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ABSOLUTE CONFIGURATIONS OF (+)-METHYL TODOMATUATE AND ITS NEW ANALOGUES, PSEUDOTSUGONAL AND AR-PSEUDOTSUGONAL, ISOLATED FROM DOUGLAS-FIR WOOD

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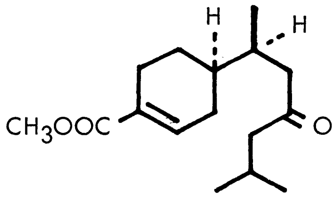
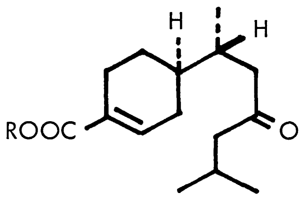
Two new sesquiterpene keto aldehydes, named pseudotsugonal and *ar*-pseudotsugonal, together with (+)-methyl todomatuate were isolated from the wood of Douglas fir (*Pseudotsuga menziesii* (Mirb.)Franco) grown in British Columbia. The absolute configurations of all these compounds have been established to possess the R,R configuration at the two asymmetric centers.

The history of the discovery, isolation, and characterisation of a compound having insect juvenile hormone activity, juvabione which was identical with the methyl ester of the known todomatuic acid, has been well documented.[1)] In 1969, Blount and his co-workers[2)] suggested by X-ray analysis of the key intermediate and also by the measurements of ORD and CD spectra of four synthetic diastereoisomers that the absolute configuration of natural (+)-juvabione has been revised to the R,S configuration (I), contrary to the R,R configuration (IIb, R=CH_3) deduced previously.[3)] Furthermore, they suggested that (+)-epijuvabione and (+)-epitodomatuic acid have the R,R configuration. Recently, Rogers and Manville[4)] isolated an insect juvenile hormone active substance, (-)-cis-(1′R)-4-(1′,5′-dimethyl-3′-oxohexyl)cyclohexane-1-carboxylic acid (III), from the wood of Douglas fir growing in British Columbia, and they deduced its structure possessing the oposite steric configuration at C-1′ to that of natural (+)-juvabione by comparison of its ORD spectrum with the data reported by Pawson et al.[5)]

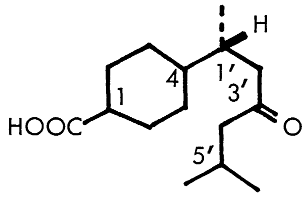
This paper describes the isolation and determination of the absolute configurations of (+)-methyl todomatuate (IIb, R=CH_3), and two new sesquiterpene keto aldehydes, named pseudotsugonal (IV) and ar-pseudotsugonal(V), from the higher boiling fraction (b.p. >110°/5 mmHg) of the volatile oil obtained from the wood of Douglas fir (Pseudotsuga menziesii (Mirb.) Franco) grown in British Columbia (the examinated material was obtained from the exhibitions of British Columbia Pavilion held in OSAKA EXPO' 70).



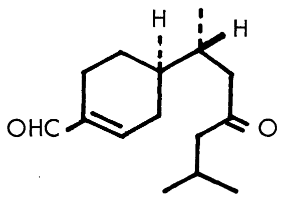
(I)



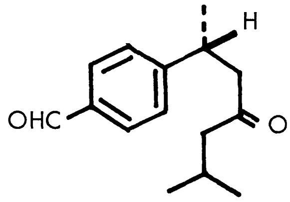
(II a , R = H)
(II b , R = CH_3)



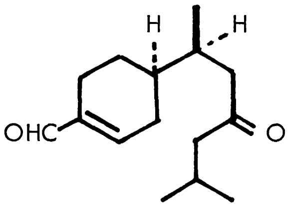
(III)



(IV)



(V)



