Tetrahedron Letters No. 3, pp. 235-238, 1970. Pergamon Press. Printed in Great Britain.

TERPENOIDS. XXVII

THE STRUCTURE OF OCCIDENOL, A NOVEL SESQUITERPENE FROM THUJA SPECIES

B. Tomita and Y. Hirose

Faculty of Agriculture, University of Tokyo, Tokyo, Japan

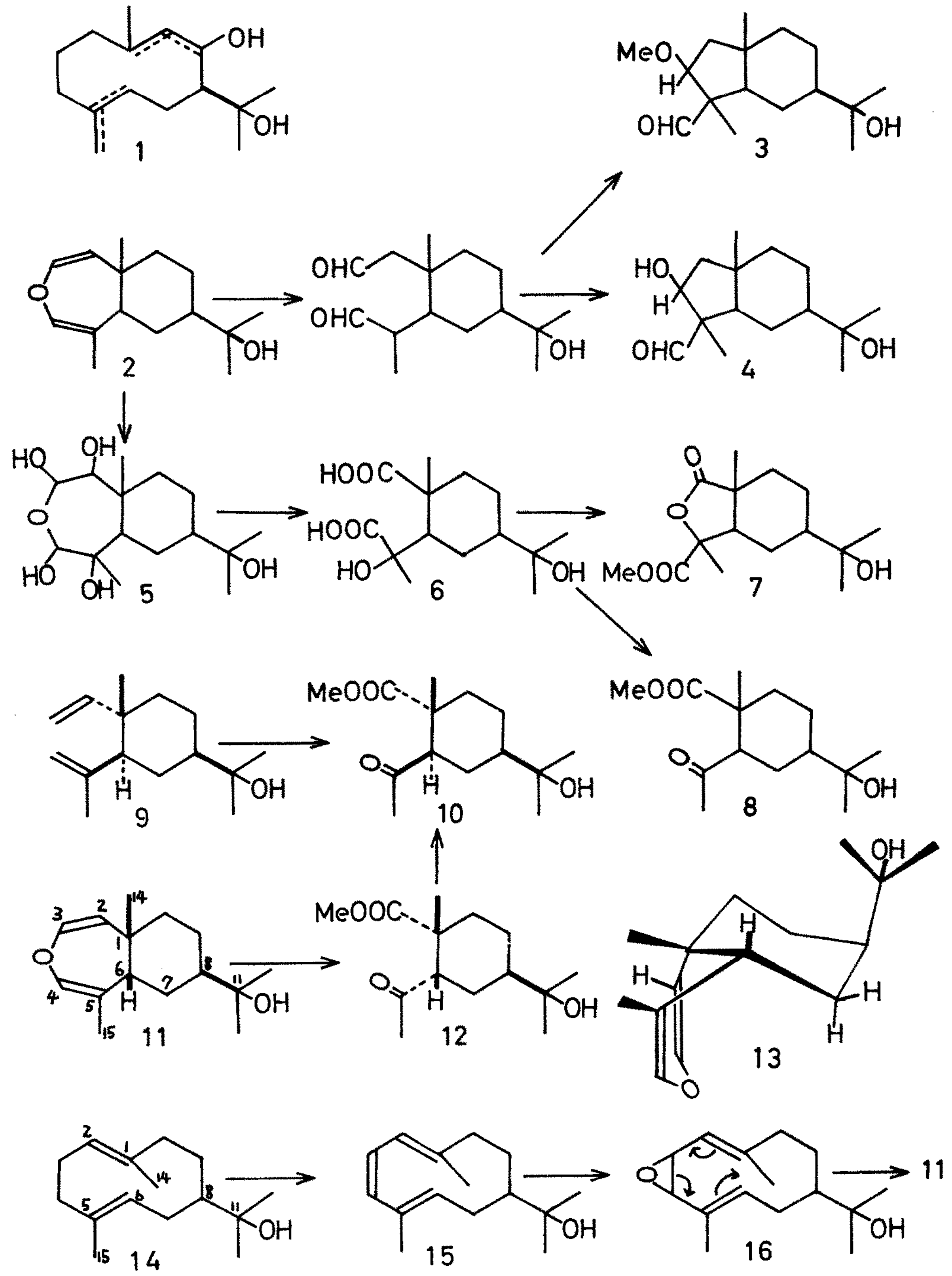
(Received in Japan 29 November 1969; received in UK for publication 18 December 1969)

