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MERCURATED ALLYLUREA DERIVATIVES AND DIURETICS CONTAINING THE SAME

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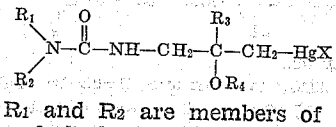
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This invention relates to mercurated allylurea derivatives and diuretics containing the same.

This application is a continuation-in-part of my copending application, Serial No. 113,494, filed August 31, 1949, now abandoned.

In various types of heart diseases, particularly congestive heart trouble, the patient becomes bloated due to sodium in the form of salt and thus water gathering in the tissues. In order to relieve this condition, various compositions have been prescribed containing diuretic compounds. These diuretics serve to excrete water and salt from the kidneys and thus from the tissues so that the heart condition is relieved. Many of the former diuretic compounds were aromatic or aliphatic amines or amides, particularly aliphatic amines or amides. Inorganic mercury compounds have been used as diuretics for many years, but only recently have organic mercury compounds been used. The early organic mercury compounds were amines and amides containing a mercury atom. Most of these prior diuretic compounds, particularly of the mercury type, were dangerous to use as they sometimes caused death by stopping the heart. When they were injected into the veins or the muscles, they sometimes destroyed or at least caused severe irritation of the tissues. This was particularly true where the injection into the muscle accidentally contacted fatty tissues.

The new compounds of this invention, which are particularly useful as the active ingredient in diuretic compositions, are mercurated allylurea compounds having essentially the structural formula:



wherein R_1 and R_2 are members of the class consisting of alkyl groups, hydrogen atoms, and cyclo-aliphatic groups in which R_1 and R_2 are joined together to form said group, R_3 is a member of the class consisting of hydrogen atoms and alkyl groups, at least one and not more than two of R_1, R_2 and R_3 being a hydrogen atom, R_4 is a member of the class consisting of hydrogen and an alkyl group, and X is a member of the class consisting of atoms of negative valence other than carbon atoms and groups including such an atom bonded directly to the mercury atom.

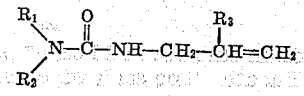
In the preferred compounds the alkyl groups of R_1 and R_2 contain not more than six carbon atoms. Also in the preferred compounds, X is

2

either halogen, hydroxyl, oxy-acyl, the residue of an acidic nitrogen compound having a replaceable hydrogen on the nitrogen atom, the residue of an alkyl thiol acid wherein the sulfur is bonded directly to the mercury atom, the alkali metal salt of this acid residue or a theophylline residue.

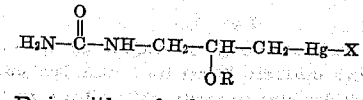
Among the preferred compounds of this invention having the above structural formula is the compound in which R_1 is methyl, R_2 is hydrogen, R_3 is hydrogen, R_4 is methyl and X is chlorine. Still others are those in which R_2, R_3, R_4 and X are the same as those in the preceding compound and in which R_1 is either ethyl, n-propyl, n-butyl, n-hexyl and cyclohexyl. In other preferred compounds, R_1 and R_2 are joined to form a piperidyl group or a morpholyl group. In other preferred compounds, R_1 and R_2 are both either ethyl groups or n-butyl groups. One of the compounds that is especially preferred is 3-chloromercuri - 2 - methoxy - 2 - methyl - propylurea. In this compound R_1 and R_2 are each a hydrogen atom, R_3 and R_4 are each a methyl group and X is a chlorine atom.

In preparing the new compounds of this invention substituted allyl ureas are used having the following structural formula:



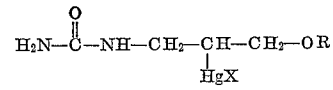
where R_1, R_2 and R_3 are as specified above. This compound is then reacted with a mercury compound to make the new compounds of this invention.

