

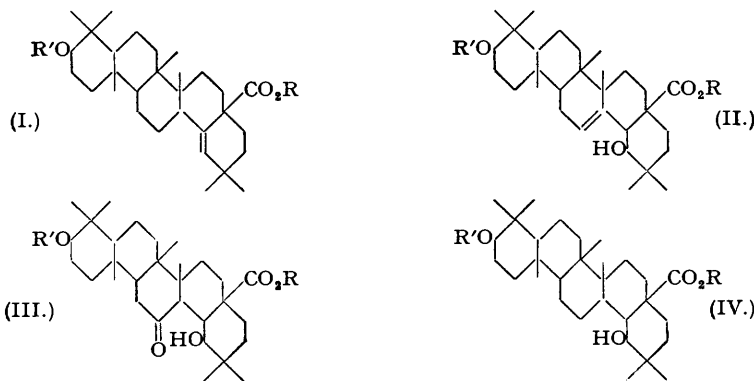
61. *Triterpenoids. Part II. The Partial Synthesis of Morolic Acid.*

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Methyl morolate acetate (methyl olean-18-enolate acetate) has been obtained by a partial synthesis based on methyl siaresinolate acetate. The synthesis provides final confirmation of the formula assigned previously (Barton and Brooks, preceding paper) to morolic acid.

In Part I of this series (preceding paper) it was concluded that morolic acid, the characteristic triterpenoid sapogenin of *Mora excelsa*, Benth., was olean-18-enolic acid (I; R = R' = H). To provide final confirmation for our views as to the structure of this acid, its partial synthesis from siaresinolic acid (II; R = R' = H) (Bilham, Kon, and Ross, *J.*, 1942, 540; Ruzicka, Grob, Egli, and Jeger, *Helv. Chim. Acta*, 1943, 26, 1218) was undertaken.

Treatment of methyl siaresinolate 2-acetate (II; R = Me, R' = Ac) with perhydrol in acetic acid afforded, in a manner characteristic of the 12(13)-ethylenic linkage (*inter al.*, Ruzicka and Cohen, *ibid.*, 1937, 20, 804; Ruzicka, Müller, and Schellenberg, *ibid.*, 1939, 22, 758; Picard, Sharples, and Spring, *J.*, 1939, 1045; Picard and Spring, *J.*, 1940, 1387), methyl 12-keto-oleananolate acetate (III; R = Me, R' = Ac). Wolff-Kishner reduction of this ketone (cf. Ruzicka and Jeger, *Helv. Chim. Acta*, 1941, 24, 1178) furnished, after methylation and acetylation, methyl dihydrosiarsinolate acetate (IV; R = Me, R' = Ac) which was smoothly dehydrated by phosphorus oxychloride in hot pyridine to give methyl olean-18-enolate acetate (I; R = Me, R' = Ac). The latter was identical in all respects with authentic methyl morolate acetate.



EXPERIMENTAL.

M. p.s are uncorrected. Unless specified to the contrary rotations were determined for the sodium D line in chloroform solution at room temperature, which varied from 15° to 25°. For rotation measurements all specimens were dried *in vacuo* at 20° below the m. p. or at 110°, whichever was the lower. Values of $[\alpha]_D$ have been approximated to the nearest degree.

Savory and Moore's alumina for chromatography was used in all cases.

In the text below the phrase "in the usual way" refers to dilution with water, extraction with ether, washing successively with aqueous potassium hydroxide, aqueous hydrochloric acid, and then water, followed by evaporation of the ethereal solution *in vacuo*. Where necessary, water was removed from the residue by azeotropic distillation with benzene *in vacuo*.

Alkaline hydrolyses were effected by using several equivalents of potassium hydroxide and refluxing the reactants for 30–60 minutes in methanolic or dioxan-methanolic solution depending on the solubility of the ester.

Oxidation of Methyl Siarsinolate Acetate with Perhydrol.—Methyl siarsinolate, m. p. 175–176°, $[\alpha]_D +45^\circ$ (c. 6.76), was converted into the acetate by heating it with excess of acetic anhydride in pyridine on the water-bath for 30 minutes. Recrystallised from methanol the acetate melted unsharply at 116–125°, in agreement with the findings of Bilham, Kon, and Ross (*J.*, 1942, 540).

Methyl siarsinolate acetate (1.10 g.) in 40 ml. of "AnalaR" glacial acetic acid was treated dropwise at 100° with a mixture of 10 ml. of acetic acid and 10 ml. of perhydrol during 60 minutes. Hot water

was then added until crystallisation began. Recrystallisation of the product from methanol containing a trace of chloroform gave *methyl 19-hydroxy-12-keto-oleananolate acetate* (400 mg., 36%), m. p. 230—232°, $[\alpha]_D^{+2}$ (c, 2.53) (Found: C, 72.8; H, 9.3. $C_{33}H_{52}O_6$ requires C, 72.75; H, 9.6%). In another experiment 730 mg. of the ketone were obtained from 2.0 g. of methyl siaresinolate acetate.

