

*The Chemistry of the Triterpenes and Related Compounds. Part XXII.\**  
*The Conversion of Lupeol into  $\psi$ -Taraxasterol (Heterolupeol).*

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$\psi$ -Taraxasterol (heterolupeol) and  $\delta$ -amyrenol have been obtained from the product of the action of boiling formic acid on lupeol.

IN continuation of the study of the acidic isomerisation of lupeol and its derivatives, the effect of boiling formic acid has been investigated, following earlier studies by Nojd (*Arch. Pharm.*, 1927, 265, 381) and by Biedebach (*ibid.*, 1943, 281, 49). Nojd isolated two formates which were hydrolysed to alcohols termed  $\alpha$ -allolupeol and  $\beta$ -allolupeol. Biedebach reported the isolation of  $\alpha$ -allolupeol and also of a new alcohol,  $\gamma$ -allolupeol, but he could not obtain  $\beta$ -allolupeol, which he suggested was impure  $\alpha$ -allolupeol. The constants of  $\gamma$ -allolupeol (m. p. 176—177°;  $[\alpha]_D +9.8^\circ$ ) and of its acetate (m. p. 268—269°;  $[\alpha]_D +19.4^\circ$ ) and benzoate (m. p. 269—271°;  $[\alpha]_D +39.5^\circ$ ) are almost identical with those of germanicol (m. p. 176—177°;  $[\alpha]_D +6^\circ$ ) and its acetate (m. p. 274°;  $[\alpha]_D +18^\circ$ ) and benzoate (m. p. 269—270°;  $[\alpha]_D +39^\circ$ ) (Simpson, *J.*, 1944, 283). In the light of the now known structures of lupeol and germanicol and their inter-relationship (Halsall, Jones, and Meakins, *J.*, 1952, 2682) it may be concluded that  $\gamma$ -allolupeol is germanicol.

In our studies on the isomerisation, lupeol was heated under reflux with formic acid (98—100%) for 2 hours. These conditions are similar to those employed by Biedebach (*loc. cit.*), but, whereas Biedebach apparently obtained a homogeneous mixture, the system remained heterogeneous in the present work; a possible factor affecting the solubility may be the presence of small amounts of water in the formic acid.

The crude formate obtained from the isomerisation was hydrolysed to a mixture of at least two alcohols which could not be separated by chromatography on alumina, and which

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formed mixed crystals of constant melting point. Its constants were not comparable with those of any of the *allolupeols* isolated by Biedebach or by Nojd. By acetylation of the mixed alcohols and careful chromatography it was possible to obtain two acetates (both  $C_{32}H_{52}O$ ), differing greatly in rotation ( $[\alpha]_D -24.6^\circ$  and  $+52^\circ$ ). The *lævorotatory* acetate absorbed strongly in the low-wave-length ultra-violet region, indicating the presence of a tetrasubstituted double bond, exocyclic to two rings. This evidence, together with the negative rotation, indicated that the acetate was  $\delta$ -amyrenyl acetate. On admixture with an authentic sample no depression of melting point occurred.

The other acetate was identified as  $\psi$ -taraxasteryl acetate. Its melting point was not depressed on admixture with, and its infra-red spectrum was identical with that of, an authentic sample. The melting point of the acetate from the isomerisation product was a little lower than that recorded in the literature for  $\psi$ -taraxasteryl acetate, which was found difficult to reproduce, however, even with authentic samples.

The  $\delta$ -amyrenol and  $\psi$ -taraxasteryl acetates were hydrolysed to their respective alcohols. The melting points of these alcohols were not depressed on admixture with authentic samples, and their infra-red spectra were respectively identical with those of  $\delta$ -amyrenol and  $\psi$ -taraxasterol.

The alcohol mixture obtained by hydrolysis of the initial isomerisation product was oxidised under mild conditions. Separation of the resulting ketones on alumina was very difficult, but two isomeric ketones with widely divergent rotations were isolated, and their constants compared well with those of  $\delta$ -amyrenone and  $\psi$ -taraxastenone. Their identities were proved by mixed melting-point determinations and by infra-red examination.

A comparison of the melting points and rotations of the derivatives of the alcohols derived from lupeol with those of the corresponding derivatives of authentic  $\delta$ -amyrenol and  $\psi$ -taraxasterol is given in the Table. The difficulty of purifying the derivatives of the alcohols obtained from the isomerisation reaction is reflected in small differences between the constants quoted, particularly in the case of  $\psi$ -taraxasterol. The formation of  $\delta$ -amyrenol under vigorous conditions was not unexpected, but the formation of  $\psi$ -taraxasterol was less predictable. As its formation is of considerable relevance to a general discussion of the acidic isomerisation of lupeol (following paper) confirmation of its presence in the isomerisation product seemed desirable.

