UNITED STATES PATENT OFFICE.

ARTHUR EICHENGRÜN, OF BONN, GERMANY.

IODOFORM COMBINATION WITH HEXAMETHYLENTETRAMINE.

SPECIFICATION forming part of Letters Patent No. 567,968, dated September 22, 1896.

Application filed December 6, 1895. Serial No. 571,257. (Specimens.)

To all whom it may concern:

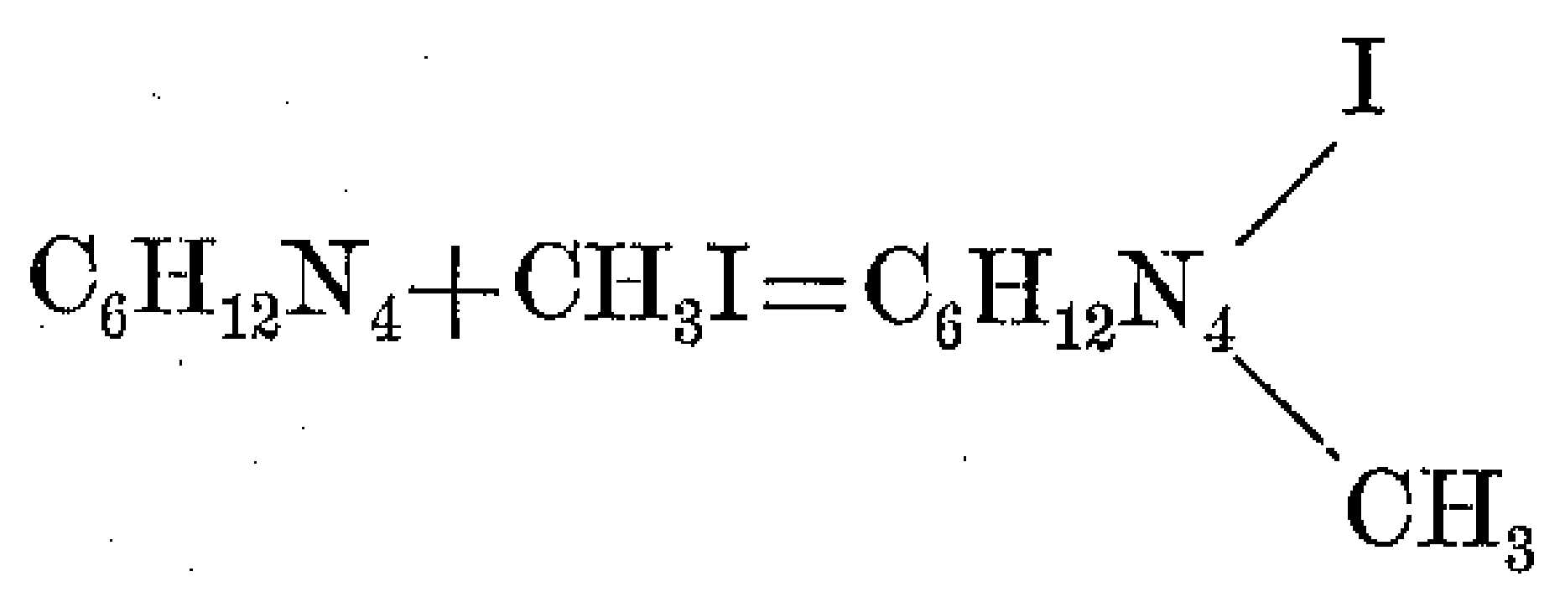
Be it known that I, ARTHUR EICHENGRÜN, a citizen of Germany, residing at Bonn, Germany, have invented new and useful Chemical Combinations to be Used for Surgical Purposes, of which the following is a specification.

Combination of Iodoform with Hexamethylentetramine and its Haloidalkyl Derivatives.

