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(54) Title: PROCESS FOR THE SYNTHESIS OF ETHERS OF AROMATIC ACIDS

(57) Abstract: Ethers of aromatic acids are produced from halogenated aromatic acids in a reaction mixture containing a copper (I) or copper (II) source and a diketone ligand that coordinates to copper.

TITLE

PROCESS FOR THE SYNTHESIS OF ETHERS OF AROMATIC ACIDS

This application claims the benefit of U.S. Provisional Application No. 60/876,570, filed 21 December 2006, which is incorporated in its entirety as a part hereof for all purposes.

Technical Field

This invention relates to the manufacture of ethers of hydroxy aromatic acids, which are valuable for a variety of purposes such as use as intermediates or as monomers to make polymers.

Background

Ethers of aromatic acids are useful as intermediates and additives in the manufacture of many valuable materials including pharmaceuticals and compounds active in crop protection, and are also useful as monomers in the production of high-performance rigid rod polymers, for example, linear rigid oligoanthranilamides for electronic applications [Wu *et al*, *Organic Letters* (2004), 6(2), 229-232] and polypyridobisimidazoles and the like [see *e.g.* Beers *et al*, *High-Performance Fibres* (2000), 93-155].

Existing processes to produce 2,5-dialkoxy- and 2,5-diarenoxyterephthalic acid involve stepwise alkylation of 2,5-dihydroxyterephthalic acid to form the corresponding 2,5-alkoxy- and 2,5-

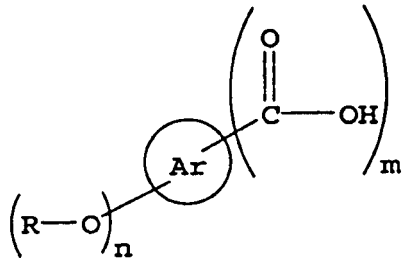
diarenoxyterephthalic esters followed by dealkylation of the ester to the acid. An n-hydroxy aromatic acid may be converted to an n-alkoxy aromatic acid by contacting the hydroxy aromatic acid under basic conditions with an n-alkyl sulfate. One suitable method of running such a conversion reaction is as described in Austrian Patent No. 265,244. Yields are moderate to low, productivity is low and a two-step process is necessary.

A need therefore remains for a process by which ethers of aromatic acids can be produced economically and with high yields and high productivity in small- and large-scale operation, and in batch and continuous operation.

Summary

The inventions disclosed herein include processes for the preparation of an ether of an aromatic acid, processes for the preparation of products into which such an ether can be converted, the use of such processes, and the products obtained and obtainable by such processes.

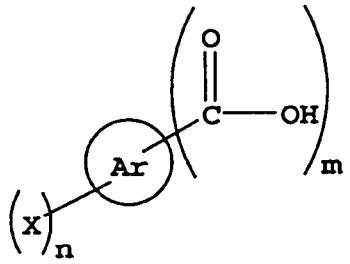
One embodiment of the processes hereof provides a process for preparing an ether of an aromatic acid, the ether being described by the structure of Formula I



I

wherein Ar is a C_6~C_{20} monocyclic or polycyclic aromatic nucleus, R is a univalent organic radical, n and m are each independently a nonzero value, and n+m is less than or equal to 8; comprising

(a) contacting a halogenated aromatic acid such as is described by the structure of Formula II



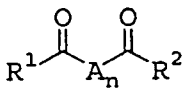
II

wherein each X is independently Cl, Br or I, and Ar, n and m are as set forth above, with

(i) a polar protic solvent, a polar aprotic solvent or an alcoholic solvent containing the alcoholate RO^-M^+ (wherein M is Na or K), wherein the polar protic solvent, polar aprotic solvent or alcoholic solvent is either ROH or is a solvent that is less acidic than ROH;

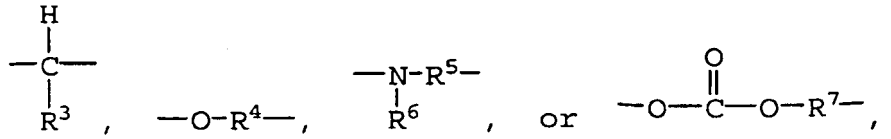
(ii) a copper (I) or copper (II) source; and

(iii) a diketone ligand that coordinates to copper, such as is described by the structure of Formula III



III

wherein A is



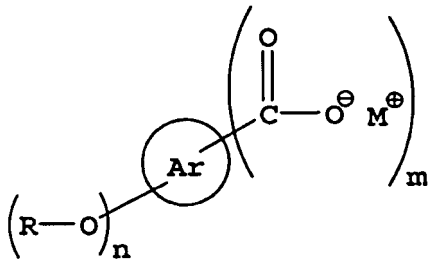
R^1 and R^2 are each independently selected from substituted and unsubstituted C_1-C_{16} n-alkyl, iso-alkyl and tertiary alkyl groups; and substituted and unsubstituted C_6 - C_{30} aryl and heteroaryl groups;

R^3 is selected from H; substituted and unsubstituted C_1-C_{16} n-alkyl, iso-alkyl and tertiary alkyl groups; substituted and unsubstituted C_6 - C_{30} aryl and heteroaryl groups; and a halogen;

R^4, R^5, R^6 and R^7 are each independently H or a substituted or unsubstituted C_1-C_{16} n-alkyl, iso-alkyl or tertiary alkyl group; and n = 0 or 1;

to form a reaction mixture;

(b) heating the reaction mixture to form the m-basic salt of the product of step (a), as described by the structure of Formula IV;



IV

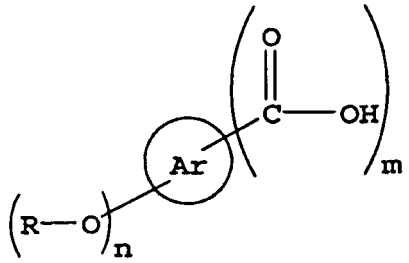
(c) optionally, separating the Formula IV m-basic salt from the reaction mixture in which it is formed; and

(d) contacting the Formula IV m-basic salt with acid to form therefrom an ether of an aromatic acid.

Another embodiment of this invention provides a process for preparing a compound, monomer, oligomer or polymer by preparing an ether of an aromatic acid that is described generally by the structure of Formula I, and then subjecting the ether so produced to a reaction (including a multi-step reaction) to prepare therefrom a compound, monomer, oligomer or polymer.

Detailed Description

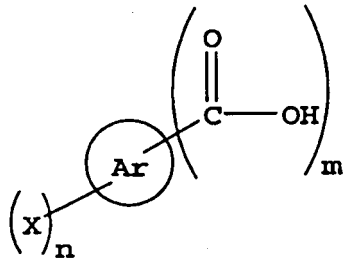
This invention provides a process having improved yield and productivity for preparing an ether of an aromatic acid, the ether being described by the structure of Formula I



I

wherein Ar is a C_6~C_{20} monocyclic or polycyclic aromatic nucleus, R is a univalent organic radical, n and m are each independently a nonzero value, and n+m is less than or equal to 8; comprising

One embodiment of the processes hereof proceeds by (a) contacting a halogenated aromatic acid such as is described by the structure of Formula II



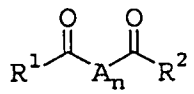
II

wherein each X is independently Cl, Br or I, and Ar, n and m are as set forth above, with

(i) a polar protic solvent, a polar aprotic solvent or an alcoholic solvent containing the alcoholate RO^-M^+ (wherein M is Na or K), wherein the polar protic solvent, polar aprotic solvent or alcoholic solvent is either ROH or is a solvent that is less acidic than ROH;

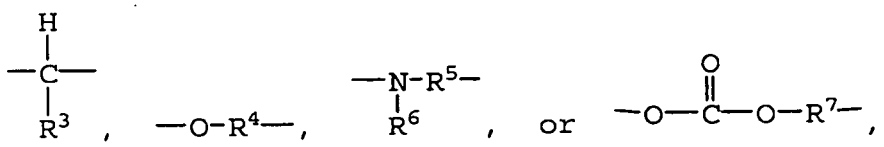
(ii) a copper (I) or copper (II) source; and

(iii) a diketone ligand that coordinates to copper, such as is described by the structure of Formula III



III

wherein A is



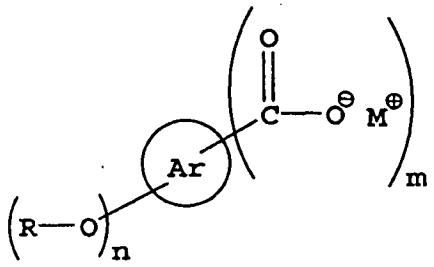
R^1 and R^2 are each independently selected from substituted and unsubstituted C_1-C_{16} n-alkyl, iso-alkyl and tertiary alkyl groups; and substituted and unsubstituted C_6 - C_{30} aryl and heteroaryl groups;

R^3 is selected from H; substituted and unsubstituted C_1-C_{16} n-alkyl, iso-alkyl and tertiary alkyl groups; substituted and unsubstituted C_6 - C_{30} aryl and heteroaryl groups; and a halogen;

R^4, R^5, R^6 and R^7 are each independently H or a substituted or unsubstituted C_1-C_{16} n-alkyl, iso-alkyl or tertiary alkyl group; and n = 0 or 1;

to form a reaction mixture;

(b) heating the reaction mixture to form the m-basic salt of the product of step (a), as described by the structure of Formula IV;



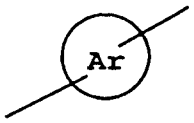
IV

(c) optionally, separating the Formula IV m-basic salt from the reaction mixture in which it is formed; and

(d) contacting the Formula IV m-basic salt with acid to form therefrom an ether of an aromatic acid.

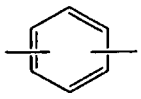
In Formulae I, II and IV, Ar is a C_6-C_{20} monocyclic or polycyclic aromatic nucleus; n and m are each independently a nonzero value and n+m is less than or equal to 8; R is a univalent organic radical; and in Formula II, each X is independently Cl, Br or I.

The radical denoted by

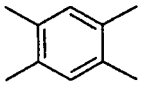


is an n+m valent C_6-C_{20} monocyclic or polycyclic aromatic nucleus formed by the removal of n+m hydrogens from different carbon atoms on the aromatic ring, or on the aromatic rings when the structure is polycyclic. The radical "Ar" may be substituted or unsubstituted; when unsubstituted, it contains only carbon and hydrogen.

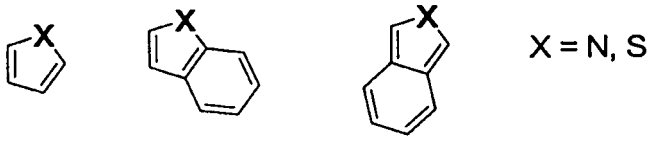
One example of a suitable Ar group is phenylene, as shown below, wherein n=m=1.

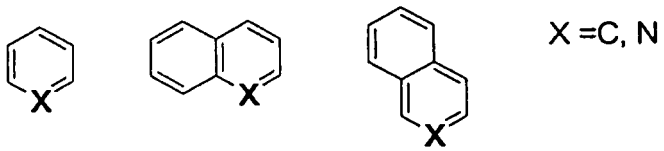


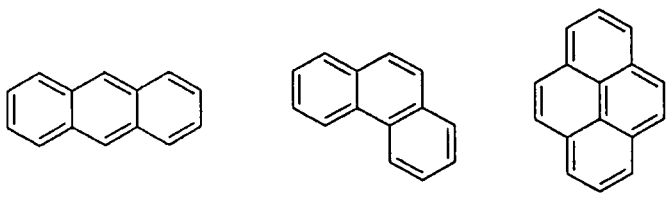
A preferred Ar group is shown below, wherein n=m=2.



