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THE STEREOCHEMISTRY OF PROTOPANAXADIOL
THE ABSOLUTE CONFIGURATION OF $C_{(20)}$ OF DAMMARENEDIOL-I AND -II

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The evidences provided by Fischer and Seiler (1) for the stereochemistry of $C_{(20)}$ of dammarenediol-II (II) in assigning that it is bearing β-hydroxyl ($C_{(20)}$:R), are erroneous , as already pointed out by Warnhoff et al.(2) and Barnes et al.(3).

The present communication deals with the absolute configuration of $C_{(20)}$ of dammarenediol-I (I) and -II (II) (4) to lead a conclusion, R for I and S for II.

As previously reported, protopanaxadiol (III) (12-β-hydroxy-dammarenediol-I) (5), a genuine sapogenin of Ginseng saponins, ginsenosides-R_{b-1}, -R_{b-2} and -R_c, afforded panaxadiol (IV) on acid treatment (6). Mild oxidation of panaxadiol (IV) with chromic acid in pyridine gave a 3-keto derivative (V), m.p. 236.5-238.5°, I.R.(in CS_2): 1715 (3-keto) and 3396 cm^{-1} (12-β-hydroxyl, intramolecularly hydrogen bonded with oxygen of the tetrahydropyrane ring), which yielded by Wolff-Kishner reduction 3-deoxypanaxadiol (VI), m.p. 192-193.5°, I.R.(in CCl_4): 3392 cm^{-1} (12-β-hydroxyl intramolecularly hydrogen bonded) and no carbonyl absorption. Oxidation of VI with Jones reagent yielded 12-keto

derivative (VII), m.p. 191-192°, I.R. (in CCl_4): 1709 cm^{-1} (12-keto) and no hydroxyl absorption, which was subjected to Baeyer-Villiger oxidation to give a lactone (VIII), m.p. 195-197°, I.R.(KBr): 1735 cm^{-1}(lactone);N.M.R.(in $CDCl_3$):τ 5.18 (1H, doublet ,J= 6.0 cps, -CO-O-C<u>H</u>-CH-). Alkaline hydrolysis of the lactone (VIII) followed by methylation of the resulted acid (IX) with diazomethane afforded an amorphous methyl ester (X), I.R.(in CCl_4): 1745, 1163 (ester) and 3350 cm^{-1}(13-hydroxyl intramolecularly hydrogen bonded). Dehydration of this ester (X) with thionyl chloride in pyridine gave an unsaturated ester (XI), which on subsequent oxidation with tert. butyl chromate yielded an amorphous unsaturated keto ester (XII),U.V. λ_{max}^{EtOH} 235 mu (ϵ 10,900); I.R.(in CCl_4): 1742, 1167 (ester), 1698 and 1625 cm^{-1}($\alpha\beta$-unsaturated five-membered ring ketone and double bond);N.M.R.(in $CDCl_3$):τ 2.55 (1H, singlet, -CO-C=C<u>H</u>-C-).

This unsaturated keto ester (XII) was oxidized with potassium permanganate in pyridine, and the acidic fraction of the product was extracted with n-hexane. The hexane-soluble part was methylated with diazomethane, and the crude methyl ester was purified by the preparative gas chromatography (7) to give oily (-) methyl cinenate (XIII), $[\alpha]_{590}^{14}$ -12.3°, $[\alpha]_{400}^{14}$ -49°, $[\alpha]_{340}^{14}$ - 103° (c= 0.2, $CHCl_3$).* The structure of XIII was confirmed by the comparison of the I.R. spectrum and the retention time of the gas chromatogram with those of racemic methyl cinenate prepared from 1,8-cineol (8).

