719. *Triterpenoids. Part VIII.* Some Derivatives of Siaresinolic Acid.*

By D. H. R. Barton, N. J. Holness, K. H. Overton, and W. J. Rosenfelder.

Methyl 12 : 19-diketo-18(α)-olean-10-enolate acetate has been prepared by stepwise reaction from siaresinolic acid and by zinc dust reduction, alkaline isomerisation, and re-acetylation of methyl 12 : 19-diketo-olea-10 : 13(18)-dienolate acetate. The partial synthesis from siaresinolic acid substantiates the formulation of the latter compound and in turn provides confirmatory evidence in favour of the correctness of the currently accepted β-amyrin formula.

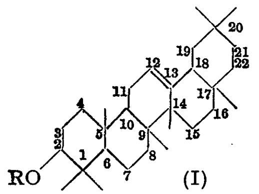
A number of derivatives of siaresinolic and oleanolic acids has been prepared.

The course of selenium dioxide oxidations in the β-amyrin series is discussed and the formation of the end products rationalised.

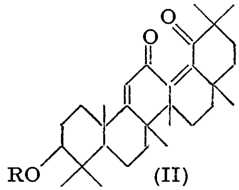
The formula (I; R = H) for β-amyrin was first proposed by R. D. Haworth (*Ann. Reports*, 1937, **34**, 327). In the great majority of respects this formula is an eminently suitable vehicle for expressing the complex chemistry of the members of the β-amyrin group of triterpenoids. It has received strong support from the formulation of β-amyradienedionol (Jacobs's "keto-diol"; Jacobs and Fleck, *J. Biol. Chem.*, 1930, **88**, 137) as (II; R = H) by Ruzicka and Jeger (*Helv. Chim. Acta*, 1941, **24**, 1236). However, Budziarek, Johnston, Manson, and Spring (*J.*, 1951, 3019) have recently discussed some aspects of β-amyrin chemistry from which, by analogy with a parallel interpretation of common reactions in the α-amyrin series, they conclude that formula (I; R = H) may not be satisfactory in every

* Part VII, *J.*, 1952, 2339.

detail. It appeared to us that the reservations expressed by Spring and his colleagues might be well-founded and that any additional evidence in favour of (I; R = H) for β-amyrin would be welcome. We turned our attention to a substantiation of the expression (II; R = H) for the key compound β-amyradienedionol.



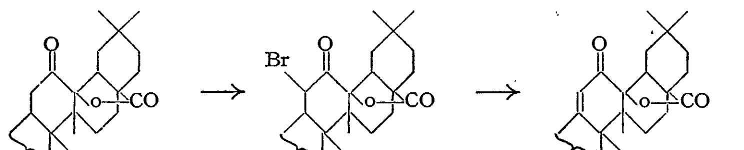
(I)



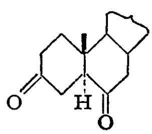
(II)

The formula advanced by Ruzicka and Jeger (*loc. cit.*) for this compound was an adequate representation for the elegant reactions which they reported. In particular it explained the formation of the cyclic pyridazine derivative on heating with hydrazine. However it appeared to us to be a curious feature of the chemistry of β-amyradienedionol that the diene-dione chromophore had never been built up by a stepwise series of reactions and that, in particular, the ketonic oxygen atoms had always been introduced simultaneously. Furthermore the formation of hydrazine derivatives as evidence for a *cisoid*-dione system as in (II; R = H) must be viewed with some reserve for it has been reported that cholestane-3 : 6-dione (III), where a comparable structural feature is absent, forms a monomolecular pyridazine derivative (Seeley and Noller, *J. Amer. Chem. Soc.*, 1948, **70**, 4260, and references there cited).

Our first attempts to build up the diene-dione chromophore by stepwise methods were based on 12-keto-oleananolic lactone acetate (IV; R = Ac). Treatment with bromine in acetic acid gave the corresponding 11-bromo-12-keto-lactone (V; R = Ac). It was hoped that refluxing this with collidine would cause loss of hydrogen bromide to give the lactone (VI; R = Ac), which might be convertible into (VII; R = Ac): in fact it caused both removal of hydrogen bromide and *reductive* opening of the lactone ring, to give 12-keto-olean-10-anolic acid acetate (VIII; R′ = H), characterised as the methyl ester (Picard, Sharples, and Spring, *J.*, 1939, 1045; Ruzicka, Jeger, and Winter, *Helv. Chim. Acta*, 1943, **26**, 265). Reduction of the 11-bromo-grouping also occurred, as some 12-keto-oleananolic lactone acetate could be recovered.



(IV) (V) (VI)



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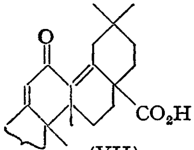
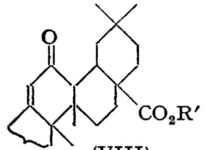
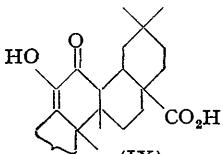


(VII)

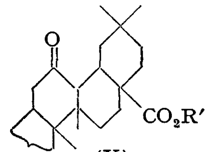


(VIII)

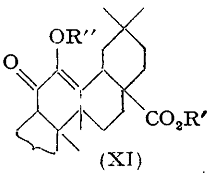
Oxidation of 12-keto-oleananolic lactone acetate (IV; R = Ac) with selenium dioxide gave a diosphenol-carboxylic acid, characterised as the methyl ester. The acid was at first formulated as (IX; R = Ac) but the methyl ester was also formed by selenium dioxide oxidation of methyl 12-keto-oleananolate acetate (X; R = Ac, R′ = Me). Ruzicka and Jeger (*Helv. Chim. Acta*, 1941, **24**, 1178) have provided compelling evidence that similar oxidation of the analogous 12-keto-β-amyranyl acetate gives a diosphenol system as in (XI). We therefore formulate the selenium dioxide oxidation product of (IV; R = Ac) as (XI; R = Ac, R′ = R″ = H). The presence of the diosphenol grouping was proved by the strong ferric chloride reaction and especially by the characteristic shift in absorption maximum when the acetate methyl ester (XI; R = Ac, R′ = Me, R″ = H) was converted by acetylation into the diacetate methyl ester (XI; R = R″ = Ac, R′ = Me).