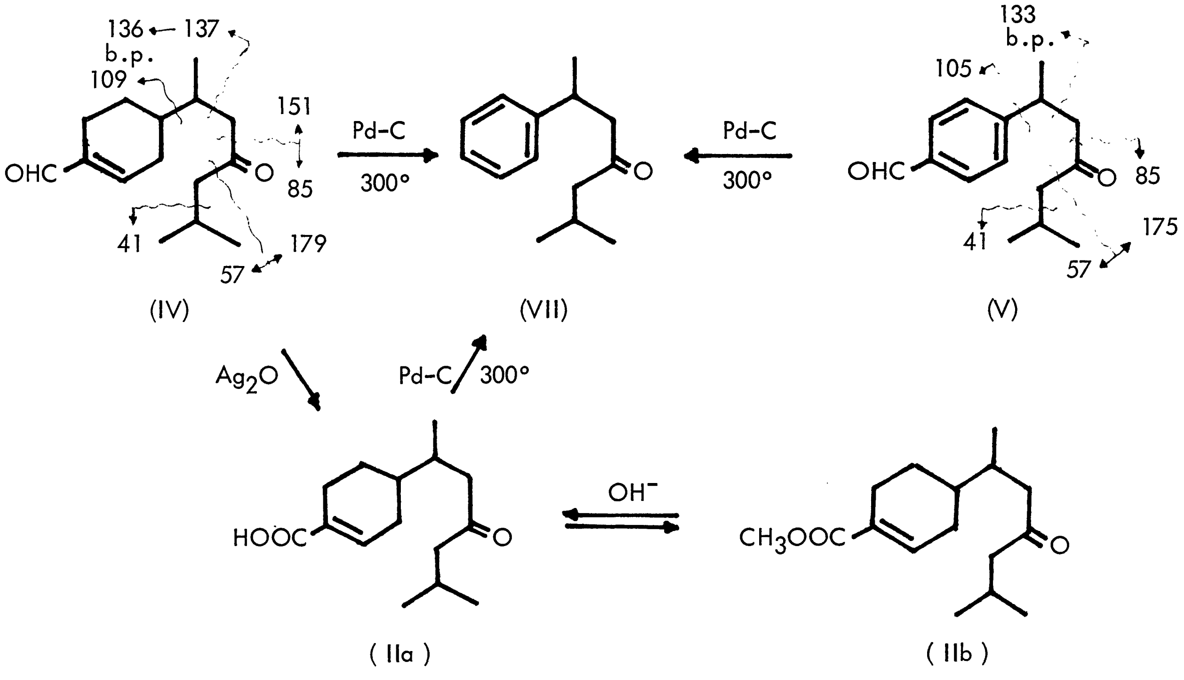
(VI)

From the fraction eluted with a mixture of ether-hexane (3 : 7) on silica gel column chromatography, ar-pseudotsugonal was isolated by preparative gas chromatography using OV-17 and Carbowax 20M columns. Pseudotsugonal and (+)-methyl todomatuate were contained in the fraction eluted with a mixture of ether-hexane (1 : 1), and were separated by the repeated gas chromatography using the same columns.

Pseudotsugonal, (IV) $[\alpha]_D^{24}$ + 85.7° (c 0.25, $CHCl_3$), has the molecular formula $C_{15}H_{24}O_2$ (M^+, m/e 236, 0.2%) based on the mass spectrometry. The UV, IR, and NMR spectral data indicated that it contains the following structural units : a -CH=C-CHO group (UV: λ_{max}^{EtOH} 232 mμ (ε 17,000); IR(neat): 1690, 2720, and 1640 cm^{-1}; NMR(CCl_4): δ 9.30 ppm (1H, s) and δ 6.64 (1H, broad m)); a C=O group IR: 1710 cm^{-1}); and three CH_3CH- groups (NMR: δ 0.86 ppm (3H, d, J = 6 Hz) and δ 0.89 (6H, d, J = 6 Hz)). The mass spectrum of it exhibits peaks at m/e 41 (42%), 57 (56), 85 (12), 109 (10), 136 (100), 151 (1), and 179 (2), suggesting the presence of an isobutyl ketone and a phellandral residues in it. These facts suggested that the structure of pseudotsugonal would be represented by IV. This structure was confirmed by the following procedures. When it was heated with 10% Pd-C at 300°, it afforded an aromatic ketone, 2-methyl-6-phenylheptan-4-one (VII); $C_{14}H_{20}O$ (M^+, m/e 204, 34%); IR(neat): 1700 cm^{-1} (C=O), 1590, 1480, 755, and 690 cm^{-1} (monosubstituted benzene ring); NMR(CCl_4): δ 0.80 ppm (6H, d, J=6 Hz, $(CH_3)_2CH$-), δ 1.19 (3H, d, J=7 Hz, Ar-CH-CH_3), and δ 7.08 (5H, s, benzene ring protons); MS: m/e 105 (100%), 57 (40) 204 (34, M^+), 85 (31), 147 (22), and 189 (20), which was also obtained from todomatuic acid by heating with Pd-C at 300°. Moreover, oxidation of pseudotsugonal with basic silver oxide afforded todomatuic acid which was identical with an authentic sample.

