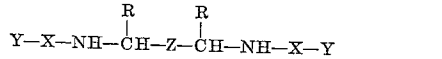
United States Patent Office 3,013,020 Patented Dec. 12, 1961

3,013,020
N,N'-BIS-PHENYL-ALKYLENE-DIAMINES

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No Drawing. Filed Jan. 24, 1958, Ser. No. 710,869
7 Claims. (Cl. 260—340.5)

This invention relates to a novel class of compounds represented by the general formula



wherein R is a cyclic or open chain lower alkyl radical, Z is an alkylene radical, X is a lower alkylene radical and Y is a radical from the group consisting of aryl and substituted aryl. It also includes pharmaceutically acceptable acid addition salts which may be formed from said compounds, in accordance with well known procedures, by using appropriate organic and inorganic acids such as hydrochloric, sulfuric, phosphoric, nitric, hydrobromic, acetic, lactic, succinic, malic, aconitic, aminoacetic and tartaric acids.

The application is a continuation-in-part of my copending application for patent Serial No. 482,880 which was filed on January 19, 1955, now abandoned.

An important object of the invention was to provide a compound or group of compounds which would indicate sufficient amebicidal activity as to be useful in chemotherapy of amebiasis and other protozoal diseases. It was also desired that such compound or compounds should when used for this purpose, be accompanied by a minimum of limiting side effects.

In various tests conducted, certain compounds of the above class were found to be particularly effective in killing the organism *Endamoeba histolytica*, strain F–22. In some instances these compounds were also found to demonstrate activity against *Trypanosoma cruzi*, the causative agent of Chargas disease or South American trypanosomiasis. Generally speaking, the tests also indicate that these compounds were of low toxicity.

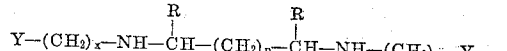
In one of these tests, the compounds were tested to determine the lowest concentration thereof which appears to kill the ameba present in a selected medium as evidenced by negative subculture. The medium used in this test was the so-called WEL medium which is a modified Boeck-Drbohlav diphasic medium such as used by the Laboratory of Tropical Diseases of the National Institutes of Health and which employs a whole egg and Locke's Solution slant with a Locke's Solution overlay. In the test procedure approximately 30 mg. of sterile rice powder was added to each test tube before use. The test organism, *Endamoeba histolytica*, strain F–22,

was maintained in association with a single species of bacteria, organism "t."

To obtain reproducible results for testing purposes, media preparation procedures were quantitated as far as possible. The amount of medium in both phases was accurately measured and the angle of the slant standardized to present equal areas of solid medium surface for use by the growing ameba and for adsorption of the test material. Stock solutions of the test material were prepared in distilled water to contain ten times the concentration to be tested. Addition of a stock solution to a tube of medium constituted the additional dilution necessary to obtain the test concentration. Control tubes received a similar amount of distilled water. Inoculum for testing procedures was provided from pooled 72 hour stock cultures, diluted with Locke's Solution to contain between 20,000 and 40,000 ameba per ml.

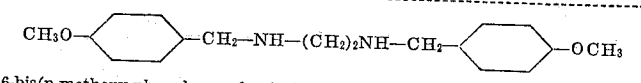
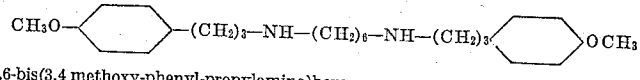
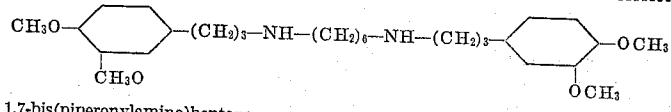
Observations were made after 48 hours incubation at 37° C. Each tube which did not show ameba or bacteria by microscopic examination, or which showed little or questionable growth or either organism was subcultured to a fresh tube of riced WEL medium and subcultures were incubated an additional 48 hours. Changes in pH were observed with a Beckmann pH meter, Model G. The tube containing the lowest concentration of test material which did not demonstrate viable ameba was considered the endpoint in the test.

