

PREPARATION OF 7-DEHYDROCHOLESTEROL, AND OF 7-OXYCHOLESTEROL.

By: ANDRÁS KRÁMLI.

From the Hungarian Biological Research Institute, Tihany, Lake
Balaton.

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7-dehydrocholesterol was first made by WINDAUS, LETTRÉ and SCHENCK (1935). Essentially their procedure was to disintegrate the dibenzoate of 7-oxycholesterol in a high vacuum at a temperature of 220°C. Then with the appearance of a molecule of benzoic acid, dehydration occurs between the carbon atoms Nos. 7 and 8 and, besides 1 molecule of benzoic acid, there results benzoate of 7-dehydrocholesterol, from which, after hydrolysis, 7-dehydrocholesterol is produced.

In the present work we speak of a process whereby the preparation of 7-dehydrocholesterol from 7-oxycholesterol takes place in one step. In the beginning we carried out the experiments with the usual methods of dehydration but they gave an unidentifiable resinous product. Good results were obtained with an oxalic acid water solution as dehydrolizing agent. Employing different concentrations of oxalic acid we found a 55—60% solution to be the most suitable. Use of a more dilute oxalic acid brought about a weaker production as judged by the rotatory power of the raw product. It is very difficult to isolate and purify the product because of the presence of subsidiary materials. Improvement in production and perfection in isolation are in process of experiment.

The starting material used, 7-oxycholesterol, was prepared by WINDAUS and co-workers from acetate of 7-ketocholesterol after MEERWEIN and PONNDORF's method with isopropylate of aluminium. In the present work the idea occurred of reducing 7-ketocholesterol in an alcoholic medium with alkali metals. As the reduction brought about by metallic sodium in the alcoholic medium results in an unidentifiable, dark product, experiments were carried out to slow down the speed

of the reaction with indifferent solvents. The best result was obtained by reduction in a mixture of dried benzene and methyl alcohol at room temperature. The reaction mixture then shows no darkening and the isolation of the product causes no difficulties.

The acetate of 7-ketocholesterol, which MAUTHNER and SUIDA (1896) first described, took place by anodic oxidation from cholesteryl acetate.

Details of experiment.

Preparation of 7-oxycholesterol.

2. g 7-ketocholesterol is dissolved in a mixture of 100 ml benzene and 180 ml abs. methyl alcohol. To this solution 16 g metallic sodium is very gradually added, while keeping it at a temperature of less than 20°C. When the sodium is entirely dissolved the mixture is poured into 500 ml water. Liquids in 2 layers result. The upper, benzene layer is separated, then washed with dilute solution of sodium hydroxide and finally several times with water. It is dried with water-free sodium sulphate and evaporated in vacuum. From the remaining light yellow oil the 7-oxycholesterol crystallises on rubbing with 50 ml petrole-ether, the resulting crystals are separated by filtration and recrystallized repeatedly in a mixture of benzene and hexan. A snow-white crystallized powder results with a melting point of 168—174°C, which heated with chloralhydrate gives a strong blue colour reaction, in a chloroform solution with concentrated sulphuric acid, a dark violet. When it is recrystallized with ethyl alcohol the melting point mounts to 176—178°C.

Remark: Acetate of 7-ketocholesterol can also be employed as starting material. The acetyl group splits off in the course of the reaction.

Preparation of 7-dehydrocholesterol.

10 g 7-oxycholesterol is dissolved in 50 ml boiling ethyl alcohol and the hot solution emulsified in 100 ml 60% oxalic acid water solution. From this emulsion the alcohol is evaporated over a water bath and the remaining mixture is boiled again until the resulting reaction-product condenses into drops of yellow oil, which takes place after about 1—1 1/2 hours of heating. The reaction mixture is cooled and the product, stiffened into a solid mass, taken up in ether. This ether

solution is washed with water, then several times with dilute solution of sodium hydroxide, then dried with water-free sodium sulphate, and evaporated. To eliminate the effect of oxidation by air the processes described are carried out in carbondioxide atmosphere.

The substance remaining after the evaporation of the ether solution is crystallized in a mixture of ether and methyl alcohol. A white substance results which, when exposed to air, turns lemon yellow, composed of small, flat crystals, strongly laevo-rotatory, which melts unsharp, with decomposition, giving up its water of crystallisation at between 100—130°C. The product dissolves well in ether, hexan and chloroform. It is difficult to dissolve in methyl alcohol and ethyl alcohol. Further purification takes place by repeated crystallization from ether-methyl alcohol, when the melting point rises to 140°C. Its chloroform solution with sulphuric acid and with chloralhydrate shows an intense violet-blue colouration.

Remark: Part of the experiments were carried out in the research laboratories of the Gedeon Richter, S. A., Pharmaceutical Mfg. Co. Budapest.

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