

**ΚΥΠΡΙΑΚΟ ΓΡΑΦΕΙΟ ΔΙΠΛΩΜΑΤΩΝ
ΕΥΡΕΣΙΤΕΧΝΙΑΣ
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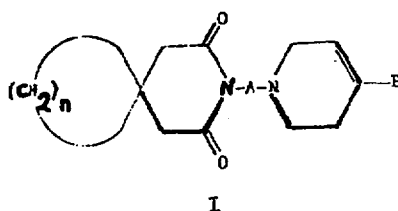
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 C2C
(71) Applicant
 Bristol-Myers Company
 345 Park Avenue
 New York
 NY 10022
 United States of
 America
(72) Inventors
 Davis L Temple
 Joseph P Yevich
 Walter G Lobeck
(74) Agents
 Langner Parry
 52-54 High Holborn
 London WC1V 6RR

(54) Azaspiroalkanes

(57) Compounds of the general formula



($n = 4$ or 5 ; $A = (CH_2)_{2-5}$; $B = Ph$
optionally substituted by a C_{1-4} alkyl
or alkoxy group or a halogen atom)
and their salts are tranquilisers. They

are prepared by standard methods, eg. dehydration of the corresponding 4-hydroxy-4-phenylpiperidine derivatives or their salts.

The preparation of 8-(4-bromobutyl)-8-azaspiro[4,5]decane-7,9-dione is described.

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SPECIFICATION

N-[(4-phenyl-1,2,3,6-tetrahydropyridin-1-yl) alkylene]azaspiroalkanediones and N-[(4-hydroxy-4-phenylpiperidin-1-yl) alkylene]azaspiroalkanediones

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Field of the Invention

N-[(4-Phenyl-1,2,3,6-tetrahydropyridin-1-yl)alkylene]-azaspiroalkanediones and N-[(4-hydroxy-4-phenylpiperidin-1-yl)alkylene]-azaspiroalkanediones are heterocyclic carbon compounds having a six-membered hetero ring including one nitrogen atom with the spiro system incorporating this

10 hetero ring (Class 546, Subclass 16).

Background of the Invention

8-(4-Phenyl-1-piperazinylalkylene)-8-azaspiro[4,5]decane-7,9-diones and 3-(4-phenyl-1-piperazinylalkylene)-3-azaspiro[5,5]undecane-2,4-diones have been prepared as psychotropic agents.

15 These are described in:

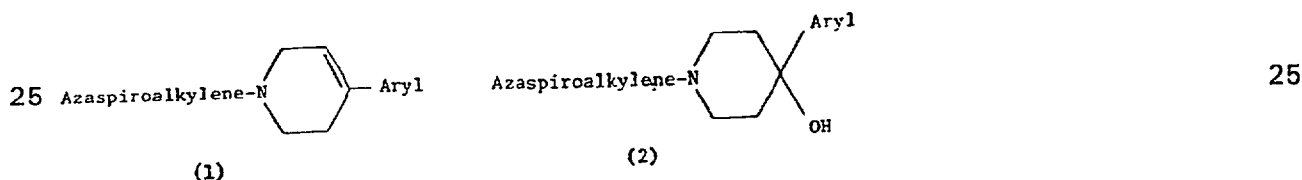
Wu, Y. H., U.S. Patent No. 3,398,151 patented Aug. 20, 1968.

Wu, Y. H., U.S. Patent No. 3,558,777 patented Jan. 26, 1971.

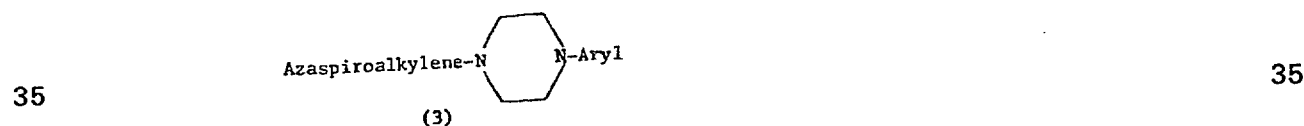
Wu, et al., *J. Med. Chem.*, 12, 876-881 (1969).