(IX)

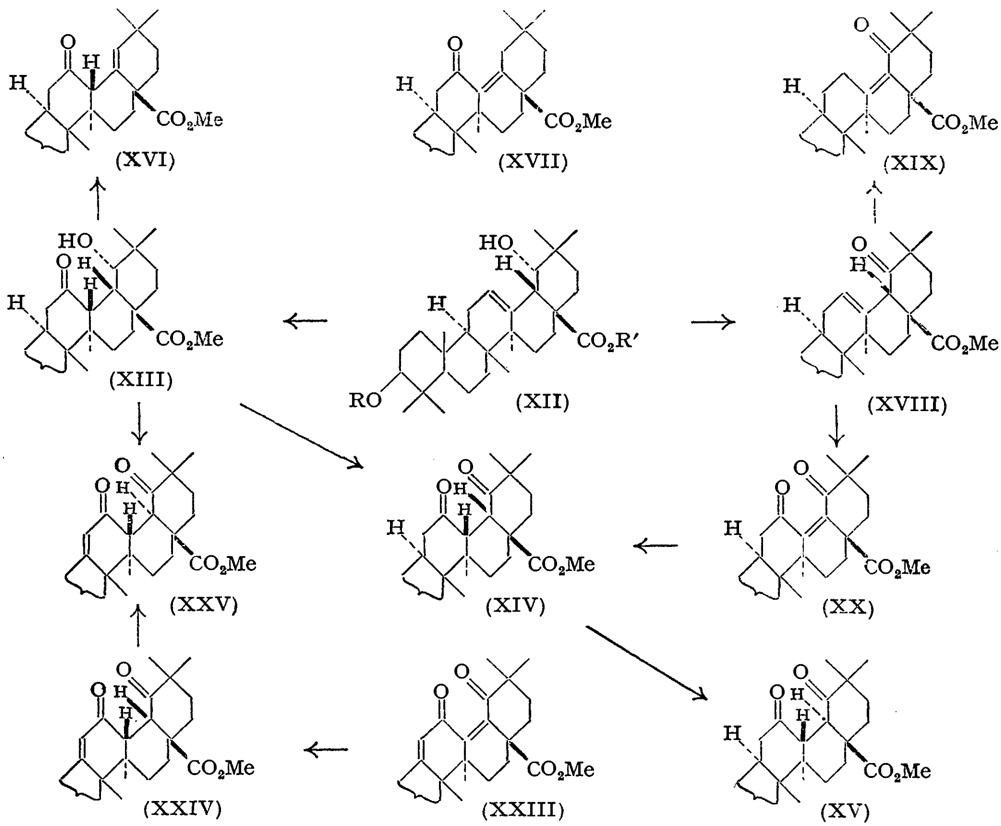


(X)



(XI)

Since these attempts to build up the required chromophore from the 12-keto-lactone seemed unpromising, attention was directed to the use of siaresinolic acid (XII; R = R′ = H) as starting material. Barton, Brooks, and Holness (*J.*, 1951, 278) have shown that the acetate methyl ester (XII; R = Ac, R′ = Me) is readily transformed into methyl 19-hydroxy-12-keto-oleananolate 2-acetate (XIII; R = Ac). Chromic acid oxidation of the latter afforded the corresponding diketone (XIV; R = Ac), which was hydrolysed and isomerised at $C_{(18)}$ by alkali to give methyl 12 : 19-diketo-18(α)-oleananolate (XV; R = H), converted by reacetylation into (XV; R = Ac).* The stereoisomeric acetates (XIV and XV; R = Ac) seemed well suited to the construction of the diene-dione system for both



contained ketonic functions at $C_{(12)}$ and $C_{(19)}$. However this did not prove to be the case.

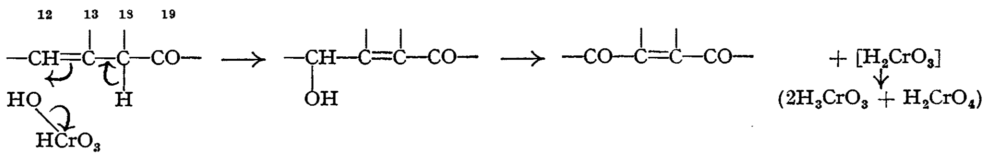
Selenium dioxide oxidation of (XIV; R = Ac) furnished the " O_7 "-acetate (Mower, Green, and Spring, *J.*, 1944, 256; cf. Jeger, Norymberski, and Ruzicka, *Helv. Chim. Acta,*

* For stereochemistry see Barton and Holness, *J.*, 1952, 78. The symbols (α) and (β) are employed in the way suggested by Halsall, Jones, and Meakins, *J.*, 1952, 2862.

