

A Simple Method for the Reduction of the 7,8-Double Bond of Steroidal 5,7-Dienes

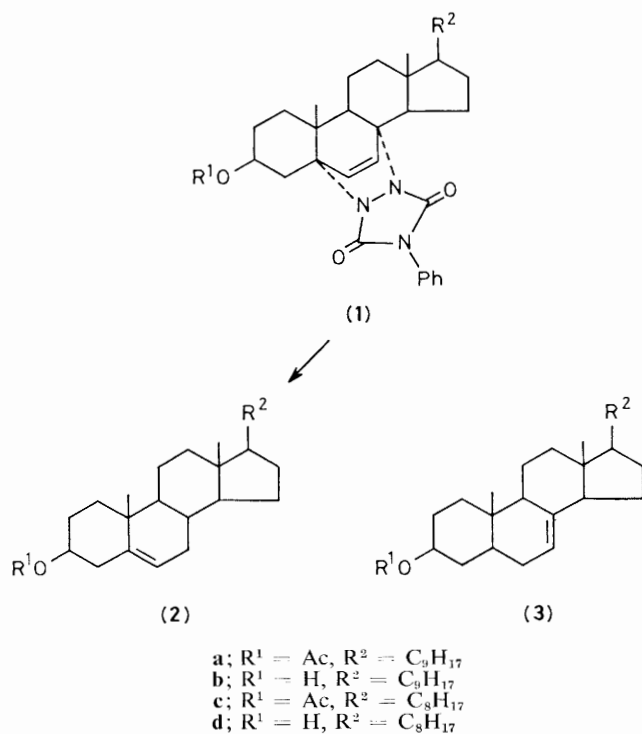
Mario Anastasia, Pierangela Ciuffreda, and Alberto Fiecchi*

Institute of Chemistry, School of Medicine, University of Milan, via Saldini, 50, I-20133 Milano, Italy

1,4-Cycloadducts of various steroidal 5,7-dienes and 4-phenyl-1,2,4-triazoline-3,5-dione gave a separable mixture (3 : 2) of the corresponding Δ^5 - and Δ^7 -sterols in good yield when treated with lithium dissolved in refluxing ethylamine.

Catalytic hydrogenation or chemical reduction of the 5,6-double bond of steroidal 5,7-dienes is a well known reaction for the formation of Δ^7 -compounds.^{1,2} In contrast no simple method is available for the reduction of the 7,8-double bond

leading to the Δ^5 -compounds. Hitherto this result has been obtained only in the 3-hydroxy-series, by protection of the 3 β -hydroxy- Δ^5 -system as the 6 β -hydroxy-3 α ,5 α -cyclo-system followed by successive transformations.³ On the other hand



the saturation of the 7,8-double bond of cholesta-5,7-dien-3 β -ol and ergosterol occurs in one step in the biological formation of cholesterol⁴ and brassicasterol.⁵

We report here the first simple method for the reduction of the 7,8-double bond by the action of lithium dissolved in ethylamine on adducts derived from steroidal 5,7-dienes and 4-phenyl-1,2,4-triazoline-3,5-dione. The reaction affords the Δ^5 -sterols accompanied by the Δ^7 -isomer in a 3:2 ratio, determined after isolation by chromatography on silica gel G-Celite-AgNO₃ (1:1:0.3; v:v:w). The reaction of the ergosterol acetate adduct (**1a**)⁶ is representative. The adduct

(**1a**) (0.5 g) dissolved in anhydrous ethylamine (5 ml) was treated with lithium (0.5 g) and the mixture was stirred at reflux for 30 min longer than required for the initial appearance of a blue colour. After the usual work-up and chromatography, brassicasterol (**2a**)[†] was obtained in 40% yield, separated from 5 α -ergost-7-en-3 β -ol (**3a**) (27% yield). Analogous results were obtained with the ergosterol adduct (**1b**)⁶ and in the cholesterol series with (**1c**) and (**1d**).⁷

When the reaction was carried out at lower temperatures the yield of the Δ^7 -sterols was greater than that of the Δ^5 -isomers. At -78 °C the reaction afforded the Δ^7 -sterols in 65–70% yield accompanied by trace amounts of the isomers. Δ^7 -compounds were the only product when liquid ammonia (-78 °C) was used as the solvent.

This method is useful owing to its simplicity and speed and it appears to be mimetic of the enzymatic route. It may be applicable to sterols lacking a 3-hydroxy group.

This work was supported by the Italian Research Council, Progetto Finalizzato Chimica Fine e Secondaria.

Received, 26th May 1982; Com. 602

References

- 1 W. Trados and A. L. Boulos, *Helv. Chim. Acta*, 1975, **58**, 668.
- 2 L. F. Fieser and M. Fieser, 'Steroids,' Reinhold, New York, 1959, p. 261, and references cited therein.
- 3 M. J. Thompson, C. F. Cohen, and S. M. Lancaster, *Steroids*, 1965, **5**, 745.
- 4 A. Fiecchi, M. Galli Kienle, A. Scala, G. Galli, E. Grossi Paoletti, F. Cattabeni, and R. Paoletti, *Proc. R. Soc. London, Ser. B*, 1972, **180**, 147.
- 5 W. R. Nes, *Adv. Lipid Res.*, 1977, **15**, 233.
- 6 D. H. R. Barton, T. Shiori, and D. A. Widdowson, *J. Chem. Soc., C*, 1971, 1968.
- 7 N. Bosworth, A. Emke, J. M. Midgley, C. J. Moore, W. B. Whalley, G. Ferguson, and W. C. Marsh, *J. Chem. Soc., Perkin Trans. 1*, 1977, 805.

[†] All compounds gave correct analyses and spectral data.