542. *Triterpenoids. Part LV.*[1] *The Stereochemistry of Alcohols Derived from Glutinone (Alnusenone).*

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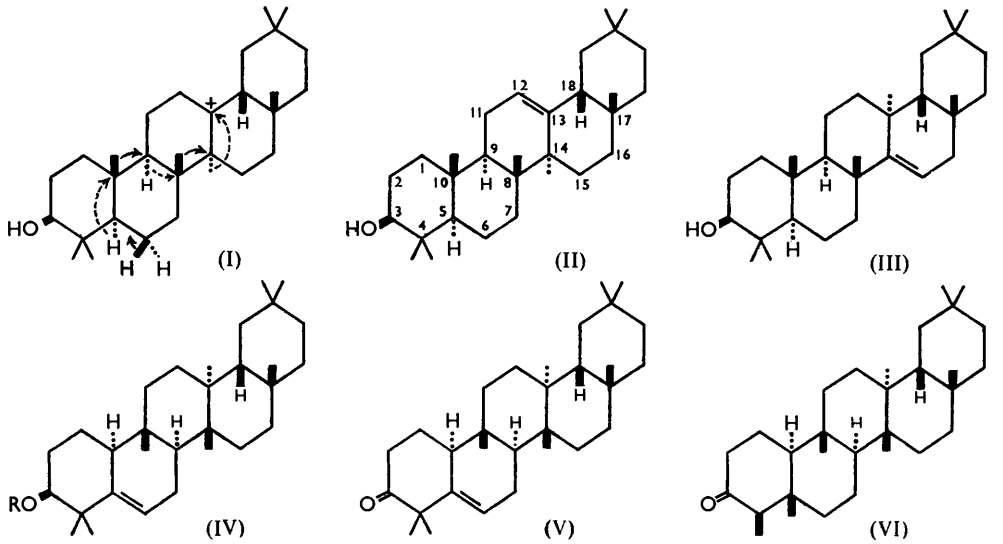
Reduction of glutinone (alnusenone) (V) with aluminium *iso*propoxide and *iso*propanol gives a mixture of glutin-5(6)-en-3α- (VII; R = H) and -3β-ol (IV; R = H). Reduction of glutin-5(10)-en-3-one (VIII) with lithium aluminium hydride gives a mixture of the epimeric alcohols glutin-5(10)-en-3β- (X; R = H) and -3α-ol (XI; R = H). The configuration of the hydroxyl group in glutin-5(10)-en-3α-ol (XI; R = H) was established by oxidation of its acetate to glutina-1(10) : 5-dien-3α-yl acetate (XIII; R = Ac), previously obtained by similar oxidation of glutin-5(6)-en-3α-yl acetate (VII; R = Ac). Likewise, the configurations of the hydroxyl group in glutin-5(10)- (X; R = H) and -5(6)-en-3β-ol (VI; R = H) were confirmed by the oxidation of the acetates to glutina-1(10) : 5-dien-3β-yl acetate (XII; R = Ac).