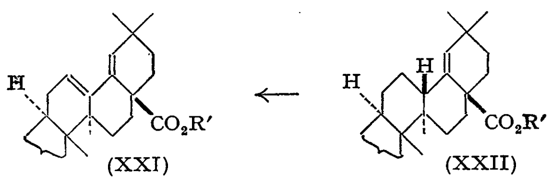
1944, **27**, 1532), which is still of unknown constitution. The isomeric diketone (XV; R = Ac) proved to be inert to selenium dioxide.

In a second approach the 12-keto-19-hydroxy-compound (XIII; R = Ac) was dehydrated by phosphorus oxychloride in pyridine to methyl 12-keto-olean-18-enolate acetate (XVI; R = Ac). All attempts to isomerise the double bond into conjugation to give (XVII) failed and it may be that the unconjugated compound is more stable than the conjugated isomer. This behaviour is in marked contrast to that of methyl 19-keto-olean-12-enolate (XVIII; R = H), which is readily isomerised by alkali to the conjugated isomer (XIX; R = H) (see Bilham, Kon, and Ross, *J.*, 1942, 540; Ruzicka, Grob, Egli, and Jeger, *Helv. Chim. Acta*, 1943, **26**, 1218).

A third approach consisted in preparation of the hitherto unknown methyl 12:19-diketo-olean-13(18)-enolate acetate (XX; R = Ac). It was found that this compound was formed, along with (XVIII; R = Ac) and a small amount of the "O_7"-acetate, by the controlled chromic acid oxidation of methyl siaresinolate acetate. It appears that (XX; R = Ac) results from the oxidation of (XVIII; R = Ac) at $C_{(12)}$ with simultaneous "migration" of the double bond into conjugation with the $C_{(19)}$-keto-group (cf. Fieser and Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., 1949, p. 227 *et seq.*). Thus (XX; R = Ac) was obtained by the chromic acid oxidation of (XVIII; R = Ac), whilst the conjugated ester (XIX; R = Ac) was recovered unchanged after being subjected to the same oxidation conditions. Furthermore (XVIII; R = Ac) was not isomerised to (XIX; R = Ac) in acetic acid under the same conditions but without the addition of chromic acid. Mechanistically this could be explained by the formal treatment:



As evidence for the constitution assigned to (XX; R = Ac), it was smoothly reduced by zinc dust and acetic acid to methyl 12:19-diketo-oleananolate acetate (XIV; R = Ac). Rigid relationships have been established between the positions of the 12(13)-double bond and the 19-hydroxyl group of siaresinolic acid (Bilham, Kon, and Ross, and Ruzicka, Grob, Egli, and Jeger, *locc. cit.*), between the positions of the 18(19)-double bond of morolic acid (XXI; R = R′ = H) and the 19-hydroxyl group of siaresinolic acid (Barton and Brooks, *J.*, 1951, 257; Barton, Brooks, and Holness, *loc. cit.*), and between the position of the diene system in *iso*dehydro-oleanolic acid (XXII; R′ = H) and the 18(19)-double bond of



(XXI) (XXII)

morolic acid. It follows then that the terminal carbon atoms of the above-mentioned diene system must correspond to the two keto-groups in methyl 12:19-diketo-olean-13(18)-enolate acetate. Since compelling evidence has been advanced (Barton and Brooks, *loc. cit.*) for the *cisoid*-character of the dienic system in *iso*dehydro-oleanolic acid the *cisoid*-nature of the unsaturated chromophore of (XX; R = Ac) follows.* The spatial

* The absorption spectrum of methyl 12:19-diketo-olean-13(18)-enolate acetate ($\lambda_{max.}$ 253 mμ, ε = 7000) shows the low intensity of absorption (cf. Barton and Brooks, *loc. cit.*; Turner and Voitle, *J. Amer. Chem. Soc.*, 1951, **73**, 1403; Braude, Bruun, Weedon, and Woods, *J.*, 1952, 1419) to be expected of a *cisoid*-chromophore. Previously Ruzicka and Jeger (*Helv. Chim. Acta*, 1941, **24**, 1236) had tentatively suggested that the hydrogenation product of 12:19-diketo-olea-10:13(18)-dienyl acetate should be formulated as 12:19-diketo-olean-13(18)-enyl acetate. Since the reported absorption was $\lambda_{max.}$ 240 mμ (ε = 10,000) it appears to us that this constitution is not acceptable. In agreement with mechanistic considerations we prefer to regard the hydrogenation product as 12:19-diketo-olean-10-enyl acetate.

relationship of the two keto-groups of (XIV; R = Ac) is thus substantiated. Attempts to convert (XX; R =Ac) into the corresponding diene-dione by oxidation with selenium dioxide or with bromine failed.

A correlation between the diene-dione, methyl 12 : 19-diketo-olea-10 : 13(18)-dienolate acetate (XXIII; R = Ac) and siaresinolic acid was finally achieved in the following way. Reduction of (XXIII; R = Ac) by zinc dust and acetic acid gave smoothly methyl 12 : 19-diketo-olean-10-enolate acetate (XXIV; R = Ac). On alkaline hydrolysis followed by reacetylation this was converted into the 18-*iso*-compound, methyl 12 : 19-diketo-18(α)-olean-10-enolate acetate (XXV; R = Ac). The latter was also obtained from (XIII; R = Ac) by bromination, oxidation to the 19-keto-derivative, and dehydrobromination by boiling acetic acid. The presence of the hydrogen bromide produced in the reaction, dissolved in the acetic acid, doubtless accounted for the inversion at $C_{(18)}$. The desired (XXV; R = Ac), although the major product of this reaction sequence, was only isolated with difficulty since it formed stable mixed crystals with a minor proportion of what appeared to be methyl 12 : 19-diketo-olea-10 : 13(18)-dienolate acetate (XXIII; R = Ac). The evidence for this, and the technique adopted for the resolution of the mixed crystals are described in the Experimental section.

