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# PATENT SPECIFICATION

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## (54) A PROCESS FOR THE NUCLEAR CHLORINATION OF XYLENOLS

(71) We, SEITETSU KAGAKU CO., LTD., a corporation organised under the laws of Japan, of 346—1, Miyanishi, Harimacho, Kako-gun, Hyogo-ken, Japan, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed to be particularly described in and by the following statement:—

This invention relates to a process for the nuclear chlorination of xyenols.

Chlorinated xyenols are important on an industrial scale as antibacterial and antifungal agents, and as agricultural chemicals and their intermediates. The chlorinated xyenols resulting from nuclear chlorination of xyenols have various isomers, and *p*-chloroxylenols have so far proved much more useful than other isomers such as *o*-chloroxylenols. Accordingly, in nuclear chlorination on an industrial scale it is desired to improve the selectivity of the reaction so as to produce *p*-chloro isomers.

Heretofore, several processes have been proposed for the nuclear chlorination of xyenols. For example, Japanese Patent Publication No. 40882/72 discloses a process for the nuclear chlorination of xyenols in a hot aqueous hydrochloric acid solution, using cupric chloride as a chlorinating agent. Japanese Patent Publication No. 35344/74 likewise discloses a process for the nuclear chlorination of xyenols in a hot aqueous hydrochloric acid solution, using cupric chloride as a catalyst, while at the same time introducing chlorine gas to the reaction system.

The above two processes can produce *p*-chloroxylenols with a high degree of selectivity. However, these processes still have various problems to be solved in their application on an industrial scale. For example, there are problems concerning the materials used to construct the reaction vessel due to the use of hot hydrochloric acid, and problems of safety due to the use of oxygen for regenerating cupric chloride. In addition the complicated procedure necessary for regenerating cupric chloride is expensive and there are

problems associated with the formation of tarry materials due to the use of chlorine gas.

Generally, it can be said that selectivity in producing *p*-chloro isomers or *o*-chloro isomers in the nuclear chlorination of xyenols depends on the one hand upon the substituents present in the xyenols and, on the other hand, on the kinds of chlorinating agents used in the chlorination. For example, in the nuclear chlorination of 3,5-xylenol with molecular chlorine, the ratio of the product *p*-chloro-3,5-xylenol to the product *o*-chloro-3,5-xylenol, which will be hereinafter referred to as "P/O ratio", can amount to only 1.5, whereas the P/O ratio is increased to 6 when using the milder chlorinating agent, sulphuryl chloride. Thus, a process for selectively producing *p*-chloroxylenols by the nuclear chlorination of xyenols with sulphuryl chloride, thereby increasing the P/O ratio, has been preferred to date.

On the other hand, in the nuclear chlorination of *o*-cresol in an adjacent art field, it has been proposed to use a catalyst in addition to sulphuryl chloride as the chlorinating agent to further increase the P/O ratio. For example, British Patent Specification No. 948,601 discloses a process for the nuclear chlorination of *o*-cresol using a halide, especially a chloride, of aluminium, iron, tin or zinc as catalyst, and German Patent No. 1,203,275 discloses a process for the nuclear chlorination of *o*-cresol, using metallic iron, tin, zinc or aluminium, or their alcoholates.

We have now made extensive studies of processes for the nuclear chlorination of xyenols on an industrial scale, and we have found that it is possible to provide an industrial process having a very high selectivity to *p*-chloro isomers in very high yield and less problems as to safety and handling by carrying out chlorination in the presence of at least one metal chloride as chlorinating catalyst and, at the same time, at least one sulphur compound as promoter.

Accordingly, the present invention provides a process for the nuclear chlorination of

xylenols, which process comprises effecting nuclear chlorination with a chlorinating agent other than sulphur chloride in the presence of from 0.01 to 10% by weight based on the weight of the xylene of a metal chloride catalyst and from 0.001 to 1% by weight based on the weight of the xylene of at least one sulphur compound.

It is an unexpected fact that selectivity to *p*-chloro isomers and yields from xylenols can both be considerably increased, irrespectively of the xylenols used as starting material, by employing both a metal chloride and a sulphur compound, for the sulphur compound itself should act to lower the selectivity, and the metal chloride itself cannot always contribute to an increase in selectivity, but is usually effective only in increasing the yield, depending upon the xylene starting material.