The Wu and Wu, et al. compounds incorporate a piperazine ring system in their structures (Formula 3) and in this respect differ from the compounds of this invention (Formula 1 and

20 Formula 2) which contain tetrahydropyridyl and piperidinyl systems, respectively.



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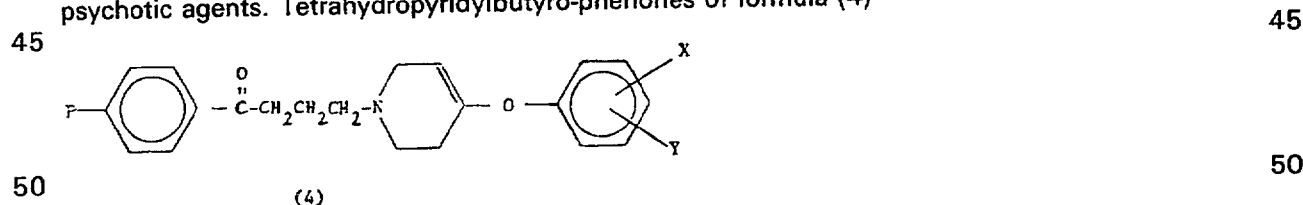
Other variations of the (3) structure, specifically substitution of various heterocycles for the aryl portion, have been described:

40 Wu, et al., U.S. Patent No. 3,717,634 patented Feb. 20, 1973.

Wu, et al., U.S. Patent No. 3,976,776 patented Aug. 24, 1976.

Wu, et al., *J. Med. Chem.*, 15, 447-479 (1972).

Certain 4-substituted-1,2,3,6-tetrahydropyridyl compounds have been described as anti-psychotic agents. Tetrahydropyridylbutyro-phenones of formula (4)



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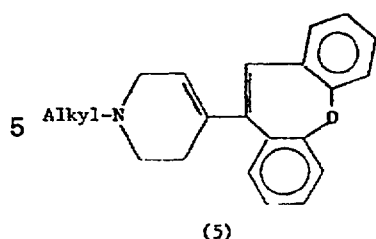
were described in:

Wise, L. D., et al., U.S. Patent No. 4,218,456 patented Aug. 19, 1980.

These compounds, with butyrophenone- and aryloxy-substituents on the tetrahydropyridine

55 ring, are structurally quite different from compounds comprising the present invention.

Anti-psychotic agents of formula (5) were described in:



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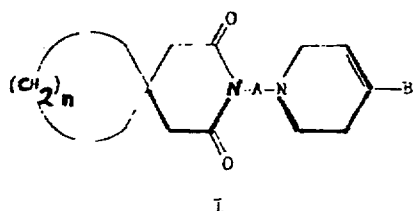
McKenzie, et al., U.S. Patent No. 4,221,714 patented Sept. 9, 1980.

These compounds, with their particular substituents on the tetrahydro-pyridine moiety, show increasing dissimilarity of structure compared with the subject compounds of this application.

15 Summary of the Invention

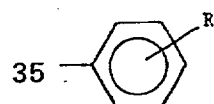
This invention is concerned with a new series of CNS-active compounds characterized by the following general structural formula (I) and the non-toxic pharmaceutically acceptable acid addition salts thereof.

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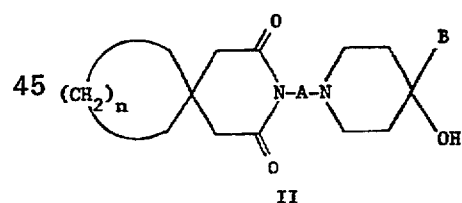
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30 In the foregoing formula, n is the integer 4 or 5; A is a divalent straight alkylene chain of 2 to 5 carbon atoms inclusive; B is



wherein R is hydrogen, lower alkyl from 1 to 4 carbon atoms inclusive, lower alkoxy of from 1 to 4 carbon atoms inclusive, or halogen.