The univalent radical R is a univalent organic radical. Preferably, R is a C_1~C_{12} alkyl group or an aryl group. More preferably, R is a C_1~C_4 alkyl group or phenyl. Examples of particularly suitable R groups include without limitation methyl, ethyl, i-propyl, i-butyl, and phenyl. Several other nonlimiting examples of R are shown below:



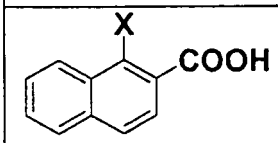
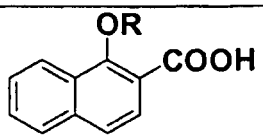
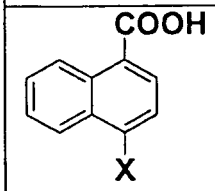
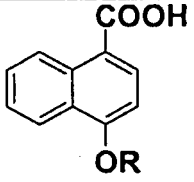
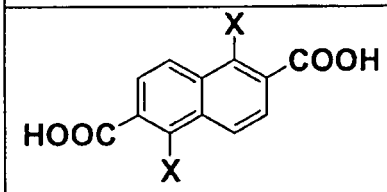
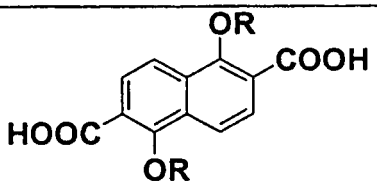
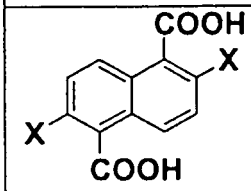
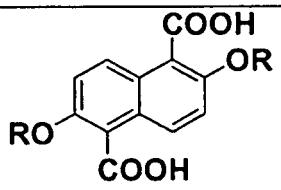
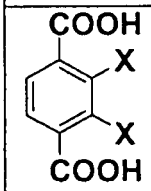
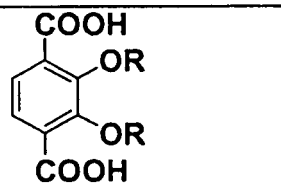
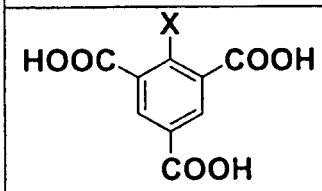
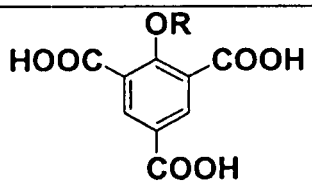
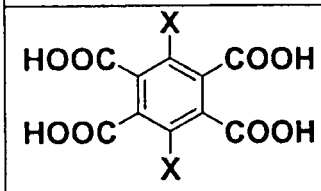
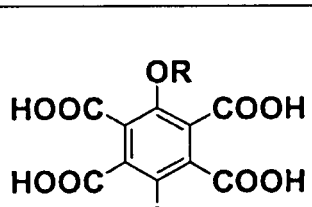
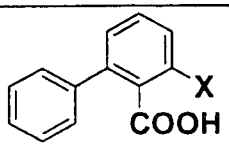
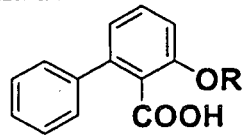


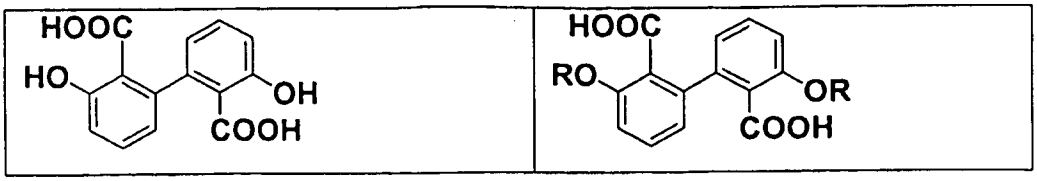


An "m-basic salt", as the term is used herein, is the salt formed from an acid that contains in each molecule m acid groups having a replaceable hydrogen atom.

Various halogenated aromatic acids, to be used as a starting material in the process of this invention, are commercially available. For example, 2-bromobenzoic acid is available from Aldrich Chemical Company (Milwaukee, Wisconsin). It can be synthesized, however, by oxidation of bromomethylbenzene as described in Sasson *et al*, *Journal of Organic Chemistry* (1986), 51(15), 2880-2883. Other halogenated aromatic acids that can be used include without limitation 2,5-dibromobenzoic acid, 2-bromo-5-nitrobenzoic acid, 2-bromo-5-methylbenzoic acid, 2-chlorobenzoic acid, 2,5-dichlorobenzoic acid, 2-chloro-3,5-dinitrobenzoic acid, 2-chloro-5-methylbenzoic acid, 2-bromo-5-methoxybenzoic acid, 5-bromo-2-chlorobenzoic acid, 2,3-dichlorobenzoic acid, 2-chloro-4-nitrobenzoic acid, 2,5-dichloroterephthalic acid, 2-chloro-5-nitrobenzoic acid, 2,5-dibromoterephthalic acid, and 2,5-dichloroterephthalic acid, all of which are commercially available. Preferably, the halogenated aromatic acid is 2,5-dibromoterephthalic acid or 2,5-dichloroterephthalic acid.

Other halogenated aromatic acids useful as a starting material in the process of this invention include those shown in the left column of the table below, wherein X = Cl, Br or I, and wherein the corresponding ether of an aromatic acid produced therefrom by the process of this invention is shown in the right column:

$(COOH)_m-Ar-(X)_n$ I	$(COOH)_m-Ar-(OR)_n$ II
	
	
	
	
	
	
	
	



In step (a), a halogenated aromatic acid is contacted with a polar protic or polar aprotic solvent or alcoholic solvent containing the alcoholate RO^-M^+, wherein R is as defined above and M is Na or K; a copper (I) or copper (II) source; and a diamine ligand that coordinates to copper.

The alcohol may be ROH, which is preferred, or it may be an alcohol that is not more acidic than ROH. For example, if R is phenyl, such that ROH is phenol, then one nonlimiting example of a less acidic alcohol that can be used in step (a) is isopropanol. Examples of suitable alcohols include without limitation methanol, ethanol, i-propanol, i-butanol, and phenol, with the proviso that the alcohol is either ROH or an alcohol that is not more acidic than ROH.

The solvent may also be a polar protic or polar aprotic solvent or a mixture of protic or polar aprotic solvent. A polar solvent, as used herein, is a solvent whose constituent molecules exhibit a nonzero dipole moment. A polar protic solvent, as used herein, is a polar solvent whose constituent molecules contain an O-H or N-H bond. A polar aprotic solvent, as used herein, is a polar solvent whose constituent molecules do not contain an O-H or N-H bond. Examples of polar solvents other than an alcohol suitable for use herein include tetrahydrofuran, N-methylpyrrolidone, dimethylformamide, and dimethylacetamide.

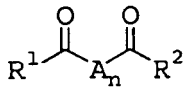
In step (a), a halogenated aromatic acid is preferably contacted with a total of from about n+m to n+m+1 equivalents of the alcoholate RO^-M^+ per equivalent of halogenated aromatic acid. Between m and m+1 equivalents is needed for forming the m-basic salt and between n and n+1 equivalents is needed for the displacement reaction. It is preferred that the total amount of alcoholate not exceed m+n+1. It is also preferred that the total amount of alcoholate not be less than m+n in order to avoid reduction reactions. One "equivalent" as used in this context is the number of moles of alcoholate RO^-M^+ that will react with one mole of hydrogen ions; for an acid, one equivalent is the number of moles of acid that will supply one mole of hydrogen ions.

As mentioned above, in step (a), the halogenated aromatic acid is also contacted with a copper (I) or (II) source in the presence of a diketone ligand that coordinates to copper. The copper source and the ligand may be added sequentially to the reaction mixture, or may be combined separately (for example, in a solution of water or acetonitrile) and added together.

The copper source is a Cu(I) salt, a Cu(II) salt, or mixtures thereof. Examples include without limitation CuCl, CuBr, CuI, Cu_2SO_4, $CuNO_3$, $CuCl_2$, $CuBr_2$, CuI_2, $CuSO_4$, and $Cu(NO_3)_2$. The selection of the copper source may be made in relation to the identity of the halogenated aromatic acid used. For example, if the starting halogenated aromatic acid is a bromobenzoic acid, CuCl, CuBr, CuI, Cu_2SO_4, $CuNO_3$, $CuCl_2$, $CuBr_2$, CuI_2, $CuSO_4$, and $Cu(NO_3)_2$ will be included among the useful

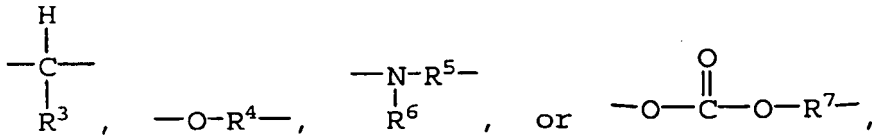
choices. If the starting halogenated aromatic acid is a chlorobenzoic acid, CuBr, CuI, $CuBr_2$ and CuI_2 will be included among the useful choices. CuBr and $CuBr_2$ are in general preferred choices for most systems. The amount of copper used is typically about 0.1 to about 5 mol% based on moles of halogenated aromatic acid.

The ligand may be a diketone as described by the structure of Formula III



III

wherein A is



R^1 and R^2 are each independently selected from substituted and unsubstituted C_1-C_{16} n-alkyl, iso-alkyl and tertiary alkyl groups; and substituted and unsubstituted C_6 - C_{30} aryl and heteroaryl groups;

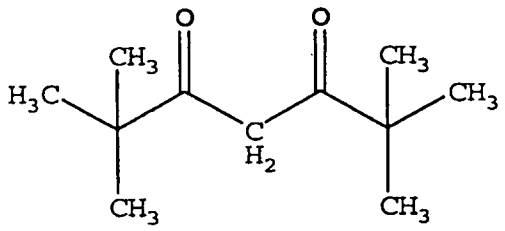
R^3 is selected from H; substituted and unsubstituted C_1-C_{16} n-alkyl, iso-alkyl and tertiary alkyl groups; substituted and unsubstituted C_6 - C_{30} aryl and heteroaryl groups; and a halogen;

R^4, R^5, R^6 and R^7 are each independently H or a substituted or unsubstituted C_1-C_{16} n-alkyl, iso-alkyl or tertiary alkyl group; and

n = 0 or 1.

The term "unsubstituted", as used with reference to an alkyl or aryl group in a diketone as described above, means that the alkyl or aryl group contains no atoms other than carbon and hydrogen. In a substituted alkyl or aryl group, however, one or more O or S atoms may optionally be substituted for any one or more of the in-chain or in-ring carbon atoms, provided that the resulting structure contains no -O-O- or -S-S- moieties, and provided that no carbon atom is bonded to more than one heteroatom. In a preferred embodiment, R^3 is H.

