

UNITED STATES PATENT OFFICE

2,527,293

5- β -NITROALKYL BARBITURIC ACIDS AND
SALTS THEREOF

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No Drawing. Application August 5, 1948,
Serial No. 42,741

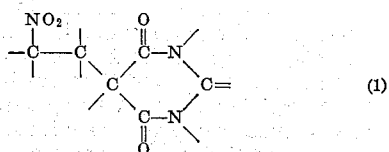
27 Claims. (Cl. 260-257)

1

This invention relates to certain derivatives of barbituric acid and related compounds and processes for preparing same. More particularly this invention relates to compounds related to barbituric acid wherein a hydrogen on the carbon atom in the 5 position is substituted with an alkyl group having a nitro group in the β position.

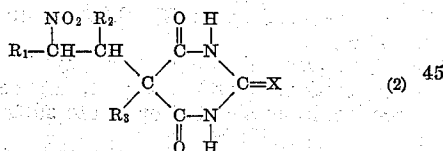
The compounds of this invention are useful as hypnotics, sedatives or soporifics. Also the compounds of this invention are useful as intermediates in the preparation of compounds having hypnotic, sedative or soporific activity, and as intermediates in the preparation of other pharmaceuticals and chemical compounds.

The compounds that are contemplated within the scope of this invention are those which have the following skeletal configuration:



It will be noted from (1) that the ring nucleus is of the barbituric acid type and is that which is found in such compounds as barbituric acid, 2-thiobarbituric acid and malonylguanidine. As is well known in the art, the acid characteristics of compounds having this skeletal arrangement are imparted by the hydrogen atoms attached to the nitrogens in the 1 and/or 3 positions, and the salts of the compounds having the above indicated skeletal configuration are to be considered as falling within the scope of this invention as defined by the appended claims. Stated in another way, this invention relates to the provision of compounds having a barbituric acid type ring nucleus wherein is provided a 2'-nitroalkyl substituent on the carbon atom in the 5 position.

More specifically, this invention relates to compounds (and their salts) having the formula:



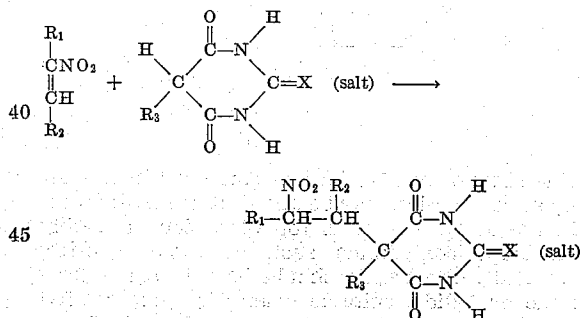
wherein R_1 is selected from the group consisting of hydrogen and alkyl, wherein R_2 is selected from the group consisting of hydrogen, alkyl and aryl, wherein R_3 is selected from the group consisting of hydrogen, alkyl and aralkyl, and wherein X is selected from the group consisting of oxygen and sulfur. Specific compounds that fall

2

within the above generalized formula and contemplated within the scope of this invention are 5-(2'-nitro-1'-ethyl-n-butyl) - barbituric acid, 5-(2'-nitro-1'-phenylethyl) - barbituric acid, 5-(2'-nitro-n-butyl) - 2-thiobarbituric acid, 5-(2'-nitro-n-butyl) - barbituric acid, 5-(2'-nitro-1'-phenylethyl) - 2-thiobarbituric acid, 5-ethyl-5-(2'-nitro-n-butyl) - barbituric acid, 5-methyl-5-(2'-nitro-n-butyl) - 2 - thiobarbituric acid, 5 - allyl-5-(2'-nitro-n-butyl) - barbituric acid, 5 - benzyl-5-(2'-nitro-n-butyl) - barbituric acid; and the salts thereof. Specific salts that may be mentioned are those of potassium, barium, calcium and those formed from a quaternary ammonium hydroxide, such as benzyltrimethylammonium hydroxide or tetraethanolammonium hydroxide. These latter salts are important as intermediates formed when one phase of this invention is carried out in accordance with a preferred embodiment, as will be hereinafter more fully explained.

