

PATENT SPECIFICATION

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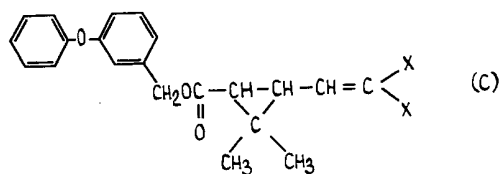
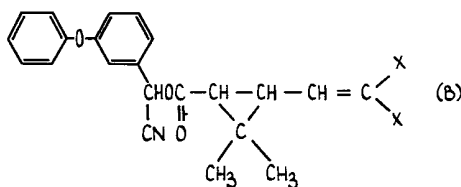
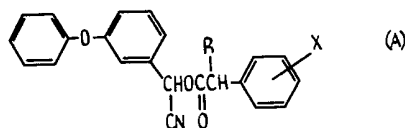


(54) PURIFICATION OF 3-PHENOXYBENZALDEHYDE

(71) We, SUMITOMO CHEMICAL COMPANY LIMITED, a corporation organized under the laws of Japan, of 15, Kitahamo-5-chome, Higashi-ku Osaka, 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 purifying 3-phenoxybenzaldehyde, and provides a said process which includes reacting crude 3-phenoxybenzaldehyde with an alkali metal—or ammonium-bisulfite or alkali metal—or ammonium-metabisulfite, in the presence of a catalyst, which catalyst is an organic quaternary ammonium salt, an inorganic acid salt of an organic tertiary amine, or a macrocyclic polyether, isolating the resulting 3-phenoxybenzaldehyde alkali metal—or ammonium-bisulfite adduct, and decomposing it by heating, or treating it with an acid or a base.

3-Phenoxybenzaldehyde purified by a process embodying the invention is an important intermediate in the synthesis of α -cyano-3-phenoxybenzyl α' -substituted-phenylacetates represented by the formula (A) [Japanese Patent Application "Kokai" (Laid Open) No. 26,425/74 and No. 126,826/74], α -cyano-3-phenoxybenzyl cyclopropanecarboxylates represented by the formula (B) [Nature, 248, 710 (1974)], 3-phenoxybenzyl chrysanthemates represented by the formula (C) (Japanese Patent Publication No. 21,473/71) and the like which have an excellent insecticidal activity.



Synthesis of 3-phenoxybenzaldehyde can be carried out in various ways according to the general methods for producing aldehydes, but the product is not sufficiently pure for use as an intermediate in synthesizing the above various insecticidal compounds. For instance, the reaction product obtained by the Sommelet reaction from 3-phenoxytoluene having a halogen atom substituted in the side chain and urotropin contains from 75% to 80% of 3-phenoxybenzaldehyde and 20% or more of non-aldehydeic compounds (Reference Example 1). Accordingly, in order for the reaction product to be usable as an intermediate in synthesizing the above useful insecticidal compounds, a commercially feasible process for its purification is prerequisite.

A conventional process for purifying an aldehyde comprises converting the aldehyde into its aldehyde bisulfite adduct, separating it from non-aldehydeic compounds, and decomposing it to recover the aldehyde [F. H. Allen and G. W. Lewbner, *Org. Synth.*, Coll. Vol. 4 866 (1963); G. B. Bochman, *ibid.*, 2, 323 (1943)]. When dealing with a strongly hydrophobic aldehyde such as 3-phenoxybenzaldehyde (which is the desired compound to be produced by the process of this invention) the reaction conditions as described below are considered to be necessary.

In converting a water-insoluble aldehyde into its aldehyde bisulfite adduct, the reaction system generally consists of substantially two phases, this being because an alkali metal- or ammonium-bisulfite is water-soluble but is not soluble in organic solvents. Accordingly, when it is desired to obtain the reaction product with a reasonable reaction rate and in a high yield, a measure frequently taken is to add to the reaction system an organic solvent which is easily mixable with water for example an alcohol so that the reactants come into contact readily with one another. When such an organic solvent is used, the intended reaction product is isolated, after removal of the solvent by distillation, by dissolving the reaction mixture in water (when producing a water-soluble aldehyde bisulfite adduct) and washing the aqueous layer with a water-insoluble solvent to remove oily non-aldehydeic compounds; or, when producing a crystalline aldehyde bisulfite adduct, by cooling the aqueous layer to precipitate the aldehyde bisulfite adduct which is then recovered by filtration. Moreover, since this reaction is reversible, a large amount of alkali metal- or ammonium-bisulfite must be added to shift the equilibrium, $\text{aldehyde} + \text{alkali metal- or ammonium-bisulfite} \rightleftharpoons \text{aldehyde bisulfite adduct}$, to the right-hand side. In many cases, the amount, in moles, of alkali metal- or ammonium-bisulfite used must be from 2 to 3 times the stoichiometric quantity or even more.