In the previous paper,[1] we have described the isolation of a crystalline compound, $C_{15}H_{24}O_2$, m.p. 42-44°, $[\alpha]_D$ - 139°, from the wood of Thuja koraiensis and its identity[2] with occidiol obtained from the wood of Thuja occidentalis, whose tentative structure was proposed as (1) by Canadian workers.[3] Our preliminary investigation suggested that occidiol was not a diol because only one proton(δ 3.95, s) as to hydroxyl group was observed on the NMR spectrum of occidiol in DMSO-d_6 solution. In this report we wish to change the name of occidiol for occidenol and describe the structural elucidation of occidenol (11) which has an unusual divinyl ether group for natural products.

Occidenol shows the following spectral data: MS M^+ m/e 236 and base peak m/e 59, IR(KBr) 3400-3500, 3080, 3040, 1670, 1655, 1300, 1285, 1200, 1130, 1100, 918 and 750 cm^{-1}, NMR[4] δ 1.11(3H, s), 1.23(6H, s), 1.65(3H, d, J=1.4 cps), 2.28(1H, ddd, J=9.6, 4.7 and 1.3 cps), 4.25(1H, dd, J=7.5 and 1.3 cps), 5.98(1H, d, J=7.5 cps), and 5.98 (1H, br s). In occidenol there was only one hydroxyl group as mentioned above and it formed part of an isopropanol group, that was suggested by the base peak m/e 59 and the signal at δ 1.23. Further, since the IR absorption band due to hydroxyl group could not be observed in the monoacetate prepared from occidenol by heating with acetic anhydride and pyridine, one of the two oxygen atoms was considered to exist in an ether group. The unique strong absorption bands at 1655, 1300, 1285 and 1200 cm^{-1} with a shoulder at 1670 cm^{-1} suggested the presence of oxygen atom attached to the double bond. Three olefinic protons and an allylic methyl group were assigned to the partial structure $-CH=CH-O-CH=C(CH_3)-$ by their chemical shifts and NMDR experiments. On hydrogenation with PtO_2 in acetic acid occidenol gave a tetrahydro derivative, which was negative to the tetranitromethane test and displayed the new multiplet at δ 3.3-3.8(4H) due to $-CH_2-O-CH_2-$ and a doublet of the secondary methyl group at δ 1.00 (J=6 cps) in its NMR spectrum instead of the signals owing to olefinic protons and an allylic methyl group in occidenol. Though the positions of the tertiary methyl and isopropanol groups were not determined, above spectral data together with the fact that the divinyl ether group was located in a seven membered ring as established followingly might lead to the plausible structure (2) for occidenol.

Acid treatment of occidenol with dil. HCl(or H_2SO_4) and methanol gave a main product separated by preparative gas chromatography which was characterized as $C_{16}H_{28}O_3$, IR 3450, 1725 and 1100 cm^{-1}, NMR δ 1.11, 1.12, 1.16, 1.23(each 3H, s), 3.22 ($-OCH_3$), 3.65(1H, dd, J=6 and 8 cps: $-O-\overset{|}{C}\underline{H}-CH_2-$), 9.32(1H, s: $-C\underline{H}O$). We proposed the structure (3) for this product. In case of acid treatment in the absence of methanol occidenol afforded a diol (4) whose oxidation product with CrO_3-pyridine showed the IR absorption band at 1750 cm^{-1} meaning the presence of a ketone in a five membered ring. Thus these acid catalyzed reactions may be postulated as shown in the scheme involving aldol condensation after hydrolysis and the divinyl ether group in occidenol is concluded to be a part of a seven membered ring system.

