To all whom it may concern:

Be it known that I, Fritzi Ach, a citizen of the Empire of Germany, residing at Mannheim, in the Empire of Germany, have invented certain new and useful Improvements in the Art of Preparing Xanthins; 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 xanthins and their derivatives, and more particularly the preparation of this class of bodies from alkylized uric acids. In order to define more exactly the ground which this invention occupies in the art, it is to be stated that a method has heretofore been found of obtaining the halogen derivatives of alkylized xanthins by the action of phosphorus-chlorid thereon, the xanthins, themselves, being then obtained by reducing the halogen derivatives. This method has been set forth in United States Patents to Emil Fischer, Nos. 565,415 and 569,490, dated October 13, 1896.

According to these patents such conversion was, however, only possible for such alkyl-uric acids as contained two alkyl groups in the alloxan ring and whose structure would be represented by the general formula:

\[
\begin{align*}
(1) & \quad \text{RN} - \text{CO} \\
(2) & \quad \text{OC}(3)\text{O} - \text{NH} \\
(3) & \quad \text{RN} - \text{C} - \text{NH}(9) \\
(4) & \quad \text{CO}(8)
\end{align*}
\]

adapting the nomenclature and system of numbering the carbon and nitrogen atoms of the purin nucleus, which have been introduced by Emil Fischer and described in Beilstein der Deutschen Chemischen Gesellschaft, Vol. 30, page 549—that is to say, only such alkyl-uric acids in which alkyl groups were bound to the molecule both at the position 1 and position 3 could according to that method be converted into xanthins. To proceed from mono-methyl-uric acids or from other dimethyl-uric acids to halogen or chlo-

roxanthins has hitherto been impossible. My investigations and experiments in this field have resulted in the discovery that all uric acids which have not been completely alkylized may be converted into the corresponding chloro-xanthins provided no alkyl group has been bound to the nitrogen atom in the position 9. In the latter case only chloro-purines would result. This discovery demonstrates that, contrary to the opinion hitherto entertained, it is immaterial for the preparation of xanthins from uric acids whether the nitrogen atoms 1 and 3—i.e., those in the alloxan ring—are alkylized or not. All that is material in this respect is that the nitrogen atom 9 be not alkylized. I have, moreover, ascertained as a result of my investigations that it is necessary to act upon the alkylized uric acid with phosphorus-oxy-chlorid alone in order to proceed to xanthins and that this result cannot be attained if the phosphorus-oxy-chlorid acts on the alkyl-uric acid in conjunction with phosphorus-penta-chlorid, for example. A comparison of the entirely and essentially different results obtained by acting on the same alkyl-uric acid first with phosphorus-oxy-chlorid together with phosphorus-penta-chlorid, according to the methods heretofore known, and then with phosphorus-oxy-chlorid alone, will serve admirably to emphasize the essence of the present invention. Thus if, for example, 7-monomethyl-uric acid is submitted to the joint action of phosphorus-oxy-chlorid and phosphorus-penta-chlorid the oxygen bound to the alloxan ring alone is replaced by chlorin, the resultant compound being 7-methyl-8-oxy-3-6-dichloropurin:

\[
\begin{align*}
\text{HN} - \text{CO} & \quad \text{N} = \text{C}, \text{Cl} \\
\text{OC} & \quad \text{C} - \text{N}, \text{CH}_2 \\
\text{HN} - \text{C} - \text{NH} & \quad \text{N} - \text{C} - \text{NH}
\end{align*}
\]

If, however, phosphorus-oxy-chlorid alone is caused to react on 7-monomethyl-uric acid, chlorin is substituted for the oxygen occupying the position 8, whereby the xanthin derivative 7-methyl-3-6-dioxy-3-chloropurin or 7-methyl-chloro-xanthin is obtained.
The chloro-xanthins are converted into the corresponding xanthins by reducing methods. It is to be noted that under my invention other alkyl radicals than the methyl group may be introduced into the xanthin molecule. Thus the 3-methyl-chloro-xanthin is readily converted into 3-methyl-1,7-diethyl-chloro-xanthin by introducing the ethyl radical into the former.

For the purposes of my invention it is unimportant whether the lower chloro-xanthins are first alkylized and then reduced, or vice versa. In both ways I may proceed to the higher alkylized xanthins, such as caffeine.

My invention, whose object is to obtain xanthins from uric acids, accordingly, broadly considered, consists in submitting alkylized uric acids, which, however, have no alkyl group at the position 9 to the action of phosphorus-oxy-chlorid. The said invention, moreover, consists in the subsequent reduction and alkylization of the resultant compounds, and, moreover, in the special products and subprocesses, all as will be hereinafter specified, and pointed out in the claims hereunto annexed.

