

PATENT SPECIFICATION

NO DRAWINGS

1,022,644



Date of Application and filing Complete Specification: Aug. 28, 1962.
No. 37788/65.

Application made in United States of America (No. 134,569) on Aug. 29, 1961.

Application made in United States of America (No. 177,174) on March 5, 1962.

(Divided out of No. 1,022,642.)

Complete Specification Published: March 16, 1966.

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Index at acceptance:—O2 C(1E7D1, 1E7F1, 1E7N5, 1E7P3)

Int. Cl.:—C 07 c

COMPLETE SPECIFICATION

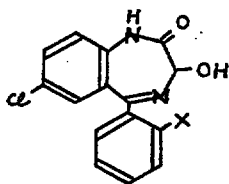
Benzodiazepine Compounds

We, AMERICAN HOME PRODUCTS CORPORATION, a corporation organised and existing under the laws of the State of Delaware, United States of America, of 685 Third Avenue, New York City 17, New York, United States of America, 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 5 - aryl - 7 - chloro - 1,3 - dihydro - 2H - 1,4 - benzodiazepin - 2 - ones having at the 3 - position a hydroxy group, or acid addition salts thereof and also to pharmaceutical preparations containing them.

The compounds of the invention have anti-convulsant, muscle-relaxing and tranquillising properties.

The compounds of the invention have the formula:



where X is hydrogen or chlorine.

Processes for preparing the compounds of the invention are part of the subject of co-pending Application No. 32910/62. (Serial No. 1,022,642).

The compounds of the invention can be administered parenterally or orally as pharmaceutical preparations containing the compound and a pharmaceutically acceptable carrier, for instance diluents, solvents, suspending agents, fillers, excipients, adhesives, colour-

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ing and flavouring materials, as desired for preparation of convenient dosage forms.

The invention is illustrated by the following Examples:

EXAMPLE 1

To a slightly warm suspension of 3.0 g. of 3 - acetoxy - 7 - chloro - 1,3 - dihydro - 5 - phenyl - 2H - 1,4 - benzodiazepin - 2 - one in 150 ml. of ethanol was added 4 ml. of 4N sodium hydroxide solution with stirring. All the solid dissolved and soon a thick white solid precipitated out. The solid was filtered, washed well with water and recrystallised from ethanol, giving 7 - chloro - 1,3 - dihydro - 3 - hydroxy - 5 - phenyl - 2H - 1,4 - benzodiazepin - 2 - one, m.p. 203°C. Analysis, calcd for $C_{15}H_{11}ClN_2O_2$: C, 62.81; H, 3.84; N, 9.27; Cl, 12.37. Found: C, 62.57; H, 3.93; N, 9.59; Cl, 12.30.

EXAMPLE 2

To a suspension of 3.4 g. of 7 - chloro - 5 - (o - chlorophenyl) - 1,3 - dihydro - 3 - acetoxy - 2H - 1,4 - benzodiazepin - 2 - one in 80 ml. of alcohol was added 6 ml. of 4N sodium hydroxide. After complete solution had taken place a solid precipitated that redissolved upon the addition of 80 ml. of water. The solution was acidified with acetic acid to give white crystals. After recrystallisation from ethanol, 3 - hydroxy - 7 - chloro - 5 - (o - chlorophenyl) - 1,3 - dihydro - 2H - 1,4 - benzodiazepin - 2 - one was isolated as a solvate with 1 mole of ethanol. When heated it loses the ethanol of solvation and melts at 166—8°C. Analysis, calcd for $C_{17}H_{13}Cl_2N_2O_2$: C, 55.60; H, 4.39; N, 7.63. Found: C, 55.68; H, 4.20; N, 7.93.

WHAT WE CLAIM IS:—

1. A 3 - hydroxy - 7 - chloro - 1,3 - dihydro - 2H - 1,4 - benzodiazepin - 2 - one having the formula

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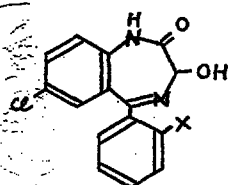
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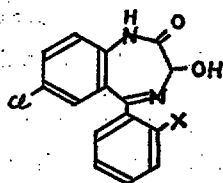
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where X is hydrogen or chlorine, or an acid addition salt thereof.

- 5 2. 3 - Hydroxy - 7 - chloro - 5 - phenyl -
1,3 - dihydro - 2H - 1,4 - benzodiazepin - 2 -
one.

3. 3 - Hydroxy - 7 - chloro - 5 - *o* - chloro-phenyl - 1,3 - dihydro - 2H - 1,4 - benzo-diazepin - 2 - one.

4. A pharmaceutical preparation having sedative, anticonvulsant and muscle relaxant properties containing a compound according to any one of claims 1-3 and a pharmaceutically acceptable carrier.

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