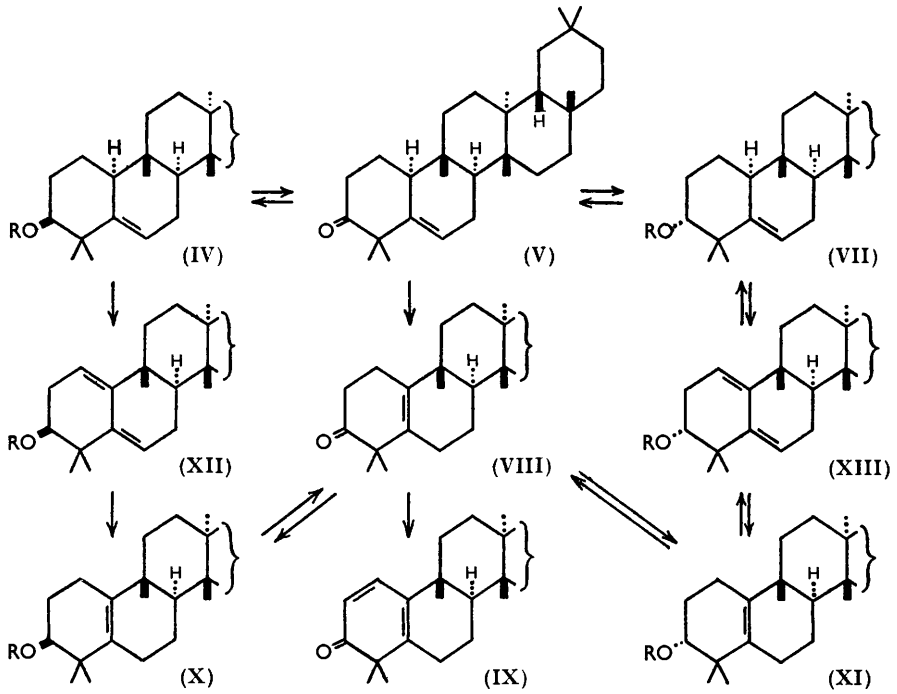
In Part LIV of this series, the constitution and stereochemistry of glutinone (alnusenone) (V) were deduced and were confirmed by partial synthesis from the saturated ketone, friedelin (VI).[1] The biogenesis of friedelin [2] from a squalene-like precursor is considered to proceed *via* the carbonium ion (I) which is also the immediate precursor of β-amyrin (II). Rearrangement of the carbonium ion by a synchronous series or by a succession of 1 : 2-shifts of the axial methyl groups or the axial hydrogen atoms attached at positions **14**, 8, 9, 10, 5, and 4, and loss of the hydrogen attached at position 3 as a proton, leads to friedelin [3] (VI). Taraxerol [4] (III) considered to be a stabilised intermediate in this biogenetic route. The biogenesis of glutinone from the carbonium ion (I) is represented as a series of 1 : 2-shifts of the axial methyl groups or axial hydrogen atoms attached at positions 14, 8, 9, 10, and 5 and loss of a proton from $C_{(6)}$. This route, which is illustrated by the arrows in (I), would lead to glutin-5(6)-en-3β-ol (IV; R = H), and the depicted changes are either followed or accompanied by oxidation of the secondary alcohol group. The possible intermediate glutin-5(6)-en-3β-ol (IV; R = H), in which the hydroxyl group is axial, has so far not been isolated from a natural source, but it has now been prepared from glutinone. Reduction of glutinone (V) with lithium aluminium hydride [5, 6] or with sodium and alcohol [5] gives an alcohol (m. p. 203—205°, $[\alpha]_D$ +61°; acetate, m. p. 235—236°, $[\alpha]_D$ +46°) in which the hydroxyl group is equatorial and consequently α-orientated. Oxidation of the alcohol regenerates glutinone and it is therefore identified as glutin-5(6)-en-3α-ol [1] (VII; R = H). We now find that reduction of glutinone (V) with aluminium

[1] Part LIV, Beaton, Spring, Stevenson, and Stewart, *Tetrahedron*, 1958, **2**, 246.
[2] Brownlie, Spring, Stevenson, and Strachan, *J.*, 1956, 2419; Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041; Takahashi and Ourisson, *Bull. Soc. chim. France*, 1956, 353; Dutler, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1955, **38**, 1268.
[3] Eschenmoser, Ruzicka, Jeger, and Arigoni, *Helv. Chim. Acta*, 1955, **38**, 1890.
[4] Beaton, Spring, Stevenson, and Stewart, *J.*, 1955, 2131.
[5] Beaton, Spring, and Stevenson, *J.*, 1955, 2616.
[6] Chapon and David, *Bull. Soc. chim. France*, 1953, 333.