Methyl 19-Hydroxy-12-keto-oleananolate.—Hydrolysis by 10% potassium hydroxide in methanolic-dioxan of the above-mentioned acetate methyl ester afforded *methyl 19-hydroxy-12-keto-oleananolate*, which recrystallised from methanol, had m. p. 234—236°, $[\alpha]_D -7^\circ$ (c, 1.60), giving a 20° depression in m. p. on admixture with starting material (Found: C, 73.0; H, 9.75. $C_{31}H_{50}O_5 \cdot 0.5CH_3 \cdot OH$ requires C, 72.9; H, 10.1%). Reacetylation by acetic anhydride in pyridine regenerated starting material, m. p. and mixed m. p. 230—232°. Benzoylation of the alcohol by benzoyl chloride in pyridine at room temperature during 24 hours furnished *methyl 19-hydroxy-12-keto-oleananolate benzoate*, which, recrystallised from methanol, had m. p. 201—203° (Found: C, 75.2; H, 8.95. $C_{38}H_{54}O_6$ requires C, 75.2; H, 9.0%).

Wolff-Kishner Reduction of Methyl 19-Hydroxy-12-keto-oleananolate Acetate.—The acetate methyl ester (690 mg.) was reduced in two batches, each being heated with 350 mg. of sodium (dissolved in 4 ml. of alcohol and 2 ml. of anhydrous hydrazine) for 15 hours at 180—200°. The reaction products were combined, worked up in the usual way, methylated with diazomethane, and acetylated with excess of acetic anhydride in pyridine on the water-bath for $\frac{1}{2}$ hour. Working up in the usual way and recrystallisation from aqueous methanol gave a product, m. p. 180—185°, $[\alpha]_D^{+19}$ (c, 3.01). This was purified by chromatography as indicated below, each fraction being crystallised once from methanol.

Fraction no.	Eluant.	M. p.
1	70 Ml. light petroleum (b. p. 40—60°)	trace, oily
2	50 Ml. 80 : 20 light petroleum (b. p. 40—60°)—benzene	trace
3	50 Ml. 75 : 25 " " " "	218—240°
4	70 Ml. " " " " "	195—198 (45 mg.)
5	70 Ml. " " " " "	199—205 (30 mg.)
6	70 Ml. " " " " "	208—210
7	70 Ml. " " " " "	—
8	70 Ml. 50 : 50 " " " "	209—211
9	70 Ml. " " " " "	—
10	70 Ml. Benzene	201—204
11	70 Ml. " " " " "	—
12	70 Ml. " " " " "	200—203
13	120 Ml. " " " " "	trace
14	70 Ml. 25 : 75-ether : benzene	trace

Fractions 7 and 8 combined had $[\alpha]_D^{+18}$ (c, 1.19). Fractions 4—12 were combined and recrystallised from methanol, to give 420 mg. (60%) of *methyl dihydrosiaresinolate 2-acetate*, m. p. 209—211°, $[\alpha]_D^{+18}$ (c, 1.19) (Found: C, 75.05; H, 10.2. $C_{33}H_{54}O_5$ requires C, 74.7; H, 10.3%). Alkaline hydrolysis of this acetate methyl ester afforded *methyl dihydrosiaresinolate*, which, recrystallised from methanol, had m. p. 205—206°, $[\alpha]_D^{+10}$ (c, 1.35) (Found: C, 75.85; H, 10.65. $C_{31}H_{52}O_4$ requires C, 76.15; H, 10.75%).

Benzoylation of methyl dihydrosiaresinolate by benzoyl chloride in pyridine over-night furnished, after working up in the usual way, *methyl dihydrosiaresinolate 2-benzoate*, which, recrystallised from chloroform-methanol, had m. p. 225—227°, $[\alpha]_D^{+37}$ (c, 1.42) (Found: C, 77.45; H, 9.6. $C_{32}H_{54}O_5$ requires C, 76.95; H, 9.55%). On the first recrystallisation of the benzoate the double m. p. 135° and 203—210°, with solidification at about 160°, was observed.

Dehydration of Methyl Dihydrosiaresinolate Acetate.—Methyl dihydrosiaresinolate acetate (90 mg.) in 3 ml. of dry pyridine was treated dropwise with 0.4 ml. of freshly distilled phosphorus oxychloride. The solution was refluxed for 4 hours in an oil-bath, cooled, diluted with water, and worked up in the usual way. The crude reaction product had m. p. 210—250° and one recrystallisation from methanol gave 40 mg. of methyl morolate acetate, m. p. 258—260°, $[\alpha]_D^{+36}$ (c, 1.59). One further recrystallisation raised the m. p. to 262—263° and there was no depression in m. p. on admixture with authentic methyl morolate acetate (Barton and Brooks, *loc. cit.*) of the same m. p. and rotation. Alkaline hydrolysis of the acetate methyl ester afforded, after one recrystallisation from methanol, methyl morolate, m. p. 225—227°, $[\alpha]_D^{+24}$ (c, 0.58), undepressed in m. p. on admixture with an authentic specimen of the same m. p. and $[\alpha]_D^{+26}$ (Barton and Brooks, *loc. cit.*).

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