995. *The Constitution and Stereochemistry of Cyclamiretin.*

By D. H. R. Barton, A. Hameed, and J. F. McGhie.

The triterpenoid sapogenin cyclamiretin has been shown to have the molecular formula $C_{30}H_{48}O_4$ and to contain one aldehyde and two secondary and one primary hydroxyl group. By degradation cyclamiretin has been shown to be an aldehydo-derivative of " genin A " (β-amyrene-3β,16α,28-triol). The aldehyde function is attached at C-10, a biogenetically unusual position for an oxygen group. The complete structure of cyclamiretin is thus defined as 3β,16α,28-trihydroxy-β-amyren-25-al.

Cyclamin, the saponin from the bulbs of *Cyclamen europaea*, is readily obtained in high yield and crystalline form. On acidic hydrolysis it affords the sapogenin cyclamiretin [1] for which the molecular formula $C_{28}H_{46}O_4$ had been proposed. The earlier work on the chemistry of cyclamiretin, which is fragmentary, has been adequately summarised elsewhere.[2,3] On dehydrogenation cyclamiretin gave sapotalene (1,2,7-trimethylnaphthalene) and 1,2,5,6-tetramethylnaphthalene,[4] so there was a strong presumption that the compound was a triterpenoid. Our investigations, summarised in the sequel, show that cyclamiretin has the molecular formula $C_{30}H_{48}O_4$ and the constitution and stereochemistry depicted in (I; X = O, R = R′ = H). It is thus a dihydroxy-aldehydo-derivative of β-amyrin.

On mild acetylation cyclamiretin furnished a diacetate (I; X = O, R = Ac, R′ = H), m. p. 248—250°. The diacetate described earlier was said [3] to have m. p. 207°. With bromine in ethanol cyclamiretin gave a monobromo-derivative, m. p. 224—225°. This agrees with the m. p. 220—223° given earlier.[3] The bromo-compound is no doubt a 12-bromo-derivative (II; X = O, R = R′ = H).[5] The earlier literature reported the formation of a monosemicarbazone. In agreement we prepared a monoxime (I; X = N·OH, R = R′ = H). With sodium acetate–acetic anhydride on the steam-bath this afforded a nitrile diacetate (III; R = Ac, R′ = H), thus proving that cyclamiretin was an aldehyde.

On reduction with potassium borohydride cyclamiretin gave a tetrol (dihydrocyclamiretin) (IV; R = R′ = H), m. p. 267—268°, which gave a triacetate (IV; R = Ac, R′ = H), m. p. 214—216°, on mild acetylation. These compounds should have been identical with the so-called tetrahydro-derivative and its triacetate, derived from sodium–ethanol reduction, in the earlier literature,[3] but the recorded m. p.s (215° and 135°, respectively) are quite different. More vigorous acetylation of dihydrocyclamiretin with sodium acetate–acetic anhydride under reflux gave a tetra-acetate (IV; R = R′ = Ac), thus showing that cyclamiretin must contain three hydroxyl groups.

Cyclamiretin diacetate was readily oxidised by selenium dioxide to a conjugated diene, the spectrum and rotation of which showed that it must have the constitution (V; R = Ac, R′ = H). Dihydrocyclamiretin triacetate gave an analogous derivative. The formation of these compounds is characteristic [6] of a β-amyrin derivative.

Mild chromic acid oxidation of cyclamiretin diacetate gave the corresponding ketone-aldehyde (VI; X = H_2, R = Ac). Oxidation for a longer period afforded the conjugated ketone (VI; X = O, R = Ac), behaviour typical of α- and β-amyrin derivatives.

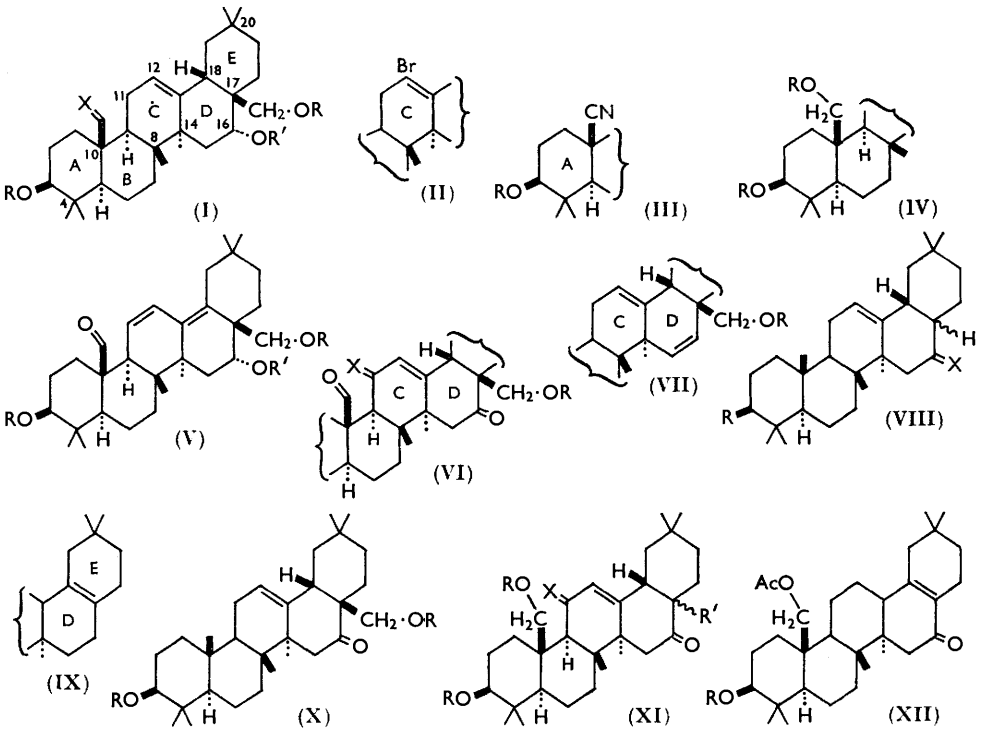
Dihydrocyclamiretin triacetate (IV; R = Ac) was smoothly dehydrated by thionyl

[1] Dafert, Gund, Muller, and Nitsche, *Arch. Pharm.*, 1926, **264**, 409.
[2] Sir John Simonsen and W. C. J. Ross, " The Terpenes," Vol. IV, Cambridge Univ. Press, 1957, p. 479.
[3] Elsevier's " Encyclopaedia of Organic Chemistry," Vol. XIV, Elsevier Publ. Co. Inc., Amsterdam, 1940, p. 597.
[4] Ruzicka, Brungger, Egli, Ehmann, Furter, and Hœsli, *Helv. Chim. Acta*, 1932, **15**, 431.
[5] Arya and Cookson, *J.*, 1957, 972.
[6] Ruzicka and Schellenberg, *Helv. Chim. Acta*, 1939, **22**, 767; Barton and Brooks, *J.*, 1951, 257.

chloride–pyridine to the anhydro-compound (VIII; R = Ac). This reaction has analogy in echinocystic acid chemistry.[7]

These preliminary experiments had led us to the view that cyclamiretin was probably a β-amyrin derivative. This was quickly confirmed in the following way. Cyclamiretin gave a dithioacetal with ethanedithiol. Desulphurisation with Raney nickel afforded deoxycyclamiretin. This was identified as the well-known " genin A " (I; $X = H_2$, $R = R' = H$).[8] Deoxycyclamiretin was also obtained by Wolff–Kishner reduction of cyclamiretin. It was characterised as the di- (I; $X = H_2$, R = Ac, R′ = H) and tri-acetate (I; $X = H_2$, $R = R' = Ac$), by oxidation to the diketo-aldehyde (not previously described), and by conversion into the diethoxycarbonyl derivative (I; $X = H_2$, R = CO_2Et, R′ = H).