Whereas the alkyl iodids usually can be easily combined with ammonia and fatty bases, in forming the iodin salts of amine, imide, nitrile, and ammonium bases, iodoform, which already differs entirely by its manner of formation and its chemical behavior from the real alkyl iodids, remains quite indifferent upon coming in contact with these bases. For this reason it is very peculiar that iodoform, as I have discovered, readily enters into a combination with the nitrile base hexamethylentetramine in producing a substance of the compositions $C_6H_{12}N_4—CHI_3$. This compound is not only formed by the action of iodoform upon the free base, but also upon the additive products which the latter forms with other substances, in which case these compounds are decomposed into their components, as such additive combinations are principally to be considered as the combinations of hexamethylenamine with phenols, with chlorids of aromatic acids, and with aldehydes—for instance, the combination of hexamethylenamine and hydrate of chloral.

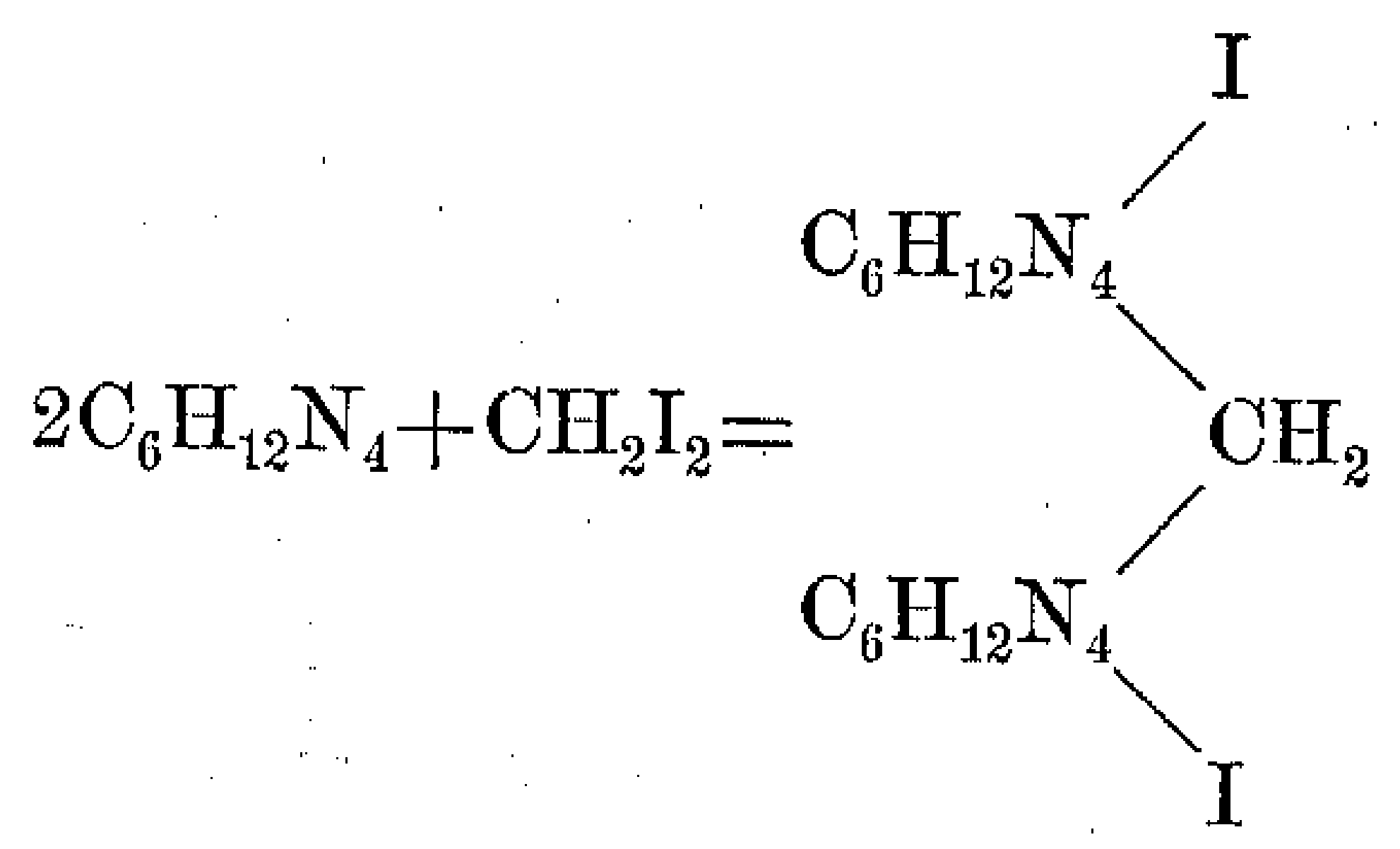
The action of iodoform on hexamethylenamine or one of its derivatives produces the above-mentioned iodoform hexamethylenamine $C_6H_{12}N_4—CHI_3$. This result is very strange for the following reasons: first, because additive combinations of iodoform and free bases are entirely unknown; second, because according to the combinations of hexamethylentetramine with real alkylhaloids (discovered by A. Wohl, *Berichte der Deutschen Chem. Gesellsch.* XIX, 1840) one should have expected that iodoform, in case of its at all entering into reaction with this base, would combine with three molecules of hexamethylenamine, thus:

(*a*)



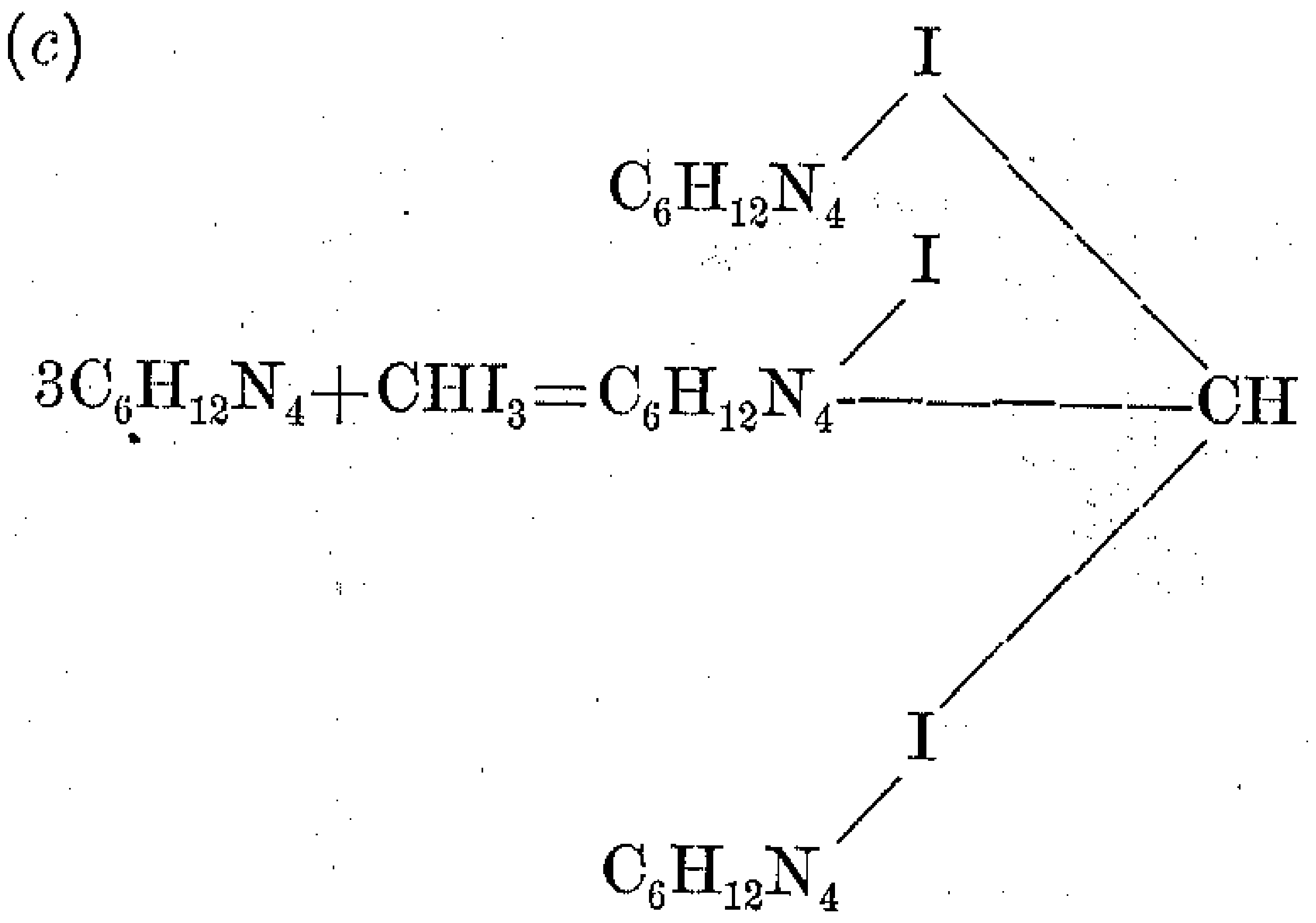
$$C_6H_{12}N_4+CH_3I=C_6H_{12}N_4\begin{array}{l}\diagup I\\ \diagdown CH_3\end{array}$$

