

PATENT SPECIFICATION

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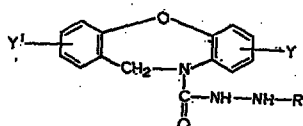
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(54) DIBENZOXAZEPINE N-CARBOXYLIC ACID HYDRAZIDES AND DERIVATIVES

(71) We, G. D. SEARLE & CO., a corporation organised and existing under the laws of the State of Delaware and whose full postal address is P.O. Box 5110 Chicago, Illinois 60680 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:—

Dibenzoxazepine N-Carboxylic Acid Hydrazides and Derivatives

The present invention relates to a group of derivative of dibenzoxazepine N-carboxylic acid hydrazides and more specifically to the compounds having a following general formula



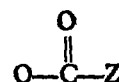
wherein Y and Y' are hydrogen, halogen, methyl or trifluoromethyl and R is higher alkanoyl, halo(lower alkanoyl), carboxy(lower alkanoyl), 3-carboxyacryloyl, phenoxy(lower alkanoyl), halophenoxy(lower alkanoyl), lower alkylsulfonyl or α -toluenesulfonyl.

The higher alkanoyl radicals referred to above contain from 7 to 12 carbon atoms and can be illustrated by heptanoyl, octanoyl, decanoyl and the corresponding branched-chain isomers. The lower alkanoyl radicals referred to above contain up to 6 carbon atoms and can be illustrated by acetyl, propionyl, butyryl, pentanoyl, hexanoyl and the branched-chain isomers thereof. The lower alkyl radicals referred to above contain 1 to 6 carbon atoms and are illustrated by methyl, ethyl, propyl, butyl and the corresponding

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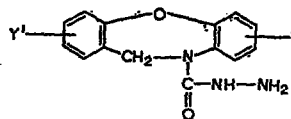
branched-chain isomers. The halogen radicals referred to above are chlorine, fluorine, bromine and iodine.

The compounds of the present invention are prepared by the reaction of a hydrazide with an acid derivative. More specifically, a hydrazide of the formula $Q'-NH-NH_2$ is reacted with an acid derivative of the formula $Q-X$ wherein X is $-OH$, halogen, $-O-$ (lower alkyl), or



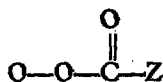
wherein Z is (lower alkyl)-O- or is connected with Q to give a cyclic compound. Q and Q' are each (lower alkylsulfonyl, α -toluenesulfonyl, higher alkanoyl, halo(lower alkanoyl), carboxy(lower alkanoyl), carboxy-acryloyl, phenoxy(lower alkanoyl), chlorophenoxy(lower alkanoyl), or Y,Y' - substituted - 10,11 - dihydrodibenz[b,f][1,4]-oxazepine - 10 - carbonyl where Y and Y' are defined as above. Q and Q' are selected so that at least one, but not more than one, contains a dibenzoxazepine group. In addition, when Q contains a sulfonyl group, X can only be halogen; and when Q contains a dibenzoxazepine group, X can only be halogen or $-O-$ (lower alkyl).

More specifically, the preferred starting material for the preparation of the present compounds is a hydrazide of the formula



wherein Y and Y' are defined as above. This is reacted with an acid halide of the formula

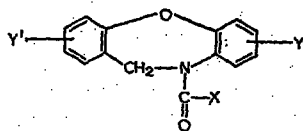
Q-halogen where halogen is preferably chlorine and Q is defined as above. The reaction is preferably carried out in the presence of an inorganic base such as sodium or potassium bicarbonate or in the presence of a tertiary amine to give the desired disubstituted hydrazine. A similar reaction takes place when the acid derivative is



in which case an anhydride is involved. Z is preferably (lower alkyl)-O- in which case a mixed anhydride is involved. This can be conveniently generated in situ by the reaction of an acid QOH with a chlorocarbonate such as ethyl chloroformate. Z can also be connected to Q to give a cyclic compound which is actually a cyclic anhydride. Examples of such useful anhydrides are maleic anhydride, succinic anhydride and glutaric anhydride. The preferred starting material depicted above can also be reacted with a compound of the formula Q-O-(lower alkyl). In this case, an ester is involved and the lower alkyl groups are preferred to be methyl or ethyl. The two reactants are heated in an inert solvent to give the desired disubstituted hydrazine. Actually, although lower alkyl esters are specified above, other active esters can be used.

