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ESTERS OF POLYHYDROXY-BENZOIC ACIDS
AND METHOD FOR THEIR PREPARATION

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This application is made under the act of March 3, 1883, as amended by the act of April 30, 1928, and the invention herein described, if patented, may be manufactured and used by or for the Government of the United States of America for governmental purposes without the payment to us of any royalty thereon.

This invention relates to esters of polyhydroxybenzoic acids and more particularly to the esters of these acids with aliphatic alcohols containing more than six carbon atoms per molecule and their preparation.

Esters of gallic acids with lower fatty alcohols can be obtained by direct esterification, frequently on heating the reactants in the presence of suitable esterification catalysts. When this procedure is followed in an attempt to esterify gallic acid with higher fatty alcohols containing more than six carbon atoms per molecule, the esterification either does not take place, or the corresponding esters are formed in such small amount that it is not feasible to isolate them from the reaction products. Similar results are obtained on heating the reactants with inert non-polar solvents such as benzene, toluene, cumene, or other non-polar organic solvents commonly utilized as entraining agents in esterification processes to facilitate removal of water from the reaction mixture.

Morris and Riemenschneider have disclosed in their application for Patent Serial No. 678,188, filed June 21, 1946, that alkyl esters of gallic acid and of some other polyhydroxybenzoic acids can be prepared by esterification of the corresponding benzyloxy-derivatives of benzoic acid and subsequent debenzoylation of the resulting ester by catalytic hydrogenation. Our method, however, is also applicable to the production of polyhydroxybenzoic acid esters of olefinic alcohols, since it obviates the hydrogenation step, which causes addition of hydrogen to the double bond of the alcohol radical and thus converts it to the corresponding alkyl group.

An object of this invention is the production of polyhydroxybenzoic acid esters of higher aliphatic alcohols by methods that are simpler and more economical than those used heretofore. A further object is the provision of a method for producing polyhydroxybenzoic acid esters of aliphatic alcohols containing more than six carbon atoms per molecule, by direct esterification. Another object is to provide new compositions of matter which are polyhydroxybenzoic acid esters of alcohols containing more than six carbons per molecule, in particular, unsaturated al-

cohols. Other objects and advantages of the invention will appear hereinafter.

We have found that esters of polyhydroxybenzoic acids with aliphatic alcohols containing more than six carbon atoms per molecule are formed by direct esterification in the presence of a polar organic solvent. In accordance with the method of our invention the polyhydroxybenzoic acid is heated with the aliphatic alcohol in the presence of a polar organic solvent, and preferably in the presence of an esterification catalyst, at a temperature and for the length of time sufficient to cause formation of the ester.

The method of this invention is applicable to polyhydroxybenzoic acids containing hydroxyl groups in para and/or meta positions to the carboxyl group, such as gallic acid, protocatechuic acid, and alpha-resorcylic acid. Aliphatic alcohols suitable for effecting esterification of these acids include saturated and unsaturated alcohols containing more than six carbon atoms per molecule, for instance n-octyl alcohol, lauryl alcohol, myristyl alcohol, cetyl alcohol, stearyl alcohol, and oleyl alcohol. Suitable polar organic solvents are polar organic solvents which under the conditions of the process are chemically inert toward the reactants and reaction products. Such polar solvents include for example, nitrobenzene, ortho-dichlorobenzene, anisole and phenetole, which can be used singly or in combination. Addition of esterification catalysts, such as sulfuric acid, toluene sulfonic acid, naphthalene sulfonic acid, or nitrobenzene sulfonic acid and similar acidic substances increases the reaction rate of the esterification process.

The expression "polar solvents" is employed here in its widely accepted sense. The following publications indicate the meaning of the term, being the widely accepted manner of defining such solvents:

"Liquids, for the sake of convenience are generally divided into two classes, polar and non-polar The dielectric constant of a compound is one of the best measures of polarity." Lewis, Squires and Broughton, "Industrial Chemistry of Colloidal and Amorphous Materials," 1942, page 15.

"Many organic solvents . . . exhibit this [electrical] conductivity. These substances are chemically active and are referred to as 'polar solvents' Solvents like alcohols and ketones, . . . have high dielectric constants and this is evidence of strong polarity. Those of low dielectric constants, like the aliphatic and aromatic hydrocarbons, are classified as non-

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polar solvents." Mellan, "Industrial Solvents," 1939, page 9.

