

ALIEN PROPERTY CUSTODIAN

PROCESS FOR THE DECOMPOSITION OF CHOLESTENONE AND OF HALOGEN DE- RIVATIVES THEREOF

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The object of our invention is a process for the decomposition of cholestenone and of halogen derivatives thereof.

Our former investigations have proved, that by a quick and cautious oxidation of cholestenone in a medium of glacial acetic acid at temperatures below 15° C and by the use of only 4.5 mol of chromium oxide to 1 mol of cholestenone, after removing the unchanged starting material and the acidic by-products, practically merely progesterone can be obtained. By other known processes for the oxidation of cholestenone with chromium oxide (see e. g. Zeitschrift für physiolog. Chemie, Vol. 252, p. 49) a mixture consisting of progesterone and of androstendione has been obtained, undergoing thereafter to highly circumstantial methods of separation, connected with considerable losses of material.

Our further experiments concerning the decomposition of the cholestenone and of some derivatives thereof have proved that almost merely androstendione can be obtained by a more vigorous and lasting action of the oxidizing agent on the starting material.

We have found that cholestenone and halogen derivatives thereof advantageously can be decomposed to androstendione by oxidation of the starting material with chromium oxide in a medium of glacial acetic acid, until practically no progesterone accompanying the androstendione can be detected in the product.

Moreover we have found that the yield and the purity of the androstendione are not satisfying, if the oxidation was carried out at elevated temperatures and with great quantities of chromic oxide. Preferably the cholestenone is oxidized at temperatures below 15° C, by the action of 4.5 mol of chromium oxide to 1 mol of cholestenone during a suitable long period, lasting 24 to 48 hours. By this method satisfying quantities of pure androstendione can be separated from the products of the reaction.

By the process according to the invention one of the derivatives of the cholestenone, the 4,5,6-tribromcholestenone can be oxidized so that almost merely androstendione is obtained from the product after having removed the bromine therefrom.

Example 1

400 grammes of cholestenone are dissolved in 25 litres of glacial acetic acid and to the solution 500 grammes (4.5 mol) of chromium trioxide dissolved in 25 litres of glacial acid are added. The temperature of the reacting mixture is kept below 13 to 15° C during the addition, as well as during 48 hours following thereafter, the content of chromium trioxide of the solution being diminished thereby about to 0.4%. The unchanged chromium trioxide is then decomposed by gradual addition of methanol, taking care

thereof of keeping the temperature below 15° C. The solution is then evaporated in vacuum, below 35° C, to a volume of 20 litres and diluted with water to a volume of 80 litres. The precipitated product is twice washed with 10 litres of benzene each time, the benzene-extract is washed with water, with 2 n-sodium hydroxyde and then with water again, dried with anhydrous sodium sulphate and evaporated in vacuum. The volatile components of the residue are separated by steam-distillation and the remaining product is dissolved in 1,5 litres of benzine. The benzine-solution is shaken out two times with 500 cubic centimetres of 2 n-sodium hydroxide each, and then with distilled water. In order to separate the androstendione the benzine-solution is extracted three times with 1500 cubic centimetres of concentrated hydrochloric acid and the united acid-solutions are diluted to a volume of 12 litres. The androstendione precipitated in a fine emulgated condition is twice shaken out with 2 litres of ether, the ether-solution is washed with water, with n-sodium hidroxide, with diluted hydrochloric acid and with water again, dried with anhydrous sodium sulphate and then evaporated to dryness, 7,2 grammes of a light-yellow coloured oil are obtained, from which after adding some ether and cooling 2,5 grammes of pure androstendione crystallize out. From the mother liquor further quantities of androstendione can be obtained. The product re-crystallized from ether shows a melting point of 167-170° C. From the benzine-solutions remaining after the treatment with hydrochloric acid 100 grammes of cholestenone can be recovered.

Example 2

62,4 grammes of pulverized crude 4,5,6-tribromcholestenone are suspended in 2500 cubic centimetres of glacial acetic acid and to the stirred solution 75 g (7.5 mol) chromium trioxide dissolved in 40 cubic centimetres of water and 400 cubic centimetres of glacial acetic acid are added during a period lasting 4 hours. During the addition the temperature of the reacting mixture is kept at 35° C and thereafter, during 24 hours, at 15° C.—50 cubic centimetres of methanol are then added to the cooled solution and, after the decomposition of the abundance of chromium trioxide the bromine is removed by adding 100 grammes of zinc powder, keeping the temperature below 35° C thereat. The filtered solution is evaporated at 35° C to a volume of 700 cubic centimetres and the residue is worked up according to the method disclosed in Example 1. The end-product is 1 gramme of a glass-like material containing 280 milligrammes of androstendione. 12 grammes of cholestenone are obtained as a by-product.

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