*iso*propoxide and *iso*propyl alcohol gives a mixture which is separated by chromatography on alumina into two homogeneous alcohols. The more strongly adsorbed component of the mixture was recognised as glutin-5(6)-en-3α-ol (VII; R = H). The less strongly



adsorbed component is an isomeric alcohol, $C_{30}H_{50}O$ (m. p. 210·5—211·5°, $[\alpha]_D$ +64°; acetate, m. p. 192—194°, $[\alpha]_D$ +79°). This also is converted into glutinone by oxidation

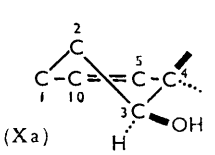


with the chromic acid–pyridine complex and is therefore identified as glutin-5(6)-en-3β-ol (IV; R = H).

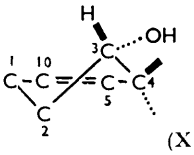
During their study, Beaton *et al.*[1] identified a ketone, obtained by the action of mineral

acid on glutinone,[7] as the isomeric glutin-5(10)-en-3-one (VIII). Its structure follows from the fact that its double bond is tetrasubstituted and that successive treatment with bromine and potassium acetate converts it into a fully conjugated homoannular dienone (IX). Glutin-5(10)-en-3-one has not so far been isolated from a natural source but this ketone, and the related glutin-5(10)-en-3β-ol (X; R = H), could represent stabilised intermediates in the biogenetic pathway between the carbonium ion (I) and friedelin (VI).

According to Beaton *et al.*,[1] reduction of glutin-5(10)-en-3-one (VIII) with lithium aluminium hydride or with sodium and alcohol gives a glutin-5(10)-en-3-ol, m. p. 241—242°, $[\alpha]_D$ −42° (acetate, m. p. 290—293°, $[\alpha]_D$ −27°), but they did not assign a configuration to the hydroxyl group in this alcohol. In the epimeric glutin-5(10)-en-3α- (XI; R = H) and -3β-ol (X; R = H), $C_{(1)}$, $C_{(4)}$, $C_{(5)}$, and $C_{(10)}$ must lie in one plane, or nearly so, and the relative positions of $C_{(2)}$ and $C_{(3)}$ will be such that ring A will adopt one of the two possible half-chair conformations. Consequently, it is possible for ring A to adopt a half-chair conformation in which the hydroxyl group is equatorial in each case, as shown in (Xa) and (XIa). The steric situation is the same as that obtaining in the epimeric *neo*ergosterols.[8] We have repeated the reduction of glutin-5(10)-en-3-one (VIII) with lithium aluminium hydride and isolated, in addition to the alcohol described by Beaton *et al.*,[1] a minor product, an isomeric alcohol, m. p. 258—259°, $[\alpha]_D$ −42° (acetate, m. p. 209—210°, $[\alpha]_D$ −49°). Since oxidation of each of the alcohols regenerates glutin-5(10)-en-3-one, they are epimeric glutin-5(10)-en-3-ols. Their configurations have been established by relating them directly to glutin-5(6)-en-3α- and -3β-ol. Oxidation of glutin-5(6)-en-3α-yl acetate (VII; R = Ac) with selenium dioxide gives a conjugated dienyl acetate,[1,7] m. p. 164—166°, $[\alpha]_D$ +35°, identified as glutina-1(10) : 5-dien-3α-yl acetate[1] (XIII; R = Ac), which shows absorption maxima at 2300, 2380 (ε 18,000) and 2480 Å.



(Xa)



(XIa)

The structure ascribed to this dienyl acetate is supported by its conversion into glutin-5(6)-en-3α-yl acetate (VII; R = Ac) on partial catalytic reduction.[1] Oxidation of the glutin-5(10)-en-3-yl acetate, m. p. 209—210°, with selenium dioxide likewise gives glutina-1(10) : 5-dien-3α-yl acetate (XIII; R = Ac), proving that the alcohol cited as minor product above is glutin-5(10)-en-3α-ol (XI; R = H). This decision was confirmed by reduction of glutina-1(10) : 5-dien-3α-yl acetate (XIII; R = Ac) with lithium and ammonia to glutin-5(10)-en-3α-ol (XI; R = H) (in poor yield). Similarly, reduction of glutina-1(10) : 5-dien-3α-ol (XIII; R = H) with potassium *tert.*-butoxide in *tert.*-butyl alcohol gave glutin-5(10)-en-3α-ol (XI; R = H) in poor yield. The partial reduction of glutina-1(10) : 5-dien-3α-ol (XIII; R = H) was effected more efficiently by using its tetrahydropyranyl ether. Reduction of this ether with lithium and ammonia followed by hydrolysis with mineral acid gave glutin-5(10)-en-3α-ol (XI; R = H) in approximately 40% yield.

