531. *The Chemistry of Triterpenes and Related Compounds. Part XLII.* Reduction of the* 7,9(11)-*Diene Group in Tetracyclic Triterpenes.*

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The reduction of the 7,9(11)-diene group in tetracyclic triterpenes with lithium in liquid ammonia has been studied. Both 1,2- and 1,4-addition of hydrogen leading to Δ^7- and Δ^8-double bonds have been found.

The isolation from fungi and resins of pure tetracyclic triterpenes containing double bonds only at the 8,9- and 24,25-positions has been frequently complicated by the presence of varying amounts of the corresponding $\Delta^{7,9(11)}$-dehydro-compounds. This difficulty has arisen in both the lanostane [1-3] and the euphane [4] series. No simple physical or chemical method for the separation of the Δ^8-compounds from the dehydro-impurities has been devised, although purification has been achieved by long and tedious fractional crystallisations.[3]

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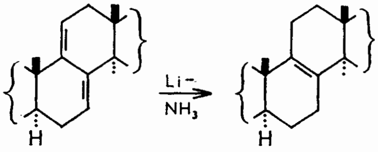
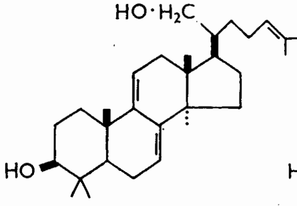
* Part XLI, *J.*, 1961, 5353.

[1] Guider, Halsall, Hodges, and Jones, *J.*, 1954, 3234.
[2] Halsall and Sayer, *J.*, 1959, 2031.
[3] Cort, Gascoigne, Holker, Ralph, Robertson, and Simes, *J.*, 1954, 3713.
[4] Halsall, Meakins, and Swayne, *J.*, 1953, 4139.

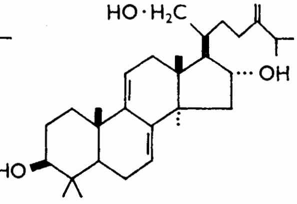
When conjugated dienes are treated with alkali metals in liquid ammonia or amines they are reduced to monoenes.[5] This reaction has now been investigated as a method for reducing the $\Delta^{7,9(11)}$-diene group in tetracyclic triterpenes with the aim of obtaining the pure Δ^8-derivatives (*e.g.*, I ⟶ II).



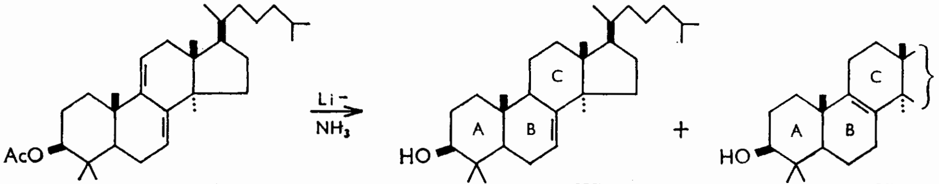
(I) (II)



(VI)



(VII)



(III) (IV) (V)

The reduction of lanosta-7,9(11)-dien-3β-yl acetate (III) with lithium in ammonia was examined. The product was shown to be an inseparable mixture of lanost-7-en-3β-ol (IV) (*ca.* 50%) and lanost-8-en-3β-ol (V) by comparing the acetylated product with the corresponding mixture, containing about 65% of the Δ^7-isomer, derived from the acidic isomerisation of lanost-8-en-3β-yl acetate.[6] The infrared spectra of the two mixtures were identical. Further, oxidation of the mixtures of alcohols obtained on hydrolysis gave mixtures, with optical rotatory dispersion curves of similar shapes, of the lanost-7- and -8-en-3-ones.

