Pergamon

Tetrahedron Letters 42 (2001) 319–322

TETRAHEDRON
LETTERS

Unusual synthesis and crystal structure of 4-tricyclanol

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Received 22 September 2000; accepted 26 October 2000

Abstract—Here we report the synthesis of 4-tricyclanol, **6**, via an unusual route and its characterisation, by single crystal X-ray diffraction studies. The crystal structure of **6** shows extended hydrophobic channels and catenated hydrogen bonding. Both of these structural features are, to our knowledge, unique in multicyclic cage alcohols. The structures of similar compounds such as 1-adamantanol and *cis*-verbinol are based on small aggregate hydrogen-bonded clusters. We propose that the catenated hydrogen-bonded structure of the crystal phase of the title compound leads to the unusual morphology of the crystalline sample. Whereas crystals of other multicyclic cage alcohols are typically cuboid in shape, those of 4-tricyclanol, are very long (20–30 mm) needles with flat rectangular cross-sections (1–2×0.3 mm). The long axis of these crystals extends in the direction of the catenated hydrogen bonding. © 2000 Elsevier Science Ltd. All rights reserved.

Reactions at the C(4) bridgehead position of nortricyclene (bicyclo[2.2.1.$0^{2,6}$]heptane) are revealing from a mechanistic viewpoint. 4-Tricyclyl triflate **1**, undergoes the slowest known S_N1 reaction,[1] whereas the $S_{RN}1$ reaction of 4-tricyclyl iodide **2**, is very rapid.[2] Extrapolation of the results from other bridgehead-substituted esters[3] suggests that the rate of thermal decomposition of the perester **3**, will be retarded significantly less than the S_N1 reaction. Furthermore, incorporation of labile functionality at the C(4) position of tricyclene is a useful way of providing stability, as in **4** and **5**.[4]

On the basis of the demonstrated ease of formation of carbanions (organolithiums) at bridgehead sites in strained molecules,[5] we generated 4-lithiotricyclene by reaction of **2** with *t*-butyl lithium, and then reacted this compound with 2-methyl-2-nitrosopropane **8**. Compound **8** is available as a solid dimer that establishes rapid equilibrium with the monomeric species in solution.

4-Iodotricyclene **2**, was treated with *t*-BuLi in a 1:2 molar ratio at −78°C in 1:1 pentane diethyl ether under argon,[5] and after 45 min 2-methyl-2-nitrosopropane (equimolar with respect to **2**) was added. After conventional workup, 4-tricyclanol **6**, identical with an authentic sample, was isolated reproducibly, in 35% yield, as the only crystalline compound.

Formation of this unexpected product **6**, may be explained as follows (Scheme 1). The nitrogen–oxygen dipole in **8** is smaller than that of a carbonyl group, and **8** can react with 4-tricyclyl lithium (4-Tc:$^-$) by two routes. These are:

1. Path (a), Scheme 1, to give **9**, which then rearranges by the aza-analogue of a Wittig rearrangement to give **10**.
2. Intermediate **10**, can be formed directly by attack of the carbanion at the 'wrong' end of the dipole, path (b), Scheme 1. From **10**, arrived at by either route, it is possible to obtain the anion of **6**, and a nitrene by heterocyclic cleavage of the nitrogen–oxygen bond, path (c).

Intermediate **10**, can fragment to the anion of **6** directly; alternatively, since **10** is an α-effect nucleophile,[6] it can attack a further molecule of **8**, path (d), to give **11**, which can then fragment to give the anion of **6**. Definitive assignment of reaction pathway is not possible at present; one reason for this is that reports of reactions of carbanions with nitroso compounds are sparse.[7] Although 4-iodotricyclene **2**, was inert toward ozone it did react with dimethyl oxirane, generated in situ from acetone, in a two phase system of chloroform with an aqueous solution of oxone (Aldrich) with phosphate buffer and in the presence of 18-crown-6 as a phase transfer catalyst.[8] From this reaction 4-tricyclanol **6**, was obtained in 75% yield.

