170. *Triterpenes of the Friedelane Series. Part III.* The Course of the Friedelene–Oleanene Rearrangement.*

By J. L. COURTNEY, R. M. GASCOIGNE, and A. Z. SZUMER.

The friedelene–oleanene rearrangement is not fully concerted since an intermediate, glutin-5(10)-ene (II), can be isolated. The latter is rearranged to olean-12-ene (VI) and in this conversion no intermediates could be detected. If taraxerene (IV) were an intermediate it would be too short-lived to be detectable by ordinary means. Thermodynamic considerations, based on conformational analysis, indicate that if intermediates are involved they would be transitory and could not be isolated.

The isolation of olean-12-ene establishes the configuration of $C_{(18)}$ in friedelane. Olean-12-ene is thought to be formed by proton elimination concerted with, and anti-parallel to, the migration of the $C_{(13)}$-methyl group.

AN outstanding feature of triterpene chemistry is the number and variety of skeletal rearrangements involving 1 : 2-shifts of hydrogen atoms, methyl groups, or ring members. Such rearrangements are probably important in the biosyntheses of terpenes and steroids, and the conversion of squalene into cyclic triterpenes is thought to involve a variety of cyclisation-rearrangements (discussed in the preceding paper) which are fully concerted. Thus no intermediate is detectable in the enzymic conversion of squalene into lanosterol.[1]

The more spectacular rearrangements which have been observed *in vitro* include migration of several methyl groups and hydrogen atoms along the general plane of the triterpene molecule. The migrating groups are invariably in the axial configuration and so are perpendicularly above or below the general plane. Several such rearrangements have been observed in the oleanane and ursane series,[2] and the friedelene–oleanene rearrangement [3] is of this type. It proceeds by addition of a proton to the double bond of friedel-3-ene (I) forming a carbonium ion which undergoes a rearrangement incorporating 1 : 2-shifts of four methyl groups and two hydrogen atoms. Elimination of a proton followed by double-bond rearrangement yields finally an equilibrium mixture of olean-13(18)-ene (VIII) and 18α-olean-12-ene (IX).[4]

It would be of interest to know whether or not the movement of the several migrating groups, in such rearrangements, is fully or partially concerted. Thus in the friedelene–oleanene rearrangement the hydrocarbons (II), (III), and (IV) (and possibly also various double-bond isomers of these) might all exist as intermediates. We have followed this rearrangement polarimetrically in various conditions. In chloroform saturated with hydrogen chloride at room temperature (low proton-donating property) friedel-3-ene is converted into a double-bond isomer which will be discussed in a later

* Part II, *J.*, 1956, 2119.

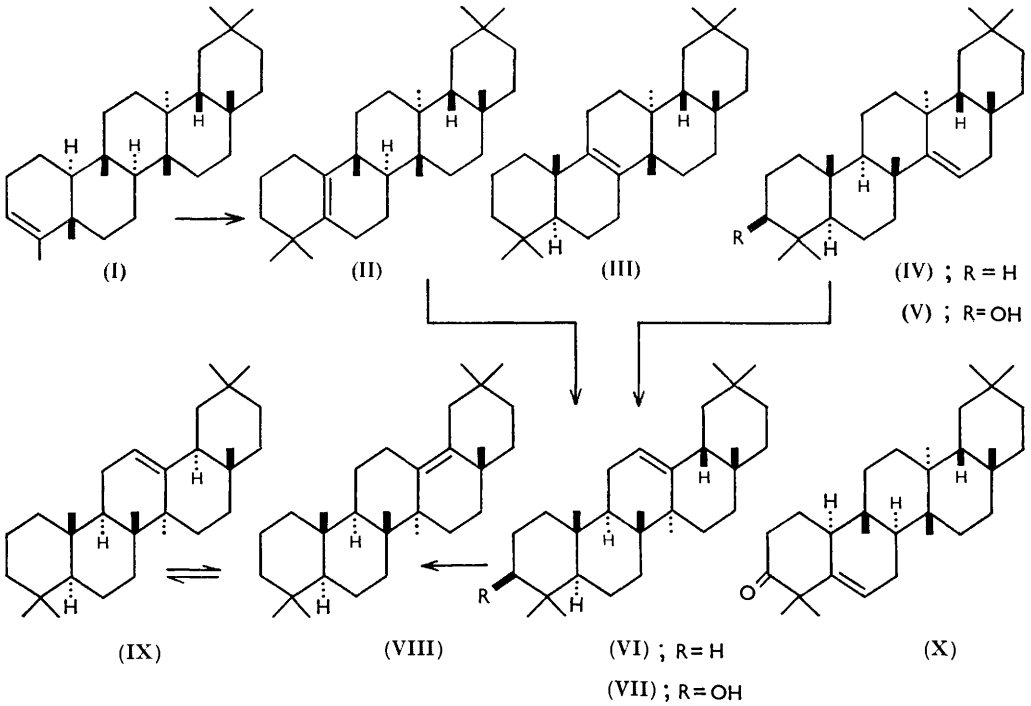
[1] Tchen and Bloch, *J. Amer. Chem. Soc.*, 1956, **78**, 1516.