An unexpected minor product from this Wolff–Kishner reduction was " norechinocystenol-A " (VIII; $X = H_2$, R = OH), characterised as its acetate (VIII; $X = H_2$,



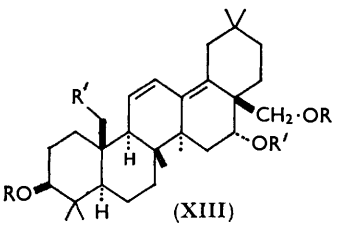
(In partial formulæ in this paper the structure implied by the braces { } is that of the last complete formula preceding.)

R = OAc) and by oxidation to the corresponding ketone[9] " norechinocystenone-A." Wolff–Kishner reduction of the latter gave " *trans*-oleanene-II." [10] In our opinion this compound must be formulated as (VIII; $X = H_2$, R = H) and not as (IX).[11] The formation of " norechinocystenol-A " must depend on alkali-promoted aerial oxidation of deoxycyclamiretin to the ketone (X; R = H) from which formaldehyde should be very

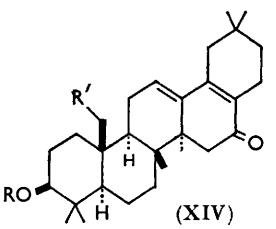
[7] Frazier and Noller, *J. Amer. Chem. Soc.*, 1944, **66**, 1267.
[8] Bischof, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1949, **32**, 1911, 1917, and references there cited.
[9] Harris and Noller, *J. Amer. Chem. Soc.*, 1944, **66**, 1005.
[10] Bilham and Kon, *J.*, 1940, 1469.
[11] Elsevier, *op. cit.*, Suppl., p. 998s; Sir John Simonsen and W. C. J. Ross, " The Terpenes," Vol. V, Cambridge Univ. Press, p. 159.

easily eliminated.[12,13] Support for this explanation was secured in the following way. Oxidation of deoxycyclamiretin diacetate (I; X = H_2, R = Ac, R′ = H) gave the ketone (X; R = Ac), which with ethanolic potassium hydroxide afforded the expected nor-ketone (VIII; X = O, R = OH) described in the literature as " norechinocystenolone." [14]

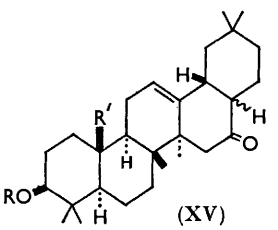
Similarly dihydrocyclamiretin triacetate (IV; R = Ac, R′ = H) was oxidised to the corresponding ketone (XI; X = H_2, R = Ac, R′ = β-CH_2·OAc) which with ethanolic potassium hydroxide afforded the nor-ketone (XI; X = H_2, R = R′ = H). When heated with acetic acid and concentrated hydrochloric acid the latter gave the conjugated ketone (XII). More prolonged chromic acid oxidation of dihydrocyclamiretin triacetate furnished the diketone (XI; X = O, R = Ac, R′ = β-CH_2·OAc). Similar experiments were carried out with dehydrodeoxycyclamiretin diacetate (XIII; R = Ac, R′ = R″ = H), which was prepared by selenium dioxide oxidation of deoxycyclamiretin diacetate (I; X = H_2, R = Ac, R′ = H). Oxidation gave the expected monoketone which with ethanolic potassium hydroxide furnished the conjugated dienone (XIV; R = R′ = H). The shift of the double bonds into conjugation would, of course, be expected for βγ, δε-diene



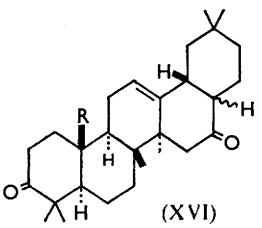
(XIII)



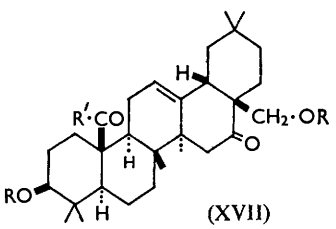
(XIV)



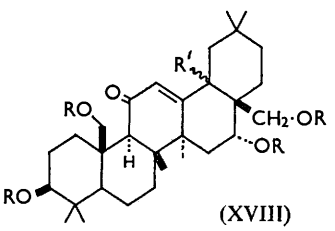
(XV)



(XVI)



(XVII)



(XVIII)

conjugation in the precursor. The same series of reactions starting from dehydrodihydrocyclamiretin triacetate (XIII; R = Ac, R′ = H, R″ = OAc) (see above) gave a monoketone which on basic hydrolysis furnished the conjugated dienone (XIV; R = H, R′ = OH), characterised as its diacetate (XIV; R = Ac, R′ = OAc).

With these experiments completed it remained to establish the position of the aldehyde group in cyclamiretin. In principle this could be attached to [see formula (I)] positions 4, 8, 10, 14, or 20. Position 14 can be dismissed at once because an (axial) aldehyde group here would form a masked aldehyde system with the axial 16-hydroxyl group (cf. aldosterone).

We considered first the possible attachment of the aldehyde group at C-4. A convenient procedure for detecting the presence of the group –CH(OH)·C·CH_2·OH is to heat the compound with copper bronze and determine the formaldehyde evolved. The chemistry of clerodin [15] provides a recent sample of this technique. Cyclamiretin and deoxycyclamiretin gave formaldehyde in the same yield as did dihydrocyclamiretin, indicating that only one formaldehydogenic grouping was present. Hederagenin methyl ester used as a control also gave essentially the same yield. In constrast, the nor-ketone

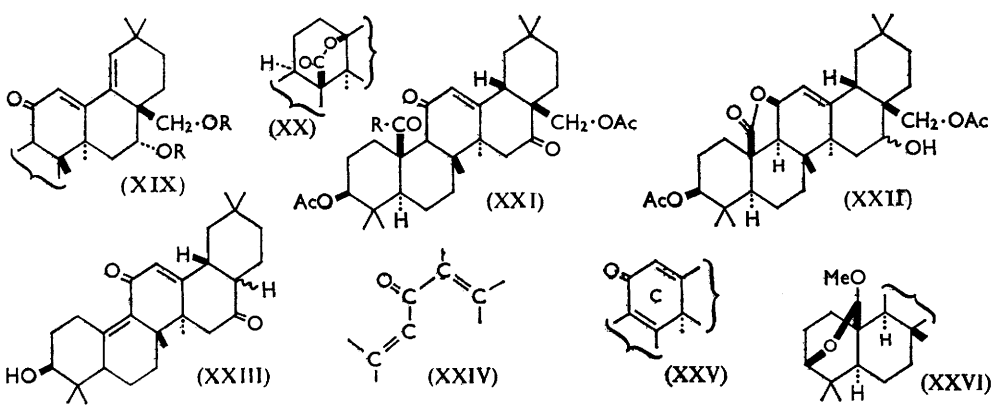
[12] Cf. Barton and de Mayo, *J.*, 1954, 887.
[13] Djerassi, Rittel, Nussbaum, Donovan, and Herran, *J. Amer. Chem. Soc.*, 1954, **76**, 6410; Djerassi and Rittel, *ibid.*, 1957, **79**, 3528.
[14] White and Noller, *J. Amer. Chem. Soc.*, 1939, **61**, 983.
[15] Barton, Cheung, Cross, Jackman, and Martin-Smith, *J.*, 1962, 5061.