On oxidation with alkaline potassium permanganate in aq. acetone at 0° and successive methylation with diazomethane occidenol gave two products; the major one, $C_{15}H_{24}O_5$, m.p. 133-135°, IR 3450, 1770(γ-lactone) and 1755 cm^{-1}(methyl ester), NMR δ 1.17(6H, s), 1.30, 1.65(each 3H, s) and 3.74($-COOCH_3$), was assigned to the structure (7). The minor one, $C_{14}H_{24}O_4$, $[\alpha]_D$ - 35°, IR 3450, 1720 cm^{-1}, NMR δ 1.08, 1.13, 1.15 (each 3H, s), 2.10($CH_3-\overset{|}{C}=O$), 2.92(1H, m), 3.64($-COOCH_3$), was also obtained by ozonolysis of occidenol followed by methylation, and its structure excluding stereochemistry was considered as (8) from these spectral data. These two methyl esters were possibly derived from (5) via (6), by lactonization and decarboxylation respectively.
The hydroxyl keto methyl ester (8) underwent hydrolysis and isomerization on treatment with ethanolic KOH at 60° to a free acid, which was methylated with diazomethane to give a new hydroxyl keto methyl ester, $C_{14}H_{24}O_4$, $[\alpha]_D$ + 15°, NMR δ 1.16(9H, s), 2.05(3H, s: $CH_3-\overset{|}{C}=O$), 2.87(1H, m) and 3.60($-COOCH_3$). This was in all respects reconciled with the hydroxyl keto methyl ester synthesized from elemol, $[\alpha]_D$ - 3°, of known absolute stereostructure (9) by the same oxidation followed by methylation. The isomerization from (8) was evidently an epimerization at the α-position to the methyl ketone group. Since the methyl ester from elemol must be shown as the stereostructure (10), the hydroxyl keto methyl ester (8) from occidenol was concluded to be represented by the structure (12) including the absolute configuration as well as the location of an iso-


OH
OH
1
MeO
H
OHC
OH
3
OHC
OHC
OH
HO
H
OHC
OH
4
2
OH
HO
OH
O
HO
OH
OH
5
HOOC
HOOC
HO
OH
6
O
O
MeOOC
OH
7
MeOOC
O
OH
8
H
OH
9
MeOOC
O
H
OH
10
3
2
14
1
O
6
8
7
11
4
5
H
15
OH
11
MeOOC
O
H
OH
12
OH
H
H
H
H
O
13
2
1
14
5
6
8
11
15
OH
14
OH
15
O
OH
16
11

propanol group. Accordingly the absolute configuration of occidenol is established as (11).

The NMR spectrum of occidenol displayed the characteristic signal at δ 2.28 which could be assigned to the allylic methine proton(H-6). Analyses of the coupling constants concerned with H-6 [$J_{2,6}$=1.3, $J_{4,6}$=0, $J_{6,7\alpha}$=9.6, $J_{6,7\beta}$=4.7 cps: established by NMDR experiments] suggest that occidenol exists in a preferred conformation (13) in which (a) the (H-6)-(C-6)-(C-1)-(C-2)-(H-2) portion exists in a coplanar W configuration,[5)-8)] (b) the (H-4)-(C-4)-(C-5)-(C-6)-(H-6) portion exists also in a coplanar configuration;[5,7,8)] (c) H-6 and H-7α are situated in a trans diaxial relationship.[5-7)]

It is interesting that occidenol possesses a cis-fusion as well as a divinyl ether group. As to the unique cis-fused ring system of a eudalene-type sesquiterpene, occidenol is closely related to occidentalol[7)] from *Thuja occidentalis* and *T. koraiensis*,[1)] and chamaecynone and its related compounds from *Chamaecyparis formosensis*[5)] with consideration of biosynthetic pathway. In our opinion, occidenol may be derived by a concerted cyclization from the hypothetic precursor (16), which would arise by biosynthetic epoxidation of 1,3,5-trans, cis, trans-cyclodecatriene (15) derived from trans-farnesol via the ten-membered intermediate (14).[9)]

REFERENCES AND FOOTNOTES

1) B. Tomita, Y. Hirose and T. Nakatsuka, *Mokuzai Gakkaishi* **15**, 76(1969)

2) The IR spectrum of occidenol was kindly supplied by Professor E. von Rudloff.

3) E. von Rudloff and G. V. Nair, *Can. J. Chem.* **42**, 421(1964)

4) The NMR spectra (100 MC) were measured in CCl_4 solutions (5-10 %) unless otherwise indicated using tetramethyl silane as an internal standard.

5) T. Asao, S. Ibe, K. Takase, Y. S. Cheng and T. Nozoe, *Tetrahedron Letters* 36(1968)

6) A. G. Hortmann, D. S. Daniel and J. Schaefer, *J. Org. Chem.* **33**, 3988(1968)

7) A. G. Hortmann and J. Barry De Roos, *J. Org. Chem.* **34**, 736(1969)

8) N. S. Bhacca and D. H. Williams, *Application of N.M.R. Spectroscopy in Organic Chemistry*, Holden-Day, San Francisco, Calif. (1964)

9) A. G. Hortmann, *Tetrahedron Letters* 5785(1968)