279. *Triterpenoids. Part XLVIII.* Olean-13(18)-ene: Isomerisation of Olean-12-ene and Related Hydrocarbons with Mineral Acid.*

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Pure olean-13(18)-ene (I) has been obtained for the first time by methods avoiding the use of mineral acid. Treatment of olean-13(18)-ene (I), olean-12-ene (II), olean-18-ene (germanicene) (III), and 18α-olean-12-ene (IV) with mineral acid gives the same equilibrium mixture of hydrocarbons, crystallisation of which yields a mixed crystal of olean-13(18)-ene (I) and 18α-olean-12-ene (IV). This mixed crystal is identical with the hydrocarbon " β-amyrene-III " obtained by Winterstein and Stein by Clemmensen reduction of olean-12-en-3-one.

TAKEDA[1] showed that Clemmensen reduction of taraxerone (skimmione; cf. Koller, Hiestand, Dietrich, and Jeger[2]) gives an unsaturated hydrocarbon, $C_{30}H_{50}$, m. p. 189—190°, $[\alpha]_D$ —20·5°, which is identical with " β-amyrene-III," previously obtained by Winterstein and Stein[3] by similar reduction of olean-12-en-3-one. According to Takeda, this hydrocarbon is olean-13(18)-ene (I), a view confirmed by Jones and his collaborators[4,5] who found, however, that the hydrocarbon prepared by the method of Winterstein and Stein and by the action of hydrochloric–acetic acid on olean-12-ene (II) is appreciably more lævorotatory ($[\alpha]_D$ —33°) than that obtained by Winterstein and Stein; the difference was commented upon by Davy *et al.*[5] who believed that their hydrocarbon was purer. During a study of the triterpenoid ketone friedelin, Brownlie, Spring, Stevenson, and Strachan[6] discovered that treatment of the derived hydrocarbon friedelene with hydrochloric–acetic acid gives an isomer which is indistinguishable from the hydrocarbon obtained by the same treatment of olean-12-ene (II). The specific rotation of this isomer, $[\alpha]_D$ —20°, is in good agreement with the values observed by Takeda[1] for olean-13(18)-ene and by Winterstein and Stein[3] for β-amyrene-III.

The melting points and specific rotations given in the literature for preparations of olean-13(18)-ene (I), in which the reaction mixture had been exposed for a long time to strong mineral acid, are annexed.

Method	M. p.	$[\alpha]_D$ ($CHCl_3$)	Ref.
Clemmensen redn. of olean-12-en-3-one	187—189·5°	—22°	3
Clemmensen redn. of olean-12-en-3-one	191·5—192·5	—32·5	4
Clemmensen redn. of taraxerone	189—190	—20·5	1
Clemmensen redn. of taraxerone	184 (183—184)	—21(—24)	2
Olean-12-ene + HCl–AcOH	190—191	—33	5
Olean-12-ene + HCl–AcOH	186—187	—20	6
" Acid-catalysed " isomerisation of olean-12-ene	186—187	—13·9	*a*
Friedelene + HCl–AcOH	186—187	—20	6
Friedelanol + PhOH + HCl	186—187	—12·5	*a*
Friedelene + $ZnCl_2$–AcOH	183—184	—18	*b*

[a] Corey and Ursprung, *J. Amer. Chem. Soc.*, 1955, **77**, 3668. [b] Dutler, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1955, **38**, 1268.

" β-Amyrene-IV," obtained[3] as an intermediate in the Clemmensen reduction of olean-12-en-3-one to " β-amyrene-III," was shown by Davy *et al.*[5] to be a mixture of

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* Part XLVII, *J.*, 1956, 456.

[1] Takeda, *J. Pharm. Soc. Japan*, 1943, **63**, 197.
[2] Koller, Hiestand, Dietrich, and Jeger, *Helv. Chim. Acta*, 1950, **33**, 1050.
[3] Winterstein and Stein, *Annalen*, 1933, **502**, 223.
[4] Ames, Halsall, and Jones, *J.*, 1951, 450.
[5] Davy, Halsall, and Jones, *ibid.*, p. 458.
[6] Brownlie, Spring, Stevenson, and Strachan, *Chem. and Ind.*, 1955, 686.

olean-12-ene (II) and olean-13(18)-ene (I). They also showed that the formation of "β-amyrene-IV" is due to the fact that the reaction was not carried to completion. According to Beaton, Spring, Stevenson, and Stewart,[7] a hydrocarbon obtained by a brief Clemmensen reduction of taraxerone by Koller *et al.*[2] is a similar mixture.

