United States Patent Office 3,074,930 Patented Jan. 22, 1963

3,074,930
6-MERCAPTOPURINE NUCLEOSIDES AND METHOD OF PREPARING THEM

George H. Hitchings, Yonkers, and Irving Goodman, White Plains, N.Y., assignors to Burroughs Wellcome & Co. (U.S.A.) Inc., Tuckahoe, N.Y., a corporation of New York

No Drawing. Filed Jan. 5, 1959, Ser. No. 784,864
Claims priority, application Great Britain Aug. 11, 1955
22 Claims. (Cl. 260—211.5)

The present invention relates to 9-glycosido-6-mercaptopurines and to a process for preparing the same.

The ability of 6-mercaptopurine to interfere with cell division has found a useful expression in the production of remissions of acute leukemia. The mechanism of action of 6-mercaptopurine is believed to be as an antagonist of the natural 6-substituted purines, which exist in cellular compositions combined through glycoside linkages.

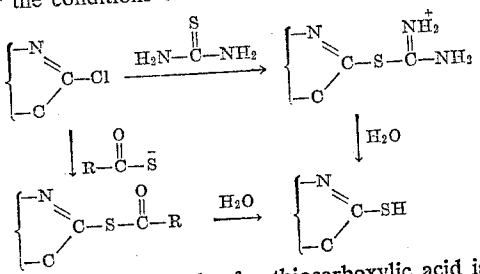
The biological activity of 6-mercaptopurine is modified, and becomes more selective in the new compounds with the result that the range of usefulness of the growth inhibitor is extended.

The usual method of preparing purine glycosides is by the reaction of a heavy metal salt of the purine with a glycosyl halide. In the present instance this method is inoperable presumably because the metal salts are attached to the sulfur of the mercaptan group. However, it has been found that 6-benzylmercaptopurine will form a suitable silver salt, and that debenzylation of the eventual 9-glycosido-6-benzylmercaptopurines can be effected by treating with sodium in liquid ammonia.

In our copending application Serial No. 574,575, now abandoned, we have described a method of preparing nucleosides of 6-marcaptopurines which consists of preparing first an acylated (thereby protected) nucleoside of a 6-chloropurine and converting that to the acylated nucleoside of a 6-mercaptopurine.

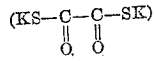
The synthesis of nucleosides of 6-chloropurines being inconvenient, though feasible, it is often preferable to start with preformed purine nucleosides available commercially. These are particularly inosine (I*a*) and guanosine (I*b*). These are first protected by acetylation or benzoylation of the sugar hydroxyls, and then converted to acylated nucleosides of 6-chloropurines by reaction with phosphorous oxychloride in the presence of a hydrogen halide acceptor. Considering the sensitivity of these nucleosides it is not surprising that this procedure is feasible only under special conditions. As the hydrogen halide-acceptor, weak tertiary organic bases are essential, and dimethyl and diethylaniline are preferred. Pyridine, picolines and lutidines can also be employed, but result in more tarformation.

The chloropurineacylnucleosides is then reacted with a sulfur-bearing reagent. For this purpose thiourea is satisfactory but a salt of a thiocarboxylic acid is even better. In both cases it is to be presumed that unstable sulfur-containing intermeriates (thio-uronium salts and thiocarboxylates) are formed and these are hydrolyzed repidly under the conditions of the reaction:



The choice of the salt of a thiocarboxylic acid is one

of convenience and accessibility rather than of chemical peculiarity. Alkali metal salts are satisfactory and other salts i.e. alkali earth metal salts usually offer no advantage. In some instances a salt of triethylamine or a similar tertiary amine (unreactive in its own right) presents advantages through having greater solubility. Among the thiocarboxylic acids thioacetic acid and dithio-oxalic acid are readily available. Potassium dithiooxalate