I will now proceed to fully disclose my invention for those skilled in the art by giving in detail a number of examples embodying what I consider the best manner of carrying said invention into effect.

1. Preparation of Halogen Derivatives of Alkylated Xanthins from the Corresponding Uric Acids.

1. Preparation of 3-methyl-chloro-xanthin from 3-methyl-uric acid. — One part of anhydrous 3-methyl-uric acid is added to five parts by volume, of phosphorus-oxy-chlorid and heated under pressure, or, in a digester, to from 130° to 140° centigrade, and maintained at this temperature for from three to four hours, the mass being steadily agitated. The resulting clear reddish-brown solution is then evaporated in vacuo for the purpose of completely removing the phosphorus-oxy-chlorid. The brownish residue, which has a tough varnish-like consistency, is thereupon brought into solution by boiling the same with about five times its quantity of alcohol or water. The alcoholic solution, which at first is clear, but soon becomes turbid on account of the precipitation of granular crystalline methyl-chloro-xanthin, is boiled for from two to three hours in a reflux-condenser and then allowed to cool. Upon then filtering the methyl-chloro-xanthin remains on the filter as a yellow granular crystalline mass.

The filtrate is then evaporated, whereby a second crystallization ensues, resulting in a further yield of the above product—methyl-chloro-xanthin. The crude product so obtained is brought into solution with dilute alkali, such as two per cent. potash-lye, treated with animal charcoal or other decolorizing agent, and finally precipitated with dilute sulfuric acid. On cooling, the new
compound is obtained in the form of yellow-
hued coarse crystals, from whose analysis
are obtained figures which show the formula
of this compound to be C₆H₅N₃O₄Cl + H₂O.
10
Its structural formula is found to be:
\[
\text{HN} - \text{C} - \text{O} \\
\text{OC} - \text{C} - \text{NH} \\
\text{CH₃} - \text{C} - \text{N} - \text{C} - \text{Cl}
\]
such formula being established by the fact of
the ready conversion of this compound into
chloro-cafein. (See under II 1a.) Therefore
designate this new compound as 3-meth-
ilylchloro-xanthin or 3-methyl-8-chloro-xan-
thin. The tenaciously-adhering yellow tint,
which is very difficult of removal, has no in-
fluence on the percentage composition of the
product.

20
Absolute decoloration of the methyl-chloro-
xanthin may be attained by thoroughly boil-
ing it with a large quantity (thirty parts to
one part of the methyl-chloro-xanthin) of
acetone. The xanthin is thereby gradually
brought into solution, while the adhering col-
inger matter remains undissolved. Upon
cooling after such solution is effected the
methyl-chloro-xanthin crystallizes in anhy-
drous fine colorless shining foliated crystals
or scales.

25
3-methyl-chloro-xanthin is soluble in about
two hundred and fifty parts boiling water,
and on cooling the solution slowly the same
crystallizes therefrom in coarse needles, which
under the microscope are found to be elong-
ated flat prisms and which contain one mole-
cule of water of crystallization. This water
of crystallization escapes on protracted heat-
ing at 120° centigrade. It is difficult of solu-
tion in boiling alcohol, in acetone, acetic-
ether, benzene, or chloroform, readily soluble
in dilute alkalies, in ammonia and soda, or
potash solutions. It is equally soluble in
40
concentrated sulfuric acid and fuming hy-
drochloric acid. From a solution in the lat-
ter the original product is precipitated by
50
water on standing for some time. Heated
with chlorin water or with dilute nitric acid
it gives a strong murexid reaction. An am-
moniacal solution of the same added to an
ammoniacal silver solution yields a gelati-
nous silver-salt which remains unchanged on
boiling.

55
3-methyl-chloro-xanthin has no melting-
point; but on being rapidly heated it begins
to turn yellow at 320° centigrade, and at about
60 345° centigrade it decomposes with efferves-
cence.