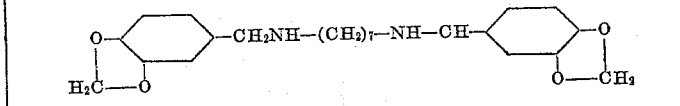
Certain of the symmetrical bis-amines of the aforesaid novel class of compounds to which this invention relates were found in the above described test to indicate a particularly low level of concentration needed to kill the ameba. Thus many of the compounds would kill the ameba when added in concentrations as low as 100 μg. per ml. of test solution while others would have a killing effect on the ameba at even lower concentrations, as for example 50 μg./ml. These compounds were found to fall within the general formula:



wherein x is an integer of 1 to 3, n is an integer of 2 to 10, when R is an alkyl radical containing 2 to 6 carbon atoms and Y is phenyl, hydroxyphenyl, alkoxyphenyl, dialkoxyphenyl, trialkoxyphenyl or methylenedioxyphenyl.

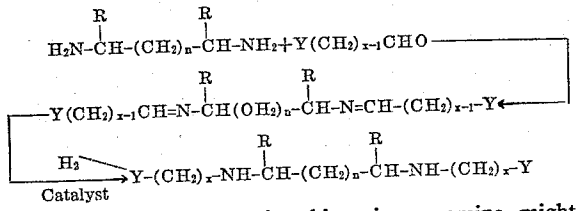
One of the surprising results of these tests was the apparent significance R has in these compounds on their amebicidal activity level. For example, the above tests were also applied to several symmetrical bis-amines which do not have an alkyl at the R position and the amebidical activity levels of these compounds were determined to be as follows:

Example	Compound	Amebicidal Activity, γ/ml., WEL
I	N,N'-bis(p-methoxy benzyl)ethylene diamine 	inactive at 1,000.
II	1,6-bis(p-methoxy-phenyl propylamino)hexane 	500.
III	1,6-bis(3,4 methoxy-phenyl-propylamino)hexane 	1,000.
IV	1,7-bis(piperonylamino)heptane	1,000–500.

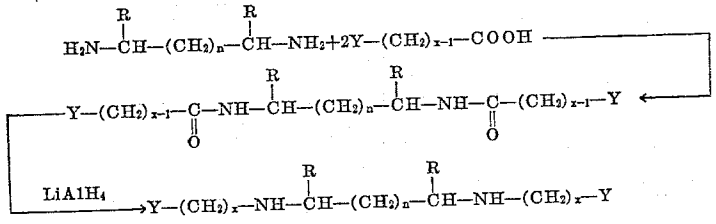
Example	Compound	Amebicidal Activity, γ/ml., WEL
V	1,3-bis(piperonylamino)-2-methyl-2-n-propylpropane 	500.

As will be seen, these compounds tested essentially inactive or required the addition of such large amounts thereof to the test solutions of ameba as to indicate they have little potential value as amebicides. The tests indicated that only those symmetrical bis-amines which have an alkyl branching on the carbons of the central moiety to which the amino groups $Y—(CH_2)_xNH—$ are attached show amebicidal activity. The inactivity of Example V also points up that it is not sufficient that the interconnecting moiety between the amino groups be branched but rather that the branching be on the carbon atoms to which the amino groups are attached. Only in the case of symmetrical bis-amines where their amino groups $Y—(CH_2)_x—NH—$ were connected at other than to the terminal carbons of the interconnecting saturated hydrocarbon or alkylene chain was any significant amebicidal activity noted. The improvement was particularly pronounced in compounds of this class where R is an open chain alkyl such as ethyl, propyl, butyl and amyl or is a cyclic-alkyl such as cyclohexyl. Although the reason is not apparent, the symmetrical bis-amines appear to be ineffective amebicides where R is hydrogen, and compounds of the general formula wherein R is aryl, substituted aryl or aralkyl do not demonstrate significant amebicidal activity in tests thus far conducted.

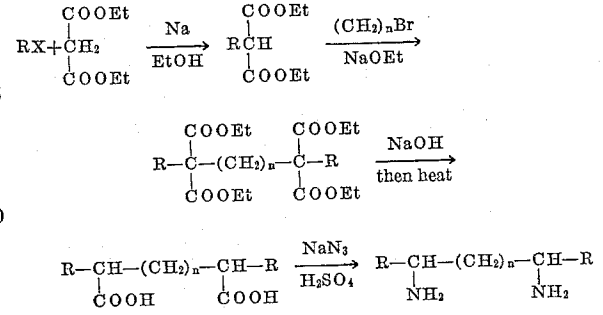
The compounds of the present invention may be prepared by reacting the bis primary amine with an appropriate aldehyde, the product of which is then hydrogenated, using a platinum or Raney nickel catalyst according to the following equations:



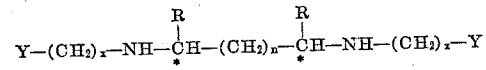
Alternatively, the starting bis primary amine might also be reacted with an appropriate organic carboxylic acid and reduced with lithium aluminum hydride according to the following:



The bis primary amines used as the starting materials to form the compounds of the class may be obtained according to the procedure of Hall, Mahboob and Turner, J. Chem. Soc. (1949) as outlined by the following series of equations:



In the group of compounds represented by the present invention, each compound and the intermediate dicarboxylic acids and diamines contain two identical asymmetrical carbon atoms as indicated by the asterisks (*) in the generic formula which follows and is therefore capable of existing both as a racemate and as a meso form.