The relatively low lævorotations of the hydrocarbons obtained by Corey and Ursprung[8] are not difficult to explain, since the isolation of a hydrocarbon of constant specific rotation from the mixture obtained by acid-isomerisation of olean-12-ene (or from friedelene) requires many crystallisations of the product during which the rotation increases slowly from *ca.* —10° to *ca.* —20°. The high lævorotations observed by Ames *et al.*[4] and by Davy *et al.*[5] are, however, anomalous.

We find that treatment of olean-12-ene with hydrochloric–acetic acid gives a product having $[\alpha]_D$ —10° ± 2°, repeated crystallisation of which yields a hydrocarbon having $[\alpha]_D$ —20° ± 2°. The specific rotation and melting point of this hydrocarbon are not changed by repeated crystallisation or by careful chromatography. The difficulty attending the isolation of the hydrocarbon of $[\alpha]_D$ —20° suggested that the initial reaction product ($[\alpha]_D$ *ca.* —10°) is an equilibrium mixture of isomers. This view was confirmed by the observation that treatment of the hydrocarbon of $[\alpha]_D$ —20°, with hydrochloric–acetic acid regenerates the mixture of $[\alpha]_D$ —10°. If the hydrocarbon, $[\alpha]_D$ —20°. is pure olean-13(18)-ene, this compound is not stable to mineral acid, a decision which led us to prepare olean-13(18)-ene by methods in which mineral acid is not used. Oleana-11 : 13(18)-dien-3β-ol[9] was hydrogenated over platinum prepared from platinum oxide from which traces of water-soluble platinum salts were removed by careful washing. The product, olean-13(18)-en-3β-ol,[10,4] was oxidised by the chromic acid–pyridine complex to olean-13(18)-en-3-one, the physical constants of which are in fair agreement with those of specimens obtained by other methods,[4] with the differences that our preparation does not show a preliminary softening before the melting point and its ultraviolet absorption spectrum does not include low-intensity bands at 2430, 2510, and 2620 Å. Reduction of olean-13(18)-en-3-one by the Wolff–Kishner method gives a hydrocarbon, m. p. 187—188°, $[\alpha]_D$ —48° ± 2°. In contrast with the behaviour of the product obtained by methods in which mineral acid is used, this hydrocarbon is easily purified, and attains a constant specific rotation after one crystallisation. We believe that it is pure olean-13(18)-ene and support for this opinion was obtained as follows.

Oleana-11 : 13(18)-dien-3β-ol was oxidised to oleana-11 : 13(18)-dien-3-one,[11] Wolff–Kishner reduction of which gave oleana-11 : 13(18)-diene, whose constants agree with those given by Ruzicka *et al.*[9] for the hydrocarbon obtained by oxidation of olean-12-ene with selenium dioxide. Hydrogenation of oleana-11 : 13(18)-diene over platinum (from purified platinum oxide) at room temperature gives olean-13(18)-ene, $[\alpha]_D$ —48°, identical with the specimen obtained as described above. Jeger and his collaborators[2] reduced oleana-11 : 13(18)-diene at 70—80° over platinum and obtained a hydrocarbon, $[\alpha]_D$ —27°. The low lævorotation of their product may have been due to the presence of traces of mineral acid in the reaction solution.