The dielectric constants of the solvents mentioned in the application and of some common inert, non-polar solvents, boiling within the range claimed are listed in the following table:

	Dielectric Constant ac- cording to Mellan	Dielectric Constant ac- cording to International Critical Tables
Nitrobenzene.....	36.10	35.7
o-Dichlorobenzene.....	9.82	7.5
Phenetole.....	4.47	4.56
Anisole.....	4.30	4.35
Benzene.....	2.23	2.23
Cumene.....		2.40
Toluene.....	2.38	2.39
p-Cymene.....	2.249	
Tetrahydronaphthalene.....	2.66	
Decahydronaphthalene.....	2.11	
o-Xylene.....	2.567	2.58
m-Xylene.....	2.40	2.37
p-Xylene.....	2.269	2.26
Methylcyclohexane.....	2.071	
n-Octane.....	1.962	1.95
n-Nonane.....	1.972	1.97
n-Decane.....	1.956	1.95

Since esterification proceeds more rapidly at higher temperature and is facilitated by removal of water from the reaction mixture it is usually advantageous to utilize polar solvents boiling above 100° C. and to conduct the reaction under reflux with concurrent separation of water. Since the reaction temperature must not, however, be sufficiently high to cause any appreciable decomposition of the polyhydroxy-benzoic acid, the operator should determine the optimum upper limit in each case. Thus for example, esterification of gallic acid in the presence of nitrobenzene is best effected by conducting the reaction under reflux and using a mixture of nitrobenzene with a lower boiling polar solvent thereby maintaining the reaction mixture at a temperature below the decomposition temperature of gallic acid. The ratio of reactants to solvent may be varied within wide limits. We have found, however, that when the polar solvent consists of a mixture of nitrobenzene with another polar organic solvent the highest yields of esters may be obtained if the amounts of polyhydroxy-benzoic acid and nitrobenzene present in the reaction mixture approximate the molar ratio of 1 to 1.

The esters of polyhydroxy-benzoic acids with aliphatic alcohols containing more than six carbon atoms are useful as antioxidants and rancidity inhibitors for fatty and oily materials and as intermediates in production of synthetic chemicals.

As illustrative embodiments of a manner in which our invention may be carried out in practice the following examples are given.

Example I

Lauryl gallate.—9.4 grams of gallic acid (anhydrous), 9.3 grams of lauryl alcohol and 0.3 gram p-toluene sulfonic acid were weighed into a flask connected to a reflux condenser fitted with a water separating device. 150 cc. of o-dichlorobenzene was added and the mixture refluxed for approximately 30 hours. The water is thus distilled off, the o-dichlorobenzene being returned by the refluxing to the flask. The temperature of the contents of the flask is thus regulated by the boiling off of the o-dichlorobenzene, employed in excess.

The contents of the flask were cooled to room

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temperature, washed with water to remove the catalyst and unreacted gallic acid, and the solvent evaporated under reduced pressure. Recrystallization of the distillation residue from benzene-petroleum ether gave 8.8 grams (52 percent of theory) of dodecyl gallate melting at 96°–97° C.

Example II

Cetyl gallate.—5.64 grams of gallic acid, 7.27 grams of cetyl alcohol, 0.5 gram of beta-naphthalene sulfonic acid and 100 cc. of nitrobenzene were refluxed as described in Example I. Since discoloration of the mixture gave reason to believe that some decomposition of gallic acid was taking place, 50 cc. of o-dichlorobenzene was added at the end of the first half hour and refluxing was continued for an additional 17½ hours.

Three grams (24 percent of theory) of hexadecyl gallate melting at 96°–98° C. was recovered from the reaction mixture by the procedure described in Example I. On further recrystallization from benzene-petroleum ether, this product yielded 2.6 grams of ester having a melting point of 98°–99° C.

A somewhat lower yield of hexadecyl gallate was obtained on heating a mixture of 5.64 grams gallic acid, 7.27 grams cetyl alcohol, 0.5 gram beta-naphthalene sulfonic acid and 100 cc. nitrobenzene at 170° C. for 24 hours, and treating the resulting reaction mixture as described in Example I. The temperature was kept constant by maintaining a pressure somewhat below atmospheric.