65
2. Preparation of 7-methyl-2,6-dioxy-8-
chloropurin or chloro-heteroxanthin from 7-
monomethyl-uric acid. — One part, by weight,
of dried and finely-powdered 7-mono-methyl-
uric acid is added to ten parts, by volume of
phosphorus-oxy-chlorid and boiled for from
twenty-four to thirty hours in a reflux-con-
denser. This treatment results in the solution
of methyl-uric acid, a clear slightly-colored
70 liquor being formed. This liquor is evapo-
rated in vacuo, and the tough, varnish-like
residue is taken up with warm alcohol. Af-
ter boiling such solution a short time the
chloro-heteroxanthin is thrown out in the
75 form of a colorless crystalline mass, which is
separated by filtration. This product is not
quite pure, but is contaminated with some
unchanged methyl-uric acid, which may be
removed by boiling with much acetone, which
80 dissolves the chloro-heteroxanthin but not
the methyl-uric acid. The acetone solution
is then evaporated, and the resulting crys-
talline residue is taken up with dilute amma-
nia, treated with decolorizing carbon, and pre-
85 cipitated with dilute sulfuric acid. The 7-
methyl-chloro-xanthin or chloro-heteroxan-
thin is thereby obtained in the form of color-
less short prismatic crystals which give
figures corresponding to the formula C₆H₅N₃
90 O₄Cl. Its structural formula is
\[
\text{HN} - \text{C} - \text{O} \\
\text{OC} - \text{C} - \text{NCH₃} \\
\text{HN} - \text{C} - \text{N} - \text{C} - \text{Cl}
\]
as is shown by its conversion into chloro-cafein.

(See II 1b.)
The chloro-heteroxanthin or 7-methyl-2,6-
dioxy-8-chloro-purin is formed about accord-
ing to the equation:
\[
\begin{align*}
3 & \text{O} - \text{O} - \text{C} - \text{NCH₃} + \text{POCl₃} = \\
& \text{HN} - \text{C} - \text{NH} - \text{C} - \text{Cl} \\
3 & \text{OC} - \text{C} - \text{NCH₃} + \text{H₃PO₄} \rightarrow \text{HN} - \text{C} - \text{N} - \text{C} - \text{Cl}
\end{align*}
\]
That this new product is a xanthin deriv-
ate is also corroborated by the fact that it
gives the murexid test with chlorin-water or
dilute nitric acid. From boiling water, in
which it is moderately soluble, it crystallizes
in short needles which are frequently aggre-
gated in bunches. It is soluble with diffi-
culty in alcohol and acetone and with very
great difficulty in benzene or chloroform. It
is readily taken up by dilute alkalies, am-
nonia, and soda or potash (carbonates) solu-
tions. An ammoniacal solution of the same, added to an ammoniacal silver solution, gives
rise to a colorless silver-salt consisting of fine
needles, which salt remains unchanged on
boiling.
Chloro-heteroxanthin has no melting point; but on being heated rapidly it becomes yellow at about 300° centigrade and is decomposed at about 340° centigrade, the decomposition being attended by dark-brown coloration and effervescence.

3. Preparation of 3-7-dimethyl-2-6-dioxy-8-chloro-purin or chloro-theobromin from 3-7-dimethyl-6-uric acid.—One part, by weight, of 3-7-dimethyl-6-uric acid which is added to the finest possible powder which has been reduced to the finest possible powder is distilled off in vacuo and the residue is dissolved with alcohol. The solution is then boiled. After a short time the chloro-theobromin which has been formed begins to crystallize out of the solution. The reaction takes place about according to the equation:

\[
\begin{align*}
\text{HN-CO} \\
3 \quad \text{OC} \quad \text{C-NCH}_3 \\
\text{CH}_3\text{N-C-N} \\
\end{align*}
\]

\[+\text{POCl}_3 = \]

\[
\begin{align*}
\text{HN-CO} \\
3 \quad \text{OC} \quad \text{C-NCH}_3 \\
\text{CH}_3\text{N-C-N} \\
\end{align*}
\]

\[+\text{H}_2\text{PO}_4.
\]

The crystals are then separated by filtration and dissolved in dilute alkali and treated with carbon for decoloration, whereupon the chloro-theobromin is thrown out by dilute sulfuric acid. The colorless product so obtained has the composition indicated by the formula \(\text{C}_9\text{H}_7\text{N}_2\text{O}_5\text{Cl}\) and the structure,

\[
\begin{align*}
\text{HN-CO} \\
\text{OC} \quad \text{C-NCH}_3 \\
\text{CH}_3\text{N-C-N} \\
\end{align*}
\]

wherefore I term it 3-7-dimethyl-2-6-dioxy-8-chloropurin or 3-7-dimethyl-8-chloroxanthin or 8-chloro-theobromin. The above structure is established by the ready and smooth conversion of this new compound into chloro-caffeine set forth under II lc.