Still other new compounds of this invention, which are particularly useful as diuretics, are mercurated propylurea compounds with a mercury substituent on the 3-carbon atom and either hydroxyl or alkoxyl on the 2-carbon atom and having the following structural formula:



wherein R is either hydrogen or alkyl and X is either halogen, hydroxyl, oxy-acyl or the residue of an acidic nitrogen compound having a replaceable hydrogen on the nitrogen atom such as theophylline, succinimide, and phthalimide residues remaining after the hydrogen on the nitrogen atom has been replaced so that the nitrogen is directly bonded to the mercury atom. Of these compounds it is preferred that the R be an alkyl group containing from 1 to 5 carbon atoms. These compounds may also have a small

proportion of a compound having the following structural formula:



Examples of the new compounds and their preparation are as follows:

Example 1

$CH_3NHCONHCH_2CH(OCH_3)CH_2HgCl$

N-(3-chloromercuri-2-methoxypropyl)-N'-methylurea

To 23 g. of a 35% aqueous solution of methylamine was added 10 g. of allylisocyanate. The mixture was concentrated at room temperature. The residue after crystallization from ethyl ether, melted at 48–49° and weighed 3.0 g. (20%).

Analysis: Calcd. for $C_5H_{10}N_2O$: N, 24.50. Found: N, 23.70.

To a solution of 2.5 g. of N-allyl-N'-methylurea in 50 cc. of methyl alcohol was added a solution of 6.4 g. of mercuric acetate in 100 cc. of methyl alcohol. After sixteen hours, the insoluble material was removed by filtration and a solution of 2.0 g. of sodium chloride in 20 ml. of water was added to the filtrate. After twenty hours, the white precipitate was collected by filtration, washed with water and crystallized from ethyl alcohol. The product melting at 176–177° weighed 1.8 g. (25%).

Analysis: Calcd. for $C_6H_{13}N_2O_2HgCl$: Hg, 52.62; N, 7.34. Found: Hg, 52.61; N, 7.13.

Example 2

$C_2H_5NHCONHCH_2CH(OCH_3)CH_2HgCl$

N-(3-chloromercuri-2-methoxypropyl)-N'-ethylurea

To 33 g. of an aqueous solution of ethylamine (33%) was added 10 g. of allyl isocyanate. The residue after concentration at room temperature was crystallized from isopropylether. The N-allyl-N'-ethylurea weighed 3.3 g. (20%) and melted at 79–80°.

Analysis: Calcd. for $C_6H_{12}N_2O$: N, 21.86. Found: N, 21.35.

To a solution of 2.4 g. of N-allyl-N'-ethylurea in 50 cc. of methyl alcohol was added a solution of 6.4 g. of mercuric acetate in 100 cc. of methyl alcohol. After twenty-four hours, the insoluble material was removed by filtration and a solution of 1.5 g. of sodium chloride in 20 cc. of water was added to the filtrate. The solid which separated upon concentration of the solution at room temperature, was washed with water and crystallized from isopropyl alcohol. The recrystallized material, melting point 140–141°, weighed 2.2 g. (30%).

Analysis: Calcd. for $C_7H_{15}N_2O_2HgCl$: Hg, 50.75; N, 7.09. Found: Hg, 50.75; N, 6.76.

Example 3

$n\text{-}C_3H_7NHCONHCH_2CH(OCH_3)CH_2HgCl$

N-(3-chloromercuri-2-methoxypropyl)-N'-n-propylurea

To 20 g. of propyl amine in 50 ml. of absolute ether was added 12.5 g. of allylisocyanate. The solution was concentrated at room temperature and the residue was crystallized from ethyl ether or from Skelly "B". The recrystallized N-allyl-N'-propylurea, melting at 96–97°, weighed 5.0 g. (25%).

Analysis: Calcd. for $C_7H_{14}N_2O$: N, 19.72. Found: N, 19.44.