Since the alcohol which is the minor component of the mixture obtained by reduction of glutin-5(10)-en-3-one with lithium aluminium hydride is identified as glutin-5(10)-en-3α-ol (XI; R = H), it follows that the epimeric major component is the 3β-alcohol (X; R = H) and this has been confirmed as follows. Oxidation of its acetate (X; R = Ac) with selenium dioxide gives glutina-1(10) : 5-dien-3β-yl acetate (XII; R = Ac), m. p. 209—210°, $[\alpha]_D$ +112°, which has absorption maxima at 2310, 2380 (ε 18,000) and 2460 Å and was

[7] Chapon, *Bull. Soc. chim. France.*, 1955, 1076, 1630.
[8] Klyne, "Progress in Stereochemistry," Butterworths Scientific Publications, London, 1954, p. 83.

characterised as the derived alcohol (XII; R = H). Similarly, oxidation of glutin-5(6)-en-3β-yl acetate with selenium dioxide also gave glutina-1(10) : 5-dien-3β-yl acetate (XII; R = Ac).

Experimental

Rotations refer to $CHCl_3$ and ultraviolet absorption spectra to EtOH solutions. Grade II alumina and light petroleum, b. p. 60—80°, were used for chromatography. M. p.s were determined in open capillaries, except those marked (K) which were determined in the Kofler apparatus.

Glutin-5(6)-en-3β-ol (IV; R = H).—A mixture of glutinone (950 mg.) and aluminium *iso*propoxide (1·25 g.) in absolute *iso*propyl alcohol (12·5 c.c.) was distilled slowly with the addition of *iso*propyl alcohol to maintain constant volume. After 4½ hr., the distillate no longer contained acetone and the solution was evaporated to dryness. The product, isolated in the usual way by means of ether, was chromatographed in light petroleum (30 c.c.) and on alumina (30 g.). Elution with light petroleum–benzene (2 : 1; 1150 c.c.) yielded fractions (246 mg.) which crystallised from chloroform–methanol to give *glutin-5(6)-en-3β-ol* as needles, m. p. (K) 210·5—211·5°, $[\alpha]_D$ +64° (*c* 0·9) (Found: C, 84·2; H, 12·0. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). A mixture with glutin-5(6)-en-3α-ol had m. p. (K) 194—196°.

Continued elution with the same solvent mixture (1500 c.c.) yielded mixtures, whereafter light petroleum–benzene (3500 c.c.) gave fractions (460 mg.) which crystallised from chloroform–methanol to yield glutin-5(6)-en-3α-ol, m. p. (K) and mixed m. p. (K) 201—203°, $[\alpha]_D$ +62° (*c* 1·9).

Glutin-5(6)-en-3β-yl Acetate (IV; R = Ac).—Glutin-5(6)-en-3β-ol was treated with pyridine and acetic anhydride at 100° for 90 min. The product, isolated in the usual manner, crystallised from chloroform–methanol, to give *glutin-5(6)-en-3β-yl acetate* as plates, m. p. (K) 192—194°, $[\alpha]_D$ +79° (*c* 1·1), $\lambda_{max.}$ 2050 Å (ε 4050) (Found: C, 82·25; H, 11·4. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%).

Hydrolysis of the acetate (35 mg.) with lithium aluminium hydride (50 mg.) in dry ether (20 c.c.) gave glutin-5(6)-en-3β-ol which crystallised from chloroform–methanol as needles, m. p. (K) and mixed m. p. (K) 210—211°, $[\alpha]_D$ +63° (*c* 0·9).