As above indicated, the compounds of this invention are barbituric acid derivatives but it will be apparent that the oxygen on the carbon atom in the 2 position of the barbituric acid nucleus may be replaced by sulfur to form the corresponding 2-thiobarbituric acid derivative or its salts, or by an imido group to form the corresponding derivative of malonylguanidine or its salts.

The compounds of this invention may be prepared by reacting a nitroolefin directly with a salt of the barbituric acid type compound whereby the nitroolefin is added to the barbituric acid type nucleus at the carbon atom in the 5 position. The over-all reaction may be represented as follows:

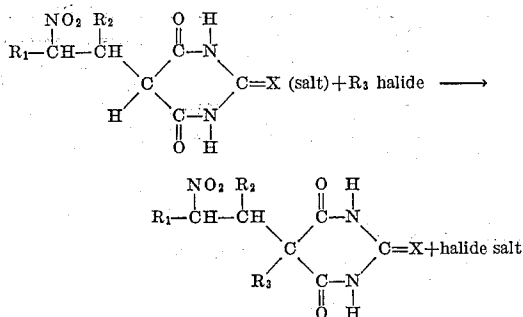


The salts of the barbituric acid type compounds which have been found to be particularly effective for carrying out the reaction are those of potassium and of benzyltrimethylammonium hydroxide. However, in most instances, other salts may readily be used, such as those of sodium, lithium, calcium, magnesium, barium, tetra-

ethanolammonium hydroxide and the like, the desirability being that such salts be soluble in the solution in which the reaction is effected.

It will be apparent that the above indicated generalized equation indicates that a convenient method has been devised in accordance with this invention for adding a β -nitroalkyl group to a compound of the barbituric acid type wherein the carbon atom in the 5 position has attached at least one unsubstituted hydrogen atom. The metallic salts of the barbituric acid type compound are very satisfactory for use in the cases where neither hydrogen on the 5 carbon atom is substituted. However, in those cases where one of the hydrogens on the 5 carbon atom has already been substituted, such as by an alkyl or an aryl group, then it is preferred to employ a quaternary ammonium salt of such a 5 monosubstituted barbituric acid derivative in the reaction with the nitroolefin. When a quaternary ammonium salt is employed (for example, a benzyltrimethylammonium salt), the addition of the nitroolefin to the carbon atom in the 5 position will readily occur even though one of the hydrogens on the 5 carbon atom has been previously substituted with another grouping, such as methyl, ethyl, n-butyl or benzyl. Thus by the use of the quaternary ammonium salts, a method has been devised for the ready preparation of 5-alkyl-5-(2'-nitroalkyl)-barbituric acid type compounds directly from the corresponding 5-alkyl compounds. Such a process and the resulting product constitute one feature of the present invention.

In accordance with a further and alternative embodiment of this invention where it is desired to provide an alkyl substituent on the carbon atom in the 5 position together with the β -nitroalkyl substituent, it has been found that this may be accomplished by the direct alkylation of a 5-(2'-nitroalkyl)-barbituric acid type compound with an alkyl halide. Thus an alkyl group is added to the nucleus at the carbon atom in the 5 position. The alkylation reaction is preferably carried out with the salt of the 5-(2'-nitroalkyl)-barbituric acid type compound, and the over-all reaction may be represented as follows:



The alkyl or aralkyl halides employed in this alkylation reaction may be any that are well known in the art to be useful for alkylation of readily alkylated compounds such as malonic ester. Generally the halide should be a chloride, bromide or iodide, suitable examples being methyl iodide, allyl bromide and benzyl chloride. Other halides, such as ethyl, propyl, n-butyl, iso-butyl, benzyl, etc. may be used.

In carrying out the addition of a nitroolefin to a salt of barbituric acid type compound as indicated in the foregoing, the salt employed is preferably one which is readily ionized in solution and is readily soluble in the solvent employed.