It is appropriate at this juncture to consider briefly the course of selenium dioxide oxidation in the β-amyrin series. The more important experimental facts are summarised in the Table. It is clear that the 12 : 19-diketo-10 : 13(18)-diene system is formed from all the possible [10 : 12-, 11 : 13(18)-, and 12 : 18-]dienes, all the monoenes so far studied, and from the only possible (10 : 12 : 18(19)-]triene system, yet it is never produced if oxygen substituents are already present, even if they are at positions 12 and/or 19. An attractive hypothesis to explain this outstanding differentiation is that all the reactions leading to the diketo-diene system proceed *via* the 10 : 12 : 18(19)-triene. Since the triene system has not been reported as an oxidation product in such reactions it is required that it should react more rapidly with selenium dioxide than any of the less unsaturated systems. This has been substantiated in qualitative experiments.

Compound	Selenium dioxide oxidation product	Ref.
β-Amyrin acetate (olean-12-enyl acetate)	12 : 19-Diketo-olea-10 : 13(18)-dienyl acetate; formed *via* olea-11 : 13(18)-dienyl acetate	1
Olean-10-enyl acetate	12 : 19-Diketo-olea-10 : 13(18)-dienyl acetate	2
Olean-13(18)-enyl acetate (δ-amyrin acetate)	12 : 19-Diketo-olea-10 : 13(18)-dienyl acetate	3
Methyl olean-18-enolate acetate (methyl morolate acetate)	Methyl 12 : 19-Diketo-olea-10 : 13(18)-dienolate acetate; formed *via* methyl olea-12 : 18-dienolate acetate	4
Olea-10 : 12-dienyl acetate	12 : 19-Diketo-olea-10 : 13(18)-dienyl acetate and 11-keto-olean-12-enyl acetate	5
Olea-10 : 12 : 18-trienyl acetate	12 : 19-Diketo-olea-10 : 13(18)-dienyl acetate	6
Methyl 12-keto-oleananolate acetate	Methyl 11-keto-12-hydroxy-olean-12-enolate acetate	7
12-Keto-olean-10-enyl acetate	" *iso*-Dienone "	8
11-Keto-olean-12-enyl acetate	" O_5 "-acetate	9
11-Keto-olea-12 : 18-dienyl acetate	" O_5 "-acetate	10
Methyl 12 : 19-diketo-oleananolate acetate	" O_7 "-acetate	7

1, Ruzicka and Jeger, *Helv. Chim. Acta*, 1941, **24**, 1236. 2, Budziarek, Johnston, Manson, and Spring, *J.*, 1951, 3019. 3, Ruzicka, Jeger, and Norymberski, *Helv. Chim. Acta*, 1942, **25**, 457. 4, Experimental, this paper; also Barton and Brooks, *J.*, 1951, 257. 5, Picard and Spring, *J.*, 1941, 35. 6, Newbold and Spring, *J.*, 1944, 532; Norymberski, Thesis, E.T.H., 1946, p. 51. 7, Experimental, this paper. 8, Green, Mower, Picard, and Spring, *J.*, 1944, 527. 9, Mower, Green, and Spring, *J.*, 1944, 256. 10, Jeger, Norymberski, and Ruzicka, *Helv. Chim. Acta*, 1944, **27**, 1532.

Experimental

M. p.s are uncorrected. Rotations were determined in chloroform solution. Values of $[\alpha]_D$ have been approximated to the nearest degree. Ultra-violet absorption spectra were measured for absolute ethanol solutions with the Unicam S.P. 500 Spectrophotometer.

Savory and Moore's standardised alumina for chromatography was used unless specified to the contrary. Light petroleum refers to that fraction of b. p. 40—60°.

The phrase " in the usual way " implies, in general, dilution with water, extraction with ether, washing successively with aqueous potassium hydroxide (or other more suitable basic reagent), aqueous hydrochloric acid, and 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 methanol or dioxan–methanol according to the solubility of the ester.

For methylations with diazomethane the acid was treated with an excess of ethereal diazomethane. After the mixture had been kept at room temperature until the evolution of nitrogen had ceased, the excess of diazomethane and the ether were removed *in vacuo* or on the steam-bath.

Bromination and Dehydrobromination of 12-*Keto-oleanolic Lactone Acetate*.—The keto-lactone acetate (4·97 g.) in "AnalaR" acetic acid (300 ml.) was treated with stirring at 40° with a 50% solution (45 drops) of hydrogen bromide in acetic acid and then with bromine in acetic acid (50 ml. of 1% v/v) at such a rate that the bromine was decolourised as soon as it was added. After 3 hours at 40° and 14 hours at room temperature the colourless plates which had separated were collected. Recrystallisation from chloroform–methanol afforded 11-*bromo*-12-*keto-oleanolic lactone acetate* (2·22 g.), chars at 250°, melts at 314—316° (decomp.), $[\alpha]_D$ $\pm 0°$ (*c*, 3·20 or 2·96) (Found: C, 64·95; H, 7·9; Br, 13·3. $C_{32}H_{47}O_5Br$ requires C, 64·9; H, 8·1; Br, 13·5%). Dilution of the filtrate and recrystallisation of the precipitate gave a further 1·97 g. of the bromo-ketone.