40 Also disclosed and claimed are compounds of Formula (II) which are useful intermediates for the preparation of (I).

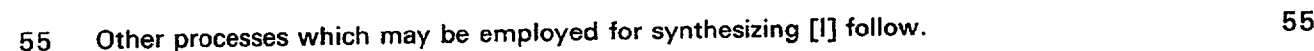
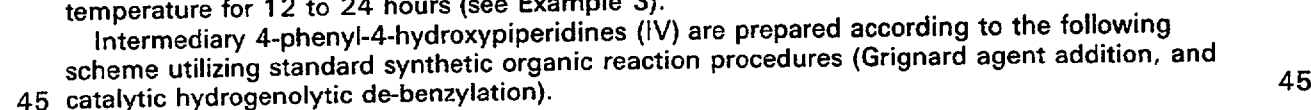
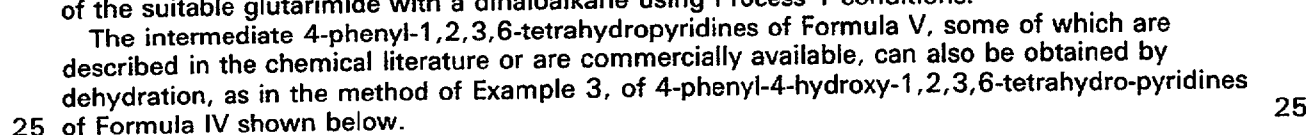


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In Formula II, n, A, and B are the same as for formula I.

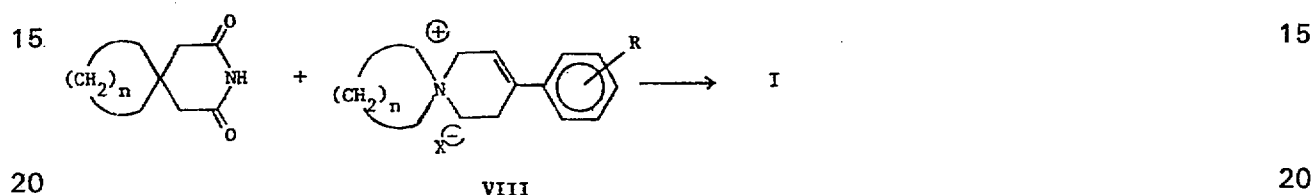
Detailed Description of the Invention

Several processes may be employed for preparation of compounds of Formula I. These processes may be adapted to variation in order to produce other compounds embraced by this invention but not specifically disclosed. Variations of methods to produce the same compounds in somewhat different fashion will also be evident to one skilled in the art. Certain examples will be given for specific illustration.

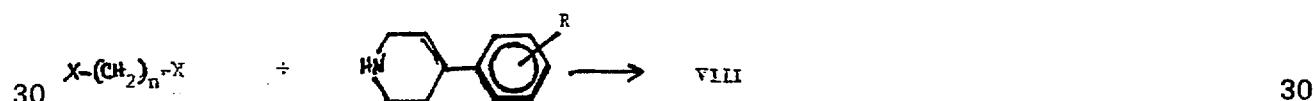


This process, wherein n, A, and R have the same meanings as previously assigned Formula I, consists of reacting a spiro-substituted glutaric anhydride of Formula (VI), many of which are described in chemical literature or are commercially available, with a 1-(ω -aminoalkyl)-4-aryl-1,2,3,6-tetrahydropyridine of Formula (VII). Adaptable methods useful for synthesis of compounds of Formula (V) may be found in the literature or described herein. An example would be reaction of an ω -cyanoalkyl halide with a suitable 4-aryl-1,2,3,6-tetrahydropyridine for an easily convertible precursor such as IV), followed by reduction of the resulting nitrile to the amine (VII). In general, the reaction of VI and VII is preferably carried out at elevated temperature in an inert organic reaction solvent – pyridine is a preferred solvent. Temperatures in the order of 100° to 200°C are preferred. A reaction period of at least 2 hrs. may be sufficient, although longer reaction times are customarily employed in the interest of obtaining maximum yield.

Process 4

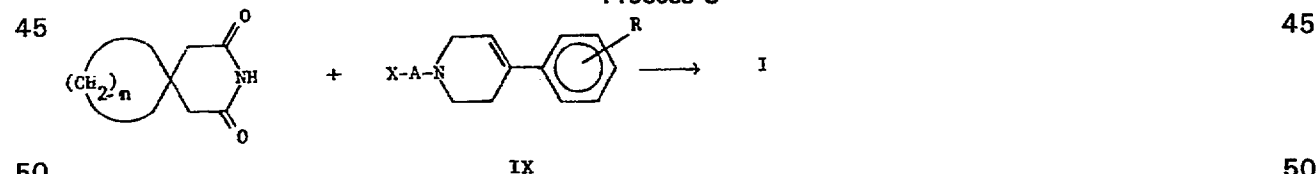


In this embodiment of the subject invention, intermediate compounds of Formula VIII, wherein n, R, and X have the same meanings as given hereinabove, are reacted with a specific glutarimide using conditions described in Process 1, of which this, Process 4, is a variant. Compounds of Formula VIII are prepared by the following scheme.