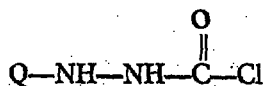
Finally, the preferred starting material can be reacted with an acid derivative Q-OH. This reaction can be carried out in an inert solvent in the presence of an agent such as dicyclohexylcarbodiimide and 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide which would remove the water formed in the course of the reaction. Alternatively, the hydrazide can be reacted with the carboxylic acid to give the hydrazonium salt which would lose water on heating to give the desired disubstituted hydrazine.

Alternatively, an acid derivative of the formula



can be reacted with a hydrazide of the formula Q-NH-NH₂ in a series of reactions similar to that detailed above.

Finally, it is possible to react a compound of the formula



with a Y,Y' - substituted - 10,11 - dihydro-

dibenz[b,f][1,4]oxazepine to give the desired products.

The compounds of the present invention are useful because of their pharmacological properties. In particular, they are antagonists of prostaglandin, 5-hydroxytryptamine and acetylcholine. They are additionally useful as topical anti-inflammatory agents, anti-diarrheal agents, and agents for reducing sebum secretion. The present compounds have minimal undesirable effects on the central nervous system.

The anti-inflammatory utility of the present compounds has been demonstrated in the following manner. A phlogistic vehicle is prepared from 4 parts of pyridine, 1 part of distilled water, 2 parts of diethyl ether, and 10 parts of 2% Croton oil in ether. Test compounds is dissolved in the indicated vehicle so that the concentration is 400 µg./cc. Similarly, hydrocortisone is dissolved in the vehicle at a concentration of 800 µg./cc. to provide a standard compound. The solutions involved are applied topically to the right ear of 10 rats (immature Sprague-Dawley rats weighing approximately 45-55 g.) with the untreated left ear serving as the control. Using the test compound solution and a syringe, 0.1 cc. is dispensed on the right ear, half on the dorsal and the other half on the ventral surface of the ears. Subsequently, the tip of the syringe used in the dispensing is used to stroke the surface of the ear back and forth five times. Six hours after the above treatment, the ears are removed and weighed individually to determine the extent of the inhibition of the phlogistic action. When tested in this way, 1-octanoyl-2-(8-chloro-10,11-dihydrodibenz[b,f][1,4]oxazepine-10-carbonyl)hydrazine was found to inhibit the inflammation and thus is useful as a topical anti-inflammatory agent.

The utility of the present compounds in inhibiting sebum secretion was demonstrated in the following way. Polysorbate 80 was added to sterile 0.9% saline solution to produce a vehicle which was 1% Polysorbate 80 and 0.9% sodium chloride. To 65 ml. of this vehicle was added 2.6 parts of 1-octanoyl-2-(8-chloro-10,11-dihydrodibenz[b,f][1,4]oxazepine-10-carbonyl)hydrazine so that 0.2 ml. of the solution would contain 8 mg. of the compound. The solution was briefly subjected to ultrasonic mixing. Using 2 groups of 12 Charles River intact male rats, the first group was injected daily with the solution containing the test compound intraperitoneally at a dose of 20 mg./kg. body weight with the second group of animals receiving the same vehicle but without the test compound and in an amount related to their body weights. On day 15 after the administration rats of both groups were shampooed with water and sodium lauryl sulfate, dried with a hair dryer, and returned

to their cages. On day 16, the rats of both groups were again shampooed with water and sodium lauryl sulfate and dried. Using hair clippers, approximately 1 g. of hair was cut from the left flank of each rat followed this second shampoo, and the hair samples were placed into tared containers. On day 24, after euthanasia, a second swath of hair was cut from the right flank of each rat and placed in tared beakers. The exact weight to the nearest 0.1 μ g. of each hair sample was determined before sending the samples to be analyzed colorimetrically for sebum content. The amount of sebum observed in the treated animals was then compared to that in the untreated animal to determine if any inhibition of secretion occurred. In the particular experiment described here, it was found that 1-octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 19 - carbonyl)-hydrazine produced a significant decrease in the sebum secretion.