[2] Spring *et al.*, *J.*, 1955, 3371, 3378; 1956, 465.

[3] (*a*) Brownlie, Spring, Stevenson, and Strachan, *Chem. and Ind.*, 1955, 686, 1156; *J.*, 1956, 2419; (*b*) Corey and Ursprung, *J. Amer. Chem. Soc.*, 1955, **77**, 3667, 3668; 1956, **78**, 5041; (*c*) Dutler, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1955, **38**, 1268.

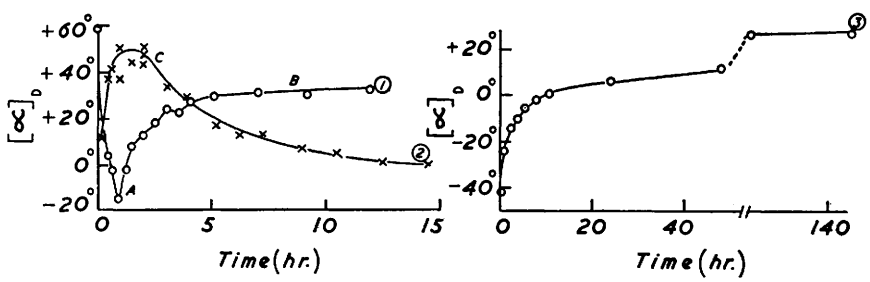
[4] Brownlie, Fayez, Spring, Stevenson, and Strachan, *J.*, 1956, 1377.

paper. However, when hydrogen chloride is passed through a solution of friedel-3-ene in boiling acetic acid more extensive changes occur. Fractional crystallisation of the mixture obtained after 1 hr. (point *A*, curve 1) yielded glutin-5(10)-ene (II), $[\alpha]_D$



$-42°$, as the major component.[5] Since this compound was converted by vigorous treatment by acid into the equilibrium mixture of olean-13(18)-ene and 18α-olean-12-ene it must be an intermediate in the friedelene–oleanene rearrangement and its

Polarimetric rate curves for the rearrangement of (1) *friedel-3-ene in boiling glacial acetic acid saturated with hydrogen chloride*; (2) *friedel-3-ene in a boiling* 1 : 20 *mixture of* 10N-*hydrochloric acid and glacial acetic acid*; (3) *glutin-5(10)-ene in chloroform saturated with hydrogen chloride at ordinary temperature.*



isolation proves that the rearrangement is not fully concerted, at least in the conditions used. The same skeletal change (I ⟶ II) occurs in the dehydrobromination of 4-bromofriedelin with silver acetate, which yields a mixture of glutin-5-en-3-one (X) and glutin-5(10)-en-3-one.[3b, 6]

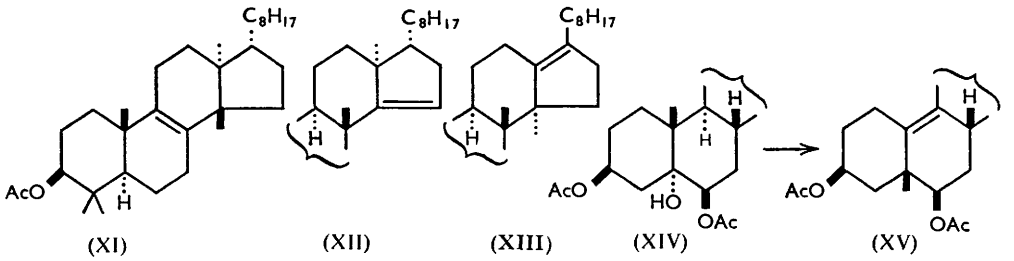
When glutin-5(10)-ene was treated with hydrogen chloride in boiling glacial acetic acid for several hours the specific rotation rose steadily to a nearly constant value and the