In one embodiment, a diketone suitable for use herein as the ligand is 2,2',6,6'-tetramethylheptanedione-3,5 (Formula V):



V

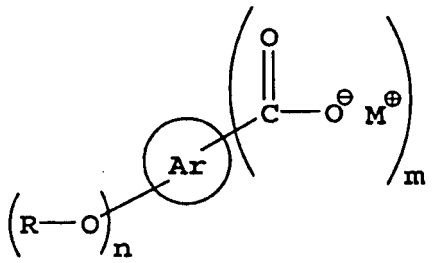
Other diketones suitable for use herein as the ligand include, without limitation, 2,4-pentanedione and 2,3-pentanedione.

A ligand suitable for use herein may be selected as any one or more or all of the members of the whole population of ligands described by name or structure above.

Various copper sources and ligands suitable for use herein may be made by processes known in the art, or are available commercially from suppliers such as Alfa Aesar (Ward Hill, Massachusetts), City Chemical (West Haven, Connecticut), Fisher Scientific (Fairlawn, New Jersey), Sigma-Aldrich (St. Louis, Missouri) or Stanford Materials (Aliso Viejo, California).

In various embodiments, the ligand may be provided in an amount of about 1 to about 8, preferably about 1 to about 2, molar equivalents of ligand per mole of copper. In those and other embodiments, the ratio of molar equivalents of ligand to molar equivalents of halogenated aromatic acid may be less than or equal to about 0.1. As used herein, the term "molar equivalent" indicates the number of moles of ligand that will interact with one mole of copper.

In step (b), the reaction mixture is heated to form the m-basic salt of the product of step (a), as described by the structure of Formula IV:



IV

The reaction temperature for steps (a) and (b) is preferably between about 40 and about 120°C, more preferably between about 75 and about 95°C. Typically, the time required for step (a) is from about

0.1 to about 1 hour. The time required for step (b) is typically from about 0.1 to about 1 hour. Oxygen may be desirably excluded during the reaction. The solution is typically allowed to cool before optional step (c) and before the acidification in step (d) is carried out.

The m-basic salt of the ether of the aromatic acid is then contacted in step (d) with acid to convert it to the hydroxy aromatic acid product. Any acid of sufficient strength to protonate the m-basic salt is suitable. Examples include without limitation hydrochloric acid, sulfuric acid and phosphoric acid.

In one embodiment, the copper (I) or copper (II) source is selected from the group consisting of CuBr, $CuBr_2$ and mixtures thereof; the ligand is selected from the group consisting of 2,2',6,6'-tetramethylheptanedione-3,5, 2,4-pentanedione and 2,3-pentanedione; and the copper (I) or copper (II) source is combined with two molar equivalents of the ligand.

The process described above also allows for effective and efficient synthesis of products made from the resulting ethers of aromatic acids such as a compound, a monomer, or an oligomer or polymer thereof. These produced materials may have one or more of ester functionality, ether functionality, amide functionality, imide functionality, imidazole functionality, thiazole functionality, oxazole functionality, carbonate functionality, acrylate functionality, epoxide functionality, urethane functionality, acetal functionality, and anhydride functionality.

Representative reactions involving a material made by the process of this invention, or a derivative of such material, include, for example, making a polyester from the ether of an aromatic acid and either diethylene glycol or triethylene glycol in the presence of 0.1% of $Zn_3(BO_3)_2$ in 1-methylnaphthalene under nitrogen, according to the method taught in US 3,047,536 (which is incorporated in its entirety as a part hereof for all purposes). Similarly, the ether of an aromatic acid is suitable for copolymerization with a dibasic acid and a glycol to prepare a heat-stabilized polyester according to the method taught in US 3,227,680 (which is incorporated in its entirety as a part hereof for all purposes), wherein representative conditions involve forming a prepolymer in the presence of titanium tetraisopropoxide in butanol at 200~250°C, followed by solid-phase polymerization at 280°C at a pressure of 0.08 mm Hg.

The ether of an aromatic acid can also be polymerized with the trihydrochloride-monohydrate of tetraaminopyridine in a condensation polymerization in strong polyphosphoric acid under slow heating above 100°C up to about 180°C under reduced pressure, followed by precipitation in water, as disclosed in US 5,674,969 (which is incorporated in its entirety as a part hereof for all purposes); or by mixing the monomers at a temperature from about 50°C to about 110°C, and then 145°C to form an oligomer, and then reacting the oligomer at a temperature of about 160°C to about 250°C as disclosed in U.S. Provisional Application No. 60/665,737, filed March 28, 2005 (which is incorporated in its entirety as a part hereof for all purposes), published as WO 2006/104974. The polymer that may be so produced may be a

pyridobisimidazole-2,6-diyl(2,5-dialkoxy-p-phenylene) polymer or a pyridobisimidazole-2,6-diyl(2,5-diareneoxy-p-phenylene) polymer such as a poly(1,4-(2,5-diareneoxy) phenylene-2,6-pyrido[2, 3-d: 5,6-d']bisimidazole) polymer. The pyridobisimidazole portion thereof may, however, be replaced by any one or more of a benzobisimidazole, benzobisthiazole, benzobisoxazole, pyridobisthiazole and a pyridobisoxazole; and the 2,5-dialkoxy-p-phenylene portion thereof may be replaced by an alkyl or aryl ether of one or more of isophthalic acid, terephthalic acid, 2,5-pyridine dicarboxylic acid, 2,6-naphthalene dicarboxylic acid, 4,4'-diphenyl dicarboxylic acid, 2,6-quinoline dicarboxylic acid, and 2,6-bis(4-carboxyphenyl)pyridobisimidazole, wherein such an ether is produced according to the methods disclosed herein.

The polymer prepared in such manner may, for example, contain one or more of the following units:

pyridobisimidazole-2,6-diyl(2,5-dialkoxy-p-phenylene) and/or pyridobisimidazole-2,6-diyl(2,5-diphenoxy-p-phenylene) units;

units selected from the group consisting of pyridobisimidazole-2,6-diyl(2,5-dimethoxy-p-phenylene), pyridobisimidazole-2,6-diyl(2,5-diethoxy-p-phenylene), pyridobisimidazole-2,6-diyl(2,5-dipropoxy-p-phenylene), pyridobisimidazole-2,6-diyl(2,5-dibutoxy-p-phenylene) and pyridobisimidazole-2,6-diyl(2,5-diphenoxy-p-phenylene);

pyridobisthiazole-2,6-diyl(2,5-dialkoxy-p-phenylene) and/or pyridobisthiazole-2,6-diyl(2,5-diphenoxy-p-phenylene) units;

units selected from the group consisting of pyridobisthiazole-2,6-diyl(2,5-dimethoxy-p-phenylene), pyridobisthiazole-2,6-diyl(2,5-diethoxy-p-phenylene),

pyridobisthiazole-2,6-diyl(2,5-dipropoxy-p-phenylene), pyridobisthiazole-2,6-diyl(2,5-dibutoxy-p-phenylene) and pyridobisthiazole-2,6-diyl(2,5-diphenoxy-p-phenylene);

pyridobisoxazole-2,6-diyl(2,5-dialkoxy-p-phenylene) and/or pyridobisoxazole-2,6-diyl(2,5-diphenoxy-p-phenylene) units;

units selected from the group consisting of pyridobisoxazole-2,6-diyl(2,5-dimethoxy-p-phenylene), pyridobisoxazole-2,6-diyl(2,5-diethoxy-p-phenylene), pyridobisoxazole-2,6-diyl(2,5-dipropoxy-p-phenylene), pyridobisoxazole-2,6-diyl(2,5-dibutoxy-p-phenylene) and pyridobisoxazole-2,6-diyl(2,5-diphenoxy-p-phenylene);

benzobisimidazole-2,6-diyl(2,5-dialkoxy-p-phenylene) and/or benzobisimidazole-2,6-diyl(2,5-diphenoxy-p-phenylene) units;

units selected from the group consisting of benzobisimidazole-2,6-diyl(2,5-dimethoxy-p-phenylene), benzobisimidazole-2,6-diyl(2,5-diethoxy-p-phenylene), benzobisimidazole-2,6-diyl(2,5-dipropoxy-p-phenylene), benzobisimidazole-2,6-diyl(2,5-dibutoxy-p-phenylene) and benzobisimidazole-2,6-diyl(2,5-diphenoxy-p-phenylene);

benzobisthiazole-2,6-diyl(2,5-dialkoxy-p-phenylene) and/or benzobisthiazole-2,6-diyl(2,5-diphenoxy-p-phenylene) units;

units selected from the group consisting of benzobisthiazole-2,6-diyl(2,5-dimethoxy-p-phenylene), benzobisthiazole-2,6-diyl(2,5-diethoxy-p-phenylene), benzobisthiazole-2,6-diyl(2,5-dipropoxy-p-phenylene), benzobisthiazole-2,6-diyl(2,5-dibutoxy-p-phenylene) and benzobisthiazole-2,6-diyl(2,5-diphenoxy-p-phenylene);

benzobisoxazole-2,6-diyl(2,5-dialkoxy-p-phenylene) and/or benzobisoxazole-2,6-diyl(2,5-diphenoxy-p-phenylene) units; and/or

units selected from the group consisting of benzobisoxazole-2,6-diyl(2,5-dimethoxy-p-phenylene), benzobisoxazole-2,6-diyl(2,5-diethoxy-p-phenylene), benzobisoxazole-2,6-diyl(2,5-dipropoxy-p-phenylene), benzobisoxazole-2,6-diyl(2,5-dibutoxy-p-phenylene) and benzobisoxazole-2,6-diyl(2,5-diphenoxy-p-phenylene).

EXAMPLES

The advantageous attributes and effects of the processes hereof may be seen in a laboratory example, as described below. The embodiments of these processes on which the example is based are representative only, and the selection of those embodiments to illustrate the invention does not indicate that conditions, arrangements, approaches, steps, techniques, configurations or reactants not described in the example are not suitable for practicing these processes, or that subject matter not described in the example is excluded from the scope of the appended claims and equivalents thereof.

As used herein, the term "conversion" refers to how much reactant was used up as a fraction or percentage of the theoretical amount. The term "selectivity" for a product P refers to the molar fraction or molar percentage of P in the final product mix. The conversion multiplied by the selectivity thus equals the maximum "yield" of P; the actual or "net" yield will normally be somewhat less than this because of sample losses incurred in the course of activities such as isolating, handling, drying, and the like. The term "purity" denotes what percentage of the in-hand, isolated sample is actually the specified substance.

The meaning of abbreviations is as follows "h" means hour(s), "mL" means milliliter(s), "g" means gram(s), "MeOH" means methanol, "mg" means milligram(s), "mmol" means millimole(s), and "mol equiv" means molar equivalent.

Example 1

In an air and moisture free environment, 4.2 g (77 mmol) of sodium methoxide is combined with 125 g of anhydrous methanol, followed by the addition of 5 g (15 mmol) of 2,5-dibromoterephthalic acid. Separately, 103 mg (0.03 mol equiv) of $CuBr_2$ and 0.06 mol equiv of 2,2',6,6'-tetramethylheptanedione-3,5 are combined under nitrogen, followed by addition of anhydrous methanol to dissolve. This solution is then added to form the reaction mixture. The reaction mixture is heated to reflux with stirring for 8 h, remaining under a nitrogen atmosphere. After cooling, the product is filtered, washed with hot MeOH and dried to yield a white solid as the bis-sodium salt. The isolated salt is then acidified with hydrochloric acid. The purity is over 95% and the net isolated yield is over 90%.