To a solution of 4.0 g. of N-allyl-N'-propylurea in 50 cc. of methyl alcohol was added a solution of 8.0 g. of mercuric acetate in 100 ml. of methyl alcohol. After sixteen hours, the insoluble material was removed by filtration and a solution of 2.0 g. of sodium chloride in 25 ml. of water was added to the filtrate. The solid which separated upon concentration at room temperature was washed with water and crystallized from isopropyl alcohol. The product melted at 120.5–121° and weighed 5.0 g. (50%).

Analysis: Calcd. for $C_8H_{17}N_2O_2HgCl$: Hg, 49.01; N, 6.84. Found: Hg, 48.78; N, 7.22.

Example 4

$n\text{-}C_4H_9NHCONHCH_2CH(OCH_3)CH_2HgCl$

N-(3-chloromercuri-2-methoxypropyl)-N'-n-butylurea

From the reaction of allylisocyanate with n-butylamine, at room temperature in anhydrous ether, N-allyl-N'-butylurea was obtained in 40% yield. This product, after washing with Skelly-B, melted at 62–64°.

Analysis: Calcd. for $C_8H_{16}N_2O$: N, 17.87. Found: N, 17.64.

By essentially the same technique used in the preceding examples, N-allyl-N'-butylurea was methoxy-mercurated. The N-(3-chloromercuri-2-methoxypropyl)-N'-n-butylurea, after crystallization from ethyl alcohol, melted at 134–135°. Yield, 30%.

Analysis: Calcd. for $C_9H_{19}N_2O_2HgCl$: Hg, 47.06; N, 6.62. Found: Hg, 47.39; N, 6.76.

Example 5

$n\text{-}C_6H_{13}NHCONHCH_2CH(OCH_3)CH_2HgCl$

N-(3-chloromercuri-2-methoxypropyl)-N'-n-hexylurea

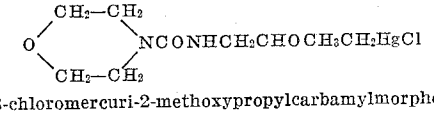
N-allyl-N-n-hexylurea was prepared by the reaction of allylisocyanate and n-hexylamine in absolute ether. The residue obtained by concentration of the reaction mixture was washed with Skelly-B. The solid product, melting at 50–52°, was isolated in 30% yield.

Analysis: Calcd. for $C_{10}H_{20}N_2O$: N, 15.20. Found: N, 14.97.

By the methoxymercuration of N-allyl-N'-n-hexylurea, by the same procedure utilized in the preceding examples, N-(3-chloromercuri-2-methoxypropyl)-N-n-hexylurea, melting at 113–116°, was isolated in 60% yield.

Analysis: Calcd. for $C_{11}H_{23}N_2O_2HgCl$: Hg, 44.44; N, 6.27. Found: Hg, 44.17; N, 6.55.

Example 6



N-3-chloromercuri-2-methoxypropylcarbamylmorpholine

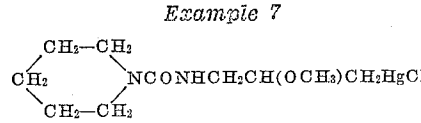
From the reaction of allylisocyanate and morpholine in ether, N-allylcarbamylmorpholine, crystallized from isopropyl ether to a constant melting point at 131–132°. Yield: 50%.

Anaylsis: Calcd. for $C_8H_{14}N_2O_2$: N, 16.46. Found: N, 16.65.

By the method used in the preceding examples, N-allylcarbamylmorpholine was converted to N-3-chloromercuri-2-methoxypropylcarbamyl morpholine. The mercurial after crystallization from ethyl alcohol melted at 112.5–113.5°. Yield: 40%.

Analysis: Calcd. for $C_9H_{17}N_2O_3HgCl$: Hg, 45.87; N, 6.41. Found Hg, 45.83; N, 6.53.

Example 7



N-3-chloromercuri-2-methoxypropylcarbamylpiperidine

N-allylcarbamylpiperidine, prepared by the reaction of allylisocyanate and piperidine in ether,

was crystallized from isopropyl ether to a constant melting point of 90–91°. Yield: 30%.