Reduction of lanosta-7,9(11)-dien-3β-ol also gave a mixed product whose m. p. 135—138° was appreciably below that of lanost-8-en-3β-ol. Lanosta-7,9(11),24-triene-3β,21-diol (VI), however, gave pure lanosta-8,24-diene-3β,21-diol in high yield with no discernible yield of the Δ^7-isomer. Similarly, eburico-7,9(11),24(28)-triene-3β,16α,21-triol (VII) also gave, in high yield, only one product which is formulated as eburico-8,24(28)-diene-3β,16α,21-triol. Eupha-7,9(11)-dien-3β-yl acetate gave a product from which, after acetylation, euph-8-en-3β-yl acetate was isolated in 85% yield. The reduction of the diene system in the euphane series was much faster than in the lanostane series.

These results indicate that in some, but not all, cases it is possible to prepare tetracyclic triterpenes containing an 8,9-double bond from the corresponding 7,9(11)-diene.

The samples of lanosta-7,9(11)-dien-3β-ol, its acetate, and the corresponding 3-ketone prepared in the course of this work had rotations ($[\alpha]_D$ +74°, +98°, and +54°) somewhat higher than those previously reported[7] ($[\alpha]_D$ +67°, +91°, and +48°).

EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected. Rotations were determined for chloroform solutions, unless otherwise stated, at room temperature. Light petroleum refers to

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[5] Birch, *Quart. Rev.*, 1950, **4**, 69; Watt, *Chem. Rev.*, 1950, **46**, 317; Birch and Smith, *Quart. Rev.*, 1958, **12**, 17.

[6] Barton, Fawcett, and Thomas, *J.*, 1951, 3147; Marker, Wittle, and Mixon, *J. Amer. Chem. Soc.*, 1937, **59**, 1368; Cavalla, McGhie, and Pradham, *J.*, 1951, 3142; Voser, Montavon, Günthard, Jeger, and Ruzicka, *Helv. Chim. Acta*, 1950, **33**, 1893.

[7] See Elsevier's " Encyclopaedia of Organic Chemistry," Vol. XIVS, p. 1250S, 1251S, and 1262S.

the fraction with b. p. 60—80°. The alumina used for chromatography had activity I—II. Known compounds gave satisfactory analyses.

Reduction of Lanosta-7,9(11)-*dien*-3β-*yl Acetate with Lithium in Liquid Ammonia.*—Lithium metal (1 g.) was added to a solution of the steroid acetate (460 mg.) in 1 : 1 ether–liquid ammonia (200 ml.). After the mixture had been stirred for 6 hr. the lithium was destroyed with ethanol, and the ammonia allowed to evaporate overnight. The resulting ether solution was washed with dilute acid, then water, and dried. Removal of the solvent gave a solid, $\lambda_{max.}$ 2520 Å (ε 290), indicating *ca.* 2·6% of 7,9(11)-diene. In a further experiment in which the lanosta-7,9(11)-dien-3β-yl acetate in ether was subjected to two successive treatments with lithium in liquid ammonia the product had m. p. 126—134° and showed no significant ultraviolet absorption.

Acetylation of the reduction product with acetic anhydride–pyridine gave a mixture of lanost-8-en-3β-yl acetate and lanost-7-en-3β-yl acetate as needles (from methanol), m. p. 129—131°, $[\alpha]_D$ +50° (*c* 1·37), $\nu_{max.}$ (in Nujol) 920 and 822 cm.$^{-1}$ (C–H out-of-plane bending). This mixture was compared with the mixture of lanost-7-en-3β-yl acetate and lanost-8-en-3β-yl acetate, m. p. 130—134°, $[\alpha]_D$ +47° (*c* 1·27), $\nu_{max.}$ (in Nujol) 920 and 822 cm.$^{-1}$, prepared by passing dry hydrogen chloride through a solution of lanosta-8-en-3β-yl acetate (1 g.) in chloroform (50 ml.) for 2·5 hr. at 20°.[6]