The potassium salts are convenient but the process is not limited to them, since, as above explained, under special conditions, the quaternary ammonium salts, such as the benzyltrimethylammonium salt, are preferred. If desired, a trace of acid may be used in the reaction mixture to inhibit the polymerization of the nitroolefin. The reaction is effected most conveniently in a solution which serves as a solvent for both the salt and the nitroolefin and does not react with or destroy either. For example, mixtures of alcohols and water have been found useful but the process is not to be considered as limited to these particular solvents. Generally speaking, when the metallic salts are employed, it is desirable to carry out the nitroolefin addition reaction at elevated temperatures since the reactants are usually more soluble in hot solvents and since elevated temperatures have a tendency to speed up the reaction. However, lower temperatures are preferred when the quaternary ammonium salts are utilized. After the addition reaction has taken place, the resulting 5-(2'-nitroalkyl) derivative may be isolated in the form of its salt by any convenient method. Often the salt form is most convenient for medicinal use or for use in preparing other compounds. If desired, salts containing other cations may be prepared by metathesis or the corresponding free barbituric acid type derivative may be obtained by cautious acidification of the salt formed in the reaction. As previously indicated, both the salts and the free acids are considered as falling within the spirit and scope of this invention.

For a more complete understanding of this invention, reference will now be made to certain specific examples wherein are indicated certain of the new compounds herein contemplated together with their method of preparation. It will be understood, however, that this invention is not to be restricted in any way by these specific examples since they are merely illustrative and not definitive of the broad aspects of the present invention.

EXAMPLE I

5-(2'-nitro-1'-ethyl-n-butyl)-barbituric acid

A mixture of 0.78 gram of 3-nitro-3-hexene, 1.0 gram of potassium barbiturate containing a trace of free barbituric acid, 5 cc. of ethyl alcohol and 2 cc. of water was refluxed for 3½ hours. The nitroolefin and the barbiturate reacted to form potassium 5-(2'-nitro-1'-ethyl-n-butyl)-barbiturate. This salt was recovered by cooling the reacted solution to room temperature and adding 5 cc. of acetone to precipitate unreacted potassium barbiturate. The solution was filtered and the filtrate was evaporated to dryness. The residue was washed with acetone. The washed dried powder was analyzed for potassium. Calculated for potassium 5-(2'-nitro-1'-ethyl-n-butyl)-barbiturate: K, 13.3%; found, K, 13.4%, 13.0%.

The free acid may be prepared from the salt by cautious treatment with an acid, such as monochloroacetic acid or dilute sulfuric acid.

EXAMPLE II

5-(2'-nitro-1'-phenylethyl)-barbituric acid

A mixture of 2.69 grams of ω -nitrostyrene, 3.00 grams of potassium barbiturate, 5.4 cc. of water and 15 cc. of 95% ethyl alcohol was refluxed for 17 hours and then diluted with 15 cc. of acetone. The precipitate obtained on cooling to room tem-

5

perature and filtering weighed 0.708 gram and contained some unreacted potassium barbiturate. The filtrate on evaporation yielded 3.23 grams of crude potassium 5-(2'-nitro-1'-phenylethyl)-barbiturate from which the purified salt was obtained by recrystallization from absolute ethyl alcohol. The free acid was liberated by treatment of an aqueous solution of the potassium salt with a solution of monochloroacetic acid.

EXAMPLE III

5-(2'-nitro-n-butyl)-2-thiobarbituric acid

A saturated solution of potassium 2-thiobarbiturate was prepared by boiling a mixture of 275 cc. of 95% ethyl alcohol and 140 cc. of water with 9.4 grams of the potassium salt. The hot solution was decanted and to it was added 6.0 grams (an excess) of 2-nitro-1-butene. The remainder of the undissolved salt was dissolved in 125 cc. of boiling water and added to the reaction mixture. The solution was allowed to cool and within a short time the lachrymatory odor of nitroolefin had disappeared. On evaporation of the solution to dryness a nearly theoretical yield of crude potassium 5-(2'-nitro-n-butyl)-2-thiobarbiturate was obtained. Impurities were removed by dissolving a 3.0 g. portion of the crude salt in 25 ml. of boiling absolute methyl alcohol, allowing to stand with 0.2 g. activated charcoal at 65° C., filtering, adding 40 ml. of dry ether to the filtrate, cooling, filtering again to remove dark-colored impurities, then evaporating the filtrate to obtain the purified salt.

