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(54) Title: PROCESSES FOR THE PREPARATION OF BISPYRIBAC SODIUM AND INTERMEDIATES THEREOF

(57) Abstract: The present disclosure relates to a process for the preparation of Bispyribac-sodium by condensing 2,6-dihydroxy benzoic acid with 2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine in the presence of at least one base and at least one solvent. The present disclosure also relates to processes for the preparation of 2,6-dihydroxy benzoic acid and 2-(alkyl sulfonyl)-4,6- dialkoxy pyrimidine.

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PROCESSES FOR THE PREPARATION OF BISPYRIBAC SODIUM AND INTERMEDIATES THEREOF

FIELD

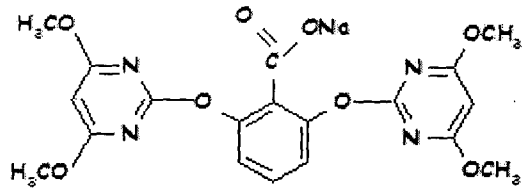
The present disclosure relates to processes for the preparation of Bispyribac sodium and intermediates thereof.

BACKGROUND

Bispyribac-sodium

IUPAC Name: sodium 2, 6-bis (4, 6-dimethoxypyrimidin-2-yloxy) benzoate

Structure:



Chemical formula: $C_{19}H_{17}N_4NaO_8$

Molecular Weight: 452.4

Physical State: white powder

Melting point: 223-224°C

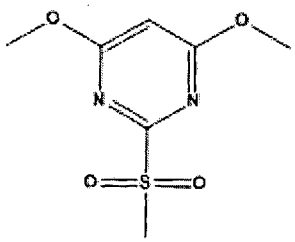
Solubility in water: 73.3g/l at 25°C

Mode of action: selective, systemic action post-emergence herbicide, absorbed by foliage and roots.

Bispyribac sodium is a systemic herbicide that moves throughout the plant tissue and works by interfering with production of a plant enzyme necessary for growth, acetolactate synthase (ALS). It is used to control grasses, sedges and broad-leaved weeds, especially *Echinochloa* spp., in direct seeded rice. It is also used to stunt growth of weeds in non-crop situations. Bispyribac sodium is broken down by microbes and has a half-life (the time it takes for half of the active ingredient to degrade) of 42-115 days. The primary degradation product of bispyribac sodium is sodium 2-(4,6 dimethoxypyrimidin-2-yl)oxy-6-(4-hydroxy-6-methoxypyrimidin-2-yl) benzoate. Bispyribac sodium does not bind to soil, is moderately persistent and somewhat mobile through the soil. Testing indicates that the aquatic

formulation of bispyribac sodium is non-toxic to fish and invertebrates. Bispyribac sodium is also non-toxic to both birds and mammals.

For synthesis of Bispyribac-sodium one of the intermediates is 4,6-dialkoxy-2-(alkylsulfonyl)pyrimidine.



4,6-dialkoxy-2-(alkylsulfonyl) pyrimidine

Synthesis of 4,6-dialkoxy-2-(alkylsulfonyl)pyrimidine has been disclosed in some of the prior art documents. For instance, WO2000046212 discloses preparation of 4.6-dimethoxy-2-(methylsulphonyl) pyrimidine. The process involves mixing 2-methylthiobarbituric acid in xylene, triphenylphosphine oxide and tetrabutylammonium chloride followed by heating and passing phosgene until reaction of the adduct is complete. In the subsequent stage, phosgene is removed from the reaction mass followed by extracting the organic phase with water and reacting with sodium methylate at 50°C to form 4,6-dimethoxy-2-methylthiopyrimidine. Further, 5 mol% of sodium tungstate and 5 mol% of tetrabutylammonium chloride are added to the reaction mixture and mixed at 85°C with 2 molar equivalents of hydrogen peroxide.

WO2002008207 discloses a process for preparing 4, 6-dimethoxy- 2- (methylsulfonyl) -1, 3-pyrimidine by reacting 4,6- dichloro-2- (methylthio) -1, 3-pyrimidine in an inert organic solvent with an alkali metal methoxide, transfer of the resulting 4, 6-dimethoxy-2-(methylthio) - 1, 3-pyrimidine into an aqueous-acidic medium and subsequent oxidation of this compound, in the presence of tricaprylmethylammonium chloride as a catalyst, wherein the oxidation is followed by a purification step in which the aqueous- acidic reaction mixture is adjusted with aqueous base to a pH in the range of 5-8 and stirred either in the presence or in the absence of an organic solvent.