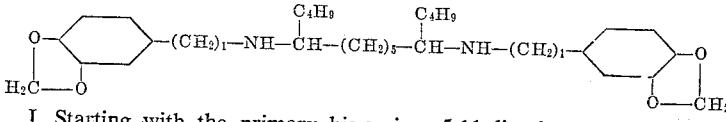


When R=n—C_4H_9 and n=5 a crystalline and a non-crystalline dicarboxylic acid were obtained. These gave diamines having identical boiling points. The diamine from the crystalline acid gave a Schiff base with piperonal which melted at 105–107°. The mixed acids gave a low melting Schiff base which could be separated by crystallization to give the high melting Schiff base plus an isomer which melted at 74–75.5°. The latter product was also isolatable in small amounts from the mother liquors from recrystallization of the Schiff base derived in two steps from the crystalline acid. This indicates incomplete separation of the isomeric acids.

The following examples are given for specific illustration of the invention but it should be understood that these are selected for illustration of the invention and are not to be considered as limitative.

EXAMPLE I

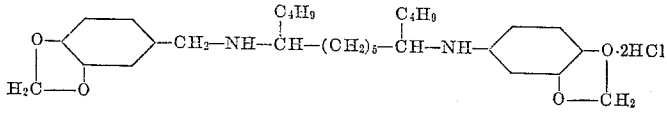
Preparation of N,N'-dipiperonyl-5,11 diaminopentadecane



I. Starting with the primary bis-amine, 5,11-diaminopentadecane prepared from the crystalline dicarboxylic acid the intermediate N,N'-dipiperonylidene-5,11-diaminopentadecane was initially prepared by mixing 260 grams or 1.07 moles of the amine with 338 g. or 2.25 moles of piperonal in three liters of absolute alcohol and 500 ml. of dry benzene. The mixture was heated to reflux and one liter of distillate was removed through a 30" column. The crystalline solid which separated on cooling of the residue, was filtered and dried. It weighed 490 g. and melted at 105–107°. A second crop weighing 55 g. and melting at 105–107° was obtained for concentration of the mother liquor. Percent N found, 5.46; calc. for $C_{31}H_{42}H_2O_4$, 5.52%. The total yield was 545 g., which is practically quantitative. In some cases recrystallization from alcohol has been necessary in order to get material of proper melting point.

II. 200 g. of the high-melting Schiff base, M.P. 105–107°, were made up to one liter with absolute alcohol. 15 grams of Raney nickel catalyst were added and the mixture was reduced at an initial hydrogen pressure of 1000 p.s.i., first at room temperature and with a final heating to 80°. Reduction was complete in two to three hours. The product was filtered and the alcohol removed by distillation to leave a colorless residue which was the desired N,N'-dipiperonyl-5,11-diaminopentadecane

III. To form a pharmaceutically acceptable acid addition salt thereof such as N,N'dipiperonyl-5,11-diaminopentadecane dihydrochloride having the formula:



the residue was then taken up in 500 ml. of anhydrous ether and added to 500 ml. of isopropanol saturated with excess anhydrous HCl. The crystalline solid, which separated, weighed 218 g., 95%, and melted at 178–180°. Recrystallization from absolute alcohol gave 202 g. of the acid addition salt which melted at 183–184°. Percent N found, 4.82; calc. for $C_{31}H_{48}Cl_2N_2O_4$, 4.80%.