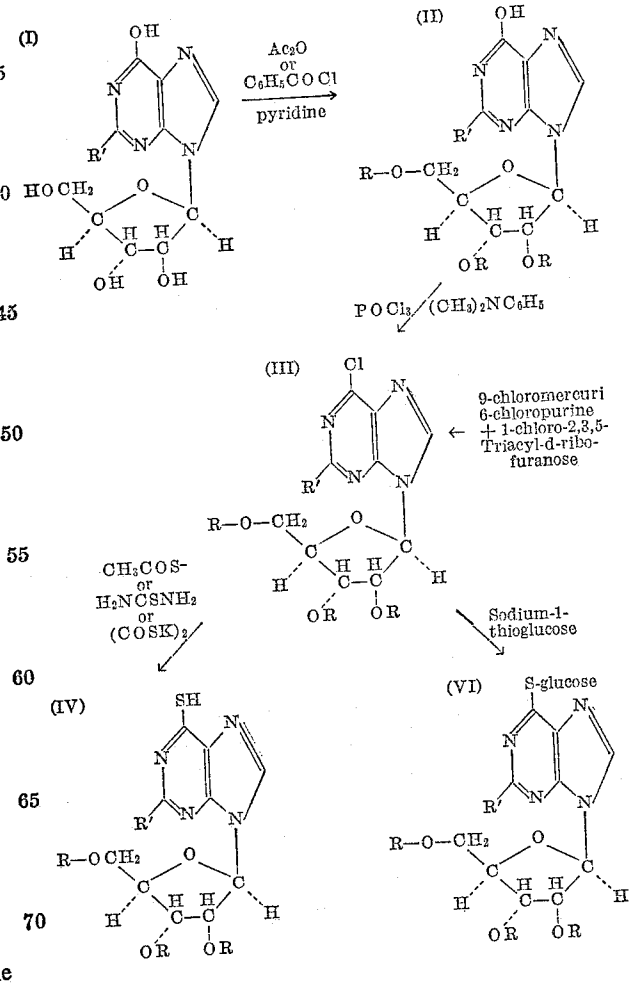


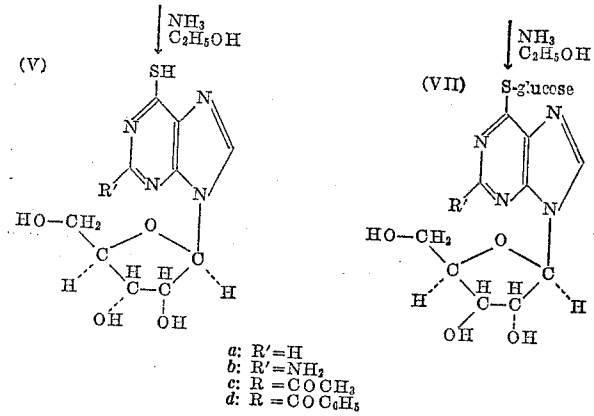
is probably the most convenient as being inexpensive and available commercially in pure form.

Finally as in other lines of synthesis, the protective acyl groups are removed, conveniently by the action of ammonia in alcoholic solution.

The 6-chloropurine acylnucleosides can also be reacted with other reagents. Of particular interest is the reaction with thiohexoses whereby are obtained 6,9-diglycosides of mercaptopurine (or of thioguanine). These compounds (VII) and their esters (VI) are of therapeutic value in their own right.

These reactions are illustrated in the chart of reactions with sodium-1-thioglucose leading to the 6-(1'-thioglucosides) (VI and VII). It is believed that these particular compounds have the β-configuration and are 1-thio-β-d-glucopyranosides. However, neither the pyranose form nor the β-configuration have yet been proved beyond question. Therefore, at this point, we refrain from writing the steric form of this portion of these compounds.





a: R'=H
b: R'=NH_2
c: R =COCH3
d: R =COC6H5

EXAMPLE 1

9-(2',3',5'-Triacetylribofuranosyl)-6-Chloropurine (IIIac)

Eight g. of chloromercuri-6-chloropurine was added to a solution of 7 g. 1-chloro-2,3,5-triacetylribofuranose in 100 ml. anhydrous xylene. The solution was refluxed for 48 hours, filtered and the filtrate was concentrated to a syrup. The product was an impure oil.