Chloro-theobromin heated with chlorin-water or with dilute nitric acid gives the mutarotid test. On heating the same rapidly it melts at about 289° to 293° centigrade to a slightly-colored liquid, which soon congeals to a crystalline mass on cooling. It dissolves in about two hundred and fifty parts of water on boiling. From such aqueous solution it is thrown out in the form of colorless vitreous shining short prisms on cooling slowly and in the form of fine needles aggregated in bunches on cooling rapidly. It is only diffusely soluble in boiling alcohol. On the other hand it is readily soluble in dilute alkalis and dilute warm ammonia. From a solution of the same in soda-lye its sodium salt is rapidly thrown out in the form of fine acicular crystals by concentrated soda-lye. If an ammoniacal solution of the same be added to an ammoniacal silver solution and the ammonia be removed by boiling, a gelatinous colorless silver-salt of the chloro-theobromin is thrown out.

II. Conversion of the Above Halogen Derivatives into Higher Alkylated Products.

1. Preparation of chloro-caffeine. (a) From 3-methyl-chloro-xanthin.—One part, by weight, of 3-methyl-chloro-xanthin, which has been described hereinabove, is brought into solution with five and four-tenth parts, by volume, of double-normal potash-lye (potassium-hydrate) and equal parts of water, and after one and one-half parts, by weight, of methyl-lodid have been added thereto the whole is heated to 90° centigrade in the pressure-tube and maintained at this temperature for two to three hours, the mass being constantly agitated. The same is then allowed to cool, when the greater portion of the chloro-caffeine which has been formed is thrown out in the form of fine needles. The balance of the chloro-caffeine is obtained by extraction from the lyes, which have previously been rendered slightly alkaline by a suitable solvent, such as chloroform, for example. The formation of chloro-caffeine takes place according to the equation:

\[
\begin{align*}
\text{HN-CO} \\
\text{OC} \quad \text{C-N+2(CH}_3\text{I)}_2+2\text{KOH} =
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3\text{N-C-N} \\
\text{CH}_3\text{N-C-N+C}_2\text{H}_5
\end{align*}
\]

\[+2\text{KI}+2\text{H}_2\text{O}.
\]

The actual amount of chloro-caffeine obtained corresponds to the theoretical yield. It is fully purified on once recrystallizing from water and has all of the characteristic properties found for chloro-caffeine by Emil Fischer, (Annalen, Vol. 213, page 263.)

(b) From 7-methyl-chloroxanthin.—Three parts, by weight, of 7-methyl-chloroxanthin or chloro-heteroxanthin, which has been here-inbefore described, are dissolved in eighteen parts, by volume, double-normal caustic-potash lye (potassium-hydrate) and thirty-six
Here, again, the theoretical and practical yield are identical.

2. Preparation of chlorotheobromin from 3-methyl-chloroaxanthin.—Six parts, by weight, of 3-methyl-chloroaxanthin are dissolved in eighteen parts, by volume, of double-normal potash-lye (potassium-hydride solution) and thirty parts, by volume, of water. There are then added to the solution seven and two-tenths parts of methyl-sulfate of potassium, and the whole is then heated to from 140° to 150° centigrade under pressure—e.g., in a digester—this temperature being maintained for from four to five hours and the mass constantly agitated. Upon cooling the chlorotheobromin 3,7-dimethyl-8-chloroaxanthin is separated out of the solution in the form of coarse yellowish-brown granular crystals. It is purified by redissolving and crystallizing out of alkali, such as potash-lye, and possesses all of the characteristic properties, as well as the melting-point, of the chlorotheobromin described under I 3. The reaction which results in its formation proceeds according to the equation:

\[
\begin{align*}
\text{HN-CO} & \quad \text{OC} \quad \text{C-N.CH}_3+\text{CH}_3\text{I}+\text{KOH} = \quad \text{CCl} \\
\text{CH}_3\text{N-C} & \quad \text{OC} \quad \text{C-N.CH}_3+2\text{KI}+3\text{H}_2\text{O} \\
\text{CH}_3\text{N-C} & \quad \text{OC} \quad \text{C-N.CH}_3+2\text{KOH} = \quad \text{CCl}
\end{align*}
\]

In this case, also, the practical yield is equivalent to the theoretical, and the chloroaxanthin is obtained pure.

(a) Fier (a).

From chlorotheobromin.—The same treatment applied to dimethyl-chloroaxanthins, such as chlorotheobromin, which is 3,7-dimethyl-2,6-dioxo-8-chloropurin or 3,7-dimethyl-8-chloroaxanthin, will again result in the trimethyl-chloroaxanthin or chloroaxanthin.

