Stereochemistry of the Biological Divinyloxiran–Dihydro-oxepin Rearrangement: *X*-Ray Studies of the Sesquiterpenoids Miscandenin and Dihydromikanolide

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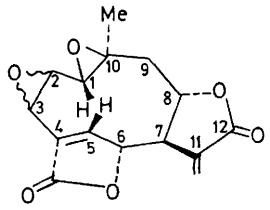
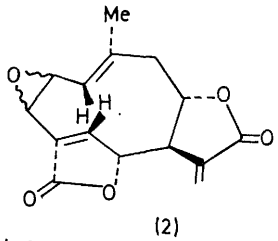
Summary The stereochemistries of the sesquiterpenoids dihydromikanolide and miscandenin have been determined by *X*-ray crystal-structure analysis: the results define the stereochemistry of the biological divinyloxiran–dihydro-oxepin rearrangement.

SEVERAL closely related sesquiterpenoid dilactones have been isolated from *Mikania* species.[1] The most prominent, mikanolide, was formulated as (**1a**) on the basis of chemical behaviour and extensive n.m.r. studies. A minor constituent, miscandenin, was assigned stereochemistry (**3a**) because of its probable derivation from the hypothetical common precursor (**2**) by way of a [3,3]sigmatropic (Cope) rearrangement. Previously studied, albeit simpler, examples of this rearrangement had produced one of the two possible *trans*-fused elemadienes *via* a chair-like transition state depending upon the conformational restraints implicit in the initial germacradiene.[2]

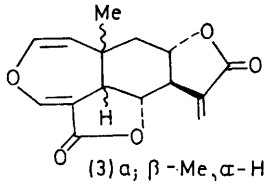
However, reconsideration of the Cope rearrangement which, as was pointed out earlier,[1] can also be looked upon as the homoelectrocyclic closure of a divinyloxiran to a dihydro-oxepin led us to the realization that the *cis*-fused divinyloxiran system and the configuration at C-6 impose limiting geometrical constraints on (**2**). These factors imply that miscandenin should be represented not by (**3a**) but either as (**3b**) [derived from (**2**) by way of rotation of the C-1,C-10 double bond through the ten-membered ring and closure *via* a boat-like transition state] or as (**3c**) [derived from (**2**) *via* a half-chair-like transition state]. The n.m.r. data of miscandenin[1] can, in fact, be accom-



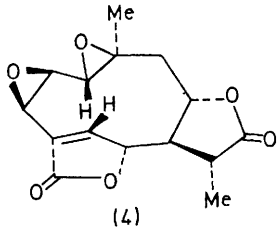
(1) a; 2,3-epoxide, *cis* and α
b; 2,3-epoxide, *cis* and β



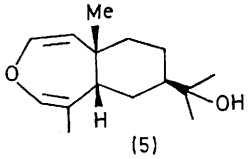
(2)



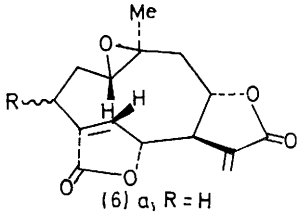
(3) a; β-Me, α-H
b; β-Me, β-H
c; α-Me, β-H



(4)



(5)



(6) a, R = H
b, R = β-OAc
c, R = α-OAc

modated more satisfactorily in terms of (**3b**) rather than (**3c**).

To settle the question, crystal structures of miscandenin and dihydromikanolide[1] have been determined in Glasgow. We find that these compounds have the stereochemistry depicted in (**3b**) and (**4**), respectively; the stereochemistry of mikanolide is therefore (**1b**) which differs from the original suggestion in the orientation of the C-2,3-epoxide. The stereochemistry of miscandenin is in accordance with the suggestion that (**1b**) and (**3b**) are formed from a common precursor (**2**) (C-2,3-epoxide, *cis* and β). The same ring junction stereochemistry has been attributed to occidenol (**5**).[3] The results require no revision in the stereochemistry of deoxymikanolide (**6a**) but intimate that scandenolide[1] could be (**6b**) rather than (**6c**).

The *X*-ray intensity data for miscandenin and dihydromikanolide were measured on a four-circle diffractometer with Mo-K_α radiation and the crystal structures elucidated by direct methods. The atomic parameters were adjusted by least-squares procedures and the analyses are at $R = 0{\cdot}070$ over 1222 reflections for (**3b**) and $R = 0{\cdot}079$ over 1486 reflections for (**4**). The molecular conformation of dihydromikanolide is very similar to the germacranolide conformation described earlier for shiromodiol.[4] The *trans* double bond in the ten-membered ring of (**4**) has a torsion angle of $-163°$ and is thus appreciably distorted from ideal geometry.

W. H. acknowledges support by a U.S. Public Health Service Grant from the National Cancer Institute. P.J.C. and G.A.S. thank the S.R.C. for a grant to purchase the diffractometer.

(*Received, 7th May* 1973; *Com.* 648.)

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