[5] Courtney, Gascoigne, and Szumer, *Chem. and Ind.*, 1956, 1479.
[6] Spring, Beaton, Stevenson, and Stewart, *Chem. and Ind.*, 1956, 1054.

hydrocarbon mixture obtained was identical (infrared spectra) with that from similar treatment of friedel-3-ene (point *B*, curve 1). An extensive fractional crystallisation of this mixture yielded glutin-5(10)-ene and olean-12-ene (VI), $[\alpha]_D$ +96°. That other compounds were present was indicated by comparison of the infrared spectrum of the mixture with that of a 1 : 1 mixture of glutin-5(10)-ene and olean-12-ene. Comparison of these spectra with the spectrum of the mixed crystal of olean-13(18)-ene and 18α-olean-12-ene suggested that one, or both, of these was present; they are known to be formed by isomerisation of olean-12-ene.[4] However, olean-12-ene is unaffected by hydrogen chloride in chloroform (room temp.) and when glutin-5(10)-ene was treated with this reagent it yielded, after 145 hr. (curve 3), a product whose infrared spectrum was very similar to that of the synthetic mixture of olean-12-ene and glutin-5(10)-ene; the spectrum gave no indication of any other component.

It is thus apparent that glutin-5(10)-ene (II) is converted into olean-12-ene (VI) and that no intermediates are detectable by the methods used. (The polarimetric curves contain some slight but reproducible irregularities; these may be due to transient formation of small amounts of double-bond isomers such as glutin-5-ene.) Of the two conceivable intermediates (III and IV) the former is unknown but the latter, taraxerene, occurs in Nature [7] and its constitution is known from that of its naturally-occurring 3β-hydroxy-derivative, taraxerol (V).[8] Beaton, Spring, Stevenson, and Stewart [8] observed that brief acid treatment of taraxeryl acetate yields β-amyrin acetate (as VII) and we have investigated the rate of conversion of taraxerene (IV) into olean-12-ene (VI). In the mildest conditions (chloroformic hydrogen chloride at room temp.) the rate was too fast to be measured, conversion into olean-12-ene being complete in less than 3 min. Hence, if taraxerene were an intermediate in the rearrangement of glutin-5(10)-ene to olean-12-ene it would not be detectable by ordinary methods. For conformational reasons, discussed below, the unknown hydrocarbon (III) would probably behave similarly.

The acid-catalysed conversion of olean-12-ene into the equilibrium mixture of olean-13(18)-ene (VIII) and 18α-olean-12-ene (IX) [4] may be regarded as the third and final stage of the friedelene–oleanene rearrangement. Friedel-3-ene was converted into this mixture in less than an hour by a boiling mixture of 10N-hydrochloric acid and acetic acid (1 : 5 v/v). In less acidic conditions (1 : 20 mixture) the conversion took about 14 hr. (curve 2) and olean-12-ene appeared to be formed (point *C*, curve 2) but could not be isolated pure; however, oxidation of the mixture with selenium dioxide in acetic acid and chromatography of the product gave olean-11 : 13(18)-diene in good yield. (Reproducibility was poor in this part of curve 2 presumably because of an interplay of double-bond rearrangements.)