EXAMPLE 2

9-Ribofuranosyl-6-Mercaptopurine (Va)

Two g. of the syrup (III) was refluxed with 0.2 g. thiourea and 0.2 g. sodium acetate in absolute ethanol for 18 hours. The resulting solution of the thiouronium salt IV was filtered, treated with H_2S to remove any remaining Hg, decolorized with Darco, concentrated to a syrup and taken up in absolute ethanol. The ethanolic solution was saturated with NH_3 and left for 18 hours at room temperature. A very small amount (50 mg.) of product was obtained.

λ max.=225, 321 at pH 1; 234, 311 at pH 11; the product gives a positive Mohlisch test and was shown by paper chromatography to have a mobility resembling that of the corresponding glucosyl derivative.

EXAMPLE 3

6-Hydroxy-9-(2,3,5-Tri-O-Acetylribofuranosyl)-Purine (IIac)

15 g. of inosine (I) is suspended in 200 ml. pyridine. To the suspension is added 100 ml. acetic anhydride. After stirring until homogeneous, the mixture is kept on the steam bath for 2 hours. The resulting clear amber-colored solution is concentrated to semi-solid state in vacuo. 250 ml. of ice water is added to the residue, whereupon the solid dissolves with the evolution of heat. Upon cooling for 5 minutes in an ice bath the white crystalline product appears. After keeping at 4° C. for one hour, the crystals are collected by filtration and washed with ice water. Yield, 19.5 g.; (89% of theory). M.P. 230°. λ max.=245 mμ (in absolute EtOH).

EXAMPLE 4

6-Chloro-9-(2,3,5-Tri-O-Acetylribofuranosyl)-Purine (IIIac)

16.0 g. of triacetylinosine (II) is intimately mixed with 10 ml. of dimethylaniline. To the mixture is added 100 ml. of $POCl_3$. The suspension is heated on the steam bath for 4 hours (anhydrous conditions). The homogeneous dark brown solution is then concentrated in vacuo on the steam bath to remove the excess $POCl_3$. The remaining brown syrup is dissolved in 250 ml. $CHCl_3$. The $CHCl_3$ solution is washed 5 times with 75 ml. portions of H_2O in a separatory funnel, after which the water washings are at pH 5 to 6. The $CHCl_3$ layer is dried over anhydrous Na_2SO_4 and is concentrated to a syrup.

Final traces of solvent are removed under high vacuum. The yield of crude product isolated as a syrup is 14.8 g. (89% of theory). λ max.=265 mμ (in H_2O).

EXAMPLE 5

6-Mercapto-9-(2,3,5-Tri-O-Acetylribofuranosyl)-Purine (IVac)

1.3 g. of (IIIac) is dissolved in 10 ml. of absolute ethanol. To this solution is added a solution containing 0.6 g. of sodium thioacetate in 10 ml. of absolute ethanol. The clear solution was refluxed on the steam bath for 1 hour. The warm solution was filtered, and upon cooling the product crystallized in the form of white plates. Yield, 800 mg. (62% of theory). λ max.=325 mμ in absolute ethanol.

EXAMPLE 6

6-Mercapto-9-(2,3,5-Tri-O-Acetylribofuranosyl)-Purine (IVac)

In ten ml. of absolute ethanol was dissolved 2.5 g. of 6 - chloro - 9 - (2,3,5-tri - O - acetylribofuranosyl)-purine (IIIac). To this was added a suspension of 1 g. of potassium dithiooxalate $(COSK)_2$ in 25 ml. of absolute ethanol. The mixture was heated at reflux for 1 hour. It was then filtered and the filtrate was concentrated in vacuo to a syrup. The syrup was taken up in 20 cc. of benzene and hexane was added to incipient precipitation. After standing 24 hours at room temperature the precipitate was filtered and washed with hexane. It had properties identical with those described above (Example 5).