Each of the formulae shown herein describes each and all of the separate, individual compounds that can be formed in that formula by (1) selection from within the prescribed range for one of the variable radicals, substituents or numerical coefficents while all of the other variable radicals, substituents or numerical coefficents are held constant, and (2) performing in turn the same selection from within the prescribed range for each of the other variable radicals, substituents or numerical coefficents with the others being held constant. In addition to a selection made

within the prescribed range for any of the variable radicals, substituents or numerical coefficents of only one of the members of the group described by the range, a plurality of compounds may be described by selecting more than one but less than all of the members of the whole group of radicals, substituents or numerical coefficents. When the selection made within the prescribed range for any of the variable radicals, substituents or numerical coefficents is a subgroup containing (i) only one of the members of the whole group described by the range, or (ii) more than one but less than all of the members of the whole group, the selected member(s) are selected by omitting those member(s) of the whole group that are not selected to form the subgroup. The compound, or plurality of compounds, may in such event be characterized by a definition of one or more of the variable radicals, substituents or numerical coefficents that refers to the whole group of the prescribed range for that variable but where the member(s) omitted to form the subgroup are absent from the whole group.

Where a range of numerical values is recited herein, the range includes the endpoints thereof and all the individual integers and fractions within the range, and also includes each of the narrower ranges therein formed by all the various possible combinations of those endpoints and internal integers and fractions to form subgroups of the larger group of values within the stated range to the same extent as if each of those narrower ranges was explicitly recited. Where a range of numerical values is stated herein as being greater than a stated value, the range is nevertheless finite and is bounded on its upper end by a value that is

operable within the context of the invention as described herein. Where a range of numerical values is stated herein as being less than a stated value, the range is nevertheless bounded on its lower end by a non-zero value.

In this specification, unless explicitly stated otherwise or indicated to the contrary by the context of usage, amounts, sizes, ranges and other quantities and characteristics recited herein, particularly when modified by the term "about", may but need not be exact, and may also be approximate and/or larger or smaller (as desired) than stated, reflecting tolerances, conversion factors, rounding off, measurement error and the like, as well as the inclusion within a stated value of those values outside it that have, within the context of this invention, functional and/or operable equivalence to the stated value.

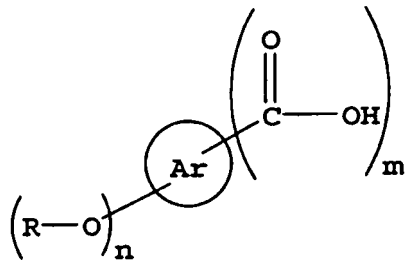
Where an embodiment of this invention is stated or described as comprising, including, containing, having, being composed of or being constituted by certain features, it is to be understood, unless the statement or description explicitly provides to the contrary, that one or more features in addition to those explicitly stated or described may be present in the embodiment. An alternative embodiment of this invention, however, may be stated or described as consisting essentially of certain features, in which embodiment features that would materially alter the principle of operation or the distinguishing characteristics of the embodiment are not present therein. A further alternative embodiment of this invention may be stated or described as consisting of

certain features, in which embodiment, or in insubstantial variations thereof, only the features specifically stated or described are present.

CLAIMS

What is claimed is:

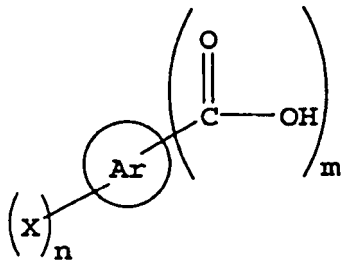
1. A process for preparing an ether of an aromatic acid, the ether being described by the structure of Formula I



I

wherein Ar is a C_6~C_{20} monocyclic or polycyclic aromatic nucleus, R is a univalent organic radical, n and m are each independently a nonzero value, and n+m is less than or equal to 8; comprising

(a) contacting a halogenated aromatic acid such as is described by the structure of Formula II



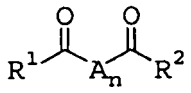
II

wherein each X is independently Cl, Br or I, and Ar, n and m are as set forth above, with

(i) a polar protic solvent, a polar aprotic solvent or an alcoholic solvent containing the alcoholate RO^-M^+ (wherein M is Na or K), wherein the polar protic solvent, polar aprotic solvent or alcoholic solvent is either ROH or is a solvent that is less acidic than ROH;

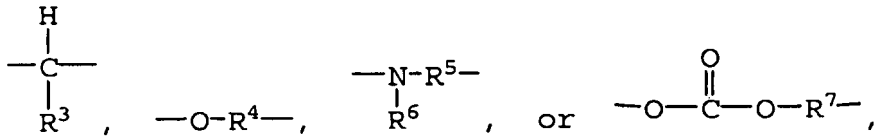
(ii) a copper (I) or copper (II) source; and

(iii) a diketone ligand that coordinates to copper, such as is described by the structure of Formula III



III

wherein A is



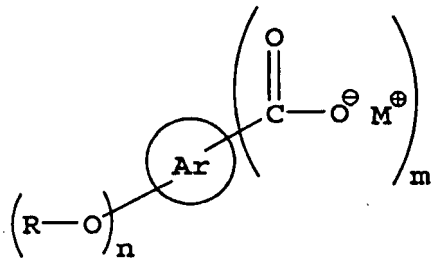
R^1 and R^2 are each independently selected from substituted and unsubstituted C_1-C_{16} n-alkyl, iso-alkyl and tertiary alkyl groups; and substituted and unsubstituted C_6 - C_{30} aryl and heteroaryl groups;

R^3 is selected from H; substituted and unsubstituted C_1-C_{16} n-alkyl, iso-alkyl and tertiary alkyl groups; substituted and unsubstituted C_6 - C_{30} aryl and heteroaryl groups; and a halogen;

R^4, R^5, R^6 and R^7 are each independently H or a substituted or unsubstituted C_1-C_{16} n-alkyl, iso-alkyl or tertiary alkyl group; and n = 0 or 1;

to form a reaction mixture;

(b) heating the reaction mixture to form the m-basic salt of the product of step (a), as described by the structure of Formula IV;



IV

(c) optionally, separating the Formula IV m-basic salt from the reaction mixture in which it is formed; and

(d) contacting the Formula IV m-basic salt with acid to form therefrom an ether of an aromatic acid.

2. A process according to Claim 1 wherein the halogenated aromatic acid is selected from the group consisting of 2-bromobenzoic acid, 2,5-dibromobenzoic acid, 2-bromo-5-nitrobenzoic acid, 2-bromo-5-methylbenzoic acid, 2-chlorobenzoic acid, 2,5-dichlorobenzoic acid, 2-chloro-3,5-dinitrobenzoic acid, 2-chloro-5-methylbenzoic acid, 2-bromo-5-methoxybenzoic acid, 5-bromo-2-chlorobenzoic acid, 2,3-dichlorobenzoic acid, 2-chloro-4-nitrobenzoic acid, 2,5-dichloroterephthalic acid, 2-chloro-5-nitrobenzoic

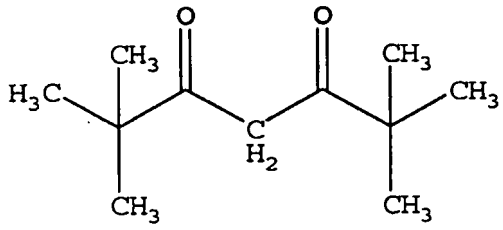
acid, 2,5-dibromoterephthalic acid, and 2,5-dichloroterephthalic acid.

3. A process according to Claim 1 wherein, in step (a), a total of about n+m to n+m+1 normal equivalents of RO^-M^+ are added to the reaction mixture per equivalent of the halogenated aromatic acid.

4. A process according to Claim 1 wherein the copper source comprises a Cu(I) salt, a Cu(II) salt, or a mixture thereof.

5. A process according to Claim 4 wherein the copper source is selected from the group consisting of CuCl, CuBr, CuI, Cu_2SO_4, $CuNO_3$, $CuCl_2$, $CuBr_2$, CuI_2, $CuSO_4$, $Cu(NO_3)_2$, and mixtures thereof.

6. A process according to Claim 1 wherein the ligand comprises 2,4-pentanedione, 2,3-pentanedione or 2,2',6,6'-tetramethylheptanedione-3,5 (as shown by the structure below):



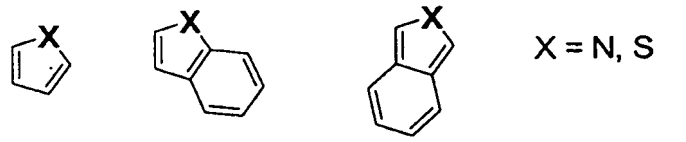
7. A process according to Claim 1 further comprising a step of combining the copper source with the ligand before adding them to the reaction mixture.

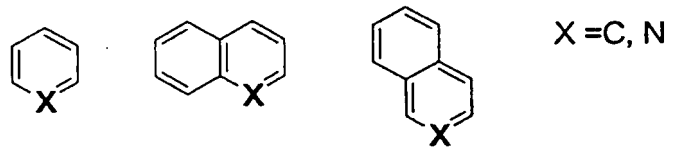
8. A process according to Claim 5 wherein the copper source comprises CuBr or $CuBr_2$.

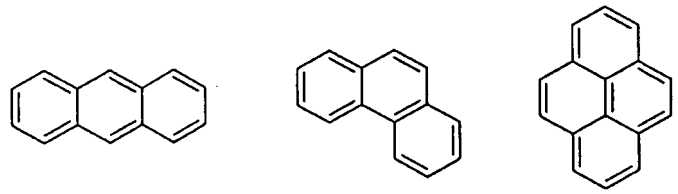
9. A process according to Claim 1 wherein copper is provided in an amount of between about 0.1 and about 5 mol% based on moles of halogenated aromatic acid.

10. A process according to Claim 1 wherein the ligand is provided in an amount of between about one and about two molar equivalents per mole of copper.

11. A process according to Claim 1 wherein R is selected from the group consisting of C_1~C_{12} alkyl groups, aryl groups and the groups described by the structures of the following formulae:







12. A process according to Claim 11 wherein R comprises a C_1~C_4 alkyl group or phenyl group.

13. A process according to Claim 1 wherein the alcoholic solvent comprises ROH.

14. A process according to Claim 1 wherein the halogenated aromatic hydroxy acid comprises 2,5-dibromoterephthalic acid or 2,5-dichloroterephthalic acid; R comprises methyl, ethyl, i-propyl, i-butyl or phenyl; the alcoholic solvent comprises ROH; the copper source comprises CuBr, $CuBr_2$, or a mixture of CuBr and $CuBr_2$; the copper source is provided in an amount of between about 0.1 and about 5 mol% based on moles of halogenated aromatic acid; the ligand comprises 2,2',6,6'-tetramethylheptanedione-3,5; and the ligand is provided in an amount of between about one and about two molar equivalents per mole of copper.

15. A process according to Claim 1 further comprising a step of subjecting the ether of the aromatic acid to a reaction to prepare therefrom a compound, monomer, oligomer or polymer.

16. A process according to Claim 15 wherein a polymer prepared comprises at least one member of the group consisting of pyridobisimidazole, pyridobisthiazole, pyridobisoxazole, benzobisimidazole, benzobisthiazole, and benzobisoxazole moieties.