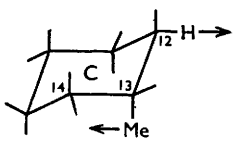
(XI) (XII) (XIII) (XIV) (XV)

The conversion of friedel-3-ene into olean-12-ene clarifies the only doubt concerning the stereochemistry of friedelane: the configuration of $C_{(18)}$ must be the same as in oleanane and the D/E ring junction must be *cis* as previously suggested.[3] Since glutin-5(10)-ene is an intermediate in the friedelene–oleanene rearrangement, no conclusions can

[7] Bruun, *Acta Chem. Scand.*, 1954, **8**, 1291.
[8] Beaton, Spring, Stevenson, and Stewart, *J.*, 1955, 2131.

be drawn from the rearrangement concerning the configurations of $C_{(5)}$ and $C_{(10)}$ in friedelane. The absolute configurations of these centres have, however, been established from other considerations.[3b, 9] The configuration of $C_{(8)}$ has been similarly established, and whether the rearrangement of glutin-5(10)-ene to olean-12-ene is concerted or not the configurations of $C_{(9)}$, $C_{(13)}$, and $C_{(14)}$ (as well as of $C_{(17)}$ and $C_{(18)}$) can be deduced from it.

Formation of olean-12-ene (VI) from glutin-5(10)-ene (II) or from taraxerene (IV) must involve elimination of a proton from $C_{(12)}$ instead of from $C_{(18)}$, even though the latter would yield the thermodynamically more stable isomer, olean-13(18)-ene (VIII). This indicates that the proton elimination is concerted with migration of the methyl group from $C_{(13)}$ to $C_{(14)}$ (see inset). The concerted process would be facilitated (and may only occur) by elimination of the proton in a direction antiparallel to the movement of the methyl group; the process would thus resemble a bimolecular elimination reaction. This geometrical requirement is satisfied by the equatorial (α) hydrogen atom at $C_{(12)}$ but not by the hydrogen atom at $C_{(18)}$ which is axial in friedelane and related structures. In the similar rearrangement of euphenyl acetate (XI) to *iso*euphenyl acetate (XIII) [10] the $C_{(17)}$-hydrogen atom may satisfy the geometrical requirement, or alternatively, a Δ^{12}-isomer, as initial product, may be isomerised to (XIII). In the rearrangement leading to Westphalen's diol (XIV ⟶ XV) [11] the direction of proton elimination appears to be the opposite of the present case; here again a $\Delta^{1(10)}$-isomer may be an intermediate or the proton elimination may not be concerted with the rearrangement.



The driving force for the friedelene–oleanene rearrangement has been attributed to the *cis*-locking of rings D and E in friedelene.[3a] This must cause marked steric instability, particularly because it results in close approach of the α-oriented axial methyl groups attached to $C_{(13)}$ and $C_{(20)}$; inspection of models shows that, in consequence, ring E must be distorted and apparently cannot be in either a pure chair or a pure boat conformation. This feature is present also in glutin-5(10)-ene, the hydrocarbon (III), and taraxerene, and is undoubtedly the main cause of the rearrangement leading to olean-12-ene since it is absent from this compound. It cannot, however, be the cause of the rearrangement of friedel-3-ene to glutin-5(10)-ene; here the conformational driving force is provided by compression energy due to the proximity (1 : 3-interaction) [12] of the axial methyl groups at $C_{(5)}$ and $C_{(9)}$ in friedel-3-ene. The magnitude of such compression energy is indicated by the estimate [13] that the diaxial conformation of *cis*-1 : 3-dimethyl*cyclo*hexane is *ca.* 5·4 kcal./mole less stable than the diequatorial conformation (1 : 3-H : Me interactions are involved as well as the Me : Me interaction).

Glutin-5(10)-ene is thus conformationally more stable than friedel-3-ene; however, the two hydrocarbons (III and IV), which are conceivable intermediates in the rearrangement of glutin-5(10)-ene to olean-12-ene, would be *less* stable than glutin-5(10)-ene. In taraxerene (IV) ring C is in a boat conformation * and in the hydrocarbon (III) rings B and C would be half-boats (cf. euphol [10a]). Also, whilst glutin-5(10)-ene contains one 1 : 3-Me : Me interaction (methyl groups at $C_{(9)}$ and $C_{(14)}$) taraxerene contains two (methyl groups at $C_{(4)}$, $C_{(10)}$, and $C_{(8)}$); the hydrocarbon (III) would contain one such interaction (methyl groups at $C_{(4)}$ and $C_{(10)}$).