EXAMPLE 7

6-Mercapto-9-Ribofuranosylpurine (Va)

95 mg. of (IV) was dissolved in 25 ml. of absolute ethanol saturated with NH_3. The solution was kept at room temperature for 18 hours after which it was concentrated in vacuo to about 5 ml. and cooled in an ice bath. 40 mg. of pure 6-MP riboside (V) was isolated (60% of theory). λ max.=225, 321 at pH 1; 234, 311 Mμ at pH 11.

EXAMPLE 8

6-Glucothiopyranosyl-9-(2,3,5-Tri-O-Acetylribofurnosyl)-Purine (VIac)

12 g. of (IIIac) is dissolved in 120 ml. absolute ethanol. To this solution is added 7 g. of sodium thioglucose. 2 H_2O in 20 ml. H_2O. The mixture was refluxed on the steam bath for 1 hour. The solution was filtered and concentrated in vacuo to a syrup. The syrup was dissolved in 200 ml. absolute ethanol. After standing for 1 hour at room temperature, the precipitate of NaCl was removd by filtration and the filtrate concentrated in vacuo to about 50 ml. Upon the addition of anhydrous ether a precipitate was formed. 13 g. of crystalline product (VIac) was isolated (66% of theory). λ max.=280 mμ (in absolute ethanol).

EXAMPLE 9

6-Glucothiopyranosyl-9-Ribofuranosylpurine (VIIa)

5 g. of (VIac) was dissolved in 70 ml. ethanolic NH_3 and kept at room temperature for 18 hours. The solution was concentrated in vacuo to 10 ml. Upon adding 10 ml. anhydrous ether, the product crystallized. Yield, 2.8 g. (72% of theory). λ max.=280 mμ (in H_2O).

EXAMPLE 10

6-Hydroxy-9-(2,3,5-Tri-O-Benzoylribofuranosyl)-Purine (IIad)

Five g. of inosine was suspended in 10 ml. of pyridine. The mixture was cooled to 0° in an ice bath. To the cold suspension, 25 ml. of $CHCl_3$ followed by 10 g. of benzoyl chloride was added. The mixture was heated at 100° for 2 hours, allowing the $CHCl_3$ to distill off. The resultant syrup was dissolved in 100 ml. of $CHCl_3$.

The $CHCl_3$ solution was washed with saturated $NaHCO_3$ solution and then with saturated $NaHSO_4$ solution followed by water. After drying over Na_2SO_4 the $CHCl_3$ solution was concentrated in vacuo to a syrup which, on treatment with anhydrous ether, formed the solid benzoyl derivative. Yield, 10 g. (92% of theory) N=9.61%. Theory N=9.68%. λ max.=230 and 265 mμ in alcohol.

EXAMPLE 11

6-Chloro-9-(2,3,5-Tri-O-Benzoylribofuranosyl)-Purine (IIIad)

Five g. of tribenzoylinosine (Example 10) was suspended in 5 ml. of dimethylaniline. To this suspension was added 61 g. of $POCl_3$ whereupon the solid dissolved. The mixture was heated at 100° for 4 hours. The resulting light yellow solution was poured into 800 ml. of ice water-$CHCl_3$ (1:1 by volume). The water layer was extracted twice with $CHCl_3$. The $CHCl_3$ layer was washed twice with saturated $NaHCO_3$ solution and then with water. After drying over Na_2SO_4 the $CHCl_3$ layer was concentrated in vacuo to a syrup. The resulting syrup was dissolved in 100 ml. of absolute alcohol and poured into 600 ml. of water. Upon acidification to pH 2 with HCl, a precipitate was formed. Yield 6 g. of crude product. λ max.=230 and 260 mμ in alcohol. The 230 mμ peak is characteristic of the benzoyl derivatives while the 260 peak is similar to that of the parent purine, 6-chloropurine with a peak at 265 (aqueous solution, pH 1). The product contains Cl (organic) and gives a positive Mohlisch test.