If two parts, by weight, of the chlorotheobromin which has been described under head I 3 be dissolved in seven volumes of double-normal potash-lye (potassium-hydride) and seven volumes of water and heated to 90° centigrade under pressure, together with one and one-half parts of methyl-iodid, this temperature being maintained for three hours and the liquid constantly agitated, the formation of chloro-axanthin will take place. The greater portion of the same is thrown out in the form of fine acicular crystals after cooling, while the remainder is obtained by extraction with a suitable vehicle, such as chloroform. The following equation explains the reaction which takes place:

\[
\begin{align*}
\text{HN-CO} & \quad \text{OC} \quad \text{C-N.CH}_3+\text{CH}_3\text{I}+\text{KOH} = \quad \text{CCl} \\
\text{CH}_3\text{N-C} & \quad \text{OC} \quad \text{C-N.CH}_3+\text{KI}+\text{H}_2\text{O} \\
\text{CH}_3\text{N-C} & \quad \text{OC} \quad \text{C-N.CH}_3+2\text{KOH} = \quad \text{CCl}
\end{align*}
\]

3. Preparation of 3-methyl-1,7-dieethyl-2,6-dioxo-8-chloropurin from 3-methyl-chloroaxanthin.—Four parts, by weight, of 3-methyl-chloroaxanthin are dissolved in twenty-three parts, by volume, of double-normal potash-lye (potassium-hydride solution) and diluted with twenty parts, by volume, of alcohol. Six and one-half parts, by weight, of ethyl-iodid are then added, and the whole is boiled for from three to four hours in a reflux-condenser. The mass is then allowed to cool, when it solidifies in the form of a pulp or fine felted needles. These are then separated by filtration, redissolved in boiling water, and recrystallized therefrom. The fine acicular crystals so obtained have the composition indicated by the formula C_{28}H_{35}N_{10}O_{10}Cl or, structurally expressed,

\[
\begin{align*}
\text{C}_2\text{H}_5\text{N-CO} & \quad \text{OC} \quad \text{C-N.CH}_3 \\
\text{CH}_3\text{N-C} & \quad \text{OC} \quad \text{C-N.CH}_3
\end{align*}
\]

The reaction to which the formation of the
new compound is due proceeds according to the equation:

\[
\begin{align*}
\text{HN} & \text{-CO} \\
\text{O} & \text{C-NH} + 2(\text{C}_2\text{H}_5\text{I}) + 2\text{KOH} = \\
\text{CH}_3\text{N} & \text{-CO} \quad \text{C}_2\text{H}_5 \\
\text{O} & \text{C-N} \quad \text{C}_2\text{H}_5 + 2\text{KI} + 2\text{H}_2\text{O} \\
\text{CH}_3 & \text{N-C-N} \quad \text{CCl}
\end{align*}
\]

This new compound, with chlorin-water, gives a strong murexid reaction. Its melting-point is 180° centigrade. It is moderately soluble in boiling and diffusely soluble in cold water. It dissolves readily in hot alcohol and in cold acetone or chloroform. It is also readily soluble in fuming hydrochloric acid, being precipitated from such solution by water. It will be noted that its structure closely resembles that of chloro-caffeine, the only difference being that in lieu of the methyl groups in the positions 1 and 7 in the latter compound it has substituted ethyl groups.

\[
\begin{align*}
\text{CH}_3 & \text{-N-CO} \quad \text{C}_2\text{H}_5 & \text{-N-CO} \\
\text{O} & \text{C-NCH}_3 \quad \text{O} & \text{C-N-C}_2\text{H}_5 \\
\text{CH}_3 & \text{-N-C-N} \quad \text{CCl} & \text{CH}_3 & \text{-N-C-N} \quad \text{CCl}
\end{align*}
\]

Chloro-caffeine or 1,3,5-tri-

methyl-4-chloro-xanthin or 1,5-
tri-methyl-4-chloro-6-dioxo-

xanthin.

III. Reduction of the Halogen Derivatives to the Corresponding Xanthins.

1. Preparation of 3-methyl-2,6-dioxypyridurin or 3-methyl-xanthin from 3-methyl-chloro-

xanthin.—If one part, by weight, of 3-methyl-

chloro-xanthin, described under head I1, is heated with ten times its weight of fuming hydriodic acid, a gradual solution and reduction of the chloro compound takes place, which is attended by a liberation of iodin. The heating (at a temperature of from 90° to 100° centigrade) is continued and phosphomuniodid added from time to time until a clear colorless solution is formed. The solution is then evaporated, whereby the iodohydroate of this new base is thrown out in the form of coarse colorless prismatic crystals. After the evaporation has been continued to complete dryness the residue is taken up with water, which causes the iodohydroate to be decomposed and the methyl-xanthin to be isolated in the form of fine colorless needles. The practical yield corresponds to the theoretical. The base is recrystallized from boiling water and so obtained in the form of fine shining needles. Its formula is \( C_8H_2N_2O_2 \) or, structurally:

\[
\begin{align*}
\text{HN} & \text{-CO} \\
\text{O} & \text{C-NH} \quad \text{CH}_3 & \text{-N-C-N} \quad \text{CCl}
\end{align*}
\]

