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PREPARATION OF THIOLESTERS FROM ALIPHATIC ACID ANHYDRIDES AND AROMATIC THIOLS

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ABSTRACT OF THE DISCLOSURE

A process for the preparation of a thiolester by reacting an aliphatic acid anhydride with an aromatic thiol in the presence of a catalytic amount of a tertiary amine.

This invention relates to an improved process for the preparation of thiolesters. More particularly it relates to a process wherein saturated aliphatic acid anhydrides are reacted with aromatic thiols in the presence of relatively small amounts of certain bases to form thiolesters.

It is known to produce thiolesters by reacting thiols with acid anhydrides; however, these known processes use at least an equimolar amount of a base, such as pyridine, triethylamine and the like; and, in some of these heretofore known processes, an excess of the equimolar amount of base is specified. The consumption of relatively large amounts of base results in relatively high production cost which is a major disadvantage of the known processes.

It is believed, therefore, that a process for the production of thiolesters from aromatic thiols and aliphatic anhydrides, which process uses only a catalytic amount of base and which process gives high yields, is a significant advance in the art.

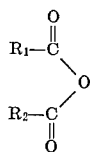
It is an object of this invention to provide an improved process for the production of aromatic thiolesters.

It is a further object of this invention to provide a high yield process for the production of aromatic thiolesters wherein said thiolesters are produced by an essentially direct reaction of an aromatic thiol with an anhydride.

Other objects, advantages, and features of this invention will become readily apparent to those skilled in the art from the detailed description which follows.

It has been discovered that aromatic thiols will react with aliphatic acid anhydrides to form aromatic thiolesters in the presence of only a catalytic amount of certain bases. The high yields obtained with the process of this invention, which uses only a catalytic amount of certain bases, are completely unexpected in view of the heretofore known processes which specify the need for at least an equimolar amount of base. The process of this invention is also unobvious because at least an equimolar amount of base is required to achieve esterification when aliphatic thiols and aliphatic acid anhydrides are used.

The saturated aliphatic anhydrides which are useful in the practice of this invention are those of the formula:



wherein R_1 and R_2 are each alkyl containing from 1 to 12 carbon atoms.

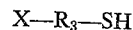
When the unsymmetrical anhydrides, that is, those anhydrides wherein R_1 and R_2 are different alkyls, are used, mixtures of the corresponding thiolesters are produced. Similarly, when a mixture of aliphatic anhydrides

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is used, a mixture of thiolesters is also produced. The mixtures of thiolesters thus produced require subsequent separation to obtain relatively pure individual products. Since any thiolester which is produced from either an unsymmetrical anhydride or a mixture of anhydrides can also be produced from the suitable symmetrical anhydride, it is preferred to use symmetrical acid anhydrides, that is, those anhydrides wherein R_1 and R_2 are the same alkyl.

Compounds illustrative of said useful symmetrical aliphatic acid anhydrides include ethanoic acid anhydride, propanoic acid anhydride, butanoic acid anhydride, pentanoic acid anhydride, hexanoic acid anhydride, heptanoic acid anhydride, octanoic acid anhydride, decanoic acid anhydride, dodecanoic acid anhydride and the anhydrides of the corresponding isomeric acids.

The aromatic thiols or mercaptans which are useful in the practice of this invention can be represented by the formula:



wherein R_3 is a member selected from the group consisting of phenylene and lower alkylated phenylene, and X is a member selected from the group consisting of hydrogen, chlorine, bromine, nitro, acetamido and lower alkoxy. It is to be noted that, as used herein, "lower alkylated phenylene" and "lower alkoxy" mean that the alkyl portion of the radical is a "lower alkyl" group, that is, an alkyl group containing from 1 to 4 carbon atoms.

Compounds which are illustrative of said useful thiols include mercaptobenzene, 2-chloro-mercaptobenzene, 3-chloro-mercaptobenzene, 4-chloro-mercaptobenzene, 2-nitro-mercaptobenzene, 4-nitro-mercaptobenzene, 4-methoxy-mercaptobenzene, 3-ethoxy-mercaptobenzene, 4-propoxy-mercaptobenzene, 4-acetamido-3-mercaptotoluene, 3-mercaptotoluene, 4-mercaptotoluene, 3-chloro-4-mercaptotoluene, 3-nitro-4-mercaptotoluene, 3-ethoxy-4-mercaptotoluene, 1-n-butyl-3-chloro-4-mercaptobenzene, 3-bromo-4-mercaptocumene and 3-nitro-4-n-propyl-mercaptobenzene.