Preparation of a Ketone Mixture from the Lithium–Liquid Ammonia Reduction Products of Lanosta-7,9(11)-*dien*-3β-*yl Acetate.*—The acetate mixture (53 mg.), m. p. 127—131°, in ether (20 ml.) was heated under reflux with lithium aluminium hydride (100 mg.) for 2 hr. The isolated product in acetone (20 ml.) was treated with 8N-chromic trioxide (1 ml.) for 3 min. at 0°. Isolation with ether and recrystallisation from ethanol (3 ml.) gave a mixture of lanost-8- and -7-en-3-one as needles, m. p. 128—133°, $[\alpha]_D$ +32° (*c* 0·38). The rotation indicates the presence of *ca.* 50% of lanosta-7-en-3-one. Optical rotatory dispersion in methanol: $[\alpha]$ (4000 Å) +120°; (3400 Å) +100°; (3000 Å inflexion) +130°; (2900 Å) +190°.

Preparation of a Ketone Mixture from Acid-isomerisation Products of Lanost-8-*en*-3β-*yl Acetate.*—The acetate mixture (300 mg.), m. p. 127—134°, was treated with 10% methanolic potassium hydroxide at 20° for 24 hr. Isolation with ether gave the alcohol mixture as a solid which was dissolved in acetone (50 ml.), cooled to 0°, and treated with 8N-chromium trioxide (3 ml.) for 3 min. Extraction with ether afforded a mixture of lanost-8- and -7-en-3-one as stout needles, m. p. 132—136°, $[\alpha]_D$ +20° (*c* 1·29). The rotation indicates the presence of *ca.* 65% of lanost-7-en-3-one. Optical rotatory dispersion in methanol: $[\alpha]$ (4000 Å) +100°; (3400 Å) +60°; (3000 Å inflexion) +100°; (2900 Å) +160°.

Reduction of Lanosta-7,9(11)-*dien*-3β-*ol.*—The alcohol (150 mg.) in ether (55 c.c.) was treated with lithium in liquid ammonia (100 c.c.) for 90 min. and the excess of metal decomposed with methanol. The product was adsorbed from light petroleum (55 c.c.) on alumina. After elution with light petroleum (100 c.c.), elution with 1 : 1 light petroleum–benzene (100 c.c.) gave a product (125 mg.) which had no ultraviolet absorption and crystallised from methanol as needles, m. p. 135—138°. Repeated recrystallisation from methanol–ethyl acetate gave needles, m. p. 140—143°, $[\alpha]_D$ +50° (*c* 0·97) (cf. authentic lanost-8-en-3β-ol, m. p. 145—146°, $[\alpha]_D$ +58°).

Lithium–Liquid Ammonia Reduction of Lanosta-7,9(11),24-*triene*-3β,21-*diol.*—Lanosta-7,9(11),24-triene-3β,21-diol[2] (100 mg.) in ether (100 ml.) was treated with lithium in liquid ammonia for 1 hr. The excess of metal was removed with methanol, and the product isolated as a waxy solid which was adsorbed from benzene (15 ml.) on alumina. Elution with 9 : 1 benzene–ether (150 ml.) afforded lanosta-8,24-diene-3β,21-diol (80 mg.) as needles (from methanol), m. p. and mixed m. p. 194—196°, $[\alpha]_D$ +40° (*c* 0·99) (lit.,[2] m. p. 189—192°), no ultraviolet light absorption. The diol on acetylation with pyridine–acetic anhydride gave 3β,21-*diacetoxylanosta*-8,24-*diene* as needles (from methanol), m. p. 121—123°, $[\alpha]_D$ +48° (*c* 1·10) (Found: C, 77·3; H, 10·3. $C_{34}H_{54}O_4$ requires C, 77·5; H, 10·35%).

Reduction of Eburico-7,9(11),24(28)-*triene*-3β,16α,21-*triol*[8] *with Lithium in Liquid Ammonia.*—The triol (150 mg.) in ether (100 ml.) was treated with lithium in liquid ammonia (100 ml.) for 2·5 hr., and the excess of lithium removed with methanol. The product was isolated and recrystallised from methanol, to give *eburico*-8,24(28)-*diene*-3β,16α,21-*triol* as needles (90% yield), m. p. 221—224°, $[\alpha]_D$ −2° (in pyridine) (*c* 0·88) (Found: C, 78·5; H, 11·3. $C_{31}H_{52}O_3$ requires C, 78·75; H, 11·6%), no ultraviolet light absorption.