The reaction, as a result of which it is obtained, is expressed in the equation:

\[
\begin{align*}
\text{HN} & \text{-CO} \\
\text{O} & \text{C-NH} + \text{H}_2\text{O} \\
\text{CH}_3 & \text{-N-C-N} \quad \text{CCl}
\end{align*}
\]

This new base as a xanthin gives a strong murexid reaction only with chlorin-water, while if it is evaporated together with moderately-concentrated nitric acid it yields a slightly-colored residue, which is dissolved in strong potash-lye, and thus forms a clear yellow solution. It requires from three hundred to three hundred and thirty parts of boiling water for solution, but is readily soluble in dilute alkalies and ammonia and also in concentrated sulfuric or hydrochloric acid. An ammonical solution of the same when added to a solution of nitrate of silver gives rise to a colorless silver salt consisting of fine needles. This silver salt dissolves in a large excess of ammonia on heating and remains unchanged on boiling. If a solution of the 3-methyl-xanthin in dilute nitric acid is added to nitrate of silver, a double salt, consisting of coarse acicular crystals intermeshed in the form of bunches, is thrown out. This double salt is readily soluble in hot water.

2. Preparation of 7-methyl-2,6-dioxo-purin or heteroxanthin from 7-methyl-8-chloro-

xanthin.—If one part, by weight, of 7-methyl-

chloro-xanthin, (described under I2) be heated on the water-bath, together with eight times
its weight of fuming hydriodic acid of the specific gravity 1.96, phosphonium-iodid being added from time to time to the mixture, a clear colorless solution is soon formed, whereby the end of the reaction is indicated. The reaction proceeds according to the equation:

\[
\begin{align*}
\text{HN} - \text{CO} & \quad \text{HN} - \text{CO} \\
\text{OC} & \quad \text{C} - \text{NCH}_2 + \text{H}_2\text{O} = \text{OC} - \text{N} + \text{HCl}.
\end{align*}
\]

The resulting liquid is evaporated to dryness, and the residue is repeatedly dissolved in water and evaporated to completely remove the hydriodic acid. The crystalline residue is then suspended in about twenty parts of hot water and soda-lye (sodium hydrate) is added until complete solution is effected, when it is allowed to cool. On cooling, the characteristic difficulty-soluble sodium salt of heteroxanthin is thrown out in the form of coarse colorless crystals. This reaction is expressed in the equation:

\[
\begin{align*}
\text{HN} - \text{CO} & \quad \text{HN} - \text{CO} \\
\text{OC} & \quad \text{C} - \text{NCH}_2 + \text{NaOH} = \\
\text{HN} - \text{CO} & \quad \text{OC} - \text{NCH}_2 + \text{H}_2\text{O}.
\end{align*}
\]

The heteroxanthin may then be liberated from the sodium salt by dissolving in hot water, supersaturating with acetic acid and separating by filtration. The heteroxanthin so obtained possesses all the characteristic properties enumerated in Emil Fischer’s patent, No. 618,045, dated January 17, 1899.

3. Preparation of 3-methyl-1,7-dimethyl-2,8-dioxypyrim or theobromin from chloro-theobromin.—If one part, by weight, of chloro-theobromin or 3,7-dimethyl-2,8-dioxo-8-chloropyrim, which has been described under head II, be heated on the water-bath with eight times its weight of fuming hydriodic acid of the specific gravity 1.96, one-half (about) part of phosphonium-iodid being added, a colorless clear solution will be obtained after the lapse of from fifteen to twenty minutes. This indicates that the reduction of the chloro-theobromin has been completed. The liquid is then evaporated to complete dryness to eliminate the surplus of hydriodic acid. The colorless crystalline residue is then taken up with water, whereby the said residue is first dissolved. After a short time, however, the formation of colorless indistinct crystals ensues. These are redissolved and recrystallized from boiling water, and they possess all the characteristic properties of theobromin. They crystallize in small colorless prisms, melt at about 345° centigrade without decomposition, and when dissolved in nitric acid they unite with nitrate of silver to form the double salt, which forms fine needles. The reducing reaction whereby the theobromin is formed from the chloro-theobromin is elucidated in the equation:

\[
\begin{align*}
\text{HN} - \text{CO} & \quad \text{HN} - \text{CO} \\
\text{OC} & \quad \text{C} - \text{NCH}_2 + \text{H}_2\text{O} = \\
\text{CH}_3\text{N} - \text{C} - \text{N} & \quad \text{HN} - \text{CO}.
\end{align*}
\]

The theoretical and practical yields of theobromin are identical.