* Conformationally the C/D ring junction of taraxerene resembles a *trans*-junction, hence rings B, C, and D are similar to *trans-syn-trans*-perhydrophenanthrene in which the central ring is in a boat conformation (Johnson, *Experientia*, 1951, **8**, 315; *J. Amer. Chem. Soc.*, 1953, **75**, 1498).

[9] Takahashi and Ourisson, *Bull. Soc. chim. France*, 1956, 353; Courtney, Gascoigne, and Szumer, *J.*, 1956, 2119; Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362.

[10] (*a*) Barton, McGhie, Pradhan, and Knight, *Chem. and Ind.*, 1954, 1325; *J.*, 1955, 876; (*b*) Arigoni, Viterbo, Dünnenberger, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1954, **37**, 2306.

[11] Petrov *et al.*, *J.*, 1938, 677; 1939, 998; 1952, 2246; Bladon, Henbest, and Wood, *J.*, 1952, 2737.

[12] Cf. Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44; Dauben and Pitzer, " Steric Effects in Organic Chemistry " (ed. Newman), Wiley, New York, 1956, Chap. 1.

[13] Beckett, Pitzer, and Spitzer, *J. Amer. Chem. Soc.*, 1947, **69**, 2488.

Since the hydrocarbons (III and IV) are conformationally less stable than glutin-5(10)-ene, and since they differ from it only in carbon skeleton, they are thermodynamically less stable (cf. preceding paper). Hence if they were intermediates in the rearrangement they would not be isolable (cf. the impossibility of isolating *cyclo*hexadiene in the hydrogenation of benzene [14]). The present work yields no evidence as to whether or not the glutin-5(10)-ene ⟶ olean-12-ene rearrangement is concerted, but indicates that positive evidence, either way, would be difficult to obtain.

The rearrangement of euphenyl acetate (XI) to *iso*euphenyl acetate (XIII) [10] is similar. Here the compound (XII) is conceivably an intermediate. It is probably identical with *apo*euphenyl acetate, prepared indirectly from butyrospermol; [15] if so, it would not be an isolable intermediate since *apo*euphenyl acetate is rearranged to *iso*euphenyl acetate by acid much more rapidly than is euphenyl acetate.[15]

The stability sequence, olean-12-ene > glutin-5(10)-ene > taraxerene, would be paralleled in β-amyrin, glutinol, and taraxerol. However, although friedel-3-ene is less stable than olean-12-ene, probably by several kcal./mole because of the steric congestion in the ring E area, nevertheless friedelin is more stable (thermochemically and probably thermodynamically) than β-amyrin. Olean-12-ene and friedel-3-ene contain the same type (and number) of bonds but β-amyrin and friedelin differ in that the former contains the bonds C–O, O–H, and C=C in place of C=O, C–H, and C–C in the latter. In terms of bond energies [16] this feature stabilises friedelin by 15 kcal./mole, which would be greater than the energy difference due to the steric factor.

Experimental

Analyses are by Dr. E. Challen and Mr. D. Weeden, and infrared spectra by Mr. I. Reece.

Specific rotations were measured in chloroform and, unless otherwise stated, in a 1 dm. tube. Chloroform used for the isomerisation experiments contained 2·0% of alcohol and the acetic acid had f. p. 14·8°. In the polarimetric runs with acetic acid as solvent each point was determined by isolating the solute (by dilution with water and extraction with chloroform) and measuring its specific rotation in chloroform solution.

Friedel-3-ene.—A solution of friedelin (20 g.) in hot benzene (400 ml.) was added to a suspension of lithium aluminium hydride (20 g.) in ether (1 l.) and the mixture was refluxed for 8 hr. Excess of lithium aluminium hydride was destroyed with ethyl acetate, and the crude *epi*friedelanol (19 g.) dissolved in pyridine (1·5 l.); phosphorus oxychloride (150 ml.) was then added slowly. The solution was left overnight, then boiled for 5 min., cooled, and poured into ice-water. The product was dissolved in benzene, and the solution filtered through alumina (500 g.), yielding friedel-3-ene (14 g.) as prisms (from alcohol–benzene), m. p. 253—256°, $[\alpha]_D$ +59° (*c* 0·5; 2 dm. tube). Lit.: [3a] m. p. 250—258°, 261—264° (vac.), $[\alpha]_D$ +53°.