(XI; X = H_2, R = R′ = H) furnished no formaldehyde. We concluded, therefore, that the aldehyde group of cyclamiretin was not attached to C-4. Further experiments provided confirmatory evidence. The monoketone (VI; X = H_2, R = Ac) from cyclamiretin diacetate was treated with ethanolic potassium hydroxide to give the nor-compound (XV; R = H, R′ = CHO). Mild chromic acid oxidation of the latter afforded the diketone-aldehyde (XVI; R = CHO). On treatment with alkali this was recovered unchanged. Had the aldehyde group been at C-4 then deformylation of the β-dicarbonyl system would have been expected.

In the chromic acid oxidation of cyclamiretin diacetate (I; X = O, R = Ac, R′ = H) the aldehyde group is partly oxidised to carboxyl to produce the keto-acid (XVII; R = Ac, R′ = OH), characterised as its methyl ester (XVII; R = Ac, R′ = OMe). Alkaline hydrolysis of the acid gave the expected nor-compound (XV; R = H, R′ = CO_2H) which with chromic acid gave the diketo-acid (XVI; R = CO_2H), again characterised as its methyl ester (XVI; R = CO_2Me). The same diketo-acid was formed as a secondary product in the chromic acid oxidation of aldehyde (XV; R = H, R′ = CHO). If the carboxyl group had been at C-4, then this diketo-acid should have been easily decarboxylated when heated. In fact, it was stable and, therefore, again the aldehyde group of cyclamiretin cannot be attached to C-4.

The possible attachment of the aldehyde group at C-20 was then examined. Dihydrocyclamiretin tetra-acetate (IV; R = R′ = Ac) (see above) was oxidised with chromic acid to the 11-ketone (XVIII; R = Ac, R′ = β-H). Bromination gave the 18-bromo-derivative (XVIII; R = Ac, R′ = Br) which on dehydrobromination furnished the conjugated dienone (XIX; R = Ac). On alkaline hydrolysis this gave the corresponding tetrol (XIX, R = H) which could be reacetylated to its precursor (XIX; R = Ac). If the aldehyde group of cyclamiretin had been at C-20 the derivative (XIX; R = H) should have lost formaldehyde easily with base (vinylogous reversed aldol condensation). The fact that this did not occur led us to the conclusion that the aldehyde was not attached to C-20.

We then considered whether the aldehyde group could be attached to C-8. If this were so, then the keto-acid truly represented as (XVII; R = Ac, R′ = OH) should have



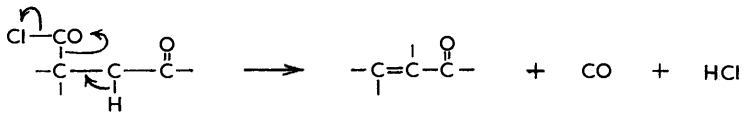
lactonised easily with acid to give a γ-lactone (as XX). In the event, (XVII; R = Ac, R′ = OH) was recovered unchanged from conditions which should have been adequate to induce lactonisation [16] if this were structurally possible.

On the basis of all this negative evidence we concluded that the aldehyde group must be attached to C-10. Since pentacyclic triterpenoids of this type are almost without

[16] Barton and Holness, *J.*, 1952, 78.

precedent [17] we sought more positive evidence to this effect. Cycalmiretin diacetate (I; X = O, R = Ac, R′ = H) was subjected to more prolonged chromic acid oxidation than hitherto, to furnish the diketo-acid (XXI; R = OH), characterised as its methyl ester (XXI; R = OMe). Reduction of the diketo-acid with potassium borohydride gave the γ-lactone (XXII). Such a lactone can only be formed from substitution on the axial groups at C-10 and C-8.

We then investigated methods of decarboxylation for position 10. The monoketo-acid (XVII; R = Ac, R′ = OH) (see above) was converted by oxalyl chloride into the acid chloride (XVII; R = Ac, R′ = Cl). With potassium ethyl xanthate this gave the corresponding ethyl xanthate (XVII; R = Ac, R′ = EtO·CS·S) which on photolysis [18] followed by alkaline hydrolysis furnished the thiol (XV; R = H, R′ = SH). We reasoned that if the same reaction sequence could be applied to an 11-ketone, then the thiol group would be β- and thus easily eliminated to give an αβ-unsaturated ketone. The diketo-acid (XXI; R = OH) (see above) was converted into its acid chloride (XXI; R = Cl) and thence into the xanthate (XXI; R = EtO·CS·S). Before we could study the photolysis of this xanthate in any detail we noted the ready decomposition of the acid chloride (XXI; R = Cl). One can consider the COCl group as a potential fragmenting group with respect to an appropriately placed ketone:



This then would also place an ethylenic linkage in conjugation with the original ketone group. Decomposition of the acid chloride (XXI; R = Cl) and alkaline hydrolysis of the product then gave the cross-conjugated dienone (XXIII). This compound had the peculiar ultraviolet absorption shown by Spring and his collaborators [19] to be characteristic of the cross-conjugated dienone system (XXIV) in two *six*-membered rings.[20] The exaltation of the *cisoid* $C_{(9)}$–$C_{(10)}$–C=C frequency could also be seen in the infrared spectrum.[21] The alternative cross-conjugated dienone (XXV) would not have these special spectroscopic properties.

As a final confirmation of the cyclamiretin formula we argued that a 10-aldehyde group should behave like the corresponding aldehyde group in steroid compounds [22] and give cyclic derivatives involving the attachment of the 3β-hydroxyl function to the 10-aldehyde. In the event treatment of cyclamiretin with methanolic hydrogen chloride gave the cyclic hemiacetal (XXVI). Acid-catalysed aqueous hydrolysis gave back cyclamiretin. Such a derivative could not, of course, have been formed if the aldehyde group had been attached to C-8.

Experimental

Ultraviolet absorption spectra were determined for EtOH, and $[\alpha]_D$ in $CHCl_3$ solutions at 15—20°. Infrared spectra were determined as Nujol mulls. All solvents for chromatography were dried and distilled. Light petroleum refers to the fraction of b. p. 40—60° unless otherwise indicated. Kiliani's chromic acid mixture was prepared from sodium dichromate (60 g.) in water (270 ml.) by addition of concentrated sulphuric acid (80 g.).

Cyclamiretin.—(*a*) *Extraction of cyclamin.* Dried, ground bulbs of *Cyclamen europaea* (1500 g.) were refluxed with 95% aqueous ethanol (7—8 l.) for 8 hr. After filtration the residue was again extracted with 95% ethanol (6 l.). The two filtrates were left at room temperature

[17] White, *Rev. Pure and Applied Chem.*, 1956, **6**, 191.
[18] Barton, George, and Tomoeda, *J.*, 1962, 1967.
[19] Beaton, Johnston, McKean, and Spring, *J.*, 1953, **3660**; Beaton, Shaw, Spring, Stevenson, Strachan, and Stewart, *J.*, 1955, 2606.
[20] Cf. Barton and Narayanan, *J.*, 1958, 963.
[21] Erskine and Waight, *J.*, 1960, 3425, and references there cited.
[22] Barton, Beaton, Geller, and Pechet, *J. Amer. Chem. Soc.*, 1961, **83**, 4076.

for 2 weeks, and the white solid filtered off and washed with ethanol (500 ml.). The combined filtrates were concentrated to half-volume and left as above before removal of the crude cyclamin, which was washed with ethanol (200 ml.). The combined solids were crystallised from 80% ethanol to furnish cyclamin (120 g.), m. p. 254° (decomp.).