The bromo-ketone (1·97 g.) was refluxed in redistilled collidine (20 ml.) in a stream of oxygen-free nitrogen for 0·5 hour. Working up in the usual way gave acidic and neutral fractions. Chromatography of the latter over alumina (elution with 1 : 1 to 1 : 4 benzene–light petroleum) gave 12-keto-oleanolic lactone acetate. Recrystallised from chloroform–methanol this had m. p. 277—279°, undepressed on admixture with authentic ketone of the same m. p.; tetranitromethane and Beilstein tests were negative. The acid fraction, after methylation and chromatography over alumina (elution with benzene and 5 : 1 to 4 : 1 benzene–ether) gave methyl 12-keto-olean-10-enolate acetate (1·02 g.). Recrystallised from methanol–light petroleum this had m. p. 203—204°, $[\alpha]_D$ +56° (*c*, 2·81), and gave no depression in m. p. on admixture with an authentic specimen (see Barton and Holness, *J.*, 1952, 78) of the same m. p. Alkaline hydrolysis afforded methyl 12-keto-olean-10-enolate. Recrystallised from methanol with a trace of chloroform this formed long needles, m. p. 231—232°, undepressed in m. p. on admixture with an authentic specimen (McKean, Manson, and Spring, *J.*, 1952, 432) of the same m. p.

Action of Selenium Dioxide on 12-*Keto-oleanolic Lactone Acetate*.—The keto-lactone (500 mg.) in "AnalaR" acetic acid (100 ml.) was refluxed with selenium dioxide (450 mg.) for 4 hours. After being worked up in the usual way the product was separated into acid (365 mg.) and neutral (130 mg.) fractions. On recrystallisation from chloroform–methanol the acidic fraction furnished 11-*keto*-12-*hydroxyolean*-12-*enolic acid acetate* as plates, m. p. 294—296° (decomp.), $[\alpha]_D$ +123° (*c*, 3·13), $\lambda_{max.}$ 289 mμ (ε = 9000), giving a strong green colour with alcoholic ferric chloride (Found: C, 72·65; H, 8·75. $C_{32}H_{48}O_6$ requires C, 72·7; H, 9·15%). Methylation with diazomethane afforded *methyl* 11-*keto*-12-*hydroxyolean*-12-*enolate acetate*. Recrystallised from chloroform–methanol in long needles, this had m. p. 217—218°, $[\alpha]_D$ +109° (*c*, 2·47), $\lambda_{max.}$ 289 mμ (ε = 9000) (Found: C, 73·6; H, 9·35. $C_{33}H_{50}O_6$ requires C, 73·05; H, 9·3%). The ester gave the same colour with ferric chloride as did the parent acid.

The above-mentioned methyl ester (400 mg.) was heated on the steam-bath with "AnalaR" pyridine (10 ml.) and acetic anhydride (5 ml.) for 45 minutes. After working up in the usual way and filtration of the product in benzene through a short column of alumina, there was obtained *methyl* 11-*keto*-12-*acetoxyolean*-12-*enolate acetate* (355 mg.). Recrystallised from methanol–light petroleum this had m. p. 210—211°, $[\alpha]_D$ +79° (*c*, 3·04), $\lambda_{max.}$ 255 mμ (ε = 5000) (Found: C, 71·9, H, 8·95. $C_{35}H_{52}O_7$ requires C, 71·85; H, 8·95%). The diacetate gave no colour with alcoholic ferric chloride.

Action of Selenium Dioxide on Methyl 12-*Keto-oleananolate Acetate*.—The keto-acetate (300 mg.) and selenium dioxide (600 mg.) were refluxed in "AnalaR" acetic acid (30 ml.) for 6 hours. Working up in the usual way furnished a neutral (to sodium carbonate) product (285 mg.). Chromatography over alumina and elution with ether afforded methyl 11-keto-12-hydroxyolean-12-enolate acetate, recrystallising from chloroform–methanol with m. p. 214—216°. There was no depression in m. p. on admixture with the same compound described above. Alcoholic ferric chloride gave a strong green colour. Pyridine–acetic anhydride and working up in the usual way furnished the diacetate; after filtration in benzene solution through alumina and recrystallisation from methanol–light petroleum, this had m. p. 210—211°, $[\alpha]_D$ +74° (*c*, 1·74), undepressed in m. p. on admixture with the diacetate of the same m. p. described above. The diacetate gave no colour with alcoholic ferric chloride.

Methyl 12-*Keto-olean*-18-*enolate Acetate*.—Methyl 19-hydroxy-12-keto-oleananolate acetate ($\lambda_{max.}$ 280 mμ; ε = 60) (1·4 g.), prepared according to the method of Barton, Brooks, and Holness (*J.*, 1951, 278), was heated under reflux with pyridine (10 ml.) and freshly distilled phosphorus oxychloride (2 ml.) for 4 hours. After being worked up in the usual way the product was chromatographed over alumina. Elution with 3 : 7-benzene–light petroleum gave *methyl* 12-*keto-olean*-18-*enolate acetate* which, recrystallised from aqueous methanol, had m. p. 178—179°, $[\alpha]_D$ +63° (*c*, 1·57) (Found: C, 74·65; H, 9·4. $C_{33}H_{50}O_5$ requires C, 75·25; H, 9·55%). It had no high intensity absorption above 220 mμ.

