Patented Dec. 11, 1951 2,578,611

UNITED STATES PATENT OFFICE

2,578,611

2,4-OXAZOLIDINEDIONES

Roger W. Stoughton, St. Louis, Mo., assignor to Mallinckrodt Chemical Works, St. Louis, Mo., a corporation of Missouri

No Drawing. Application December 20, 1947, Serial No. 793,039

18 Claims. (Cl. 260—294.7)

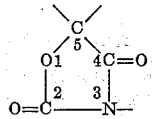
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This invention relates to 2,4-oxazolidinediones and more particularly to 2,4-oxazolidinediones which contain a dialkylaminoalkyl substituent.

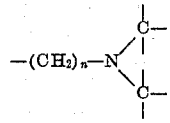
Among the objects of this invention are the provision of new chemical compounds; the provision of 2,4-oxazolidinediones which possess analgesic properties; the provision of such compounds which possess analgesic properties at levels considerably below the toxic level; the provision of useful intermediates for the preparation of such compounds; the provision of compounds of the class described which may be readily prepared from available materials, and the provision of methods for the preparation of such compounds. Other objects will be in part apparent and in part pointed out hereinafter.

The invention accordingly comprises the ingredients and combinations of ingredients, the proportions thereof, steps and sequence of steps, and features of composition and synthesis, analysis, or metathesis, which will be exemplified in the products and processes hereinafter described, and the scope of the application of which will be indicated in the following claims.

In the present invention the compounds referred to include a secondary-amino alkyl group, i. e., an alkyl group bearing a nitrogen atom bonded to two other carbon atoms, substituted in the oxazolidinedione ring in either the 3 or the 5 position:



Oxazolidinedione derivatives containing alkyl or aryl substituents are described in my U. S. Patents 2,338,064, 2,372,861, 2,349,795, 2,349,796, and 2,349,313, for example, but in the compounds of the present invention one substituent in either the 3 or 5 position must be a secondary aminoalkyl group.

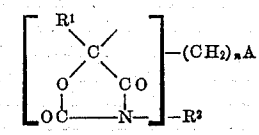


While the 2,4-oxazolidinedione compounds previously disclosed represent useful therapeutic compounds, such therapeutic value has been due to their anesthetic, hypnotic and anti-convulsive action and not to any substantial analgesic action. Similarly, simple tertiary amines have not been found to possess analgesis properties. How-

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ever, it has now been found in the present invention that when the tertiary amine structure is combined in the same molecule with the oxazolidinedione ring, i. e., when the ring is substituted with a secondary aminoalkyl group, compounds are formed which have an entirely different physiological action than the known oxazolidinediones. These compounds possess valuable analgesic properties which fit them for use when relief of pain is the object of the therapeutic treatment. The previously known 2,4-oxazolidinediones have shown no useful analgesic activity and in this respect are to be contrasted with the compounds of the present invention whose analgesic activity is of an entirely different order.

The compounds of the present invention may be represented by the following type formula:



wherein n is a small whole number, R^1 is a lower alkyl or aryl group, R^2 is hydrogen, a lower alkyl, or an aryl group, and A is a nitrogen atom bonded to two carbon atoms, i. e., A is a secondary amino group which may be acyclic or part of a cyclic structure.

The analgesic activity of the compounds of the present invention may be tested in accordance with the method described by Winder, Pfeiffer and Maison, Arch. int. pharmacodyn., 72, 329 (1946). When so tested the compounds of the present invention show analgesic activity and in addition certain of them possess other properties which are of therapeutic value. In contrast to the simple alkyl substituted derivatives, the aminoalkyl derivatives of the present invention show little or no hypnotic or sedative action, but produce analgesia in doses much below those which cause toxic symptoms.

