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# PATENT SPECIFICATION

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COMPLETE SPECIFICATION

## Penicillin Compounds with Benzimidazoles

We, CHEMIE GRÜNENTHAL G.M.B.H., of Stolberg, Rhineland, Germany, a Body Corporate organised under the laws of Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to novel salt-like penicillin compounds and the production thereof.

Specification No. 683,409 claims a salt of penicillin with an organic base possessing antihistamine activity. The following are the antihistamine bases mentioned by name in the specification: α-(N-phenyl-N-benzylamino) acetamidine; 2-(N-phenyl-N-benzylamino) acetamidine; 2-(N-phenyl-N-benzylamino-methyl)-4:5-dihydroglyoxaline; N-(2-dimethyl-aminopropyl)-phenothiazine; 2-(N-*p*-methoxy-benzyl-N-Beta-dimethylamino-ethyl)-amino-pyrimidine; 2-(N-*p*-methoxybenzyl-N-Beta-dimethylamino-ethyl)-aminopyridine; d1-1-(4'-chlorobenzhydryl)-4-methylpiperazine.

We have now discovered that salt-like penicillin compounds derived from a penicillin and from 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole can be tolerated in larger doses than penicillin salts of the above-named bases without producing undesirable side effects, such as allergic symptoms.

According to the invention the novel compounds are made by reacting in solution a penicillin with the 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole, or by reacting in solution a metal salt of a penicillin, such as an alkali metal salt, with a salt of the 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole, for example a hydrogen halide salt, whereupon the desired compound separates as a sparingly soluble precipitate. Examples of solvents in which the salts of the two substances can be reacted are water and/or alcohols having 1—6 carbon atoms or ketones having 3—7 carbon atoms; examples of solvents in which the free substances can be reacted are alcohols having 1—6 carbon atoms, ketones having 3—7 carbon atoms, ethers, esters and halogeno-hydrocarbons. The new compounds can be produced from various qualities of penicillin, for example from amorphous or crystalline penicillin.

As compared to administration of penicillin and the benzimidazole compound separately, administration of the new compounds of the invention has the advantage that the two substances produce their specific actions without undesirable delay and that the new compound gives a very desirable prolonged penicillin effect.

The new compounds are preferably employed in the form of suspensions, for example in isotonic solutions.

### EXAMPLE 1.

A solution of 35.6 g. of the sodium salt of penicillin G in 75 cc. of water is cooled to 1 to 5° C. and is treated with a similarly cooled solution of 36.2 g. of 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole hydrochloride in 1 litre of water. The emulsion thus produced forms a crystalline precipitate on stand-for a long time in the ice-chest. The white crystalline precipitate, after trituration with cold water, is filtered off and washed with water. The salt thus obtained is then dried in a vacuum desiccator. The melting point is determined by dipping into a bath at 105° C. and raising the temperature at approximately 5° C. per minute, giving a melting point of 147 to 148.7° C. with foaming.

### EXAMPLE 2.

The same compound can also be made as follows:—

A cold solution of 66.8 g. of free penicillin G in 250 cc. of chloroform is treated with a solution of 65.1 g. of 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole dissolved in 500 cc. of chloroform. At first no precipitate is formed. The chloroform solution is concentrated at low temperature and then diluted with

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hexane which produces turbidity. The salt first separates in a viscous form and becomes solid on prolonged trituration on standing. The melting point is 144 to 146° C. with foaming.

What we claim is:—

1. A salt-like compound of a penicillin and 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole.

2. A salt-like compound of penicillin G and 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole.

3. A process for the production of a salt-like penicillin compound as claimed in claim 1, wherein a penicillin is reacted in solution with the 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole.

4. A process for the production of a salt as claimed in claim 1, wherein a metal salt of a penicillin, such as an alkali metal salt, is reacted in a solution with a salt of the 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole, for example a hydrogen halide salt.

5. A process as claimed in claim 4, wherein a metal salt of penicillin, preferably an alkali metal salt of penicillin, is reacted with 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole hydrochloride.

6. A process for the production of the salt-like penicillin compound claimed in claim 2, substantially as described with reference to either of the examples.

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What we claim is:—

1. A salt-like compound of a penicillin and 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole.

2. A salt-like compound of penicillin G and 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole.

3. A process for the production of a salt-like penicillin compound as claimed in claim 1, wherein a penicillin is reacted in solution with the 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole.

4. A process for the production of a salt as claimed in claim 1, wherein a metal salt of a penicillin, such as an alkali metal salt, is reacted in a solution with a salt of the 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole, for example a hydrogen halide salt.

5. A process as claimed in claim 4, wherein a metal salt of penicillin, preferably an alkali metal salt of penicillin, is reacted with 1-*p*-chlorbenzyl-2-pyrrolidylmethyl-benzimidazole hydrochloride.

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