In the following examples, which illustrate the invention, quantities are indicated in parts by weight unless parts by volume are specified, and temperatures are indicated in degrees Centigrade ($^{\circ}$ C.). Nuclear magnetic resonance spectra were determined on a 60 megaHertz instrument using tetramethylsilane as an internal reference, and are indicated in Hertz (cycles per second). Ultraviolet absorption maxima are given in millimicrons ($m\mu$), and infrared absorption maxima in microns (μ).

Example 1

To a solution of 0.5 part of 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carboxylic acid hydrazide and 19.6 parts of acetonitrile was added 0.30 part of sodium bicarbonate followed by 0.56 part of octanoyl chloride. The solution was stirred for 48 hours at room temperature, after which time the solvent was removed under reduced pressure and the resulting oil recrystallized by trituration with cyclohexane. Recrystallization of the solid from cyclohexane yielded 1 - octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)-hydrazine, melting at about 127—129 $^{\circ}$ C.

When the above procedure was repeated using the appropriate acid chloride in place of the octanoyl chloride and optionally using potassium carbonate in place of the sodium carbonate, the following compounds were obtained:

1 - Heptanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 131—132 $^{\circ}$ C.

1 - Decanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 112—114 $^{\circ}$ C.

1 - (5 - Chloropentanoyl) - 2 - (8 - chloro -

10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl(hydrazine melting at about 148—149 $^{\circ}$ C.

1 - (4 - Chlorobutanoyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 154—156 $^{\circ}$ C.

1 - (6 - Chlorohevanoyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine which is characterized by nuclear magnetic resonance peaks, in a dilute solution of deuteriochloroform and deuterated water, at about 80, 130 (broad triplet), 170 (broad triplet), 300 and 450 Hertz. The combined integration of the peaks at 80, 130 and 170 Hertz is that expected for 10 protons.

1 - (5 - Bromopentanoyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 157—159 $^{\circ}$ C.

Example 2

When the procedure of Example 1 was repeated using triethylamine in place of the sodium bicarbonate and using the appropriate acid chloride in place of the octanoyl chloride, the following compounds were obtained:

1 - Phenoxyacetyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 157—158 $^{\circ}$ C. with decomposition.

1 - (3 - Phenoxypropionyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine which is characterized by nuclear magnetic resonance peaks, in a dilute solution of deuteriochloroform and deuterated water, at about 150, 240, 300 and 450 Hertz. The integration of the envelope at about 450 Hertz is that expected for 12 protons.

1 - (4 - Chlorophenoxyacetyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 138—139 $^{\circ}$ C.

1 - [3 - (4 - Chlorophenoxy)propionyl] - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine characterized by nuclear magnetic resonance peaks, in a dilute solution of deuteriochloroform and deuterated water, at about 150, 240, 300 and 450 Hertz. The integration of the envelope at about 450 Hertz is that expected for 11 protons.

Example 3

When the procedure of Example 1 was repeated using sodium carbonate as the base and an appropriate sulfonyl chloride in place of the octanoyl chloride, the following compounds were obtained:

1 - (n - butylsulfonyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 148—150 $^{\circ}$ C.

- 1 - Methylsulfonyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, characterized by nuclear magnetic resonance peaks, in a dilute solution of deuteriochloroform and deuterated water, at about 190, 300 and 450 Hertz.
- 5 1 - (α - toluenesulfonyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 218—220°C.

Example 4

- The procedure of Example 1 was repeated using the appropriate dibenzoxazepine - 10 - carboxylic acid hydrazide in place of the chloro-substituted compound used therein and the following compounds were obtained:

- 1 - Octanoyl - 2 - (8 - trifluoromethyl - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 97—100°C.

- 1 - Octanoyl - 2 - (10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine which is characterized by nuclear magnetic resonance peaks, in deuterio - dimethylsulfoxide, at about 50 broad triplet), 80, 130 (triplet), 300 and 450 Hertz. The integration of the 450 Hertz region indicates the presence of 8 protons.

- 1 - Octanoyl - 2 - (8 - bromo - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine characterized by infrared absorption maxima, in a potassium bromide disc, at about 3.0, 5.9, 6.1 and 18.0 microns.

- 1 - Octanoyl - 2 - (8 - methyl - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, characterized by nuclear magnetic resonance peaks, in a dilute solution of deuteriochloroform and deuterated water, at about 50 (broad triplet), 80, 120 (triplet), 140, 300 and 450 Hertz.

