(54) Title: IMPROVED METHOD FOR THE PREPARATION OF 4-METHYLSULFONYL-BENOIC ACID DERIVATIVES AND INTERMEDIATES

(57) Abstract

This invention relates to an improved process for preparing a herbicidal intermediate compound having structural formula (I), wherein groups X are independently selected from C₁₋₆ alkyl, halo C₁₋₆ alkyl, CN, halogen, C₆₋₁₄ alkoxy, nitro, or S(O)ₓR² where R² is C₁₋₆ alkyl and m is 0, 1 or 2, n is O or an integer of from 1 to 4 and R² is hydrogen or C₁₋₆ alkyl and intermediate compounds.

$$\text{COOH}$$

$$\text{SO}_2\text{CH}_2\text{R}^2$$

$$\text{X}^n$$

(I)
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IMPROVED METHOD FOR THE PREPARATION OF 4-METHYLSULFONYL-BENZOIC ACID DERIVATIVES AND INTERMEDIATES

BACKGROUND OF THE INVENTION

The compounds 2-(chloro, bromo, nitro or methyl)-4-methylsulfonyl benzoic acid are intermediates that are useful in the preparation of a class of herbicidal compounds including 2-(2’chloro-4’-(methyisulfonyl-benzoyl)-1,3-cyclohexanedione. These herbicidal compounds and their preparation from the acid chloride or acid cyanide of the above 2-(chloro, bromo, nitro or methyl)-4-methylsulfonyl benzoic acid and a substituted or unsubstituted 1,3-cyclohexanedione are described in several patents including U.S. Patent 4,780,127.

U.S. Patent 4,692,545 teaches a method of preparing compounds having the structural formula:

\[
\text{COOR}^1 \quad \text{X'} \\
\text{SR} \\
\text{NO}_2
\]

wherein X’ is chlorine, bromine, or nitro and R and R\(^1\) are alkyl by reacting a compound having the structural formula:

\[
\text{COOR}^1 \quad \text{X'} \\
\text{NO}_2
\]
wherein X' and R¹ are as defined with an alkyl mercaptan (R-SH) including methyl mercaptan in the presence of an inorganic base and a polar aprotic solvent.

U.S. Patent 4,704,467 teaches an identical reaction except that it is run in the presence of an inorganic base and a phase transfer catalyst and a non-polar aprotic solvent. The alkyl esters of 2-(chloro, bromo or nitro)-4-methyl thio benzoic acid are easily oxidized to the corresponding alkyl ester of 2-chloro-4-methylsulfonyl benzoic acid by conventional techniques.

The esters of 2-(chloro, bromo, or nitro)-4-methyl thio benzoic acid are converted to the corresponding benzoic acids by known techniques.

A method of producing sulphonyl benzoic acids by oxidation of sulphonyl alkyl benzene derivatives is disclosed in WO 90/6302, WO 90/13537 and EP 505965-A. This method generally requires harsh reaction conditions. In WO 90/6302, a process is described which requires the use of strongly acid conditions (70% nitric acid) and temperatures of over 170°C. The processes described in WO 90/13537 and EP 505965-A required elevated pressure and a temperature of greater than 120°C.

SUMMARY OF THE INVENTION

One embodiment of this invention relates to an improved process for preparing an herbicidal intermediate compound having the structural formula (I):

\[
\text{COOH} \quad \text{(I)}
\]

\[
\begin{array}{c}
\text{(X)n} \\
\text{SO_2CH_2R^2}
\end{array}
\]
wherein groups X are independently selected from C\textsubscript{1-6} alkyl, halo C\textsubscript{1-6} alkyl, CN, halogen, C\textsubscript{1-6} alkoxy, nitro, or S(O)\textsubscript{m} R\textsuperscript{3}

where R\textsuperscript{3} is C\textsubscript{1-6} alkyl and m is 0, 1 or 2, n is 0 or an integer of from 1 to 4 and R\textsuperscript{2} is hydrogen or C\textsubscript{1-6} alkyl by the following reaction scheme:

Procurement by conventional means or purchase of a substituted phenol of formula (II):

\[
\begin{array}{c}
\text{OH} \\
\text{SO}_2\text{CH}_2\text{R}^2 \\
(X)_n
\end{array}
\]  

(II)

wherein R\textsuperscript{2}, X and n are as hereinbefore defined;

reacting the phenol of formula (II) with a sulfonic acid anhydride of formula (IIIA):

\[
O(SO_2R^4)_2
\]  

(IIIA)

wherein R\textsuperscript{4} is C\textsubscript{1-4} alkyl substituted by one or more halogen atoms such as fluorine, or with a compound of formula (IIIB)

\[
R^4\text{SO}_2Y
\]  

(IIIB)

wherein R\textsuperscript{4} is C\textsubscript{1-4} alkyl substituted by one or more halogen atoms such as fluorine, and Y is a halogen atom to produce a compound of formula (IV):

\[
\begin{array}{c}
\text{OSO}_2\text{R}^4 \\
\text{SO}_2\text{CH}_2\text{R}^2 \\
(X)_n
\end{array}
\]  

(IV)
wherein $R^2$, $R^4$, X and n are as hereinbefore defined. The reaction is suitably effected in a solvent at 0-100°C in the presence of a base;

reacting the compound of formula (IV) with carbon monoxide and water in the presence of a palladium salt, a compound containing a phosphine ligand, and a base to give the desired acid of formula (I). The reaction is preferably effected in a solvent at 25-150°C.