Olean-13(18)-ene, $[\alpha]_D$ —48°, is unstable to mineral acid. Treatment of the hydrocarbon with hydrochloric–acetic acid yields a mixture, $[\alpha]_D$ —12°, from which, after repeated crystallisation, a hydrocarbon, m. p. 187—188°, of constant specific rotation, $[\alpha]_D$ —20°, was isolated, and this is identical with the hydrocarbon obtained by the same treatment of olean-12-ene. With the object of identifying the hydrocarbon, $[\alpha]_D$ —20°, olean-18-ene (germanicene) (III) and 18α-olean-12-ene (IV) were prepared, the former by the recorded method[12] and the latter by oxidation of 18α-olean-12-en-3β-ol[13] with chromic acid–pyridine, followed by Wolff–Kishner reduction of the product, 18α-olean-12-en-3-one. Treatment

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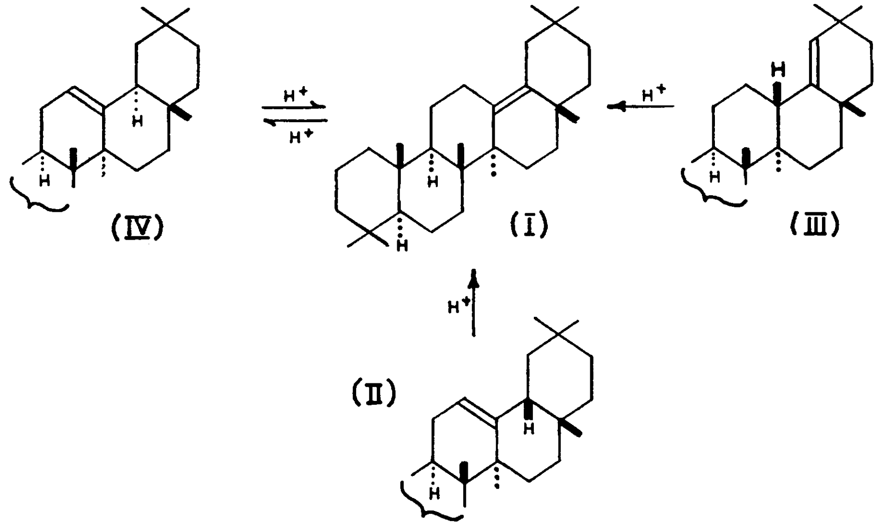
[7] Beaton, Spring, Stevenson, and Stewart, *J.*, 1955, 2131.
[8] Ref. *a* in Table.
[9] Ruzicka, Müller, and Schellenberg, *Helv. Chim. Acta*, 1939, **22**, 767.
[10] Ruzicka and Jeger, *ibid.*, 1941, **24**, 1236.
[11] Shaw, Spring, and Stevenson, *J.*, 1956, 465.
[12] David, *Bull. Soc. chim. France*, 1949, **16**, 427; Barton and Brooks, *J.*, 1951, 257; Halsall, Jones, and Meakins, *J.*, 1952, 2862.
[13] Allan and Spring, *J.*, 1955, 2125.

of each of the hydrocarbons (III) and (IV) with hydrochloric–acetic acid gives a mixture, repeated crystallisation of which yields the hydrocarbon, $[\alpha]_D$ —20°, identical with the product obtained by similar treatment of either olean-12-ene or olean-13(18)-ene.

18α-Olean-12-ene, $[\alpha]_D$ +37°, has m. p. 186—188° and olean-13(18)-ene, $[\alpha]_D$ —48°, has m. p. 187—188° and random mixtures of the two hydrocarbons do not show greatly depressed melting points. This suggested that the hydrocarbon, $[\alpha]_D$ —20°, m. p. 187°, is an inseparable (or difficulty separable) mixed crystal of olean-13(18)-ene (2 parts) and 18α-olean-12-ene (1 part). This view was confirmed by the preparation of a mixture of these two hydrocarbons in these proportions, a single crystallisation of which gave a hydrocarbon, m. p. 186—187°, $[\alpha]_D$ —20°, identical with that isolated from the mixtures obtained by treatment of olean-12-ene, olean-13(18)-ene, olean-18-ene, or 18α-olean-12-ene with hydrochloric–acetic acid.

