

UNITED STATES PATENT OFFICE

2,551,378

ALKYLENE-BIS-CARBAMYLAMINO- AND GUANIDYLCYCLOHEXANES

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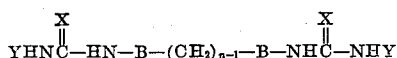
5 Claims. (Cl. 260-552)

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This invention relates to nitrogen-substituted dialicyclic compounds and more particularly to new and useful amido derivatives of dialicyclic diamines.

This invention has as an object the preparation of new derivatives of dialicyclic diamines. A further object is the preparation of new intermediates for resins. Another object is the preparation of new pest control agents, and new intermediates for pharmaceuticals. Other objects will appear hereinafter.

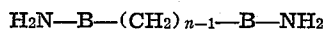
These objects are accomplished by the invention of new compounds of the formula



wherein n is an integer from one to five, each X is oxygen, sulfur, or imino ($=\text{NH}$), each Y is hydrogen or methylol ($-\text{CH}_2\text{OH}$), and B is a six-membered divalent alicyclic hydrocarbon radical having a cyclohexane nucleus and any other hydrocarbon substituent being monovalent hydrocarbon radicals bonded to ring carbon of said cyclohexane nucleus. Thus the compounds are bis-guanidines (iminocarbamides), bis-thioureas (thiocarbamides) and bis-ureas (carbamides) derived from dialicyclic diamines represented by the formula $\text{H}_2\text{N—B—(CH}_2\text{)}_{n-1}\text{—B—NH}_2$ in which the symbols, n and B, have the same

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wherein n is an integer from one to five, each R is hydrogen or a methyl radical, not more than one such methyl radical being present on each of the rings, each X is oxygen, or sulfur, i. e., a chalcogen of integral atomic number $8n$ wherein n is an integer of up to two, and each Y is hydrogen or methylol ($-\text{CH}_2\text{OH}$). These preferred compounds are then the bis-guanidines (iminocarbamides), the bis-thioureas (thiocarbamides), and the bis-ureas (carbamides) derived from the symmetrical dialicyclic diamines represented by the general formula,

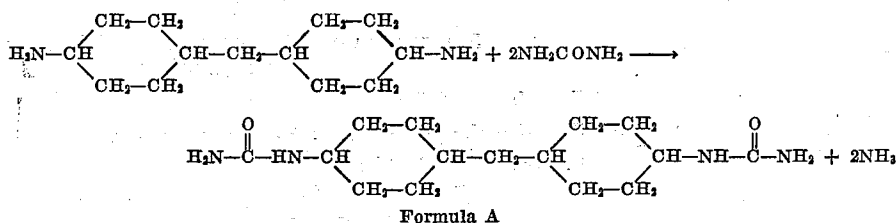


15 wherein n is an integer of from one to five and B is a cycloalkylene radical, i. e., a divalent saturated hydrocarbon radical having a cyclohexane nucleus, said radical containing at least six and preferably not more than seven carbons, the two valences of the radical stemming from ring carbons of the cyclohexane nucleus, preferably in the 1,4-positions to each other, and any hydrocarbon substituent on said nucleus being bonded to a ring carbon which is other than a radical valence bearing carbon and preferably in an ortho or meta position to that bearing the amino group.

The following examples in which parts are by weight are illustrative of the invention.

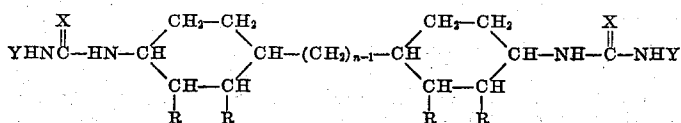
EXAMPLE I

Preparation of 1,1'-(methylenedi-1,4-cyclohexylene)diurea



meaning as indicated above for the new compounds of the invention.

A preferred embodiment of the invention comprises the new symmetrical compounds represented by the formula



A mixture of 9 parts of urea and 10.5 parts of di(4-aminocyclohexyl)methane (prepared as described in the copending application of Kirk, Schreiber and Whitman, Serial No. 615,912, filed September 12, 1945, now abandoned by the hydro-

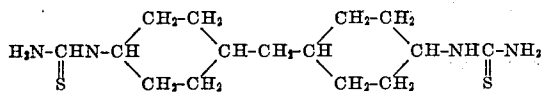
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genation at 100° C. and a hydrogen pressure of 135 atmospheres of di(p-aminophenyl)methane in dioxane over ruthenium dioxide) was heated gradually to 140° C. where it was maintained for 1.5 hours. At this point, ammonia evolution, which had started at about 110° C., ceased.