Glutin-5(10)-ene.—When a stream of hydrogen chloride was passed through a suspension of finely ground friedel-3-ene (3 g.) in boiling acetic acid (2 l.) the friedel-3-ene soon dissolved. After 1 hr. the solution was concentrated to *ca.* 250 ml. and the product was repeatedly recrystallised from alcohol–benzene, yielding glutin-5(10)-ene as laths, m. p. 226—227°, $[\alpha]_D$ −42° (*c* 0·9)(Found: C, 87·7; H, 12·1. Calc. for $C_{30}H_{50}$: C, 87·7; H, 12·3%). Chapon [17] records m. p. 226°, $[\alpha]_D$ −38°, for a hydrocarbon which must have been glutin-5(10)-ene (cf. ref. 5).

Glutin-5(10)-ene was also obtained, somewhat impure (m. p. 222—225°, $[\alpha]_D$ −32°), by fractional crystallisation of the least soluble fraction from the following experiment.

Olean-12-ene.—Hydrogen chloride was passed through a solution of friedel-3-ene (3 g.) in boiling acetic acid (2 l.) for 7 hr. The solution was then concentrated (first to *ca.* 500 ml.) so as to give three crops of crystals. The third crop, which was initially gummy, after one recrystallisation from acetic acid had $[\alpha]_D$ +70° and on repeated recrystallisation yielded olean-12-ene, m. p. 160—161°, $[\alpha]_D$ +96° (*c*, 1·0), identical (infrared spectra) with an authentic

[14] Janz, *J. Chem. Phys.*, 1954, **22**, 751.
[15] Lawrie, Hamilton, Spring, and Watson, *J.*, 1956, 3272.
[16] Wheland, "Resonance in Organic Chemistry," Wiley, New York, 1955, p. 88, cf. p. **115** *et seq.*
[17] Chapon, *Bull. Soc. chim. France*, 1955, 1076, 1630.

specimen. It was characterised by oxidation with selenium dioxide in acetic acid to olean-11 : 13(18)-diene, m. p. 215—217°, $[\alpha]_D$ −66° (*c*, 0·7), $\lambda_{max.}$ 2420, 2510, 2600 Å (ε 26,400, 30,600, and 19,800), identical (infrared spectra) with an authentic specimen.

Olean-12-ene was also obtained, slightly impure (m. p. 157—159°, $[\alpha]_D$ +91°), by fractional crystallisation of the material from the acetic acid mother-liquors from the above-described preparation of glutin-5(10)-ene.

Taraxer-14-ene.—Taraxerol (isolated from *Litsea dealbata* [18]) was oxidised with chromic acid according to Koller *et al.*,[19] yielding taraxerone, m. p. 241—244°, $[\alpha]_D$ +10° (*c* 2·0). Wolff–Kishner reduction of taraxerone (190 mg.) with anhydrous hydrazine at 200° for 16 hr. and filtration of a solution of the product in hexane through alumina yielded taraxer-14-ene (130 mg.) which crystallised from methanol–chloroform in laths, m. p. 242—244°, $[\alpha]_D$ +3° (*c* 1·0). Lit.: [20] m. p. 238—243°, $[\alpha]_D$ +3°, and m. p. 240—241°, $[\alpha]_D$ + 3°.

When hydrogen chloride was passed through a solution of taraxer-14-ene (48 mg.) in chloroform (10 ml.) the specific rotation rose to +98° in less than 3 min. and remained constant thereat. The product obtained by evaporation of the solvent had infrared absorption identical with that of olean-12-ene and after one recrystallisation from chloroform–methanol had m. p. 161—162°.

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ORGANIC CHEMISTRY DEPARTMENT,
N.S.W. UNIVERSITY OF TECHNOLOGY, SYDNEY. [*Received, May 13th,* 1957.]

[18] Dunstan, Hughes, and Smithson, *Austral. J. Chem.*, 1953, **6**, 321.
[19] Koller, Hiestand, Dietrich, and Jeger, *Helv. Chim. Acta*, 1950, **33**, 1050.
[20] Brooks, *J.*, 1955, 1675; Elsevier's "Encyclopædia of Organic Chemistry," Vol. 14, p. 1195S.