Analysis: Calcd. for $C_9H_{16}N_2O$: N, 16.65. Found: N, 16.61.

To a solution of N-allylcarbamylpiperidine in hot methyl alcohol was added a mixture of mercuric acetate, acetic acid and methyl alcohol. After the reaction mixture was heated under reflux for one hour, the insoluble material was removed by filtration. A solution of sodium chloride in water was added to the filtrate and the mixture was concentrated at room temperature. The residue was washed with water and with ethyl alcohol and recrystallized from isopropyl ether. The recrystallized material melted at 119–120°.

Analysis: Calcd. for $C_{10}H_{19}N_2O_2HgCl$: Hg, 46.08; N, 6.43. Found: Hg, 45.85; N, 6.47.

Example 8

$(C_2H_5)_2NCONHCH_2CHOCH_3CH_2HgCl$

N-(3-chloromercuri-2-methoxypropyl)-N',N'-diethylurea

N-allyl-N',N'-diethylurea was prepared by the reaction of allylisocyanate and diethylamine. The product, distilling at 109–110° at 1 mm. Hg, was obtained in 65% yield. $n_D^{20}=1.4741$.

Analysis: Calcd. for $C_8H_{16}N_2O$: N, 17.93. Found: N, 18.04.

To a solution of N-allyl-N',N'-diethylurea in methyl alcohol was added a mixture of mercuric-acetate, acetic acid and methyl alcohol. After one day, the insoluble material was removed by filtration and an aqueous solution of sodium chloride was added to the filtrate. The mixture was concentrated at room temperature. The oily residue, N-(3-chloromercuri-2-methoxypropyl)-N',N'-diethylurea, did not solidify.

Example 9

$(n\text{-}C_4H_9)_2NCONHCH_2CHOCH_3CH_2HgCl$

N-(3-chloromercuri-2-methoxypropyl)-N',N'-dibutylurea

From the reaction of dibutylamine with allylisocyanate, N-allyl-N',N'-dibutylurea was obtained in 30% yield. The product boiled at 114–118° at 1 mm. Hg. $n_D^{20}=1.4692$.

Analysis: Calcd. for $C_{12}H_{24}N_2O$: N, 13.19. Found: N, 13.03.

To a hot solution of N-allyl-N',N'-dibutylurea in methyl alcohol was added a mixture of mercuric acetate, acetic acid and methyl alcohol. After the reaction mixture was heated under reflux for sixteen hours, the insoluble material was removed by filtration. A solution of sodium chloride in water was added to the filtrate and the mixture was concentrated at room temperature. The oily residue, after washing with water and drying in vacuo over sulfuric acid, solidified. After washing with Skelly B, the solid melted at 69–70°. Yield: 35%.

Analysis: Calcd. for $C_{13}H_{27}N_2O_2HgCl$: Hg, 41.85; N, 5.84. Found: Hg, 41.25; N, 5.94.

Example 10

$NH_2CONHCH_2C(OCH_3)CH_2HgCl$

CH_3

3-chloromercuri-2-methoxy-2-methyl-propylurea

A solution of 213 g. of methallylamine in 200 cc. of cold water was neutralized with 147 g. of sulfuric acid. To this solution was added gradually a solution of 195 g. of sodium cyanate in 1000 cc. of warm water. After twenty hours, the solid was removed by filtration and the filtrate was concentrated in vacuo. The residue after concentration was poured into 1200 cc. of absolute ethyl alcohol. The solid material was removed by filtration and the filtrate was concentrated in vacuo. The residual methallylurea, after crystallization from ethyl acetate melted at 119–120°. Yield: 190 g. (55%).

Analysis: Calcd. for $C_5H_{10}N_2O$: N, 24.54. Found: N, 24.37.

