[Chem. Pharm. Bull. 19(12)2653—2654(1971)]
UDC 547.914.2:02.04

Stereochemistry on the Rearranged Compound (Benzilic Acid Rearrangement) of Methyl 6,7-Dioxo-5α,10α-podocarpa-8,11,13-trien-15-oate[1]

Ten years ago, a British group[2] and our group[3] independently reported the chemical conversion of *l*-abietic acid (I) to a hydrofluorene compound (III) considered to have a gibberellin skeleton. The skeletal conversion was completed by the benzilic acid rearrangement of a diketone (II).

Discussion on stereochemistry of the rearranged acid (III) was made only by the former group, who reported that III gave a mixture of anhydrides (IV′ and V). Acetoxy anhydride

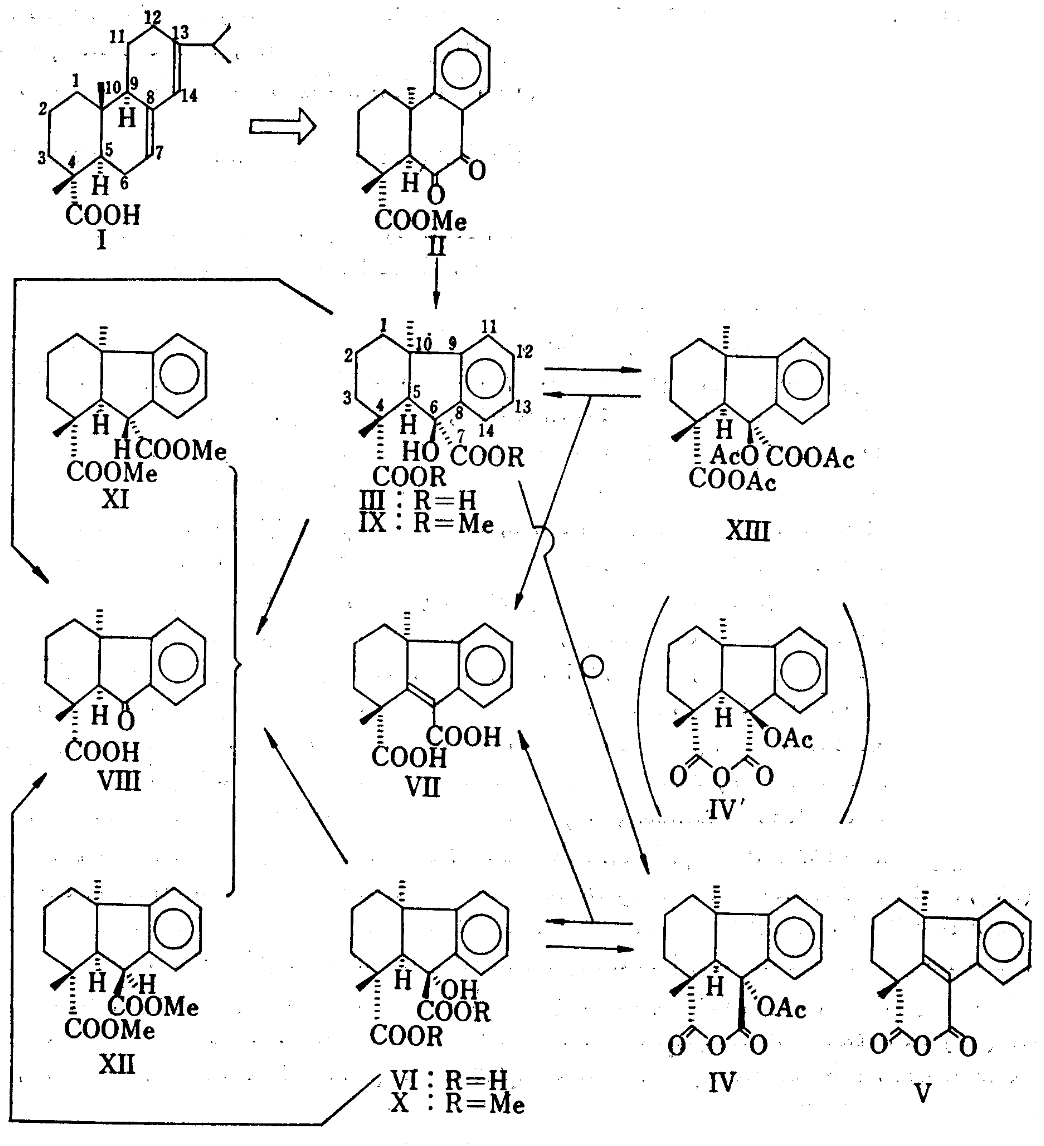

Chart 1

---

[1] A part of this work was presented at the 91st Annual Meeting of the Pharmaceutical Society of Japan at Fukuoka, April, 1971 (Meeting Abstracts, p. 758). New compounds indicated by molecular formula gave satisfactory analytical values and were homogeneous on gas liquid chromatography. Nuclear magnetic resonance (NMR) spectra were measured at 60 Mc in $CDCl_3$ *vs.* Me_4Si as internal reference. The hydrofluorene compounds were obtained from l-abietic acid in this work and the usual numbering for diterpenes was used for the hydrofluorene derivatives.

