United States Patent Office.

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BROMOTHEOPHYLLIN AND PROCESS OF MAKING SAME.

SPECIFICATION forming part of Letters Patent No. 571,353, dated November 17, 1896.

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To all whom it may concern:

Be it known that I, EMIL FISCHER, a citizen of Germany, residing at Berlin, Germany, have invented a certain new and useful Compound, Bromotheophyllin, and Process of Preparing the Same; 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.

This invention relates to the manufacture of derivatives of theophyllin; and it consists in the new compound, bromotheophyllin, and the process of obtaining the same, all as will be hereinafter set forth, and more particularly

pointed out in the claims.

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I have found, as the result of experiments, that a compound which I term, "bromotheophyllin," and which has the formula C₅H 20 (CH₂)₂BrN₄O₂, or

$$CH_3.N-C.B_1$$
 $COC-NH$
 $COC-NH$
 COC
 $CH_3.N-C=N$

may be obtained by heating theophyllin together with bromin under pressure.

The following is the preferred method in which I propose to carry my invention into practice: One part of finely-powdered theophyllin, which has been dried at 110° centi-

grade, is heated with five parts bromin to 100° centigrade and retained at that temperature for several hours in a tightly-closed vessel. Thereupon, to remove the excess of bromin, the vessel is opened and the temperature of the contents is raised to 150° centigrade and held there until the evolution and escape of free bromin has ceased. The residue is then triturated or otherwise comminuted and then treated with aqueous sulfurous acid

in excess and gently heated, for the purpose of completely discolorizing the same. The crude bromotheophyllin so obtained is then completely purified by dissolving it in lye, such as soda-lye, and treated with animal charcoal. Thereupon the product is precipitated out of the lye-bath by acid, and the

5° precipitate is then recrystallized with alcohol. This_bromo derivative of the ophyllin pos-

sesses certain valuable properties, viz: The physiological action of it on the organism is the same as that of caffein and theobromin. Doses 0.5 to 1.5 grains.

Bromotheophyllin is soluble with some difficulty in warm alcohol, and from such solutions it crystallizes in small, thin, colorless, spear-shaped crystals, which melt at a temperature which is not quite constant and 60 which is between 315° and 320° centigrade. In melting they are colored brown and completely decomposed.

In water the bromotheophyllin is soluble with great difficulty, even at a high heat. It 65 is readily taken up in dilute alkalies, including ammonia, while strong alkalies precipitate its alkali salts from its aqueous solution in crystalling forms.

in crystalline form.

The silver salt of bromotheophyllin is pre-70 cipitated from an ammoniacal solution of the same.

By the addition of silver nitrate to an ammoniacal solution of the bromotheophyllin the silver salt of the same is precipitated first 75 as an amorphous colorless precipitate, which becomes granular, however, on boiling. This silver salt is soluble in much ammonia, and upon evaporating the ammonia by boiling it separates in the form of a colorless crystal- 80 line precipitate consisting of very small needles. Its formula, as above stated, is:

$$CH_{3}.N-C.Br$$
 $CO C-NH$
 $CO C-NH$
 $CO_{3}.N-C=N$
 $CO_{3}.N-C=N$

or $C_5H(CH_3)_2BrN_4O_2$.

What I claim, and desire to secure by Let- 90 ters Patent, is—

1. The process which consists in mixing theophyllin with bromin, and then heating the mixture, substantially as set forth.

2. The process which consists in mixing 95 theophyllin with bromin, and then heating the mixture under pressure, substantially as set forth.

3. The process which consists in mixing theophyllin with bromin in the proportion 100 of one part of the former to five parts of the latter, then heating the mixture to 100° cen-

tigrade, and retaining the same at this temperature in a closed vessel, substantially as set forth.

4. The process which consists in the following steps: first, mixing theophyllin and bromin in the proportion of one part of the former to five parts of the latter, then heating the mixture in a closed vessel to 100° centigrade, and retaining it at that temperature for several hours, then opening the vessel and raising the temperature to about 150° centigrade, to drive off the excess of bromin, substantially as set forth.

5. The process which consists in mixing theophyllin with bromin, then heating the mixture under pressure, and then driving off the excess of bromin and purifying the residue, substantially as set forth.

6. The process which consists in the following steps: first, mixing theophyllin and bromin in the proportion of one part of the former to five parts of the latter, then heating the mixture in a closed vessel to 100° centigrade, and retaining it at that temperature for several hours, then opening the vessel and raising the temperature to about 150°

centigrade, to drive off the excess of bromin,

and then purifying the residue, substantially as set forth.

7. The process which consists in mixing 30 theophyllin with bromin in the proportion of one part of the former to five parts of the latter, then heating the mixture to 100° centigrade, and retaining the same at this temperature in a closed vessel, then driving off 35 the excess of bromin, then decolorizing the residue, then dissolving the crude bromotheophyllin obtained in lye and treating with animal charcoal, and finally precipitating it by acid and recrystallizing the precipitate 40 from alcohol, substantially as set forth.

8. As a new compound, bromotheophyllin having the formula hereinbefore stated, whose melting-point is between 315° and 320° centigrade, which is soluble with difficulty in alcohol and water, but readily taken up by dilute alkalies.

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

EMIL FISCHER.

Witnesses:

OSCAR GUNNERLING, P. REHLÄNDER.