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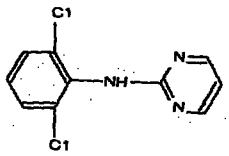
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(19)

(54) N-2,6-DICHLOROPHENYL-2-AMINOPYRIMIDINE AND THERAPEUTIC COMPOSITIONS CONTAINING IT

(71) We, SOCIETE D'ETUDES DE PRODUITS CHIMIQUES, a Company organised and existing under the laws of France, of 4, rue Theodule Ribot, 75017 Paris, France, 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:—

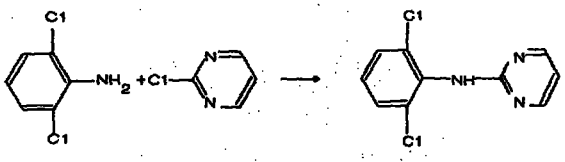
The invention relates to a new compound which is of interest in the pharmaceutical field, to its preparation and to therapeutic compositions containing it. The new compound is N-2,6-dichlorophenyl-2-aminopyrimidine, which has the formula



This compound is of interest as it indicates analgesic activity, as has been shown by tests of the pain syndrome using acetic acid (Koster) or phenyl benzoquinone (Siegmund).

The compound of the invention is a yellow crystalline product with the formula $C_{10}H_7Cl_2N_3$ and a melting point of 190°C. It is soluble in chloroform and dimethylsulphoxide at room temperature, but insoluble in water, ethanol and transcutol.

It may be prepared according to the invention by reacting 2,6-dichloroaniline and 2-chloropyrimidine, in solution in dimethyl formamide and in the presence of sodium hydride, preferably at a temperature not exceeding 40°C. The reaction proceeds according to the following scheme:



The invention is illustrated by the following Example:

Example

In a 2-litre reactor fitted with warming, cooling ond stirring means there were poured 250 ml of dimethylformamide and 24.5 g of sodium hydride (0.51 mol). The mixture was warmed to 40—50°C and there was then added a solution containing, in 300 ml of dimethylformamide, 82.6 g (0.51 mol) of 2,6-dichloroaniline. Stirring was maintained for 75 minutes, by which time a brown solution was obtained. This solution was cooled to 20°C and it was slowly added, over a period of 90 minutes, to a solution containing, in 200 ml of dimethylformamide, 59.5 g (0.51 mol) of 2-chloropyrimidine. During the addition the temperature rose to 35°C.

Stirring was maintained overnight and the dimethylformamide was evaporated. The residue was treated 3 times with diisopropyl ether which led to a pasty product which was washed with water and recrystallized from 300 ml of acetonitrile. After separation and drying there were obtained 61 g (yield 61%) of a yellowish crystalline

product melting at 190°C, analysis of which was in agreement with the general formula $C_{10}H_7Cl_2N_3$.

Toxicity

The *per os* toxicity has been determined on female mice and rats; on mice the LD 50 is over 6.5 g/Kg and on rats the LD 50 is 4.72 g/Kg. The compound according to the invention presents accordingly a low toxicity. This has been confirmed by sub-chronic oral administration to rats.

Pharmacology

The compound of the invention has been submitted to various tests which have shown a marked analgesic action which has been evidenced by the Koster's test (ED 50 *per os* 3 mg/Kg) and by the Siegmund's test (ED 50 *per os* 4.5 mg/Kg).

Clinical Tests

The compound of the invention has been used for clinical tests on 21 cases of various pains including 2 cancer cases, 6 broken bones and 3 coxarthritis.

Of those cases, only 1 was not at all affected by treatment, 1 has to be considered as doubtful, 12 were very favourable (strong attenuation of the pain) and 7 resulted in total relief.

All the patients treated had previously received some other treatment without result.

Concurrently with the compound of the invention, a placebo preparation was also administered and it was noticed that in no case did the placebo have any action.

All the cases treated received 2 or 3 times *per diem* a gelatine capsule containing 30 mg of active substance. As to the tolerance, no significant phenomenon has been noticed. Duration of the treatments: from 2 to 18 days.

Posology

The compound according to the invention may be presented in any therapeutically acceptable form such as tablets, gelatine capsules and suspensions. Preferably the presentation is in gelatine capsules, each containing from 10 to 100 mg of the compound of the invention.

WHAT WE CLAIM IS:—

1. N-2,6-dichlorophenyl-2-aminopyrimidine.

2. A process for the preparation of N-2,6-dichlorophenyl-2-aminopyrimidine, comprising reacting 2,6-dichloroaniline and 2-chloropyrimidine, in solution in dimethyl formamide and in the presence of sodium hydride.

3. A process according to claim 2, wherein the reaction is effected at a temperature not exceeding 40°C.

4. A process according to claim 2, substantially as disclosed in the Example herein.

5. A therapeutic composition in unit dosage form, each dosage unit containing from 10 to 100 mg of N-2,6-dichlorophenyl-2-aminopyrimidine.

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