Example 1

A solution of 70 grams of sodium bisulfite in 600 ml. of water was placed in a one liter three necked flask fitted with a mechanical stirrer, thermometer and dropping funnel. The solution was cooled in an ice bath and 83 grams of diethylaminoacetone (prepared by the method of Magee and Henze, J. Am. Chem. Soc., 60, 2148 (1938)) was added. When this addition was complete a solution of 43 grams of sodium cyanide in 150 ml. of water was added dropwise at

such a rate that the temperature was maintained below 5° C. After stirring for two hours the oil layer was separated and the aqueous layer extracted with three 75 ml. portions of ether. The ether extracts were combined with the main fraction and dropped into 700 ml. of concentrated hydrochloric acid, the temperature of which was kept below 5° C. After standing overnight at room temperature this solution was evaporated to dryness on the steam bath. The residue was treated with 200 ml. of alcohol and the insoluble ammonium chloride was filtered off. This was washed with another 200 ml. of alcohol and to these combined filtrates 200 ml. of carbon tetrachloride was added. This mixture was then distilled through a fractionating column into an automatic water separator which returned the dry alcohol-carbon tetrachloride mixture to the distilling flask. This apparatus is described in Organic Synthesis Col., vol. 1, 1st ed., page 257. The distillation was continued until no more water separated. This required approximately forty hours. The remaining solvent was removed by distillation under reduced pressure. The residue was taken up in 100 ml. of cold water and after clarification with activated carbon, solid potassium carbonate was added until the solution was basic to phenolphthalein. A yellowish oil separated. This was extracted with ether and distilled under reduced pressure. The fraction boiling at 84–86° C. at 8 mm. pressure amounted to 90.3 grams (70%). This was ethyl β-diethylamino-α-hydroxyisobutyrate.

Example 2

Thirty grams of ethyl β-diethylamino-α-hydroxyisobutyrate and 9 grams of dry urea were added to a cool solution of 3 grams of sodium in 100 ml. of absolute alcohol. This mixture was refluxed for ten hours and the alcohol was then removed under reduced pressure. The residue was dissolved in 50 ml. of cold water and extracted with two 25 ml. portions of ether. The other extracts were discarded and the aqueous solution, after clarification with activated carbon was acidified with 11 ml. (exactly one equivalent) of concentrated hydrochloric acid. The product was extracted with ether and after the ether has been removed by distillation it solidified. It was finally recrystallized from petroleum ether. A yield of 13 grams with a melting point of 71–72° C. was obtained. This was 5-diethylaminomethyl-5-methyl-2,4-oxazolidinedione.

Example 3

The hydrochloride of 5-diethylaminomethyl-5-methyl-2,4-oxazolidinedione was prepared by adding 25 ml. of an ether solution of anhydrous hydrogen chloride to a solution of 7 grams of the free base in 50 ml. of anhydrous ether. On standing a crystalline hydrochloride was obtained. It melted at 191–194° C. Analysis: Calcd. for $C_9H_{17}ClN_2O_3$: Cl, 14.98. Found: Cl, 14.98. This compound was found to have analgesic properties.

Example 4

To a solution of 30 grams of 5-diethylaminomethyl-5-methyl-2,4-oxazolidinedione in 75 ml. of water, 15.6 ml. of 35° Bé. sodium hydroxide sodium hydroxide solution was added. This solution was neutral to phenolphthalein but slightly basic to litmus. After cooling in an ice bath 15.5 ml. (10% excess) of dimethyl sulfate was added keeping the temperature below 10° C. After stirring for one hour it was allowed to warm up to room temperature. Sodium carbonate was then added with cooling until the solution was basic to litmus. The product was extracted with three 25 ml. portions of ether and distilled under reduced pressure. A yield of 20 grams of 5-diethylaminomethyl - 3,5 - dimethyl-2,4-oxazolidinedione was obtained with a boiling point of 87–92° C. at 1 mm. pressure.