EXAMPLE 12

6-Mercapto-9-(2,3,5-Tri-O-Benzoylribofuranosyl)-Purine (IVad)

One g. of the 6-chloronucleoside of Example 11 was dissolved in 25 ml. of absolute alcohol. To this was added a solution containing 0.4 g. of sodium thioacetate in 5 ml. of alcohol. The mixture was heated under reflux for one hour. On cooling for 18 hours at 4° C., a fluocculant precipitate was formed. The solution was acidified with 0.1 N HCl and filtered. Yield, 400 mg. N=9.35%; theory, N=9.42%. λ max.=230, 265 and 322 mμ in abs. alcohol.

EXAMPLE 13

6-Glucothiopyranosyl-9-(2,3,5-Tri-O-Benzoylribofuranosyl)-Purine (VIad)

Two g. of the chloronucleoside of Example 11 was dissolved in 50 ml. of absolute ethanol. To this solution was added a solution containing 1 g. of sodium thioglucose dihydrate in 5 ml. of water. The mixture was heated at 100° for 15 minutes, then filtered. From the filterate was isolated 0.8 g. of crude product with λ max.=228 and 280 mμ in 50% ethanol. The 280 mμ peak is characteristic of the 6-purinethoiglycosides. Upon hydrolysis this yields 6-mercaptopurine. The product still contains the benzoyl groups as shown by the 228 mμ peak.

EXAMPLE 14

2-Amino-6-Hydroxy-9-(2,3,5-Tri-O-Acetylribofuranosyl)-Purine (IIbc)

Fifty g. of guanosine (commercial grade) was suspended in 500 ml. of pyridine. To this was added 250 ml. of acetic anhydride. The mixture was heated at 100° for 17 hours. The resulting solution was poured into 1600 ml. of water and extracted with $CHCl_3$ (3–200 ml. portions). The $CHCl_3$ solution was washed twice with saturated $NaHSO_4$ solution (2 x 200 ml.), twice with 200 ml. portions of H_2O, dried over Na_2SO_4, and concentrated to a syrup in vacuo. The syrup, on trituration with anhydrous ether formed a crude solid product (63 g.). λ max.=258 mμ at pH 6; 265 mμ at pH 12. The product shows U.V. characteristics similar to guanosine as would be expected.

EXAMPLE 15

2-Amino-6-Chloro-9-(2,3,5-Tri-O-Acetylribofuranosyl)-Purine (IIIbc)

Twenty-five g. of the above ester was suspended in 35 ml. of dimethylaniline. To this was added 240 g. of $POCl_3$. The mixture was heated at 100° under reflux for 4 hours. The resulting solution was concentrated in vacuo on the steam bath to a syrup. The syrup was dissolved in 200 ml. of $CHCl_3$, which solution was extracted several times with 75 ml. portions of H_2O until the pH of the washings was about 4. After drying over Na_2SO_4 the $CHCl_3$ layer was concentrated in vacuo to a syrup. To this was added anhydrous ether. The resulting hygroscopic solid was dried in vacuo. Yield 12 g. λ max. 252 and 285 mμ in alcohol. Contains chlorine (organic). Positive Mohlisch test.

EXAMPLE 16

2-Amino-6-Mercapto-9-(2,3,5-Tri-O-Acetylribofuranosyl)-Purine (IVbc)

One g. of the above chloro compound was dissolved in 25 ml. of absolute alcohol. To this was added a solution of 0.5 g. of sodium thioacetate in 5 ml. of absolute alcohol. The mixture was refluxed for 2 hours, filtered, and concentrated to dryness in vacuo. The solid residue was treated with 50 ml. of water. A precipitate formed with U.V. characteristics similar to the parent purine compound, thioguanine. U.V., λ max. at 250 and 340 mμ in absolute alcohol. The 340 peak is characteristic of the mercapto group of thioguanine. A positive Mohlisch test indicates the presence intact of the ribosyl group.