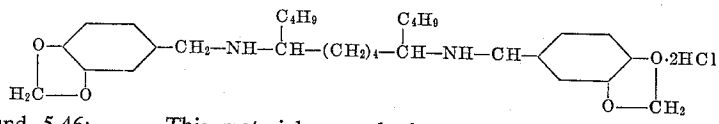
IV. By exhaustive recrystallization of material isolated from the mother liquors from the preparation of a large batch of the high melting Schiff base, the low melting Schiff base having a melting point of 74–75.5° was also isolated. Percent N found, 5.48; calc. for $C_{31}H_{42}N_2O_4$, 5.52%. 21.5 grams of this low melting Schiff base was similarly reduced, as in the case of the higher melting Schiff base, in absolute alcohol using a Raney nickel catalyst. The reduced product was also converted to its dihydrochloride and recrystallized from a mixture of absolute alcohol and ethyl acetate to yield the low melting

isomer of N,N'dipiperonyl-5,11-diaminopentadecane 2 HCl which melted at 175–176° mixed M.P. with the high melting isomer, 163–165°. Percent N found was 4.77 as compared with the theoretical of 4.80% calculated for $C_{31}H_{48}Cl_2N_2O_4$.

Both isomers were tested for their amebicidal activity level by the WEL test described above and the level of the N,N'dipiperonyl-5,11-diaminopentadecane prepared from the higher melting Schiff base was measured at 50–100 μg./ml. WEL. and that from the lower melting Schiff base was 100 μg./ml.

EXAMPLE 2

Preparation of N,N'dipiperonyl-5,10-diaminotetradecane dihydrochloride

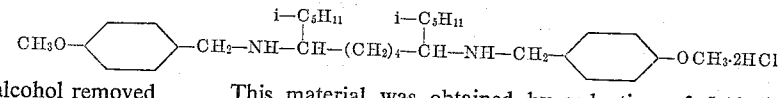


This material was obtained by reduction of 5,10-diaminotetradecane and piperonal according to the procedure of Example 1. After crystallization from water the dihydro chloride melted at 193–195° C. Percent Cl found 13.01; calc'd for $C_{30}H_{46}Cl_2N_2O_4$, 12.45%.

Its amebicidal activity level was measured and found to be 100 μg./ml. WEL.

EXAMPLE 3

Preparation of N,N'-di(p-methoxybenzyl)-5,10-diamino-2,13-dimethyltetradecane

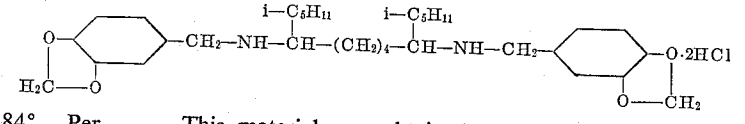


This material was obtained by reduction of 5,10-diamino-2,13-dimethyl tetradecane and p-methoxybenzaldehyde according to the procedure of Example 1. The dihydrochloride to which the reduced product was converted melted at 53–54°. Percent N found was 4.79; calculated for $C_{32}H_{54}Cl_2N_2O_2$, 4.92%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 4

Preparation of N,N'-dipiperonyl-5,10-diamino-2,13-dimethyltetradecane dihydrochloride



This material was obtained by reduction of 5,10-diamino-2,13-dimethyltetradecane and piperonal according to the procedure of Example 1. The dihydrochloride to which the reduced product was converted melted at 86–88°. Percent N found was 4.82; calculated for

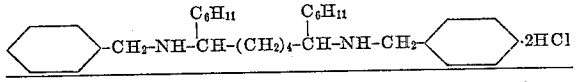
$C_{32}H_{50}Cl_2N_2O_4$

4.69%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 5

Preparation of N,N'-dibenzyl-1,6-dicyclohexyl-1,6-diamino-hexane dihydrochloride

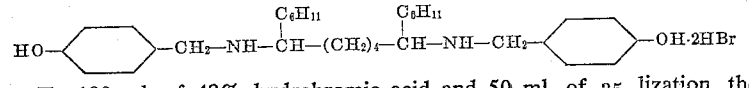


This material was obtained by reduction of 1,6-diamino-1,6-dicyclohexylhexane and benzaldehyde according to the procedure of Example 1. The dihydrochloride which was subsequently obtained melted at 259–264°. Percent N found was 5.30; calculated for $C_{32}H_{50}Cl_2N_2$, 5.26%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 6

Preparation of N,N'-di(p-hydroxybenzyl)-1,6-diamino-1,6-dicyclohexylhexane dihydrobromide