Oxidation of Glutin-5(6)-en-3β-ol.—The complex from chromium trioxide (100 mg.) and pyridine (1 c.c.) was added to a solution of glutin-5(6)-en-3β-ol (32 mg.) in pyridine (0·5 c.c.) and the mixture kept at room temperature for 17 hr. A solution of the product, isolated in the usual way, in light petroleum (10 c.c.) was filtered through alumina (5 g.), and the column eluted with the same solvent (300 c.c.). The eluate crystallised from chloroform–methanol, to give glutin-5(6)-en-3-one as plates, m. p. (K) and mixed m. p. (K) 244—245°, $[\alpha]_D$ +31° (*c* 1·2).

Glutin-5(10)-en-3β-yl Acetate (X; R = Ac).—Lithium aluminium hydride (450 mg.) was added to a suspension of glutin-5(10)-en-3-one (m. p. 251—253°, $[\alpha]_D$ −91·5°) (750 mg.) in ether (200 c.c.) and kept at room temperature for 1 hr. The product, isolated in the usual way, was treated with pyridine (5 c.c.) and acetic anhydride (5 c.c.) at 100° for 30 min. and the crystals which separated on cooling were collected (mother-liquor A) and recrystallised from chloroform–methanol, to give glutin-5(10)-en-3β-yl acetate (450 mg.) as plates, m. p. (K) 297—299°, $[\alpha]_D$ −23° (*c* 1·7). Beaton *et al.*[1] give m. p. 290—293°, $[\alpha]_D$ −27°, for " alnus-5(10)-en-3ξ-yl acetate."

A suspension of glutin-5(10)-en-3β-yl acetate (55 mg.) in ether (25 c.c.) was treated with lithium aluminium hydride (50 mg.) and refluxed for 5 min. The product was isolated in the usual manner and crystallised from light petroleum from which glutin-5(10)-en-3β-ol separated as needles, m. p. 244—245°, $[\alpha]_D$ −42·5° (*c* 0·8) (Found: C, 84·35; H, 11·5. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%). Beaton *et al.*[1] give m. p. 241—242°, $[\alpha]_D$ −42°, for " alnus-5(10)-en-3ξ-ol."

Glutin-5(10)-en-3α-yl Acetate (XI; R = Ac).—The acetic anhydride–pyridine mother-liquor A (above) was diluted with water and extracted with ether. The extracted solid (225 mg.) crystallised from chloroform–methanol, to give *glutin-5(10)-en-3α-yl acetate* (50 mg.) as needles, m. p. 209—210°, $[\alpha]_D$ −49° (*c* 1·4), $\lambda_{max.}$ 2050 Å (ε 5100) (Found: C, 82·0; H, 11·5. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%).

Treatment of glutin-5(10)-en-3α-yl acetate with lithium aluminium hydride, and crystallisation of the product from chloroform–methanol, gave *glutin-5(10)-en-3α-ol* as plates, m. p. (K)

258—259°, $[\alpha]_D$ −42° (*c* 1·6), $\lambda_{max.}$ 2060 Å (ε 4300) (Found: C, 83·4; H, 11·9. $C_{30}H_{50}O,\frac{1}{3}MeOH$ requires C, 83·4; H, 11·8%). A mixture with glutin-5(10)-en-3β-ol had m. p. (K) 238—242°.

Glutin-5(10)-en-3-one (VIII).—(*a*) A solution of glutin-5(10)-en-3α-ol (40 mg.) in pyridine (1 c.c.) was added to the chromium trioxide (40 mg.)–pyridine (0·5 c.c.) reagent and kept at room temperature for 15 hr. A solution of the product, isolated in the usual way, in light petroleum was chromatographed on alumina (6 g.). Elution with the same solvent yielded glutin-5(10)-en-3-one as plates (from chloroform–methanol), m. p. (K) and mixed m. p. (K) 251—253°, $[\alpha]_D$ −97° (*c* 1·3). (*b*) Oxidation of glutin-5(10)-en-3β-ol by the method described above gave glutin-5(10)-en-3-one as plates, m. p. (K) and mixed m. p. (K) 251—253°, $[\alpha]_D$ −96° (*c* 1·6).