Analysis: Calculated for potassium 5-(2'-nitro-n-butyl)-2-thiobarbiturate: K, 13.79%; found, K, 13.56%, 13.53%.

The corresponding barium and calcium salts were separately prepared by adding concentrated solutions of barium chloride and calcium nitrate, respectively, to separate concentrated clarified solutions of the potassium salt. The barium and calcium salts, respectively, precipitated out. These alkaline earth metal salts were much less soluble in water than was the potassium salt, but were nevertheless somewhat soluble.

The free 5-(2'-nitro-n-butyl)-2-thiobarbituric acid was prepared (1) by the cautious addition of a very dilute solution of sulfuric acid to an aqueous solution of the barium salt, and (2) by a similar addition of a solution of oxalic acid to a solution of the calcium salt.

EXAMPLE IV

5-(2'-nitro-n-butyl)-barbituric acid

A boiling solution of 12.0 grams of potassium barbiturate in 200 cc. of water was added during the course of a few minutes to a solution of 8.5 grams of 2-nitro-1-butene in 135 cc. of 95% ethyl alcohol. The mixture was allowed to stand until the next day (although the reaction was completed within a short time) and on evaporation yielded 18.6 grams of crude potassium 5-(2'-nitro-n-butyl)-barbiturate. In order to obtain the free acid, 7.0 grams of this crude salt were dissolved in 20 cc. of water and the solution was acidified by the addition of a solution of 2.0 grams of concentrated sulfuric acid in 20 cc. of water over a period of 30 minutes, keeping the solution cooled and well stirred. During this period the weight of free acid which separated in the form of white crystals was 2.7 grams. An additional quantity of the free acid was recovered by extracting the aqueous mother liquor with ethyl ether. After recrystallization, the acid

6

melted at 155° C. Analysis: Calculated for 5-(2'-nitro-n-butyl)-barbituric acid: C, 41.92%, H, 4.83%; found: C, 41.97%, H, 4.91%.

In the foregoing examples an embodiment of this invention has been illustrated wherein the potassium salts of barbituric acid were employed. As previously indicated, and in accordance with one preferred embodiment of this invention, it has been found under certain conditions advantageous to use a quaternary ammonium salt of the barbituric acid type compound instead of the alkali metal salt. When such quaternary ammonium salts are employed, the reaction may then be carried out in more concentrated solutions and at lower temperatures. Likewise the use of these salts is particularly desirable when it is desired to react a nitroolefin with a barbituric acid type derivative which already has one alkyl or aryl substituent on the carbon atom in the 5 position since very much improved yields are obtained (see particularly Example VIII). The next four examples are illustrative of processes in which a quaternary ammonium salt of the barbituric acid type compound is employed in reactions involving nitroolefins.

EXAMPLE V

5-(2'-nitro-n-butyl)-barbituric acid

A neutral solution was prepared by adding 7.2 grams of barbituric acid to 22.5 grams of Triton B, cooling being effected as necessary to maintain the temperature below about 50° C. (Triton B is a commercial preparation of benzyltrimethylammonium hydroxide in a 40% aqueous solution which is sold and distributed by Rohm & Haas Co., of Philadelphia, Pa.). To this solution was added 5.06 grams of 2-nitro-1-butene in small portions with stirring, employing a water bath to prevent the temperature from rising above about 40° C. The odor of the nitroolefin was no longer observed after a short period. After the solution had been allowed to stand for four days (this period of standing not being necessary), it was centrifuged to remove a small amount of solid matter. Thereafter the 5-(2'-nitro-n-butyl)-barbituric acid benzyltrimethylammonium salt was treated in the supernatant liquid by the addition of 4.0 grams of concentrated sulfuric acid dissolved in 20 cc. of water. The dilute acid was added dropwise with stirring over a 30 minute period, keeping the solution cooled. The weight of crude product which separated in the form of tan crystals was 13.3 grams. A single recrystallization from isopropyl alcohol was sufficient to yield nearly pure 5-(2'-nitro-n-butyl)-barbituric acid melting at 152° to 154° C.