The catalyst used in the process of the present invention is a metal chloride as usually employed in ionic-type chlorination reactions. Examples of such metal chlorides are ferric chloride, aluminium chloride, antimony trichloride, antimony pentachloride, tellurium chloride, stannic chloride, titanium tetrachloride, bismuth trichloride, mercuric chloride and zinc chloride.

The sulphur compound used in the process of the present invention may be an organic sulphur compound such as a thiophene, for example, thiophene itself, 2-methylthiophene and tetrahydrothiophene; and aliphatic mercaptan having from 1 to 15 carbon atoms, for example, methylmercaptan, ethylmercaptan, *n*-butylmercaptan, *t*-butylmercaptan, hexylmercaptan, and dodecylmercaptan; an organic sulphide, for example, dimethyl sulphide, dimethyl disulphide, diisobutyl sulphide, vinyl sulphide and benzyl sulphide; an organic sulfoxide, for example, dimethyl sulfoxide; carbon disulphide; thiourea; thioglycolic acid; L-cysteine; and L-cystine. Also, inorganic sulphur compounds may be used such as sulphuric acid, sodium thiosulphate, thionyl chloride, and antimony sulphide.

In the process of the present invention, it is necessary to use from 0.01 to 10% by weight of at least one metal chloride as catalyst, on the basis of the weight of xylene to be chlorinated. In the case of less than 0.01% by weight of the metal chloride, the catalytic effect is low, whereas in the case of more than 10% by weight, yields of non-preferred dichloro isomers is increased, resulting in reduction in yield of the desired monochloro isomers, particularly *p*-chloroxylenol.

It is also necessary to use from 0.001 to 1% by weight, of at least one organic or inorganic sulphur compound as promoter, again on the basis of the weight of xylene to be chlorinated. In the case of 0.001% by weight or more of the sulphur compound as the promoter, the addition effect becomes remarkable, increasing the yield of *p*-chloro isomers

and maintaining a high P/O ratio, whereas in the case of more than 1% by weight, the yield of di-chloro isomers is increased, and consequently *p*-chloroxylenol is decreased lowering the P/O ratio. Preferably the amount of sulphur compound employed is from 0.01 to 0.1% by weight based on xylene.

Xylenols which can be chlorinated in the process of the present invention include 2,3-xylene, 2,5-xylene, 2,6-xylene, 3,5-xylene. The process of the present invention is most suitable for the nuclear chlorination of the para position of 3,5-xylene, which is of industrial significance.

In the nuclear chlorination according to the present invention, any of chlorine gas, phosphorus pentachloride, and sulphuryl chloride may be used as the chlorinating agent. Especially when an approximately theoretical amount of sulphuryl chloride is used on the basis of the xylene, the nuclear chlorination proceeds mildly, suppressing production of dichloroxylenols, and other unwanted by-products.

The present process can be carried out with or without a solvent, but it is usually desirable to carry out the process after the xylene has been dissolved in a suitable solvent. Examples of solvents which may be used are chlorinated hydrocarbons such as carbon tetrachloride, trichloroethylene, perchloroethylene and dichlorobenzene.

Since some xylenols have a high melting point, a high temperature is inevitably required for their nuclear chlorination in the liquid state in the absence of a solvent. Thus, by the use of a solvent, nuclear chlorination can be carried out at a low temperature and in such instances can have the effect of preventing the formation of tarry by-products by avoiding reaction at a high temperature. The amount of solvent employed may vary within wide limits, but it is usually desirable to employ an amount which will completely dissolve the xylene.

Another advantage of using a solvent, obtained in most cases in the present invention, is deposition and precipitation of only *p*-chloroxylenols from solution owing to differences in solubility, and the resulting simple separation by filtering only the precipitated *p*-chloroxylenols. Since the precipitated *p*-chloroxylenols are crystallized out of the reaction mixture solution, substantially the same effect as that of recrystallization can be obtained, thus avoiding a further separate step of purification.

The present process can be carried out without any special restriction to reaction conditions merely by adding the required amounts of metal chloride catalyst and sulphur compound promoter to the xylene, and then introducing the desired chlorinating agent into the reaction system. Usually, it is advantageous to use a chlorinated hydrocarbon solvent, and to carry out the nuclear chlorination in

the solvent. In that case, the nuclear chlorination reaction is carried out at such a temperature as to keep the xyleneol starting material, the catalyst and the sulphur compound in a liquid state, preferably at a temperature of from 5° to 45°C., so that purification and separation of *p*-chloroxylenols as a main product will be facilitated. The nuclear chlorination reaction can be carried out under atmospheric pressure, usually without any difficulty, but also may be carried out either at elevated pressure or at a reduced pressure, if desired. The process may also be carried out either batch-wise or continuously.