Glutina-1(10) : 5-dien-3α-yl Acetate (XIII; R = Ac).—A solution of selenium dioxide (35 mg.) in water (0·1 c.c.) was mixed with one of glutin-5(10)-en-3α-yl acetate (35 mg.) in acetic acid (25 c.c.), and the mixture refluxed for 5 hr. The product, isolated in the usual way, was chromatographed in light petroleum (5 c.c.) on alumina (5 g.). Elution with the same solvent (150 c.c.) yielded fractions which crystallised from chloroform–methanol, to give glutina-1(10) : 5-dien-3α-yl acetate as needles, m. p. (K) and mixed m. p. (K) 164—166°, $[\alpha]_D$ +35° (*c* 0·5), $\lambda_{max.}$ 2310 and 2380 Å (ε 15,000 and 17,000), inflexion at 2480 Å (ε 10,000). Beaton *et al.*[1] give m. p. 164—166° $[\alpha]_D$ +35°.

Glutina-1(10) : 5-dien-3α-ol (XIII; R = H).—Treatment of the dienyl acetate with lithium aluminium hydride and crystallisation of the product from chloroform–methanol gave glutina-1(10) : 5-dien-3α-ol as prismatic needles, m. p. (K) and mixed m. p. (K) 198—200°, $[\alpha]_D$ +84° (*c* 1·6), $\lambda_{max.}$ 2330 and 2400 Å (ε 16,000 and 18,000), inflexion at 2480 Å (ε 11,000). Beaton *et al.*[1] give m. p. 195—197°, $[\alpha]_D$ +83°.

Glutina-1(10) : 5-dien-3β-yl Acetate (XII; R = Ac).—(*a*) A solution of selenium dioxide (100 mg.) in water (0·1 c.c.) was mixed with a solution of glutin-5(10)-en-3β-yl acetate (100 mg.) in acetic acid (50 c.c.). After 3 hours' refluxing, the solvent was removed and a solution of the product in light petroleum (10 c.c.) was chromatographed on alumina (8 g.). Crystallisation of the fractions eluted by light petroleum (175 c.c.) from chloroform–methanol gave *glutina-1(10) : 5-dien-3β-yl acetate* as plates (75 mg.), m. p. 209—210°, $[\alpha]_D$ +112° (*c* 1·0), $\lambda_{max.}$ 2310, 2380, and 2460 (inflex.) Å (ε 16,500, 18,000, and 11,000) (Found: C, 82·3; H, 10·9. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%). It gives a deep orange colour with tetranitromethane. (*b*) Glutin-5(6)-en-3β-yl acetate (80 mg.) in acetic acid (20 c.c.) was treated with a solution of selenium dioxide (80 mg.) in water (0·1 c.c.) and acetic acid (2 c.c.), and kept at 60—70° for 1 hr. The filtered solution was evaporated to dryness and a solution of the residue in light petroleum (5 c.c.) chromatographed on alumina (10 g.). Elution with the same solvent (750 c.c.) yielded fractions which crystallised from chloroform–methanol, to give glutina-1(10) : 5-dien-3β-yl acetate as blades (68 mg.), m. p. (K) and mixed m. p. (K) 209—210°, $[\alpha]_D$ +112·5° (*c* 1·1), $\lambda_{max.}$ 2320 and 2380 Å (ε 15,000 and 16,500), inflexion at 2470 Å (ε 10,000).

Glutina-1(10) : 5-dien-3β-ol (XII; R = H).—A solution of the dienyl acetate (40 mg.) in ether (15 c.c.) was refluxed with lithium aluminium hydride (100 mg.) for 30 min. The product, in light petroleum–benzene (2 : 1; 15 c.c.), was chromatographed on alumina (5 g.), and the fraction eluted by benzene–ether (20 : 1; 100 c.c.), crystallised from methanol, to give *glutina-1(10) : 5-dien-3β-ol* as needles, m. p. (K) 195—197°, $[\alpha]_D$ +110° (*c* 0·6), $\lambda_{max.}$ 2320, 2390, and 2470 (inflex.) Å (ε 15,000, 16,000, and 10,000) (Found: C, 84·9; H, 11·7. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%).

