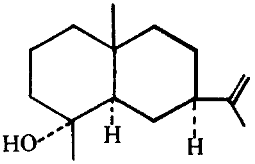
Tetrahedron Letters No.28, pp. 3223-3225, 1968. Pergamon Press. Printed in Great Britain.

The Synthesis and Absolute Configuration of Juniper Camphor and Selin-11-en-4α-ol. The Structure of Intermedeol (1)

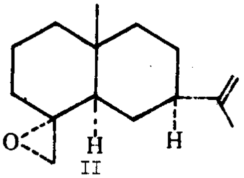
G. L. Chetty (2), V. B. Zalkow (3) and Leon H. Zalkow
School of Chemistry
Georgia Institute of Technology, Atlanta, Georgia

(Received in USA 7 March 1968; received in UK for publication 20 April 1968)

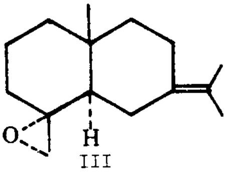
Recently Corbett and Smith (4) reported the isolation of a new sesquiterpene (selin-11-en-4α-ol) to which structure I was assigned. Intermedeol (5), which has been assigned a structure enantiomeric with I was found on direct comparison (6) not to be identical with selin-11-en-4α-ol by m.p., t.l.c. and by I.R., n.m.r. and mass spectra. In particular, the n.m.r. olefinic signal for intermedeol appeared 0.15 ppm further downfield than the corresponding signal in selin-11-en-4α-ol and the mass spectrum showed an intense peak (93%) at m/e 135 for selin-11-en-4α-ol, whereas in intermedeol this peak showed only a relative intensity of 38%.



I



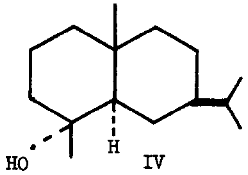
II



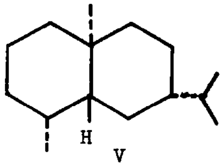
III

In order to determine whether structure I corresponded to the New Zealand sesquiterpene or to the enantiomer of intermedeol we set about to synthesize I unequivocally. Treatment of a commercial sample of eudesmol (~ 75% β isomer by g.l.c.) (7) with m-chloroperbenzoic acid gave in quantitative yield a mixture of two epoxides (ratio 3:2), which was directly dehydrated with phosphorus oxychloride in pyridine to give in 80% yield a mixture consisting of II and III (ratio 1:1). An attempt to prepare II and III by pyrolysis of the epoxy acetates gave a complex mixture consisting of aldehydes. Reduction of the mixture of II and III with lithium aluminum hydride, followed by chromatography on alumina gave in approximately a 1:1 ratio juniper camphor (IV) and selin-11-en-4α-ol (I).

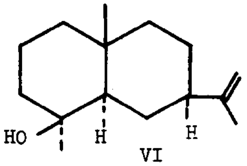
The juniper camphor thus obtained was identical in all respects (except optical rotation)



IV



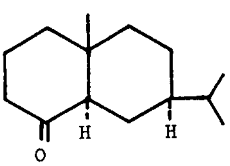
V



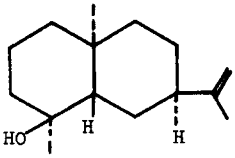
VI

with an authentic sample of (±) juniper camphor (8) but synthetic IV gave a (-) plain O.R.D. curve whereas natural optically active juniper camphor (9) showed an enantiomeric (+) O.R.D. curve. Thus natural optically active juniper camphor is now known to be the enantiomer of IV. Synthetic I ((-) O.R.D. curve) was identical in all respects with the New Zealand selin-4-en-11α-ol (I) thus verifying the structure and absolute configuration of the latter.

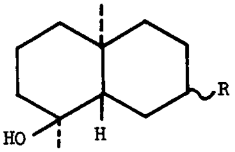
Thus, the structure of intermedeol remained in doubt. The most surprising observation was that intermedeol gave (-) selinane (V) on hydroganation (Pd/C), dehydrogenation ($POCl_3$/pyridine) and finally hydrogenation (Pt/C). The (-) selinane thus obtained was identical with (+) selinane prepared from β-eudesmol in refractive index, I.R. (thick-film), n.m.r. and mass spectra and differed only in optical rotation ($[d]_D^{32}$ -10.5° from intermedeol, $[d]_D^{32}$ + 12.5° from eudesmol). That intermedeol did not differ structurally from I only in the stereochemistry of the C-4 hydroxyl group was clear since another sesquiterpene, neo-intermedeol (VI) (10), of unequivocal structure, is known to have an axial C-4 hydroxyl group. Hydrogenation of intermedeol in the presence of Pt/C did not give dihydrojuniper camphor and this dihydrointermedeol on dehydration with $POCl_3$/pyridine, then oxidation with osmium tetroxide and lead tetraacetate and finally epimerization with base gave a ketone ((-) Cotton effect) not identical with VII (11) ((-) Cotton effect) prepared from eudesmol by acetylation, ozonolysis, pyrolysis and hydrogenation.



VII



VIII



IX C-7 β-acetyl
X C-7 α-acetyl
XI C-7 α-isopropenyl

Thus, it was suspected that intermedeol possessed structure VIII and that this was in fact so shown as follows. On treatment with potassium permanganate and sodium periodate, intermedeol gave in 75% yield hydroxy-ketone IX (δ0.90, 1.02, 2.14 ppm), which on refluxing in ethanolic potassium hydroxide was quantitatively converted into epimeric hydroxy-ketone X (δ0.88, 1.08, 2.10 ppm). The latter ketone gave XI on treatment with methylenetriphenylphosphorane. The selin-4-en-4α-ol thus obtained (XI) was identical in all respects with synthetic I except that XI gave an enantiomeric (+) plain O.R.D. curve. Thus the structure and absolute configuration of intermedeol are correctly represented by structure VIII.

The formation of (-) selinane from VIII is most readily explained by assuming that in the presence of Pd/C the double bond in VIII migrated to give an isopropylidene group which then absorbed hydrogen from the less hindered side. Double bond migration is particularly facile in the presence of palladium (12).

Acknowledgements: We thank the National Institutes of Health (5-R01-AM-10099-03) for financial support of this research. We thank the National Science Foundation for purchase of the Varian M-66 mass spectrometer used in this investigation.

References

1. Terpenes XXIII. Terpenes XXII, Tetrahedron Letters, in press.
2. Postdoctoral Fellow, 1966-1968.
3. Initial experiments performed by V.B. Zalkow at Oklahoma State University, 1963-1965.
4. R. E. Corbett and R. A. J. Smith, Tetrahedron Letters, 1009 (1967).
5. L. H. Zalkow, V. B. Zalkow and D. R. Brannon, Chem. and Ind., 38 (1963).
6. We thank Professor Corbett for supplying n.m.r. and I.R. spectra of selin-11-en-4α-ol and for an authentic sample for g.l.c., t.l.c. and mass spectral comparisons in our laboratory.
7. Since β-eudesmol has been totally synthesized (R. P. Houghton, D. C. Humber and A. R. Pinder, Tetrahedron Letters, 353 (1966) this synthesis comprises a total synthesis.
8. Kindly supplied by Academician F. Sorm, Czechoslovak Academy of Science.
9. This sample originated with Professor G. V. Pigulevskii, University of Lenningrad.
10. V. B. Zalkow, A. M. Shaligram and L. H. Zalkow, Chem. and Ind., 194 (1964).
11. B. Lacoume and L. H. Zalkow, Tetrahedron Letters, 588 (1966).
12. R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, Inc., 1965, p. 68.