The solid white residue (11 parts) remaining after extraction of the hard reaction product with 1450 parts of boiling water was, as shown by analysis, 1,1'-(methylenedi-1,4-cyclohexylene)diurea (see Formula A) melting above 230° C. *Analysis*.—Calculated for $C_{15}H_{22}N_4O_2$: N, 18.9%. Found: N, 18.69%; 19.02%.

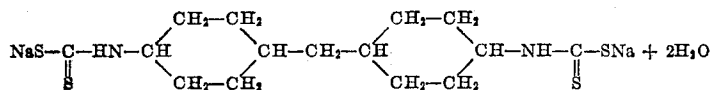
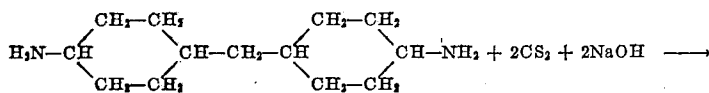
EXAMPLE II

Preparation of 1,1'-(methylenedi-1,4-cyclohexylene)bis(2-thiourea)

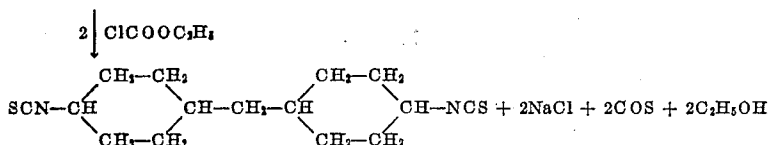


Formula B

a. METHYLENEDI-1,4-CYCLOHEXYLENE DIISOTHIOCYANATE



Formula C



Formula D

A solution of 284 parts of di(4-aminocyclohexyl)-methane, and 103 parts of dioxane was added dropwise to a stirred mixture of 208 parts of carbon disulfide, 108 parts of sodium hydroxide and 800 parts of water. During this addition, the temperature of the reaction mixture was allowed to rise from 20° C. to 45° C. after which the mixture was heated cautiously on the steam bath for 0.5 hour, being careful to avoid foaming. The resulting suspension of disodium

extract was successively washed with dilute sodium hydroxide, dilute hydrochloric acid and finally with water. After drying the ether extract over calcium chloride and removal of the ether by distillation, 374 parts of crude, yellow, oily product was obtained. Crystallization of this oily product was induced by stirring with 200 parts of methanol at room temperature and the resulting solid, which was separated by filtration, was subsequently recrystallized from a mixture of 240 parts of n-butanol and 200 parts of methanol. This yielded, after filtration and drying, 184 parts of crystalline methylenedi-1,4-cyclohexylene diisothiocyanate. *Analysis*.—Calculated for $C_{15}H_{22}N_2S_2$: C, 61.2%; H, 7.5%; N, 9.5%; S, 21.8%. Found: C, 61.0%; H, 7.7%; N, 9.3%; S, 21.7%.

b. 1,1'-(METHYLENEDI-1,4-CYCLOHEXYLENE) BIS (2-THIOUREA)

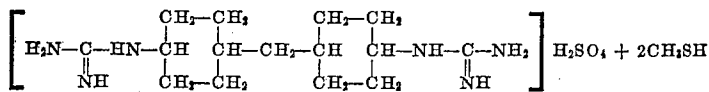
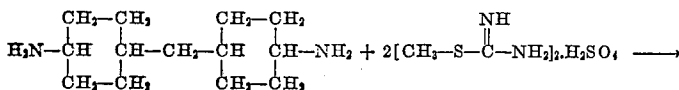
20 Product of above Formula D + 2NH₃(C₄H₉OH)-bis-thiourea of Formula B

One hundred (100) parts of the diisothiocyanate prepared as described above was refluxed

with 243 parts of n-butanol until a clear solution was obtained. Ammonia gas was then bubbled into this refluxing (114° C.) solution for eight hours. The solution was cooled in ice and the resulting white crystalline 1,1'-(methylenedi-1,4-cyclohexylene)bis(2-thiourea) [see above Formula B] which was filtered, washed with acetone and dried amounted to 74 parts. *Analysis*.—Calculated for $C_{15}H_{22}N_4S_2$: N, 17.0%. Found: N, 16.99%; 16.84%.