On applying the above-mentioned conventional purification process using a bisulfite to the purification of 3-phenoxybenzaldehyde, we have found that certain difficulties accompany the process. The procedure which we adopted and the difficulties encountered are now described.

A crude aldehyde (containing about 80% of 3-phenoxybenzaldehyde and 20% of non-aldehydeic compounds) was dissolved in toluene or chlorobenzene contacted with an aqueous solution of sodium bisulfite (3 molar-equivalents to one of the aldehyde) for a long period of time with vigorous stirring and application of heat to obtain only the unreacted starting materials and none of the aldehyde bisulfite adduct (Reference Example 2). When a water-soluble alcohol was used as an auxiliary solvent, as shown in Reference Example 3, conversion to the aldehyde bisulfite adduct was substantially improved but not sufficiently and a large amount of unreacted 3-phenoxybenzaldehyde was recovered in a very impure state from the filtrate. In this case, moreover, filterability of the crystals of the sodium bisulfite adduct was too poor for the satisfactory isolation of the product by filtration on a commercial scale. In addition, a decreased yield of the isolated product, is obtained from increased quantities of free aldehyde due to the significant solubility of the adduct in alcohol unfavourably shifting the equilibrium. The disadvantages listed above bring about much difficulty in the commercialization of this conventional purification process.

We conducted studies to overcome these difficulties and found, unexpectedly, that by using an organic quaternary ammonium salt, an inorganic acid salt of an organic tertiary amine, or a macrocyclic polyether as a catalyst, a 3-phenoxybenzaldehyde bisulfite adduct of high purity and in easily filterable form could be obtained in a high yield under mild conditions without using an auxiliary solvent such as an alcohol.

Although research into the use of organic quaternary ammonium salts and macrocyclic polyethers as phase transfer catalysts has become very active in recent

years, no report on the addition reaction of an aldehyde and bisulfite as in the process of the present invention appears to have been published.

In a preferred process embodying the present invention the reaction system comprises two phases, an aqueous one and an organic one. The amount of water to be used is not particularly limited. It is sufficient to use a minimal amount of water required for dissolving an alkali metal- or ammonium-bisulfite or metabisulfite, or to use a suitable amount of water for keeping the crystals, which precipitate during the course of reaction, in a slurry form of suitable fluidity.

Since crude 3-phenoxybenzaldehyde is a liquid, solvents are not necessarily used. However, it is not objectionable to use a solvent to facilitate the removal of impurities in filtering the bisulfite adduct. The solvent used for providing the organic phase of the reaction medium is preferably one which does not contain, as functional group, either a ketone or aldehyde group and which is not easily dissolved in water. Examples of suitable solvents are aromatic hydrocarbons such as benzene, toluene, xylene and ethylbenzene; halogenated aromatic hydrocarbons such as fluorobenzene, chlorobenzene, bromobenzene and dichlorobenzene; aliphatic or cycloaliphatic hydrocarbons such as pentane, hexane, heptane and cyclohexane; halogenated aliphatic hydrocarbons such as dichloromethane, chloroform, carbon tetrachloride, 1,1-dichloroethane, 1,2-difluoroethane, 1,1,1-trichloroethane, perchloroethylene, pentachloroethane, bromoform, 1,2-dibromoethane and 1,1,2,2-tetrabromoethane; and fatty acid esters such as ethyl acetate. Mixtures of these solvents may also be used.