To synthesize compounds of Formula VIII, a 4-aryl-1,2,3,6-tetrahydro-pyridine (V) is combined with three equivalents of a dihaloalkane in an inert organic solvent in the presence of a strong base. Strong bases which may be employed consist of alkali metal oxides, hydrides, amides, or carbonates with sodium carbonate and potassium carbonate being particularly preferred. Suitable organic solvents, usually with boiling points in the range of about 80° to 160°C, include liquid hydrocarbons, hydrocarbon nitriles, dimethylformamide, hydrocarbon ethers, and the like. The reaction is conveniently carried out at the boiling point of the medium selected. Suitable reaction periods range from 2 to 24 hrs. with the duration of the reaction period depending to some extent upon the temperature and reaction solvent selected. In general, formation of quaternary compounds of Formula VII are facilitated by higher reaction temperatures.

Process 5



Process 5 illustrates the reaction of one equivalent of an intermediate compound of Formula IX, wherein A, R, and X are as hereinabove defined, with one equivalent of a specific glutarimide using the reaction conditions outlined above for Process 4.

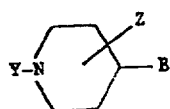
The haloalkyl reactant of Formula IX is prepared according to standard organic procedures. By way of example, reaction of the tetrahydropyridines of Formula V with alkanol halides of the formula HO-A-X provides intermediates of the Formula X.



65 This intermediate is then esterified according to conventional techniques well known to the art to 65

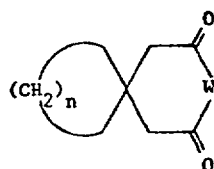
provide the Formula IX reactants. For instance, thionyl chloride acting upon the compounds of Formula X provides the Formula IX intermediates in which X is chlorine. In a similar fashion, bromides and iodides are prepared. Phosphates, sulfates, tosylates, mesylates corresponding to Formula IX are obtained with conventional laboratory techniques.

The foregoing embodiments of the process of the present invention for the preparation of compounds of Formula I are considered to be a unitary process. Thus, the 4-phenyltetrahydropyridylalkylene-azaspiroalkanediones of Formula I are prepared in accordance with the unitary process of the present invention by reacting a tetrahydropyridine, or its precursor, depicted by Formula XI



XI

wherein Y is selected from the group consisting of hydrogen (Formula IV and V), H_2N-A- (Formula VII), $X-A-$ (Formula IX), or $(CH_2)_n$ (Formula VIII), and A, n, and X are as hereinbefore defined; and Z is 4-hydroxy (for the precursor), or Z is a 3,4-double bond; with a spiroglutaric acid derivative, depicted by Formula XII



XII

wherein n is as hereinbefore defined and W is O (Formula VI) when Y is H_2N-A- ; or W is N-H when Y is $X-A-$ or $(CH_2)_n =$; or W is N-A-X when Y is hydrogen; in an inert organic liquid medium at an elevated temperature. In the instances when the precursor-type intermediates of Formula XI, Z is 4-hydroxy, were used as reactants, a dehydration step must intervene for preparation of the invention compounds of Formula I.

Biological testing of the subject compounds of formula I in animals demonstrates psychotropic activity of the sort which characterizes tranquilizers. The term tranquilizer used herein encompasses anxiolytic and neuroleptic actions. Conventional screening tests can be utilized in determining the psychotropic profile of the instant compounds such as:

1. Conditioned avoidance response in fasted rats treated orally. These data were obtained by the method described in the above Wu, et al. patents and publications.

2. Dopamine receptor binding assay reflecting neuroleptic activity (Burt, Crease, and Snyder, *Molec. Pharmacol.* 12:800 (1976); Burt, Crease, and Snyder, *Science* 196:326 (1977); Crease, Burt, and Snyder, *Science* 192:481 (1976).

3. Apomorphine stereotype behavior test in non-fasted rats which determines the ability of centrally acting compounds to block apomorphine-induced stereotyped behavior. This preclinical test gives an indication of potential neuroleptic efficacy (Janssen, et al., *Arzneimittel-Forsch.*, 17:841 (1966)).