As used herein the term "alkyl" includes straight or branched chain groups such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, isobutyl and t-butyl. The term "halogen" includes chlorine, bromine, iodine and fluorine. The term "alkoxy" includes methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, sec-butoxy and t-butoxy. The term "halo-alkyl" includes the alkyl groups defined above in which one or more hydrogen is replaced by chloro, bromo, iodo or fluoro.

The reaction may also be performed using an alcohol $R^5\text{OH}$ where $R^5$ is $C_{1-6}$ alkyl in place of the water. The product of such a reaction would be the benzoate ester of formula

\[
\begin{align*}
\text{COOR}^5 \\
\text{SO}_2\text{CH}_2\text{R}^2
\end{align*}
\]

wherein $R^2$ and $R^5$ are as hereinbefore defined. The ester could then be hydrolysed to the required acid of formula (I) by conventional techniques.

The intermediate products of formula (IV) are novel and as such form a further aspect of the invention.
DETAILED DESCRIPTION OF THE INVENTION

The phenols of formula (II) may be made by conventional techniques from 4-halophenyl alkyl sulphones. Thus, for example, 3,4-dichlorophenyl methyl sulphone can be converted to 2-chloro-4-methylsulphonyl phenol by treatment with potassium hydroxide in a solvent such as DMSO at 100-189°C; or to 2-nitro-4-methylsulphonyl phenol by treatment with an excess of sodium nitrite in DMSO at 100-189°C.

The process preferably uses compounds of formula (IIIA) to react with compounds of formula (II).

A preferred anhydride of formula (IIIA) is trifluoromethanesulfonic anhydride (triflic anhydride). Suitable solvents are those such as halogenated alkanes or ethers. A preferred solvent is dichloromethane. Preferably the reaction is performed at 5-25°C.

The base may suitably be a tertiary amine or an alkaline earth or alkali metal carbonate, bicarbonate or hydroxide. A preferred base is pyridine.

In the reaction of the compound of formula (IV) with carbon monoxide, the solvent may suitably be any polar aprotic solvent such as acetonitrile, dioxane, DMSO or DMF. A preferred solvent is DMF. The reaction is preferably performed at 40-100°C. The base may suitably be any non-nucleophilic base such as sodium acetate or a tertiary amine. A preferred base is triethylamine.

Suitable palladium salts for use in the reaction are the salts of organic or mineral acids. Preferred salts are the acetate, carbonate and chloride salts. An especially preferred salt is palladium acetate. Suitable compounds containing phosphine ligands include triphenylphosphine, tri-
butylphosphine and preferably 1,3-bis(diphenylphosphino)propane.

The process of this invention can be better understood by reference to the following examples.

EXAMPLE 1

Preparation of 2-chloro-4-(methylsulfonyl)phenyl trifluoromethanesulfonate

2-(chloro-4-(methylsulfonyl) phenol (6.5 g), pyridine (5.1 ml) and dichloromethane (65 ml) were introduced into a 250 ml flask under a nitrogen atmosphere. After cooling to 5°C, trifluoromethanesulfonic anhydride (5.8 ml) was added dropwise over a 10 minute period. The mixture slowly warmed to 15°C. After 20 minutes, the mixture was washed with 200 ml water and then 200 ml concentrated hydrochloric acid. The organic solution was dried over magnesium sulphate and the solvent removed under reduced pressure to give the title compound as a white solid (10.35 g, 97.2% yield) m.p. 98-99°C.

EXAMPLE 2

Preparation of 2-chloro-4-(methylsulfonyl) benzoic acid

The triflate prepared in Example 1 (1 g), triethylamine (0.82 ml), 1,3-bis(diphenylphosphino)propane (0.07 g), palladium acetate (0.02 g), water (1.1 ml) and DMF (10 ml) were mixed together in a 50 ml flask. Carbon monoxide was bubbled through the mixture for 15 minutes which was then heated to 60°C for one hour. The required acid was produced in 38% yield.
What is claimed is:

1. A process for preparing a substituted benzoic acid of formula (I)

```
COOH
\[\text{(X)}_n\]
SO₂CH₂R²
```

wherein each X is independently selected from C_{1-6} alkyl, halo C_{1-6} alkyl, CN, halogen, C_{1-6} alkoxy, nitro, and S(O)ₘR³ where R³ is C_{1-6} alkyl and m is 0, 1 or 2, n is 0 or an integer of from 1 to 4 and R² is hydrogen or C_{1-6} alkyl, the process comprising

(a) reacting a compound of formula (II)

```
OH
\[\text{(X)}_n\]
SO₂CH₂R²
```

wherein R², X and n are as hereinbefore defined with a compound of formula (IIIA)

```
O(SO₂R⁴)₂
```

(IIIA)

wherein R⁴ is C_{1-4} alkyl substituted by one or more halogen atoms or with a compound of formula (IIIB)

```
R⁴SO₂Y
```

(IIIB)
wherein R\(^4\) is C\(_{1-4}\) alkyl substituted by one or more halogen atoms, and Y is a halogen atom to produce a compound of formula (IV):

\[
\text{OSO}_2\text{R}^4
\]

\[
\text{SO}_2\text{CH}_2\text{R}^2
\]

wherein R\(^2\), R\(^4\), X and n are as hereinbefore defined;

b) reacting the compound of formula (IV) with carbon monoxide and water in the presence of palladium salt, a compound containing a phosphine ligand and a base.