EXAMPLE 17

2-Amino-6-Mercapto-9-β-D-ribofuranosylpurine (IVb)

One-tenth g. of 2-amino-6-mercapto-9-triacetylribofuranosylpurine (Example 16) was dissolved in 2.5 cc. of alcohol saturated with ammonia. The solution was allowed to stand over-night at room temperature and was then evaporated in vacuo. The residue, after washing with absolute ethanol was a brown amorphous powder. It gave a positive Mohlisch test and had the ultraviolet absorption of a thioguanine derivative. (λ max. (H_2O 260 and 340 mμ. At pH 11, λ max. 250 and 320 mμ. The peaks at 340 and 320 mμ are very distinct and characteristic.)

EXAMPLE 18

Tribenzoyl Guanosine (IIbd)

Benzoylation was accomplished by the method described for the benzoylation of inosine (Example 10). The product was isolated as a crystalline solid, M.P. 205–8°. N=11.36%. Calculated N=11.75%. λ max. =230, 270 in alcohol.

EXAMPLE 19

2-Amino-6-Chloro-9-(2,3,5-Tri-O-Benzoylribofuranosyl)-Purine (IIIbd)

Five g. of tribenzoylinosine (Example 18) was chlorinated with $POCl_3$ as described in Examples 11 and 15. The product was isolated as an amorphous powder, probably a salt of H_3PO_4. It contains chlorine (organic), N, and P. Analysis for N: Found, N=9.57%; calculated for 1 mole H_3PO_4, N=9.85%. λ max.=230, 280 mμ in alcohol.

EXAMPLE 20

2-Amino-6-Glucothiopyranosyl-9-(2,3,5-Tri-O-Benzoylribofuranosyl)-Purine (VIbd)

One-half g. of the 6-chloro compound of Example 19 was treated with 0.25 g. of thioglucose dihydrate by the

method of Examples 8 and 13. The product was isolated as a white crystalline solid. λ max.=230 and 300 mμ. Upon hydrolysis, the thioglucosyl linkage is split leaving a product, 2-amino-6-mercapto-9-tribenzoylribofuranosylpurine, with λ max. 230 and 340 at pH 1 and 230 and 312 at pH 11. The 230 peak indicates that the benzoyl ribose portion of the molecule is intact.

What we claim is:

1. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine, 2-amino-6-mercaptopurine, purine-6-thioglycoside and 2-aminopurine-6-thioglycoside which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine, reacting the latter with a reagent selected from the class consisting of thiourea, the alkali thiohexoses and the salts of aliphatic thiocarboxylic acids and deacylating the product with alcoholic ammonia to yield the desired nucleoside.

2. The method of preparing nucleosides selected from the class consisting of nucleosides of purine-6-thioglycoside and 2-aminopurine-6-thioglycoside which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine, reacting the latter compound with a thiohexose and deacylating the product with alcoholic ammonia.

3. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine and 2-amino-6-mercaptopurine which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine, reacting the latter compound with thiourea and deacylating the product with alcoholic ammonia.

4. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine and 2-amino-6-mercaptopurine which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine, reacting the latter compound with an alkali salt of thioacetic acid and deacylating the product with alcoholic ammonia.

5. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine and 2-amino-6-mercaptopurine which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine, reacting the latter compound with an alkali salt of dithiooxalic acid and deacylating the product with alcoholic ammonia.

6. The method of preparing an O-acylated nucleoside which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine and reacting the latter compound with an alkali thiohexose.

7. The method of preparing an O-acylated nucleoside which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine and reacting the latter compound with thiourea.

8. The method of preparing an O-acylated nucleoside which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine and reacting the latter compound with an alakali salt of thioacetic acid.

9. The method of preparing an O-acylated nucleoside which comprises converting a reagent of the class consisting of inosine and guanosine to its O-acyl derivative, reacting the acylated nucleoside with phosphorus oxychloride in the presence of a hydrogen halide acceptor, so as to form the acylated nucleoside of the corresponding 6-chloropurine and reacting the latter compound with an alkali salt of dithiooxalic acid.

10. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-thioglycosido purine and 2-amino-6-thioglycosido purine which comprises converting a reagent of the class consisting of O-triacylinosine and O-triacylguanosine into its 6-chloro derivative by reaction with phosphorus oxychloride in the presence of a hydrogen halide acceptor, reacting the 6-chloro compound with an alkali thiohexose to form the 6-thioglycoside and deacylating this product with alcoholic ammonia.

11. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine and 2-amino-6-mercaptopurine which comprises converting a compound of the class consisting of O-triacylinosine and O-triacylguanosine to its 6-chloro derivative by reaction with phosphorus oxychloride in the presence of a hydrogen halide acceptor, reacting the 6-chloro compound with thiourea to give the 6-mercapto derivative and deacylating the latter with alcoholic ammonia.

12. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine and 2-amino-6-mercaptopurine which comprises converting a compound of the class consisting of O-triacylinosine and O-triacylguanosine to its 6-chloro derivative by reaction with phosphorus oxychloride in the presence of a hydrogen halide acceptor, reacting the 6-chloro compound with an alkali salt of thioacetic acid to give the 6-mercapto derivative and deacylating the latter with alcoholic ammonia.

13. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine and 2-amino-6-mercaptopurine which comprises converting a compound of the class consisting of O-triacylinosine and O-triacylguanosine to its 6-chloro derivative by reaction with phosphorus oxychloride in the presence of a hydrogen halide acceptor, reacting the 6-chloro compound with an alkali salt of dithiooxalic acid to give the 6-mercapto derivative and deacylating the latter with alcoholic ammonia.

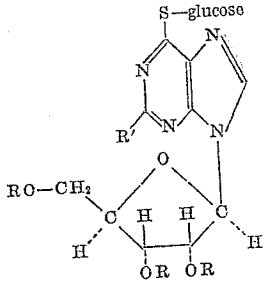
14. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-thioglycosido purine and 2-amino-6-thioglycosido purine which comprises reacting a compound selected from the class consisting of the triacylnucleosides of 6-chloropurine and the triacylnucleosides of 2-amino-6-chloropurine with an alkali thiohexose to form the 6-thioglycoside and deacylating this product with alcoholic ammonia.

15. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine and 2-amino-6-mercaptopurine which comprises reacting a compound selected from the class consisting of the triacylnucleosides of 6-chloropurine and the triacylnucleosides of 2-amino-6-chloropurine with an alkali salt of thioacetic acid to give the 6-mercapto derivative and deacylating the latter with alcoholic ammonia.

16. The method of preparing nucleosides selected from the class consisting of nucleosides of 6-mercaptopurine

and 2-amino-6-mercaptopurine which comprises reacting a compound selected from the class consisting of the triacylnucleosides of 6-chloropurine and the triacylnucleosides of 2-amino-6-chloropurine with an alkali salt of dithiooxalic acid to give the 6-mercapto derivative and deacylating the latter with alcoholic ammonia.

17. A compound represented by the formula:



wherein R is selected from the class consisting of CH_3CO, C_6H_5CO and hydrogen and R' is selected from the class consisting of the amino group and hydrogen.

18. Purine-9-β-d-ribofuranoside-6-thioglucoside.

19. Purine-9-β-d-triacetylriboside-6-thioglucoside.

20. 2-aminopurine - 9 - β-d-ribofuranoside-6-thioglucoside.

21. 2-aminopurine - 9 - β-d-triacetylribofuranoside-6-thioglucoside.

22. 2 - amino-6-chloropurine-9-β-d-triacetylribofuranoside.

References Cited in the file of this patent

UNITED STATES PATENTS

2,746,961	Hitchings et al.	May 22, 1956
2,852,505	Baker	Sept. 16, 1958
2,852,506	Goldman et al.	Sept. 16, 1958

OTHER REFERENCES

Friedkin: Biochem et Biophys Acta 18, pp. 447–448 (1955). (Cited in Chem. Abstracts 40, 3516, 1956.)

Johnson, Jr., et al.: J. Am. Chem. Soc. 78, 3863 (1956).