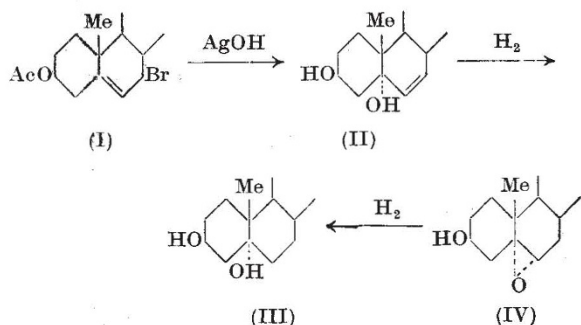


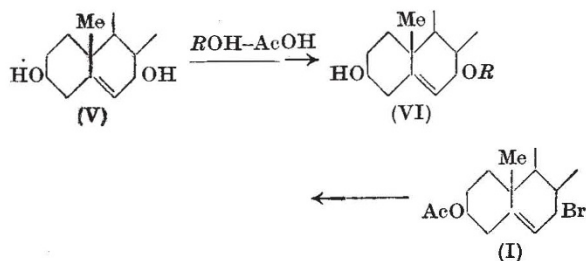
### Etherifications Accompanying Girard Treatment for the Separation of Ketonic Substances

THE reagents devised by Girard and Sandulesco<sup>1</sup> for the separation of ketonic substances are widely employed in a variety of fields, especially for the isolation of ketonic steroids. Although the conditions under which these reagents are normally employed are comparatively mild, it has now been shown that, in certain cases, etherification of reactive alcohols can occur.

During the investigation of the reactions of 'β'-7-bromocholesteryl acetate<sup>2</sup> (I), we have discovered that one of the products obtained by alkaline hydrolysis is Δ<sup>5</sup>-cholestene-3-(β):5(α)-diol (II). This compound, m.p. 181°, is readily hydrogenated to cholestane-3(β):5(α)-diol (III), previously prepared<sup>3</sup> by hydrogenation of α-cholesterol-oxid<sup>4</sup> (IV).



Only two Δ<sup>5</sup>-cholestene-3(β):5-diols, differing in configuration at C<sub>5</sub>, can possibly exist, and two such 'diols' had already been tentatively assigned this structure. Bergström and Wintersteiner<sup>4</sup> obtained a compound, m.p. 138°, from 'β'-7-hydroxycholesterol (V) by refluxing in ethanol containing 10 per cent of acetic acid. Prelog, Ruzicka and Stein<sup>5</sup> isolated a compound, m.p. 155.5–156°, from the non-saponifiable portion of extracts of pig spleen, which they suggested might be an isomer of the Bergström and Wintersteiner diol. The reactions of these two substances were consistent with the formulations suggested, but in neither case was any rigorous structural proof obtained, for example, by hydrogenation, etc.



We have now shown that the former compound is actually 'β'-7-ethoxycholesterol (VI; R = Et), formed by a facile acid-catalysed etherification reaction; substitution of methanol for ethanol in this reaction gives 'β'-7-methoxycholesterol (VI; R = Me), m.p. 158°. These formulations are supported by analytical data, including methoxyl and ethoxyl determinations.

Treatment of 'β'-7-bromocholesteryl acetate (I) either with sodium methoxide or with silver nitrate and methanol, followed by alkaline hydrolysis, also yields 'β'-7-methoxycholesterol (VI; R = Me). It was observed that its physical constants and those of its acetate and benzoate were in close agreement with those of the supposed diol obtained from pig spleen<sup>5</sup>, and mixed melting point determinations, kindly carried out by Dr. Prelog, confirmed the identity of the products.

Bergström and Wintersteiner<sup>4</sup> first isolated what has now been shown to be the 7-ethoxy-compound, following the Girard separation of the ketonic and non-ketonic materials obtained by aerial oxidation of cholesterol, the separation being effected in the usual manner in ethanol solution in the presence of acetic acid. Although these workers realized that the 7-hydroxy-compound had undergone some change during the treatment, their supposition of an isomerization reaction was incorrect. Prelog *et al.*<sup>5,6</sup> employed the Girard reagent in methanol, and it is reasonably certain that the 7-methoxy-steroid does not occur in the natural material, but that it is formed during the Girard separation from 'β'-7-hydroxycholesterol originally present in the extract.

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Nov. 18.

<sup>1</sup> Girard, A., and Sandulesco, G., *Helv. Chim. Acta*, **19**, 1095 (1936).

<sup>2</sup> Henbest, H. B., Jones, E. R. H., Bide, A. E., Peever, R. W., and Wilkinson, P. A., *Nature*, **158**, 169 (1946).

<sup>3</sup> Plattner, Pl. A., Petzalkler, Th., and Lang, W., *Helv. Chim. Acta*, **27**, 513 (1944). Plattner, Pl. A., and Lang, W., *Helv. Chim. Acta*, **27**, 1872 (1944).

<sup>4</sup> Bergström, S., and Wintersteiner, O., *J. Biol. Chem.*, **143**, 503 (1942); **141**, 597 (1941).

<sup>5</sup> Prelog, V., Ruzicka, L., and Stein, P., *Helv. Chim. Acta*, **26**, 2222 (1943).

<sup>6</sup> Prelog, V., and Ruzicka, L., *Helv. Chim. Acta*, **26**, 986 (1943).

### Analysis of Boron Trifluoride: a Double Compound of Silicon Tetrafluoride and Trimethylamine

IN connexion with nuclear cross-section studies in which boron trifluoride was used as a reference gas, a method of analysis of this gas was devised based on the condensation of boron trifluoride with acetyl fluoride to form acetyl fluoborate. This material is involatile at -120° C., and volatile impurities from the boron trifluoride can easily be pumped off and their volume determined<sup>1</sup>.

During these studies, particular attention was paid to silicon tetrafluoride as the most likely volatile impurity remaining in the gas after two fractional distillations *in vacuo* at -160° C.

The volume of the sample of boron trifluoride to be analysed was determined in a calibrated bulb attached to the vacuum apparatus, in which mercury cut-offs were used throughout in place of stopcocks. It was then frozen out in liquid nitrogen in a bulb attached to a 300-c.c. reaction vessel, and an excess of acetyl fluoride prepared by the method of Nesmejaow and Kahn<sup>2</sup> afterwards condensed in the same trap. On warming, the gases volatilized and reacted. The contents of the vessel were pumped out slowly through an efficient liquid-nitrogen trap, the temperature of the condensate was raised to -120°, and the silicon tetrafluoride collected and