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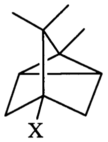
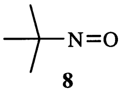
PII: S0040-4039(00)01903-1



1 $X = OSO_2CF_3$
2 $X = I$
3 $X = COOOCMe_3$
4 $X = I(OCOAr)_2$
5 $X = IF_2$
6 $X = OH$
7 $X = IO$



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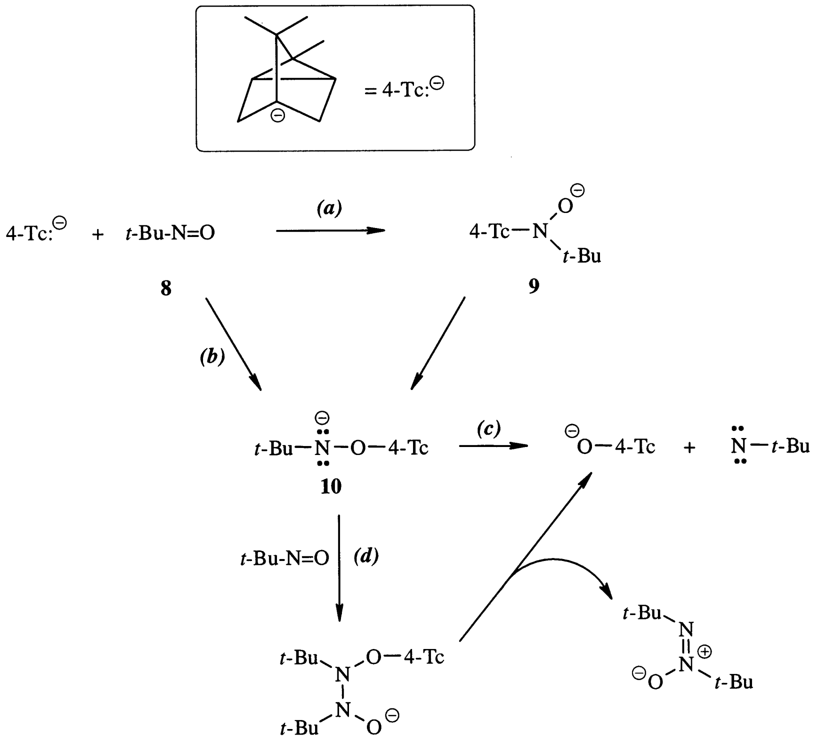
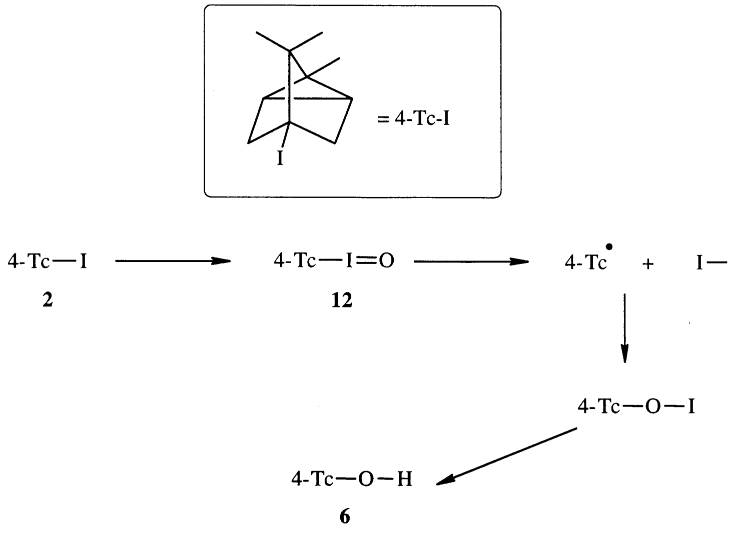


Scheme 1.