EXAMPLE VI

5-(2'-nitro-1'-phenylethyl)-2-thiobarbituric acid

The benzyltrimethylammonium salt of 2-thiobarbituric acid was prepared by adding to 2.25 grams of Triton B enough 2-thiobarbituric acid (about 0.760 grams) to produce a neutral solution. After 30 minutes a solution of 0.70 gram of 1-nitro-2-phenylethylene in 2.5 cc. of absolute ethyl alcohol was added. The solution remained clear on standing overnight but upon seeding deposited crystals of the benzyltrimethylammonium salt of 5-(2'-nitro-1'-phenylethyl)-2-thiobarbituric acid. The crystals were washed with 5 cc. of ethyl alcohol and were dried. The crystals had a melting point of 190° to 191° C. and 1.45 grams were recovered. The corresponding free

7

acid was obtained by dissolving 0.80 gram of the salt in 50 cc. of water to form a saturated solution and then adding 1 cc. of 3 N. hydrochloric acid at room temperature. The free acid separated out in the form of white crystals.

EXAMPLE VII

5-(2'-nitro-1'-phenylethyl)-barbituric acid

The benzyltrimethylammonium salt of barbituric acid was prepared by dissolving 1.3 grams of barbituric acid in 4.5 grams of Triton B. To this solution, previously clarified by centrifuging, was added a solution of 1.4 grams of 1-nitro-2-phenylethylene in 5 cc. of absolute ethyl alcohol with stirring. After a few minutes, white crystals of the benzyltrimethylammonium salt of 5-(2'-nitro-1'-phenylethyl)-barbituric acid began to precipitate. This salt was recovered by filtration and washed with a mixture of ethyl alcohol and water. It weighed 3.0 grams and decomposed at 175° C. An additional 0.9 gram of the salt was recovered from the mother liquor.

The free acid was obtained by dissolving 1.0 gram of the salt in 5 cc. water at 60° C. and adding 1 cc. of 3 N. hydrochloric acid dropwise with stirring. The oily droplets of the acid which first separated soon solidified in an amount corresponding to 0.62 gram.

EXAMPLE VIII

5-ethyl-5-(2'-nitro-n-butyl)-barbituric acid

The benzyltrimethylammonium salt of 5-ethylbarbituric acid was prepared by dissolving 1.85 grams of 5-ethylbarbituric acid in 4.4 grams of Triton B and 2.5 cc. of 95% ethyl alcohol to form a neutral solution. To this solution 1.17 grams of 2-nitro-1-butene were added dropwise with stirring employing an ice bath to prevent the temperature from rising above 50° C. The lachrymatory odor of the nitroolefin disappeared at once. The following day 20 cc. of water were added to the reaction mixture and it was centrifuged to remove some gummy material which separated. The resulting clear solution of the benzyltrimethylammonium salt of 5-ethyl-5-(2'-nitro-n-butyl)-barbituric acid was acidified by the addition of 1.0 gram of concentrated sulfuric acid dissolved in 8 cc. of water dropwise with stirring and cooling over a 10 minute period. Additional gummy material formed was separated and the clarified solution was allowed to evaporate until crystals formed which were recovered by filtration, washed with water and dried. The weight of crystals was 0.3 gram. After recrystallization from methyl ethyl ketone, the purified acid melted at 152.5° C. Analysis: Calculated for 5-ethyl-5-(2'-nitro-n-butyl)-barbituric acid: N, 16.34%; found: N, 16.47%.

In the immediately preceding four examples, the benzyltrimethylammonium salts of barbituric acid and 2-thiobarbituric acid have been specifically disclosed. However, it will be apparent to one skilled in the art that other quaternary ammonium salts may be employed if desired. For example, tetraethanolammonium salts have been used. As will be apparent to one skilled in the art, those quaternary ammonium salts that are preferred for use are those which are soluble to a substantial degree in the solvents employed for the nitroolefin addition reaction.