These experiments show that the equilibrium mixture, $[\alpha]_D$ —10°, obtained from each of the hydrocarbons (I)—(IV) by treatment with mineral acid, is the same and contains olean-13(18)-ene and 18α-olean-12-ene. We believe that these are the only components, because a mixture of the two hydrocarbons in the ratio 4 : 3 is indistinguishable from the equilibrium mixture in its behaviour on crystallisation—the mixed crystal, $[\alpha]_D$ —20°, is obtained. Further, a mixture of equal parts of 18α-olean-12-ene, olean-13(18)-ene, and germanicene differs from the equilibrium mixture since it forms crystals, the specific rotation of which ($[\alpha]_D$ ±0°) does not change after five crystallisations. Although the mixed crystal of olean-13(18)-ene and 18α-olean-12-ene, $[\alpha]_D$ —20°, could not be isolated from the three-component mixture by crystallisation, treatment of the latter with hydrochloric–acetic acid gives the equilibrium mixture, $[\alpha]_D$ —10°, from which the mixed crystal, $[\alpha]_D$ —20°, was obtained by crystallisation. For these reasons, the behaviour of the hydrocarbons (I)—(IV) with mineral acid is represented as shown in the annexed scheme.



The mineral acid-isomerisation of simple derivatives of the hydrocarbons (I), (II), (III), and (IV) probably follows the same pattern as that established for the parents. The nature of the product obtained by crystallisation of the equilibrium mixture will depend upon the relative solubilities of the two components and upon any tendency to form insoluble mixed crystals. We have repeated the acid-isomerisation of olean-12-en-3-one (cf. Ames *et al.*[4]) and after a tedious fractional crystallisation isolated olean-13(18)-en-3-one. This specimen has a slightly lower melting point than that obtained by oxidation of olean-13(18)-en-3β-ol; like the latter preparation it gives pure olean-13(18)-ene, $[\alpha]_D$ —48° ± 2°, when reduced by the Wolff–Kishner method.

EXPERIMENTAL

Rotations were measured in $CHCl_3$ and ultraviolet absorption spectra in EtOH solutions. Grade II alumina and light petroleum, b. p. 60—80°, were used for chromatography.

Olean-13(18)-*en*-3β-*ol*.—A solution of oleana-11 : 13(18)-dien-3β-ol[9] (m. p. 226—228°, $[\alpha]_D$ −71°; 1·0 g.) in *cyclo*hexane (50 c.c.) and acetic acid (180 c.c.) was shaken for 16 hr. with hydrogen and platinum. The catalyst was prepared from platinum oxide (250 mg.) from which soluble salts were removed by careful washing with distilled water. The product was isolated in the usual way and crystallised from aqueous methanol, to yield olean-13(18)-en-3β-ol as needles, m. p. 212—213°, $[\alpha]_D$ −52° (*c*, 1·2). Lit. :[10, 4] m. p. 213—213·5°, $[\alpha]_D$ −52°, and m. p. 212—212·5°, $[\alpha]_D$ −50·5°.

Olean-13(18)-*en*-3-*one*.—A mixture of olean-13(18)-en-3β-ol (800 mg.) in pyridine (20 c.c.) and the complex obtained by adding chromium trioxide (800 mg.) to pyridine (30 c.c.) was shaken occasionally for 16 hr., then diluted with ether, and the product was isolated in the usual way but avoiding the use of mineral acid. Purification by chromatography on alumina, followed by crystallisation from acetone–methanol gave olean-13(18)-en-3-one, as blades, m. p. 200—201°, $[\alpha]_D$ −10° (*c*, 2·3).

Oleana-11 : 13(18)-*diene*.—A mixture of oleana-11 : 13(18)-dien-3-one[11] (m. p. 236—238°, $[\alpha]_D$ −48·5°; 400 mg.), sodium methoxide (from 1·0 g. of sodium) in methanol (40 c.c.), and hydrazine hydrate (100%; 5 c.c.) was kept at 200° (autoclave) for 16 hr. The product was worked up in the usual way and crystallised from chloroform–methanol, to yield oleana-11 : 13-(18)-diene as blades, m. p. 217—218°, $[\alpha]_D$ −66° (*c*, 1·3), $\lambda_{max.}$ 2420, 2500, and 2600 Å (ε 27,000, 30,000, and 20,000). A specimen prepared by oxidation of olean-12-ene with selenium dioxide[9] separated from chloroform–methanol as blades, m. p. 218—219°, $[\alpha]_D$ −65° (*c*, 0·9). Lit. :[9, 1] m. p. 218—219°, $[\alpha]_D$ −73°; m. p. 222—224°, $[\alpha]_D$ −67°.