It is probable that the iodosyl compound **12** (Scheme 2) is a transient intermediate, which undergoes homolysis to a radical pair (Scheme 2). Recombination of the components of this radical pair with formation of a bond between 4-Tc$^\bullet$ and the oxygen of I–O$^\bullet$, gives a hypoiodite, which is the precursor of 4-tricyclanol **6**. This pathway, outlined in Scheme 2, has some precedent in the reaction of 1-iodoadamantane with peroxy acid to give 1-adamantanol.[9] Although there have been a couple of reports of the isolation of aliphatic compounds, R–IO, either at very low temperatures, or for very short lifetimes,[10] it appears that few, if any, such compounds will have any longevity.

4-Tricyclanol **6**, was isolated from solution by removal of solvent with a rotary evaporator. When the sample of **6** so obtained was left to stand in a stoppered flask under normal laboratory conditions it sublimed to produce long very thin needles. This behaviour is unusual for an alcohol and prompted us to determine the crystal structure using the synchrotron radiation source at Daresbury. Although single crystal data for multicyclic cage alcohols are fairly rare, recent examples have included both 1-adamantanol and *cis*-verbinol. In both these cases the small single crystals were cuboid in shape. Observed in both of these structure determinations was clustered hydrogen bonding resulting in the formation of hydrogen-bonded tetramers and trimers respectively within the unit cells.[11,12] These localised interactions are presumably favoured by the large aliphatic substituent at the C–O–H carbon and consequently lend no driving force to the anisotropic growth of the crystal phase along any of the coordinate axes. In contrast to these structures, the single crystal structure



Scheme 2.

determination[†,13,14] carried out by us on a sublimed sample of 4-tricyclanol **6**, reveals both an aliphatic channel, and catenated hydrogen-bonding extending along the *c* axis of the sample (Fig. 1).

The asymmetric unit of 4-tricyclanol is shown in Fig. 2. The O–H bond of the hydroxyl groups of each 4-tricyclanol is directed towards the hydroxyl oxygen atom of a neighbouring molecule, whose O–H bond in turn is directed towards the hydroxyl oxygen of the next molecule. The successive hydrogen-bonded molecules, are related by the operations of threefold screw axes (3_1, or 3_2) resulting in the formation of helical chains in the (001) direction, represented schematically in Fig. 3. This unusual configuration is presumably the consequence of the steric bulk of the tricyclic cage. In particular the steric effect of the two methyl substituents adjacent to the O-bearing carbon atom may preclude the formation of small hydrogen-bonded aggregates like those observed in the structures of 1-adamantanol and *cis*-verbinol. Both of these molecules are significantly less sterically crowded about the OH group. In 4-tricyclanol the chains of hydrogen bonded molecules are held together by van der Waals' interactions in a hexagonal-type array. As a consequence of this arrangement crystal growth is strongly anisotropic favouring growth in the *c* direction and resulting in the formation of one-dimensional channels. These channels contain $\bar{3}$ centres and are lined with methyl groups (C11) from six different chains; the diameter of these channels (C···C) is 6.16 Å (H···H distance = 5.8 Å).

