Retro-1,4-cycloaddition of Adducts Derived from Steroidal-5,7-dienes and 4-Phenyl-1,2,4-triazoline-3,5-dione

By MASAO TADA* and ATSUSHI OIKAWA

(*The Research Institute for Tuberculosis and Cancer, Tohoku University, Seiryomachi* 4–1, *Sendai* 980, *Japan*)

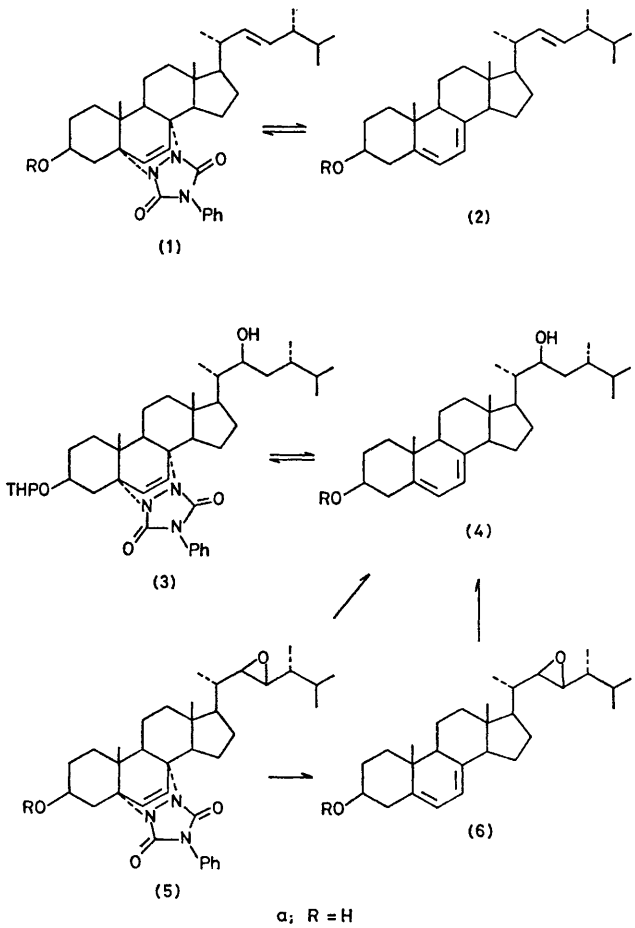
Summary Heating at 120 °C of 1,4-cycloadducts of various steroidal-5,7-dienes and 4-phenyl-1,2,4-triazoline-3,5-dione with mineral base in an appropriate solvent gives the corresponding steroidal-5,7-dienes in high yields.

CONJUGATED dienes may be protected by reaction with a dienophile; 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) undergoes cycloaddition to steroidal-5,7-dienes providing 1,4-cycloadducts.[1,2] Barton *et al.*[2] reported that the diene system could be regenerated in high yield by treatment of these adducts with lithium aluminium hydride. As part of our investigation of reversible protection of steroidal-5,7-diene systems, we report here a simple method for the retro-1,4-cycloaddition of adducts derived from steroidal-5,7-dienes and PTAD.

The adduct (**1b**)[2](1 mmol) and anhydrous K_2CO_3 (1 mmol) in dimethyl sulphoxide† were heated at 120 °C for 7 h with stirring to give ergosteryl acetate (**2b**) in quantitative yield. An analogous result was obtained with the ergosterol adduct (**1a**).[1,2] The retro-1,4-cycloaddition of (**1c**), m.p. 154—155 °C, obtained from either (**1a**) or (**2c**),[3] in the presence of anhydrous K_2CO_3 in Me_2SO also afforded (**2c**) in quantitative yield. When pyridine was used in place of K_2CO_3, the retro-addition of adducts (**1**) proceeded so slowly that 90% of (**1**) was recovered. In the conversion of (**1**) into (**2**), Me_2SO and *NN*-dimethylformamide were better solvents than ethylene glycol or methyl cellosolve. Yields were optimum at 120 °C and for 7 h reaction. Cleavage of (**1b**) using an aqueous solvent system was accompanied by removal of the acetyl group of (**1b**) to furnish ergosterol (**2a**)

† All solvents were dried with molecular sieves and all new compounds gave correct analyses and spectral data.

in 88% yield. Adduct (**3**) (m.p. 142—144 °C; 74%) derived from the ether (**4c**) was converted into (**4c**) in 95% yield under similar conditions. Treatment of (**4c**) with dilute HCl in ethanol gave the diol (**4a**) in high yield. Crump *et al.* reported that the reduction of (**5b**) with $LiAlH_4$ gave the 22-hydroxy derivative (**4a**), the position of the hydroxy group being confirmed by mass spectroscopy.[4] Treatment of (**5c**) with $LiAlH_4$ in an analogous fashion gave a 3:1 mixture of the 22-hydroxy compound (**4c**), m.p. 169—170 °C, and the 23-hydroxy compound, m.p. 133—134 °C, the locations of the hydroxy groups being established by mass spectral analysis of their trimethylsilyl derivatives, prepared with *NO*-bis(trimethylsilyl)acetamide in pyridine. Treatment of (**4c**) with acetic anhydride and *p*-chlorobenzoyl chloride in pyridine afforded the acetate, m.p. 163—164 °C, and the *p*-chlorobenzoate, m.p. 201—202 °C, respectively.



Treatment of the adduct (**5b**),[4] derived from (**1b**), under similar conditions resulted in retro-cycloaddition without affecting the epoxide ring to give 22,23-epoxyergosteryl acetate (**6b**), m.p. 133—134 °C, in 83% overall yield from (**1b**). The adduct (**5c**) was prepared by epoxidation of (**1c**) with *m*-chloroperbenzoic acid in CH_2Cl_2. The analogous conversion of (**5c**) gave 22,23-epoxyergosteryl tetrahydropyranyl ether (**6c**), m.p. 138—139 °C, in 91% yield based on (**1c**). Hydrolysis of (**6c**) with HCl in ethanol furnished 22,23-epoxyergosterol (**6a**), m.p. 138—139 °C, in 94% yield. Compound (**6a**) was also obtained in 95% yield by heating (**6b**) for 10 min with 2N KOH in refluxing aqueous methanol. Reduction of (**6c**) with $LiAlH_4$ gave both (**4a**) and the 23-hydroxy derivative in a ratio of 1:4, in contrast to the reduction of the adduct (**5c**).

Treatment of the 1,4-cycloadduct (m.p. 156—157 °C) of 7-dehydrocholesterol and PTAD in an analogous fashion gave a 52% yield of 7-dehydrocholesterol.

This method is useful because of its simplicity and the high yields obtained as well as its applicability to compounds having groups which are sensitive to $LiAlH_4$.

We thank Dr. Kyozo Ogura, Tohoku University, for the mass spectral determinations and helpful discussions.

(*Received, 2nd May* 1978; *Com.* 470.)

[1] S. H. Gilani and D. J. Triggle, *J. Org. Chem.*, 1966, **31**, 2397.
[2] D. H. R. Barton, T. Shioiri, and D. A. Widdowson, *Chem. Comm.*, 1970, 939; *J. Chem. Soc.* (*C*), 1971, 1968.
[3] M. Z. Nazer, *J. Org. Chem.*, 1965, **30**, 1737.
[4] D. R. Crump, D. H. Williams, and B. Pelc, *J.C.S. Perkin I*, 1973, 2731.

Printed by Heffers Printers Ltd Cambridge England