(*b*) *Hydrolysis of cyclamin.* The saponin (50 g.) in water (1500 ml.) was refluxed with 10% aqueous sulphuric acid (1500 ml.) for 12 hr. The dark brown powder that separated was filtered off, washed with water, and then refluxed with ether (1500 ml.) for 2 hr. The ethereal extract was washed with 2% aqueous sodium hydroxide and with water and then treated with charcoal. After filtration, the pale yellow ethereal solution was dried (Na_2SO_4) and the ether removed *in vacuo*. Crystallisation from ethanol afforded *cyclamiretin* (I; X = O, R = R′ = H) as needles (7·5 g.), m. p. 239—240°, $[\alpha]_D$ +48° (*c* 1·42), $\nu_{max.}$ 3460 and 3378 (OH) and 1712 (CHO) cm.$^{-1}$ (Found: C, 76·1; H, 10·1. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·25%). Cyclamiretin consumed one mol. of perbenzoic acid overnight at room temperature.

(*c*) *Derivatives of cyclamiretin.* Treatment of cyclamiretin with pyridine–acetic anhydride overnight at room temperature gave the *diacetate* (I; X = O, R = Ac, R′ = H). This crystallised from ethanol as needles, m. p. 248—250°, $[\alpha]_D$ +38° (*c* 0·65), $\nu_{max.}$ 3484 (OH), 1739 and 1244 (OAc), and 1712 (CHO) cm.$^{-1}$ (Found: C, 73·1; H, 9·2. $C_{34}H_{52}O_6$ requires C, 73·35; H, 9·4%).

Cyclamiretin (100 mg.) in ethanol (5 ml.) was treated on the steam-bath with bromine (2% in ethanol) until the yellow colour persisted. Crystallisation from methanol gave *bromocyclamiretin* (II; X = O, R = R′ = H) (80 mg.), m. p. 224—225°, $[\alpha]_D$ +80° (*c* 0·60), $\nu_{max.}$ 3460 and 3378 (OH) and 1712 (CHO) cm.$^{-1}$ (Found: C, 65·65; H, 8·65; Br, 14·1. $C_{30}H_{47}BrO_4$ requires C, 65·3; H, 8·6; Br, 14·3%).

Cyclamiretin Oxime.—Cyclamiretin (100 mg.) in pyridine (2 ml.) containing hydroxylamine hydrochloride (100 mg.) was left at room temperature overnight. Crystallisation from ethanol gave *cyclamiretin oxime* (I; X = N·OH, R = R′ = H) as needles (75 mg.), m. p. 275—276°, $[\alpha]_D$ +61° (*c* 0·70), $\nu_{max.}$ 3472 and 3322 (OH) cm.$^{-1}$ (Found: C, 73·65; H, 9·95; N, 3·1. $C_{30}H_{49}NO_4$ requires C, 73·9; H, 10·15; N, 2·85%).

The oxime (50 mg.) was heated on the steam-bath for 3 hr. with acetic anhydride (2 ml.) containing fused sodium acetate (100 mg.). Crystallisation from methanol gave the *nitrile diacetate* (III; R = Ac, R′ = H) as needles (30 mg.), m. p. 306—308°, $[\alpha]_D$ +38° (in pyridine, *c* 2·04), $\nu_{max.}$ 3366 (OH), 2265 (CN), and 1739 and 1244 (OAc) cm.$^{-1}$ (Found: C, 73·4; H, 9·1; N, 2·6. $C_{34}H_{51}NO_5$ requires C, 73·75; H, 9·3; N, 2·55%).

Dihydrocyclamiretin and its Derivatives.—Cyclamiretin (100 mg.) in benzene (8 ml.) and methanol (12 ml.) was treated overnight at room temperature with potassium borohydride (100 mg.). Crystallisation from ethanol furnished *dihydrocyclamiretin* (IV; R = R′ = H) as needles (85 mg.), m. p. 267—268°, $[\alpha]_D$ +60° (in pyridine, *c* 0·71), $\nu_{max.}$ 3322 (OH) cm.$^{-1}$ (Found: C, 73·2; H, 10·6. $C_{30}H_{50}O_4$ requires C, 73·1; H, 10·65%). Treatment with pyridine–acetic anhydride overnight at room temperature afforded *dihydrocyclamiretin triacetate* (IV; R = Ac, R′ = H). From methanol this formed needles, m. p. 214—216°, $[\alpha]_D$ +28° (in pyridine, *c* 0·71), $\nu_{max.}$ 3508 (OH) and 1734 and 1240 (OAc) cm.$^{-1}$ (Found: C, 72·2; H, 9·25. $C_{36}H_{56}O_7$ requires C, 71·95; H, 9·4%).

Dihydrocyclamiretin (200 mg.) in acetic anhydride (5 ml.) containing fused sodium acetate (200 mg.) was refluxed for 4 hr. Crystallisation from methanol afforded *dihydrocyclamiretin tetra-acetate* (IV; R = R′ = Ac) as needles (170 mg.), m. p. 134—136°, $[\alpha]_D$ −32° (*c* 0·37), $\nu_{max.}$ 1735 and 1240 (OAc) cm.$^{-1}$ (Found: C, 70·7; H, 9·4. $C_{38}H_{58}O_8$ requires C, 71·0; H, 9·1%).

Dehydrocyclamiretin Diacetate.—Cyclamiretin diacetate (100 mg.) in glacial acetic acid (5 ml.) was refluxed with selenium dioxide (100 mg.) for 1 hr. Chromatography of the product over alumina (grade V), elution with benzene, and crystallisation from methanol, gave *dehydrocyclamiretin diacetate* (V; R = Ac, R′ = H) as needles (50 mg.), m. p. 158—160°, $[\alpha]_D$ −60° (*c* 1·72), $\lambda_{max.}$ 250 mμ (ε 23,700) (Found: C, 73·2; H, 9·35. $C_{34}H_{50}O_6$ requires C, 73·6; H, 9·1%).

Dehydrodihydrocyclamiretin Triacetate.—Dihydrocyclamiretin triacetate (100 mg.) in glacial acetic acid (5 ml.) was refluxed with selenium dioxide (100 mg.) for 1 hr. Chromatography as above and crystallisation from ether–methanol afforded *dehydrodihydrocyclamiretin triacetate* (XIII; R = Ac, R′ = H, R″ = OAc) as plates (55 mg.), m. p. 185—187°, $[\alpha]_D$ −48° (*c* 1·26), $\lambda_{max.}$ 250 mμ (ε 25,000) (Found: C, 72·3; H, 9·2. $C_{36}H_{54}O_7$ requires C, 72·2; H, 9·1%).