To a solution of 20 g. of methallylurea in 200 cc. of methyl alcohol was added a hot mixture of 55 g. of mercuric acetate, 5 cc. of glacial acetic acid and 300 cc. of methyl alcohol. After the reaction mixture was heated under reflux for sixteen hours, the solid material was removed by filtration and a solution of 12 g. of sodium chloride in 50 ml. of water was added to the filtrate. The precipitate was collected by filtration, washed with water and crystallized from ethyl alcohol. The 3-chloro-mercuri-2-methoxy-2-methylpropylurea melting at 168.5–169.5° weighed 36 g. (55%).

Analysis: Calcd. for $C_6H_{13}N_2O_2HgCl$: Hg, 52.62; N, 7.35. Found: Hg, 53.07; N, 7.48.

Example 11

$$H_2N-\overset{\overset{O}{\|}}{C}-HN-CH_2-\underset{\underset{OCH_3}{|}}{CH}-CH_2-HgCl$$

3-chloromercuri-2-methoxy-propylurea

$C_5H_{11}ClN_2O_2Hg$ M. W.=368

To a refluxing solution of 100 g. of allyl urea in 600 ml. of absolute methanol there was added with stirring a suspension of 319 g. of mercuric acetate in 600 ml. of absolute methanol and 60 ml. of glacial acetic acid; complete solution resulted. After 6 hours of refluxing the solution was cooled and clarified by filtration. To this solution there was added 59 g. of sodium chloride in 240 ml. of water. After a short time a heavy white precipitate settled out. This was filtered, washed and dried, resulting in 250 g. (68% yield) with a M. P. 141–142° C. After crystallization from ethyl alcohol, it melted at 149½–150½° C.

Analysis: Calc: N, 7.63; Hg, 54.8. Found: N, 7.79; Hg, 54.7.

Example 12

$$H_2N-\overset{\overset{O}{\|}}{C}-NH-CH_2-\underset{\underset{OCH_3}{|}}{CH}-CH_2-Hg-Br$$

3-bromomercuri-2-methoxy-propylurea

$C_5H_{11}BrN_2O_2Hg$ M. W.=412

If in place of the sodium chloride of Example 11, there is used sodium bromide, a precipitate of the bromo-mercuri compound results in 60% yield. It was recrystallized from alcohol and melts at 161–161½° C.

Analysis: Calc: N, 6.80; Hg, 48.8. Found: N, 6.55; Hg, 48.8.

Example 13

$$H_2N-\overset{\overset{O}{\|}}{C}-NH-CH_2-\underset{\underset{OCH_3}{|}}{CH}-CH_2-Hg-OH$$

3-hydroxymercuri-2-methoxy-propylurea

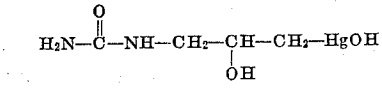
$C_5H_{12}N_2O_3Hg$ M. W.=349

Allyl urea was mercurated in methanolic solution with mercuric acetate as in Example 11. After refluxing, the solution was clarified and concentrated to a viscous liquid. Two molar equivalents of a solution of sodium hydroxide were added and the resulting solution again concentrated to a viscous liquid. On standing it solidified. The solid was granulated by suspension in alcohol (SDA-30) and washed well. The

yield was 75% of white material, M. P. 181–182° C.

Analysis: Calc: N, 8.03; Hg, 57.6. Found: N, 8.30; Hg, 57.2.

Example 14



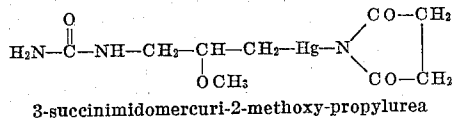
3-hydroxymercuri-2-hydroxy-propylurea

$C_4H_{10}N_2O_3Hg$ M. W.=335

To a solution of 80 g. of allyl urea in 180 ml. of hot water there was added a hot solution of 250 g. of mercuric acetate in 170 ml. of water and 48 ml. of acetic acid. The resulting mixture was refluxed for 1¼ hours. To one-fifth of the solution thus formed, there was added with cooling and stirring approximately 80 g. of 20% sodium hydroxide solution. A gummy precipitate resulted. The supernatant solution was decanted and an additional 20 g. of sodium hydroxide solution was added. A white precipitate formed; this was washed with water and then ethyl alcohol, whereupon it showed the following melting point: turns green at 140° C., black by 205° and becomes a black semi-fluid mass with gas evolution at ca. 230° C.