Hydrolysis with methanolic potassium hydroxide and working up in the usual way afforded *methyl* 12-*keto-olean*-18-*enolate*, m. p. 228—230° (from aqueous methanol) $[\alpha]_D$ +74° (*c*, 1·07) (Found: C, 75·7; H, 10·45. $C_{31}H_{48}O_4,0·5CH_3·OH$ requires C, 75·5; H, 10·6%). It had no high-intensity absorption above 220 mμ.

In an attempt to effect rearrangement of the 18(19)-double bond to the 13(18)-position, the acetate (80 mg.) in dry methanol (16 ml.) was treated with a solution of sodium (800 mg.) in dry methanol (8 ml.). The absorption spectrum of the solution was determined at intervals. There was no indication of the development of high-intensity selective absorption above 220 mμ even after 120 hours at room temperature or 3 hours' refluxing. Working up in the usual way gave methyl 12-keto-olean-18-enolate, m. p. 232—234°, undepressed in m. p. on admixture with authentic material (see above). The absorption spectrum of the recovered ketone was also checked.

Methyl 12 : 19-*Diketo-oleananolate Acetate*.—Methyl 19-hydroxy-12-keto-oleananolate (1·3 g.) (Barton, Brooks, and Holness, *loc. cit.*) in "AnalaR" acetic acid (50 ml.) was treated with "AnalaR" chromium trioxide (200 mg.) in 90% acetic acid (10 ml.) and left overnight at room temperature. After working up in the usual way, recrystallisation from methanol containing a trace of chloroform furnished *methyl* 12 : 19-*diketo-oleananolate acetate* (1·15 g.), m. p. 262—264°, $[\alpha]_D$ +66° (*c*, 1·13), $\lambda_{max.}$ 284 mμ (ε = 90) (Found: C, 73·05; H, 9·2. $C_{33}H_{50}O_6$ requires C, 73·05; H, 9·3%).

Selenium Dioxide Oxidation of Methyl 12 : 19-*Diketo-oleananolate Acetate*.—The diketone (750 mg.) in "AnalaR" acetic acid (30 ml.) was heated under reflux with selenium dioxide (750 mg.) for 18 hours. After being worked up in the usual way the product was chromatographed over alumina. Elution with benzene furnished the "O_7"-acetate (330 mg.). Recrystallised from methanol as fine needles, this had m. p. 258—259° after sintering at 248—249°, $[\alpha]_D$ +24° (*c*, 2·23), $\lambda_{max.}$ 225 mμ (ε = 3900), $\lambda_{infl.}$ 292 mμ (ε = 380) (Found: C, 71·2; H, 8·05. Calc. for $C_{33}H_{46}O_7$: C, 71·45; H, 8·35%). There was no depression in m. p. on admixture with an authentic specimen of the "O_7"-acetate of the same m. p. prepared according to the method of Mower, Green, and Spring (*J.*, 1944, 256).

Methyl 12 : 19-*Diketo*-18(α)-*oleananolate Acetate*.—The 18(β)-diketone (220 mg.) was heated under reflux with 10% methanolic potassium hydroxide (25 ml.) for 1 hour. After being worked up in the usual way the product was recrystallised from aqueous methanol, to give *methyl* 12 : 19-*diketo*-18(α)-*oleananolate*, m. p. 284—285°, $[\alpha]_D$ +11° (*c*, 2·06) (Found: C, 74·2; H, 9·55. $C_{31}H_{48}O_5$ requires C, 74·35; H, 9·65%). Acetylation with pyridine–acetic anhydride on the water-bath for 30 minutes gave the corresponding *acetate*. Recrystallised from aqueous methanol this had m. p. 304—305°, $[\alpha]_D$ +17° (*c*, 2·04), $\lambda_{max.}$ 283—284 mμ (ε = 100) (Found: C, 73·0; H, 9·35. $C_{33}H_{50}O_6$ requires C, 73·05; H, 9·3%). On attempted oxidation with selenium dioxide as for the 18(β)-isomer (see above), the acetate was recovered unchanged (m. p. and mixed m. p., ultra-violet spectrum) in almost quantitative yield.

Chromic Acid Oxidation of Methyl Siaresinolate Acetate.—The acetate methyl ester (6·0 g.) in "AnalaR" acetic acid (250 ml.) was treated at 40° with "AnalaR" chromium trioxide (2·5 g.) in 95% acetic acid (150 ml.), added dropwise with stirring during 8 hours. Next morning the excess of chromium trioxide was destroyed with methanol (50 ml.), and the mixture worked up in the usual way, to give acid (0·53 g.) and neutral (4·6 g.) fractions. Chromatography (17 fractions) of the neutral fraction over alumina gave the following products: Elution with benzene afforded first methyl 19-keto-olean-12-enolate acetate (715 mg.) (recrystallised from chloroform–methanol), m. p. 243—244°, $[\alpha]_D$ +98° (*c*, 2·27), then material which, when rechromatographed over alumina, gave the "O_7"-acetate (30 mg.), m. p. 256—258°, $\lambda_{max.}$ 225 mμ (ε = 4200), $\lambda_{infl.}$ 288—298 mμ (ε = 250), undepressed in m. p. on admixture with an authentic specimen (see above), and finally *methyl* 12 : 19-*diketo-olean*-13(18)-*enolate acetate* (450 mg.).

Recrystallised from methanol the last had m. p. 248—250°, $[\alpha]_D$ −120° (*c*, 1·21), $\lambda_{max.}$ 253 mμ (ε = 7000) (Found: C, 72·9, 73·65; H, 8·65, 8·65. $C_{33}H_{48}O_6$ requires C, 73·3; H, 8·95%).

