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PATENT SPECIFICATION

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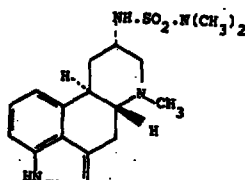
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79Y SC
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(54) 6-METHYL-8 α -N,N-DIMETHYLSULPHAMOYLAMINOERGOLINE I

(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 relates to 6 - methyl - 8 α - N,N - dimethylsulphamoyl aminoergoline I of formula I



The compound may be obtained by acylating 6 - methyl - 8 α - aminoergoline with a reactive functional derivative of an acid of formula (CH₃)₂ . NSO₂ H.

The process may be carried out in conventional manner for such acylations. A suitable reactive functional derivative is the chloride or bromide. The process may be effected as follows (all temperatures are in degrees Centigrade and are uncorrected):—

2.41 g (10 millimols) of 6 - methyl - 8 α - aminoergoline I are dissolved in a mixture of 200 cc of methylene chloride and 25 cc of absolute pyridine, and a solution of 3.58 g (25 millimols) of dimethylsulphamoyl chloride in 25 cc of methylene chloride is added dropwise with stirring at room temperature. After stirring for 12 hours, the reaction solution is poured into an excess of a 2N sodium carbonate solution, the precipitate is filtered off, dried in the air and subsequently chromatographed on silicagel. The title com-

pound is eluted with 2% of methanol in methylene chloride. M.P. 223—226°C from ethanol; yellowish needles. [α]_D²⁰ = -51.6° (c=0.5 in pyridine).

Acid addition salt forms of the compound of formula I may be obtained in conventional manner from the free base form, and vice versa.

The compound of formula I exhibits pharmacological activity. In particular, the compound exhibits prolactin secretion inhibition activity as indicated in standard tests, for example, in rats by an inhibition of ovum implantation as follows:

The compound under investigation is administered to female rats 5 days after coitus and shown to be sperm positive according to the vaginal smear test. The rats are sacrificed on day 12 and their uteri are examined by means of the Salewski reaction for proof that the nidation process has been interrupted (Arch. exp. Path. Pharm. 247, 367 (1967)).

The compound is, therefore, indicated for use as an prolactin secretion inhibitor agent. For this use an indicated daily dose is from 0.05 to 10 mg, conveniently administered in divided doses 2 to 4 times a day in unit dosage form containing from 0.01 to 5 mg, or in sustained release form.

The compound of formula I may be administered in pharmaceutically acceptable acid addition salt form. Such acid addition salt forms exhibit the same order of activity as the free base form and are readily prepared in conventional manner. The present invention also provides a pharmaceutical composition comprising a compound of formula I, in free base form or in pharmaceutically acceptable acid addition salt form, in association with a pharmaceutical carrier or diluent. Such com-

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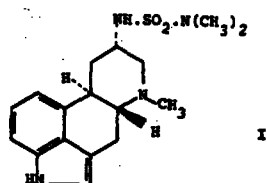
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positions may be formulated in conventional manner, so as to be, for example, a solution or a tablet.

WHAT WE CLAIM IS:—

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



10 which comprises acylating 6 - methyl - 8α - aminoergoline with a reactive functional derivative of an acid of formula $(CH_3)_2NSO_2H$.

2. A process for the production of a compound of formula I, as stated in claim 1, substantially as hereinbefore described with reference to the Example.

3. A compound of formula I, whenever produced by a process according to claim 1 or 2.

4. A compound of formula I, as defined in claim 1.

5. A compound according to claims 3 or 4 in free base form.

6. A compound according to claim 3 or 4 in acid addition salt form.

7. A pharmaceutical composition comprising a compound according to claim 3 or 4 in free base form or in pharmaceutically acceptable acid addition salt form in association with a pharmaceutical carrier or diluent.

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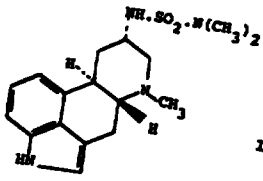
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positions may be formulated in conventional manner, so as to be, for example, a solution or a tablet.

WHAT WE CLAIM IS:—

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



2. A process for the production of a compound of formula I, as stated in claim 1, substantially as hereinbefore described with reference to the Example.

3. A compound of formula I, whenever produced by a process according to claim 1 or 2.
4. A compound of formula I, as defined in claim 1.
5. A compound according to claims 3 or 4 in free base form.
6. A compound according to claim 3 or 4 in acid addition salt form.
7. A pharmaceutical composition comprising a compound according to claim 3 or 4 in free base form or in pharmaceutically acceptable acid addition salt form in association with a pharmaceutical carrier or diluent.

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