

## UNITED STATES PATENT OFFICE

2,603,643

2-AMINO-4-HYDROXY-6-POLYHYDROXY-  
ALKYL PTERIDINE AND METHODS OF  
OXIDIZING SAME

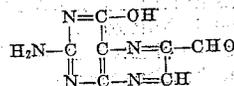
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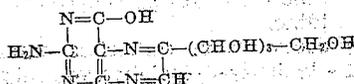
12 Claims. (Cl. 260—251.5)

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The present invention relates to the manufacture of a pteridin derivative, more specifically of 2-amino-4-hydroxy-6-pteridyl-aldehyde, which can be represented by the formula



It has been found according to the present invention that 2-amino-4-hydroxy-6-pteridyl-aldehyde can be obtained by condensing, in faintly acidic solution, 2,4,5-triamino-6-hydroxypyrimidine with a ketohexose and subsequently oxidizing the 2-amino-4-hydroxy-6-(tetrahydroxybutyl)-pteridine which can be represented by the following formula



with an oxidant suitable for effecting glycolic cleavage. The condensation may be carried out in the presence of hydrazine. Potassium periodate, lead tetra. acetate and red lead ( $\text{Pb}_3\text{O}_4$ ), for instance, are suitable as oxidants.

The product thus obtained is useful as an intermediate for the preparation of folic acid.

*Example 1*

10 parts by weight of 2,4,5-triamino-6-hydroxy-pyrimidine-dihydrochloride, 12 parts by weight of d-fructose, 12.8 parts by weight of sodium acetate (crystallised with 3  $\text{H}_2\text{O}$ ), and 120 parts of water are warmed on a steam bath while carbondioxide is passed through. Within a few minutes a clear solution is formed and shortly thereafter a precipitate begins to separate. After lapse of 4½ hours, the reaction mixture is cooled, the precipitate is sucked off, successively washed with water, alcohol and ether and dried at 80° C. The yield amounts to 2 parts by weight. The crude 2-amino-4-hydroxy-6-(tetrahydroxybutyl)-pteridine thus obtained can be used as such for the preparation of 2-amino-4-hydroxy-6-pteridyl-aldehyde, as described below; if desired, it may however be purified by recrystallisation from hot water after addition of charcoal. A yellowish microcrystalline powder decomposing above 280° C. without melting is obtained.

30 parts by weight of 2-amino-4-hydroxy-6-(tetrahydroxybutyl)-pteridine are dissolved in 5000 parts by volume of 10 per cent. aqueous acetic acid. A solution of 67.5 parts by weight of lead tetra. acetate in 1000 parts by volume

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of glacial acetic acid is added dropwise in the course of 2 hours at a temperature of 80° C. while stirring. Then an amount, equivalent to the lead salts present, of sulphuric acid, is added as well as 10 parts by weight of charcoal and stirring is continued for a short time. The hot solution is filtered and the filtrate is concentrated in vacuo to about 500 parts by volume. After cooling down the precipitate of 2-amino-4-hydroxy-6-pteridyl-aldehyde is sucked off, successively washed with water, alcohol and ether and dried at 80° C. The yield amounts to 14.2 parts by weight.

*Example 2*

15 18.8 parts by weight of 2,4,5-triamino-6-hydroxy-pyrimidine. hydrochloride, 14.6 parts by weight of sodium acetate (containing 3 mols of water of crystallisation), 7 parts by weight of glacial acetic acid, 19.2 parts by weight of d-fructose and 6 parts by weight of hydrazine hydrate are heated for 7 hours in 180 parts of water on a steam bath. It was found to be advantageous to displace the air in the reaction vessel by an inert gas such as carbon dioxide or nitrogen in order to prevent oxidation of the 2,4,5-triamino-6-hydroxy-pyrimidine. At the beginning of the reaction all the solid substances gradually dissolve and later the condensation product formed separates in solid form. After cooling, the reaction mixture is filtered by suction, successively washed with water, alcohol and ether and dried at 80° C. The yield amounts to 16.3 parts by weight of 2-amino-4-hydroxy-6-(tetrahydroxybutyl)-pteridine. A pure product is obtained by dissolving the condensation product in 100 per cent. formic acid, treating the solution with charcoal and precipitating by the addition of water.

This compound is transformed into 2-amino-4-hydroxy-6-pteridyl-aldehyde, according to the indications in Example 1.

*Example 3*

A mixture of 321 parts by weight of 2,4,5-triamino-6-hydroxy-pyrimidine-dihydrochloride, 270 parts by weight of 1-sorbose, 320 parts by weight of anhydrous sodium acetate, 270 parts by weight of glacial acetic acid, 83 parts by weight of hydrazine hydrate and 1800 parts of water is heated to 80° C. while stirring well. This results first in the formation of a complete solution and sometime later 2-amino-4-hydroxy-6-(tetrahydroxybutyl)-pteridine begins to separate. After stirring for 6 hours at the temperature indicated above the mixture is cooled down to room temper-