4. Preparation of 3-methyl-1,7-diethyl-2,8-dioxypyrim.—This new body is obtained by reduction of 3-methyl-1,7-diethyl-2,6-dioxo-8-chloropyrim or 3-methyl-1,7-diethyl-8-chloroxanthin, which has been described under head II. If one part, by weight, of this chloroxanthin be heated with ten parts, by weight, of fuming hydriodic acid to 90° centigrade, solution is speedily effected. The heating is then continued on a boiling water-bath so long until with the addition of phosphonium-iodid in sufficient quantity to take up the liberated iodin a clear solution is formed. This solution is then evaporated to dryness and the crystalline residue is taken up with water and supersaturated with alkali. Through this treatment the new base separates as a colorless oil, which very soon congeals, forming fine acicular crystals. The base is then extracted with a suitable vehicle, such as chloroform or ether, whereupon the extract is evaporated and the colorless residue recrystallized from benzene. From the benzene solution, to which ligroin is preferably added, the methyl-diethyl-dioxopyrim crystallizes in the form of splendidly-developed vitreous colorless prisms, whose analysis gives figures which correspond well to the formula C₈H₅N₂O₂. The structural formula of the base is

\[
\begin{align*}
\text{C}_8\text{H}_5\text{N} - \text{CO} & \quad \text{OC} - \text{N} - \text{C}_2\text{H}_5 \\
\text{CH}_3\text{N} - \text{C} - \text{N} & \quad \text{HN} - \text{CO}.
\end{align*}
\]
The reducing process is expressed in the equation:

\[
\begin{align*}
C_5H_4N-C&-\text{H} + H_2 = C_5H_4N\text{-CO} + HCl. \\
C_5H_4N-C-N& + HCl = C_5H_4N-C&-\text{H} + H_2 \\
\end{align*}
\]

20 As a xanthin this new body with chlorin-water gives a strong murexid reaction. It melts at from 137° to 138° centigrade. It is readily soluble in water, alcohol, chloroform, benzene, ether, and concentrated hydrochloric or sulfuric acid. From an aqueous solution this mass is precipitated by concentrated alkaline 1yes as a colorless oil which soon solidifies to a crystalline mass.

IV. Alkylizing Subsequent to Reducing the Halogen Derivatives.

Alkylization of 3-methyl-xanthin.—In preparing the higher alkylated xanthins from the chloro-xanthins described under I it is not indispensably necessary to first further alkylate the chloro-xanthins and then to reduce such higher alkylated products; but the order of these steps may be equally well reversed by first reducing the chloro-xanthins and then alkylating the reduced products. My invention therefore, broadly considered, consists in reducing and alkylizing the chloro-xanthins irrespective of the order of these two steps.

1. Preparation of 3,7-dimethyl-xanthin (theobromin) from 3-methyl-xanthin.—Seven parts, by weight, of 3-methyl-xanthin are dissolved in twenty-six parts, by volume, of potash-lye (potassium-hydrate solution) of double normal strength, and fifty parts, by volume, of water, and, after adding thereto eight parts, by weight, of methyl-iodid, heated to 80° centigrade and maintained at this temperature for three hours while constantly agitating the mass. After cooling, the liquid will be found to be filled with a pulpy mass of colorless crystals. The mother-liquor is removed from these crystals by filtration or otherwise, and they are then redissolved in and recrystallized from boiling water. The colorless crystals so obtained possess all of the characteristic properties of natural theobromin. The reaction takes place according to the equation:

\[
\begin{align*}
\text{HN}\text{-CO} + \text{C\text{-NH} + 2(CH}_3\text{)} &\text{+ 2KOH = CH}_3\text{\text{-C\text{-N} + H}_2\text{O + KI} } \\
\text{CH}_3\text{\text{-C\text{-N} + H}_2\text{O + KI} } &\text{HC\text{-NH} + 2KCI + 2H}_2\text{O } \\
\end{align*}
\]