Example III

Oleyl gallate.—4.71 grams of gallic acid, 8.93 grams of oleyl alcohol, 0.5 gram of p-toluene sulfonic acid and 150 cc. of o-dichlorobenzene were refluxed for 29½ hours during which time an additional 0.4 gram of p-toluene sulfonic acid was added by increments.

The mixture was allowed to cool to room temperature and filtered. 2.36 grams of unreacted gallic acid was thus recovered. The filtrate was then washed three times with equal volumes of hot water. The o-dichlorobenzene was removed by distillation under vacuum and the residue taken up in a mixture of benzene and petroleum ether from which the ester was allowed to crystallize. Approximately 1 gram of crystalline octadecenyl gallate melting at 83°–85° C. was obtained which after crystallization gave a crystalline material, M. P. 85.5°–86.5° C. Similar results were obtained when a mixture of 145 cc. o-dichlorobenzene and 5 cc. of nitrobenzene was used as the solvent mixture.

Example IV

Octyl gallate.—3.4 grams of gallic acid, 5.4 grams of 1-octanol and 0.2 gram of naphthalene beta-sulfonic acid were refluxed for 14 hours in a mixture of 40 cc. anisole and 2.1 cc. nitrobenzene. After steam distillation of the reaction mixture the residual ester was extracted with 100 cc. of benzene and crystallized to yield 2.2 grams (39 percent) of octyl gallate melting at 94.8°–95.3° C.

Example V

Lauryl gallate.—A mixture of 3.6 grams of gallic acid, 8 grams n-dodecyl alcohol, 0.2 gram naphthalene beta-sulfonic acid, 45 cc. anisole and 2.2 cc. nitrobenzene was refluxed for 15 hours. The ester was recovered as described in Example

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IV and recrystallized from benzene-petroleum ether mixture: 5.5 grams (77 percent) of dodecyl gallate, M. P. 96.5°–97.0° C. was obtained. An additional 4 grams of crude ester (M. P. 85°) crystallized from the mother liquor.

Example VI

Lauryl gallate.—A mixture of 51 grams gallic acid, 112 grams lauryl alcohol, 2.5 grams naphthalene beta-sulfonic acid, 535 cc. anisole and 31 cc. nitrobenzene was refluxed for 20 hours. 67.8 grams (66.8 percent) of dodecyl gallate, M. P. 96°–97° C. was recovered by the procedure given in Example V.

Example VII

Myristyl gallate.—A mixture of 3 grams gallic acid, 7.5 grams myristyl alcohol, 0.2 gram naphthalene-beta-sulfonic acid, 40 cc. phenetole and 2.2 cc. nitrobenzene was refluxed for 9 hours. The ester recovered as in Example IV was recrystallized from benzene-petroleum ether yielding 2.6 grams (41 percent) of tetradecyl gallate, M. P. 98.3° C.

Example VIII

Cetyl gallate.—A mixture of 3.4 grams gallic acid, 9.6 grams cetyl alcohol, 0.2 gram naphthalene-beta-sulfonic acid, 40 cc. anisole and 2.1 cc. nitrobenzene was refluxed for 15 hours. The ester recovered as in Example IV was recrystallized to yield 2.1 grams (27 percent) of hexadecyl gallate, M. P. 93°–94° C.

Example IX

Octadecyl gallate was prepared by reacting 3.4 grams of gallic acid with 11.4 grams of 1-octadecanol according to the procedure described in Example VIII. The yield was 7.2 grams (86 percent) of crude octadecyl gallate, M. P. 91°–93° C. A purified ester melting at 101.5°–103.5° C. was obtained by recrystallization.

Example X

Lauryl protocatechuate.—A mixture of 0.9 gram protocatechuic acid, 2.6 grams lauryl alcohol, 0.05 gram naphthalene-beta-sulfonic acid, 20 cc. anisole and 0.7 gram nitrobenzene was refluxed for 7 hours. Dodecyl-3, 4-dihydroxybenzoate, M. P. 102.7°–103.6° C. was recovered from the reaction mixture by a procedure analogous to those described in the foregoing examples. The yield was 0.9 gram (47 percent of the calculated).

Example XI

Lauryl alpha-resorcylate, M. P. 86°–89° C. was obtained by reacting 3,5-dihydroxybenzoic acid with lauryl alcohol, according to the procedure described in Example X.