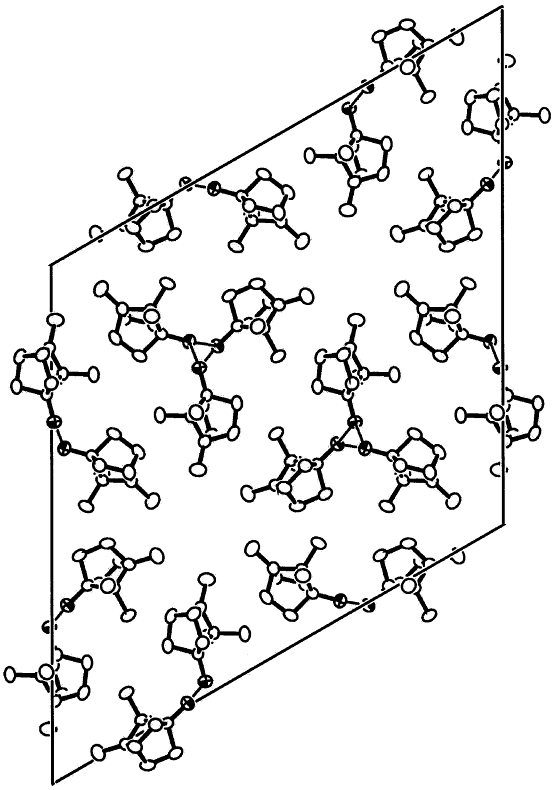


Figure 1. Projection of the channel structure of 4-tricyclanol along the (001) direction. C atoms are represented by open ellipsoids, O atoms by shaded ellipsoids and H atoms are omitted. The O–H···O hydrogen bonds are indicated.

[†] Crystal structure determination of 4-tricyclanol, $C_{10}H_{16}O$: M = 152.23, trigonal, space group, $R\bar{3}$ (no. 148), a = 25.413(4), c = 7.263(1) Å, V = 4062 Å^3, Z = 18, T = 150 K, λ = 0.6923 Å (synchrotron radiation), μ = 0.070 mm^{-1}, 9423 reflections measured, 2490 reflections unique, 2068 reflections observed (R_{int} = 0.0278). The crystal structure was solved using direct methods and refined by full-matrix least-squares on F^2. Final refinement of the 104 least-squares parameters converged to $wR(F^2_{\text{all data}})$ = 0.1318, $R(F_{\text{all data}})$ = 0.0580. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 148068.

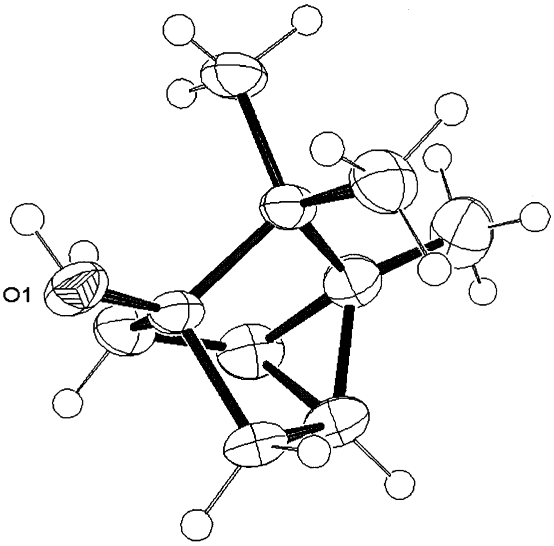


Figure 2. The asymmetric unit of 4-tricyclanol (50% ellipsoids).

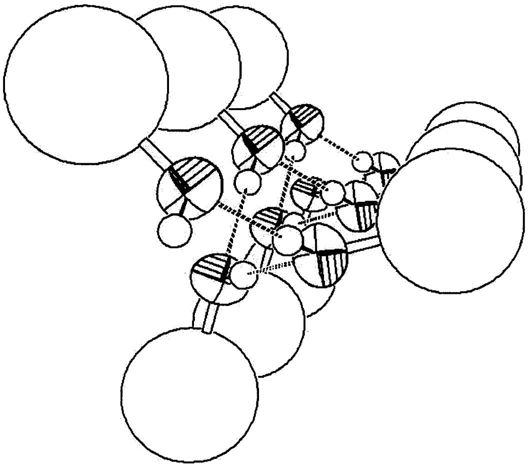


Figure 3. Schematic representation of the hydrogen bonding (shown as dashed bonds) between the hydroxyl groups, leading to the formation of helical chains. The multicyclic cages are shown as large circles for clarity.

Acknowledgements

We gratefully acknowledge the provision of time on DARTS, the UK national synchrotron radiation service at the CLRC Daresbury Laboratory, through funding by the EPSRC.

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