Chromic Acid Oxidation of Dihydrocyclamiretin Triacetate.—The triacetate (100 mg.) in glacial

acetic acid (10 ml.) was treated with chromium trioxide (50 mg.) in the same solvent (10 ml.) at room temperature for 5 min. (1 atom of oxygen uptake). Chromatography over alumina (grade V) and elution with benzene–light petroleum (1 : 3) furnished the *ketone* (XI; X = H_2, R = Ac, R′ = β-CH_2·OAc). This crystallised from methanol as needles (65 mg.), m. p. 140—142°, $[\alpha]_D$ +30° (*c* 0·92), $\nu_{max.}$ 1735 and 1244 (OAc) and 1715 (ketone) cm.$^{-1}$ (Found: C, 71·8; H, 9·25. $C_{36}H_{54}O_7$ requires C, 72·2; H, 9·1%).

Dihydrocyclamiretin triacetate (100 mg.) in glacial acetic acid (10 ml.) was treated with chromium trioxide (100 mg.) in the same solvent (10 ml.) at room temperature overnight (3 atoms of oxygen uptake). Chromatography over alumina (grade V) and elution with benzene–light petroleum (1 : 3) gave the *diketone* (XI; X = O, R = Ac, R′ = β-CH_2·OAc). This crystallised from methanol as needles (50 mg.), m. p. 182—184°, $[\alpha]_D$ +36° (*c* 0·72), $\lambda_{max.}$ 244 mμ (ε 13,800), $\nu_{max.}$ 1733 and 1242 (OAc), 1712 (ketone), and 1660 (cyclohexenone) cm.$^{-1}$ (Found: C, 70·3; H, 8·6. $C_{36}H_{52}O_8$ requires C, 70·55; H, 8·55%).

Treatment of the ketone (XI; X = H_2, R = Ac, R′ = β-CH_2·OAc) 100 mg.) with 1% ethanolic potassium hydroxide (10 ml.) under reflux for 1 hr. gave, after crystallisation from chloroform–methanol, the *dihydroxy-ketone* (XI; X = H_2, R = R′ = H) as needles (65 mg.), m. p. 231—233°, $[\alpha]_D$ −87° (*c* 0·56), $\nu_{max.}$ 3356 (OH) and 1706 (ketone) cm.$^{-1}$ (Found: C, 78·4; H, 10·4. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·45%). This compound (50 mg.), heated under reflux in glacial acetic acid (4 ml.) and concentrated hydrochloric acid (1·0 ml.) for 1 hr., gave, on crystallisation from methanol, the conjugated *ketone diacetate* (XII) (35 mg.), m. p. 267—268°, $[\alpha]_D$ +9° (*c* 0·36), $\lambda_{max.}$ 251 mμ (ε 9000) (Found: C, 74·55; H, 9·5. $C_{33}H_{50}O_5$ requires C, 75·25; H, 9·55%).

Anhydrodihydrocyclamiretin Triacetate (VII; R = Ac).—Dihydrocyclamiretin triacetate (100 mg.) in pyridine (5 ml.) was treated dropwise at 0° with thionyl chloride (1·0 ml.) and then left at ambient temperature for 5 min. Chromatography over alumina (grade V) and elution with ether–light petroleum (1 : 4) gave *anhydrodihydrocyclamiretin triacetate* (VII, R = Ac). This crystallised from chloroform–methanol as rods (64 mg.), m. p. 130—132°, $[\alpha]_D$ +32° (*c* 0·65), $\nu_{max.}$ 1740 and 1244 (OAc) cm.$^{-1}$ (Found: C, 74·2; H, 9·3. $C_{36}H_{54}O_6$ requires C, 74·2; H, 9·35%).

Pyrolyses with Copper Bronze.—(*a*) *Positive experiments.* Hederagenin methyl ester (100 mg.), mixed with copper bronze (200 mg.), was heated at 270—280° under oxygen-free nitrogen for 1 hr., the effluent gas being passed into a saturated aqueous solution of dimedone. The precipitate was filtered off, recrystallised from aqueous alcohol, and identified (m. p. and mixed m. p.) as the formaldehyde–dimedone derivative (8·9 mg.). In the same way portions (100 mg.) of the following compounds were shown to give the formaldehyde derivative (yields, in parentheses, in mg. of purified derivative): cyclamiretin (6·8 mg.), dihydrocyclamiretin (8·2 mg.), and deoxycyclamiretin (8·0 mg.).

(*b*) *Negative experiments.* Tested under the same conditions, lanostanol and the 28-norketone (XI; X = H_2, R = R′ = H) gave no formaldehyde.

25-*Deoxycyclamiretin.*—(*a*) *Through the dithioacetal.* Cyclamiretin (200 mg.) in acetic acid (10 ml.) containing ethanedithiol (0·3 ml.) and boron trifluoride–ether (2 ml.) was kept at room temperature for 5 hr. Crystallised from aqueous ethanol, the *dithioacetal* (190 mg.) had m. p. 152—154° (Found: C, 67·5; H, 9·65; S, 11·4. $C_{32}H_{52}O_3S_2,H_2O$ requires C, 67·8; H, 9·95; S, 11·3%). This dithioacetal (150 mg.) in ethanol (20 ml.) was refluxed overnight with alkali-free Raney nickel (500 mg.). Crystallisation from ethanol gave 25-deoxycyclamiretin (I; X = H_2, R = R′ = H) as needles (125 mg.), m. p. 228—230°, $[\alpha]_D$ +46° (*c* 0·73), $\nu_{max.}$ 3276 (hydroxy) cm.$^{-1}$ (Found: C, 78·3; H, 11·3. Calc. for $C_{30}H_{50}O_3$: C, 78·55; H, 11·0%). Crystallisation from ethyl acetate gave plates, m. p. 248—250°, $[\alpha]_D$ +50° (*c* 1·36). Identity with " genin A," obtained from echinocystic acid, was established by m. p. and mixed m. p. Acetylation with pyridine–acetic anhydride overnight at room temperature gave, after crystallisation from chloroform–methanol, the diacetate (I; X = H_2, R = Ac, R′ = H), m. p. 184—185°, $[\alpha]_D$ +34° (*c* 1·52) (Found: C, 75·4; H, 9·9. Calc. for $C_{34}H_{54}O_5$: C, 75·25; H, 10·05%), identical (m. p. and mixed m. p.) with " genin A " diacetate. Treatment with pyridine–acetic anhydride for 3 days at room temperature gave the triacetate (I; X = H_2, R = R′ = Ac). This crystallised from methanol as needles, m. p. 159—160°, $[\alpha]_D$ −9° (*c* 0·96) (Found: C, 73·65; H, 9·7. Calc. for $C_{36}H_{56}O_6$: C, 73·95; H, 9·65%), and was identified as " genin A " triacetate (m. p. and mixed m. p.).

Deoxycyclamiretin (50 mg.) in dry pyridine (1 ml.) was treated at 0° with freshly distilled ethyl chloroformate (100 mg.) and then allowed to warm to room temperature. Crystallisation

from methanol gave the *diethoxycarbonyl derivative* (I; X = H_2, R = CO_2Et, R′ = H) as needles (40 mg.), m. p. 150—152°, $[\alpha]_D$ +38° (*c* 0·66) (Found: C, 71·95, H, 9·85. $C_{36}H_{58}O_7$ requires C, 71·75; H, 9·7%).

Treatment of deoxycyclamiretin (100 mg.) in " AnalaR " acetone (10 ml.) with Kiliani chromic acid mixture (1 ml.) at room temperature for 10 min. afforded the *diketo-aldehyde*. This crystallised from methanol as needles (55 mg.), m. p. 187—188°, $[\alpha]_D$ +68° (*c* 0·73), $\nu_{max.}$ 1710 (aldehyde and ketones) $cm.^{-1}$ (Found: C, 79·35; H, 9·95. $C_{30}H_{44}O_3$ requires C, 79·6; H, 9·8%).