The mixed acetates were oxidised with osmium tetroxide. The product consisted mainly of unchanged acetate, but a small fraction which was strongly adsorbed on deactivated alumina was isolated. By comparison of its infra-red spectrum with that of an authentic sample, this fraction was shown to be  $\psi$ -taraxastanetriol 3-acetate.

	Derivatives from isomerisation reaction			Literature values	
	M. p.	$[\alpha]_D$	Mixed m. p.	M. p.	$[\alpha]_D$
$\delta$ -Amyrenol .....	210—212°	-46.5°	210—213°	212—212.5°	-50.5° <sup>1</sup>
$\delta$ -Amyrenyl acetate .....	206—207	-24.5	209—210	207.5—209	-34 <sup>1</sup>
$\delta$ -Amyrenone .....	198—201	-3	199—203	199.5—202.5	-12 <sup>1</sup>
$\psi$ -Taraxasterol .....	202—215	+46	200—213	217—219	+50 <sup>2</sup>
				198—200	+47 <sup>3</sup>
$\psi$ -Taraxasteryl acetate .....	225—231	+52	226—233	240—241	— <sup>2</sup>
				234—235	+53 <sup>3</sup>
$\psi$ -Taraxastenone .....	166—168	+81	166.5—171.5	174—175	+81 <sup>4</sup>

<sup>1</sup> Ames, Halsall, and Jones, *J.*, 1951, 450. <sup>2</sup> Lardelli, Krusi, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1948, **31**, 1159. <sup>3</sup> Burrows and Simpson, *J.*, 1938, 2042. <sup>4</sup> Ames, Beton, Bowers, Halsall, and Jones, following paper.

#### EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected. Rotations were determined in chloroform. The alumina used for chromatography had an activity I—II.

*The Action of Boiling Formic Acid on Lupeol.*—Lupeol (24 g.) was heated under reflux in formic acid (98—100%; 400 c.c.) for 2 hr. The solution was deep violet in colour, but much undissolved solid was present throughout the reaction. After filtration, the filtrate was diluted with water, and the resulting precipitate combined with the formic acid insoluble material. A portion of the combined precipitates (17.6 g.) was washed with boiling ethanol (800 c.c.) which left an insoluble amorphous material. This sublimed, giving plates, m. p. 220—224°. The

washings yielded needles (m. p. after sublimation, 215—225°) on cooling. These were filtered off and combined with the insoluble material. The mixture was hydrolysed by heating under reflux with 5% ethanolic potassium hydroxide (300 c.c.). Dilution with water and acidification with dilute sulphuric yielded a solid which was crystallised from ethanol giving needles, m. p. 182—183.5°,  $[\alpha]_D + 3^\circ$  (*c*, 1.0) (Found: C, 84.5; H, 11.9. Calc. for  $C_{30}H_{50}O$ : C, 84.4; H, 11.8%). Light absorption:  $\epsilon_{2100 \text{ \AA}} = 5900$ ,  $\epsilon_{2150 \text{ \AA}} = 3500$ ,  $\epsilon_{2200 \text{ \AA}} = 1960$ , and  $\epsilon_{2330 \text{ \AA}} = 1430$ .

A portion (0.65 g.) was chromatographed on alumina (100 g.). All the fractions obtained melted at temperatures between 180° and 190°.

*Acetylation of the Mixed Alcohols and Separation of the Mixed Acetates.*—The mixed alcohols (1.0 g.) were dissolved in pyridine (25 c.c.), acetic anhydride (25 c.c.) was added, and the mixture was kept at 20° for 16 hr. The solution was evaporated to dryness with methanol, and then the solid was taken up in methanol and the evaporation repeated. After several repetitions of the process the solid finally obtained (1.09 g.) was adsorbed from light petroleum on alumina (100 g.) and eluted as follows [each fraction was eluted with 250 c.c. of solvent; with fractions 1—9 this was light petroleum; fractions 10 and 11 were eluted with light petroleum—benzene (9 : 1)].

Fraction	Wt., mg.	M. p.	Form	Fraction	Wt., mg.	M. p.	Form
1 + 1a	17	187—196°	Rods	7	50	212.5—223°	Needles
2	220	202—205.5	"	8	44	215—226.5	"
3	184	205.5—208.5	"	9	77	218—230	"
4	146	198—204	Needles	10	67	218—231	"
5	112	202—213	"	11	25	200—216	"
6	90	210—221	"				

Fractions 2 and 3 were combined and crystallised from ethanol, giving  $\delta$ -amyrenyl acetate as platelets, m. p. 206—207°,  $[\alpha]_D - 24.5^\circ$  (*c*, 0.6) (Found: C, 82.35; H, 11.15. Calc. for  $C_{32}H_{52}O_2$ : C, 82.0; H, 11.2%). Light absorption:  $\epsilon_{2100 \text{ \AA}} = 9500$ ,  $\epsilon_{2150 \text{ \AA}} = 6000$ ,  $\epsilon_{2200 \text{ \AA}} = 3550$ , and  $\epsilon_{2330 \text{ \AA}} = 2600$ . The m. p. of a mixture with an authentic sample of  $\delta$ -amyrenyl acetate (m. p. 208°) was 209—210°.

