added and the mixture was extracted with ethyl acetate. The combined organic extracts were dried (Na_2SO_4), and solvent was removed from the filtrate under reduced pressure to yield a mixture of the diol isomers as a white solid. These were separated by chromatography on silica to yield first the *anti*,*anti*-diol (0.15 g, 34%) and then the required *syn*,*syn* isomer **17** (0.17 g, 39%). M.p. 256−259 °C. ^{1}H NMR ($CDCl_3$): δ = 1.17 (s, 2 H, OH), 1.70−1.72 (m, 2 H), 1.93−2.00 (m, 2 H), 2.23−2.35 (m, 4 H). ^{13}C NMR [D_6]DMSO): δ = 19.0 (CH_2), 23.7 (CH_3), 30.1 (CH), 40.6 (CH), 48.4 (CH), 55.7 (CH), 79.6 (C). IR (paraffin mull): ṽ = 3260 s, 1300 m, 1280 m, 1260 m, 1230 w, 1190 w, 1150 m, 1120 m, 1090 m, 960 w, 930 m, 890 w, 840 w, 710m cm^{-1}. MS: *m/z* (%) = 220 (36) [M^+], 177 (52), 159 (42), 140 (46), 131 (25), 122 (47), 107 (29), 97 (47), 91 (73), 81 (36), 80 (46), 79 (62), 77 (50), 71 (47), 69 (31), 67 (23), 55 (25), 43 (100). $C_{14}H_{20}O_2$ (220.3): calcd. C 76.32, H 9.15; found C 76.17, H 8.96.

4,8-Dimethylbicyclo[3.3.1]nona-3,7-diene-2-*endo*,6-*endo*-diol (18): A solution of diketone **33**[37] (1.06 g, 6.0 mmol) in dry ether (30 mL) was added slowly with stirring to a slurry of $LiAlH_4$ (0.68 g, 0.018 mol) in dry diethyl ether (30 mL) at 0 °C. When addition was complete, the ice bath was removed and the solution was allowed to stir at room temp. overnight. Excess $LiAlH_4$ was decomposed by cautious addition of wet ether. Satd. aq. NH_4Cl solution was then added, and the reaction mixture was extracted several times with diethyl ether. The combined organic extracts were dried (Na_2SO_4), and solvent was evaporated from the filtrate to give **18** as a white solid (0.76 g, 70%). M.p. 170−171 °C (from diethyl ether). ^{1}H NMR [D$_6$]DMSO): δ = 1.64 (t, 2 H, *J* 3.1 Hz), 1.77 (s, 6 H), 2.16 (t, 2 H, *J* 3.1 Hz), 4.35 (br. s, 2 H), 4.56 (d, 2 H, *J* 4.1 Hz, exch. with D_2O), 5.26 (s, 2 H). ^{13}C NMR [D$_6$]DMSO): δ = 25.2 (CH_3), 31.0 (CH_2), 39.1 (CH), 71.7 (CH), 127.1 (CH), 136.4 (C). IR (paraffin mull): ṽ = 3275 s, 3225 s, 2700 m, 1660 w, 1330 s, 1300 w, 1280 w, 1150 m, 1125 w, 1095 w, 1040 s, 1020 m, 1000 s, 970 m, 890 m, 825 w, 785w cm^{-1}. MS: *m/z* (> 20% & [M$^+$]): 180 (1.4) [M$^+$], 162 (61) [M − H_2O]$^+$, 147 (100), 129 (25), 119 (31), 91 (41), 41 (46). $C_{11}H_{16}O_2$ (180.2): calcd. C 73.30, H 8.95; found C 73.40, H 9.10.

2,4,6,8-Tetramethylbicyclo[3.3.1]nona-3,7-diene-2-*endo*,6-*endo*-diol (19): A solution of diketone **33**[37] (1.76 g, 0.01 mol) in dry diethyl ether (100 mL) was stirred at −10 °C, and methyllithium (28.6 mL, 1.4 M solution in ether, 0.04 mol) was then added by syringe through a septum. After 30 min, the cooling bath was removed, and the reaction mixture was allowed to stir at room temp. overnight. Excess CH_3Li was decomposed by cautious addition of wet ether. Solvent was then removed under reduced pressure, satd. aq. NH_4Cl solution was added, and the reaction mixture was extracted several times with ethyl acetate. The combined organic extracts were dried (Na_2SO_4) and solvent was evaporated from the filtrate to give a pale yellow, sticky solid. This was triturated with a small volume of diethyl ether and then filtered to give **19** as a yellowish oil (1.56 g, 75%). M.p. 179−180 °C (from ethyl acetate). ^{1}H NMR [D$_6$]DMSO: δ = 1.20 (s, 6 H), 1.73 (s, 6 H), 1.74 (t, 2 H, *J* 3.15 Hz), 1.87 (t, 2 H, *J* 3.15 Hz), 4.05 (s, 2 H, exch. with D_2O), 5.09 (s, 2 H). ^{13}C NMR [D$_6$]DMSO: δ = 26.2 (CH_3), 31.0 (CH_3), 31.4 (CH_2), 44.7 (CH), 73.2 (C), 130.5 (CH), 135.9 (C). IR (paraffin mull): ṽ = 3375 s, 3335 s, 1660 w, 1345 w, 1305 m, 1245 w, 1230 w, 1190 w, 1140 m, 1105 s, 1075 m, 1045 m, 1025 m, 955 m, 915 m, 855 m, 825w cm^{-1}. MS: *m/z* (> 20% & [M − 18]$^+$): 208 (not obs.) [M$^+$], 190 (8) [M − 18]$^+$, 175 (90), 157 (68), 147 (49), 142 (24), 133 (32), 119 (22), 91 (21), 55 (22), 43 (100). $C_{13}H_{20}O_2$ (208.3): calcd. C 74.96, H 9.68; found C 75.12, H 9.86.

Determination of the Crystal Structures of 17−19: Crystals of **17** were grown from acetone, and **18** and **19** both from chloroform. Reflection data were measured with an Enraf−Nonius CAD-4 diffractometer in θ/2θ scan mode, using graphite-monochromated copper radiation (λ = 1.5418 Å). Data for **19** were corrected for absorption,[51] but those of the other two structures were not, as the crystals were irregular fragments. Reflections with $I > 3\sigma(I)$ were considered observed. The positions of all atoms in the asymmetric unit were determined by direct phasing (SIR92).[52] Hydroxy hydrogen atoms were included at positions from difference Fourier maps, while all other hydrogen atoms were included in calculated positions. Hydrogen atoms were assigned thermal parameters equal to those of the atom to which they were bonded. Positional and anisotropic thermal parameters for the non-hydrogen atoms were refined using full-matrix least squares.[53] Reflection weights used were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o) = [\sigma^2(I_o) + (0.04I_o)^2]^{1/2}$. The weighted residual is defined as $R_w = (\Sigma w\Delta^2/\Sigma wF_o^2)^{1/2}$. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-ray Crystallography.[54] Supplementary crystallographic data (excluding structure factors) for the structures **17−19** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-162504 to -162506, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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believe that our search is comprehensive for all dialcohol ladder structures involving only C, H and two HO groups contained in the 5.19 version of the CSD, but we would appreciate being notified of any omissions.

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