(*b*) *By Wolff–Kishner reduction under anhydrous conditions.* Cyclamiretin (2·0 g.) was reduced under the conditions detailed by Barton, Ives, and Thomas.[23] Chromatography over alumina (grade V) and elution with benzene and with benzene–ether (1 : 1), followed by fractional crystallisation from ethanol, afforded doexycyclamiretin (I; X = H_2, R = R′ = H) (" genin A ") (1·2 g.), identified by m. p., mixed m. p. (crystallised both from ethanol and from ethyl acetate), $[\alpha]_D$, and infrared spectrum (Found: C, 78·5; H, 11·25%), and " norechinocystenol-A " (VIII; X = H_2, R = OH). The latter crystallised from ethanol as needles (350 mg.), m. p. 185—187°, $[\alpha]_D$ +15° (*c* 1·25), $\nu_{max.}$ 3370 (OH) $cm.^{-1}$ (Found: C, 84·55; H, 11·6. Calc. for $C_{29}H_{48}O$: C, 84·4; H, 11·7%). The identity of the " norechinocystenol-A " was confirmed by conversion into the acetate (VIII; X = H_2, R = OAc) and by oxidation to the ketone. The latter was reduced by the Wolff–Kishner procedure to the corresponding hydrocarbon which was identified as " *trans*-oleanene-II " (VIII; X = H_2, R = H) by m. p., mixed m. p., and $[\alpha]_D$ (Found: C, 87·45; H, 12·5. Calc. for $C_{29}H_{48}$: C, 87·8; H, 12·2%). The authentic specimen came from the collection of triterpenoids of the late Professor G. A. R. Kon, F.R.S.[10]

Conversion of Deoxycyclamiretin into " Norechinocystenolone."—Deoxycyclamiretin diacetate (100 mg.) in " AnalaR " acetone (10 ml.) was treated with Kiliani chromic acid mixture (0·5 ml.) at room temperature for 5 min. Crystallisation from methanol gave the known [24] ketone diacetate (X; R = Ac) as needles (80 mg.), m. p. 216—217°, $[\alpha]_D$ −9° (*c* 0·88), $\nu_{max.}$ 1740 and 1240 (OAc) and 1706 (ketone) $cm.^{-1}$ (Found: C, 75·55; H, 9·6. Calc. for $C_{34}H_{52}O_5$: C, 75·5; H, 9·7%). This ketone (50 mg.) in ethanolic 1% potassium hydroxide (10 ml.) was refluxed for 1 hr. Crystallisation from chloroform–methanol gave " norechinocystenolone " (VIII; X = O, R = OH)[14] (40 mg.), m. p. 223—225°, $[\alpha]_D$ −96° (in dioxan, *c* 0·75), $\nu_{max.}$ 3360 (OH) and 1706 (ketone) $cm.^{-1}$ (Found: C, 81·6; H, 11·0. Calc. for $C_{29}H_{46}O_2$: C, 81·65; H, 10·85%).

Dehydrodeoxycyclamiretin Diacetate and its Derivatives.—Deoxycyclamiretin diacetate (200 mg.) in glacial acetic acid (10 ml.) was refluxed with selenium dioxide (200 mg.) for 1 hr. Selenium was removed and then the acetic acid *in vacuo*. Crystallisation of the residue from methanol afforded *dehydrodeoxycyclamiretin diacetate* (XIII; R = Ac, R′ = R″ = H) (150 mg.), m. p. 165—166°, $[\alpha]_D$ −52° (*c* 0·73), $\lambda_{max.}$ 250 mμ (ε 22,800) (Found: C, 75·5; H, 9·55. $C_{34}H_{52}O_5$ requires C, 75·5; H, 9·7%).

Dehydrodeoxycyclamiretin diacetate (100 mg.) in " AnalaR " acetone (10 ml.) was treated with Kiliani chromic acid mixture (0·5 ml.) at room temperature for 5 min. Crystallisation from methanol gave the *ketone* as needles (80 mg.), m. p. 210—211°, $[\alpha]_D$ −68° (*c* 0·68), $\lambda_{max.}$ 250 mμ (ε 22,000) (Found: C, 75·55; H, 9·3. $C_{34}H_{50}O_5$ requires C, 75·8; H, 9·35%). This ketone (50 mg.) in 1% ethanolic potassium hydroxide (10 ml.) was refluxed for 1 hr. The product was acetylated with pyridine–acetic anhydride overnight at room temperature. The resulting *acetate* (XIV; R = Ac, R′ = H) crystallised from chloroform–methanol as needles (25 mg.), m. p. 221—222°, $[\alpha]_D$ −38° (*c* 0·34), $\lambda_{max.}$ 240 and 297 mμ (ε 7000 and 13,600, respectively) (Found: C, 79·5; H, 9·9. $C_{31}H_{46}O_3$ requires C, 79·8; H, 9·9%).

Dehydrodihydrocyclamiretin Triacetate Derivatives.—The triacetate (100 mg.) in " AnalaR " acetone (10 ml.) was treated with Kiliani chromic acid mixture (0·5 ml.) with agitation for 5 min. at room temperature. After dilution with water the excess of chromic acid was destroyed with sulphur dioxide. Chromatography over alumina (grade V), elution with light petroleum–benzene (4 : 1), and crystallisation from methanol gave the *ketone triacetate* as needles (70 mg.), m. p. 205—206°, $[\alpha]_D$ −64° (*c* 0·55), $\lambda_{max.}$ 250 mμ (ε 24,000) (Found: C, 72·55; H, 9·3. $C_{36}H_{52}O_7$ requires C, 72·45; H, 9·0%).

The ketone (100 mg.) in ethanolic potassium hydroxide (1%, 10 ml.) was refluxed for 1 hr. Crystallisation of the product from methanol gave the *dienone* (XIV; R = H, R′ = OH)

[23] Barton, Ives, and Thomas, *J.*, 1955, 2056.
[24] Margot and Reichstein, *Pharm. Acta Helv.*, 1942, **17**, 113.

(60 mg.), m. p. 194—195°, $[\alpha]_D$ −36° (*c* 0·63), $\lambda_{max.}$ 240 and 296 mμ (ε 6700 and 15,000, respectively), $\nu_{max.}$ 3405 (OH) and 1670 (conjugated ketone) cm.$^{-1}$ (Found: C, 78·75; H, 10·0. $C_{29}H_{44}O_3$ requires C, 79·05; H, 10·05%). On treatment with pyridine–acetic anhydride overnight at room temperature the corresponding *diacetate* (XIV; R = Ac, R′ = OAc) was formed. This crystallised as plates (from chloroform–methanol) (35 mg.), m. p. 220—221°, $[\alpha]_D$ −27° (*c* 0·36) (Found: C, 75·25; H, 9·2. $C_{33}H_{48}O_5$ requires C, 75·55; H, 9·2%).