Hydrolysis of the acetate with an ethereal solution of lithium aluminium hydride yielded  $\delta$ -amyrenol which crystallised from ethanol as needles, m. p. 210—212° undepressed on admixture with an authentic sample (m. p. 213—214.5°),  $[\alpha]_D - 46.5^\circ$  (*c*, 0.64).

Fractions 4—8 were combined and crystallised from ethanol, giving the mixed acetates as needles (0.27 g.), m. p. 205—210°,  $[\alpha]_D + 19.8^\circ$  (*c*, 0.5).

Fraction 9 crystallised from ethanol to give  $\psi$ -taraxasteryl acetate as plates, m. p. 225—231° ( $[\alpha]_D + 52^\circ$  (*c*, 0.89) (Found: C, 81.75; H, 11.2. Calc. for  $C_{32}H_{52}O_2$ : C, 82.0; H, 11.2%). Light absorption  $\epsilon_{2100 \text{ \AA}} = 3000$ ,  $\epsilon_{2150 \text{ \AA}} = 1300$ ,  $\epsilon_{2200 \text{ \AA}} = 340$ , and  $\epsilon_{2330 \text{ \AA}} = 50$ . The m. p. of a mixture with an authentic sample of  $\psi$ -taraxasteryl acetate (m. p. 238—240°) was 226—233°.

Hydrolysis of the acetate with an ethereal solution of lithium aluminium hydride yielded  $\psi$ -taraxasterol, which crystallised from ethanol and nitromethane as needles, m. p. 202—215°,  $[\alpha]_D + 46^\circ$  (*c*, 0.94). The m. p. of a mixture with an authentic sample (m. p. 206—212°) was 200—213°.

Fraction 10 was crystallised from methanol, yielding plates, m. p. 200—228°,  $[\alpha]_D + 61.5^\circ$  (*c*, 0.70). The constants indicate that the fraction was mainly  $\psi$ -taraxasteryl acetate, with possibly a small amount of lupenyl-I acetate.

*Oxidation of the Mixed Alcohols and Separation of the Mixed Ketones.*—The mixed alcohols (0.47 g.) were kept at 20° for 2 hr. with Kiliani's reagent (120 c.c.) [chromic acid (1.5 g.), acetic acid (120 c.c.), acetone (225 c.c.), and water (15 c.c.)]. Dilution with water and extraction with ether yielded an oil (0.45 g.) which crystallised from ethanol to give needles (0.42 g.), m. p. 183°. These were adsorbed from light petroleum on alumina (42 g.), and fractions were eluted as follows. (i) With light petroleum (700 c.c.): solid (44 mg.), m. p. 177—195°. (ii) With light petroleum—benzene (19 : 1) (175 c.c.): solid (90 mg.), m. p. 155—190°. (iii) With light petroleum—benzene (19 : 1) (525 c.c.): oil (138 mg.). Fraction (i) was crystallised from ethanol, giving  $\delta$ -amyrenone as rods, m. p. 198—201° undepressed on admixture with an authentic sample (m. p. 199.5—201.5°),  $[\alpha]_D - 3.2^\circ$  (*c*, 0.5). Fraction (iii) was crystallised from ethanol, nitromethane, and methanol, giving  $\psi$ -taraxastenone as fine needle clusters, m. p. 166—168° undepressed on admixture with an authentic sample (m. p. 170—173°),  $[\alpha]_D + 81^\circ$  (*c*, 0.2).

*The Action of Osmium Tetroxide on the Mixed Acetates.*—A solution of osmium tetroxide (303 mg.) in dry ether (15 c.c.) was added to a solution of the mixed acetates (0.79 g.) in dry ether (20 c.c.). After 7 days at 20° the reaction mixture was shaken with a solution of mannitol (14 g.) and potassium hydroxide (1.4 g.) in water (140 c.c.) for 8 hr. From the ethereal phase a solid residue (0.726 g.), m. p. 179—197°, was obtained. It was adsorbed from light petroleum

on deactivated alumina (75 g.). After elution with light petroleum (750 c.c.) of a fraction (0.496 g.) consisting of unchanged mixed acetates, elution with ether (500 c.c.) gave an amorphous residue (60 mg.) which was crystallised from nitromethane, giving  $\psi$ -taraxastanetriol 3-acetate as needles, m. p. 278° (transition to short needles at 240°),  $[\alpha]_D +41.5^\circ$  (Found: C, 76.25; H, 10.95.  $C_{32}H_{54}O_4$  requires C, 76.25; H, 10.95%). An authentic sample (m. p. 276°) of  $\psi$ -taraxastanetriol 3-acetate was prepared from pure  $\psi$ -taraxasteryl acetate in a similar manner, and on admixture of the two samples of triol 3-acetate no depression of melting point was found.

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