2. A process according to claim 1 wherein the compound of formula (II) is reacted with a compound of formula (IIIA).

3. A process according to claim 2 wherein the compound of formula (IIIA) is trifluoromethanesulphonic anhydride.

4. A process according to claim 1 wherein the compound containing a phosphine ligand is 1,3-bis(diphenylphosphino)propane.

5. A process according to claim 1 wherein the palladium salt is palladium acetate.

6. A process according to claim 1 wherein the compound of formula (I) is
7. A process for preparing a substituted benzoic acid of formula (I)

\[
\begin{align*}
\text{COOH} \\
\text{Cl} \\
\text{SO}_2\text{CH}_3
\end{align*}
\]

wherein each \( X \) is independently selected from \( \text{C}_1-6 \) alkyl, halo \( \text{C}_1-6 \) alkyl, CN, halogen, \( \text{C}_1-6 \) alkoxy, nitro, and \( S(0)\text{mR}^3 \) where \( R^3 \) is \( \text{C}_1-6 \) alkyl and \( m \) is 0, 1 or 2, \( n \) is 0 or an integer of from 1 to 4 and \( R^2 \) is hydrogen or \( \text{C}_1-6 \) alkyl, the process comprising

(a) reacting a compound of formula (II)

\[
\begin{align*}
\text{OH} \\
\text{(X)}_n \\
\text{SO}_2\text{CH}_2\text{R}^2
\end{align*}
\]

wherein \( R^2 \), \( X \) and \( n \) are as hereinbefore defined with a compound of formula (IIIA)

\[
\begin{align*}
\text{O(SO}_2\text{R}^4)_2
\end{align*}
\]

wherein \( R^4 \) is \( \text{C}_1-4 \) alkyl substituted by one or more halogen atoms or with a compound of formula (IIIB)
wherein \( R^4 \) is \( C_{1-4} \) alkyl substituted by one or more halogen atoms, and \( Y \) is a halogen atom to produce a compound of formula (IV):

\[
\text{OSO}_2^4 \text{R}^4
\]

\[
\text{(IV)}
\]

wherein \( R^2, R^4, X \) and \( n \) are as hereinbefore defined;

b) reacting the compound of formula (IV) with carbon monoxide and an alcohol of formula \( R^5\text{OH} \) where \( R^5 \) is \( C_{1-6} \) alkyl in the presence of a palladium salt, a compound containing a phosphine ligand and a base to produce a benzoate ester of the formula

\[
\text{COOR}^5
\]

and

c) hydrolyzing the benzoate ester.

8. A process according to claim 7 wherein the compound containing a phosphine ligand is 1,3-bis(diphenylphosphino)propane.

9. A process according to claim 8 wherein the palladium salt is palladium acetate.
10. A compound of formula (IV)

\[
\begin{array}{c}
\text{OSO}_2\text{CF}_3 \\
\text{X}_n \\
\text{SO}_2\text{CH}_2\text{R}^2
\end{array}
\] (IV)

wherein each X is independently selected from C\text{\textsubscript{1-6}} alkyl, halo C\text{\textsubscript{1-6}} alkyl, CN, halogen, C\text{\textsubscript{1-6}} alkoxy, nitro, and S(0)\text{\textsubscript{m}}R\text{\textsuperscript{3}} where R\text{\textsuperscript{3}} is C\text{\textsubscript{1-6}} alkyl and m is 0, 1 or 2, n is 0 or an integer of from 1 to 4 and R\text{\textsuperscript{2}} is hydrogen or C\text{\textsubscript{1-6}} alkyl.

11. A compound according to claim 10 wherein the compound is

\[
\begin{array}{c}
\text{OSO}_2\text{CF}_3 \\
\text{Cl} \\
\text{SO}_2\text{CH}_3
\end{array}
\]
### INTERNATIONAL SEARCH REPORT

**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)

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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)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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<td>A</td>
<td>WO,A,90 06302 (ICI AMERICAS) 14 June 1990 cited in the application see the whole document</td>
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<td>JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL COMMUNICATIONS, no.12, June 1987 LETCHWORTH GB, pages 904-905, R.E. DOLLE, ET AL.: 'Palladium catalysed alkoxy carbylation of phenols to benzoate esters' see the whole document</td>
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**Date of the actual completion of the international search**

14 December 1994

**Date of mailing of the international search report**

22.12.94

**Name and mailing address of the ISA**

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