The compounds of the present invention may be administered to mammals to exert their anxiolytic and neuroleptic effects in the same way and in similar dosage amounts as was suitable for the compounds cited in the above Wu, et al. patents which are incorporated herein in entirety by reference.

Accordingly, another embodiment of the present invention concerns a process for eliciting a tranquilizing effect in a psychotic or neurotic mammal which comprises administering to said mammal a non-toxic effective tranquilizing dose of from 0.01 to 40 mg. per kg. of body weight of said mammal of a Formula I compound or a non-toxic pharmaceutically acceptable acid addition salt thereof.

Appropriate pharmaceutically acceptable carriers, diluents, and adjuvants as set forth in the aforementioned Wu, et al. patents together with the instant compounds may be employed to prepare desired compositions for use in the tranquilizing process. Thus, an embodiment of the invention is directed to a pharmaceutical composition in dosage unit form suitable for systemic administration to a mammalian host comprising a pharmaceutical carrier and an amount of a compound claimed in Claim 1 to provide an effective dose of from 0.1 to 40 mg. per kg. of body weight of said host.

65 Description of Specific Embodiments

The compounds which constitute this invention, their methods of preparation, and their biologic actions will appear more fully from a consideration of the following examples and appended claims which are given for the purpose of illustration only and are not to be construed as limiting the invention in sphere or scope.

- 5 In examples which follow, used to illustrate the foregoing processes, temperatures are expressed in degrees centigrade ($^{\circ}$). Melting points are uncorrected. The nuclear magnetic resonance (NMR) spectral characteristics refer to chemical shifts (δ) expressed as parts per million (ppm) versus tetramethylsilane (TMS) as reference standard. The relative area reported for the various shifts in the H NMR spectral data corresponds to the number of hydrogen atoms of a particular functional type in the molecule. The nature of the shifts as to multiplicity is reported as broad single (bs), singlet (s), multiplet (m), doublet (d), triplet (t), or doublet of doublets (dd). Abbreviations employed are DMSO- d_6 (deuterodimethylsulfoxide), $CDCl_3$ (deuteriochloroform), and are otherwise conventional. The infrared (IR) spectral descriptions include only absorption wave numbers (cm^{-1}) having functional group identification value. The IR determinations were employed using potassium bromide (KBr) as diluent. The elemental analyses are reported as percent by weight. 15

Process 1

EXAMPLE 1

- 20 8-[4-(4-Phenyl-1,2,3,6-tetrahydropyridin-1-yl)butyl]-8-azaspiro[4.5]decane-7,9-dione Hydrochloride (Ia; $n = 4$, A = butyl, B = phenyl) 20

A solution of 0.02 mole each of 4-phenyl-1,2,3,6-tetrahydropyridine (V), 8-(4-bromobutyl)-8-azaspiro[4.5]decane-7,9-dione (III), and triethylamine in 30 ml. ethanol was heated in a high pressure reaction vessel at $150^{\circ}C$. for 6 hrs., sealed under a nitrogen atmosphere. The reaction solution was evaporated to dryness *in vacuo* and the residue partitioned between $CHCl_3$ and H_2O . The $CHCl_3$ layer was dried ($MgSO_4$), filtered and concentrated to a residue which was dissolved in 20 to 30 ml. ethanol and acidified with ethereal HCl. The solid was collected by filtration and recrystallized from ethanol to give 2.5 g. of the hydrochloride salt, m.p. $215-217^{\circ}C$. 25

- 30 Anal. Calcd. for $C_{24}H_{32}N_2O_2 \cdot HCl$: C, 69.14; H, 7.98; N, 6.72. Found: C, 68.82; H, 7.78; N, 6.60. 30

NMR (DMSO- d_6): 1.52 (12,m); 2.64 (4,s); 3.11 (6,m); 3.68 (4,m); 6.14 (1,m); 7.39 (5,m). IR (KBr): 690, 745, 1119, 1350, 1360, 1680, 1725, 2570, and 2930 cm^{-1} .

