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IN VITRO STUDIES OF TETRACYCLIC DITERPENOID BIOSYNTHESIS

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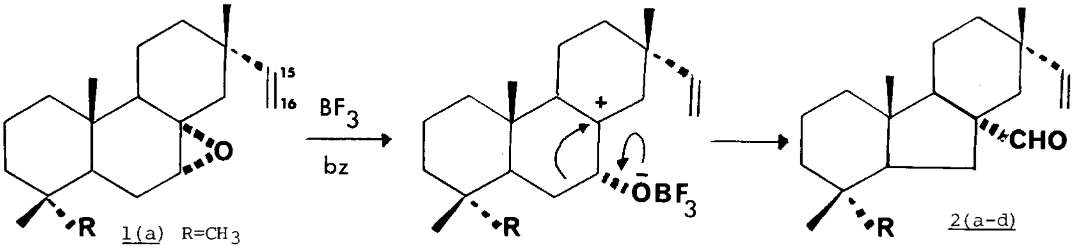
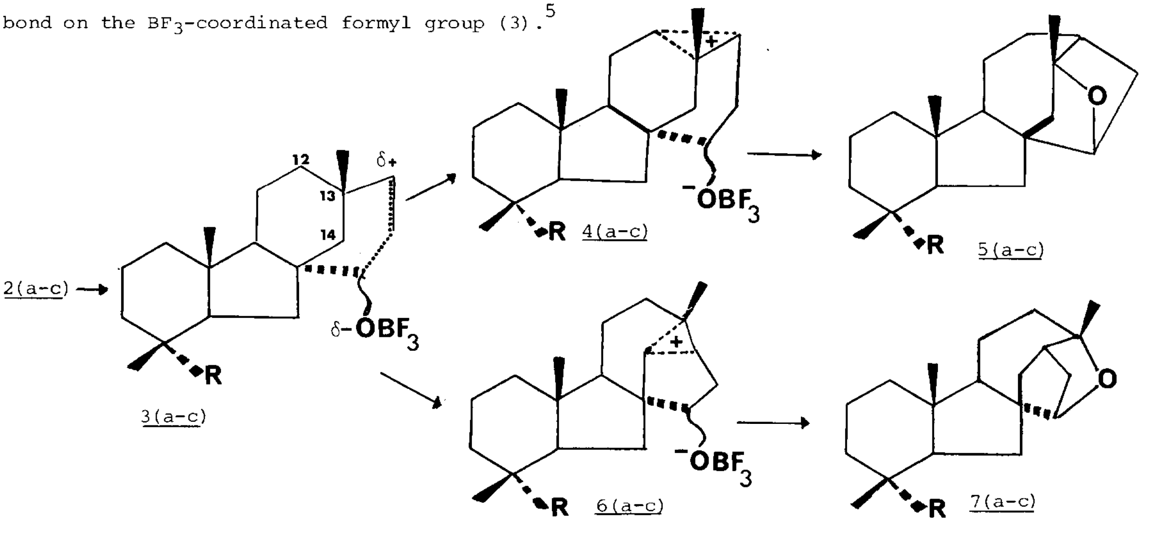
Abstract: The structure of a novel pentacyclic diterpene ether (7) is presented.

In the boron trifluoride diethyletherate catalysed rearrangement of the 7,8-epoxyisopimar-15-ene skeleton (1a-c) a pentacyclic ether is formed.[1,2] The structure and mode of formation of the ether was of considerable interest as the 15-ene was involved and potentially represented a demonstration of the involvement of the vinyl group in the type of cyclisation required by the postulated route for tetracyclic diterpenoid biosynthesis.[3] Isolation of an aldehyde with the rearranged skeleton (2c-d)[2,4,5] however, precluded that possibility since (2c) on further reaction gave the pentacyclic ether (7c).[2]



1(a) $R=CH_3$
1(b) $R=CH_2OCO\phi$
1(c) $R=CO_2CH_3$
1(d) $R=CH_3$;15,16-dihydro

There are a number of possible structures for the pentacyclic ether that could be considered, but two, (5 and 7), were more favoured. These could arise from the two possible non-classical ions (4 and 6)(or their classical equivalents) that are formed following attack of the double bond on the BF_3-coordinated formyl group (3).[5]



It is not possible to distinguish mechanistically between these, since both C12/C13 (leading to (4)) or C13/C14 (leading to (5)) can assume favourable orientations for participation because of the conformational mobility of the reacting structure (3). Although ^{13}C- and ^{1}H nmr and LIS studies established the structural fragment $CH_3\text{-}\overset{|}{\underset{|}{C}}\text{-}O\text{-}\overset{|}{C}H\text{-}CH_2\text{-}\overset{|}{\underset{|}{C}}H$, they did not allow a differentiation between (5a-b) and (7a-b) and consequently a single crystal X-ray structure analysis was undertaken.

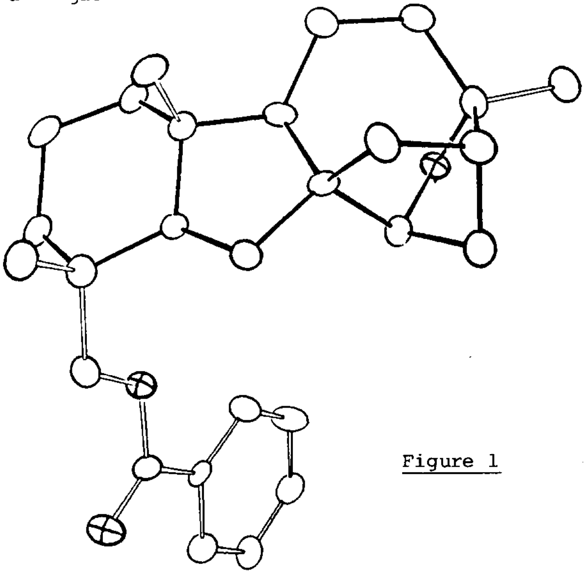


Figure 1

Crystals of the ether (7b) belong to the orthorhombic system, space group $P2_12_12_1$, with a=12.2267(8), b=10.5934(7), c=17.8426(11)Å; z=4. Intensity data with 2θ<114° were collected using an Hilger and Watts four-circle diffractometer, nickel filtered CuKα(λ=1.5418Å) radiation and the θ-2θ scan technique. Of the 1802 reflections measured, 1128 were judged observed ($|F_o^2|>3\sigma(F_o^2)$) and used in refinement. Application of the MULTAN[6] system of programmes yielded a plausible model which was completed and refined using conventional Fourier and least-squares methods. A conventional R factor of 0.072 was obtained on convergence with anisotropic thermal parameters for the non-hydrogen atoms, idealised positions for the aromatic carbon atoms and hydrogen atoms included in calculated positions in the final cycle of refinement.[7]

The X-ray analysis established the structure and stereochemistry of the ether as (7) which is shown in perspective in Figure 1 in which the oxygen atoms are distinguished. This confirms the tentative proposal for the structure put forward by Delmond et al.[2]

Thus, despite the participation of the vinyl group in a cyclisation, the mechanism leading to the ether (7) diverges significantly from any biosynthetic proposal.

Notes and References

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7. The structural and thermal parameters, bond distances and the observed and calculated structure factors are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratories, Lensfield Road, Cambridge CB2 1EW, England.

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