Derivatives of Dihydrocyclamiretin Tetra-acetate.—Dihydrocyclamiretin tetra-acetate (500 mg.) in glacial acetic acid (20 ml.) was treated with chromium trioxide (200 mg.) in the same solvent (5 ml.) overnight at room temperature. Chromatography over alumina (grade V) and elution with light petroleum–benzene (1 : 1), followed by crystallisation from chloroform–methanol, gave the 11-*ketone* (XVIII; R = Ac, R′ = β-H) as needles (280 mg.), m. p. 140—142°, $[\alpha]_D$ +20° (*c* 1·32), $\lambda_{max.}$ 247 mμ (ε 12,500), $\gamma_{max.}$ 1738 and 1242 (OAc) and 1680 (cyclohexenone) cm.$^{-1}$ (Found: C, 69·25; H, 8·65. $C_{38}H_{58}O_9$ requires C, 69·5; H, 8·6%).

This ketone (200 mg.) in glacial acetic acid (10 ml.) was treated dropwise with bromine in the same solvent (3%; 3 ml.) on the steam-bath until the colour persisted. Crystallisation of the product from methanol gave the 18-*bromo*-11-*ketone* (XVIII; R = Ac, R′ = Br) (160 mg.), m. p. 158—160°, $[\alpha]_D$ +42° (*c* 0·76), $\lambda_{max.}$ 248 mμ (ε 8500) (Found: C, 62·15; H, 7·75; Br, 10·35. $C_{38}H_{55}BrO_9$ requires C, 61·95; H, 7·65; Br, 10·85%).

This bromo-ketone (200 mg.) in dimethylformamide (10 ml.; freshly distilled) was refluxed with stirring with lithium carbonate (200 mg.) for 8 hr. The product, crystallised from methanol, was the conjugated *dienone tetra-acetate* (XIX; R = Ac) as needles (110 mg.), m. p. 193—194°, $[\alpha]_D$ +166° (*c* 0·61), $\lambda_{max.}$ 284 mμ (ε 13,500) (Found: C, 69·8; H, 8·25. $C_{38}H_{54}O_9$ requires C, 69·7; H, 8·3%). Treatment of this dienone (50 mg.) with 5% methanolic potassium hydroxide (10 ml.) for 12 hr. and crystallisation of the product from methanol gave the *tetrahydroxy-dienone* (XIX; R = H) as needles (25 mg.), m. p. 297—299°, $[\alpha]_D$ +45° (*c* 0·36), $\lambda_{max.}$ 285 mμ (ε 12,000) (Found: C, 73·75; H, 9·3. $C_{30}H_{46}O_5$ requires C, 74·05; H, 9·55%). On acetylation with acetic anhydride and sodium acetate under reflux it re-formed the dienone tetra-acetate (XIX; R = Ac) (m. p., mixed m. p., and infrared spectrum).

Derivatives of Cyclamiretin Diacetate.—The diacetate (500 mg.) in "AnalaR" acetone (50 ml.) was agitated with Kiliani chromic acid mixture (3 ml.) at room temperature for 5 min. After dilution with water the excess of oxidant was destroyed with sulphur dioxide. The product was separated into neutral and acidic fractions. Crystallisation of the neutral fraction from methanol furnished the *ketone diacetate* (VI; X = H_2, R = Ac) as needles (250 mg.), m. p. 175—177° (Found: C, 73·45; H, 9·1. $C_{34}H_{50}O_6$ requires C, 73·6; H, 9·1%). Crystallisation of the acidic fraction in the same way gave the *ketone-acid* (XVII; R = Ac, R′ = OH) (80 mg.), m. p. 274—277°, $[\alpha]_D$ +14° (*c* 0·96), $\nu_{max.}$ 3150 (CO_2H), 1745 (OAc), 1720 (CO_2H), and 1700 (ketone) cm.$^{-1}$ (Found: C, 71·4; H, 8·6. $C_{34}H_{50}O_7$ requires C, 71·55; H, 8·85%). This acid (50 mg.) in chloroform (20 ml.) was saturated with dry hydrogen chloride at room temperature and left overnight. Removal of the solvent gave back the acid unchanged.

The ketone-acid (XVII; R = Ac, R′ = OH), treated with ethereal diazomethane in the usual way, afforded the corresponding *methyl ester* (XVII; R = Ac, R′ = OMe). Recrystallised from chloroform–methanol this had m. p. 212—214°, $[\alpha]_D$ +9°, $\nu_{max.}$ 1750 (OAc) and 1720 (CO_2Me and ketone) cm.$^{-1}$ (Found: C, 71·5; H, 9·05. $C_{35}H_{52}O_7$ requires C, 71·9; H, 8·95%).

The keto-acid (XVII; R = Ac, R′ = OH) (50 mg.) in 1% ethanolic potassium hydroxide (10 ml.) was refluxed for 1 hr. Crystallisation from methanol gave the *nor-keto-acid* (XV; R = H, R′ = CO_2H) (35 mg.), m. p. 280—282°, $[\alpha]_D$ −45° (*c* 0·33), $\nu_{max.}$ 3450 (OH), 1728 (CO_2H), and 1700 (ketone) cm.$^{-1}$ (Found: C, 76·05; H, 9·7. $C_{29}H_{44}O_4$ requires C, 76·25; H, 9·7%). Oxidation with Kiliani chromic acid mixture as in the examples already cited gave the diketo-acid (XVI; R = CO_2H) described in detail below.

The Diketo-aldehyde (XVI; R = CHO) *and its Derivatives.*—The ketone diacetate (VI; X = H_2, R = Ac) (see above) (200 mg.) in 2% ethanolic potassium hydroxide (10 ml.) was refluxed for 1 hr. Crystallisation of the product from methanol afforded the *nor-ketone* (XV; R = H, R′ = CHO) (140 mg.), m. p. 205—207°, $[\alpha]_D$ −88° (*c* 0·63), $\nu_{max.}$ 3650 (OH) and 1700 (ketone) cm.$^{-1}$ (Found: C, 78·6; H, 10·0. $C_{29}H_{44}O_3$ requires C, 79·05; H, 10·05%). This compound (100 mg.) in "AnalaR" acetone (10 ml.) was agitated with Kiliani chromic acid mixture (0·5 ml.) for 1 min. After working up as above, crystallisation from chloroform–methanol gave the *diketo-aldehyde* (XVI; R = CHO) as needles (75 mg.), m. p. 234—236°, $[\alpha]_D$ −75° (*c* 0·54), $\nu_{max.}$ 1700 (ketones and aldehyde) (Found: C, 79·25; H, 9·35. $C_{29}H_{42}O_3$

requires C, 78·9; H, 9·55%). This diketo-aldehyde was recovered unchanged after 8 hours' refluxing in 10% ethanolic potassium hydroxide under nitrogen.

The diketo-aldehyde (XVI; R = CHO) (200 mg.) in " AnalaR " acetone (10 ml.) was agitated with Kiliani chromic acid mixture (0·5 ml.) at room temperature for 5 min. After dilution with water and destruction of the excess of oxidant with sulphur dioxide, the product was separated into acidic and neutral (negligible) fractions. Crystallisation of the former from methanol gave the desired *diketo-carboxylic acid* (XVI; R = CO_2H) as needles (150 mg.), m. p. 250—252°, $[\alpha]_D$ −69° (*c* 0·86), $\nu_{max.}$ 3350 (CO_2H), 1728 (CO_2H), and 1700 (ketones) cm.$^{-1}$ (Found: C, 76·2; H, 9·1. $C_{29}H_{42}O_4$ requires C, 76·6; H, 9·3%). The acid was recovered unchanged after 1 hour's refluxing in benzene under nitrogen. Treatment with ethereal diazomethane in the usual way gave the *methyl ester* (XVI; R = CO_2Me), needles (43 mg.) (from methanol), m. p. 220—221°, $[\alpha]_D$ −65° (*c* 0·45), $\nu_{max.}$ 1700 (CO_2Me and ketones) cm.$^{-1}$ (Found: C, 76·7; H, 9·5. $C_{30}H_{44}O_4$ requires C, 76·9; H, 9·45%).