According to the present invention *p*-chloroxylenols can be obtained with high selectivities in high yields, and furthermore since no oxygen is used in catalyst regeneration in contrast to the above described prior art processes, it is not necessary to take precautions against explosion of the xyleneol starting materials. Also, since hot hydrochloric acid is not used, it is unnecessary to employ special safety precautions or to use special acid-resistant materials to construct the reaction vessel. In addition, the fact that the present process can be carried out at temperatures approximating to room temperature is a great advantage in handling, and, furthermore, complicated steps for the necessary regeneration of cupric chloride can be avoided. Accordingly, the present invention can provide an improved and economical process.

Following is a description by way of example to illustrate processes in accordance with the invention, and including comparative Examples.

#### Example 1.

Into a four-necked separable flask having a capacity of 1,000 ml, provided with a stirrer, a thermometer, a nozzle for introducing a chlorinating agent, and a reflux cooler were charged 600 g of tetrachloroethylene and 122 g (1 mole) of 3,5-xyleneol. Then, 0.2 g (0.16% by weight on the basis of 3,5-xyleneol) of anhydrous ferric chloride as a catalyst and 0.6 g (0.49% by weight on the basis of 3,5-xyleneol) of thiophene as a promoter were added thereto, and the resulting mixture was sufficiently stirred and subjected to reaction while adding 135 g of sulphuryl chloride as a chlorinating agent drop by drop at a rate of 0.8 g/minute and keeping the temperature at 20°C. In the course of reaction, the product *p*-chloro-3,5-xyleneol started to deposit. After the completion of dropwise addition of sulphuryl chloride, the temperature of the reaction solution was raised to 65°C by means of a water bath to remove the dissolved acidic gas, and completely to dissolve the reaction product into the tetrachloroethylene. A portion of the resulting solution was sampled and analyzed by gas-chromatography. As a result, it was

found that the solution had the following composition excluding the solvent tetrachloroethylene and the catalyst thiophene:

|                               |               |
|-------------------------------|---------------|
| <i>p</i> -chloro-3,5-xyleneol | 89.4% by mole |
| <i>o</i> -chloro-3,5-xyleneol | 8.5% by mole  |
| 2,4-dichloro-3,5-xyleneol     | 0.4% by mole  |
| 3,5-xyleneol                  | 0.7% by mole  |
| P/O ratio=10.5                |               |

The reaction solution was slowly cooled to 15°C with stirring, the deposited crystals were filtered and dried, and 119 g of white crystals were obtained. The crystals had the following composition according to gas chromatographic analysis.

|                               |                 |
|-------------------------------|-----------------|
| <i>p</i> -chloro-3,5-xyleneol | 99.7% by weight |
| 3,5-xyleneol                  | 0.3% by weight  |

#### Comparative Example 1.

The chlorination reaction was carried out under the same conditions as in Example 1, except that only 0.8 g of anhydrous ferric chloride as the catalyst were used in the absence of the promoter. The resulting reaction solution had the following composition:

|                               |               |
|-------------------------------|---------------|
| <i>p</i> -chloro-3,5-xyleneol | 81.0% by mole |
| <i>o</i> -chloro-3,5-xyleneol | 14.9% by mole |
| 2,4-dichloro-3,5-xyleneol     | 2.0% by mole  |
| 3,5-xyleneol                  | 1.5% by mole  |
| Others                        | 0.6% by mole  |
| P/O ratio=5.43                |               |

106 g of crystals were obtained by the same crystallization operation as in Example 1 with a yield of 68.0%.