In order to demonstrate that aspect of this invention which relates to the preparation of 5-alkyl-5-(2'-nitroalkyl)-barbituric acid type com-

8

pounds by alkylation in accordance with this invention, the following three examples are given:

EXAMPLE IX

5-methyl-5-(2'-nitro-n-butyl)-2-thiobarbituric acid

A solution was prepared comprising 73 cc. of absolute methyl alcohol, 14.5 cc. of methyl iodide and 7.0 grams of potassium 5-(2'-nitro-n-butyl)-2-thiobarbiturate, the latter being prepared in accordance with the method indicated in Example III. The solution was refluxed for 24 hours, then filtered and the filtrate evaporated to dryness. The crude product was purified by dissolving in 24 ml. of hot alcohol, then throwing out of solution by addition of water and cooling. After two further crystallizations from isopropyl alcohol it was obtained in the form of crystals melting at 203° C. with decomposition. Analysis: Calculated for 5-methyl-5-(2'-nitro-n-butyl)-2-thiobarbituric acid: C, 41.69, H, 5.05; found: C, 41.85, H, 5.02.

EXAMPLE X

5-allyl-5-(2'-nitro-n-butyl)-barbituric acid

A solution was prepared containing 105 cc. of 95% ethyl alcohol, 7.0 grams of allyl bromide and 7.0 grams of potassium 5-(2'-nitro-n-butyl)-barbiturate, the latter having been prepared in accordance with the method indicated in Example IV above. The resulting solution was refluxed for 24 hours, cooled and filtered to remove by-products. The filtrate was evaporated to dryness and recrystallized first from hot absolute ethanol solution, by addition of water and cooling, then from isopropyl alcohol by addition of n-butyl ether to produce crystals of 5-allyl-5-(2'-nitro-n-butyl)-barbituric acid, melting at 133° to 133.5° C. Analysis of the acid showed: Calculated: C, 49.03, H, 5.62; found: C, 49.10, H, 5.66.

EXAMPLE XI

5-benzyl-5-(2'-nitro-n-butyl)-barbituric acid

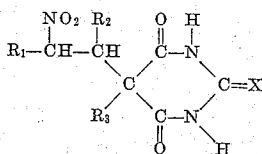
A solution was prepared containing 104 cc. of 91% ethyl alcohol, 5.0 grams of benzyl chloride and 4.5 grams of potassium 5-(2'-nitro-n-butyl)-barbiturate. The solution was refluxed for 24 hours, cooled and filtered to remove potassium chloride. The filtrate was evaporated to dryness and the residue was recrystallized first from hot absolute alcohol, by addition of water and cooling, then from 95% alcohol to form white crystals which melted with decomposition at 225° to 227° C. The acid prepared showed upon analysis: Calculated: C, 56.38, H, 5.36; found: C, 56.42, H, 5.41.

It will be apparent from the foregoing examples that a new series of compounds has been prepared which are particularly useful as intermediates in the preparation of certain pharmaceuticals related to barbituric acid and its analogues. Broadly speaking, the invention contemplates compounds and processes wherein the barbituric acid type ring nucleus is substituted in the 5 position by a β -nitroalkyl group. In its broadest aspects the invention contemplates not only the derivatives of barbituric acid, but also the derivatives of 2-thiobarbituric acid, malonylguanidine, their respective salts and other derivatives. For example, the N-alkyl derivatives of compounds of this type are contemplated within the spirit and scope of this invention and may be prepared by reacting a nitroolefin with the N-alkyl derivative salts in the manner indicated in the foregoing.

While several particular embodiments of this invention are shown above, it will be understood, of course, that the invention is not to be limited thereto, since many modifications may be made, and it is contemplated, therefore, by the appended claims, to cover any such modifications as fall within the true spirit and scope of this invention.

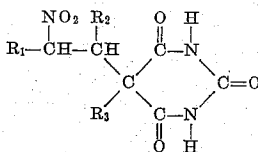
What is claimed is:

1. A compound selected from the class consisting of acids having the formula:



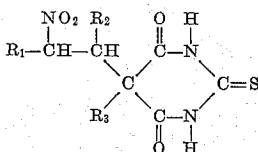
wherein R₁ is selected from the group consisting of hydrogen and alkyl, wherein R₂ is selected from the group consisting of hydrogen, alkyl and aryl, wherein R₃ is selected from the group consisting of hydrogen, alkyl and aralkyl; and wherein X is selected from the group consisting of oxygen and sulfur; and the salts of said acids.