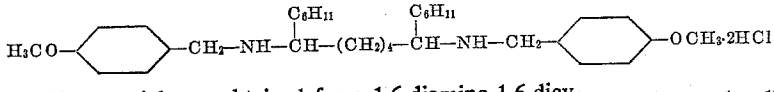


To 100 ml. of 48% hydrobromic acid and 50 ml. of glacial acetic acid was added 12 g. of N,N'-dibenzyl-1,6-dicyclohexyl-1,6-diaminohexane dihydrochloride from Example 5 and the mixture was refluxed for 4 hours. The acetic acid was removed by distillation. On cooling the residue a thick brown syrup separated. The aqueous layer was poured off and the syrup was partially dried by heating in a water bath under vacuum, dissolved in hot isopropyl alcohol and dried over magnesium sulfate. The dried solution was concentrated to 100 ml. and diluted with 100 ml. of hot ethyl acetate. A crystalline product separated. Percent N found was 4.25; calculated for $C_{32}H_{50}Br_2N_2O_2$, 4.28%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 7

Preparation of N,N'-di(p-methoxybenzyl)-1,6-diamino-1,6-dicyclohexylhexane dihydrochloride

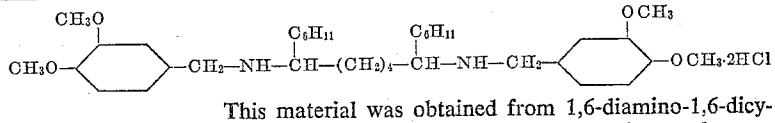


This material was obtained from 1,6-diamino-1,6-dicyclohexylhexane p-methoxybenzaldehyde according to the procedure of Example 1. The dihydrochloride melted to 257–258°. Percent N found was 4.79; calculated for $C_{34}H_{54}Cl_2N_2O_2$, 4.72%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 8

Preparation of N,N'-diveratryl-1,6-diamino-1,6-dicyclohexylhexane dihydrochloride

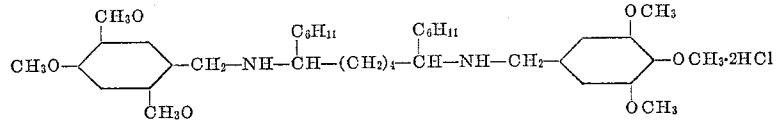


This material was obtained from 1,6-diamino-1,6-dicyclohexylhexane and veratraldehyde according to the procedure of Example 1. After crystallization, the dihydrochloride melted at 237–245°. Percent N found was 4.32; calculated for $C_{36}H_{58}Cl_2N_2O_4$, 4.28%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 9

Preparation of N,N'-di(3,4,5-trimethoxybenzyl)-1,6-diamino-1,6-dicyclohexylhexane dihydrochloride

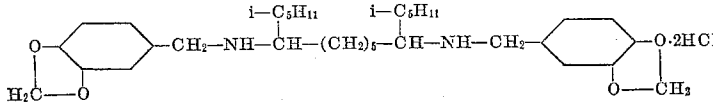


This material was obtained from 1,6-diamino-1,6-dicyclohexylhexane and 3,4,5-trimethoxybenzaldehyde according to the procedure of Example 1. After crystallization, the dihydrochloride melted at 236–239°. Percent N found was 3.86; calculated for $C_{38}H_{62}Cl_2N_2O_6$, 3.93%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 10

Preparation of N,N'-dipiperonyl-5,11-diamino-2,14-dimethylpentadecane dihydrochloride

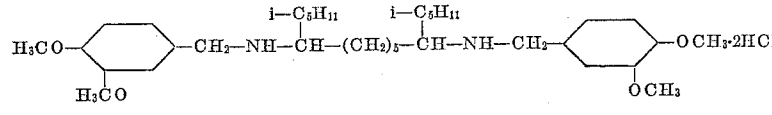


This material was obtained from 5,11-diamino-2,14-dimethylpentadecane and piperonal according to the procedure of Example 1. After crystallization, the dihydrochloride melted at 74–76°. Percent N found was 4.71; calculated for $C_{33}H_{52}Cl_2N_2O_4$, 4.58%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 11

Preparation of N,N'-diveratryl-5,11-diamino-2,14-dimethylpentadecane dihydrochloride

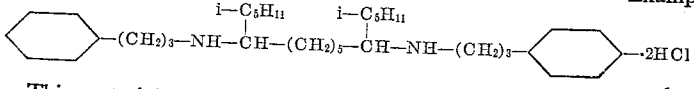


This material was obtained from 5,11-diamino-2,14-dimethylpentadecane and veratraldehyde according to the procedure of Example 1. After crystallization from the solvent, the dihydrochloride melted at 67–69°. Percent N found was 4.55; calculated for $C_{35}H_{60}Cl_2N_2O_4$, 4.36%.