EXAMPLE III

Preparation of 1,1'-(methylenedi-1,4-cyclohexylene)diguanidine



Formula E

salt of N,N'-(methylenedi-1,4-cyclohexylene)bis-(thiocarbamic acid) [see Formula C] was then cooled to about 40° C. and 321 parts of ethyl chlorocarbonate added dropwise with stirring. The mixture was then heated on a steam bath for 0.5 hour. After cooling to room temperature, the separated oily solid was extracted from the reaction mixture with diethyl ether. The ether

Chemically equivalent amounts of di(4-aminocyclohexyl)-methane (21 parts) and S-methylisothiourea sulfate (27.8 parts) were heated in a methanol/water (10 parts/65 parts) solution on the steam bath for one hour when evolution of methyl mercaptan, very rapid at the beginning of the reaction, had practically ceased. Most of the solvents were then removed by distillation

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gen is replaced by HOCH₂— groups and although the invention has been illustrated in particularity, other dialicyclic diamines which can be suitably employed in the examples in place of di(4-aminocyclohexyl)methane for the preparation

of the new compounds of the invention include di(4-aminocyclohexyl), [(Balas and Sevchenko, Collection Czechoslov. Chem. Communications 3, 171-6 (1931))]; bis(4-amino-3-methylcyclohexyl), bis(4-amino-3-methylcyclohexyl)-methane, 1,2-bis(4-aminocyclohexyl)ethane and 1,3-bis(4-aminocyclohexyl)propane as prepared by the hydrogenation, at 75-250° C. and a hydrogen pressure of at least 100 lbs./sq. in., of the corresponding amino-, nitro-, or nitroso-phenyl compound over ruthenium dioxide catalyst, as disclosed in the application of Kirk et al., Serial No. 615,912, filed September 12, 1945; bis(4-amino-2-methylcyclohexyl)methane (prepared by the hydrogenation at 75-250° C. and a hydrogen pressure of 1500-2700 lbs./sq. in. of 2,2'-dimethyl-4,4'-diaminodiphenylmethane as disclosed in Bolton and Kirk, Serial No. 615,918, filed September 12, 1945, now U. S. Patent 2,512,606); 1,4-bis(4-aminocyclohexyl)butane [Ferber, Ber. 62B 192 (1929)]. Because of their cheapness and satisfactory reactivity to yield the new carbamido compounds of the invention, the dialicyclic diamines, such as those just mentioned, which contain two saturated six-membered cycloaliphatic rings having up to seven carbons are preferred.

Of the new compounds of the invention, the bis-ureas and bis-thioureas, i. e., those carbamido compounds defined by the structural formula in column 1 wherein Y is hydrogen and X is a chalcogen (oxygen or sulfur) of integral atomic number $8n$, n being an integer of up to two, are preferred since they are usually the most easily prepared. The most preferred are the bis-ureas because they are readily derived in highest yield from low cost urea by reaction with the dialicyclic diamines and, moreover, they can be smoothly and economically converted by formaldehyde condensation to the methylol derivatives from which the cheapest and most attractive molded articles have been produced.

While other well-known methods can usually be employed to prepare the new carbamido compounds of this invention, the processes described in the examples are, in general, satisfactory and preferred. Employing the method of the examples for the preparation of the bis-ureas of the invention, the molal ratio of the dialicyclic diamines to urea may vary between 1:1 to 1:5 or more. It is preferable, however, to use a molal excess of urea. The reaction may be satisfactorily operated at temperatures of from 80-200° C., depending to a large extent on the dialicyclic diamine being treated. In general, the preferred temperature is between 125-160° C. The time of reaction can vary widely, for example, from 1 to 24 hours or more, depending on the temperature and the attendant rate of ammonia evo-

cause solution of the diisothiocyanate at the reaction temperature, 100-150° C. Reaction time can vary from 1 to 24 hours or more, but usually 5 to 15 hours is sufficient time for satisfactory results.

