UNITED STATES PATENT OFFICE.

LORENZ ACH, OF MANNHEIM, GERMANY, ASSIGNOR TO C. F. BOEHRINGER & SOEHNE, OF MANNHEIM-WALDHOF, GERMANY.

PROCESS OF PREPARING ALKYLIZED PURINS.

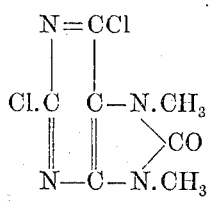
SPECIFICATION forming part of Letters Patent No. 676,861, dated June 25, 1901.

Application filed July 23, 1897. Serial No. 645,691. (Specimens.)

To all whom it may concern:

Be it known that I, LORENZ ACH, a citizen of the Empire of Germany, residing at Mannheim, in the Empire of Germany, have invented certain new and useful Improvements in Preparing Alkylized Purins; and I do hereby declare the following to be a full, clear, and exact description of the invention, such as will enable others skilled in the art to which it appertains to make and use the same.

The present application relates to the art of obtaining derivatives of the class of compounds known as "purins," and described, for example, in *Berichte der Deutschen Chemischen Gesellschaft*, Vol. 17, pages 328 and 1786, and *Abstracts of the British Chemical Society*, Vol. 44, page 996. It relates more particularly to the preparation of alkylized halogen purin derivatives, such as the alkylized dichloropurins, of which dichlor-oxy-dimethyl-purin having the formula



is an example. (*Berichte*, Vol. 17, pages 328 and 1787; *Abstracts*, Vol. 44, page 996.) These bodies have formerly been obtained from various alkyl derivatives of uric acid and xanthin, such as theobromin or caffein, by causing phosphorus penta-chlorid in connection with phosphorus oxy-chlorid acting as a solvent to act upon them. (*Berichte der Deutschen Chemischen Gesellschaft*, Vol. 17, page 330, and Vol. 28, page 2480.) These processes, however, involve the use of expensive raw materials and are hence inapplicable for the production of these compounds on a commercial scale.

It is the purpose of this invention to overcome these objections, and with this purpose in view the same consists in a method which primarily involves the action of haloid ethers upon halogen oxy-purins free from alkyl radicals, which I have been the first to obtain and for which I have filed an application for Letters Patent of the United States, executed concurrently herewith and filed June 14, 1897, Serial No. 640,762, the said application describing and claiming the same and the method of their preparation.

My invention also consists in such further steps, methods, and features as will be hereinafter set forth and then particularly pointed out in the claims hereunto annexed.

I have found as the result of my experiments and investigations that, for example, alkylized dichlor-oxy-purins may readily be obtained by the reaction which takes place when such alkylizing agents as halogen-alkyls or other esters suitable for alkylizing purposes—such as alkyl nitrates, alkyl sulfates, di-alkyl sulfates, the alkyl esters of benzyl-sulfo-acids, &c.—are brought together with the salts of dichlor-oxy-purin. For this purpose the dry salts may be taken or they may be employed in aqueous solution or dissolved in concentrated or dilute alcohol. In all cases the reaction takes place smoothly and without difficulty. By the action of one or two molecules of the haloid ether upon the acid salt or the neutral salt, respectively, one or both hydrogen atoms respectively of the imido groups of the dichlor-oxy-purin are replaced by an alkyl radical. When the methyl radical is thus introduced, we obtain bodies which have already been obtained in other ways—viz., β-dichlor-oxy-methyl-purin, (E. Fischer in *Berichte der Deutschen Chemischen Gesellschaft*, Vol. 28, page 2490,) or dichlor-oxy-dimethyl-purin, (E. Fischer in *Berichte der Deutschen Chemischen Gesellschaft*, Vol. 17, page 333.)