Its amebicidal activity level was measured as described above and determined to be 100–50 μg./ml. WEL.

EXAMPLE 12

Preparation of N,N'-di(3-phenylpropyl)-5,11-diamino-2,14-dimethylpentadecane dihydrochloride

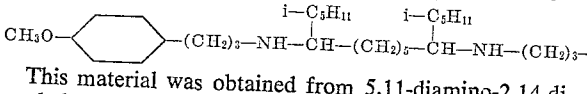


This material was obtained from 5,11-diamino-2,14-dimethylpentadecane and cinnamaldehyde according to the procedure of Example 1. Percent N found was 4.87; calculated for $C_{35}H_{60}Cl_2N_2$, 4.83%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 13

Preparation of N,N'-di[3-(p-methoxyphenyl) propyl]-5,11-diamino-2,14-dimethylpentadecane dihydrochloride

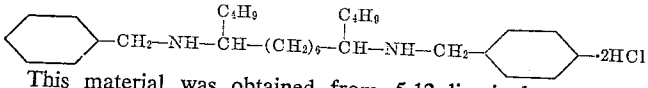


This material was obtained from 5,11-diamino-2,14-dimethylpentadecane and p-methoxycinnamaldehyde according to the procedure of Example 1. The dihydrochloride melted at 233-236°. Percent N found was 4.34; calculated for $C_{37}H_{64}Cl_2N_2O_2$, 4.38%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 14

Preparation of N,N'-dibenzyl-5,12-diamino-hexadecane dihydrochloride

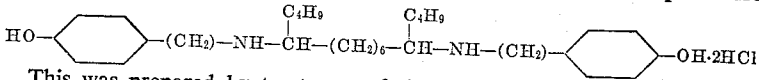


This material was obtained from 5,12-diaminohexadecane and benzaldehyde according to the procedure of Example 1. The dihydrochloride to which the reduced product was converted melted at 186–188°. Percent N found was 5.55; calculated for $C_{30}H_{50}Cl_2N_2$, 5.50%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 15

Preparation of N,N'-di(p-hydroxybenzyl) - 5,12-diamino-hexadecane dihydrobromide

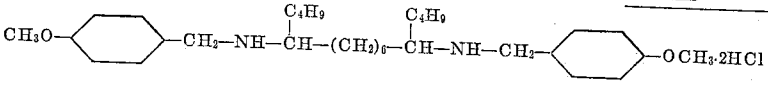


This was prepared by treatment of the compound of Example 16 with 48% HBr as described in connection with Example 6 above. The dihydrobromide melted at 180–182°. Percent N found was 4.42; calculated for $C_{30}H_{50}Br_2N_2O_2$, 4.44%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 16

Preparation of N,N'-di(p-methoxybenzyl) - 5,12, diamino-hexadecane dihydrochloride

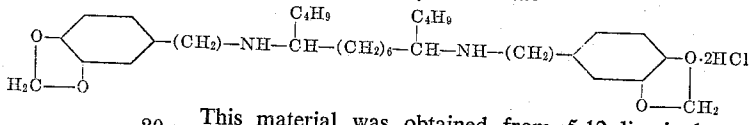


This was obtained from 5,12-diaminohexadecane and p-methoxybenzaldehyde according to the procedure of Example 1. The dihydrochloride to which the reduced product was converted melted at 160–164°. Percent N found was 4.96; calculated for $C_{32}H_{54}Cl_2N_2O_2$, 4.96%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 17

Preparation of N,N'dipiperonyl - 5,12-diaminohexadecane dihydrochloride

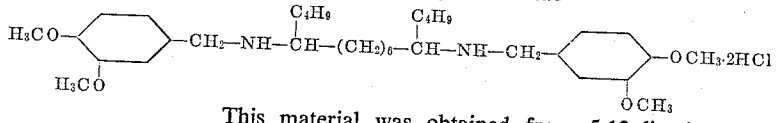


This material was obtained from 5,12-diaminohexadecane and piperonal according to the procedure of Example 1. The dihydrochloride melted at 186–189°. Percent N found was 4.72; calculated for $C_{32}H_{50}Cl_2N_2O_4$, 4.68%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 18