Olean-13(18)-*ene*.—(*a*) A solution of oleana-11 : 13(18)-diene (240 mg.) in *cyclo*hexane (50 c.c.) and acetic acid (150 c.c.) was shaken for 17 hr. with hydrogen and platinum (from 150 mg. of oxide). Working up in the usual way and three crystallisations of the product (m. p. 184—185°, $[\alpha]_D$ −48·5°) from chloroform–methanol yielded *olean*-13(18)-*ene* as blades, m. p. 187—188°, $[\alpha]_D$ −48°, −48·5° (*c*, 1·4, 1·2), ε_{2100} 7000 (Found : C, 88·0; H, 12·3. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%). (*b*) Olean-13(18)-en-3-one was reduced by the Wolff–Kishner method under the conditions described above. The product was worked up in the usual way, but avoiding the use of mineral acid, and crystallised from chloroform–methanol to yield olean-13(18)-ene as blades, m. p. 186—187°, $[\alpha]_D$ −48° (*c*, 1·1). A different experiment gave olean-13(18)-ene, m. p. 184—185°, $[\alpha]_D$ −50° (*c*, 2·4).

18α-*Olean*-12-*en*-3-*one*.—A solution of 18α-olean-12-en-3β-yl acetate (Budziarek *et al.*[14]) in ether was refluxed with lithium aluminium hydride, to give 18α-olean-12-en-3β-ol as fibrous needles (from chloroform–methanol), m. p. 209—210°, $[\alpha]_D$ +45° (*c*, 2·2). Allan and Spring[13] give m. p. 213—214°, $[\alpha]_D$ +50°, for this compound. A mixture of the alcohol (800 mg.) in pyridine (8 c.c.) and the complex prepared by adding chromium trioxide (800 mg.) to pyridine (8 c.c.) was kept for 18 hr. with occasional shaking. The product was isolated in the usual way but avoiding the use of mineral acid, and crystallised from chloroform–methanol to give 18α-*olean*-12-*en*-3-*one* (660 mg.) as plates, m. p. 209—210°, $[\alpha]_D$ +80° (*c*, 2·2) (Found : C, 84·5; H, 11·6. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). It gives a yellow colour with tetranitromethane.

18α-*Olean*-12-*ene*.—Reduction of 18α-olean-12-en-3-one by the Wolff–Kishner method as described above, and crystallisation of the product from chloroform–methanol, yielded 18α-*olean*-12-*ene* as plates, m. p. 186—188°, $[\alpha]_D$ +37° (*c*, 3·5) (Found : C, 87·7; H, 12·3. $C_{30}H_{50}$ requires C, 87·7; H, 12·3%). It gives a yellow colour with tetranitromethane. Mixtures of this hydrocarbon with different proportions of olean-13(18)-ene, m. p. 187—188°, $[\alpha]_D$ −48°, melted at or above 180°.

Olean-13(18)-*ene*–18α-*Olean*-12-*ene Mixture*.—(*a*) Olean-12-ene (m. p. 159—161°, $[\alpha]_D$ +94°; 300 mg.) in hot acetic acid (150 c.c.) was treated during 15 min. with concentrated hydrochloric acid (37 c.c.), and the mixture refluxed for 18 hr. and then evaporated under reduced pressure. The dried residue {$[\alpha]_D$ −10° (*c*, 3·0)} crystallised from chloroform–methanol to give blades, m. p. 181—184°, $[\alpha]_D$ −11° (*c*, 2·3). Several recrystallisations of these from the same solvent gave the crystal mixture (yield, 55%), m. p. 186—187°, $[\alpha]_D$ −18° (*c*, 2·1), further recrystallisation of which did not change the melting point or specific rotation.

(*b*) Germanicene[12] (olean-18-ene; m. p. 173—175°, $[\alpha]_D$ +6°; 150 mg.) was treated with

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[14] Budziarek, Manson, and Spring, *J.*, **1951**, **3336**.

hydrochloric-acetic acid as described under (*a*). The total equilibrium mixture had $[\alpha]_D$ −10° (*c*, 3·0) and after three crystallisations from chloroform–methanol it gave the mixed crystal as blades (85 mg.), m. p. 186—187°, $[\alpha]_D$ −18° (*c*, 1·5), unchanged by recrystallisation.