35 EXAMPLE 2 35

8-(4-Bromobutyl)-8-azaspiro[4.5]decane-7,9-dione (IIIa; $n = 4$, A = butyl, X = Br)

A slurry of 33.4 g. (0.2 mole) of 3,3-tetramethylene glutarimide, 86.4 g. (0.4 mole) of 1,4-dibromobutane, and 89% (0.6 mole) of K_2CO_3 (pulverized) in 500 ml. toluene was refluxed for 20 hrs. The reaction mixture was filtered while hot. The filtrate was concentrated and distilled *in vacuo* to afford a 58% yield of product, b.p. $160-167^{\circ}C/0.1\text{ mmHg}$. 40

Process 2 Dehydration

EXAMPLE 3

- 45 8-[4-(4-[2-Methoxyphenyl]-1,2,3,6-tetrahydropyridin-1-yl)butyl]-8-azaspiro[4.5]decane-7,9-dione Hydrochloride (Ic; $n = 4$, A = butyl, B = 2-methoxyphenyl) 45

8-[4-(4-Hydroxy-4-(2-methoxyphenyl)-1-piperidiny)butyl]-8-azaspiro[4.5]decane-7,9-dione (IIC, 3 g.) was stirred at room temperature in 20 ml. trifluoroacetic acid for 18 hrs. The reaction solution was concentrated *in vacuo* to a residue which was partitioned between dilute NH_4OH solution and $CHCl_3$. The organic layer was dried (Na_2SO_4) and concentrated to an oil which was converted to the hydrochloride salt with ethereal HCl in ethanol. The crude salt was isolated and recrystallized twice in acetonitrile-ethyl ether to give 1.5 g. of product (50%), m.p. $159-161^{\circ}C$. 50

Anal. Calcd. for $C_{25}H_{34}N_2O_3 \cdot HCl$: C, 67.18; H, 7.90; N, 6.27. Found: 67.11; H, 7.68; N, 6.33.

- 55 NMR (DMSO- d_6): 1.49 (12,m); 2.60 (4,s); 3.04 (6,m); 3.64 (4,m); 3.74 (3,s); 5.74 (1,m); 7.00 (4,m); 11.15 (1,bs). 55

IR (KBr): 760, 1125, 1255, 1355, 1435, 1670, 1722, 2480, and 2955 cm^{-1} .

Process 2 Hydrolysis intermediate

EXAMPLE 4

- 60 8-[4-(4-Hydroxy-4-[2-methoxyphenyl]-1-piperidiny) butyl]-8-azaspiro[4.5]decane-7,9-dione Hydrochloride (IIc; $n = 4$, A = butyl, B = 2-methoxyphenyl) 60

4-Hydroxy-4-(2-methoxyphenyl)piperidine (2 g., IVc where R = 2-MeO-prepared as set forth below); 8-[4-(1-bromobutyl)-8-azaspiro[4.5]decane-7,9-dione (2.4 g, IIIa); K_2CO_3 (2.3 g.); and KI (0.15 g) were combined in 80 ml. acetonitrile and refluxed for 18 hrs. The reaction mixture was filtered while hot and the filtrate concentrated *in vacuo* to a residue which was dissolved in 65

70 ml. CHCl_3 . The CHCl_3 solution was washed twice, using 50 ml. H_2O ; dried with MgSO_4 ; filtered and concentrated to 3.7 g. of oil. Conversion of the oil to the hydrochloride salt (ethanol and ethereal HCl) and recrystallization for ethanol gave a 73% yield of product, m.p. 246–248°C.

5 *Anal.* Calcd. for $\text{C}_{25}\text{H}_{36}\text{N}_2\text{O}_4 \cdot \text{HCl}$: C, 64.58; H, 8.03; N, 6.03. Found: C, 64.33; H, 7.82; N, 6.02.

NMR ($\text{DMSO}-d_6$): 1.56 (14,m); 2.64 (4,s); 3.10 (8,m); 3.68 (2,m); 3.84 (3,s); 5.30 (1,bs); 7.09 (3,m); 7.54 (1,m); 10.80 (1,bs).

IR (KBr): 755, 1120, 1238, 1350, 1430, 1672, 1720, 2710, 2930, and 3300 cm^{-1} .

