# DEMETHYLATION IN THE SYNTHESIS OF OCTESTROL

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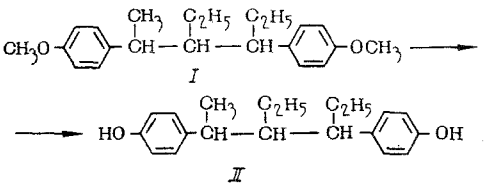
The synthesis of octestrol [2,4-di(hydroxyphenyl)-3-ethylhexane] (II), which is used for the treatment of failure of ovarian function, involves in the last stage the conversion of methoxyl groups into phenolic hydroxyls:



I



II

This reaction is effected by heating I in ethanol solution with alkali at 210°C and 90 atm in an autoclave.

It is highly undesirable to carry out this reaction at high pressures in an aggressive solvent, and at high temperatures.

Literature methods for the conversion of ethers into phenols fall into two main categories, i.e., reaction of the former with either basic or acidic reagents [1].

Our attempts to carry out such conversions in the synthesis of octesterol at atmospheric pressure were not crowned with success. The desired product was either not obtained at all, or it was obtained in very low yields.

In order to avoid the use of high pressures in the synthesis, we reacted I with a fivefold excess of potassium hydroxide in diethylene glycol at 245° and atmospheric pressure. By boiling this mixture for 12 h, octestrol was obtained in a yield of 74.7%.

Current technology at the Kharkov plant for endocrine preparations gives a yield of 73.7% of desired product.

The quality of the material obtained by the new method satisfies the requirements of the USSR State Pharmacopeia, 10th edition.

## EXPERIMENTAL

A mixture of 50 g of I, 85 g of potassium hydroxide, and 270 ml of diethylene glycol was boiled on a bath of Wood's metal for 12 h, diluted with 1.5 liters of water, and acidified with hydrochloric acid until acid to Congo Red. The precipitate was filtered off, washed with water, and dried. The technical product was dissolved in 300 ml of dichloroethane, 1 g of decolorizing charcoal was added, and the mixture was heated for 10 min and filtered. On cooling to 0 to −5°, the II crystallized from the filtrate in a yield of 34 g (74.5%), mp 161-162°.

## LITERATURE CITED

1. K. Byuler and D. Pirson, in: Synthesis of Organic Compounds [in Russian], Part 1, Moscow (1973), p. 288.

Kharkov Plant for Endocrine Preparations. Kharkov Scientific-Research Institute for Endocrinology and the Chemistry of Hormones. Translated from Khimiko-Farmatsevticheskii Zhurnal, Vol. 11, No. 3, pp. 91-92, March, 1977. Original article submitted August 3, 1976.