1 545 576

PATENT SPECIFICATION (11) 1 545 576

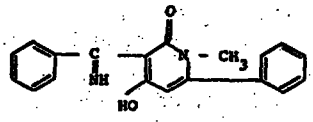
(21) Application No. 38667/78 (22) Filed 9 March 1976
(62) Divided out of No. 1545575
(31) Convention Application No. 558419
(32) Filed 14 March 1975
(31) Convention Application No. 584764
(32) Filed 9 June 1975 in
(33) United States of America (US)
(44) Complete Specification published 10 May 1979
(51) INT CL² C07D 213/69
(52) Index at acceptance
C2C 1377 1530 214 215 220 226 22Y 250 251 255 25Y 305 30Y 328 351 352 365 36Y 386 625 672 699 700 761 762 802 80Y MG TR

(72) Inventor JEFFREY NADELSON

(54) 3-(α-IMINOBENZYL)-4-HYDROXY-6-PHENYL-1 METHYL-2(IH)-PYRIDONE

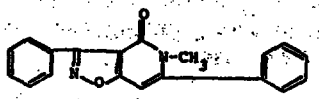
(71) We, SANDOZ LTD., of 35 Lichtstrasse, 4002 Basle, Switzerland, a Swiss Body Corporate, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention provides 3 - (α - iminobenzyl) - 4 - hydroxy - 6 - phenyl - 1 - methyl - 2 (IH) - pyridone, of formula I,



I

The invention also provides a process for the production of the compound of formula I, comprising reducing the compound of formula II

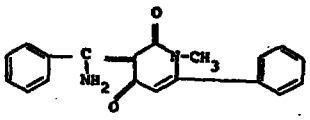


II

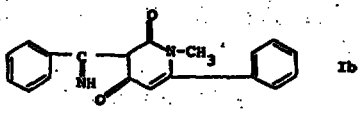
in an inert organic solvent. The reduction may suitably be effected in conventional manner, for example by catalytic hydrogenation.

The resulting compound of formula I may be isolated and purified using conventional techniques. Where required, the free hydroxy form of the compound may be converted into base salt forms in conventional manner, and *vice versa*.

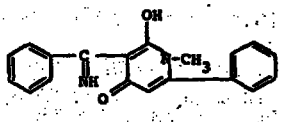
As will be appreciated, the compound of formula I may exist in tautomeric forms of formulae Ia, Ib and Ic:



Ia



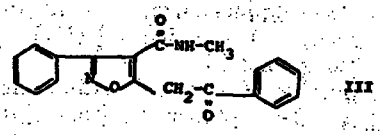
Ib



Ic

While reference is made herein solely to the form of formula I, or the corresponding chemical name, it is to be understood that the invention is not intended to be limited to, or to the production or use of, any particular form of the compound.

The compound of formula II may be produced by cyclising the compound of formula III



III

in the presence of an acid and a solvent. The resulting compound of formula II may be isolated and purified using conventional techniques.

The compound of formula III is claimed in our application No. 38668/78 (Serial No. 1545577), and may be produced by the methods described therein.

The compound of formula I possesses pharmacological activity. In particular it possesses minor tranquillising activity as indicated by its ability to antagonize chronic convulsions and death in mice given about 35 mg/kg of the test compound followed immediately by 45 to 250 mg/kg, i.p., of N - sulfamoylazepine; and by its ability to reduce conflicts as defined in the Geller

Conflict Test [Irving Geller, Psychopharmacologia, I, 42—492 (1960)].

The compound of formula I is therefore indicated for use as a minor tranquilliser. An indicated suitable daily dosage is from 10 to 1000 mg, suitably administered in divided dosages of from 2.5 to 500 mg, two to four times daily, or in retard form.

The compound may be administered in free hydroxy form or in the form of pharmacologically acceptable base salts, which salt forms have the same order of activity as the free form. Suitable salt forms include alkali metal forms, in particular lithium, sodium and potassium salt forms, and alkaline earth metal forms, in particular magnesium or calcium salt forms.

The compound may be admixed with conventional pharmaceutically acceptable diluents and carriers, and, optionally, other excipients, and administered in such forms as hard-filled capsules and tablets.

The following Example illustrates the invention:

EXAMPLE

a) 5 - Methyl - 3,6 - diphenyl - isoxazolo [4,5 - c]pyridin - 4 (5H) - one [compound II]

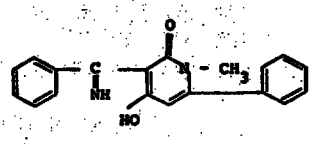
A mixture of 26.1 g (0.0815 mole) of N - methyl - 5 - phenacyl - 3 - phenylisoxazole - 4 - carboxamide and 261 ml of 2M sulphuric acid is refluxed for 24 hours. The mixture is cooled and extracted with methylene chloride. The methylene chloride layer is washed with water and then brine, dried over anhydrous magnesium sulphate, filtered and evaporated *in vacuo*. The residue is triturated with ether and then recrystallised from ethanol to give the heading compound, m.p. 149—151.1°C.

b) 3 - (α - Iminobenzyl) - 4 - hydroxy - 6 - phenyl - 1 - methyl - 2 (1H) - pyridone [compound I]

A mixture of 16.5 g (0.0545 mole) of N - methyl - 3,6 - diphenyl - isoxazolo[4,5 - c] pyridin - 4 (5H) - one, 330 ml of ethanol and 1.65 g of 10% palladium on carbon is hydrogenated at 50 p.s.i. and room temperature. The hydrogenation is ceased after 1 equivalent of hydrogen is absorbed (ca. 2.5 hours). The mixture is treated with methylene chloride and the catalyst is removed by filtration. The solvents are removed *in vacuo* to a volume of ca. 50 ml and then ether is added to precipitate solids which are removed by filtration to give the heading compound, m.p. 238°—240°C. The above compound is dissolved in methanol and treated with sodium hydroxide solution to yield after evaporation the sodium salt of 3 - (α - iminobenzyl) - 4 - hydroxy - 6 - phenyl - 1 - methyl - 2 (1H) - pyridone.

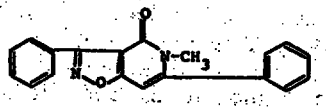
WHAT WE CLAIM IS:—

1. A process for the production of the compound of formula I,



I

comprising reducing the compound of formula II



II

in an inert organic solvent.

2. A process as claimed in Claim 1, substantially as described in the example.

3. The compound of formula I, stated in Claim 1, whenever prepared by a process as claimed in Claim 1 or Claim 2.

4. The compound of formula I, stated in Claim 1.

5. The compound of formula I, stated in Claim 1 in base salt form.

6. A pharmaceutical composition comprising the compound as claimed in Claim 3 or Claim 4, in free hydroxy form or in the form of a pharmaceutically acceptable base salt, in association with a pharmaceutically acceptable diluent or carrier.

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Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa, 1979.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.

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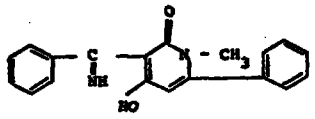
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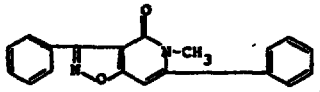
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