[2] J.F. Grove and B.J. Riley, *J. Chem. Soc.*, **1961**, 1105.

[3] A. Tahara, *Chem. Pharm. Bull.* (Tokyo), **9**, 252 (1961); A. Tahara and O. Hoshino, *ibid.*, **9**, 655 (1961).

was estimated to have the structure (IV') by its ability to form an anhydride ring and the ready *trans*-elimination between 5-hydrogen atom and 6-acetoxy group. Based on this fact, they concluded that the original diacid had the structure (III) among the four possible stereoisomers due to asymmetric 5- and 6-carbon centers. In contrast, our recent examination of the molecular model suggested the difficulty of the anhydride (IV') to be formed and stereochemistry of the diacid (III) is still open to discussion.

In the same way as reported by Grove, *et al.*,[2] III was acetylated (Ac_2O, reflux) and gave two kinds of anhydride; One of mp 207—209° (decomp.), $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1792, 1757; τ: 8.62, 8.38 (4- or 10-Me), and the other of mp 161—163°, $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1811, 1761, 1737, 1235; τ: 9.33 (4-Me), 8.63 (10-Me), 7.93 (6-OAc), 7.35 (5α-H). They were assumed to correspond to Grove's anhydrides (V, mp 208—209° (decomp.) and IV', mp 163—165°) by comparison with their physical constants. However, contrary to Grove's report, the acetoxy anhydride (IV; Grove's formula IV') was not recovered by alkaline hydrolysis (1N KOH, room temp.)[4] but was converted to a new isomeric hydroxy-diacid (VI), $C_{17}H_{20}O_5 \cdot H_2O$, mp 143.5—144.5°, in company with VII.[3]

Therefore, the structure of these isomeric diacids (III and VI) was reexamined from following experiments.

i) The new diacid (VI) was oxidized (CrO_3, AcOH) to give authentic 6-oxo-acid (VIII) already led from the isomer[2,3] (III). Thus, it is evident that the hydroxyl group in VI was situated at the same 6-position as that in III.

ii) Catalytic hydrogenolysis (10% Pd-C, AcOH, H_2SO_4) of the corresponding methyl esters[2] (IX) and (X), $C_{19}H_{24}O_5$, bp 145—150°/0.001 mmHg (bath temp.), similarly gave a mixture of XI and XII[5] in a ratio of 1: 3 and 3: 1, respectively. Structure of the resulting diesters (XI and XII) was reported to be *cis*-A/B ring fusion in our previous paper,[5] so that the hydroxy diesters (IX and X) should have the same *cis*-A/B ring fusion.

iii) As a result of the above experiments, the two hydroxy diacids (III and VI) were proved to be stereoisomers with respect to the C-6 configuration alone. Successively, their stereochemistry was investigated. Mild acetylation (Ac_2O, room temp.) of VI readily gave the anhydride (IV; Grove's formula IV') ,while that of III only gave a triacetate (XIII), $C_{23}H_{26}O_8$, $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 1825, 1752, 1713; τ: 7.92, 7.78, 7.74 (3×OAc), whose hydrolysis (1N KOH, room temp.) gave III and VII. The experiments are notably compared to the more drastic acetylation of III which gave IV and V as described before. Considering the molecular model, the structure (IV) must be assumed for the acetoxy anhydride having a *cis*-A/B ring fusion and another formula (IV') previously reported[2] can be ruled out.

Accordingly, the new diacid (VI) should have the same configuration as that of the anhydride (IV), and the diacid obtained by benzilic acid rearrangement should have the structure of III. As a result of this structural assignment, it can be considered that a unique epimerization at C-6 has occurred during the anhydride ring formation (III→IV).

Drastic acetylation (Ac_2O, reflux) of III gave an unsaturated anhydride (V) and an acetoxy anhydride (IV) in a ratio of 1.4:1, in contrast to the ratio of 1:2.2 by the same acetylation of VI. The observable tendency of the dehydration (*trans*-elimination, III$>$VI) further supports the assigned structures.

In conclusion, the acetoxy anhydride (IV'), Grove's important compound for elucidation of hydroxy diacid (III), should be revised to formula IV. However, the diacid (III) in question was correctly assigned[2] by chance, because an interesting epimerization at C-6 had fortunately occured during the acetylation of III (to IV).

---

4) The hydrolysis reported by Grove, *et al.* was carried out under alkaline condition (0.1N NaOH, room temp.) to recover only the starting material. Our reexamination under the same condition gave Δ^5-diacid (VII).

5) A. Tahara and Y. Ohtsuka, *Chem. Pharm. Bull.* (Tokyo), **18**, 859 (1970).