10

Process 4 Dehydration

EXAMPLE 5

8-[4-(4-[4-Chlorophenyl]-1,2,3,6-tetrahydropyridin-1-yl)butyl]-8-azaspiro[4.5]decane-7,9-dione Hydrochloride (Ib; $n = 4$, A = butyl, B = 4-chlorophenyl)

15 8-(4-(4-[4-Chlorophenyl]-4-hydroxy-1-piperidiny)butyl)-8-azaspiro[4.5]decane-7,9-dione hydrochloride (II, 2 g) was added in portions to a stirred reaction medium consisting of 2 g. P_2O_5 in 10 ml. H_3PO_4 . After completion of addition the stirred mixture was heated to 170° and kept in that range for 3 hr. After being allowed to cool and stand at room temperature for 12 hours, the reaction mixture was hydrolyzed, while being kept cool with an ice bath, using 10 ml. H_2O . The hydrolyzed mixture was made basic, using sat'd Na_2CO_3 solution, and extracted with ether. The ether extract was dried (MgSO_4) and concentrated to a residual oil which was converted to the hydrochloride salt using a dilute ethanolic solution of HCl . Addition of ether caused precipitation of solid which was collected by filtration and dried to give 0.5 g. product (26%), m.p. 222–224°C.

25 *Anal.* Calcd. for $\text{C}_{24}\text{H}_{31}\text{ClN}_2\text{O}_2 \cdot \text{HCl}$: C, 63.86; H, 7.15; N, 6.21. Found: C, 63.52; H, 7.18; N, 6.10.

NMR ($\text{DMSO}-d_6$): 1.52 (12,m); 2.64 (4,s); 3.12 (6,m); 3.67 (4,m); 6.19 (1,m); 7.45 (4,m); 11.35 (1,bs).

IR (KBr): 810, 1125, 1355, 1670, 1723, 2580, and 2955 cm^{-1} .

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EXAMPLE 6

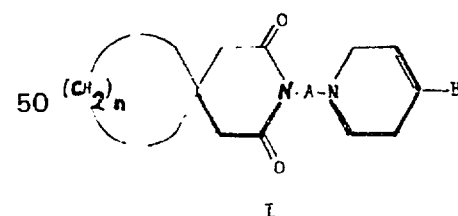
8-[4-(4-[4-Chlorophenyl]-4-hydroxy-1-piperidiny)butyl]-8-azaspiro[4.5]decane-7,9-dione Hydrochloride (IIb; $n = 4$, A = butyl, B = 4-chlorophenyl)

35 4-(4-Chlorophenyl)-4-hydroxypiperidine (4 g., IVb where R = 4-Cl—prepared as set forth below); IIIa (5.7 g.); Et_3N (1.9 g.) were all dissolved in 50 ml. ethanol and heated at 150°C. in a sealed reaction vessel for 6 hr. After cooling, the reaction mixture was concentrated to a residue and partitioned between CHCl_3 and 1M NaOH . The CHCl_3 layer was separated, dried (MgSO_4) and concentrated to 18.6 g. of grease-like residue. This material was dissolved in ethanol and acidified with ethereal HCl . Filtration gave 6.9 g. of HCl salt, m.p. 242–244°C. (decompose).

40 *Anal.* Calcd. for $\text{C}_{24}\text{H}_{33}\text{ClN}_2\text{O}_3 \cdot \text{HCl} \cdot 1/4\text{H}_2\text{O}$: C, 61.41; H, 7.31; N, 5.97. Found: C, 60.88; H, 7.34; N, 5.88.

CLAIMS

45 1. A compound selected from the group consisting of a compound having the formula (I)



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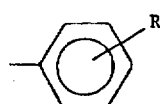
wherein

n is the integer 4 or 5;

A is a divalent straight alkylene chain of 2 to 5 carbon atoms inclusive;

B is

60



wherein R is hydrogen, lower alkyl from 1 to 4 carbon atoms inclusive, lower alkoxy of from 1 to 4 carbon atoms inclusive, or halogen;
and the non-toxic pharmaceutically acceptable acid addition salts thereof.

2. The compound of claim 1, 8-[4-(4-phenyl-1,2,3,6-tetrahydropyridin-1-yl)butyl]-8-azaspiro[4.5]decane-7,9-dione (Ia) or a pharmaceutically acceptable acid addition salt thereof. 5