Because of the very low solubility either in water or in any of the above solvents, almost all of the 3-phenoxybenzaldehyde bisulfite adduct formed by the reaction crystallizes out of the reaction medium and shifts the reaction equilibrium to favour the formation of adduct. Accordingly, the amount of an alkali metal- or ammonium-bisulfite which need be used as starting material can be greatly reduced as compared with the corresponding conventional process. An approximately quantitative yield of the adduct may be obtained by using from 1.0 to 1.5 moles of an alkali metal- or ammonium-bisulfite (or half this amount in the case of a metabisulfite) for 1 mole of 3-phenoxybenzaldehyde.

Alkali metal- or ammonium-bisulfite or metabisulfites which can be employed in processes embodying the present invention include sodium bisulfite, potassium bisulfite, sodium metabisulfite, potassium metabisulfite and ammonium bisulfite.

Examples of compounds which can be used as catalysts in the process are listed below:

Organic quaternary ammonium salts represented by the general formula $R_1R_2R_3R_4NX$ (where R_1 represents an alkyl group having from 1 to 20 carbon atoms inclusive and which may be branched, a phenyl group, a benzyl group or a 3-phenoxybenzyl group; R_2 , R_3 and R_4 , which may be the same or different, each represents an alkyl group having from 1 to 12 carbon atoms inclusive and which may be branched; and X represents a halogen atom or hydroxyl group).

Examples of these are chlorides, bromides, iodides or hydroxides of benzyltriethylammonium, benzyltrimethylammonium, benzyltripropylammonium, phenyltriethylammonium, tetrabutylammonium, tetrapropylammonium, tetraethylammonium, tetramethylammonium, triethylpropylammonium, 3-phenoxybenzyltriethylammonium, and cetyltrimethylammonium.

Inorganic acid salts of organic tertiary amines.

Examples of these are hydrochlorides, hydrobromides, sulfates, nitrates, sulfites, bisulfates, or bisulfites of triethylamine, trimethylamine, triethanolamine, N-methylpyrrolidine and triethylenediamine.

Macrocyclic polyethers are described in an article by A. C. Knipe, J. Chem. Education 53, 618 (1976) and are generally regarded as being cyclic polyethers having at least four oxygen atoms in the polyether ring [C. J. Pedersen, J. Amer. Chem. Soc. (1967), 89, 7017].

Examples of these are 2,3,11,12-dibenzo-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene(dibenzo-18-crown-6), 2,3,11,12-dicyclohexyl-1,4,7,10,13,16-hexaoxacyclooctadecane (dicyclohexyl-18-crown-6), 4,7,13,18-tetraoxa-1,10-diazabicyclo [8,5,5]eicosane, 4,7,13,16,21-pentaoxa-1,10-diazabicyclo [8,8,5] tricosane, 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo [8,8,8] hexacosane, and 5,6-benzo-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo [8,8,8]-hexacosane.

The amount of these catalysts to be added may be selected from the range of from 1 to 300 millimole-equivalents inclusive per molar equivalent of the reactant aldehyde, but for improved reaction efficiency it is preferably selected from the

range of from 10 to 100 millimole-equivalents inclusive.

The reaction can be carried out at a temperature of from about 0° to 80°C, but is usually carried out under mild temperature conditions of from 10° to 60°C.

The 3-phenoxybenzaldehyde bisulfite adduct formed by the reaction crystallizes in an easily filterable form and can be collected by suitable means such as vacuum filtration, pressure filtration or centrifugal filtration. If necessary, small amounts of non-aldehydic organic substances adhering to the crystals can be removed with an organic solvent.

The 3-phenoxybenzaldehyde alkali metal- or ammonium-bisulfite adducts formed by processes embodying this invention are decomposed to yield purified 3-phenoxybenzaldehyde by treating them in a known manner, such as by treating them with inorganic acids, for example, hydrochloric, sulfuric, nitric, sulfurous, and phosphoric acids, organic acids, for example, acetic acid and formic acid, or bases, for example, alkali metal hydroxides, e.g. sodium hydroxide, potassium hydroxide, and ammonium hydroxide, and carbonates, e.g. sodium carbonate, potassium carbonate, sodium bicarbonate, and potassium bicarbonate [F. H. Allen and D. W. Lewbner, *Org. Synth.*, Coll. Vol. 4, 866 (1963); G. B. Bochman, *ibid.* 2, 323 (1943)].

