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CONFORMATIONAL ANALYSIS OF THE ANTI-TRICYCLO[5.1.0.0.^{3,5}]OCTANE RING SYSTEM: COMPARISON OF SOLUTION AND SOLID-STATE GEOMETRIES

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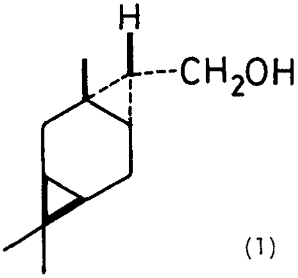
Abstract: The six-membered ring of an *anti*-tricyclo [5.1.0.0.^{3,5}] octane derivative is shown by X-ray crystallography to be almost planar. The precise conformation agrees remarkably well with that obtained for the molecule in solution using lanthanide shift reagents.

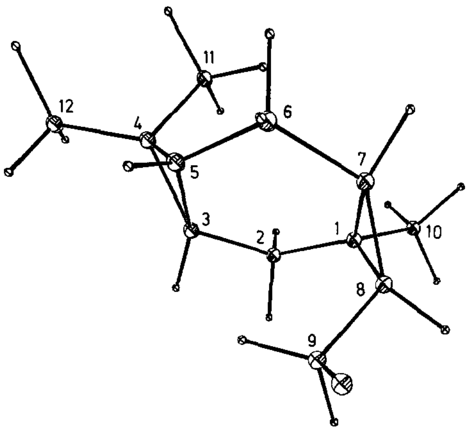
Although the conformation of the six-membered ring of *anti*-tricyclo[5.1.0.0.^{3,5}]-octanes and related compounds has been investigated[1,2] by a variety of methods, it has been pointed out[2] that none of these allows a precise conformational assignment to be made. On the basis of an NMR study[3] involving lanthanide shift reagents (LSR) we suggested that the cyclohexane ring in (1) assumes a very shallow boat conformation, being in fact almost planar. Although the approach adopted was rigorous and the results obtained as judged by the R-factor (0.03) quite definite, two factors suggested that additional evidence in support of this conclusion might be desirable. Firstly the nature of the site, an hydroxymethylene group, at which the LSR was complexed to the molecule, precluded the application of the generally accepted procedure[4] for the use of LSR in conformational analysis, which involves the positioning of the paramagnetic atom relative to some conformationally rigid part of the structure prior to an analysis of the conformationally mobile elements of the molecule. Secondly, the result itself could be interpreted in terms of a rapidly equilibrating, approximately equimolar, mixture of boat and inverted-boat conformers. Although again, on the basis of a comparison of the R-factors given by the single conformer and equilibrating mixture models respectively, this appeared to be excluded, it seemed appropriate to obtain further evidence for this unusual conformation.



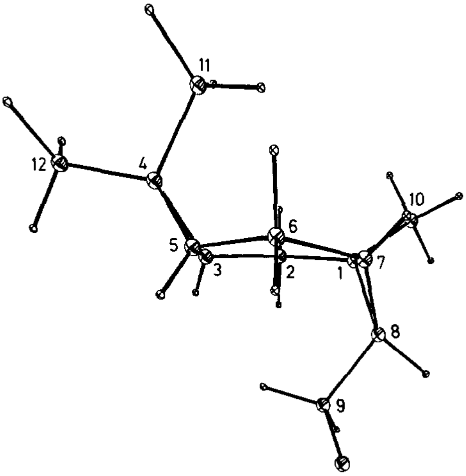
(1)

Thus for these reasons, and also because of the continuing interest in comparisons of solid-state and solution conformations, an X-ray crystal structure[5] was obtained for the alcohol (1),[6] (-)-8α-hydroxymethyl-1β,4,4-trimethyl-anti-cis-anti-tricyclo-[5.1.0.0.^{3,5}]octane. *The ORTEP representation (A) of this structure confirms* configurational assignments made for this alcohol previously;[6] the perspective shown in (B) emphasises the near planarity of the six-membered ring. A comparison of the solution and solid-state conformations is possible using the dihedral angles (2), (3) and (4) which define the conformation of the ring; these are available from the previous LSR study and were also calculated from the X-ray data. It can be seen (Table) that only in respect of the position of the hydroxymethylene group is there any difference between the solution and the crystal structures. In the crystal the hydroxymethylene group is almost perfectly staggered relative to the cyclopropane ring; the observed conformation in solution, which involves significant eclipsing interactions, is presumably the result of a LSR induced change in a part of the molecule which is very close to the binding site.[7]

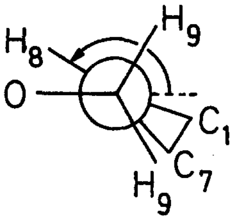
The excellent agreement between the results obtained by the two methods confirms the use of LSR as a valuable method for the precise determination of the conformation of suitable molecules in solution. It also indicates the usefulness of the computer programme LISCA[8] used in this case. It remains to investigate whether the conformation and the agreement between the solution and solid-state structures are dependent on the substituents of the cyclopropane rings. Although in the case of the former there appears to be some evidence[9] to suggest that this should be the case, it seems possible that ring strain may be the deciding factor in determining the conformation of this cyclohexane ring.



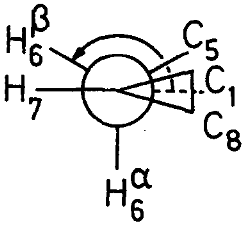
A



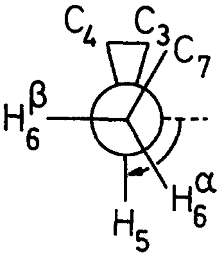
B



(2)



(3)



(4)

Dihedral Angle	(2)	(3)	(4)
LSR	153.5°	140.2°	68.6°
X-Ray	118.8°	139.7°	74.7°

Table

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5. Crystal Data: trigonal space group $R3_2$; a = 12.422(3), b = 12.422(3), c = 6.220(2) Å; Z = 3. Intensity measurements were made on a Hilger and Watts Y290 diffractometer with MoK_α radiation; the data were collected within the range $2 < \theta < 24^o$ and contained 243 unique reflections which had $I > 3\sigma I$. The structure was solved by direct methods and refined by full matrix least squares techniques. The number of variable parameters used was 56 and the structure was refined to final values of R = 9.11 and R^1 = 10.59. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Center, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK. Any request should be accompanied by the full literature citation for this communication.

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