Example 5

The hydrochloride of 5-diethylaminomethyl-3,5-dimethyl-2,4-oxazolidinedione was prepared by the method described in Example 3. It had a melting point of 166 to 167° C. Analysis: Calcd. for $C_{10}H_{19}ClN_2O_3$: Cl, 14.17. Found: Cl, 14.14. This compound was found to have analgesic properties.

Example 6

Eethyl β - di - n - butylamino - α - hydroxyisobutyrate was prepared by the method described in Example 1, except an equivalent amount of di-n-butylaminoacetone (prepared by the method of Magee and Henze) was substituted for the diethylaminoacetone. The product was oil which boiled at 116–120° C. at 5 mm. pressure.

Example 7

5 - di-n-butylaminomethyl-5-methyl - 2,4 - oxazolidinedione was prepared by the method described in Example 2 by substituting an equivalent amount of ethyl β-di-n-butylamino-α-hydroxyisobutyrate for ethyl diethylamino-α-hydroxyisobutyrate. A yield of 71% of an oil boiling at 149–154° C. was obtained.

Example 8

The hydrochloride of 5-di-n-butylaminomethyl-5-methyl-2,4-oxazolidinedione was prepared by the method described in Example 3. This product appeared to be amorphous. It melted at 71–74° C. Analysis: Calcd. for $C_{13}H_{25}ClN_2O_3$, Cl, 12.11. Found: Cl, 12.75.

Example 9

5-di-n-butylaminomethyl - 3,5 - dimethyl-2,4-oxazolidinedione was prepared by the methylation of 5-di-n-butylaminomethyl-5-methyl-2,4-oxazolidinedione according to the method described in Example 4. A yield of 80% of a colorless oil boiling at 113–117° C. at 1 mm. pressure was obtained.

Example 10

5-di-n-butylaminomethyl - 3,5 - dimethyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It was recrystallized from ether containing 10% ethanol. The pure salt melted at 107–110° C. Analysis: Calcd. for $C_{14}H_{27}ClN_2O_3$: Cl, 11.56. Found: Cl, 11.59. This compound was found to have analgesic properties.

Example 11

Ethyl δ - diethylamino-α-hydroxy - α - methylvalerate was prepared by the method described in Example 1 by the substitution of an equivalent amount of 5-diethylaminopentanone-2 for the diethylamioacetone. The product was an oil which boiled at 129–131° C. at 11 mm. pressure.

Example 12

Ethyl δ-diethylamino-α-hydroxy - α - methylvalerate was condensed with urea according to the procedure described in Example 2. The alcohol was not removed from the reaction mixture

but alcoholic hydrogen chloride was added and the sodium chloride which precipitated was filtered off. The alcohol was then distilled under reduced pressure. The residue was taken up in warm acetone and allowed to crystallize. A yield of 60% of crude 5-(3-diethylamino) propyl-5-methyl-2,4-oxazolidinedione hydrochloride was obtained. It was finally recrystallized from ter.-butyl alcohol. The pure salt melted at 158–159° C. Analysis: Calcd. for $C_{11}H_{21}ClN_2O_3$: Cl, 13.42. Found: Cl, 13.35. This substance had analgesic properties.

Example 13

5-(3-diethylamino) propyl - 3,5 - dimethyl-2,4-oxazolidinedione was prepared by the methylation of 5-(3-diethylamino) propyl-5-methyl-2,4-oxazolidinedione by the method described in Example 4. It was obtained in 80% yield as an oil boiling at 135–140° C. at 4 mm. pressure.

Example 14

5 - (3 - diethylamino) propyl-3,5-dimethyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It was recrystallized from an alcohol-ether mixture. The melting point of the pure hydrochloride was 132–133° C. Analysis: Calcd. for $C_{12}H_{23}ClN_2O_3$, Cl, 12.73. Found: Cl, 12.71.

