

METHYLSTEROIDS*

VI. THE " ISOMERIZATION " OF LANOST-8-EN-3,7,11-TRIONE†

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In 1941 when the structure of lanost-8-en-3,7,11-trione (I) was unknown, Wieland and Joost (1941) reported its conversion to an isomer when a solution in 10 per cent. methanolic potassium hydroxide was refluxed for 4 days. The melting point (232° C) of this isomer appeared to us to be too high for a triketone of this series, and moreover, with the structure now known, isomerization appeared impossible. Nevertheless, experiment showed that prolonged refluxing did, as Wieland and Joost reported, give a material with this high melting point, and we have now shown this to be di-(3,7,11-trioxolanost-8-en-2 ξ yl)methane (II).

In the region around 270 m μ the ultraviolet absorption spectra of I and the new material were identical, showing that the chromophore was unchanged, and that no additional unsaturation had been introduced near a carbonyl group. The infra-red absorption spectra showed no major differences between the two compounds, and in particular no hydroxyl group was present. A molecular weight determination (Rast) showed that in some way two molecules of the triketone had combined, but the data excludes a simple aldol condensation (Wallach 1896).

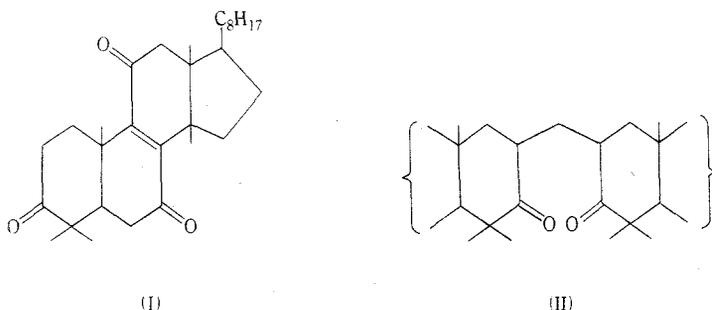
The most likely alternative seemed to be a coupling by a methylene group derived from formaldehyde either present in the solvent or formed from it by base-catalysed hydrogen transfer. This was established by refluxing I with paraformaldehyde in methanolic potassium hydroxide when the product (II) was deposited in 80 per cent. yield within a minute of the addition of paraformaldehyde. In the absence of added paraformaldehyde the yield was less than 50 per cent. even after several hours. The configuration at the 2-position is not assigned, because although it is likely that the substituent is equatorial, the extreme insolubility of the product causes it to precipitate before equilibration could occur. This condensation, which is analogous to the dimedone-formaldehyde reaction, has been studied with simple cyclic ketones by Cologne, Dreux, and Delplace (1954).

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† For Part V of this series see Barnes (1958).

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Lanost-8-en-3-one and cholestan-3-one underwent similar reactions in methanolic alkali, but not with higher alcohols, so that this condensation in methanol is likely to be general for steroidal 3-ketones. The products (type II) were rather unreactive and no satisfactory derivatives were prepared. Oximation gave products which could not be purified and which had nitrogen contents indicating reaction of more than one carbonyl. Pyrolyses also gave no recognizable product.



Experimental

(i) *General*: See Part V (Barnes 1958).

(ii) *Condensation of Ketones with Formaldehyde*:

- (1) Lanost-8-en-3,7,11-trione (I; 0.5 g) was dissolved in methanol (10 ml) and added to a solution of sodium hydroxide (15 g) in methanol (100 ml). Paraformaldehyde (200 mg) in dilute methanolic sodium hydroxide (10 ml) was added to the refluxing solution. After 30 sec further reflux the deposited crystals (400 mg, 80%) were filtered off and recrystallized from acetone, acetic acid, or *n*-propanol. Only from the last was unsolvated *di*-(3,7,11-trioxolanost-8-en-2 ξ yl)methane obtained having m.p. 239–240 °C (sealed tube), $[\alpha]_D +245^\circ$, λ_{max} , 270 m μ ϵ 9,000 (Found: C, 79.5; H, 10.3%; mol. wt., $900 \pm 5\%$. Calc. for $C_{61}H_{92}O_6$: C, 79.5; H, 10.0%; mol. wt., 921).
- (2) In a similar way lanost-8-en-3-one reacted with formaldehyde to give *di*-(3-oxo-lanost-8-en-2 ξ yl)methane, m.p. 233–234 °C (sealed tube), $[\alpha]_D \pm 0^\circ$, λ_{max} , 290 m μ ϵ 80 (Found: C, 84.5; H, 11.5%. Calc. for $C_{61}H_{100}O_2$: C, 84.7; H, 11.7%).
- (3) In a similar way cholestan-3-one gave *di*-(3-oxo-cholestan-2 ξ yl)methane, m.p. 259–261 °C (sealed tube), $[\alpha]_D +10^\circ$ (Found: C, 84.0; H, 11.5%. Calc. for $C_{55}H_{82}O_2$: C, 84.1; H, 11.8%).

References

- BARNES, C. S. (1958).—*Aust. J. Chem.* **11**: 546.
 COLOGNE, J., DREUX, J., and DELPLACE, H. (1954).—*C.R. Acad. Sci. Paris* **238**: 1237.
 WALLACH, O. (1896).—*Ber. dtsh. chem. Ges.* **29**: 2965.
 WIELAND, H., and JOOST, E. (1941).—*Liebigs Ann.* **546**: 103.