2. A barbituric acid derivative selected from the class consisting of compounds having the formula:



wherein R₁ is selected from the group consisting of hydrogen and alkyl, wherein R₂ is selected from the group consisting of hydrogen, alkyl and aryl and wherein R₃ is selected from the group consisting of hydrogen, alkyl, and aralkyl; and the salts of said compounds.

3. A 2-thiobarbituric acid derivative selected from the class consisting of compounds having the formula:



wherein R₁ is selected from the group consisting of hydrogen and alkyl, wherein R₂ is selected from the group consisting of hydrogen, alkyl and aryl and wherein R₃ is selected from the group consisting of hydrogen, alkyl, and aralkyl; and the salts of said compounds.

4. A compound selected from the group consisting of the 5-(2'-nitroalkyl) barbituric acids and their salts.

5. A compound selected from the group consisting of the 5-(2'-nitroalkyl) 2-thiobarbituric acids and their salts.

6. 5-Benzyl - 5 - (2'-nitro-n-butyl) - barbituric acid.

7. 5-Methyl - 5 - (2'-nitro-n-butyl) - 2-thiobarbituric acid.

8. 5-Ethyl-5-(2'-nitro - n - butyl) - barbituric acid.

9. A process of preparing a compound having a barbituric acid type ring nucleus substituted in the 5 position with a β-nitroalkyl group which comprises reacting a nitroolefin in which the nitro group is attached to one of the doubly bound carbon atoms with a salt of a compound

selected from the group consisting of barbituric acid and 2-thiobarbituric acid to produce the said compound having a barbituric acid ring type nucleus substituted in the five-position with a β-nitroalkyl group.

10. A process of preparing a 5-(2'-nitroalkyl) barbituric acid derivative which comprises reacting a nitroolefin in which the nitro group is attached to one of the doubly bound carbon atoms with a salt of barbituric acid to produce a 5-(2'-nitroalkyl) barbituric acid derivative.

11. The process recited in claim 10 wherein said salt is a quaternary ammonium salt of barbituric acid.

12. The process recited in claim 10 wherein said salt is a benzyltrimethylammonium salt of barbituric acid.

13. The process recited in claim 10 wherein said salt is an alkali metal salt.

14. The process recited in claim 10 wherein said salt is a potassium salt.

15. A process of preparing a 5-(2'-nitroalkyl) - 2-thiobarbituric acid derivative which comprises reacting a nitroolefin in which the nitro group is attached to one of the doubly bound carbon atoms with a salt of 2-thiobarbituric acid to produce a 5-(2'-nitroalkyl) - 2-thiobarbituric acid derivative.

16. The process recited in claim 15 wherein said salt is a quaternary ammonium salt of barbituric acid.

17. The process recited in claim 15 wherein said salt is a benzyltrimethylammonium salt of barbituric acid.

18. The process recited in claim 15 wherein said salt is an alkali metal salt.

19. The process recited in claim 15 wherein said salt is a potassium salt.

20. A process for the preparation of a 5-(2'-nitroalkyl) - 5-alkyl derivative of a compound selected from the group consisting of barbituric acid and 2-thiobarbituric acid which comprises reacting a nitroolefin in which the nitro group is attached to one of the doubly bound carbon atoms with a quaternary ammonium salt of a 5-alkyl derivative of said compound to produce a 5-(2'-nitroalkyl) - 5-alkyl derivative of a compound selected from the group consisting of barbituric acid and 2-thiobarbituric acid.

21. The process recited in claim 20 wherein said salt is a benzyltrimethylammonium salt of said derivative.

22. A process of alkylating in the 5 position a compound selected from the group consisting of the salts of 5-(2'-nitroalkyl) - barbituric acid and of 5-(2'-nitroalkyl) - 2-thiobarbituric acid which comprises reacting said compound with an alkyl halide.

23. The process recited in claim 22 wherein said halide is selected from the group consisting of chloride, bromide and iodide.

24. A compound selected from the group consisting of 5-(2'-nitroalkyl) - 5-alkyl barbituric acids.

25. A compound selected from the group consisting of 5-(2'-nitroalkyl) - 5-alkyl thiobarbituric acids.

26. A compound selected from the group consisting of 5-(2'-nitroalkyl) - 5-aralkyl barbituric acids.

27. A compound selected from the group consisting of 5-(2'-nitroalkyl) - 5-aralkyl thiobarbituric acids.

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No references cited.