Although the molar ratio of aromatic thiol to aliphatic acid anhydride can be varied throughout a relatively wide range, such as from about 1:1000 to about 1000:1, and still produce at least some of the aromatic thiolester, it is preferred for economy and optimum yield to approximate molar equivalents of reactants; that is, one mole of aromatic thiol per mole of aliphatic acid anhydride.

Generally, the acid anhydrides are liquids within the temperature range employed in the practice of this invention and will dissolve the aromatic thiols, thus eliminating the need for an extrinsic solvent. Although temperature is not critical, for ease of operation and for optimum yields, it is preferred to operate within the temperature range of from about 10° C. above the freezing point to about 5° C. below the boiling point of the solution of the thiol in the anhydride. Since, in most cases, a temperature range of from about 20° C. to about 80° C. can be used, this relatively moderate range is especially preferred.

In general, those bases which (a) are soluble in the solution of thiol in the anhydride, (b) do not react with either the anhydride, thiol or thiolester and (c) have sufficient basic properties to "catalyze" the reaction can be used in the practice of this invention. The compounds which have been found to have the foregoing suitable properties are those selected from the group consisting of pyridine, lower alkylated pyridine and tertiary amines of the formula



wherein R , R' and R'' are each lower alkyl.

Compounds illustrative of said useful bases include triethylamine, tripropylamine, tributylamine, ethylisopropylmethylamine, dimethylethylamine, di-isobutylmethyl-

aromatic thiolesters are prepared from aromatic thiols and aliphatic acid anhydrides. Selected examples of such preparations are given in the following table.

Ex.	Thiol	Acid Anhydride	Tertiary Amine	Thiolester
3.....	4-nitro-mercaptobenzene.....	Dodecanoic acid anhydride.....	Pyridine.....	4-nitrophenyl thioldodecanoate.
4.....	3-chloro-4-mercaptotoluene.....	Butanoic acid anhydride.....	do.....	2-chloro-p-tolyl thiolbutanoate.
5.....	1-bromo-4-mercaptobenzene.....	Propanoic acid anhydride.....	Triethylamine.....	4-bromophenyl thiolpropionate.
6.....	4-acetamido-3-mercaptotoluene.....	Ethanoic acid anhydride.....	Tributylamine.....	2-acetamido-m-tolyl thiolacetate.
7.....	4-methoxy-mercaptobenzene.....	Heptanoic acid anhydride.....	Dimethylethylamine.....	4-methoxyphenyl thiolheptanoate.
8.....	3-chloro-mercaptobenzene.....	Butanoic acid anhydride.....	Tripropylamine.....	3-chlorophenyl thiolbutanoate.
9.....	4-dimethylamino mercaptobenzene.....	Decanoic acid anhydride.....	2-methylpyridine.....	4-dimethylaminophenyl thioldodecanoate.
10.....	3-ethoxy-4-mercaptotoluene.....	Octanoic acid anhydride.....	Di-isobutylmethylamine.....	2-ethoxy-p-tolyl thioloctanoate.
11.....	3-chloro-4-isopropyl-mercaptobenzene.....	Propanoic acid anhydride.....	Tributylamine.....	3-chloro-4-isopropylphenyl thiolpropionate.
12.....	2-chloro-mercaptobenzene.....	Hexanoic acid anhydride.....	Triethylamine.....	2-chlorophenyl thiolhexanoate.
13.....	4-mercaptotoluene.....	Pentanoic acid anhydride.....	Ethylisobutylmethylamine.....	p-Tolyl thiolpentanoate.
14.....	4-n-butyl-mercaptobenzene.....	Ethanoic acid anhydride.....	Triethylamine.....	4-n-butylphenyl thiolacetate.
5.....	3-ethoxy mercaptobenzene.....	Butanoic acid anhydride.....	do.....	3-ethoxyphenyl thiolbutanoate.

amine, pyridine, 2-methylpyridine, 3-methylpyridine, 2-propylpyridine, 2,4-dimethylpyridine, 2-ethylpyridine, 4-isopropylpyridine, 2,4,6-trimethylpyridine.

The reaction of this invention can be conducted using amounts of base as low as about 0.01% based upon the weight of the thiol. In most instances, however, it is preferred to use between about 0.1% and about 3% of said base based upon the weight of the thiol to insure efficient reactions. It is completely unexpected that such a significant reduction in the amount of base can be made in view of the prior art which teaches that at least equimolar quantities of bases must be used. When compared with prior processes, a vast reduction in the amount of base is achieved resulting in a major improvement in the process. Larger amounts of bases can be employed but are not preferred since the excess usage serves no purpose except to needlessly increase the cost of the process.