Example 15

Ethyl α-hydroxy-β-(4 - morpholinyl) isobutyrate was prepared by the method described in Example 1 from 1-(4-morpholinyl) acetone (prepared by the method of Mason and Ross, J. Am. Chem. Soc., 62, page 2882 (1940)). The product was an oil which boiled at 112–114° C., at 5 mm. pressure.

Example 16

5-methyl-5-(4 - morpholinyl) methyl - 2,4 - oxazolidinedione was prepared by the method described in Example 2 from ethyl α-hydroxy-β-(4-morpholinyl)-isobutyrate. The product was recrystallized from boiling water. A yield of 42% of pure product melting at 126–127° C. was obtained.

Example 17

5-methyl - 5 - (4 - morpholinyl) methyl-2,4-oxazolidinedione hydrochloride was prepared by the method described in Example 3. It melted at 247° C. with decomposition. Analysis: Calcd. for $C_9H_{15}ClN_2O_4$ Cl, 14.14. Found: Cl, 14.03. This compound was found to have analgesic properties.

Example 18

3,5-dimethyl - 5 - (4-morpholinyl) methyl-2,4-oxazolidinedione was prepared by the methylation of 5-methyl-5-(4-morpholinyl) methyl-2,4-oxazolidinedione according to the method described in Example 4. It was recrystallized from twenty parts of light petroleum ether and had a melting point of 59–60° C.

Example 19

3,5 - dimethyl - 5 - (4-morpholinyl) methyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It was recrystallized from absolute ethanol. The pure hydrochloride melted at 225° C. with decomposition. Analysis: Calcd. for $C_{10}H_{17}ClN_2O_4$, Cl, 13.40. Found: Cl, 13.39. This substance had analgesic properties.

Example 20

Ethyl α - hydroxy - β - (1-piperidyl) isobutyrate

was prepared by the method described in Example 1 from 1-piperidyl acetone (prepared by the method of Magee and Henze). The product was an oil which boiled at 66–67° C. at 6 mm. pressure.

Example 21

5 - methyl - 5-(1-piperidyl) methyl-2,4-oxazolidinedione was prepared by the method described in Example 2 from ethyl α-hydroxy-β-(1-piperidyl) isobutyrate. The product, when recrystallized from benzene, melted at 124–125° C. It was obtained in 61% yield.

Example 22

The hydrochloride of 5-methyl-5-(1-piperidyl) methyl-2,4-oxazolidinedione was prepared by the method described in Example 3. It melted at 238–240° C. with decomposition. Analysis: Calcd. for $C_{10}H_{17}ClN_2O_2$, Cl, 14.19. Found: Cl, 14.15. This compound was found to have analgesic properties.

Example 23

3,5 - dimethyl - 5 - (1-piperidyl) methyl-2,4-oxazolidinedione was prepared by the methylation of 5 - methyl-5-(1-piperidyl) methyl-2,4-oxazolidinedione according to the method described in Example 4. The product was recrystallized from five parts of light petroleum ether. A yield of 61% of a product melting at 140–141° C. was obtained.

Example 24

3,5 - dimethyl - 5 - (1-piperidyl) methyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It melted at 241° C. with decomposition. Analysis: Calcd. for $C_{11}H_{19}ClN_2O_3$, Cl, 13.50. Found: Cl, 13.49. This compound was found to have analgesic properties.

Example 25

In a 500 ml. three-necked flask equipped with a mercury sealed stirrer, reflux condenser and dropping funnel, 2.3 grams of sodium was dissolved in 100 ml. of absolute ethanol. When solution was complete 18 grams of 5-phenyl-2,4-oxazolidinedione was added and then a solution of 20 grams of diethylaminoethyl chloride (prepared by the method of Breslow, Yost, Walker and Hauser, J. Am. Chem. Soc., 66, 1922 (1944)) in 50 ml. of absolute ethanol was added dropwise. The mixture was then refluxed for seven hours, the precipitated sodium chloride was filtered off and the ethanol removed by distillation. The residue was taken up in dilute hydrochloric acid and after clarification with activated carbon potassium carbonate was added until the solution was basic to phenolphthalein. The yellow oil that separated was distilled under reduced pressure. It boiled at 173–175° C. at 1.5 mm. pressure and was 3-(β-diethylaminoethyl) 5-phenyl-2,4-oxazolidinedione. It was obtained in 65% yield.