(*c*) A solution of 18α-olean-12-ene (150 mg.) in acetic acid (120 c.c.) and concentrated hydrochloric acid (20 c.c.) was refluxed for 18 hr. After several crystallisations from chloroform–methanol, the product formed blades, m. p. 185—186°, $[\alpha]_D$ −18° (*c*, 2·3), unchanged by recrystallisation.

(*d*) The same treatment of olean-13(18)-ene, $[\alpha]_D$ −48°, gave a product which crystallised from chloroform–methanol as blades, m. p. 182—184°, $[\alpha]_D$ −12°. Three recrystallisations from the same solvent gave the mixed crystal of 18α-olean-12-ene and olean-13(18)-ene, m. p. 187—188°, $[\alpha]_D$ −19·5° (*c*, 2·3), unchanged by repeated recrystallisation.

(*e*) A mixture of olean-13(18)-ene, $[\alpha]_D$ −48° (40 mg.), and 18α-olean-12-ene (20 mg.) was crystallised from chloroform–methanol, to give blades which after recrystallisation from the same solvent had m. p. 186—187°, $[\alpha]_D$ −21° (*c*, 3·1); the m. p. and specific rotation did not change on recrystallisation.

A mixture of olean-13(18)-ene ($[\alpha]_D$ −48°; 50·4 mg.) and 18α-olean-12-ene (37·8 mg.), crystallised from chloroform–methanol, gave blades m. p. 183—186°, $[\alpha]_D$ −13°, three crystallisations of which from the same solvent gave the mixed crystal (45 mg.), m. p. 186—187°, $[\alpha]_D$ −18° (*c*, 1·5), unchanged after further crystallisation.

(*f*) A mixture of 18α-olean-12-ene (100 mg.), germanicene (100 mg.), and olean-13(18)-ene ($[\alpha]_D$ −48°, 100 mg.) was crystallised five times from chloroform–methanol during which the rotation ($[\alpha]_D$ ±1°) did not change. The mixture was reconstituted and treated with hydrochloric–acetic acid as described above. The total equilibrium mixture had $[\alpha]_D$ −10° (*c*, 2·6) and after three crystallisations from chloroform–methanol gave the mixed crystal (125 mg.) as blades, m. p. 186—187°, $[\alpha]_D$ −18° (*c*, 2·1).

The mixed crystals obtained by the methods (*a*)—(*f*) were undepressed in m. p. when mixed with each other. Treatment of the mixed crystal, $[\alpha]_D$ −19°, with hydrochloric–acetic acid, as described above, gave the equilibrium mixture which separated from chloroform–methanol as blades, m. p. 184—185°, $[\alpha]_D$ −10·4° (*c*, 1·0). Careful chromatography of the mixed crystal did not separate it into its components.

Acid Equilibration of Olean-12-*en*-3-*one* (cf. Ames *et al.*[4]). Olean-12-en-3-one (1·3 g.; m. p. 178—180°, $[\alpha]_D$ +113°) in benzene (13 c.c.) was treated with acetic acid (110 c.c.) and concentrated sulphuric acid (19·5 c.c.), and the mixture warmed to 80°, then kept for 14 days at room temperature. The separated crystalline solid {530 mg., m. p. 165—185°, $[\alpha]_D$ +2° (*c*, 1·9)} was crystallised successively from chloroform–methanol, ethanol (twice), acetone–methanol, and ethanol, to yield olean-13(18)-en-3-one as blades, m. p. 194—197° (softening at 173°), $[\alpha]_D$ −10° (*c*, 2·1). A mixture with the specimen of olean-13(18)-en-3-one, m. p. 200—201°, described above had m. p. 194—198°. The infrared spectra of the two specimens were identical; we thank Dr. G. Eglinton for making this comparison. Reduction, by the Wolff–Kishner process described above, of the specimen of olean-13(18)-en-3-one obtained by acid-isomerisation of olean-12-en-3-one, and crystallisation of the product from chloroform–methanol, gave olean-13(18)-ene as short needles, m. p. and mixed m. p. 184—185°, $[\alpha]_D$ −48° (*c*, 3·2).

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