#### Example 2.

The chlorination reaction was carried out under the same conditions as in Example 1, using the same reaction apparatus as in Example 1, except that there were employed 600 g of carbon tetrachloride as the solvent, 1.55 g of anhydrous aluminium chloride as the catalyst and 0.01 g of dodecylmercaptan as the promoter. The resulting reaction solution had the following composition:

|                               |               |
|-------------------------------|---------------|
| <i>p</i> -chloro-3,5-xyleneol | 89.3% by mole |
| <i>o</i> -chloro-3,5-xyleneol | 7.0% by mole  |
| 2,4-dichloro-3,5-xyleneol     | 2.1% by mole  |
| 3,5-xyleneol                  | 1.0% by mole  |
| Others                        | 0.6% by mole  |
| P/O ratio=12.7                |               |

#### Comparative Example 2.

The chlorination reaction was carried out under the same conditions as in Example 2 except that only 1.6 g of anhydrous aluminium chloride was used as the catalyst. The resulting reaction solution had the following composition:

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4

1,505,321

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*p*-chloro-3,5-xyleneol 83.0% by mole  
*o*-chloro-3,5-xyleneol 12.0% by mole  
 2,4-dichloro-3,5-xyleneol 3.0% by mole  
 3,5-xyleneol 1.0% by mole  
 Others 0.8% by mole  
 P/O ratio=6.80

Example 3.  
 The chlorination reaction was carried out under the same conditions as in Example 1, but with variations in the kind of promoters used and in the amount of catalyst as shown in Table 1 below. 10

TABLE 1

| Run No. | Metal chloride as catalyst |     | Sulphur compound as promoter |        |
|---------|----------------------------|-----|------------------------------|--------|
| 3-1     | Anhydrous ferric chloride  | 1 g | Dodecylmercaptan             | 0.02 g |
| 3-2     | "                          | "   | 98% Sulphuric acid           | 0.8 g  |
| 3-3     | "                          | "   | t-Butylmercaptan             | 0.3 g  |

The resulting reaction solutions had the compositions shown in Table 2 below.

TABLE 2

Composition of reaction solution (% by mole)

| Run No. | <i>p</i> -Chloro isomer | <i>o</i> -Chloro isomer | Dichloro isomer | 3,5-xyleneol | Others | P/O  |
|---------|-------------------------|-------------------------|-----------------|--------------|--------|------|
| 3-1     | 90.3                    | 6.4                     | 0.2             | 2.8          | 0.3    | 14.1 |
| 3-2     | 86.7                    | 10.0                    | 1.8             | 0.8          | 0.7    | 8.7  |
| 3-3     | 88.8                    | 8.3                     | 1.3             | 1.0          | 0.6    | 10.7 |

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 Example 4.  
 The chlorination reaction was carried out under the same conditions as in Example 1, using the same reaction apparatus as in Example 1, except that there were employed, 600 g of *o*-dichlorobenzene as the solvent, 8.5 g of titanium tetrachloride as the catalyst, and 0.02 g of dodecylmercaptan as the promoter. The resulting reaction solution had the following composition:

25  
 30  
*p*-chloro isomer 91.5% by mole  
*o*-chloro isomer 6.3% by mole  
 dichloro isomer 1.3% by mole  
 3,5-xyleneol 0.3% by mole  
 Others 0.6% by mole  
 P/O ratio=14.4

WHAT WE CLAIM IS:—

35  
 1. A process for the nuclear chlorination of xyleneols, which process comprises effecting nuclear chlorination with a chlorinating agent other than sulphur chloride in the presence

of from 0.01 to 10% by weight based on the weight of the xyleneol of a metal chloride catalyst and from 0.001 to 1% by weight based on the weight of the xyleneol of at least one sulphur compound. 40

2. A process according to claim 1, wherein the metal chloride catalyst is ferric chloride, aluminium chloride, antimony trichloride, antimony pentachloride, tellurium chloride, stannic chloride, titanium tetrachloride, bismuth trichloride, mercuric chloride and zinc chloride. 45

3. A process according to claim 1 or claim 2, wherein the sulphur compound is an aliphatic mercaptan having from 1 to 15 carbon atoms. 50

4. A process according to claim 3, wherein the aliphatic mercaptan is dodecylmercaptan or butylmercaptan. 55

5. A process according to claim 1 or claim 2, wherein the sulphur compound is a thiophene or sulphuric acid.

6. A process according to claim 1 or claim

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1,505,321

5 *p*-chloro-3,5-xyleneol 83.0% by mole  
*o*-chloro-3,5-xyleneol 12.0% by mole  
 2,4-dichloro-3,5-xyleneol 3.0% by mole  
 3,5-xyleneol 1.0% by mole  
 Others 0.8% by mole  
 P/O ratio=6.80

Example 3.

The chlorination reaction was carried out under the same conditions as in Example 1, but with variations in the kind of promoters used and in the amount of catalyst as shown in Table 1 below.