For the preparation of the bis-guanidines, it is preferable to use at least chemically equivalent amounts of the S-alkyl isothioureia, for example, S-methyl, S-ethyl, etc., or the corresponding mineral acid salts such as the hydrochlorides or sulfates, and the dialicyclic diamines at temperatures (80-150° C.) where alkyl mercaptan is evolved at a satisfactory rate. Although the reaction may be carried out without diluent it is preferable to employ diluents such as water, organic solvents, such as alcohols, e. g., methanol, ethanol, propanol, butanol, etc., or mixtures of organic solvents and water.

Although the methylol derivatives of the invention, for example, the methylol derivatives of the bis-ureas, can be produced by the use of the chemically equivalent amounts of formaldehyde, it is preferable to operate with molal excesses, for example, 100-500% excesses, of this aldehyde. Aside from the n-butanol shown in the example, other alcohols, for example, ethanol, propanol, butanol, pentanol, etc., may be used for the condensation reaction of the herein described carbamido compounds with formaldehyde. Such formaldehyde condensation, whether in an alcohol or water medium, is carried out at a pH of from 7 to 11, preferably 8 to 9.5 and at a temperature of 50-125° C.

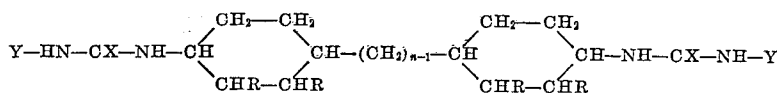
With the exception of the methylol derivatives which are for the most part amorphous solids, the new carbamido compounds of this invention are, ordinarily, high melting crystalline solids insoluble in water and most organic solvents such as ethanol, benzene, acetone, etc. The methylol derivatives, although substantially insoluble in water and hydrocarbon solvents, are appreciably soluble in acetone, alcohols, e. g., ethanol, propanol, butanol, etc.

In addition to the use of the new compounds of this invention as resin-forming materials for application in the manufacture of molded articles and coating compositions, they are also useful as intermediates for pharmaceuticals and as pest control agents, particularly the bis-thioureas for the insect-proofing of woolen fabrics.

The foregoing detailed description has been given for clearness of understanding only and no unnecessary limitations are to be understood therefrom. The invention is not limited to the exact details shown and described for obvious modifications will occur to those skilled in the art.

What is claimed is:

1. A symmetrical compound of the formula



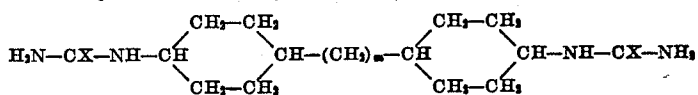
lution, a criterion of the completion of the reaction. High boiling, inert, organic solvents may be used but these are not ordinarily required.

Likewise in the preparation of the bis-thioureas of the invention, the molal ratio of the dialicyclic diisothiocyanate to ammonia may vary between 1:1 to 1:20 or more. The reaction is, in general, most suitably conducted with molal excesses of ammonia and preferably with polar organic solvents, such as butanol, pentanol, cyclohexanol, dioxane, etc., employed in amounts sufficient to

wherein n is an integer from one to five, each Y is the same member of the class consisting of hydrogen and methylol, each X is the same member of the class consisting of O, S, and NH, and each R is a member of the class consisting of hydrogen and monovalent saturated hydrocarbon radicals.

2. A compound according to claim 1 wherein X is a chalcogen of integral atomic number of $8n$, n being a positive integer not greater than 2.

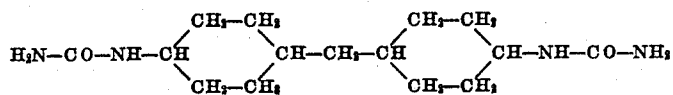
3. A symmetrical compound of the formula



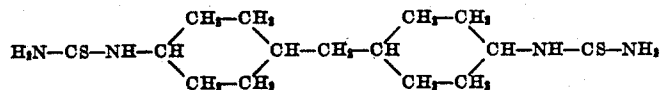
wherein each X is the same chalcogen of atomic

weight not greater than 33 and m is a cardinal number not greater than 4.

4. A compound of the formula



5. A compound of the formula



JAMES EMORY KIRBY.

REFERENCES CITED

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

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Number	Name	Date
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