Example 26

3 - β - diethylaminoethyl-5-phenyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. After recrystallization from a 50% alcohol-ether mixture it melted at 123–125° C. Analysis: Calcd. for $C_{15}H_{21}ClN_2O_3$, Cl, 11.31. Found: Cl, 11.34. This compound was found to have analgesic properties.

Example 27

3 - β-dimethylaminoethyl-5,5-diphenyl-2,4-oxazolidinedione was prepared from β-dimethyl-

aminoethyl chloride (prepared from dimethylaminoethanol by the method of Breslow, Yost, Walker and Hauser) and 5,5-diphenyl-2,4-oxazolidinedione according to the method described in Example 25. Upon acidifying the reaction mixture the hydrochloride of the base separated. This was collected and the free base liberated with sodium carbonate solution. It was recrystallized from water and when pure melted at 60.5–62° C. A yield of 44% of theory was obtained.

Example 28

3 - β-dimethylaminoethyl-5,5-diphenyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It melted at 194–197° C. and was only slightly soluble in water. Analysis: Calcd. for $C_{19}H_{21}ClN_2O_3$, Cl, 9.80. Found: Cl, 9.80. This compound was found to have analgesic properties.

Example 29

3 - β-diethylaminopropyl-5,5-diphenyl-2,4-oxazolidinedione was prepared from diethylaminopropyl chloride (prepared from diethylaminoisopropanol by the method of Breslow, Yost, Walker and Hauser) and 5,5-diphenyl-2,4-oxazolidinedione according to the method described in Example 25. It was obtained as an oil in 67% yield.

Example 30

3-β-diethylaminopropyl - 5,5-diphenyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It was recrystallized from an alcohol-ether mixture and when pure had a melting point of 96°–100° C. Analysis: Calcd. for $C_{22}H_{27}ClN_2O_3$, Cl. 8.78. Found: Cl, 8.83. This compound was found to have analgesic properties.

Example 31

3-γ-di-n-butylaminopropyl - 5,5 - diphenyl-2,4-oxazolidinedione was prepared from γ-di-n-butylaminopropyl chloride (prepared from γ-di-n-butylaminopropanol by the method of Breslow, Yost, Walker and Hauser) and 5,5-diphenyl-2,4-oxazolidinedione according to the method described in Example 25. A yield of 31% of an oil was obtained.

Example 32

3-γ-di-n-butylaminopropyl - 5,5 - diphenyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It was recrystallized from an alcohol-ether mixture. The pure salt melted at 141–145°C. Analysis: Calcd. for $C_{26}H_{35}ClN_2O_3$, Cl, 7.71. Found: Cl, 7.93. This compound was found to have analgesic properties.

Example 33

3-β-di-n-butylaminoethyl - 5,5 - diphenyl - 2,4-oxazolidinedione was prepared from di-n-butylaminoethylchloride (prepared from di-n-butylaminoethanol by the method of Breslow, Yost, Walker and Hauser) and 5,5-diphenyl-2,4-oxazolidinedione according to the method described in Example 25. The free base was soluble in water but was extracted with ether and recrystallized from petroleum ether. It had a melting point of 41–43° C. The yield was 70% of the theoretical.

Example 34

3-β-di-n-butylaminoethyl - 5,5 - diphenyl - 2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It was recrystallized from an alcohol-ether mixture. The pure salt melted at 114–118°C. Analysis: Calcd. for $C_{25}H_{33}ClN_2O_3$, Cl, 7.95. Found: Cl, 7.98. This compound was found to have analgesic properties.