1. The first part of the document discusses the importance of maintaining accurate records of all transactions and activities. It emphasizes that proper record-keeping is essential for transparency and accountability, particularly in financial matters. The text suggests that organizations should implement robust systems to track every detail, from small expenses to major investments.

2. The second section focuses on the role of leadership in fostering a culture of integrity and ethical behavior. It argues that leaders must set a clear example and communicate the organization's values consistently. By doing so, they can ensure that all employees understand the expectations and are motivated to act accordingly. This section also touches upon the importance of regular communication and feedback loops between management and staff.

3. The third part of the document addresses the challenges of managing a large and diverse workforce. It highlights the need for effective communication and collaboration across different departments and regions. The text suggests that organizations should invest in training and development programs to enhance the skills and knowledge of their employees. Additionally, it stresses the importance of creating a supportive and inclusive work environment where everyone feels valued and empowered to contribute.

4. The fourth section discusses the importance of financial management and budgeting. It notes that organizations must carefully monitor their finances to ensure they are operating within their means and achieving their financial goals. The text suggests that organizations should conduct regular financial reviews and adjust their budgets as needed. It also emphasizes the importance of maintaining accurate financial records and reporting to stakeholders.

5. The fifth part of the document focuses on the importance of innovation and continuous improvement. It argues that organizations must constantly seek new ways to improve their products, services, and processes. This involves encouraging creativity and experimentation among employees and investing in research and development. The text suggests that organizations should establish a culture of innovation where failure is seen as a learning opportunity rather than a setback.

6. The sixth section discusses the importance of risk management and compliance. It notes that organizations must identify and mitigate potential risks to their operations and reputation. This involves conducting regular risk assessments and implementing appropriate controls. The text also emphasizes the importance of staying up-to-date with relevant laws and regulations to ensure full compliance. Organizations should also consider the impact of their actions on the environment and society, and strive to minimize any negative effects.

7. The seventh part of the document focuses on the importance of customer satisfaction and loyalty. It argues that organizations must understand their customers' needs and preferences and strive to exceed their expectations. This involves providing excellent customer service and offering high-quality products and services. The text suggests that organizations should implement feedback mechanisms to gather customer input and use it to improve their offerings. It also emphasizes the importance of building strong relationships with customers and fostering a sense of loyalty.

8. The eighth section discusses the importance of sustainability and social responsibility. It notes that organizations have a responsibility to contribute positively to society and the environment. This involves adopting sustainable practices, such as reducing waste and energy consumption, and supporting social causes. The text suggests that organizations should report on their sustainability efforts and engage with stakeholders to discuss their impact. It also emphasizes the importance of being transparent about the organization's activities and the challenges it faces.

9. The ninth part of the document focuses on the importance of talent management and succession planning. It argues that organizations must attract, develop, and retain top talent to ensure their long-term success. This involves creating a clear career path for employees and providing opportunities for growth and advancement. The text suggests that organizations should implement a structured process for identifying and developing potential successors for key positions. It also emphasizes the importance of maintaining a diverse and inclusive workforce.

10. The final section of the document discusses the importance of strategic planning and execution. It notes that organizations must have a clear vision and strategy for the future and work effectively to achieve their goals. This involves setting clear objectives and priorities, allocating resources accordingly, and monitoring progress regularly. The text suggests that organizations should involve all levels of the organization in the planning process to ensure buy-in and commitment. It also emphasizes the importance of being flexible and adaptable in the face of changing circumstances.

Certificate of Correction

Patent No. 2,527,293

October 24, 1950

CARL T. BAHNER

It is hereby certified that error appears in the printed specification of the above numbered patent requiring correction as follows:

Column 1, line 9, for "soporifices" read *soporifics*; column 5, line 30, for "fitering" read *filtering*; column 6, line 60, for "nitrol" read *nitro*;

and that the said Letters Patent should be read as corrected above, so that the same may conform to the record of the case in the Patent Office.

Signed and sealed this 2nd day of January, A. D. 1951.

[SEAL]

THOMAS F. MURPHY,
Assistant Commissioner of Patents.