3α-2′-Tetrahydropyranyloxyglutina-1(10) : 5-diene.—Toluene-*p*-sulphonic acid (0·5 mg.) was added to a solution of glutina-1(10) : 5-dien-3α-ol (350 mg.) in benzene (15 c.c.) and dihydropyran (1·5 c.c.), and the mixture kept at room temperature for 16 hr. A solution of the product, isolated in the usual way, in light petroleum (40 c.c.) was chromatographed on alumina (30 g.). The fractions eluted by light petroleum (300 c.c.) were crystallised from chloroform–methanol, to give *3α-2′-tetrahydropyranyloxyglutina-1(10) : 5-diene* as needles (after gelation), m. p. (K) 171—173°, $[\alpha]_D$ +70° (*c* 1·6), $\lambda_{max.}$ 2340 (inflex.), 2400, and 2380 (inflex.) Å (ε 13,500, 14,500, and 9600) (Found: C, 82·9; H, 11·3. $C_{35}H_{56}O_2$ requires C, 82·6; H, 11·1%).

Glutin-5(10)-en-3α-ol (XI; R = H).—(*a*) Lithium (300 mg.) was added to a solution of 3α-2′-tetrahydropyranyloxyglutina-1(10) : 5-diene (285 mg.) in ether (150 c.c.) and liquid ammonia (300 c.c.), and the mixture stirred for 1 hr. Ethanol (10 c.c.) was added and the product, isolated in the usual way, was refluxed in benzene (10 c.c.), ethanol (20 c.c.), and concentrated hydrochloric acid (0·25 c.c.) for 90 min.; the hydrolysed product was then

chromatographed in light petroleum (20 c.c.) on alumina (10 g.). Elution with light petroleum–benzene (1 : 6; 425 c.c.) yielded fractions which crystallised from chloroform–methanol, to give glutin-5(10)-en-3α-ol as plates (95 mg.), m. p. (K) and mixed m. p. (K) 258—259°, $[\alpha]_D$ −42° (*c* 1·6), $\lambda_{max.}$ 2040 Å (ε 4300). This alcohol with pyridine and acetic anhydride at 100° gave its acetate as needles, m. p. (K) and mixed m. p. (K) 209—210°, $[\alpha]_D$ −49° (*c* 1·4).

(*b*) Lithium (150 mg.) was added to a solution of glutina-1(10) : 5-dien-3α-yl acetate (100 mg.) in ether (50 c.c.) and liquid ammonia (100 c.c.), and the mixture stirred for 1 hr. After addition of ethanol (10 c.c.), the ammonia was allowed to evaporate. The product, isolated in the usual way, was acetylated with pyridine and acetic anhydride and chromatographed on alumina (10 g.). Elution with light petroleum (175 c.c.) yielded a fraction (15 mg.) which after three recrystallisations from chloroform–methanol gave glutin-5(10)-en-3α-yl acetate as needles, m. p. (K) and mixed m. p. (K) 207—208°, $[\alpha]_D$ −48° (*c* 0·3).

(*c*) Potassium (6·5 g.) was added to a solution of glutina-1(10) : 5-dien-3α-ol (100 mg.) in *tert.*-butyl alcohol (100 c.c.), the mixture was heated at 100° for 18 hr., then diluted with water, and the product was isolated in the usual way and chromatographed in light petroleum–benzene (9 : 1; 15 c.c.) on alumina (10 g.). Elution with this solvent mixture (125 c.c.) yielded fractions which crystallised from chloroform–methanol, to give glutin-5(10)-en-3α-ol as plates (12 mg.), m. p. 247—251°, $[\alpha]_D$ −36° (*c* 0·7), raised to m. p. (K) and mixed m. p. (K) 254—256° on recrystallisation. A mixture of the alcohol and glutin-5(10)-en-3β-ol had m. p. 235°.

One of us (A. C. P.) thanks the Department of Scientific and Industrial Research for the award of a Research Studentship.

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[*Received, December 27th*, 1957.]