Preparation of N,N'-diveratryl - 5,12 diaminohexadecane dihydrochloride

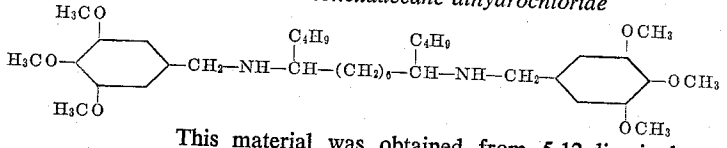


This material was obtained from 5,12-diaminohexadecane and veratraldehyde according to the procedure of Example 1. The dihydrochloride melted at 163–166°. Percent N found was 4.47; calculated for $C_{34}H_{58}Cl_2N_2O_4$, 4.45%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 19

Preparation of N,N'-di(3,4,5-trimethoxybenzyl) - 5,12-diaminohexadecane dihydrochloride

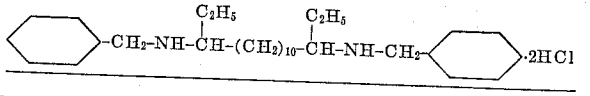


This material was obtained from 5,12-diaminohexadecane and 3,4,5-trimethoxybenzaldehyde according to the procedure of Example 1. The dihydrochloride melted at 130–134°. Percent N found was 4.00; calculated for $C_{36}H_{62}Cl_2N_2O_4$, 4.07%.

Its amebicidal activity level was measured as described above and determined to be 100 μg./ml. WEL.

EXAMPLE 20

Preparation of N,N' dibenzyl-3,14-diaminohexadecane dihydrochloride

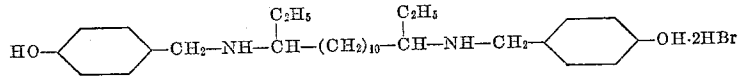


This material was obtained from 3,14-diaminohexadecane and benzaldehyde according to the procedure of Example 1. Percent N found was 5.66; calculated for $C_{30}H_{50}Cl_2N_2$, 5.51%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 21

Preparation of N,N'-di-p-hydroxybenzyl - 3,14-diaminohexadecane dihydrobromide

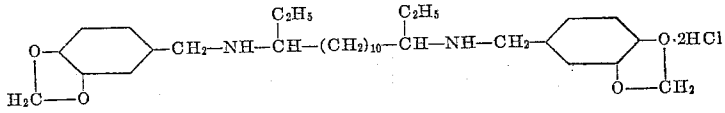


This was prepared by demethylation of the corresponding dimethyl ether with 48% HBr, as described in Example 6 above. Percent N found was 4.35; calculated for $C_{30}H_{50}Br_2N_2O_2$, 4.44%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 22

Preparation of N,N'-dipiperonyl - 3,14-diaminohexadecane dihydrochloride

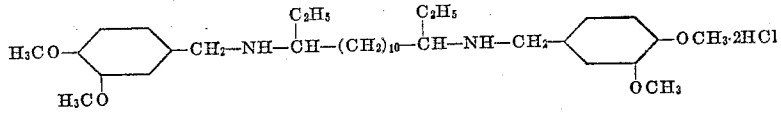


This material was obtained from 3,14-diaminohexadecane and piperonal according to the procedure of Example 1. Percent N found was 4.91; calculated for $C_{32}H_{50}Cl_2N_2O_2$, 4.70%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 23

Preparation of N,N'-diveratryl-3,14-diaminohexadecane dihydrochloride

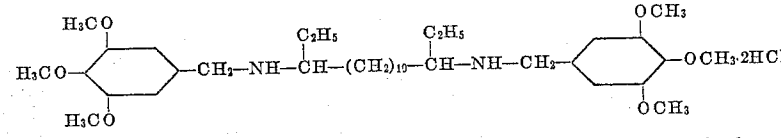


This material was obtained from 3,14-diaminohexadecane and veratraldehyde according to the procedure of Example 1. Percent N found was 4.50; calculated for $C_{34}H_{58}Cl_2N_2O_4$, 4.46%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 24

Preparation of N,N'-di(3,4,5-trimethoxybenzyl)-3,14-diaminohexadecane dihydrochloride

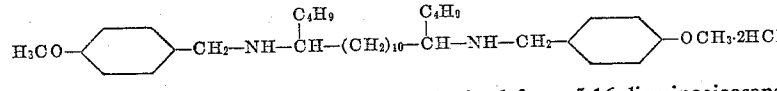


This material was obtained from 3,14-diaminohexadecane and 3,4,5-trimethoxybenzaldehyde according to the procedure of Example 1. Percent N found was 4.09; calculated for $C_{36}H_{62}Cl_2N_2O_6$, 4.07%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 25