- 1 - Octanoyl - 2 - (2 - methyl - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine characterized by nuclear magnetic resonance peaks, in deuteriochloroform solution and deuterated water, at about 50 (broad triplet), 80, 130 triplet), 140, 300 and 450 Hertz. The region of 140 Hertz indicated a 3 proton singlet and the width at half weight ($W_{1/2}$) is about 2.5 Hertz.

- Also obtained in a similar manner was 1 - (5 - chloropentanoyl) - 2 - (8 - trifluoromethyl - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 121.5—123.5°C.

Example 5

- To one part of 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carboxylic acid hydrazide dissolved in 50 parts by volume of a 1:1 benzene-ethylene chloride solution, there was added in one portion 0.34 part of maleic anhydride. The mixture was stirred at room temperature for 24 hours and the solvent was evaporated to leave a residual oil.

This was crystallized first from benzene ethyl acetate and then from a mixture of ethyl acetate, cyclohexane and ethanol to give 1 - (3 - carboxyacryloyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 171—172°C.

When the above procedure was repeated using glutaric anhydride and succinic anhydride in place of the maleic anhydride, the products obtained were, respectively, 1 - (4 - carboxybutyryl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 173—176°C. with decomposition and 1 - (3 - carboxypropionyl) - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine melting at about 177—179°C. with decomposition.

Example 6

0.3 Part of octanoic acid hydrazide was dissolved in dimethylsulfoxide containing 0.2 part of sodium bicarbonate. 8 - Chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)chloride was added dropwise to the mixture. The solution was stirred for 48 hours at room temperature and then the solvent was removed under reduced pressure. The resulting residual oil was triturated with cyclohexane to give a solid which was then recrystallized from cyclohexane to give 1 - octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine which was identical to the product obtained by the method described in the first paragraph of Example 1.

When heptanoic acid hydrazide, decanoic acid hydrazide, 5 - chloropentanoic acid hydrazide and 4 - chlorobutanoic acid hydrazide were each substituted for the octanoic acid hydrazine and the procedure described above was repeated, the corresponding disubstituted hydrazines were obtained in each instance. Each of the products obtained in this way is identical to the material prepared by the method described in Example 1.

Example 7

To a solution of 0.53 part of methyl 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carboxylate in benzene was added with stirring 0.3 part of octanoic acid hydrazide until the hydrazide was dissolved. The reaction was then heated under reflux until completed. The solvent was removed under reduced pressure and the resulting oil crystallized by trituration with cyclohexane. Recrystallization from cyclohexane yielded 1 - octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, which product was identical to that obtained in the first paragraph of Example 1.

Substitution of an equivalent quantity of

ethyl 8 - chloro - 10,11 - dihydrodibenz-
[b,f][1,4]oxazepine - 10 - carboxylate and
heptanoic acid hydrazide in the procedure
detailed in the foregoing paragraph afforded
1 - heptanoyl - 2 - (8 - chloro - 10,11 -
dihydrodibenz[b,f][1,4]oxazepine - 10 -
carbonyl)hydrazine, which product was iden-
tical to that obtained in the second paragraph
of Example 1.

Example 8

0.26 Part of octanoic acid was dissolved in
tetrahydrofuran and to the resulting solution
was added 0.2 part of trimethylamine with
cooling. 0.19 Part of ethyl chloroformate was
then added. The solution was stirred for one
hour and then 0.55 part of 8 - chloro -
10,11 - dihydrodibenz[b,f][1,4]oxazepine -
10 - carboxylic acid hydrazide was added in
tetrahydrofuran while the reaction mixture
was allowed to come to room temperature.
When the reaction was complete the tetra-
hydrofuran was removed by distillation and
the residue was crystallized by trituration with
cyclohexane. Recrystallization from cyclo-
hexane yielded 1 - octanoyl - 2 - (8 - chloro -
10,11 - dihydrodibenz[b,f][1,4]oxazepine -
10 - carbonyl)hydrazine, which product was
identical to that obtained in the first para-
graph of Example 1.