17. A process according to Claim 16 wherein a polymer prepared comprises a pyridobisimidazole-2,6-diyl(2,5-dialkoxy-p-phenylene) polymer.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/025917

A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BUCK E ET AL: "Ullmann diaryl ether synthesis: rate aceleration by 2,2,6,6-tetramethylheptane-3,5-dione" ORGANIC LETTERS, ACS, WASHINGTON, DC, US, vol. 4, no. 9, 2002, pages 1623-1626, XP002403679 ISSN: 1523-7060 the whole document	1-17
Y	JP 06 080609 A (NIPPON CHEMICAL IND) 22 March 1994 (1994-03-22) the whole document	1-17

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 April 2008	02/05/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bedel, Christian

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2007/025917

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
JP 6080609 A	22-03-1994	JP 3285391 B2	27-05-2002

[19] 中华人民共和国国家知识产权局

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[32] 2006.12.21 [33] US [31] 60/876,570
[86] 国际申请 PCT/US2007/025917 2007.12.18
[87] 国际公布 WO2008/079225 英 2008.7.3
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权利要求书 4 页 说明书 16 页

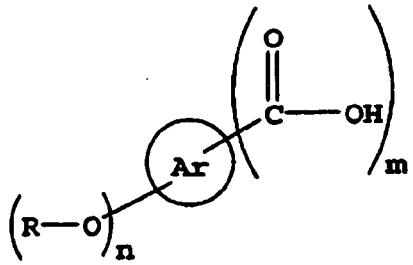
[54] 发明名称

芳香酸的醚的合成方法

[57] 摘要

本发明公开了在包含铜(I)或铜(II)源以及与铜配位的二酮配体的反应混合物中，由卤代芳香酸来制备芳香酸的醚。

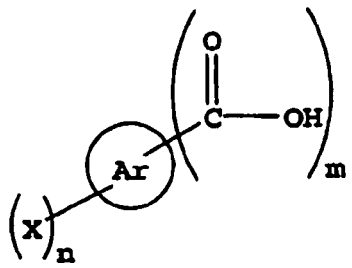
1. 用于制备芳香酸的醚的方法，所述醚由式 I 结构来描述



I

其中 Ar 为 C_6-C_{20} 单环的或多环的芳基核，R 为一价的有机基团，n 和 m 各自独立地为非零值，并且 n+m 小于或等于 8；所述方法包括

(a) 使如式 II 的结构所述的卤代芳香酸



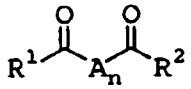
II

其中每个 X 独立地为 Cl、Br 或 I，并且 Ar、n 和 m 为如上所述，与以下物质接触：

(i) 包含醇化物 RO^-M^+（其中 M 为 Na 或 K）的极性质子溶剂、极性非质子溶剂或醇溶剂，其中所述极性质子溶剂、极性非质子溶剂或醇溶剂为 ROH 或酸性小于 ROH 的溶剂；

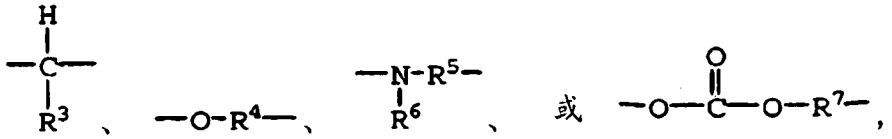
(ii) 铜(I)或铜(II)源；和

(iii) 与铜配位的二酮配体，如式 III 的结构所描述



III

其中 A 为



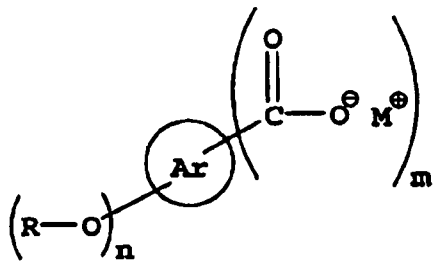
R^1和 R^2各自独立地选自取代和未取代的 C_1-C_{16}正烷基、异烷基和叔烷基；以及取代和未取代的 C_6-C_{30}芳基和杂芳基；

R^3选自 H；取代和未取代的 C_1-C_{16}正烷基、异烷基和叔烷基；取代和未取代的 C_6-C_{30}芳基和杂芳基；以及卤素；

R^4、R^5、R^6和 R^7各自独立地为 H 或取代或未取代的 C_1-C_{16}正烷基、异烷基或叔烷基；并且 n = 0 或 1；

以形成反应混合物；

(b) 加热所述反应混合物以形成如式 IV 结构描述的步骤(a)产物的 m-代盐；



IV

(c) 任选地，从其中形成式 IV 的 m-代盐的反应混合物中分离出式 IV 的 m-代盐；和

(d) 使所述式 IV 的 m-代盐与酸接触，以由此形成芳香酸的醚。

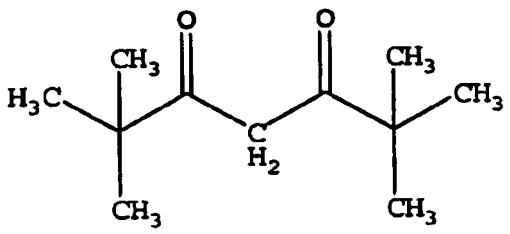
2. 根据权利要求 1 的方法，其中所述卤代芳香酸选自 2-溴苯甲酸、2,5-二溴苯甲酸、2-溴-5-硝基苯甲酸、2-溴-5-甲基苯甲酸、2-氯苯甲酸、2,5-二氯苯甲酸、2-氯-3,5-二硝基苯甲酸、2-氯-5-甲基苯甲酸、2-溴-5-甲氧基苯甲酸、5-溴-2-氯苯甲酸、2,3-二氯苯甲酸、2-氯-4-硝基苯甲酸、2,5-二氯对苯二甲酸、2-氯-5-硝基苯甲酸、2,5-二溴对苯二甲酸、以及 2,5-二氯对苯二甲酸。

3. 根据权利要求 1 的方法，其中在步骤(a)中，以总共约 n+m 至 n+m+1 标准当量的 RO^-M^+ 每当量所述卤代芳香酸的量，将所述 RO^-M^+ 添加到所述反应混合物中。

4. 根据权利要求 1 的方法，其中所述铜源包括 Cu(I)盐、Cu(II)盐、或它们的混合物。

5. 根据权利要求 4 的方法，其中所述铜源选自 CuCl、CuBr、CuI、Cu_2SO_4、$CuNO_3$、$CuCl_2$、$CuBr_2$、CuI_2、$CuSO_4$、$Cu(NO_3)_2$、以及它们的混合物。

6. 根据权利要求 1 的方法，其中所述配体包括 2,4-戊二酮、2,3-戊二酮或 2,2',6,6'-四甲基-3,5-庚二酮（如以下结构所示）：



。

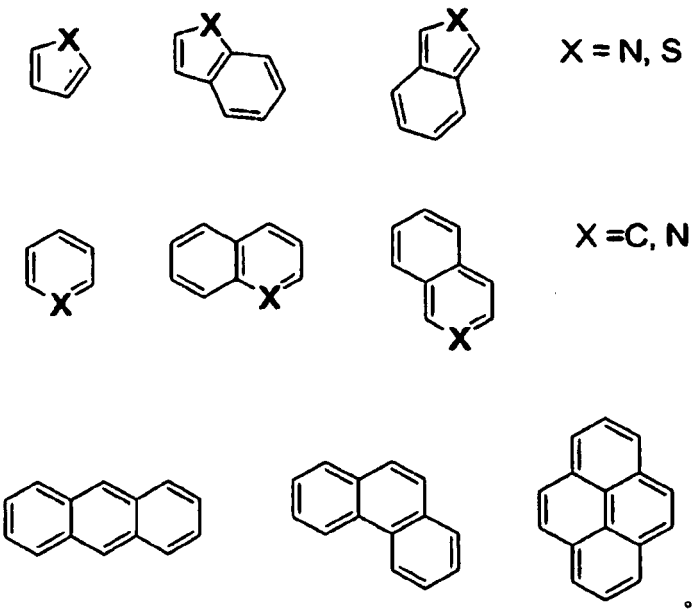
7. 根据权利要求 1 的方法，所述方法还包括在将所述铜源和所述配体加入到所述反应混合物中之前将它们进行结合的步骤。

8. 根据权利要求 5 的方法，其中所述铜源包括 CuBr 或 $CuBr_2$。

9. 根据权利要求 1 的方法，其中所提供的铜的量按卤代芳香酸的摩尔数计为约 0.1mol% 至约 5mol%。

10. 根据权利要求 1 的方法，其中所提供的配体的量为约一至约二摩尔当量每摩尔铜。

11. 根据权利要求 1 的方法，其中 R 选自 C_1-C_{12}烷基、芳基以及由下式结构描述的基团：



12. 根据权利要求 11 的方法，其中 R 包括 C_1-C_4烷基或苯基。
13. 根据权利要求 1 的方法，其中所述醇溶剂包括 ROH。
14. 根据权利要求 1 的方法，其中所述卤代芳族羟基酸包括 2,5-二溴对苯二甲酸或 2,5-二氯对苯二甲酸；R 包括甲基、乙基、异丙基、异丁基或苯基；所述醇溶剂包括 ROH；所述铜源包括 CuBr、$CuBr_2$、或 CuBr 和 $CuBr_2$的混合物；所提供的铜源的量按卤代芳香酸的摩尔数计为约 0.1mol% 至约 5mol%；所述配体包括 2,2',6,6'-四甲基-3,5-庚二酮；并且所提供的配体的量为约一至约二摩尔当量每摩尔铜。
15. 根据权利要求 1 的方法，所述方法还包括使所述芳香酸的醚经历反应以由此制备化合物、单体、低聚物或聚合物的步骤。
16. 根据权利要求 15 的方法，其中所制备的聚合物包括以下部分中的至少一员：吡啶并二咪唑、吡啶并二噻唑、吡啶并二噁唑、苯并二咪唑、苯并二噻唑、以及苯并二噁唑部分。
17. 根据权利要求 16 的方法，其中所制备的聚合物包括吡啶并二咪唑-2,6-二基(2,5-二烷氧基对亚苯基)聚合物。

芳香酸的醚的合成方法

本专利申请要求享有 2006 年 12 月 21 日提交的美国临时申请 60/876,570 的优先权，其全文引入作为本文的一部分，以用于各种目的。

技术领域

本发明涉及羟基芳香酸的醚的制备，所述羟基芳香酸的醚非常有价值，可用于多种用途，例如用作中间体或用作制备聚合物的单体。

发明背景

芳香酸的醚在许多有价值的物质（包括药物和在作物保护中起作用的化合物）的制造中用作中间体和助剂，并且还在高性能刚性聚合物的生产中用作单体，所述高性能刚性聚合物为例如用于电器件应用的线性刚性低聚(2-氨基苯甲酰胺)[Wu 等人,Organic Letters (2004), 6(2), 第 229 至 232 页]和聚吡啶并二咪唑等[参见例如 Beers 等人,High-Performance Fibres (2000), 第 93 至 155 页]。

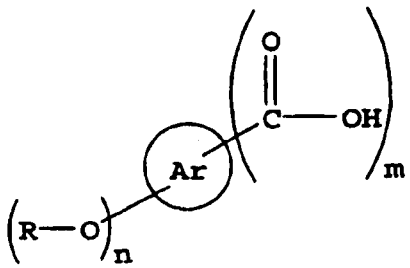
现有的生产 2,5-二烷氧基-和 2,5-二芳氧基对苯二甲酸的方法涉及将 2,5-二羟基对苯二甲酸逐步烷基化以形成相应的 2,5-烷氧基-和 2,5-二芳氧基对苯二甲酸酯，随后将酯脱烷基化成酸。可通过使羟基芳香酸在碱性条件下与 n-烷基硫酸酯接触来将 n-羟基芳香酸转化成 n-烷氧基芳香酸。进行此转化反应的一种适宜方法描述于奥地利专利 265,244 中。收率为中等收率到低收率，产率为低产率并且需要两步处理。