Example 35

3,-β - (1 - piperidyl) ethyl-5,5-diphenyl-2,4-oxazolidinedione was prepared from β-(1-piperidyl) ethyl chloride (prepared from β-piperidyl ethanol by the method of Breslow, Yost, Walker and Hauser) and 2,4-oxazolidinedione according to the method described in Example 25. The free base was extracted with ether and recrystallized from a benzene-petroleum ether mixture. An almost quantitative yield of product melting at 101–104° C. was obtained.

Example 36

3-β-(1-piperidyl) ethyl - 5,5 - diphenyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It melted at 152–156° C. Analysis: Calcd. for $C_{22}H_{25}ClN_2O_3$, Cl, 8.84. Found: Cl, 8.45. This compound was found to have analgesic properties.

Example 37

3-β-(4-morpholinyl) ethyl-5,5-diphenyl-2,4-oxazolidinedione was prepared from β-(4-morpholinyl) ethyl chloride (prepared from β-morpholinyl ethanol by the method of Breslow, Yost, Walker and Hauser) and 5,5-diphenyl-2,4-oxazolidinedione according to the method described in Example 25. The base was recrystallized from water. An almost quantitative yield of product melting at 133–136.5° C. was obtained.

Example 38

3-β-(4-morpholinyl) ethyl-5,5-diphenyl-2,4-oxazolidinedione was converted to its hydrochloride by the method described in Example 3. It melted at 189–192° C. Analysis: Calcd. for $C_{21}H_{23}ClN_2O_4$, Cl, 8.80. Found: Cl, 8.62. This compound was found to have analgesic properties.

It is to be understood that other salts of the aminoalkyloxazolidinediones such as the hydrobromide, the sulfate, or phosphate, for example, may be employed in place of the hydrochloride if desired.

In general, it is preferred that the valuable therapeutic properties of the compounds of the present invention be utilized in analgesic compositions. For convenience, it is preferred to employ solutions of the salts rather than the free bases. The pharmacological studies referred to above were carried out using the hydrochlorides.

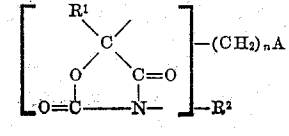
The bases and their salts may be used in hypodermic or oral tablets, in solutions, pills, elixirs, syrups, or in other convenient forms of administration.

In view of the above, it will be seen that the several objects of the invention are achieved and other advantageous results attained.

As many changes could be made in the above processes and products without departing from the scope of the invention, it is intended that all matter contained in the above description shall be interpreted as illustrative and not in a limiting sense.

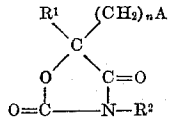
I claim:

1. Aminoalkyl oxazolidinediones of the formula:



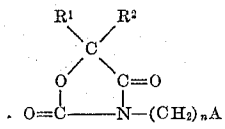
wherein n is a small whole number, R^1 is selected from the group consisting of lower alkyl and aryl groups, R^2 is selected from the group consisting of hydrogen, lower alkyl, and aryl groups, and A is a secondary amino group.

2. Aminoalkyl oxazolidinediones of the formula:



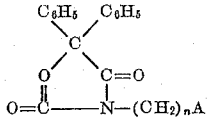
wherein n is a small whole number, R^1 is selected from the group consisting of lower alkyl and aryl groups, R^2 is selected from the group consisting of hydrogen, lower alkyl, and aryl groups, and A is a secondary amino group.

3. Aminoalkyl oxazolidinediones of the formula:



wherein n is a small whole number, R^1 is selected from the group consisting of lower alkyl and aryl groups, R^2 is selected from the group consisting of hydrogen, lower alkyl, and aryl groups, and A is a secondary amino group.

4. Aminoalkyl oxazolidinediones of the formula:



wherein n is a small whole number and A is a secondary amino group.