Analysis: Calc: N, 8.36; Hg, 60.0. Found: N, 8.74; Hg, 60.3.

Example 15



3-succinimidomercuri-2-methoxy-propylurea

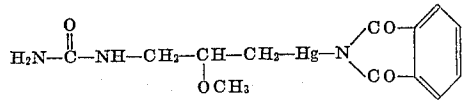
$C_9H_{15}N_3O_4Hg$ M. W.=430

To a solution of 2.5 g. of succinimide in 50 ml. of water there was added 9 g. of 3-hydroxymercuri-2-methoxy-propylurea (Example 13).

The practically complete solution which resulated was clarified and the filtrate concentrated at room temperature. The resulting solid which precipitated was crystallized from ethyl alcohol and then melted at 159–169° C.

Analysis: Calc: N, 9.77; Hg, 46.7. Found: N, 9.59; Hg, 46.4.

Example 16



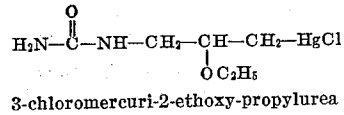
3-phthalimidomercuri-2-methoxy-propylurea

$C_{13}H_{15}N_3O_4Hg$ M. W.=478

If in place of the succinimide of Example 15 there is used an equimolecular amount of phthalimide, solution is effected when hot water is used. The hot solution was clarified and cooled. The precipitate resulting on cooling was filtered and recrystallized from alcohol, M. P. 186–187° C.

Analysis: Calc: N, 8.7; Hg, 42.1. Found: N, 8.7; Hg, 41.3.

Example 17



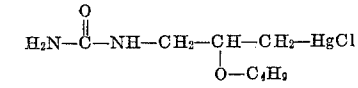
3-chloromercuri-2-ethoxy-propylurea

$C_6H_{13}N_2O_2HgCl$ M. W.=381

To a refluxing solution of 85 g. of allyl urea in 500 ml. of absolute ethanol there was added 271 g. of mercuric acetate in 800 ml. of ethanol and 50 ml. of glacial acetic acid over a period of one hour. After refluxing an additional ½ hr. the solution was allowed to cool and was clarified by filtration. To ⅓ of the resulting solution there was added 16.3 g. of sodium chloride in 70 ml. of water. On stirring a white precipitate slowly formed. This was filtered, washed with water and dried, 33 g. (30% yield). On crystallization from ethyl alcohol the product melted at 150–152° C.

Analysis: Calc: N, 7.36; Hg, 52.7. Found: N, 7.38; Hg., 52.6.

Example 18



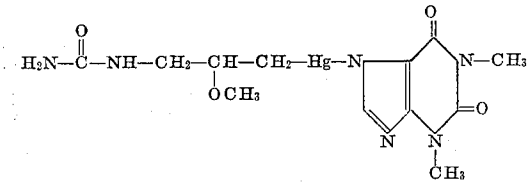
3-chloromercuri-2-n-butoxy-propylurea

$C_8H_{17}N_2O_2ClHg$ M. W.=409

In place of ethanol in Example 17, the reaction was run in normal butanol at approximately 70° C. and the resulting solution concentrated and sodium chloride solution added, there was obtained on further concentration, followed by crystallization from water, the corresponding n-butoxy analog, of M. P. 120–122° C.

Analysis: Calc: N, 6.85; Hg, 49.2. Found: N, 6.84; Hg, 49.0.