Example 9

0.26 Part of octanoic acid and 0.42 part
of dicyclohexylcarbodiimide were dissolved in
tetrahydrofuran and stirred at room tempera-
ture. Then 0.55 part of 8 - chloro - 10,11 -
dihydrodibenz[b,f][1,4]oxazepine - 10 -
carboxylic acid hydrazide was added drop-
wise with stirring until the reaction was com-
plete. The substituted urea by-product was
separated by filtration and the solvent was
removed from the filtrate by distillation. The
residue was then crystallized from cyclo-
hexane to yield 1 - octanoyl - 2 - (8 - chloro -
10,11 - dihydrodibenz[b,f][1,4]oxazepine -
10 - carbonyl)hydrazine, which product was
identical with that obtained in the first para-
graph of Example 1.

Example 10

To a solution of 0.55 part of 8 - chloro -
10,11 - dihydrodibenz[b,f][1,4]oxazepine -
10 - carboxylic acid hydrazide in dimethyl-
formamide was added dropwise 0.3 part of
ethyl octanoate and the solution was stirred
and heated until the reaction was complete.
Then, the dimethylformamide was removed
by distillation at reduced pressure and the
residual material was triturated with cyclo-
hexane to cause it to crystallize. Recrystalliza-
tion from cyclohexane yielded 1 - octanoyl -
2 - (8 - chloro - 10,11 - dihydrodibenz[b,f]-
[1,4]oxazepine - 10 - carbonyl)hydrazine,
which product was identical to that obtained
in the first paragraph of Example 1.

Example 11

To 0.55 part of 8 - chloro - 10,11 -
dihydrodibenz[b,f][1,4]oxazepine - 10 -
carboxylic acid hydrazide was added with
stirring 0.26 part of octanoic acid and the
solution was stirred until the reaction was
complete. The hydrazonium carboxylate which
crystallized was filtered from the solution.
The hydrazonium carboxylate was then placed
in a flask equipped with a glass tube to allow
the system to be flushed with nitrogen. The
hydrazonium carboxylate was then heated
between 100 and 250°C. under nitrogen until
the reaction was complete. The residue was
then crystallized from cyclohexane, yielding
1 - octanoyl - 2 - (8 - chloro - 10,11 -
dihydrodibenz[b,f][1,4]oxazepine - 10 -
carbonyl)hydrazine, which product was iden-
tical with that obtained in the first paragraph
of Example 1.

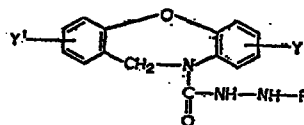
Example 12

0.3 Part of octanoic acid hydrazide was
dissolved in dichloromethane and cooled to
0°C. and then 0.4 part of triethylamine was
added. 0.18 Part of phosgene in dichloro-
methane was added dropwise until no further
salt precipitation occurred. 0.44 Part of 8 -
chloro - 10,11 - dihydrodibenz[b,f][1,4]-
oxazepine was added with stirring in one por-
tion and the solution was then allowed to
warm to room temperature. Stirring was
continued until the reaction was completed.
The salts were filtered, and the filtrate was
evaporated by distillation at reduced pressure,
and the product was crystallized by trituration
with cyclohexane. Recrystallization from
cyclohexane yielded 1 - octanoyl - 2 - (8 -
chloro - 10,11 - dihydrodibenz[b,f][1,4]-
oxazepine - 10 - carbonyl)hydrazine, which
product was identical to that obtained in
the first paragraph of Example 1.

WHAT WE CLAIM IS:—

1. Compounds of the general formula

(I)



wherein Y and Y' are hydrogen, halogen,
methyl, or trifluoromethyl; and R is higher
alkanoyl, halo(lower alkanoyl), carboxy(lower
alkanoyl), 3 - carboxyacryloyl, phenoxy(lower
alkanoyl), halophenoxy(lower alkanoyl), (lower
alkyl)sulfonyl or α -toluenesulfonyl.

2. 1 - Octanoyl - 2 - (8 - chloro - 10,11 -
dihydrodibenz[b,f][1,4]oxazepine - 10 -
carbonyl)hydrazine.

3. 1 - Heptanoyl - 2 - (8 - chloro - 10,11 -
dihydrodibenz[b,f][1,4]oxazepine - 10 -
carbonyl)hydrazine.

ethyl 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carboxylate and heptanoic acid hydrazide in the procedure detailed in the foregoing paragraph afforded 1 - heptanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, which product was identical to that obtained in the second paragraph of Example 1.

