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A PARTIAL SYNTHESIS OF MASLINIC ACID

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Abstract—A partial synthesis of maslinic acid from oleanolic acid is described.

IN a previous paper,[1] it was demonstrated that maslinic acid, isolated from the husks of *Olea europaea* and identified with crategolic acid,[2] is a 2,3-dihydroxy-Δ^{12}-28-carboxy oleanene. The selective acetylation of the hydroxy group in position 2 suggests the $2\alpha,3\beta$ configuration for the hydroxy groups.

This paper reports a partial synthesis of maslinic acid, starting from the well-known oleanolic acid. The synthesis confirms that maslinic acid is the $2\alpha,3\beta$-dihydroxy Δ^{12} 28 carboxy oleanene.

During our work on the hydroboration of unsaturated steroids, a method[3] to obtain *trans* α diols through hydroboration, followed by oxidation with alkaline hydrogen peroxide, of enol esters of saturated ketones was found. In particular, the enol acetate of 5α-cholestane-3-one furnished a 50% yield of $2\alpha,3\beta$-dihydroxy-5α-cholestane.

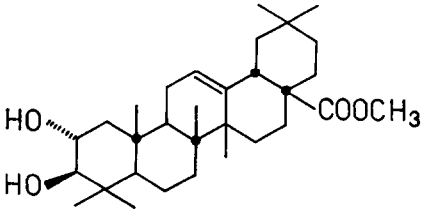

FIG. 1. Maslinic acid methyl ester

It is remarkable that, of the two possible α-diols, only one, namely the one resulting from an attack of the diborane from the back (α) side of the molecule was obtained: a similar attack from the front (β) side would lead to the $2\beta,3\alpha$-cholestandiol. The stereospecificity of the reaction is due to the shielding effect that the methyl group in position 10 exerts on the front side of the molecule.[4]

Analogously, through hydroboration followed by oxidation with alkaline hydrogen peroxide of the enol acetate of 3-keto Δ^{12}-28 carbomethoxy oleanene, the $2\alpha,3\beta$-dihydroxy, Δ^{12}, 28 carbomethoxy oleanene should result: the methyl group in position 10 exerting the same influence as in the above mentioned case. An accurate examination of the models led to the conclusion that the presence of a pair of methyls in the 4 position should be more favourable to a rear rather than to a front attack.

[1] L. Caglioti, G. Cainelli and F. Minutilli, *Gazz. Chim. Ital.* **91**, 1387 (1961).

[2] We wish to thank Prof. R. Tscesche who provided a sample of methyl crataegolate for identification purposes.

[3] L. Caglioti and G. Cainelli, *R. C. Accad. Lincei* (8) **30**, 224 (1961); L. Caglioti, G. Cainelli, G. Maina and A. Selva, *Gazz. Chim. Ital.* In press.

[4] L. F. Fieser, *Experientia* **6**, 312 (1960).

The enol acetate of I was obtained by treating the ketone with isopropenylacetate containing traces of concentrated sulphuric acid, resulting in a very high yield of II, m.p. 178°, $[\alpha]_D^{20°} = +110°$. After mild basic saponification of II, compound I was reformed thus proving that during the acid treatment there was no undesired isomerization of the double bond.

The hydroboration of II was effected under very mild conditions as the molecule presents, beside the unsaturated groups from the enol acetate, two other groups which could possibly be attacked by the same reagent, i.e. the carbomethoxy group in 28 and the double bond 12–13. Of these two groups, the carbomethoxy group should react very slowly[5] or not at all. Concerning the 12–13 double bond, the great resistance of this double bond to catalytic hydrogenation indicates that it should not react with diborane.

These hypotheses were confirmed experimentally. Compound II after hydroboration and oxidation with alkaline hydrogen peroxide, yielded 50% of starting material (saponified to I), 10% of 3β-hydroxy-Δ^{12}-28 carbomethoxy oleanene[6] and 25% of a compound III which compared with the methylester of maslinic acid proved identical.

Considering the amount of starting material recovered, the yield of III is high, and comparable with the yield of 2α,3β-dihydroxy-5α-cholestane obtained by the hydroboration of cholestanone enol acetate.

In this second experiment, only one of the two possible isomers was obtained, thus confirming that the two hydroxy groups of maslinic acid have the 2α,3β configuration tentatively proposed.

EXPERIMENTAL

Enol acetate (II). A mixture of I (1 g), isopropenylacetate (20 ml) and conc H_2SO_4 (4 drops) was warmed for 12 hr and 5 ml of the liquid distilled off. Then, pyridine (3 ml) were added and the reaction mixture taken up in ether washed with water and dried. Recrystallization of the residue from dil methanol yielded 0·8 g of white needles, m.p. 178°, (Found: C, 77·41; H, 10·07. $C_{33}H_{50}O_4$ requires: C, 77·60; H, 9·87%). $[\alpha]_D^{20}$ +110°

Saponification of II. Compound II (50 mg) were treated for 12 hr at room temp with 10 ml of a 5% solution of KOH in MeOH. Then, the reaction mixture taken up with ether was washed with water and dried. Recrystallization of the solid residue from dil methanol yielded 38 mg of a product identical with I.

Hydroboration of II. Compound II (1 g) dissolved in dry ether (50 ml) was treated for 1 hr at O° with an excess of diborane in an atmosphere of dry nitrogen. The reaction mixture, after standing for 2 more hr at room temp was treated with 20 ml of 5% KOH-MeOH and 5 ml of 30% H_2O_2. After 15 min, the mixture was taken up in ether, washed with water, with a solution 5% of $FeSO_4$, with water again and dried. The residue was chromatographed on 20 g of Alox Woehm act. II: 502 mg of 3-keto-Δ^{12}-28-carbomethoxy oleanene, were eluted with 200 ml of benzene, 85 mg of 3β-hydroxy-Δ^{12}-28-carbomethoxy oleanene with 100 ml of ether, and finally 245 mg of 2α, 3β-dihydroxy-Δ^{12}-28-carbomethoxy oleanene were eluted with a mixture of ether-MeOH 10:1. (Found: C, 76·66; H, 10·54. $C_{31}H_{50}O_4$ requires: C, 76·50; H, 10·36%).

We thank Prof. A. Quilico for his great interest in our work.

[5] H. C. Brown, *Tetrahedron* **12**, 117 (1961).

[6] Analogously, in the case of 5α-cholestan-3-one enol acetate, a small quantity of 5α-cholestan-3β-ol was isolated.