As described above, compared with the above mentioned conventional process which requires the troublesome operations of removing the alcohol by distillation and recovering it, processes embodying the invention make it possible to reduce the amount of alkali metal- or ammonium bisulfite employed and to select freely the reaction medium. Further, when using processes embodying this invention, owing to the favourable volume utilization factor of the equipment which can be attained, highly purified 3-phenoxybenzaldehyde can be produced more simply and economically on a commercial scale.

Processes embodying the invention are illustrated in more detail with reference to Examples thereof and by comparison with Reference Examples illustrating conventional processes.

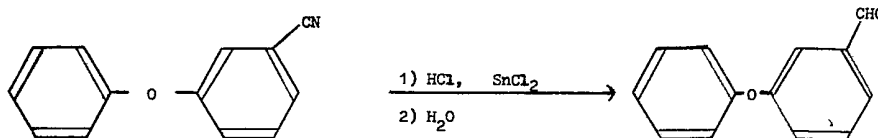
Reference Example 1

[S. J. Angyl, *Organic Reactions*, Vol. 8, 197 (1954)]

(1) To 82 g of 3-phenoxybenzyl bromide-hexamethylenetetramine addition product (0.19 mole), were added 70 ml of glacial acetic and 70 ml of water and the mixture was refluxed for 8 hours with heating. After being cooled to room temperature, the reaction mixture was extracted twice with 60 ml of dichloromethane and the organic layer was washed with 50 ml of water, freed from the dichloromethane by distillation to obtain 38 g of a crude product containing 77.0% of 3-phenoxybenzaldehyde (as determined by GC-MS method using dibutyl terephthalate as internal standard).

(2) A known process for preparing 3-phenoxybenzaldehyde [G. Lock and F. H. Kempter, *Monatsh.*, 67, 24 (1935)].

The reaction proceeds according to the following scheme:



Hydrogen chloride was introduced until saturation into a solution of 37.9 g of anhydrous stannous chloride (0.2 mole) in 200 ml of anhydrous ether. To the resulting solution, was added 9.5 g of 3-phenoxybenzonitrile (0.1 mole) and the mixture was stirred for 10 hours at room temperature. After addition of 200 ml of water and thorough stirring, the insoluble matter was removed by filtration. The filtrate was separated and the ether layer was further washed three times with 50 ml of water. After removal of the ether by distillation, the residue was distilled to obtain 8.5 g of crude 3-phenoxybenzaldehyde boiling at 100° to 115°C/0.45 mmHg which contained 71.4% of 3-phenoxybenzaldehyde.

Reference Example 2

To 280 g of a 20% aqueous solution of sodium bisulfite (0.538 mole of sodium bisulfite), was added dropwise a solution containing 45.0 g of crude 3-phenoxybenzaldehyde (79.7% purity (0.181 mole of 3-phenoxybenzaldehyde) and containing no other aldehydic compounds) in 90 g of chlorobenzene, taking 2 hours with stirring at room temperature. Because no crystals were deposited from the reaction medium the reaction temperature was elevated to 60°C and stirring was continued at this temperature for further 5 hours. No crystal deposit was observed. The reaction was discontinued and the reaction solution was separated. The organic layer was freed from the chlorobenzene to recover 44.3 g of crude 3-phenoxybenzaldehyde of 77.8% purity.

Reference Example 3

To a solution prepared by mixing 160 g of a 15% aqueous solution of sodium bisulfite (0.231 mole of sodium bisulfite) and 160 ml of methanol, was added 14.0 g of an organic mixture containing 54.0% of 3-phenoxybenzaldehyde (0.038 mole of 3-phenoxybenzaldehyde) and no other aldehydic compounds. The resulting mixture was stirred at 70°C for 4 hours. The reaction mixture was freed from the methanol by distillation and cooled to room temperature. The precipitated white crystals were collected by filtration and washed three times with 30 ml of ethanol to obtain 10.9 g (94.8% yield) of white crystals. After removal of the ethanol, the filtrate was extracted with 50 ml of ethyl acetate and the aqueous layer was removed. On removing the ethyl acetate by distillation, 7.1 g of a concentrated residue containing 12.0% of 3-phenoxybenzaldehyde were obtained.

