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TRANS- AND CIS-A/B-RING FUSED ISOMER OF 1α-CARBOMETHOXY-1,11α-DIMETHYL-HEXAHYDROFLUORENE*

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According to the interesting biogenetical and structural relationship between gibberellins and other diterpenoids, the transformation of abietic acid (I) to the hydrofluorene derivatives (II and III), regarded as a basic skeleton of gibberellin, was previously achieved by application of the benzilic acid rearrangement.[1] Under the same intention, attempts were made for the synthesis of isomeric hydrofluorenes (V and VI) having an evident trans- and cis-A/B-ring juncture, respectively.

The methyl ester (VIII), b.p.$_4$ 175-177°, ν_{max}^{film} 1730, 1710, 1605 cm^{-1}, τ 8.66(C_{11}-Me), 8.49(C_1-Me), 6.98(C_{10}-H), 6.32(COOMe), of hydrofluorenone (VII) synthesized from abietic acid,[1,2] was reduced with $NaBH_4$ followed by dehydration with $POCl_3$-pyridine

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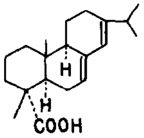
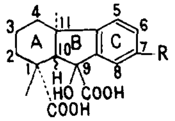
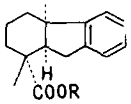
* This work will be published in detail elsewhere. New compounds indicated by m.p. and b.p. gave satisfactory analytical values and gas-liquid chromatographic purity (The authors thank Dr. N.Ikekawa, this Institute, for his advice on the measurement of gas-liquid chromatography). All NMR spectra were measured at 60 mc in CCl_4(5-10% solution) vs. Me_4Si as internal reference.



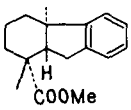
(I)



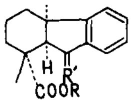
(II) R=H
(III) R=OH
or OMe



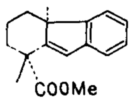
(IV) R=H
(V) R=Me



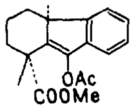
(VI)



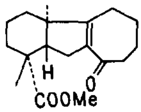
(VII) R=H, R'=O
(VIII) R=Me, R'=O
(IX) R=Me, R'=<$^{OH}_{H}$



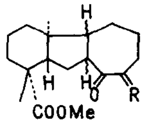
(X)



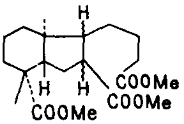
(XI)



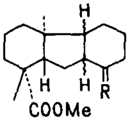
(XII)



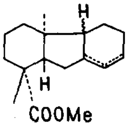
(XIII) R=H_2
(XIV) R=CH– 



(XV)



(XVI) R=O
(XVII) R=<$^{OH}_{H}$



(XVIII)

or conc. HCl-MeOH to give Δ^9-hydrofluorene (X), m.p. 74-76° ν_{max}^{KBr} 1730, 1610 cm^{-1}, τ 8.92(C_{11}-Me), 8.49(C_1-Me), 6.44(COOMe), 3.53(C=CH-Ar), through oily hydroxy compound (IX), $b.p._6$ 195-200°, $\nu_{max}^{CCl_4}$ 3590, 1730 cm^{-1} and also (VIII) was acetylated with KOAc-Ac_2O to yield the enol-acetate (XI), m.p. 150-153°, ν_{max}^{KBr} 1755, 1720, 1635, 1210 cm^{-1}.

For the hydrogen addition to $\Delta^{9,10}$-double bond, both compounds (X and XI) were hydrogenated (Pd-C, AcOH, H_2SO_4) to give a mixture of saturated compounds, which was chromatographed on neutral alumina and separated into the stereoisomers, cis-hydrofluorene (V), m.p. 58-60°, ν_{max}^{KBr} 1730 cm^{-1}, τ 8.84(C_{11}-Me, C_1-Me), 6.37(COOMe) and trans-isomer (VI), m.p. 83-84°, ν_{max}^{KBr} 1715 cm^{-1}, τ 9.18(C_{11}-Me), 8.75(C_1-Me), 6.38(COOMe), in a ratio of 8 to 1 (same product ratio from the both compounds (X and XI)).