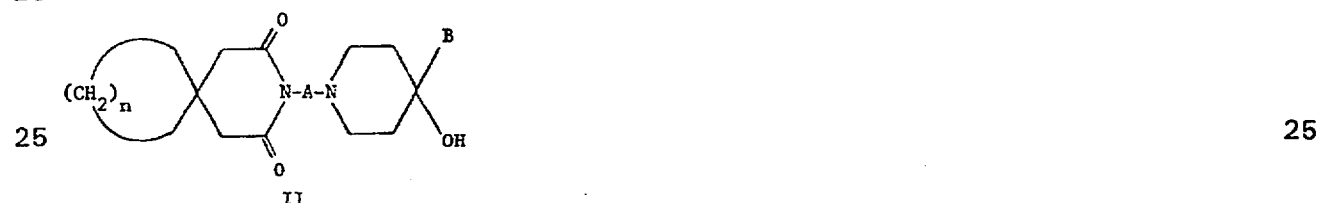
3. The compound of claim 1, 8-[4-(4-[4-chlorophenyl]-1,2,3,6-tetrahydropyridin-1-yl)butyl]-8-azaspiro[4.5]decane-7,9-dione (Ib) or a pharmaceutically acceptable acid addition salt thereof.

4. The compound of claim 1, 8-[4-(4-[2-methoxyphenyl]-1,2,3,6-tetrahydropyridin-1-yl)butyl]-8-azaspiro[4.5]decane-7,9-dione (Ic) or a pharmaceutically acceptable acid addition salt thereof. 10

5. The process for eliciting a tranquilizer effect in a psychotic or neurotic mammal which comprises administering to said mammal a non-toxic effective tranquilizing dose of from 0.01 to 40 mg. per kg. of body weight of said mammal of a compound claimed in claim 1 by the oral or a parenteral route.

6. A pharmaceutical composition in dosage unit form suitable for systemic administration to a mammalian host comprising a pharmaceutical carrier and an amount of a compound claimed in claim 1 to provide an effective non-toxic dose of from 0.01 to 40 mg. per kg. of body weight of said host. 15

7. A compound selected from the group consisting of a compound having the formula (II) 20



wherein n, A, and B are the same as recited above in Claim 1.

8. The compound of Claim 7, 8-[4-(4-[4-chlorophenyl]-4-hydroxy-1-piperidiny)butyl]-8-azaspiro[4.5]decane-7,9-dione (IIb) or a pharmaceutically acceptable acid addition salt thereof. 30

9. The compound of Claim 7, 8-[4-(4-hydroxy-4-[2-methoxyphenyl]-1-piperidiny)butyl]-8-azaspiro[4.5]decane-7,9-dione (IIc) or a pharmaceutically acceptable acid addition salt thereof.

10. A process for preparing azaspiroalkanediones having the formula 35



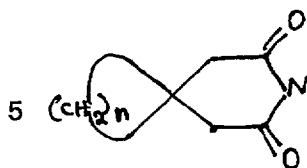
wherein n is a cardinal number which is 4 or 5, A is a divalent straight chain alkylene moiety containing from 2 to 5 carbon atoms, B is a group of the formula 45



wherein R is hydrogen, lower alkyl having from 1 to 4 carbon atoms, or halogen, by reacting a tetrahydropyridine or its precursor, having the formula 55



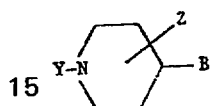
wherein Y is hydrogen, H_2NA- , $XA-$ or $(CH_2)_n-$ in which A, n and Y are as defined above, and Z is a 4-hydroxy (in the case of the precursor), or Z is a 3,4-double bond with a spiroglutaric acid derivative and having the formula 65



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- 10 in which n is as defined above and W is O when Y is H₂NA- or W is NH when Y is XA-, or W is (CH₂)_n = , or W is NAX when Y is hydrogen, in an inert organic liquid medium at an elevated temperature, but when in the precursor type intermediate of the aforesaid formula

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X1

- 20 are used as reactants, then the process further includes a dehydration step.
11. A pharmaceutical compound as defined in any one of Claims 1 to 4 for use in a method of treatment of the human or animal body.
12. A compound according to Claim 8 for use as a tranquilizer.
13. A compound according to Claim 1 substantially as hereinbefore specifically described in each of the examples for the use hereinbefore specifically described.
- 25 14. A compound as described in Claim 1 substantially as hereinbefore specifically described in each of the examples.
15. A pharmaceutical composition according to Claim 6 substantially as hereinbefore specifically described in examples.
- 30 16. A process for making a compound as defined in Claim 10 substantially as hereinbefore specifically described in the examples.
17. A compound when produced by a process as claimed in any one of claims 10 and 16.
18. A compound as defined in Claim 7 substantially as hereinbefore described in the examples.