To a mixture comprising 40 g of a 5% aqueous sodium hydroxide solution and 15 ml of toluene, was added 10.0 g of the 3-phenoxybenzaldehyde-sodium bisulfite adduct obtained above. The resulting mixture was stirred for 2 hours at room temperature under a nitrogen stream. After settling, the aqueous layer was removed. The toluene layer was washed with 5 ml of 1% hydrochloric acid and then with an aqueous sodium chloride solution. After removal of the toluene by distillation, 6.0 g (90.9% yield) of a colourless, clear liquid containing 96.7% of 3-phenoxybenzaldehyde were obtained.

Example 1

To a solution prepared by dissolving 2.3 g of benzyltriethylammonium chloride (0.010 mole) in 123.3 g of a 20% aqueous solution of sodium bisulfite (0.237 mole of sodium bisulfite), while being stirred at room temperature, was added dropwise taking 2 hours, a solution prepared by dissolving 45.0 g of crude 3-phenoxybenzaldehyde (79.7% purity (0.181 mole of 3-phenoxybenzaldehyde) and containing no other aldehydic compounds) in 90 g of chlorobenzene. Immediately after commencement of the dropwise addition, white crystals began to precipitate out of the reaction medium. After completion of the dropwise addition, stirring was continued for further two hours. The crystals were then collected by filtration, washed three times with 45 g of chlorobenzene, and dried to obtain 53.0 g (98.3% yield) of 3-phenoxybenzaldehyde-sodium bisulfite adduct.

To a mixture comprising 158.8 g of a 5% aqueous sodium hydroxide solution and 60 ml of toluene, was added 40.0 g of the 3-phenoxybenzaldehyde sodium bisulfite adduct (0.132 mole) obtained above. The resulting mixture was stirred for 2 hours at room temperature under a nitrogen stream. After settling and removal of the aqueous layer, the toluene layer was washed with 20 ml of 1% hydrochloric acid and then with an aqueous sodium chloride solution. On removal of the toluene, 25.4 g (96.9% yield) of a colourless, clear liquid containing 98.5% of 3-phenoxybenzaldehyde were obtained.

Example 2

To a solution prepared by dissolving 1.3 g of triethylamine hydrochloride (0.009 mole) in 69.2 g of a 35.8% aqueous solution of sodium bisulfite (0.238 mole of sodium bisulfite) while being stirred at room temperature, was added dropwise taking 2 hours, a solution prepared by dissolving 50 g of crude 3-phenoxybenzaldehyde (72.5% purity (0.183 mole of 3-phenoxybenzaldehyde) and containing no other aldehydic compounds) in 80 g of toluene. Immediately after commencement of the dropwise addition, white crystals began to precipitate out of

the reaction medium. After completion of the addition, stirring was continued for further 2 hours. The crystals were collected by filtration, washed three times with 50 g of toluene, and dried to obtain 54.5 g (98.5 % yield) of 3-phenoxybenzaldehyde sodium bisulfite adduct.

- 5 To 40.0 g of the above adduct (0.132 mole), was added 90 g of water. To the
resulting mixture, while being kept under reflux by heating, was added dropwise,
taking one hour, 15 g of 50% sulfuric acid. The sulfur dioxide evolved during the
reaction was removed by absorption with a 10% aqueous sodium hydroxide
10 solution. After completion of the dropwise addition, refluxing was continued for 30
minutes. The reaction mixture was cooled to room temperature and extracted with
50 ml of toluene. The toluene layer was washed twice with 15 ml of water and
concentrated to obtain 25.2 g (96.0% yield) of a colourless, clear liquid containing
98.1% of 3-phenoxybenzaldehyde.
- 15 In the following Table are shown other Examples, wherein various organic
solvents, catalysts, and bisulfites or metabisulfites were employed, other conditions
having been similar to those in Example 1.