In order to obtain a reliable proof for the structure of these isomers, the trans-compound (VI) was synthesized by another indubitable route as follows. *Since c-homohydrofluorene (XII),* previously transformed from abietic acid,[3] has a rigid structure with the same configuration at C_1, C_{10} and C_{11} as in deoxy-enantio-podocarpic acid, the compound (XII) was used as the starting material for the above purpose. Catalytic hydrogenation(Pd-C, EtOH) of (XII) under pressure of 50 lb./inch^2 afforded a saturated ketone (XIII), m.p. 104-106°, ν_{max}^{KBr} 1715, 1695 cm^{-1}, τ 9.47 (C_{11}-Me), 8.80(C_1-Me), 6.41(COOMe), configuration of whose B/C-ring juncture still remains obscure. The corresponding furfurylidene blocked derivative (XIV), m.p. 103-105°, ν_{max}^{KBr} 1720, 1680, 1605, 1545 cm^{-1}, of (XIII) was oxidized by ozonization at -70° followed by decomposition of the ozonide with 30% H_2O_2-conc.

HCl and the resultant diacid ester was methylated to give a triester (XV), b.p.$_1$ 220–225°(bath temp.), $\nu_{max}^{CCl_4}$ 1735, 1725 cm^{-1}, τ 9.50(C$_{11}$-Me), 8.84(C$_1$-Me), 6.42, 6.38(COOMe).

Dieckmann cyclization of the triester (XV) catalysed by sodium hydride and successive decarboxylation with conc. HCl afforded a six-membered ring ketone (XVI), m.p. 75–100°, $\nu_{max}^{CCl_4}$ 1735 cm^{-1}, whose gas-liquid chromatogram (two peaks) showed that the crystals are presumably a mixture of <u>trans</u>- and <u>cis</u>-stereoisomer in respect to the B/C-ring juncture. The mixed ketone (XVI) was reduced with $NaBH_4$ to give an oily alcohol (XVII), $\nu_{max}^{CCl_4}$ 3650, 1735 cm^{-1}, which consisted of four stereoisomers due to configuration of B/C-ring juncture and a hydroxy group on basis of the gas-liquid chromatogram (four peaks). In order to effect aromatization of the C-ring, the mixed alcohol (XVII) was dehydrated with $POCl_3$-pyridine and then dehydrogenated with sulfur in quinoline to yield the aimed <u>trans</u>-hydrofluorene (VI) through an unsaturated compound (XVIII), $\nu_{max}^{CCl_4}$ 1735 cm^{-1}. The synthesized <u>trans</u>-hydrofluorene (VI) having an undeniable structure, was completely identical with the minor product of the catalytic reduction of (X and XI) discussed above and, therefore, its major reduction product should be the <u>cis</u>-hydrofluorene (V).

Previously, two synthetic routes had been accomplished for the <u>cis</u>-hydrofluorene; an optically active acid (IV) from abietic acid <u>via</u> hydrofluorenone (VII) by M. Ohta[2] and the corresponding racemic ester (V) through the total synthesis by U. R. Ghatak's group.[4] These compounds were assumed to have <u>cis</u>-A/B-ring juncture by Ghatak <u>et al</u>., but a more rigorous evidence on its stereochemistry is desirable. Comparison of methyl ester of the Ohta's optically active acid (IV)(m.m.p., I.R., retention time of G.C.) and the Ghatak's racemic ester (V)[**] (I.R.($CHCl_3$), retention time of G.C.) with our secure sample (V), proved the previous assumption (cis-A/B-ring) to be correct. Furthermore, reduction of hydrofluorenone (VIII) by catalytic hydrogenolysis (Pd-C, AcOH, H_2SO_4) gave cis-hydrofluorene (V) and, therefore, (VIII) must also have a cis-A/B-ring juncture.

The interesting mode of the catalytic reduction of Δ^9-compounds (X and XI)(cis-isomer (V) is the major and trans-isomer (VI) is the minor product) will be discussed in detailed report.

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References

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(2) M.Ohta, Chem. Pharm. Bull.(Tokyo) **5**, 256(1957).

(3) A.Tahara and O.Hoshino, Tetrahedron Letters **1966**, 3825.

(4) U.R.Ghatak, J.Chakravarty and A.K.Banerjee, Tetrahedron Letters **1965**, 3145.

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