The following examples further illustrate the invention. All parts, percentages and proportions are by weight unless otherwise indicated.

EXAMPLE 1

4-chlorophenyl thiolacetate

About 1,440 parts of 1-chloro-4-mercaptobenzene are charged into a conventional reaction vessel equipped with an agitator. While agitating, about 1,020 parts of ethanoic acid anhydride are dissolved in the 1-chloro-4-mercaptobenzene. After about 10 parts of triethylamine are added, an exothermic reaction occurs. Fractional distillation of the crude product, after the reaction is completed, yields about 1,690 parts of a product having a boiling point of 142° C. at 15 mm. Hg and a melting point of 31-32° C. The infrared absorption spectrum has the expected carbonyl absorption band of 1680 to 1704 cm.⁻¹. The compound is identified as 4-chlorophenyl thiolacetate, and the yield, based upon the raw materials charged, is about 91%.

EXAMPLE 2

Phenyl thiolacetate

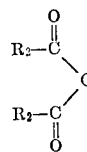
About 1,020 parts of ethanoic acid anhydride are charged into a conventional reaction vessel equipped with an agitator. While agitating, about 1,100 parts of mercaptobenzene are dissolved in the ethanoic acid anhydride. About 2 parts of triethylamine are added, and an exothermic reaction occurs with the temperature rising to about 75° C. After the temperature rise has ceased, the reaction product is distilled yielding about 1,370 parts of a product having a boiling point of 60° C. at 0.5 mm. Hg. The infrared absorption spectrum gives the expected carbonyl band of from about 1,684 to 1,704 cm.⁻¹. Analytical determination of elemental content indicates the formula of the product to be C₈H₈OS. The yield of phenyl thiolacetate is about 90% based upon the reactants charged.

Following the procedure of Examples 1 and 2, other

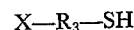
While the invention has been described herein with regard to specific embodiments, it is not so limited. It is to be understood that variations and modifications thereof may be made by those skilled in the art without departing from the spirit and scope of the invention.

What is claimed is:

1. In a process for the production of thiolesters wherein an aliphatic acid anhydride of the formula,



wherein R₁ and R₂ are each alkyl containing from 1 to 12 carbon atoms is reacted with an aromatic thiol of the formula,



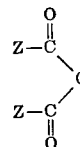
wherein R₃ is a member selected from the group consisting of phenylene and lower alkylated phenylene; and X is a member selected from the group consisting of hydrogen, chlorine, bromine, nitro, acetamido, and lower alkoxy, the improvement comprising reacting said aliphatic acid anhydride and said aromatic thiol in the presence of from about 0.01% to about 3.0% by weight, based upon said aromatic thiol, of a base selected from the group consisting of pyridine, lower alkylated pyridine and lower alkyl tertiary amines.

2. A process as defined in claim 1 wherein said base is present in amounts of from at least about 0.1% to about 3.0% by weight based upon said aromatic thiol.

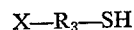
3. A process as defined in claim 1 wherein said base is triethylamine.

4. A process as defined in claim 1 wherein said base is pyridine.

5. In a process for the production of thiolesters wherein a symmetrical aliphatic acid anhydride of the formula,



wherein Z is alkyl containing from 1 to 12 carbon atoms is reacted with an aromatic thiol of the formula,



wherein R₃ is a member selected from the group consisting of phenylene and lower alkylated phenylene, and X is a member selected from the group consisting of hydrogen, chlorine, bromine, nitro, acetamido and lower alkoxy, the improvement comprising reacting said aliphatic acid anhydride and said aromatic thiol in the

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presence of from about 0.01% to about 3.0% by weight, based upon said aromatic thiol, of a base selected from the group consisting of pyridine, lower alkylated pyridine and lower alkyl tertiary amines.

6. A process as defined in claim 5 wherein said base is present in amounts of from about 0.1% to about 3.0% by weight based upon said aromatic thiol.

7. A process as defined in claim 6 wherein said base is triethylamine.

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8. A process as defined in claim 6 wherein said base is pyridine.

References Cited

Schleppnik et al., J. Org. Chem., vol. 29, pp. 1663, 1910-1915 (1964).

CHARLES B. PARKER, *Primary Examiner*.

D. R. PHILLIPS, *Assistant Examiner*.