Further Derivatives of the Keto-acid (XVII; R = Ac, R′ = OH).—The keto-acid (500 mg.) in dry benzene (20 ml.) containing oxalyl chloride (1 ml.) was kept at room temperature for 12 hr. Removal of the solvent and crystallisation from light petroleum–benzene gave the *acid chloride* (XVII; R = Ac, R′ = Cl) (390 mg.), m. p. 186—187°, $\nu_{max.}$ 1800 (acid chloride), 1748 (OAc), and 1700 (ketone) cm.$^{-1}$ (Found: C, 68·9; H, 8·2; Cl, 5·8. $C_{34}H_{49}ClO_6$ requires C, 69·3; H, 8·3; Cl, 6·05%). This acid chloride (300 mg.) in dry acetone (150 ml.) was treated at −35° with potassium ethyl xanthate (150 mg.) in the same solvent (100 ml.) added in 30 min. with stirring under nitrogen. After a further hr. at −35° the acetone was removed at < room temperature *in vacuo*. Crystallisation from light petroleum–benzene gave (XVII; R = Ac, R′ = EtO·CS·S) (280 mg.), m. p. 207—210° (decomp.), $[\alpha]_D$ +13° (*c* 1·26), $\lambda_{max.}$ 387 mμ (ε 60) (Found: C, 65·5; H, 8·35; S, 9·15. $C_{37}H_{54}O_7S_2$ requires C, 65·85; H, 8·05; S, 9·5%).

The *xanthate* (200 mg.) in dry benzene (25 ml.) was irradiated under reflux in nitrogen with a 200-w tungsten lamp [18] until the yellow colour had essentially disappeared (2 hr.). The benzene was removed *in vacuo* and the product was refluxed with 1% ethanolic potassium hydroxide (10 ml.) for 1 hr. under nitrogen. Crystallisation from methanol gave the *thiol* (XV; R = H, R′ = SH) as needles (90 mg.), m. p. 185—186°, $[\alpha]_D$ −52° (*c* 0·42) (Found: C, 75·5; H, 9·8; S, 6·85. $C_{28}H_{44}O_2S$ requires C, 75·65; H, 9·95; S, 7·2%).

Further Derivatives of Cyclamiretin Diacetate.—Cyclamiretin diacetate (1·0 g.) in glacial acetic acid (50 ml.) was treated overnight at room temperature with chromium trioxide (600 mg.) in the same solvent (25 ml.). After dilution with water and destruction of excess of oxidant with sulphur dioxide the acidic product was crystallised from chloroform–methanol, to furnish the *diketo-acid* (XXI; R = OH) as needles (550 mg.), m. p. 278—280°, $[\alpha]_D$ +29° (*c* 0·63), $\lambda_{max.}$ 245 mμ (ε 12,000), $\nu_{max.}$ 3180 (CO_2H), 1750 (OAc), 1720 (ketone), and 1680 (cyclohexenone) cm.$^{-1}$ (Found: C, 69·6; H, 8·4. $C_{34}H_{48}O_8$ requires C, 69·85; H, 8·25%). The corresponding *methyl ester* (XXI; R = OMe), prepared with ethereal diazomethane, crystallised from methanol as flat needles, m. p. 212—214°, $[\alpha]_D$ +25° (*c* 0·33), $\nu_{max.}$ 1750 (OAc), 1720 (CO_2Me and ketone) and 1670 (cyclohexenone) cm.$^{-1}$ (Found: C, 69·9; H, 8·4. $C_{35}H_{50}O_8$ requires C, 70·2; H, 8·4%).

The diketo-acid (XXI; R = OH) (see above) (500 mg.) in dry benzene (20 ml.) was treated with oxalyl chloride (1·0 ml.) at room temperature for 12 hr. Removal of the solvent and excess of oxalyl chloride *in vacuo* gave the desired acid chloride (XXI; R = Cl) which had $\nu_{max.}$ 1800 (acid chloride), 1750 (OAc), 1720 (ketone), and 1670 (cyclohexenone) cm.$^{-1}$. When this acid chloride was treated with potassium ethyl xanthate as in the example given above it gave the corresponding *xanthate* (XXI; R = EtO·CS·S). Crystallised from light petroleum (b. p. 60—80°)–benzene, this had m. p. 215—216°, $[\alpha]_D$ +24° (*c* 0·96), $\lambda_{max.}$ 244 mμ (ε 11,000) (Found: C, 64·25; H, 7·25; S, 8·85. $C_{37}H_{52}O_8S_2$ requires C, 64·5; H, 7·6; S, 9·3%).

This acid chloride (XXI; R = Cl) (200 mg.) was heated at 200—230° for 30 min. in a slow stream of nitrogen (evolution of 1 mol. of hydrogen chloride). The product in 2% ethanolic potassium hydroxide (10 ml.) was refluxed for 30 min., to give the *hydroxy-diketone* (XXIII). Recrystallised from methanol (70 mg.) this had m. p. 210—211°, $[\alpha]_D$ −44° (*c* 0·63), $\lambda_{max.}$ 264 and 288 mμ (ε 8500 and 6500, respectively), $\nu_{max.}$ 3400 (OH), 1700 (ketone), 1640 (cyclohexadienone), and 1600 (exalted *cisoid* C=C) cm.$^{-1}$ (Found: C, 78·9; H, 9·25. $C_{28}H_{40}O_3$ requires C, 79·2; H, 9·5%).

When the diketo-acid (XXI; R = OH) (50 mg.) in methanol (10 ml.) was treated overnight with potassium borohydride (50 mg.) at room temperature it gave the *lactone* (XXII).

Recrystallised from methanol (30 mg.) this had m. p. 292—293°, $[\alpha]_D$ +22° (*c* 0·73), with no high-intensity ultraviolet absorption (Found: C, 71·2; H, 8·75. $C_{34}H_{50}O_7$ requires C, 71·55; H, 8·85%).

Action of Methanolic Hydrogen Chloride on Cyclamiretin.—The sapogenin (100 mg.) in methanol (50 ml.) was saturated at room temperature with dry hydrogen chloride and left overnight. Removal of the solvent *in vacuo* and crystallisation from moist ether gave the *hemi-acetal* (XXVI) (60 mg.), m. p. 302—304°, $[\alpha]_D$ +53° (*c* 0·53), $\nu_{max.}$ 3480 (OH) cm.$^{-1}$, τ ($CDCl_3$) 6·66 (O–Me), 5·78 (–O–C*H*·OMe), 8·79 (allyl-attached >CMe), 9·03 (>CMe), 9·09 (2>CMe), 9·14 (>CMe) and 9·24 (>CMe) (Found: C, 76·25; H, 10·3. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·35%). This compound (30 mg.) in tetrahydrofuran (10 ml.) and 5% aqueous hydrochloric acid (3 ml.) was stirred overnight at room temperature. Crystallisation of the product from ethanol gave back cyclamiretin (20 mg.), identified by m. p., mixed m. p., and infrared spectrum.

IMPERIAL COLLEGE, LONDON, S.W.7.
DEPARTMENT OF CHEMISTRY, CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY,
LONDON, S.W.3.
[*Received, June 4th,* 1962.]