[8] Bowers, Halsall, and Sayer, *J.*, 1954, 3070.

Reduction of Eupha-7,9(11)-*dien*-3β-*yl Acetate*.—The diene (500 mg.) in ether (50 ml.) was treated with lithium in liquid ammonia for 2 hr. The excess of metal was removed with ammonium chloride, and the product (485 mg.) was treated with acetic anhydride–pyridine. The product was isolated with ether and adsorbed from light petroleum (30 ml.) on alumina (30 g.). Elution with light petroleum (200 ml.) gave euph-8-en-3β-yl acetate (420 mg.) which recrystallised from methanol–ethyl acetate as needles, m. p. and mixed m. p. 124—126°, $[\alpha]_D$ +34° (*c* 1·01). Elution with benzene (300 c.c.) gave an impure acetate (40 mg.) as needles, m. p. 135—143°, $[\alpha]_D$ +20° (*c* 1·3), which was not investigated further.

Lanosta-7,9(11)-*dien*-3β-*yl Acetate* (*Dihydroagnosteryl Acetate*).—" iso-Cholesterol " (10·3 g.) in ethyl acetate (300 c.c.) was hydrogenated at 20° over Adams catalyst (0·5 g.). After filtration and evaporation of the solvent the product was acetylated. The lanost-8-enyl acetate was isolated as needles, m. p. 103—110°, raised by recrystallisation from methanol–ethyl acetate to 117—119°, and by several recrystallisations from methanol–ethyl acetate or methanol–chloroform to 120—122°, $[\alpha]_D$ +62° (*c* 0·98). Light absorption: max. 2430 Å [ε = 624 (4% diene content)].

The acetate (4·0 g.) in benzene (100 c.c.) was treated with a 0·25M-benzene solution of perbenzoic acid (1 : 1 mol., 42 c.c.) at 20° for several days. The solution was washed with 10% sodium hydrogen carbonate solution and water and dried (Na_2SO_4). The residual " oxide," m. p. 138—140°, obtained after removal of the benzene, was dissolved in acetic acid (80 c.c.) and brought to reflux temperature. Twelve drops of concentrated sulphuric acid were added, and the solution was allowed to cool to 20°. Dilution with water and isolation with ether gave a solid which was adsorbed from light petroleum (200 c.c.) on alumina (200 g.). Elution with light petroleum (1 l.) gave dihydroagnosteryl acetate, m. p. 165—168°, raised by recrystallisation from methanol–acetone and methanol–ethyl acetate to 170—172°, $[\alpha]_D$ +98° (*c* 1·07), $\lambda_{max.}$ 2360, 2430, and 2510 Å (ε 16,600, 19,500, and 12,800).

The acetate was hydrolysed with methanolic potassium hydroxide containing some chloroform, to give dihydroagnosterol as needles, m. p. 150—154°, raised by recrystallisation from methanol–acetone to 158—159°, $[\alpha]_D$ +74° (*c* 0·98). This had $\lambda_{max.}$ 2360, 2430, and 2510 Å (ε 14,950, 17,800, and 11,700).

Dihydroagnosterol (500 mg.) was oxidised with chromic acid in the usual manner,[9] to give lanosta-7,9(11)-dien-3-one as plates (from methanol–ethyl acetate), m. p. 127—129°, raised by recrystallisation from methanol–acetone to 130—132°, $[\alpha]_D$ +54° (*c*, 1·05). This ketone had $\lambda_{max.}$ 2360, 2430, and 2510 Å (ε 15,950, 17,200, 11,500).

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[9] Bowers, Halsall, Lemin, and Jones, *J.*, 1953, 2548.