Example No.	Solvent	Catalyst	Molar ratio of catalyst *1)	Bisulfite or meta-bisulfite	Molar ratio of bisulfite or meta-bisulfite *1)	Yield of adduct (%)	Purity *2)
3	Xylene	Tetrabutylammonium bromide	0.05	NaHSO ₃	1.2	96.8	99.1
4	Benzene	Cetyltrimethylammonium chloride	0.05	KHSO ₃	1.3	99.1	98.2
5	Heptane	Dibenzo-18-crown-6	0.04	NaHSO ₃	1.4	98.3	98.4
6	Perchloroethylene	4,7,13,18-Tetraoxa-1,10-diazabicyclo-[8,8,5]eicosane	0.04	Na ₂ S ₂ O ₅	0.7	97.0	98.8
7	None	Benzyltrimethylammonium bromide	0.03	NaHSO ₃	1.3	97.3	97.5
8	Benzene	Tetraethylammonium bromide	0.01	NaHSO ₃	1.4	97.3	98.2
9	Toluene/heptane (1/1)	Benzyltriethylammonium chloride	0.05	NaHSO ₃	1.4	99.7	97.9
10	Chloroform	Benzyltriethylammonium hydroxide	0.05	Na ₂ S ₂ O ₅	0.6	97.2	98.3
11	Chlorobenzene	3-Phenoxybenzyltriethylammonium bromide	0.03	Na ₂ S ₂ O ₅	0.7	98.6	97.9
12 *3)	Toluene	N-methylpyrrolidine sulfate	0.08	NH ₄ HSO ₃	1.5	98.5	97.3
13	Xylene	Triethylamine bisulfite	0.03	KHSO ₃	1.4	99.0	98.0
14	1,2-Dichloroethane	Dodecylbenzyl-diethylammonium chloride	0.02	Na ₂ S ₂ O ₅	0.7	97.3	98.0
15 *4)	Benzene/ethyl acetate (1/1)	Tetrapropylammonium bromide	0.10	Na ₂ S ₂ O ₅	0.7	97.9	97.8
16 *5)	Chlorobenzene/perchloroethylene (2/1)	Phenyltriethylammonium iodide	0.06	KHSO ₃	1.3	98.5	97.9

Note:—

- 1) Molar ratios of catalysts and bisulfite or metabisulfite are based on 3-phenoxybenzaldehyde.
- 2) Purity of the 3-phenoxybenzaldehyde obtained by decomposition of the adduct in a conventional manner.
- 3) Reaction temperature in Example 12 was 45°C.
- 4) Reaction temperature in Example 15 was 10°C.
- 5) Reaction temperature in Example 16 was 60°C.

WHAT WE CLAIM IS:—

- 5 1. A process for purifying 3-phenoxybenzaldehyde which includes reacting crude 3-phenoxybenzaldehyde with an alkali metal- or ammonium- bisulfite or an alkali metal- or ammonium- meta- bisulfite in the presence of a catalyst, which catalyst is an organic quaternary ammonium salt, in inorganic acid salt of an organic tertiary amine or a macrocyclic polyether as herein before defined, isolating the resulting 3-phenoxybenzaldehyde bisulfite adduct, and decomposing it by heating or treating it with an acid or a base. 5
- 10 2. A process according to Claim 1, wherein the molar ratio of the catalyst to the 3-phenoxybenzaldehyde is from 0.001 to 0.3 inclusive. 10
3. A process according to Claim 2, wherein the molar ratio of the catalyst to the 3-phenoxybenzaldehyde is from 0.01 to 0.1.
- 15 4. A process according to Claim 1, wherein a said bisulfite is used and the molar ratio of the said bisulfite to the 3-phenoxybenzaldehyde is from 1.0 to 1.5 inclusive, or a said metabisulfite is used and molar ratio of the said metabisulfite to the 3-phenoxybenzaldehyde is from 0.5 to 0.75 inclusive. 15
5. A process according to any one of the preceding Claims wherein the reaction temperature is from 0° to 80°C inclusive.
- 20 6. A process according to Claim 5, wherein the reaction temperature is from 10° to 60°C inclusive. 20
7. A process according to Claim 1, wherein the reaction medium is water or a mixture of water and an organic solvent containing neither a ketone group nor an aldehyde group and having a low solubility in water.
- 25 8. A process according to Claim 1 for the purification of 3-phenoxybenzaldehyde, which process is substantially as herein described and exemplified. 25
9. 3-Phenoxybenzaldehyde whenever purified by a process according to any one of the preceding claims.

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