(*b*)



$$2C_6H_{12}N_4+CH_2I_2=\begin{array}{l}I\\ \diagup\\ C_6H_{12}N_4\\ \diagdown\\ CH_2\\ \diagup\\ C_6H_{12}N_4\\ \diagdown\\ I\end{array}$$

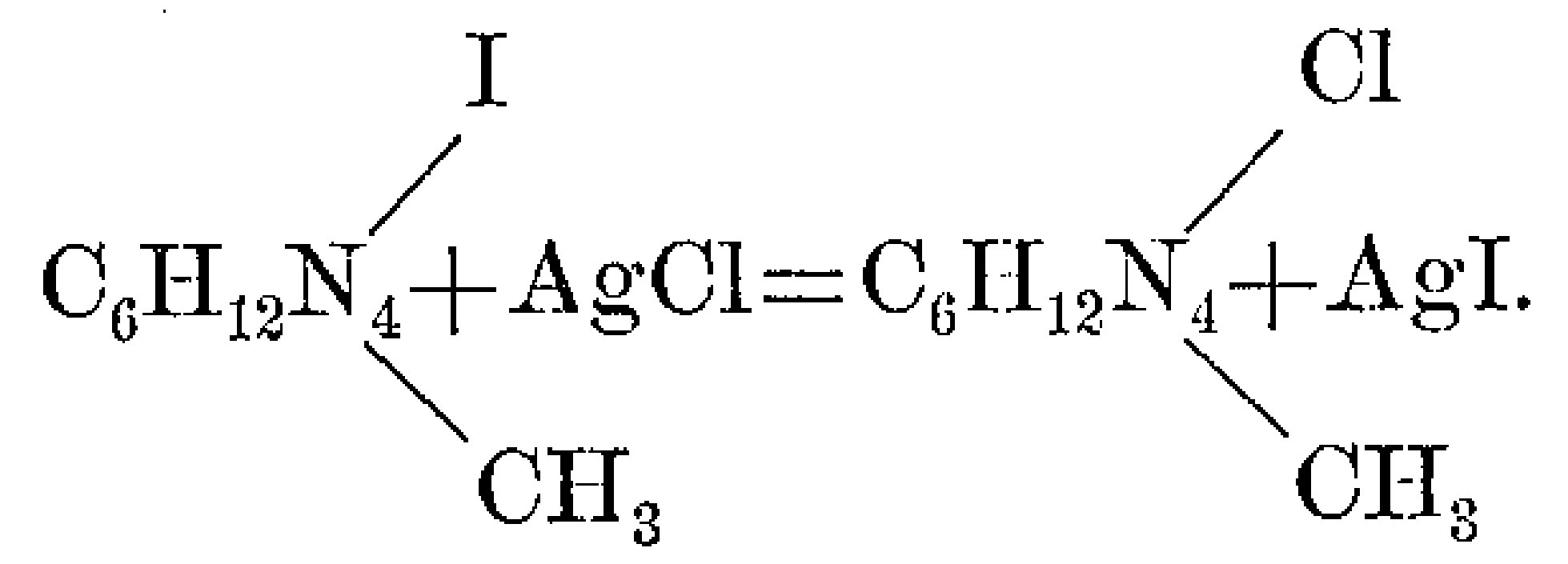
(*c*)