Methyl 12 : 19-diketo-olean-12(18)-enolate acetate (50 mg.) in " AnalaR " acetic acid (10 ml.) was stirred under reflux with excess of zinc dust for 2 hours. After being worked up in the usual way and recrystallisation from methanol, the product had m. p. 259—261° $[\alpha]_D$ +66° (*c*, 0·68), undepressed in m. p. on admixture with methyl 12 : 19-diketo-oleananolate acetate (see above). For confirmation of the identity, the reduction product was refluxed with 10% methanolic potassium hydroxide (10 ml.) for 1 hour. After working up in the usual way, reacetylation (pyridine–acetic anhydride on the steam-bath for 30 minutes), and filtration in benzene through alumina, recrystallisation from methanol gave methyl 12 : 19-diketo-18(α)-oleananolate acetate, m. p. 302—304°, undepressed in m. p. on admixture with authentic material (see above).

Chromic Acid Oxidation of Methyl 19-*Keto-olean*-12- *and* -13(18)-*enolate Acetates.*—Methyl 19-keto-olean-12-enolate acetate (120 mg.), in " AnalaR " acetic acid (7·0 ml.), was treated at 40° with " AnalaR " chromium trioxide (60 mg.) in 95% acetic acid (5 ml.) dropwise during 8 hours. After being kept overnight the reaction mixture was worked up as above. Chromatography gave unchanged starting material and methyl 12 : 19-diketo-olean-13(18)-enolate acetate, $\lambda_{max.}$ 254 mμ (ε = 7500), the identity of both compounds being confirmed by m. p. and mixed m. p.

Oxidation of methyl 19-keto-olean-13(18)-enolate acetate (100 mg.) under the same conditions revealed very little uptake (<20% of the theoretical) of chromium trioxide during 2 days at 40°. Working up as above gave back starting material (80 mg.) (m. p. and mixed m. p.).

Methyl 19-keto-olean-13(18)-enolate acetate (100 mg.) in " AnalaR " acetic acid (25 ml.) was kept at 40° for 8 hours; working up gave back unchanged starting material (95 mg.) (m. p. and mixed m. p.).

Chromic Acid Oxidation of Siaresinolic Acid.—Siaresinolic acid (2·0 g.) in " AnalaR " acetic acid (300 ml.) was oxidised as for the methyl ester acetate (see above), but with a proportionate amount of chromium trioxide and working up at room temperature. This gave an acid (1·86 g. and a neutral (0·18 g.) fraction. The acid fraction was methylated and chromatographed over alumina. Elution with benzene gave methyl 2 : 19-diketo-olean-12-enate, m. p. 205—208° (from methanol), converted by being heated under reflux for 1 hour with 25% potassium hydroxide solution and then remethylation into methyl 2 : 19-diketo-olean-13(18)-enate, m. p. 190—192° (from methanol), $\lambda_{max.}$ 252 mμ (ε = 8500). Elution with 9 : 1 ether–benzene and recrystallisation from ethyl acetate–light petroleum afforded *methyl* 2 : 12 : 19-*triketo-olean*-13(18)-*enate* (340 mg.), m. p. 226—228°, $[\alpha]_D$ −137° (*c*, 1·00), $\lambda_{max.}$ 251 mμ (ε = 8700) (Found: C, 74·3; H, 8·85. $C_{31}H_{44}O_5$ requires C, 74·95; H, 8·95%).

Methyl 12 : 19-*Diketo-olean*-10-*enolate Acetate.*—Methyl 12 : 19-diketo-olea-10 : 13(18)-dienolate acetate (205 mg.) (Ruzicka, Grob, and van der Sluys-Veer, *Helv. Chim. Acta*, 1939, **22**, 788) in " AnalaR " acetic acid (20 ml.) was stirred under reflux with excess of zinc dust (400 mg.) for 4 hours. After being worked up in the usual way the product was recrystallised from chloroform–methanol, to give *methyl* 12 : 19-*diketo-olean*-10-*enolate acetate*, m. p. 268—270°, $[\alpha]_D$ +128° (*c*, 1·34), $\lambda_{max.}$ 245 mμ (ε = 12,000) (Found: C, 72·85; H, 8·9. $C_{33}H_{48}O_6$ requires C, 73·3; H, 8·95%).

Methyl 12 : 19-*diketo*-18(α)-*olean*-10-*enolate Acetate.*—The 18(β)-diketone (see above) (1·0 g.) was heated under reflux with 10% methanolic potassium hydroxide (200 ml.) for 1 hour. After being worked up in the usual way the product was acetylated (pyridine–acetic anhydride on the steam-bath for 30 minutes) and then chromatographed over alumina. Elution with benzene gave ten small fractions which were not investigated further. Elution with ether–benzene afforded *methyl* 12 : 19-*diketo*-18(α)-*olean*-10-*enolate acetate* (500 mg.). Recrystallised from methanol this had m. p. 319—320°, $[\alpha]_D$ +82—83° (*c*, 2·62—0·54), $\lambda_{max.}$ 242 mμ (ε = 10,800) (Found: C, 73·25; H, 8·85. $C_{33}H_{48}O_6$ requires C, 73·3; H, 8·95%). The 18(α)-diketone was also formed when the 18(β)-diketone (135 mg.) was heated under reflux with selenium dioxide (135 mg.) in " AnalaR " acetic acid (10 ml.) for up to 5 hours. After being worked up in the usual way and filtered in benzene through alumina the 18(α)-diketone was obtained in essentially quantitative yield (m. p. and mixed m. p.).

