## A CONVERSION OF CHOLEST-4-EN-3-ONE INTO CHOLEST-5-EN-ONE\*

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Cholest-4-en-3-one (I) has been converted into cholest-5-en-3-one (III) (Birch 1950) through the salt II (R=K) obtained by the action of potassium amide in liquid ammonia on the enol-acetate (II, R=Ac) of I. This type of movement of a double bond from a conjugated to an unconjugated position is potentially of considerable use in synthesis and has been employed in the total synthesis of some non-aromatic steroids (Cardwell et al. 1951, 1953; Woodward et al. 1951). In connection with other work in this field (Birch, Quartey, and Smith 1952) processes are being sought which are more practicable than that already used. The cholestenone conversion has been used as a model, although in the meantime the chief problem with which it is associated—the preparation in good yield of cholesterol-has been solved by a one-stage hydrolysis and reduction with sodium borohydride (Belleau and Gallagher 1951; Dauben and Eastham 1951). It is also of considerable interest that tert.-butyl magnesium chloride causes enolization of I to give II (R=MgCl) (Belleau and Gallagher 1951), although potassium amide failed to do so (Birch 1950). In view of these results we have abandoned further work on the preparation of cholesterol.

Potassium amide in ammonia was originally used merely to demonstrate the feasibility of the process; it was realized that the reagent has drawbacks from a practical point of view. An attempt was first made to replace it with ethyl magnesium bromide. From the product cholest-5-en-3-one could be isolated in poor yield but was accompanied by a large proportion of non-ketonic material which was not further examined. Attention was then turned to methyl-

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anilinomagnesium bromide, which would be expected to cause fission of the enol-acetate by analogy with the reaction of anilinomagnesium bromide with esters (Hardy 1936). In fact, a 50 per cent. yield of III was obtained without difficulty. The reagent should be useful with molecules containing other active groups, and other ketones are now being examined. Attempts to prepare enamines by the action of piperidine in boiling benzene on I or II (R=COCH<sub>3</sub>) did not give the compounds of the desired structure, since the action of acid regenerated I together with what may be polymers. According to the results of Mannich and Kniss (1941) any 3-piperidinocholesta-3,5-diene should have given rise to III.\*

The Grignard reagent from magnesium  $(0 \cdot 295 \text{ g}; 3 \text{ mol})$ , ethyl bromide and methylaniline  $(2 \cdot 16 \text{ g}; \text{ excess})$  in ether (25 c.c.) was cooled in ice and the enol-acetate (II, R=Ac)  $(1 \cdot 70 \text{ g})$  in a small volume of ether added. After 1 hr at room temperature hydrochloric acid (5 per cent.) was added, the ether layer separated and rapidly washed with dilute acetic acid (10 per cent.), water, saturated sodium bicarbonate solution, water, and then dried (sodium sulphate). After evaporation of the solvent the residue was twice crystallized from ethanol to give cholest-5-en-3-one  $(0 \cdot 75 \text{ g})$ , m.p.  $122-124 \,^{\circ}\text{C}$ ,  $[\alpha]_D - 2 \cdot 2^{\circ}$  (in chloroform). It was further characterized by reduction with lithium aluminium hydride to cholesterol, m.p.  $144-145 \,^{\circ}\text{C}$ , undepressed by an authentic specimen, m.p.  $147-148 \,^{\circ}\text{C}$ ,  $[\alpha]_D - 39 \cdot 5^{\circ}$  (in chloroform).

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<sup>\*</sup> Note added in Proof.—Since this work was completed Heyl and Herr (1953) have shown that a 3,5-dienamine can be prepared using pyrrolidine. We confirm this, but find the substance unexpectedly difficult to hydrolyse, and under conditions leading to hydrolysis only the 4-unsaturated ketone is obtained.