Example 8

0.26 Part of octanoic acid was dissolved in tetrahydrofuran and to the resulting solution was added 0.2 part of trimethylamine with cooling. 0.19 Part of ethyl chloroformate was then added. The solution was stirred for one hour and then 0.55 part of 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carboxylic acid hydrazide was added in tetrahydrofuran while the reaction mixture was allowed to come to room temperature. When the reaction was complete the tetrahydrofuran was removed by distillation and the residue was crystallized by trituration with cyclohexane. Recrystallization from cyclohexane yielded 1 - octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, which product was identical to that obtained in the first paragraph of Example 1.

Example 9

0.26 Part of octanoic acid and 0.42 part of dicyclohexylcarbodiimide were dissolved in tetrahydrofuran and stirred at room temperature. Then 0.55 part of 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carboxylic acid hydrazide was added dropwise with stirring until the reaction was complete. The substituted urea by-product was separated by filtration and the solvent was removed from the filtrate by distillation. The residue was then crystallized from cyclohexane to yield 1 - octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, which product was identical with that obtained in the first paragraph of Example 1.

Example 10

To a solution of 0.55 part of 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carboxylic acid hydrazide in dimethylformamide was added dropwise 0.3 part of ethyl octanoate and the solution was stirred and heated until the reaction was complete. Then, the dimethylformamide was removed by distillation at reduced pressure and the residual material was triturated with cyclohexane to cause it to crystallize. Recrystallization from cyclohexane yielded 1 - octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, which product was identical to that obtained in the first paragraph of Example 1.

Example 11

To 0.55 part of 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carboxylic acid hydrazide was added with stirring 0.26 part of octanoic acid and the solution was stirred until the reaction was complete. The hydrazone carboxylate which crystallized was filtered from the solution. The hydrazone carboxylate was then placed in a flask equipped with a glass tube to allow the system to be flushed with nitrogen. The hydrazone carboxylate was then heated between 100 and 250°C. under nitrogen until the reaction was complete. The residue was then crystallized from cyclohexane, yielding 1 - octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, which product was identical with that obtained in the first paragraph of Example 1.

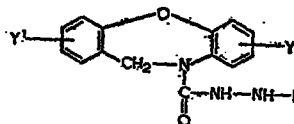
Example 12

0.3 Part of octanoic acid hydrazide was dissolved in dichloromethane and cooled to 0°C. and then 0.4 part of triethylamine was added. 0.18 Part of phosgene in dichloromethane was added dropwise until no further salt precipitation occurred. 0.44 Part of 8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine was added with stirring in one portion and the solution was then allowed to warm to room temperature. Stirring was continued until the reaction was completed. The salts were filtered, and the filtrate was evaporated by distillation at reduced pressure, and the product was crystallized by trituration with cyclohexane. Recrystallization from cyclohexane yielded 1 - octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine, which product was identical to that obtained in the first paragraph of Example 1.

WHAT WE CLAIM IS:—

1. Compounds of the general formula

(I)



wherein Y and Y' are hydrogen, halogen, methyl, or trifluoromethyl; and R is higher alkanoyl, halo(lower alkanoyl), carboxy(lower alkanoyl), 3 - carboxyacryloyl, phenoxy(lower alkanoyl), halophenoxy(lower alkanoyl), (lower alkyl)sulfonyl or α -toluenesulfonyl.

2. 1 - Octanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine.

3. 1 - Heptanoyl - 2 - (8 - chloro - 10,11 - dihydrodibenz[b,f][1,4]oxazepine - 10 - carbonyl)hydrazine.



4. 1 - (5 - chloropentanoyl) - 2 - (8 - as hereinbefore described with reference to
chloro - 10,11 - dihydrodibenz[b,f][1,4]- any of the Examples.
oxazepine - 10 - carbonyl)hydrazine.
5. 1 - Decanoyl - 2 - (8 - chloro -
10,11 - dihydrodibenz[b,f][1,4]oxazepine -
10 - carbonyl)hydrazine.
6. 1 - (4 - Chlorobutanoyl) - 2 - (8 -
chloro - 10,11 - dihydrodibenz[b,f][1,4]-
oxazepine - 10 - carbonyl)hydrazine.
- 10 7. Compounds of the general formula (I)

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