Methyl 12 : 19-*Diketo*-18(α)-*olean*-10-*enolate Acetate from Methyl* 19-*Hydroxy*-12-*keto-oleananolate Acetate.*—The hydroxy-ketone (1·0 g.) (see above) in " AnalaR " acetic acid (30 ml.) was treated with a 50% solution (5 drops) of hydrogen bromide in acetic acid and then with 1% (v/v) bromine in acetic acid (9·51 ml., 1 mol.) added during 1·5 hours at 40°. After being kept at room temperature overnight and worked up in the usual way this gave only a neutral product (1·0 g.). A satisfactory crystalline compound could not be isolated at this stage. The crude reaction product in "AnalaR" acetic acid (100 ml.) was treated with chromium trioxide (125 mg.) in 95% acetic acid (10 ml.) during 1 hour at 40°. A further 50 mg. of chromium trioxide were then added and the solution was kept for a further hour at 40°. After being worked up in the usual way the product, which could not be crystallised, was dissolved in "AnalaR" acetic acid (30 ml.), a 50% solution (4 drops) of hydrogen bromide in acetic acid added, and the solution refluxed for 1 hour. After being worked up in the usual way the neutral product (750 mg.) was chromatographed over alumina. Elution with 4 : 1 benzene–light petroleum and crystallisation from methanol gave in long needles a substance (50 mg.), m. p. 243—244°, $[\alpha]_D$ +58° (*c*, 2·87), +55° (*c*, 1·13), $\lambda_{max.}$ 319 mμ (ε = 15,000) (Found: C, 75·9; H, 9·1%) which was free from bromine. It was not investigated further. Elution with 10 : 1 to 2 : 3 ether–benzene gave seven fractions with m. p.s ranging from 246—249° to 311—314°. These were combined and rechromatographed. Elution with 10 : 1 ether–benzene afforded mixed crystals of methyl 12 : 19-diketo-olean-13(18)-en- and -10 : 13(18)-dien-olate acetates which, recrystallised from methanol, had m. p. 307—309°, $[\alpha]_D$ +34° (*c*, 1·85), +37° (*c*, 1·52), $\lambda_{max.}$ 242 mμ (ε = 9400), $\lambda_{infl.}$ 280 mμ (ε = 2700). A mixture of these two compounds, prepared in such a ratio as to have the same specific rotation, had m. p. 309—310° and an identical ultra-violet absorption spectrum, and was undepressed in m. p. on admixture with above the mixed crystals. Both mixtures gave no depression in m. p. on admixture with methyl 12 : 19-diketo-olean-10-enolate acetate. Repeated crystallisation failed to resolve either the artificial mixture, or that obtained by partial synthesis. Further chromatography was only partly successful.

The mixed crystals (380 mg.) in "AnalaR" acetic acid (30 ml.) were stirred under reflux with zinc dust (500 mg.) for 1·5 hours. After being worked up in the usual way the product (350 mg.) was chromatographed over alumina. Elution with benzene gave material which was not investigated further. Elution with 1 : 19 ether–benzene furnished, after crystallisation from methanol, without difficulty, methyl 12 : 19-diketo-18(α)-olean-10-enolate acetate (130 mg.), m. p. 318—320°, $[\alpha]_D$ +80° (*c*, 2·26—2·12), $\lambda_{max.}$ 242 mμ (ε = 10,800) (Found: C, 72·6; 73·2; H, 8·95, 8·6. Calc. for $C_{33}H_{48}O_6$: C, 73·3; H, 8·95%), undepressed in m. p. on admixture with material of the same m. p., rotation, and absorption spectrum prepared (see above) from methyl 12 : 19-diketo-olean-10 : 13(18)-dienolate acetate.

*Action of Selenium Dioxide on Methyl Olea-*12 : 18*-dienolate Acetate.*—The methyl ester acetate (methyl *iso*dehydro-oleanolate acetate; Barton and Brooks, *J.*, 1951, 257) (100 mg.) in "AnalaR" acetic acid (25 ml.) was heated under reflux with an equal weight of selenium dioxide for 16 hours. Working up in the usual way gave a neutral product which on chromatography over alumina, elution with 1 : 19 to 1 : 4 ether–benzene, and recrystallisation from chloroform–methanol gave methyl 12 : 19-diketo-olea-10 : 13(18)-dienolate acetate (60 mg.), m. p. 247—248°, $\lambda_{max.}$ 277 mμ (ε = 14,000), undepressed in m. p. on admixture with an authentic specimen (Ruzicka, Grob, and van der Sluys-Veer, *loc. cit.*) of the same m. p. and absorption spectrum.

Relative Selenium Dioxide Oxidation Rates.—The compound (20 mg.), mixed with an equal weight of selenium dioxide, was dissolved in "AnalaR" acetic acid (5 ml.) and rapidly brought to reflux (paraffin-bath). The time required for deposition of red selenium was noted. The following relative oxidation rates were observed: β-amyratrienyl benzoate (Newbold and Spring, *J.*, 1944, 532) (<1 min.), methyl olean-12 : 18-dienolate acetate (Barton and Brooks, *loc. cit.*) (5 mins.), methyl oleanolate acetate (10 mins.), morolic acid, olean-13(18)-enolic acid, and methyl olea-11 : 13(18)-dienolate (all 10—30 mins.).

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