Preparation of N,N'(p-methoxybenzyl)-5,16-diaminoeicosane dihydrochloride

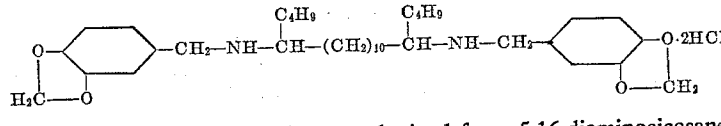


This material was obtained from 5,16-diaminoeicosane and p-methoxybenzaldehyde according to the procedure of Example 1. Percent N found was 4.57; calculated for $C_{36}H_{62}Cl_2N_2O_2$, 4.47%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 26

Preparation of N,N'-dipiperonyl-5,16-diaminoeicosane dihydrochloride

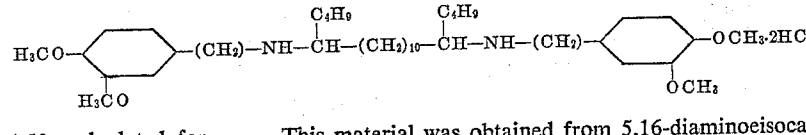


This material was obtained from 5,16-diaminoeicosane and piperonal according to the procedure of Example 1. Percent N found was 4.34; calculated for $C_{36}H_{58}Cl_2N_2O_4$, 4.29%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 27

Preparation of N,N'-diveratryl-5,16-diaminoeicosane dihydrochloride

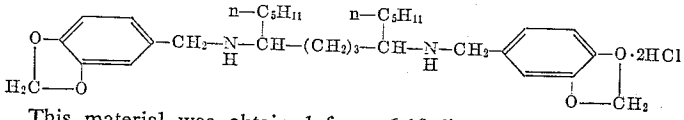


This material was obtained from 5,16-diaminoeisocane and veratraldehyde according to the procedure of Example 1. Percent N found was 404; calculated for $C_{38}H_{66}Cl_2N_2O_4$, 4.08%.

Its amebicidal activity level was measured as described above and determined to be 50 μg./ml. WEL.

EXAMPLE 28

Preparation of N,N'-dipiperonyl-6,10-diaminopentadecane dihydrochloride

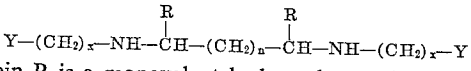


This material was obtained from 6,10-diaminopentadecane and piperonal according to the procedure of Example 1. Percent N found 4.79; calculated for $C_{13}H_{48}Cl_2N_2O_4$, 4.80%.

Its amebicidal activity level was measured as described above and determined to be 10 μg./ml. WEL.

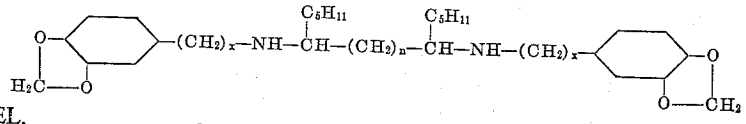
Having described my invention, I claim:

1. A compound selected from the group consisting of bis-amines of the formula



wherein R is a monovalent hydrocarbon radical selected from the group consisting of alkyl of 2 to 5 carbon atoms and cyclohexyl, Y is a moiety from the group consisting of phenyl, monohydroxyphenyl, monomethoxyphenyl, dimethoxyphenyl, trimethoxyphenyl and methylenedioxyphenyl, x is an integer of 1 to 3 and n is an integer of 2 to 10, and pharmaceutically acceptable acid addition salts thereof.

2. A symmetrical bis-amine having the formula:

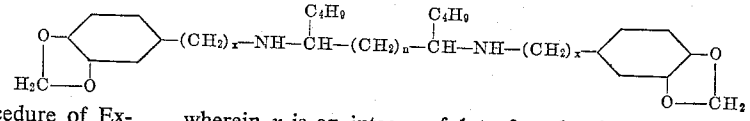


wherein n is an integer of 2 to 10 and x is an integer of 1 to 3.

3. N,N'-dipiperonyl-5,11-diaminopentadecane.

4. N,N'-dipiperonyl-5,10-diaminotetradecane.

5. A symmetrical bis-amine having the formula:



wherein x is an integer of 1 to 3 and n is an integer of 2 to 10.

6. N,N'-dipiperonyl-3,14-diaminohexadecane.

7. N,N'-dipiperonyl-6,10-diaminopentadecane.

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