因此，仍然需要能够经济地制备芳香酸的醚并在小规模和大规模作业以及批量和连续作业中具有高收率和高产率的方法。

发明详述

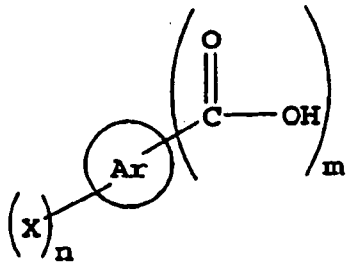
本文所公开的发明包括：制备芳香酸的醚的方法、此种醚可转化成的产物的制备方法、此类方法的使用、以及由此类方法获得的和可获得的产物。

本文方法的一个实施方案提供了制备芳香酸的醚的方法，所述醚可由式 I 结构描述



其中 Ar 为 C_6-C_{20}单环的或多环的芳基核，R 为一价的有机基团，n 和 m 各自独立地为非零值，并且 n+m 小于或等于 8；所述方法包括

(a) 使如式 II 结构所述的卤代芳香酸



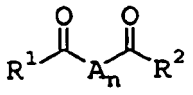
II

其中每个 X 独立地为 Cl、Br 或 I，并且 Ar、n 和 m 为如上所述，与以下物质接触：

(i) 包含醇化物 RO^-M^+（其中 M 为 Na 或 K）的极性质子溶剂、极性非质子溶剂或醇溶剂，其中所述极性质子溶剂、极性非质子溶剂或醇溶剂为 ROH 或酸性小于 ROH 的溶剂；

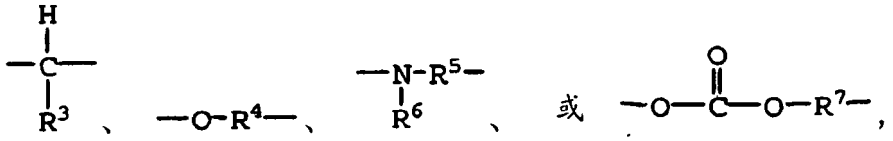
(ii) 铜(I)或铜(II)源；和

(iii) 与铜配位的二酮配体，如式 III 的结构所描述



III

其中 A 为



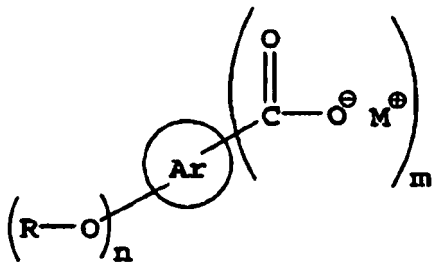
R^1和 R^2各自独立地选自取代和未取代的 C_1-C_{16}正烷基、异烷基和叔烷基；以及取代和未取代的 C_6-C_{30}芳基和杂芳基；

R^3选自 H；取代和未取代的 C_1-C_{16}正烷基、异烷基和叔烷基；取代和未取代的 C_6-C_{30}芳基和杂芳基；以及卤素；

R^4、R^5、R^6和 R^7各自独立地为 H 或取代或未取代的 C_1-C_{16}正烷基、异烷基或叔烷基；并且 n = 0 或 1；

以形成反应混合物；

(b) 加热该反应混合物以形成如式 IV 的结构所描述的步骤(a)产物的 m-代盐；



IV

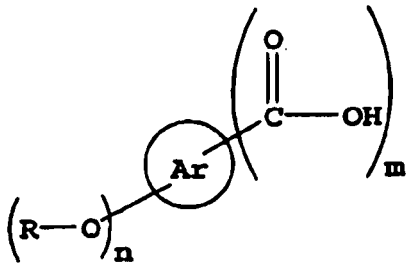
(c) 任选地，从其中形成式 IV 的 m-代盐的反应混合物中分离出式 IV 的 m-代盐；和

(d) 使式 IV 的 m-代盐与酸接触，以由此形成芳香酸的醚。

本发明的另一个实施方案提供了制备化合物、单体、低聚物或聚合物的方法，所述方法通过制备一般由式 I 的结构所描述的芳香酸的醚，然后使如此生产出的醚经历反应（包括多步反应）以此来制备化合物、单体、低聚物或聚合物。

发明详述

本发明提供了用于制备芳香酸的醚的具有改善的收率和产率的方法，所述醚可由式 I 的结构来描述

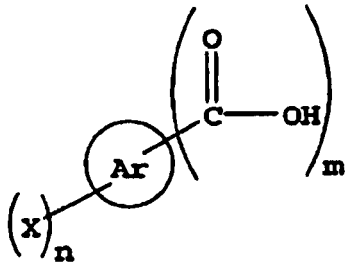


I

其中 Ar 为 C_6-C_{20}单环的或多环的芳基核，R 为一价的有机基团，n 和 m 各自独立地为非零值，并且 n+m 小于或等于 8；所述方法包括

本文方法的一个实施方案通过以下步骤进行:

(a) 使如式 II 结构所述的卤代芳香酸



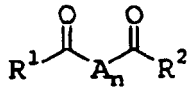
II

其中每个 X 独立地为 Cl、Br 或 I，并且 Ar、n 和 m 为如上所述，与以下物质接触:

(i) 包含醇化物 ROM^+（其中 M 为 Na 或 K）的极性质子溶剂、极性非质子溶剂或醇溶剂，其中所述极性质子溶剂、极性非质子溶剂或醇溶剂为 ROH 或酸性小于 ROH 的溶剂；

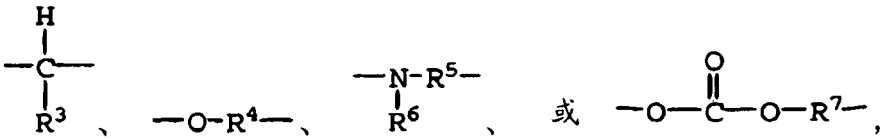
(ii) 铜(I)或铜(II)源；和

(iii) 与铜配位的二酮配体，例如式 III 的结构所描述



III

其中 A 为



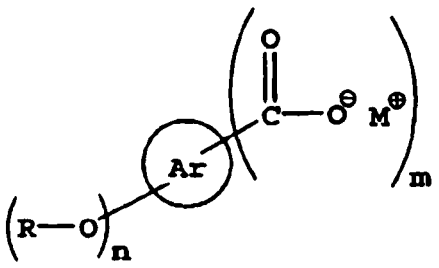
R^1和 R^2各自独立地选自取代和未取代的 C_1-C_{16}正烷基、异烷基和叔烷基；以及取代和未取代的 C_6-C_{30}芳基和杂芳基；

R^3选自 H；取代和未取代的 C_1-C_{16}正烷基、异烷基和叔烷基；取代和未取代的 C_6-C_{30}芳基和杂芳基；以及卤素；

R^4、R^5、R^6和 R^7各自独立地为 H 或取代或未取代的 C_1-C_{16}正烷基、异烷基或叔烷基；并且 n = 0 或 1；

以形成反应混合物；

(b) 加热该反应混合物以形成如式 IV 的结构所描述的步骤(a)产物的 m-代盐；



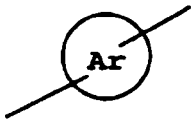
IV

(c) 任选地，从其中形成式 IV 的 m-代盐的反应混合物中分离出式 IV 的 m-代盐；和

(d) 使式 IV 的 m-代盐与酸接触，以由此形成芳香酸的醚。

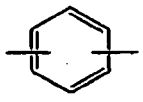
在式 I、II 和 IV 中，Ar 为 C_6-C_{20}单环的或多环的芳基核；n 和 m 各自独立地为非零值，并且 n+m 小于或等于 8；R 为一价的有机基团；并且在式 II 中，每个 X 独立地为 Cl、Br 或 I。

由下式

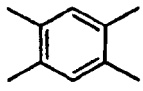


表示的基团为 n+m 价的 C_6-C_{20}单环的或多环的芳基核，所述芳基核通过从芳环或多个芳环（当结构是多环的时）上的不同碳原子中脱掉 n+m 个氢而形成。基团“Ar”可以是取代的或未取代的；当是未取代的时，其仅包含碳和氢。

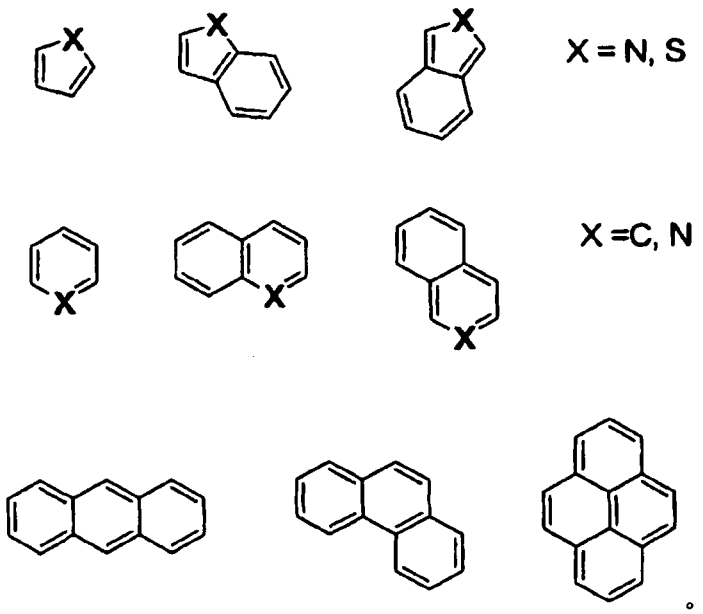
合适的 Ar 基团的一个实例是如下所示的亚苯基，其中 n=m=1。



一种优选的 Ar 基团如下所示，其中 n=m=2。



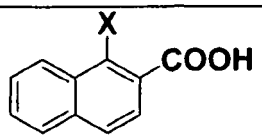
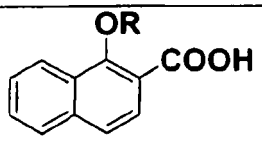
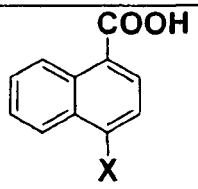
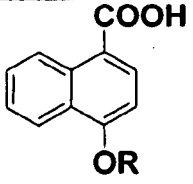
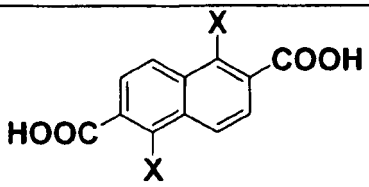
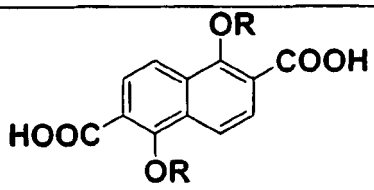
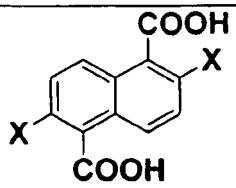
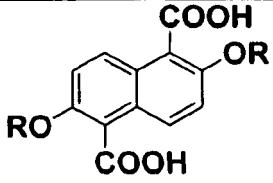
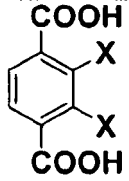
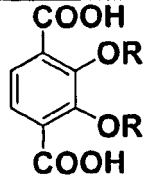
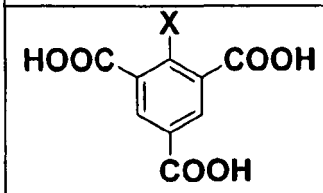
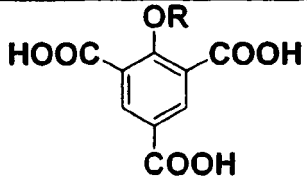
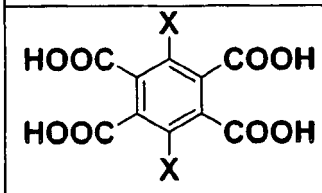
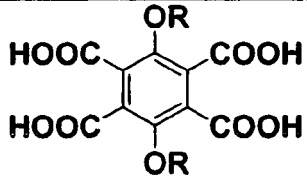
一价基团 R 为一价的有机基团。R 优选为 C_1-C_{12}烷基或芳基。R 更优选为 C_1-C_4烷基或苯基。尤其适合的 R 基团的实例无限制地包括甲基、乙基、异丙基、异丁基和苯基。以下示出了 R 的几个其它非限制性实例:

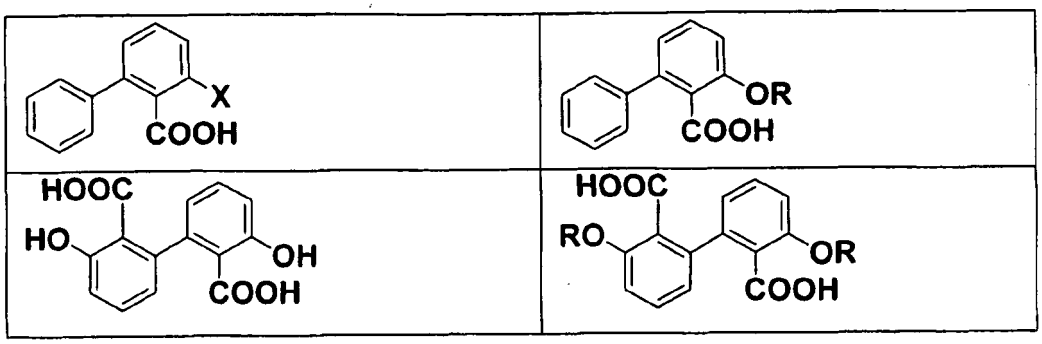


如本文所用，术语“m-代盐”是由酸形成的盐，所述酸在每个分子中包含 m 个具有可置换氢原子的酸基。

在本发明方法中待用作原料的各种卤代芳香酸是可商购获得的。例如，2-溴苯甲酸可得自 Aldrich Chemical Company（Milwaukee，Wisconsin）。然而如 Sasson 等人在 Journal of Organic Chemistry (1986), 51(15), 2880 至 2883 中所述，其可通过苄基溴的氧化来合成。其它可用的卤代芳香酸无限制地包括 2,5-二溴苯甲酸、2-溴-5-硝基苯甲酸、2-溴-5-甲基苯甲酸、2-氯苯甲酸、2,5-二氯苯甲酸、2-氯-3,5-二硝基苯甲酸、2-氯-5-甲基苯甲酸、2-溴-5-甲氧基苯甲酸、5-溴-2-氯苯甲酸、2,3-二氯苯甲酸、2-氯-4-硝基苯甲酸、2,5-二氯对苯二甲酸、2-氯-5-硝基苯甲酸、2,5-二溴对苯二甲酸、以及 2,5-二氯对苯二甲酸，所有这些均可商购获得。所述卤代芳香酸优选为 2,5-二溴对苯二甲酸或 2,5-二氯对苯二甲酸。

本发明的方法中，其它可用作原料的卤代芳香酸包括下表左栏中示出的那些，其中 X = Cl、Br 或 I，并且其中通过本发明方法由此制得的相应的芳香酸的醚示于右栏中：

$(COOH)_m—Ar—(X)_n$ I	$(COOH)_m—Ar—(OR)_n$ II
	
	
	
	
	
	
	



在步骤(a)中，使卤代芳香酸与以下物质接触：包含醇化物 RO^-M^+ 的极性质子溶剂或极性非质子溶剂或醇溶剂，其中 R 为如上所定义并且 M 为 Na 或 K；铜(I)或铜(II)源；以及与铜配位的二胺配体。

所述醇可以是 ROH，其是优选的，或者可以是酸性小于 ROH 的醇。例如，如果 R 为苯基，使得 ROH 为苯酚，则步骤(a)中可用的酸性较弱的醇的一个非限制性实例是异丙醇。合适的醇的实例无限制地包括甲醇、乙醇、异丙醇、异丁醇、和苯酚，前提条件是所述醇是 ROH 或酸性小于 ROH 的醇。

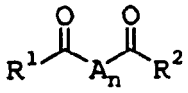
所述溶剂可以是极性质子溶剂或极性非质子溶剂或质子溶剂和极性非质子溶剂的混合物。如本文所用，极性溶剂是组分分子表现出非零偶极矩的溶剂。如本文所用，极性质子溶剂是组分分子包含 O-H 或 N-H 键的极性溶剂。如本文所用，极性非质子溶剂是组分分子不包含 O-H 或 N-H 键的极性溶剂。适用于本文的除了醇以外的极性溶剂的实例包括四氢呋喃、N-甲基吡咯烷酮、二甲基甲酰胺、以及二甲基乙酰胺。

在步骤(a)中，使卤代的芳香酸优选以总共约 n+m 至 n+m+1 当量的醇化物 RO^-M^+ 每当量卤代芳香酸的量与醇化物接触。需要介于 m 和 m+1 之间的当量来用于形成 m-代盐，并且需要介于 n 和 n+1 之间的当量来用于取代反应。醇化物的总量优选不超过 m+n+1。醇化物的总量还优选不小于 m+n 以避免还原反应。如本文中所使用，一“当量”是将与一摩尔氢离子反应的醇化物 RO^-M^+ 的摩尔数。对于酸而言，一个当量是指将提供一摩尔氢离子的酸的摩尔数。

如上所述，在步骤(a)中，卤代芳香酸还在与铜配位的二酮配体的存在下与铜(I)或(II)源接触。铜源和配体可以依次加入到反应混合物中，或可以单独结合（例如在水溶液或乙腈溶液中结合）并一同添加。

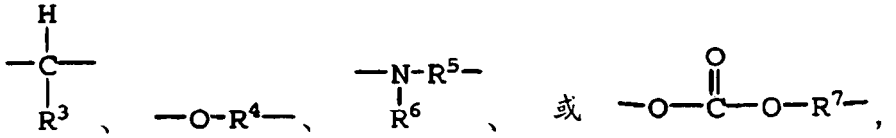
所述铜源为 Cu(I)盐、Cu(II)盐、或它们的混合物。实例无限制地包括 CuCl、CuBr、CuI、Cu_2SO_4、$CuNO_3$、$CuCl_2$、$CuBr_2$、CuI_2、$CuSO_4$、和 $Cu(NO_3)_2$。可根据所用卤代芳香酸的特性来选择铜源。例如，如果起始卤代芳酸为溴苯甲酸，则 CuCl、CuBr、CuI、Cu_2SO_4、$CuNO_3$、$CuCl_2$、$CuBr_2$、CuI_2、$CuSO_4$、和 $Cu(NO_3)_2$可包括在可用的选择中。如果起始卤代芳酸为氯苯甲酸，则 CuBr、CuI、$CuBr_2$和 CuI_2可包括在可用的选择中。对大多数体系而言，CuBr 和 $CuBr_2$一般是优选的选择。所用铜的量基于卤代芳香酸的摩尔数计通常为约 0.1 至约 5mol%。

所述配体可以是如式 III 的结构所描述的二酮



III

其中 A 为



R^1和 R^2各自独立地选自取代和未取代的 C_1-C_{16}正烷基、异烷基和叔烷基；以及取代和未取代的 C_6-C_{30}芳基和杂芳基；

R^3选自 H；取代和未取代的 C_1-C_{16}正烷基、异烷基和叔烷基；取代和未取代的 C_6-C_{30}芳基和杂芳基；以及卤素；

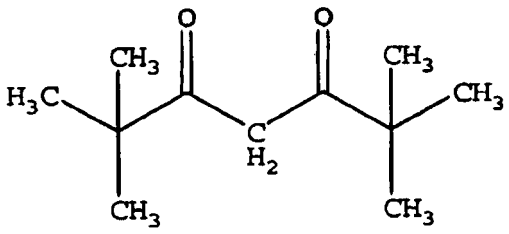
R^4、R^5、R^6和 R^7各自独立地为 H 或取代或未取代的 C_1-C_{16}正烷基、异烷基或叔烷基；并且

N=0 或 1。

当用于如上所述的二酮中的烷基或芳基时，术语“未取代的”是指所述烷基或芳基不包含碳和氢之外的原子。然而，在取代的烷基或芳基中，一个或多个 O 或 S 原子可任选地取代链中或环中的任何一个或多个碳原

子，前提条件是所得的结构不包含 -O-O- 或 -S-S- 部分，并且任何碳原子不能键合超过一个杂原子。在一个优选的实施方案中，R^3为 H。

在一个实施方案中，在本文中适于用作配体的二酮为 2,2',6,6'-四甲基-3,5-庚二酮（式 V）：



V

。

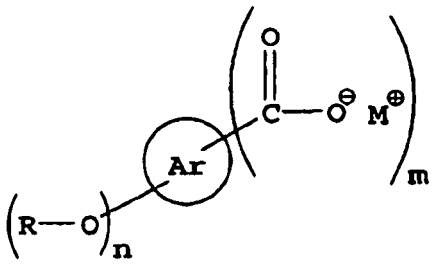
在本文中适于用作配体的其它二酮无限制地包括 2,4-戊二酮和 2,3-戊二酮。

适用于本文的配体可以选用以上名称或结构描述的所有配体中的任何一种或多种或全部。

适用于本文的各种铜源和配体可以由本领域已知的方法制备，或者可从供应商如 Alfa Aesar(Ward Hill, Massachusetts)、City Chemical (West Haven, Connecticut)、Fisher Scientific(Fairlawn, New Jersey)、Sigma-Aldrich (St. Louis, Missouri) 或 Stanford Materials (Aliso Viejo, California) 处商购获得。

在各种实施方案中，可以按约 1 至约 8，优选约 1 至约 2 摩尔当量配体每摩尔铜的量来提供配体。在那些以及其它实施方案中，配体的摩尔当量与卤代芳酸的摩尔当量的比率可小于或等于约 0.1。如本文所用，术语“摩尔当量”是指将与一摩尔铜相互作用的配体的摩尔数。

在步骤(b)中，加热反应混合物以形成如式 IV 的结构所描述的步骤(a)产物的 m-代盐：



IV 。

步骤（a）和（b）的反应温度优选介于约 40 和约 120℃之间，更优选介于约 75 和约 95℃之间。步骤(a)所需的时间通常为约 0.1 至约 1 小时。步骤(b)所需的时间通常为约 0.1 至约 1 小时。在反应期间，可能需要除氧。在任选的步骤(c)之前并且在步骤(d)中的酸化进行之前，通常使溶液冷却。

然后在步骤（d）中，使芳香酸的醚的 m-代盐与酸接触，以将其转化成羟基芳香酸产物。任何强度足以将 m-代盐质子化的酸均是适宜的。实例无限制地包括：盐酸、硫酸和磷酸。