Example 19



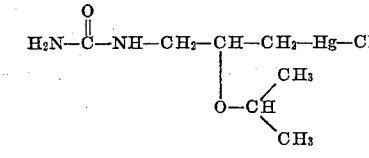
3-ureido-2-methoxy-propyl-mercury-theophylline

$C_{12}H_{18}N_6O_4Hg$ M. W.=511

In place of the succinimide of Example 15, there was used an equimolecular amount of theophylline, solution was effected when hot water was used. The solution was clarified, cooled and concentrated at room temperature. Upon drowning in acetone a precipitate appeared and became granular on stirring. This was filtered, washed with acetone and then crystallized from ethyl alcohol, whereupon it melted at 180–182° C. Further crystallization raised the M. P. to 188–188½° C.

Analysis: Calc: Hg, 39.3. Found: Hg, 39.1.

Example 20



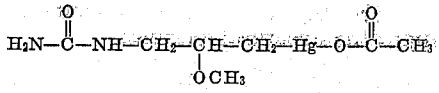
3-chloromercuri-2-isopropoxy-propylurea

$C_7H_{15}N_2O_2HgCl$ M. W.=395

In place of ethanol in Example 17, the reaction was run in isopropanol at approximately 55° C., sodium chloride solution added, the solution filtered, concentrated and the resulting solid recrystallized from alcohol. The corresponding isopropoxy analog of M. P. 149–150° C. was obtained.

Analysis: Calc: N, 7.09; Hg, 50.9. Found: N, 7.17; Hg, 51.0.

Example 21



3-acetoxymercuri-2-methoxy-propylurea

$C_7H_{14}N_2O_4Hg$ M. W.=391

Allylurea was mercurated in methanolic solution with mercuric acetate as in Example 11. The clarified solution was concentrated at room temperature to a viscous liquid. This on being allowed to stand slowly deposited a solid, but was too viscous to filter. By trituration with acetone a solid was obtained melting at 122–3° C. This was crystallized from isopropyl alcohol and then melted at 126–127° C.

Analysis: Calc: N, 7.16; Hg, 51.4. Found: N, 7.30; Hg. 51.4.

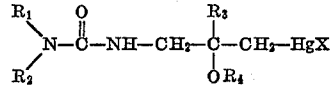
The invention described herein is also related to the copending application of Emmanuel Leon Foreman, Serial No. 113,493, filed August 31, 1949. In this application also R_1, R_2 and R_3 are each a hydrogen atom and R_4 is either hydrogen or alkyl. In this copending application, X is an atom other than carbon and having a negative valence or a group including such an atom bonded directly to the mercury.

The new compounds are used with the ordinary carriers, such as in aqueous solutions, as diuretics and may be injected either intravenously, subcutaneously or intramuscularly. When so injected, there is noted a marked increase in urinary output. This increase ordinarily lasts about five hours after which the output of liquids returns to its normal level. In treating patients having large amounts of water and salt in the tissues, the injections are continued until a constant weight in the patient is obtained. After this constant weight has been obtained, no more need be given until such time as there is noted a marked weight increase. The new mercurated allylureas are non-toxic even when given in relatively large amounts and are superior to other prior mercury compounds in eliminating a greater amount of liquid and salt in a given time.

The foregoing detailed description is given for clearness of understanding only and no unnecessary limitations are to be understood therefrom, for some modifications will be obvious to those skilled in the art.