$$3C_6H_{12}N_4+CHI_3=\begin{array}{l}I{-}C_6H_{12}N_4\\ I{-}C_6H_{12}N_4\\ I{-}C_6H_{12}N_4\end{array}\!\!\gt CH$$

The reason that the process does not turn out in aforesaid manner, (formula *c*,) but, instead, that the compound $C_6H_{12}N_4—CHI_3$ is formed, is that this substance is a molecular additive combination, whereas the products obtained by Wohl are iodin salts of new bases, (methyl, ethyl, methylene, ethylene, hexamethylentetramine,) which are real atomistic combinations. This can be seen from the entirely-different chemical properties. Iodoform hexamethylenamine is a white subtile powder, which melts at 178° centigrade and cannot be dissolved either in water or in ether or in alcohol. Upon coming in contact with diluted acids or alkalies, and even being agitated with water, it separates into iodoform and hexamethylenamine. By the action of silver nitrate no precipitation of silver iodid is formed, but iodoform liberated, and a double salt of silver nitrate and hexamethylenamine formed. By the action of silver chlorid and platinum chlorid the same decomposing effect is produced. On the other hand, the compounds of Wohl have the characteristic properties of iodin salts of ammonium bases. They are easily soluble in water and crystallize unaltered by evaporating the aqueous solution. The iodin is completely removed by treatment with silver nitrate.

When heated with silver chlorid, Wohl's compounds are converted into the corresponding chlorin salts from which platinchlorid—double salts—can be prepared:

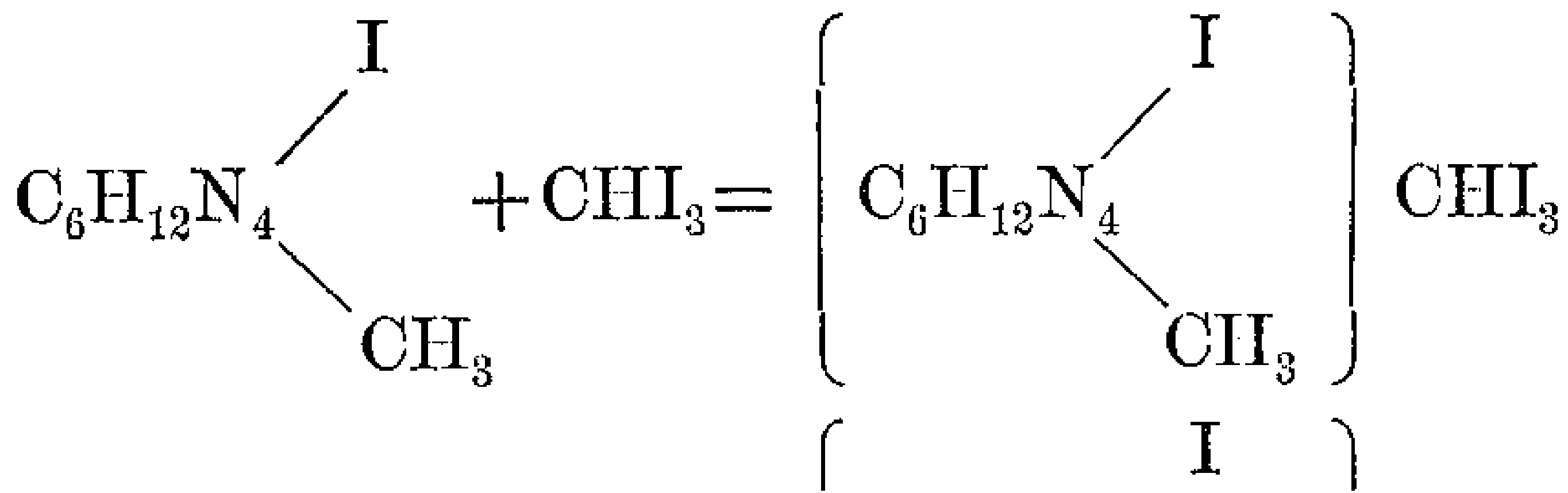


$$C_6H_{12}N_4\begin{matrix}I\\CH_3\end{matrix}+AgCl=C_6H_{12}N_4\begin{matrix}Cl\\CH_3\end{matrix}+AgI.$$

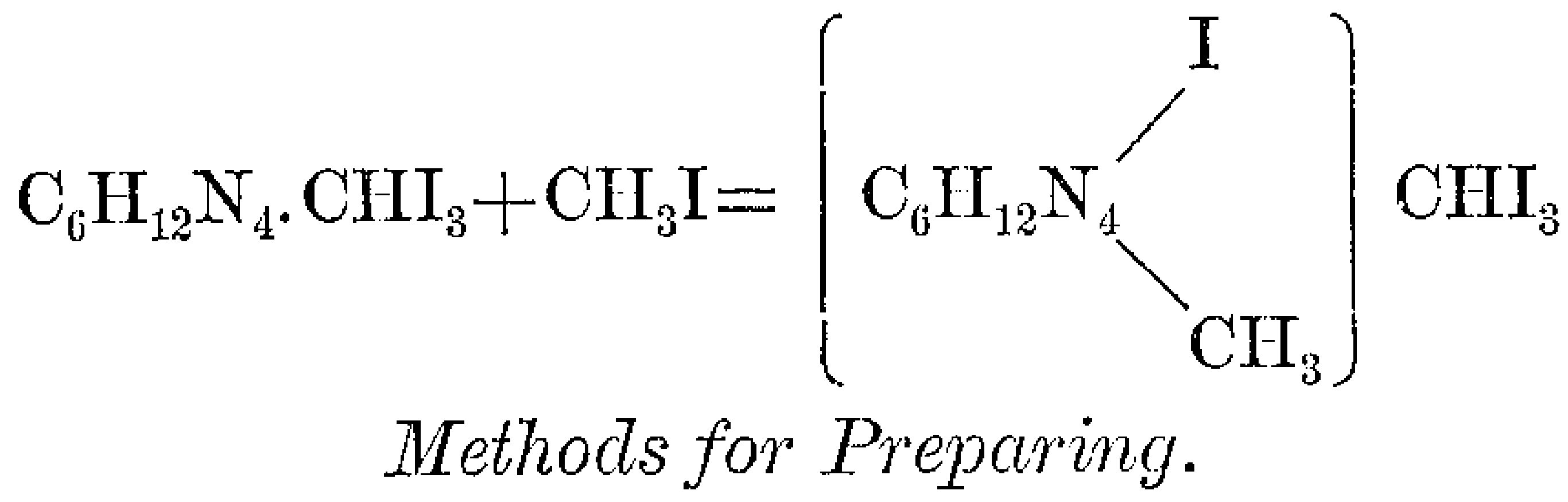
but:

$$C_6H_{12}N_4-CHI_3+AgCl=C_6H_{12}N_4AgCl+CHI_3.$$

When heated in alcoholic solution, Wohl's compounds become altered, as, for instance, the ethiodid hexamethylenamine, melting at 144° centigrade, is converted into a compound melting at 180° centigrade, but never under any circumstances do they decompose into their components as iodoform hexamethylenamine does. If hydrate of potash be added to a concentrated watery solution, the compounds of Wohl are precipitated without being altered. This reaction doubtless shows that they are salts of quaternary ammonium bases. As such compounds they are not able to form a combination with another haloidalkyl, but just as well as hexamethylenamine itself they are also able to form additive combinations with iodoform. These new compounds have the same chemical properties as iodoform hexamethylenamine. They cannot be dissolved in water and become decomposed with acids and alkalies in liberating iodoform. Equally as well as by the action of iodoform on haloidalkyl hexamethylenamine they can be obtained by the action of haloidalkyl iodoform hexamethylenamine.



$$C_6H_{12}N_4\begin{matrix}I\\CH_3\end{matrix}+CHI_3=\left[C_6H_{12}N_4\begin{matrix}I\\CH_3\end{matrix}\right]CHI_3$$



$$C_6H_{12}N_4.CHI_3+CH_3I=\left[C_6H_{12}N_4\begin{matrix}I\\CH_3\end{matrix}\right]CHI_3$$

Methods for Preparing.

Example I: Fourteen grains hexamethylenamine are dissolved in absolute alcohol, then 39.4 grains of iodoform are added, and the mixture heated a short time by means of a water-bath. A white fine powder is then deposited consisting of iodoform hexamethylentetramine and having the above-mentioned properties. Instead of taking pure hexamethylentetramine one may mix the alcoholic solutions of its components with a solution of iodoform.

Example II: 23.4 grains of monophenolhexamethylenamine are dissolved in alcohol, then 39.4 grains iodoform added, and the precipitated iodoform hexamethylenamine filtered. The mother liquor contains all the phenol.

Example III: Dissolve 30.5 grains chloralhexamethylenamine in chloroform, add a hot solution of 39.4 grains iodoform in the same dissolvent, and apply a gentle heat to promote the action. After cooling one separates the precipitation from the solution containing the hydrate of chloral and washes the iodoform hexamethylenamine with alcohol.

Example IV: Dissolve 29.6 grains ethyliodid hexamethylentetramine in absolute alcohol, add an alcoholic solution of 39.4 grains iodoform, and heat for a short time. On cooling a mass of lemon-yellow crystals is deposited consisting of iodoform ethylhexamethyleniodid. They melt at 128° centigrade, are not soluble in water, readily soluble in hot alcohol. If the alcoholic solution is heated too long, another compound is formed, melting at 172° centigrade. It seems to be an isomeric of the above combination.

Example V: One dissolves iodoform hexamethylenamine in amyl acetate and adds to the hot solution methyliodide. On cooling the iodoform methylhexamethylenaminiodid is obtained in light-yellow needles, which are easily dissolved in alcohol and melt at 179° centigrade. By the same methods one obtains the other combinations of iodoform with alkyl-haloid derivatives of hexamethylenamine; as, for instance, methylene-iodid-hexamethylenamine forms, with iodoform an additive product, crystallizing in small yellow needles, melting at 174° centigrade. Bromethylhexamethylenamine (melting at 155° centigrade) forms with iodoform a new compound, which is easily soluble in alcohol and crystallizes in light-yellow prisms, melting at 114° centigrade.

What I claim as my invention, and desire to secure by Letters Patent of the United States, is—

The herein-described compositions of matter to be used for surgical purposes, consisting of crystalline inodorous additive combinations of iodoform with hexamethylentetramine or its haloidalkyl derivatives, which are not soluble in water and become decomposed into their components by the action of acids or alkalies, liberating iodoform.

Signed at Cologne, in the Empire of Germany, this 23d day of November, A. D. 1895.

ARTHUR EICHENGRÜN.

Witnesses:
Sophie Nagel,
Maria Nagel.