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3,772,299

p'-ALKOXY-ERGOTAMINES

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No Drawing. Filed May 25, 1971, Ser. No. 146,829
Claims priority, application Switzerland, May 26, 1970,

7,793/70

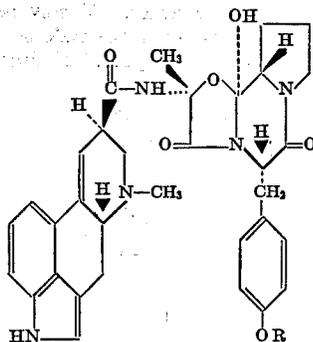
Int. Cl. C07d 51/64

U.S. Cl. 260-268 PE

2 Claims

ABSTRACT OF THE DISCLOSURE

The present invention concerns new compounds of the formula:

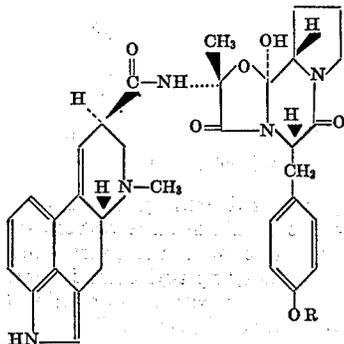


wherein R is lower alkyl of 1 to 4 carbon atoms, and their pharmaceutically acceptable acid addition salts.

The compounds and their pharmaceutically acceptable acid addition salts are useful in promoting uterus contractions. Furthermore, they are useful in the treatment of migraine type headaches and circulatory disorders.

The present invention relates to heterocyclic compounds and more specifically to ergot alkaloids.

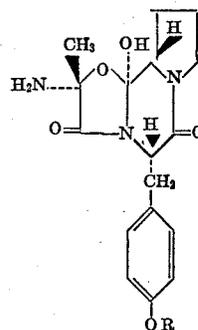
The present invention provides new heterocyclic compounds of Formula I,



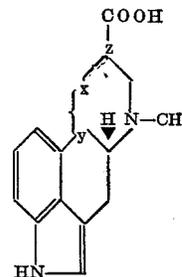
wherein R is lower alkyl of 1 to 4 carbon atoms, and acid addition salts thereof.

The present invention also provides a process for the production of a compound of Formula I or an acid addition salt thereof, which comprises reacting an acid addition salt of a compound of Formula II,

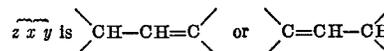
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15 wherein R is as defined above,
with a reactive functional derivative of a compound of Formula III,



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25
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35 wherein



in an inert organic solvent or solvent mixture, in the presence of a basic condensation agent, preferably at a temperature of -20° to 0° C., and, when required, converting the resulting compound into an acid addition salt.

40 A suitable reactive functional derivative of a compound of Formula III which may be used is the mixed anhydride with trifluoroacetic acid. This may be produced by reacting a compound of Formula III with trifluoroacetic acid in the presence of trifluoroacetic acid, in an inert organic solvent or solvent mixture, at a temperature of -20° to -10° C. An acid addition salt of a compound of Formula II in an inert organic solvent or solvent mixture is then added to the resulting mixed anhydride in the presence of a tertiary organic base, at a temperature of -20° to -10° C., and the reaction mixture is allowed to react for a short period at a temperature of about -10° to 0° C.

55 It is possible to use other mixed anhydrides, e.g. with sulphuric acid, as reactive derivatives of compounds of Formula III. The acid chloride hydrochloride or the acid azide, or the addition product with the imidoaldehyde of an N-di(lower)alkyl substituted carboxylic acid amide, e.g. dimethyl formamide or dimethyl acetamide, may likewise be used.

60 A preferred method of effecting the process comprises using as compound of Formula III a mixture of lysergic acid, isolysergic acid and 6-methyl- $\Delta^{8,9}$ -ergolene-8-carboxylic acid, which mixture may, for example, be obtained by saprophytic cultivation of the fungus strain of the species *Claviceps paspali* Stevens and Hall. A culture