I claim:

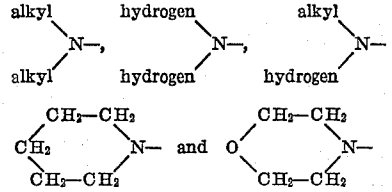
1. The new compound having essentially the structural formula:



wherein the radical

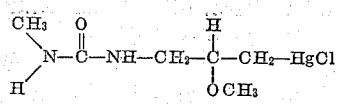


is selected from the class consisting of

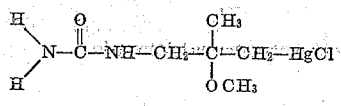


radicals, R_3 is a member of the class consisting of hydrogen atoms and alkyl groups, R_4 is a member of the class consisting of a hydrogen atom and alkyl groups, and X is a member of the class consisting of a halogen, a hydroxyl, an oxy-acyl, the residue of acidic nitrogen compounds theophylline, succinimide, and phthalimide having a replaceable hydrogen on the nitrogen atom, the residue of an alkyl thiol acid wherein the sulfur is bonded directly to the mercury atom, and the alkali metal salts of said thiol acid residue, at least one and not more than two of R_1, R_2, and R_3 being a hydrogen atom when X includes a sulfur atom linked to the mercury atom.

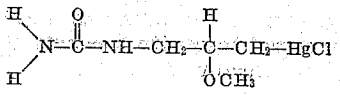
2. The new compound having essentially the structural formula:



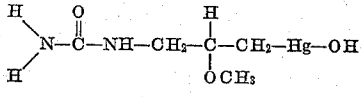
3. The new compound having essentially the structural formula:



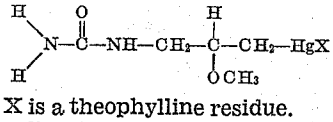
4. The new compound having essentially the structural formula:



5. The new compound having essentially the structural formula:

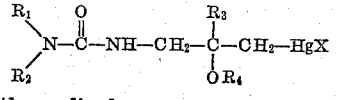


6. The new compound having essentially the structural formula:



wherein X is a theophylline residue.

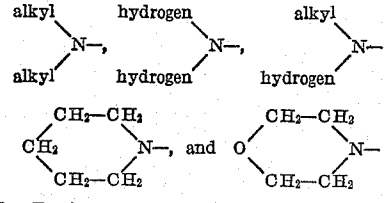
7. As a diuretic, a pharmaceutical carrier having associated therewith a compound having essentially the structural formula:



wherein the radical



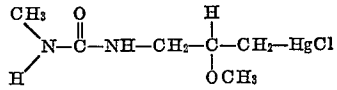
is selected from the class consisting of



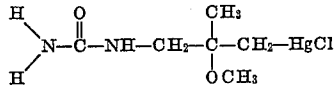
radicals, R_3 is a member of the class consisting of hydrogen atoms and alkyl groups, R_4 is a member of the class consisting of a hydrogen atom and alkyl groups, and X is a member of the class consisting of a halogen, a hydroxyl, an oxy-acyl, the residue of acidic nitrogen compounds theophylline, succinimide, and phthalimide, having a replaceable hydrogen on the nitrogen atom, the residue of an alkyl thiol acid wherein the sulfur is bonded directly to the mercury atom, and the alkali metal salts of said thiol acid residue, at

least one and not more than two of R_1, R_2, and R_3 being a hydrogen atom when X includes a sulfur atom linked to the mercury atom.

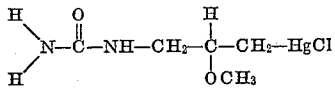
8. As a diuretic, a pharmaceutical carrier having associated therewith a compound having essentially the structural formula:



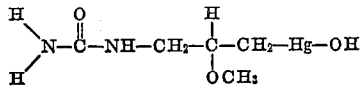
9. As a diuretic, a pharmaceutical carrier having associated therewith a compound having essentially the structural formula:



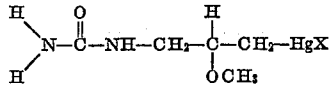
10. As a diuretic, a pharmaceutical carrier having associated therewith a compound having essentially the structural formula:



11. As a diuretic, a pharmaceutical carrier having associated therewith a compound having essentially the structural formula:



12. As a diuretic, a pharmaceutical carrier having associated therewith a compound having essentially the structural formula:



wherein X is a theophylline residue.

RALPH L. ROWLAND.

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