The yield in caffein obtained corresponds to the theoretical yield.
7-dimethyl-chloro-xanthin, and the methods of preparing the same and also of reducing and alkylizing them in illustration of my invention, I do not herein claim these new com-
5 pounds nor the specific methods involved in
their preparation, since these form the sub-
jects-matter of and are claimed in my appli-
cations, Serial Nos. 670,843 and 673,849, filed
concurrently herewith, (Cases K and L.)
10 Nor do I herein claim the new compound, 3-
methyl-xanthin (having the methyl group in
the position 3) or the specific process of pre-
paring the same, although they have been
15 herein described in illustration of my inven-
tion, broadly considered, nor specifically the
process of first reducing and then alkylizing
the 3-methyl-chloro-xanthin, since all of these
are claimed in my application, Serial No.
672,843, filed March 4, 1898. The invention
covered in the present application, however,
consists in the method broadly of alkylizing
and reducing the 3-methyl-chloro-xanthin when the same is considered irrespective of
the order of these two steps. Finally I do
25 not herein claim the compound 3-methyl-1-
7-dimethyl-2-dioxypurin or 3-methyl-1-7-di-
eethyl-xanthin or the specific methods of pre-
paring the same, since these form the sub-
ject-matter of and are claimed in my appli-
cation, Serial No. 724,838, filed July 32, 1899.
30 What I claim, and desire to secure by Let-
ters Patent of the United States, is—
1. The process in the art of preparing xan-
35 thins which consists in acting upon alkylized
uric acids having no alkyl group in the posi-
tion 9 with phosphorus-oxy-chlorid.
2. In the art of preparing xanthins the pro-
cess which consists in adding phosphorus-oxy-
40 chlorid to an alkyl-uric acid having no alkyl
group in the position 9 and heating the mix-
ture.
3. In the art of preparing xanthins the pro-
cess which consists in adding phosphorus-oxy-
45 chlorid to an alkyl-uric acid having no alkyl
group in the position 9 and heating the mix-
ture, then evaporating the resulting solution
to remove surplus of phosphorus-oxy-chlorid,
then dissolving the residue after evaporation
with alcohol or water and boiling such solu-
tion.
50 4. In the art of preparing xanthins the pro-
cess which consists in adding phosphorus-oxy-
chlorid to an alkyl-uric acid having no alkyl
group in the position 9, heating the mixture,
then evaporating the resulting solution to re-
move surplus of phosphorus-oxy-chlorid, then
dissolving the residue after evaporation with
alcohol or water and boiling such solution,
then allowing the solution to cool and filter-
ing to evaporate the crystalline alkyl-chloro-
xanthin from the mother-liquor.
5. The process which consists in treating

an alkyl-uric acid, having no alkyl group in
the position 9, with phosphorus-oxy-chlorid,
and then after isolating the resultant chloro-
xanthin, alkylizing the same.
6. The process which consists in treating
an alkyl-uric acid, having no alkyl group in
the position 9, with phosphorus-oxy-chlorid
and then after isolating the resultant com-
pound, submitting the same to alkylization
and reduction.
7. The process which consists in treating
3-methyl-uric acid with phosphorus-oxy-
chlorid.
8. The process which consists in heating 3-
methyl-uric acid with phosphorus-oxy-chlorid
under pressure, then evaporating the result-
ant clear solution to recover the excess of
oxygen-chlorid, then boiling the residue in alco-
hol, then cooling and filtering, all substan-
tially in the proportions and under the con-
ditions set forth.
9. The process which consists in heating 3-
methyl-uric acid with phosphorus-oxy-chlorid
under pressure, then evaporating the result-
ant clear solution to recover the excess of
oxygen-chlorid, then boiling the residue in
alcohol, then cooling and filtering, then dis-
solving the crystalline crude product in alkali
to which a decolorizing agent is added, and
precipitating with acid, all substantially in
the proportions and under the conditions set
forth.
10. A new chemical compound, 3-methyl-
chloro-xanthin, which has the formula here-
above given, is difficult of solution in boil-
ing alcohol, in acetone, acetice ether, benzene
or chloroform, but readily soluble in dilute
alkalies, in ammonia soda or potash solutions,
soluble in concentrated sulfuric or fuming
hydrochloric acid, has no melting-point, but
on being rapidly heated, begins to turn yellow
at about 320°, centigrade, decomposing at
about 345°, centigrade, with effervescence,
and crystallizes from boiling water on cooling
in coarse needles, containing one molecule of
water of crystallization, which escapes on
heating at 130° centigrade.
11. The process which consists in submit-
ting 3-alkyl-chloro-xanthin to the action of
reducing and of alkylizing agents.
12. The process which consists in submit-
ting 3-methyl-chloro-xanthin to the action of
reducing and of methylating agents.
13. The process which consists in submit-
ting 3-methyl-chloro-xanthin to the action of
a methylating agent.
In testimony whereof I affix my signature
in presence of two witnesses.

FRITZ ACH.

Witnesses:
JACOB ADRIAN,
LORENZ ACH.