ar-Pseudotsugonal (V), $[\alpha]_D^{24}$ -23.9° (c 0.57, $CHCl_3$) has the molecular formula $C_{15}H_{20}O_2$ (M^+, m/e 232, 45%). Its IR spectrum is quite similar to that of cuminaldehyde and shows the band at 1720 cm^{-1} due to a carbonyl group and the bands at 1700, 2740, 1600, 1575, 850, and 840 cm^{-1} due to a p-substituted benzaldehyde group. The NMR spectrum of it shows a doublet at δ 0.83 ppm (6H, d, J=6 Hz, $(CH_3)_2CH$-), a doublet at δ 1.24 (3H, d, J=7 Hz, Ar-CH-CH_3) a singlet at δ 9.87 (1H, s, Ar-CHO), and a multiplet located between δ 7.2~8.0 (4H, m, benzene ring protons)). The mass spectrum of it shows the presence of an isobutyl ketone group (m/e 41 (37%), 57 (64), 85 (65), and 175 (21)) and a cuminaldehyde residue (m/e 77 (21%), 91 (16), 105 (23), 133 (100), and 149 (25)). Heating of it with 10% Pd-C at 300° gave the aromatic ketone (VII). All spectral data and the chemical evidence suggested that ar-pseudotsugonal is the aromatic derivative of pseudotsugonal, p-(1′,5′-dimethyl-3′-oxohexyl)benzaldehyde shown in V.

Methyl todomatuate (IIb, R=CH_3), $[\alpha]_D^{24}$ +67.7° (c 0.31, $CHCl_3$) was isolated from the same fraction containing pseudotsugonal. It was identified with an authentic sample by direct comparison. Hydrolysis of it with alcoholic potassium hydroxide afforded (+)-todomatuic acid.



The Absolute Stereochemistry of Pseudotsugonal, ar-Pseudotsugonal, and (+)-Methyl todomatuate.

In view of the absolute stereochemistry of 4-p-tolylpentanol,[6] ar-turmerone,[7] α-curcumene,[8] and nuciferal and nuciferol,[9] it would be certain that ar-pseudotsugonal possesses the R configuration at C-1′ in V.

All of the spectral data (UV, IR, NMR, MS, ORD, and CD), except for the lower optical rotatory value, of methyl todomatuate isolated from the wood of Douglas fir were completely identical with those of the methyl ester of natural todomatuic acid (Dr. Isoe's sample). But, the ORD and CD spectra of our methyl todomatuate were identical with those of " (+)-epijuvabione" not with "natural (+)-juvabione", which were reported by Pawson et al.5)

The ORD and CD spectral data of pseudotsugonal are shown as follows; ORD (c 0.0228, ethanol, 24°) : $[\phi]_{600}$ +70°, $[\phi]_{370}$ +640°, $[\phi]_{356}$ +665°, $[\phi]_{330}$ 0°, $[\phi]_{318}$ -200°, $[\phi]_{306}$ 0°; CD (0.030 M, ethanol, 24°): $[\theta]_{374}$ 0, $[\theta]_{366}$ +143, $[\theta]_{342}$ +396, $[\theta]_{333}$ +451, $[\theta]_{296}$ -770, $[\theta]_{290}$ 0. These data were not identical with those of (4R, 1'S)-(1',5'-dimethyl-3'-oxohexyl)cyclohexene-1-carboxaldehyde (VI) having the R,S configuration which was synthesized by Pawson et al.5) From these results, therefore, it would be also certain that pseudotsugonal possesses the R,R configuration at the two asymmetric centers.

Thus above results led us to the following conclusions; pseudotsugonal, ar-pseudotsugonal, and (+)-methyl todomatuate isolated from the wood of Douglas fir, as well as natural "original" todomatuic acid and the saturated keto acid (III), have the same R,R configuration; and it seems that the authentic sample (Prof. Cerny's sample,[*1] Czechoslovakian origin, it gave todomatuic acid having m.p. 64-65° by hydrolysis) of "natural (+)-juvabione" used for the identification by Pawson et al.5) is not identical with our methyl todomatuate (its parent todomatuic acid has m.p. 57-59°).

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*1) We could not get the authentic sample from Prof. V. Cerny, Czechoslovak Academy of Science, Inst. of Organic Chem. and Biochem. Private Communication.

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