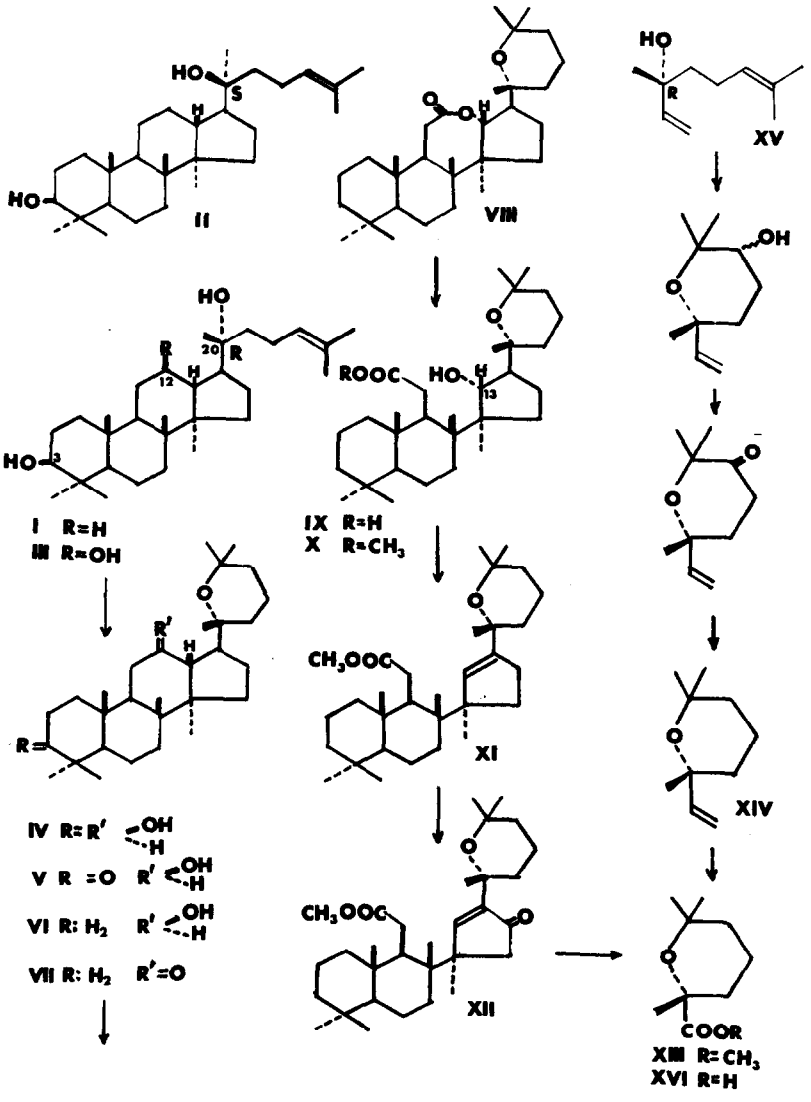
The optically active trimethylvinyl-tetrahydropyrane (XIV) was prepared from (-) linalool (XV) by the procedure known in

the literatures (9,10). On oxidation with potassium permanganate and sodium periodate (11), XIV yielded (-) cinenic acid (XVI), m.p. 47.5-48.5°, $[\alpha]_{590}^{27}$ -7.3°, $[\alpha]_{400}^{27}$ - 26.0°, $[\alpha]_{340}^{27}$ - 54.8° (c= 6.6, $CHCl_3$)*, whose I.R. spectrum in CCl_4 and Rf value of the thin layer chromatogram (on Silica Gel G impregnated with oxalic acid, using chloroform as the developing solvent) were identical with those of racemic cinenic acid.

(-) Cinenic acid (XVI) was methylated with diazomethane to give oily (-) methyl cinenate, $[\alpha]_{590}^{29}$ - 10.1°, $[\alpha]_{400}^{29}$ - 37.6°, $[\alpha]_{340}^{29}$ - 81.8°(c= 2.1, $CHCl_3$)*, whose I.R. spectrum and the retention time of the gas chromatogram were identical with those of racemic methyl cinenate.

The absolute configuration of (-) linalool (XV) has already been assigned as R by Conforth et al. (12), and it has also been established that XIV retains the same absolute configuration as that of XV (9,10). Accordingly, (-) cinenic acid (XVI) as well as its methyl ester (XIII) with negative optical rotation should have R-configuration. Since protopanaxadiol (III) was already correlated to dammarenediol-I (I) (5), it can be concluded that the absolute configuration of $C_{(20)}$ of dammarenediol-I (I) is represented as R, then that of dammarenediol-II (II) is S configuration.

Recently we have learned from Dr. Ohloff that his group came to the same conclusion on the absolute configuration of (-) cinenic acid (XVI) (13). On the other hand, Dr. Biellmann has informed us that he assigned S-configuration for $C_{(20)}$ of dipterocarpol (= 3-keto-3-deoxydammarenediol-II)as shown in his report jointly published(14).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III R=OH
ROOC
HO
H
13
IX R=H
X R=CH3
O
R'
H
R=
IV R=R' OH H
V R =O R' OH H
VI R: H2 R' OH H
VII R: H2 R'=O
CH3OOC
XI
XIV
CH3OOC
O
XII
COOR
XIII R=CH3
XVI R=H

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*Note:Optical activities were measured on a Spectrophotometer Model ORD/UV-5, Japan Spectroscopic Co.Ltd.