

Dienone-Phenol Rearrangement of Sulphur-containing Derivatives of Steroids

James Y. Satoh,^{*a} Amos M. Haruta,^a Toyoyuki Satoh,^a Keiichi Satoh,^a and Thomas T. Takahashi^b

^a Department of Chemistry, St. Paul's (Rikkyo) University, Nishi-Ikebukuro, Toshima-ku, Tokyo 171, Japan

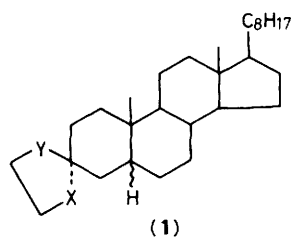
^b Department of Chemistry, The Jikei University School of Medicine, Kokuryo, Chofu, Tokyo 182, Japan

Dienone-phenol rearrangement occurs in the reaction of an oxathiolane and dithiolane of 3-oxo-steroids with copper(II) bromide to give 4-methyl-19-norcholesta-1,3,5,(10)-trieno[1,2-*b*]-dihydroxathiine and -dihydrodithiine, respectively.

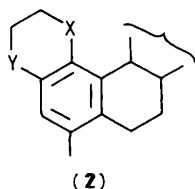
Reports on dienone-phenol type rearrangements in steroids have been limited almost entirely to highly unsaturated compounds, such as cross-conjugated dienone and trienone derivatives,¹ or labile compounds,^{2a} such as epoxy-derivatives.^{2b-d} No research of this type has been reported for sulphur-containing derivatives of steroids. We now report that rearrangement occurs in the reaction of oxathiolane derivatives of 3-oxo-steroids, which are stable saturated compounds, with copper(II) bromide to give 4-methyl-19-norcholesta-1,3,5(10)-trieno[1,2-*b*]-dihydroxathiine, (**2a**).

The reaction was carried out as follows. A solution of the 3 α -O-oxathiolane (**1a**) (1 g) of 5 α -cholestan-3-one and cop-

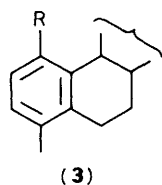
per(II) bromide (2.5 g, 5 mol equiv.) in dioxane (40 ml) was refluxed for 3 h. The mixture was poured into ice-cold water and the resultant precipitate was filtered off. The filtrate was extracted with diethyl ether, and then the extract was chromatographed on silica-gel with light petroleum-benzene. Crystallization of the first fraction from methanol-ethanol gave 4-methyl-19-norcholesta-1,3,5(10)-trieno[1,2-*b*]-dihydroxathiine (**2a**), 525 mg, 52%; m.p. 106–107.5 °C; i.r. (KBr-disk, cm⁻¹) 863; ¹H n.m.r. (CDCl₃, δ) 2.15 (s, 3H, Ar-CH₃), 2.95–3.15 (br. t, 2H, S-CH₂), 4.15–4.45 (br. t, 2H, O-CH₂), 6.50 (s, 1 H, Ar-H); *m/z* 440. In order to determine the configuration of the product of aromatization,



- a; X = O, Y = S, 5 α -H d; X = S, Y = O, 5 β -H
 b; X = S, Y = O, 5 α -H e; X = Y = S, 5 α -H
 c; X = O, Y = S, 5 β -H f; X = Y = S, 5 β -H



- a; X = O, Y = S
 b; X = Y = S



- a; R = OH
 b; R = H

compound (2a) was desulphurized with Raney-Ni catalyst, and then C-O bond cleavage was carried out with boron tribromide. Crystallization of the reaction product from hexane gave 1-hydroxy-4-methyl-19-norcholesta-1,3,5(10)-triene (3a): m.p. 146–147 °C (lit.^{1a} 145–146 °C); i.r. (KBr-disk, cm⁻¹) 805, 808; ¹H n.m.r. (CDCl₃, δ) 2.10 (s, 3H, Ar-CH₃), 4.28 (s, 1H, Ar-OH), 6.27 and 6.69 (AB-type, *J* 7 Hz, 2H, Ar-H).

Compound (1b) (the 3 α -S-oxathiolane derivative of 5 α -cholestan-3-one) and a mixture of (1c) and (1d) (the 3 α -O- and 3 α -S-oxathiolane derivatives of 5 β -cholestan-3-one) react smoothly, as does (1a), to give (2a) in 40 and 37% yields respectively.

In the cases of dithiolanes (1e) and (1f) of 5 α - and

5 β -cholestan-3-one, the reaction proceeded as for the oxathiolanes to give the Δ -aromatized steroid (2b), 76%; oil; ¹H n.m.r. (CDCl₃, δ) 2.12 (s, 3H, Ar-CH₃), 2.95–3.45 (m, 4H, S-CH₂), 6.88 (s, 1H, Ar-H). Since crystallization of this product was not successful, the aromatization product was reductively desulphurized with Raney-Ni. Crystallization of the reduction product from methanol-water gave 4-methyl-19-norcholesta-1,3,5(10)-triene (3b); m.p. 50–51 °C (lit.³ 49 °C); i.r. (KBr-disk, cm⁻¹) 776, 736; ¹H n.m.r. (CDCl₃, δ) 2.13 (s, 3H, Ar-CH₃), 6.85 (m, 3H, Ar-H).

In the case of the dioxolane derivative, bromination took place only at the α -position,⁴ but the rearrangement could not be observed. It may be concluded from this phenomenon that the progress of the present reaction is determined by the affinity between the Cu^{II} ion and the heteroatom of the acetal ring.

The present work is the first case of a dienone-phenol rearrangement, including a double 1,2-shift of an alkyl group (C-9) via a cationic spiran intermediate, for sulphur-containing derivatives of a steroid by copper(II) bromide. Accordingly, the present work is not only a valuable application of copper(II) bromide in organic chemistry, but also an available synthetic pathway for steroids containing a sulphur atom.

Received, 12th August 1986; Com. 1157

References

- (a) H. H. Inhoffen and Huang-Minlon, *Naturwissenschaften*, 1938, **26**, 756; (b) J. Romo, C. Djerassi, and G. Rosenkranz, *J. Org. Chem.*, 1950, **15**, 896; (c) R. L. Clarke, K. Dobriner, A. Mooradian, and C. M. Martini, *J. Am. Chem. Soc.*, 1955, **77**, 661; (d) J. A. Waters and B. Witkop, *J. Org. Chem.*, 1969, **34**, 1601; (e) J. Elks, J. F. Oughton, and L. Stephenson, *J. Chem. Soc.*, 1961, 4531.
- (a) J. Libman and Y. Mazur, *Chem. Commun.*, 1971, 729; (b) J. R. Hanson, *ibid.*, 1971, 1119; (c) *ibid.*, 1971, 1343; (d) D. Baldwin and J. R. Hanson, *J. Chem. Soc., Chem. Commun.*, 1974, 211.
- H. Dannenberg and H.-G. Neumann, *Liebigs Ann. Chem.*, 1961, **646**, 148.
- J. Y. Satoh, C. T. Yokoyama, A. M. Haruta, K. Nishizawa, M. Hirose, and A. Hagitani, *Chem. Lett.*, 1974, 1521.