5. A substance selected from the group consisting of 2,4-oxazolidinediones containing at least two substituents, one of said substituents being selected from the group consisting of lower alkyl and aryl groups and another substituent being a secondary-amino alkyl group, and acid addition salts thereof.

6. A substance selected from the group consisting of 5-substituted-2,4-oxazolidinediones containing at least two substituents one of said substituents being selected from the group consisting of lower alkyl and aryl groups and another substituent being a secondary-amino alkyl group, and acid addition salts thereof.

7. A substance selected from the group consisting of 5 -diethylaminomethyl- 5 -methyl- 2,4-oxazolidinedione, 5-diethylaminomethyl - 3,5-dimethyl- 2,4 -oxazolidinedione, 5- di- n -butylaminomethyl-5-methyl- 2,4 -oxazolidinedione, 5-di-n-butylaminomethyl-3,5 -dimethyl- 2,4 -oxazolidinedione, 5-(3 - diethylamino) propyl - 5-

methyl - 2,4 - oxazolidinedione, 5-(3-diethylamino) propyl-3,5-dimethyl-2,4- oxazolidinedione, 5 -methyl- 5-(4- morpholinyl) -methyl- 2,4- oxazolidinedione, 3,5-dimethyl-5-(4-morpholinyl) - methyl - 2,4 - oxazolidinedione, 5-methyl-5-(1-piperidyl) -methyl-2,4-oxazolidinedione, 3,5 - dimethyl-5-(1-piperidyl) -methyl- 2,4 -oxazolidinedione, 3-(β-diethylaminoethyl) -5-phenyl-2,4-oxazolidinedione, 3-β-dimethylaminoethyl-5,5-diphenyl-2,4-oxazolidinedione, 3 -β- diethylaminopropyl-5,5-diphenyl-2,4-oxazolidinedione, 3-γ-di-n-butylaminopropyl- 5,5 -diphenyl- 2,4 -oxazolidinedione, 3-β -di -n- butylaminoethyl- 5,5 -diphenyl-2,4-oxazolidinedione, 3-β-(1-piperidyl) - ethyl-5,5-diphenyl-2,4-oxazolidinedione, 3-β-(4-morpholinyl) ethyl-5,5-diphenyl-2,4 -oxazolidinedione, and acid addition salts thereof.

8. A substance selected from the group consisting of a 5,5 -diphenyl- 3 -secondary - amino alkyl-2,4-oxazolidinedione and its acid addition salts.

9. 5-diethylaminomethyl- 5 -methyl- 2,4 -oxazolidinedione hydrochloride.

10. 5 -di- n -butylaminomethyl- 3,5 -dimethyl-2,4-oxazolidinedione hydrochloride.

11. 5-(3 -diethylamino) propyl- 5 -methyl- 2,4-oxazolidinedione hydrochloride.

12. 3-β-dimethylaminoethyl-5,5 -diphenyl- 2,4-oxazolidinedione hydrochloride.

13. 3-β-(1 -piperidyl) ethyl- 5,5 -diphenyl- 2,4-oxazolidinedione hydrochloride.

14. A substance selected from the group consisting of 5-diethylaminomethyl-5-methyl-2,4-oxazolidinedione and acid addition salts thereof.

15. A substance selected from the group consisting of 5-di-n-butylaminomethyl- 3,5 -dimethyl-2,4-oxazolidinedione and acid addition salts thereof.

16. A substance selected from the group consisting of 3-β-(1-piperidly) ethyl-5,5-diphenyl-2,4-oxazolidinedione and acid addition salts thereof.

17. A substance selected from the group consisting of 5-(3-diethylamino) propyl-5-methyl-2,4-oxazolidinedione and acid addition salts thereof.

18. A substance selected from the group consisting of 3-β-dimethylaminoethyl-5,5-diphenyl-2,4-oxazolidinedione and acid addition salts thereof.

ROGER W. STOUGHTON.

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The following references are of record in the file of this patent:

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