

## Dienone-Phenol Rearrangement of Sulphur-containing Derivatives of Steroids

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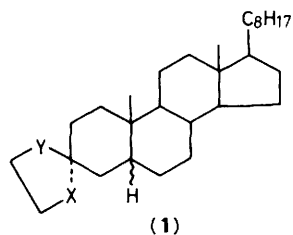
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Dienone-phenol rearrangement occurs in the reaction of an oxathiolane and dithiolane of 3-oxo-steroids with copper(II) bromide to give 4-methyl-19-norcholesta-1,3,5,(10)-trieno[1,2-*b*]-dihydroxathiine and -dihydrodithiine, respectively.

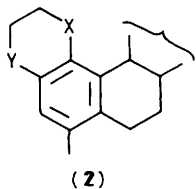
Reports on dienone-phenol type rearrangements in steroids have been limited almost entirely to highly unsaturated compounds, such as cross-conjugated dienone and trienone derivatives,<sup>1</sup> or labile compounds,<sup>2a</sup> such as epoxy-derivatives.<sup>2b-d</sup> No research of this type has 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 $\alpha$ -O-oxathiolane (**1a**) (1 g) of 5 $\alpha$ -cholestan-3-one and cop-

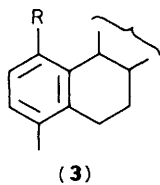
per(II) bromide (2.5 g, 5 mol equiv.) in dioxane (40 ml) was refluxed for 3 h. The mixture was poured into ice-cold water and the resultant precipitate was filtered off. The filtrate was extracted with diethyl ether, and then the extract was chromatographed on silica-gel with light petroleum-benzene. 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<sup>-1</sup>) 863; <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>,  $\delta$ ) 2.15 (s, 3H, Ar-CH<sub>3</sub>), 2.95–3.15 (br. t, 2H, S-CH<sub>2</sub>), 4.15–4.45 (br. t, 2H, O-CH<sub>2</sub>), 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 $\alpha$ -H      d; X = S, Y = O, 5 $\beta$ -H  
 b; X = S, Y = O, 5 $\alpha$ -H      e; X = Y = S, 5 $\alpha$ -H  
 c; X = O, Y = S, 5 $\beta$ -H      f; X = Y = S, 5 $\beta$ -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.<sup>1a</sup> 145–146 °C); i.r. (KBr-disk, cm<sup>-1</sup>) 805, 808; <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>,  $\delta$ ) 2.10 (s, 3H, Ar-CH<sub>3</sub>), 4.28 (s, 1H, Ar-OH), 6.27 and 6.69 (AB-type, *J* 7 Hz, 2H, Ar-H).

Compound (**1b**) (the 3 $\alpha$ -S-oxathiolane derivative of 5 $\alpha$ -cholestan-3-one) and a mixture of (**1c**) and (**1d**) (the 3 $\alpha$ -O- and 3 $\alpha$ -S-oxathiolane derivatives of 5 $\beta$ -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 $\alpha$ - and

5 $\beta$ -cholestan-3-one, the reaction proceeded as for the oxathiolanes to give the A-aromatized steroid (**2b**), 76%; oil; <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>,  $\delta$ ) 2.12 (s, 3H, Ar-CH<sub>3</sub>), 2.95–3.45 (m, 4H, S-CH<sub>2</sub>), 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.<sup>3</sup> 49 °C); i.r. (KBr-disk, cm<sup>-1</sup>) 776, 736; <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>,  $\delta$ ) 2.13 (s, 3H, Ar-CH<sub>3</sub>), 6.85 (m, 3H, Ar-H).

In the case of the dioxolane derivative, bromination took place only at the  $\alpha$ -position,<sup>4</sup> 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<sup>II</sup> 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.

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## 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.