The following examples will serve to illustrate my invention in detail, and they embody what I at present consider the best method of carrying out my invention:

1. Alkylizing a dry salt—Preparation of dimethyl-chlor-oxy-purin.—Four hundred grains, corresponding to one molecule of the dry neutral lead salt of dichlor-oxy-purin, ($PbC_5N_4OCl_2$,) are heated with three hundred grams (corresponding to two molecules) of methyl iodid and one hundred and fifty cubic centimeters of ether to from 100° to 110° centigrade in a closed vessel and maintained at this temperature for twelve hours. The resulting mass is boiled out or extracted with

alcohol. The dichlor-oxy-dimethyl-purin separates out from the concentrated filtrate in needles of fine appearance, which melt at 187° centigrade after recrystallizing out of alcohol. The following equation expresses the reaction taking place:

$$PbC_5N_4OCl_2+2ICH_3=(CH_3)_2C_5N_4OCl_2+PbI_2.$$

2. Alkylizing in dilute alcohol solution—Preparation of mono-methyl-chlor-oxy-purin.—One kilogram of dichlor-oxy-purin (corresponding to one molecule) is dissolved in water by the addition of seven hundred grams (corresponding to two molecules) of caustic potash. The solution is mixed with equal volume of alcohol and cooled off. Then seven hundred grams (corresponding to one molecule) of methyl iodid is added, and the mixture is allowed to stand for forty-eight hours in a cooling-chamber or refrigerator. The reaction takes place according to the following equation:

$$K_2C_5N_4OCl_2+ICH_3=K(CH_3)C_5N_4OCl_2+KI.$$

The resulting dichlor-oxy-methyl-purin is then separated out in fine crystals after evaporating off the alcohol and acidulating, according to the following equation:

$$K(CH_3)C_5N_4OCl_2+HCl=(CH_3)HC_5N_4OCl_2+KCl.$$

Other caustic alkalies may be used in the above process, and both reactions may be carried out by using other haloid ethers than the methyl iodid or other esters suitable for alkylizing purposes—such as alkyl nitrates, alkyl sulfates, dialkyl sulfates, alkyl esters of benzyl-sulfo-acids, &c.—as explained above. However, I consider methyl iodid the best example. Other haloid-oxy-purin derivatives may also be employed. It is manifest, therefore, that the methods above described may be greatly varied without departing from my invention.

It is to be observed that my invention under one of its aspects involves the action upon a salt of dichlor-oxy-purin with an alkylizing ester, whether such salt is already formed, as in the first example hereinabove given, or is formed during the process, as in the second example, and the second claim hereunto appended covers both of these methods.

What I claim, therefore, and desire to secure by Letters Patent, is—

1. The process which consists in acting upon the salt of a di-haloid-purin with an alkylizing agent.

2. The process which consists in acting upon a salt of dichlor-oxy-purin with an ester suitable for alkylizing.

3. The process which consists in acting upon the salt of a di-haloid-oxy-purin with a haloid ether.

4. The process which consists in acting upon a salt of dichlor-oxy-purin with methyl iodid.

5. The process which consists in treating dichlor-oxy-purin with an alkali and then acting upon the salt so formed with an alkylizing ester.

6. The process which consists in dissolving dichlor-oxy-purin together with an alkali and subsequently treating the solution with an alkylizing ester.

7. The process which consists in dissolving dichlor-oxy-purin in water, together with caustic alkali, then adding alcohol and cooling, and then adding a haloid ether and cooling.

8. The process which consists in dissolving dichlor-oxy-purin in water together with caustic potash, then adding alcohol and cooling, then treating with methyl iodid, and finally cooling.

9. The process, which consists in dissolving dichlor-oxy-purin in water, together with caustic potash, then adding alcohol and cooling, then treating with methyl iodid and cooling, and finally separating the resulting dichlor-oxy-methyl-purin by evaporating the alcohol.

In testimony whereof I affix my signature in presence of two witnesses.

LORENZ ACH.

Witnesses:
FR. ACH,
JACOB ADRIAN.