在一个实施方案中，所述铜(I)或铜(II)源选自 CuBr、$CuBr_2$以及它们的混合物；所述配体选自 2,2',6,6'-四甲基-3,5-庚二酮、2,4-戊二酮和 2,3-戊二酮；并且铜(I)或铜(II)源与两摩尔当量的配体结合。

上述方法还能够有效并且高效地合成由所得的芳香酸的醚制备的产品，例如化合物、单体、或者它们的低聚物或聚合物。这些制备的物质可以具有酯官能团、醚官能团、酰胺官能团、酰亚胺官能团、咪唑官能团、噻唑官能团、噁唑官能团、碳酸酯官能团、丙烯酸酯官能团、环氧化物官能团、尿烷官能团、缩醛官能团、以及酸酐官能团中的一种或多种。

涉及使用本发明的方法制备的物质或此类物质的衍生物的代表性反应包括例如依照 US 3,047,536（其全文引入作为本文的一部分，以用于各种目的）中提出的方法，在氮气下并且在存在 0.1% $Zn_3(BO_3)_2$的情况下，在 1-甲基萘中由芳香酸的醚与二甘醇或三甘醇来制备聚酯。类似地，依照 US 3,227,680（其全文引入作为本文的一部分，以用于各种目的）中提出的方法，芳香酸的醚适合与二元酸和二元醇进行共聚以制备热稳定的聚酯，其中代表性的条件包括在存在四异丙氧基钛的情况下，在 200-250℃下，在丁醇中形成预聚物，然后在 280℃、0.08mmHg 的压力下进行固相聚合。

芳香酸的醚还可以如 US 5,674,969（其全文引入作为本文的一部分，以用于各种目的）中所公开，在减压下在缓慢加热至 100℃以上至约 180℃下，在强的多磷酸中与四氨基吡啶的三盐酸盐一水合物以缩聚方式聚合，然后在水中沉淀；或者如提交于 2005 年 3 月 28 日公布为 WO 2006/104974 的美国临时申请 60/665,737（其全文引入作为本文的一部分，以用于各种目的）中所公开，通过在约 50℃至约 110℃的温度下混合单体，然后在 145℃下形成低聚物，然后使低聚物在约 160℃至约 250℃下反应。如此产生的聚合物可以是吡啶并二咪唑-2,6-二基(2,5-二烷氧基对亚苯基)聚合物或吡啶并二咪唑-2,6-二基(2,5-二芳氧基对亚苯基)聚合物，例如聚(1,4-(2,5-二芳氧基)亚苯基-2,6-吡啶并[2,3-d: 5,6-d′]二咪唑)聚合物。然而，它们的吡啶并二咪唑部分可以被置换为苯并二咪唑、苯并二噻唑、苯并二噁唑、吡啶并二噻唑和吡啶并二噁唑中的任何一种或多种；并且它们的 2,5-二烷基对亚苯基部分可被间苯二甲酸、对苯二甲酸、2,5-吡啶二甲酸、2,6-萘二甲酸、4,4′-二苯基二甲酸、2,6-喹啉二甲酸、以及 2,6-双(4-羧基苯基)吡啶并二咪唑的一种或多种的烷基醚或芳基醚取代，其中依照本文所公开的方法生产这样的醚。

以此方式制备的聚合物可例如包含以下单元中的一种或多种：

吡啶并二咪唑-2,6-二基(2,5-二烷氧基对亚苯基)和/或吡啶并二咪唑-2,6-二基(2,5-二苯氧基对亚苯基)单元；

选自吡啶并二咪唑-2,6-二基(2,5-二甲氧基对亚苯基)、吡啶并二咪唑-2,6-二基(2,5-二乙氧基对亚苯基)、吡啶并二咪唑-2,6-二基(2,5-二丙氧基对亚苯基)、吡啶并二咪唑-2,6-二基(2,5-二丁氧基对亚苯基)和吡啶并二咪唑-2,6-二基(2,5-二苯氧基对亚苯基)的单元；

吡啶并二噻唑-2,6-二基(2,5-二烷氧基对亚苯基)和/或吡啶并二噻唑-2,6-二基(2,5-二苯氧基对亚苯基)单元；

选自吡啶并二噻唑-2,6-二基(2,5-二甲氧基对亚苯基)、吡啶并二噻唑-2,6-二基(2,5-二乙氧基对亚苯基)、吡啶并二噻唑-2,6-二基(2,5-二丙氧基对亚苯基)、吡啶并二噻唑-2,6-二基(2,5-二丁氧基对亚苯基)和吡啶并二噻唑-2,6-二基(2,5-二苯氧基对亚苯基)的单元；

吡啶并二噁唑-2,6-二基(2,5-二烷氧基对亚苯基)和/或吡啶并二噁唑-2,6-二基(2,5-二苯氧基对亚苯基)单元;

选自吡啶并二噁唑-2,6-二基(2,5-二甲氧基对亚苯基)、吡啶并二噁唑-2,6-二基(2,5-二乙氧基对亚苯基)、吡啶并二噁唑-2,6-二基(2,5-二丙氧基对亚苯基)、吡啶并二噁唑-2,6-二基(2,5-二丁氧基对亚苯基)和吡啶并二噁唑-2,6-二基(2,5-二苯氧基对亚苯基)的单元;

苯并二咪唑-2,6-二基(2,5-二烷氧基对亚苯基)和/或苯并二咪唑-2,6-二基(2,5-二苯氧基对亚苯基)单元;

选自苯并二咪唑-2,6-二基(2,5-二甲氧基对亚苯基)、苯并二咪唑-2,6-二基(2,5-二乙氧基对亚苯基)、苯并二咪唑-2,6-二基(2,5-二丙氧基对亚苯基)、苯并二咪唑-2,6-二基(2,5-二丁氧基对亚苯基)和苯并二咪唑-2,6-二基(2,5-二苯氧基对亚苯基)的单元;

苯并二噻唑-2,6-二基(2,5-二烷氧基对亚苯基)和/或苯并二噻唑-2,6-二基(2,5-二苯氧基对亚苯基)单元;

选自苯并二噻唑-2,6-二基(2,5-二甲氧基对亚苯基)、苯并二噻唑-2,6-二基(2,5-二乙氧基对亚苯基)、苯并二噻唑-2,6-二基(2,5-二丙氧基对亚苯基)、苯并二噻唑-2,6-二基(2,5-二丁氧基对亚苯基)和苯并二噻唑-2,6-二基(2,5-二苯氧基对亚苯基)的单元;

苯并二噁唑-2,6-二基(2,5-二烷氧基对亚苯基)和/或苯并二噁唑-2,6-二基(2,5-二苯氧基对亚苯基)单元;和/或

选自苯并二噁唑-2,6-二基(2,5-二甲氧基对亚苯基)、苯并二噁唑-2,6-二基(2,5-二乙氧基对亚苯基)、苯并二噁唑-2,6-二基(2,5-二丙氧基对亚苯基)、苯并二噁唑-2,6-二基(2,5-二丁氧基对亚苯基)和苯并二噁唑-2,6-二基(2,5-二苯氧基对亚苯基)的单元。

实施例

可以在如下所述的实验室实施例中看到本发明的方法的有利属性和效果。实施例所基于的这些方法的实施方案仅仅是代表性的,并且选择那些实施方案来例证本发明并不表示该实施例中未描述的条件、排列、方式、步骤、技术、构型或反应物就不适用于实施这些方法,也不表示该实施例中未描述的主题就被排除在所附权利要求及其等同物的范围之外。

如本文所用，术语“转化率”是指以理论量的分数或百分比表示的被用去的反应物量。术语产物 P 的“选择度”是指最终产物混合物中 P 的摩尔分数或摩尔百分比。因此，转化率乘以选择度等于 P 的最大“收率”；由于在诸如分离、处理、干燥等活动过程中样本会有损耗，因此实际收率或“净”收率一般将略微小于最大收率。术语“纯度”是指所指定的物质在所得的分离的样品中实际所占的百分比。

缩写的含义如下：“h”是指小时，“mL”是指毫升，“g”是指克，“MeOH”是指甲醇，“mg”是指毫克，“mmol”是指毫摩尔，并且“mol equiv”是指摩尔当量。

实施例 1

在无空气和水分的环境中，将 4.2g(77mmol) 甲氧化钠与 125g 无水甲醇结合，随后加入 5g (15mmol) 2,5-二溴对苯二甲酸。在氮气下，将 103mg (0.03mol equiv) $CuBr_2$ 和 0.06mol equiv 的 2,2',6,6'-四甲基-3,5-庚二酮单独结合，随后添加无水甲醇至溶解。然后添加该溶液以形成反应混合物。将该反应混合物保持在氮气气氛下，在搅拌下加热至回流 8h。在冷却后，将产物滤出，使用热的 MeOH 洗涤并且干燥以收获作为二钠盐的白色固体。然后将分离出的盐用盐酸酸化。纯度大于 95%，并且净分离的收率大于 90%。

本文所示的每个式描述了全部的不同的单独的化合物，其可通过以下方式以那样的式形成：（1）在指定范围内选择可变的基团、取代基或数值系数中的一种，而所有的其它可变的基团、取代基或数值系数保持不变，和（2）在指定范围内轮流进行同样的选择，以选择每种其它的可变的基团、取代基或数值系数，而其它的保持不变。除了在任何可变的基团、取代基或数值系数的指定范围内所做的由该范围所述的组的仅仅一员的选择之外，多个化合物还可以通过选择整组基团、取代基或数值系数中的一种以上但少于所有成员来进行描述。当在任何可变的基团、取代基或数值系数的指定范围内所做的选择是包含以下的子组：（i）由该范围所描述的整个组中成员的仅仅一员，或者（ii）整个组的一种以上但少于所有成员时，则所选择的成员是通过忽略掉整个组中未被选择以形成子组的那些成员而选择出来的。在此情况下，所述化合物或多个化合物可以被一

种或多种可变的基团、取代基或数值系数的定义来表征，其涉及指定范围的可变的整个组，但是其中形成子组时被忽略掉的成员不在整个组内。

凡在本文中表述某一数值范围之处，所述范围包括其端点，以及位于所述范围内的所有单个的整数和分数，并且还包括由其中那些端点和内部整数和分数的所有各种可能组合形成的每一个较窄范围，以在所述范围内形成更大数值群的子群，其程度如同每一个那些较窄范围均被明确表述一样。当本文中的数值范围被描述为大于某设定值时，所述范围仍然是有限的，并且被如本文所描述的发明上下文中可操作的值限定其上限。当本文中的数值范围被描述为小于某设定值时，所述范围仍然被非零值限定其下限。

在本说明书中，除非在使用情形下另外明确指明或相反指明，本文所述的含量、大小、范围以及其它量和特性，尤其是当由术语“约”修正时，可以但不必精确，并且还可接近和/或大于或小于（按需要）所述值，反映偏差、转换因子、四舍五入、测量误差等，并且将在所述值之外的在本发明上下文中具有与所述值相等功能和/或操作的那些值包括在所述值内。

应当理解，当将本发明的实施方案陈述或描述为包含、包括、含有、具有某些特征，以及由某些特征构成或组成时，除了明确地陈述或描述的特征之外，实施方案中可能出现一个或多个特征，除非陈述或描述明确地指出相反情况。然而，可以将本发明的可供选择的实施方案陈述或描述为基本上由某些特征组成，在该实施方案中，会在很大程度上改变该实施方案的操作原理或特点的实施方案特征是不存在于其中的。可以将本发明的另外的可供选择的实施方案陈述或描述为由某些特征组成，在该实施方案或其非实质变型中，仅存在具体陈述或描述的特征。