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TABLE 1

| Run No. | Metal chloride as catalyst |     | Sulphur compound as promoter |        |
|---------|----------------------------|-----|------------------------------|--------|
| 3-1     | Anhydrous ferric chloride  | 1 g | Dodecylmercaptan             | 0.02 g |
| 3-2     | "                          | "   | 98% Sulphuric acid           | 0.8 g  |
| 3-3     | "                          | "   | t-Butylmercaptan             | 0.3 g  |

The resulting reaction solutions had the compositions shown in Table 2 below.

TABLE 2

Composition of reaction solution (% by mole)

| Run No. | <i>p</i> -Chloro isomer | <i>o</i> -Chloro isomer | Dichloro isomer | 3,5-xyleneol | Others | P/O  |
|---------|-------------------------|-------------------------|-----------------|--------------|--------|------|
| 3-1     | 90.3                    | 6.4                     | 0.2             | 2.8          | 0.3    | 14.1 |
| 3-2     | 86.7                    | 10.0                    | 1.8             | 0.8          | 0.7    | 8.7  |
| 3-3     | 88.8                    | 8.3                     | 1.3             | 1.0          | 0.6    | 10.7 |

Example 4.

20 The chlorination reaction was carried out under the same conditions as in Example 1, using the same reaction apparatus as in Example 1, except that there were employed, 600 g of *o*-dichlorobenzene as the solvent, 8.5 g of titanium tetrachloride as the catalyst, and 0.02 g of dodecylmercaptan as the promoter. The resulting reaction solution had the following composition:

25 *p*-chloro isomer 91.5% by mole  
*o*-chloro isomer 6.3% by mole  
 dichloro isomer 1.3% by mole  
 3,5-xyleneol 0.3% by mole  
 Others 0.6% by mole  
 P/O ratio=14.4

WHAT WE CLAIM IS:—

35 1. A process for the nuclear chlorination of xyleneols, which process comprises effecting nuclear chlorination with a chlorinating agent other than sulphur chloride in the presence

of from 0.01 to 10% by weight based on the weight of the xyleneol of a metal chloride catalyst and from 0.001 to 1% by weight based on the weight of the xyleneol of at least one sulphur compound.

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2. A process according to claim 1, wherein the metal chloride catalyst is ferric chloride, aluminium chloride, antimony trichloride, antimony pentachloride, tellurium chloride, stannic chloride, titanium tetrachloride, bismuth trichloride, mercuric chloride and zinc chloride.

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3. A process according to claim 1 or claim 2, wherein the sulphur compound is an aliphatic mercaptan having from 1 to 15 carbon atoms.

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4. A process according to claim 3, wherein the aliphatic mercaptan is dodecylmercaptan or butylmercaptan.

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5. A process according to claim 1 or claim 2, wherein the sulphur compound is a thiophene or sulphuric acid.

6. A process according to claim 1 or claim



1,505,321

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- 2, wherein the sulphur compound is an organic sulphide, dimethyl sulphoxide, carbon disulphide, thiourea, thioglycolic acid, L-cysteine or L-cystine. 25
- 5 7. A process according to claim 1 or claim 2 wherein the sulphur compound is sodium thiosulphate, thionyl chloride or antimony sulphide. 30
- 10 8. A process according to any one of the preceding claims, wherein the sulphur compound is employed in an amount of from 0.01 to 0.1% by weight based on the weight of the xlenol. 35
- 15 9. A process according to any one of the preceding claims, wherein the xlenol is 3,5-xlenol. 40
- 20 10. A process according to any one of the preceding claims, wherein the chlorinating agent is chlorine gas or phosphorus pentachloride.
11. A process according to any one of claims 1 to 9 wherein the chlorinating agent is sulphuryl chloride.
12. A process according to any one of the preceding claims, wherein the nuclear chlorination is carried out in a chlorinated hydrocarbon solvent.
13. A process according to claim 12, wherein the solvent is carbon tetrachloride, trichloroethylene, perchloroethylene or dichlorobenzene.
14. A process according to claim 12 or claim 13 wherein the nuclear chlorination is carried out at a temperature of from 5° to 45°C.
15. A process according to claim 1 substantially as hereinbefore described with reference to any one of Examples 1 to 4.
16. A chlorinated xlenol when produced by a process according to any one of the preceding claims.

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