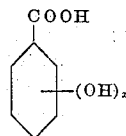
Example XII

A mixture consisting of 3.4 grams gallic acid, 5.5 grams lauryl alcohol, 0.2 gram naphthalene-beta-sulfonic acid and 40 cc. of phenetole was refluxed for 10 hours. Lauryl gallate was isolated from the reaction mixture by a procedure similar to those described in the foregoing examples.

The above examples are not to be construed as limiting the scope of the invention. Our processes include application of the above procedures to other olefinic alcohols, such as 3-hexen-1-ol, 4-hexen-1-ol, and to higher molecular weight olefinic alcohols, such as elaidyl alcohol.

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Having thus described our invention, we claim:
1. A process of producing an ester of a polyhydroxybenzoic acid of the general formula:



in which x is an integer from 2 to 3 and in which the positions ortho to the carboxyl group are free of substituents; comprising heating said acid with an alcohol of the formula $R-CH_2OH$, in which R is a radical taken from the group consisting of olefine and saturated alkyl radicals having more than five carbon atoms, said heating being in the presence of an acid esterification catalyst and under reflux and return of solvent with concurrent separation of water, the solvent being a polar organic solvent medium which under the conditions of the process is chemically inert toward the reactants and the reaction products and which boils above 100° C. and not higher than the boiling point of nitrobenzene, and below the decomposition temperature of the polyhydroxybenzoic acid, the solvent medium being a substituted hydrocarbon taken from the group consisting of nitrobenzene, ortho-dichlorobenzene, anisole, and phenetole.

2. The process described in claim 1 in which the solvent medium is a mixture of nitrobenzene and another solvent of said group, the nitrobenzene being present in the reaction in minor amount with respect to the said solvent, and recovering the ester of the acid and the alcohol.

3. The process defined in claim 1 in which the acid is gallic acid.

4. The process defined in claim 1 in which the acid is protocatechuic acid.

5. The process defined in claim 1 in which the acid is 3,5-dihydroxy benzoic acid.

6. The process defined in claim 1 in which the alcohol is a normal saturated aliphatic alcohol containing from 8 to 18 carbon atoms per molecule.

7. The process defined in claim 1 in which the alcohol is oleyl alcohol.

8. The process defined in claim 1 in which the alcohol is lauryl alcohol.

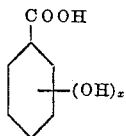
9. The process defined in claim 1 in which the alcohol is n-octadecyl alcohol.

10. The process of preparing oleyl gallate comprising heating to reflux oleyl alcohol with gallic acid in a medium of ortho-dichlorobenzene in the presence of minor amounts of nitrobenzene with respect to the weight of the gallic acid.

11. The process described in claim 10 in which the reaction is in the presence of p-toluene sulfonic acid.

12. A process comprising refluxing a mixture of protocatechuic acid, lauryl alcohol, anisole and nitrobenzene, and recovering lauryl protocatechuate from the reaction mixture, the anisole being in molar excess with respect to the protocatechuic acid, the nitrobenzene being in minor amount with respect to the anisole.

13. A process of producing an ester of a polyhydroxybenzoic acid of the formula:



in which x is an integer from 2 to 3 and in which the positions ortho to the carboxyl group are free of substituents; comprising heating said acid with an alcohol of the formula $R-CH_2OH$, in which R is a radical taken from the group consisting of olefine and saturated alkyl radicals having more than five carbon atoms, said heating being under reflux in a mixture of nitrobenzene and anisole.

14. The process described in claim 1 in which the solvent medium is a mixture of nitrobenzene and another solvent of said group having a boiling point below nitrobenzene, the molar ratio of polyhydroxybenzoic acid to nitrobenzene being about 1 to 1.

15. The process described in claim 1 in which the solvent medium is a mixture of nitrobenzene and another solvent of said group having a boiling point below nitrobenzene.

16. The process described in claim 1 in which the solvent is a mixture of nitrobenzene and anisole.

17. The process described in claim 1 in which the polyhydroxybenzoic acid is taken from the group consisting of gallic acid, protocathechuic acid, and 3,5-dihydroxy benzoic acid, the alcohol being taken from the group consisting of oleyl, lauryl, n-octyl, myristyl, cetyl, and stearyl.

18. The process of claim 1 in which the alcohol is monohydric.

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