CN 101747283 discloses a method for the preparation of 4,6-dimethoxy-2-(methanesulfonyl) pyrimidine which involves chlorination of 4,6-dihydroxy-2-(methylthio)pyrimidine to obtain

4,6-dichloro-2-(methylthio)pyrimidine which on methoxylation gives 4,6-dimethoxy-2-(methylthio)pyrimidine followed by oxidation. The process disclosed in CN 101747283 particularly employs trifluoromethane sulfonic acid salt, quaternary ammonium salt or organic bases catalyst in methoxylation reaction. The catalyst is selected from the group consisting of copper trifluoromethane sulfonate, trifluoromethane sulfonate, tin trifluoromethyl sulfonate, trioctyl methyl chloride ammonium, tertiary ammonium chloride and triethylamine.

Another intermediate for the synthesis of Bispyribac-sodium is Resorcylic acid, also known as 2, 6-dihydroxybenzoic acid. The synthesis of 2, 6-dihydroxybenzoic acid has been disclosed in various prior art documents such as:

GB 9165481963 discloses the synthesis of 2, 6-dihydroxybenzoic acid by carboxylating andydrous mono-potassium salt of resorcinol, at 130 °C, in the presence of a solvent having the formula $RCON(R^1)_2$,where R is hydrogen or a lower alkyl group and R^1 is a lower alkyl group having 1 to 4 carbon atoms. N, N'-dimethylformamide and N, N'-diethylformamide are the preferable solvents choices. An alkali salt of resorcinol may be formed *in situ* by reacting resorcinol with alkali metal hydroxide, carbonate or bicarbonate. Isolation of 2, 6-dihydroxybenzoic acid is effected by acidification with hydrochloric acid followed by fractional crystallization.

US 5304677 discloses synthesis of 2, 6-dihydroxybenzoic acid by dissolving resorcinol in a suitable solvent followed by blowing carbon dioxide into the solution in the presence of a basic compound until the absorption of carbon dioxide ceases. Alcohols, alkoxy-alcohols, dimethylformamide, water and mixtures thereof may be used as solvents. The basic compound may be potassium carbonate, potassium hydroxide or sodium carbonate and is used approximately in an amount equimolar to resorcinol. The reaction may be carried out within a temperature range of 100 to 200 °C under atmospheric pressure or under carbon dioxide gas pressure of 30 kg/cm^2. The patent also discloses decomposition of 2, 4-dihydroxybenzoic acid from the resultant mixture by acidification of the basic aqueous solution with an organic or a mineral acid to a pH between 5 and 7 and heating the mixture from 90 °C to the boiling temperature of the aqueous solution. After completion of the decomposition reaction, sulfuric acid is added to the mixture to attain a pH of 3 which is followed by filtering off the insoluble matter. Sulfuric acid is further added to the filtrate

until the pH value reaches 1, after which the 2, 6-dihydroxybenzoic acid is finally isolated by filtration at 5 °C.

The prior art methods for the preparation of Bispyribac sodium, 4,6-disubstituted 2-alkylsulfonylpyrimidine and 2, 6-dihydroxybenzoic acid, however, suffer from several disadvantages such as presence of high impurity content, low yield, slow rate of reaction and low cost-effectiveness. Therefore, there is a felt need for simple, economic and high yielding processes for the preparation of these compounds.

OBJECTS

Some of the objects of the present disclosure which at least one embodiment is adapted to provide, are described herein below:

It is an object of the present disclosure to provide a simple and high yielding process for the preparation of Bispyribac-sodium.

It is another object of the present disclosure to provide a time saving process for the preparation of Bispyribac- sodium.

It is another object of the present disclosure to provide a process for the preparation of Bispyribac-sodium which employs mild base rendering the process economic.

Another object of the present disclosure is to provide a process for the preparation of Bispyribac- sodium which obviates the use of strong acids.

Another object of the present disclosure is to provide a process for the preparation of 4,6-dialkoxy 2-(alkylsulfonyl)pyrimidine.

Still another object of the present disclosure is to provide a simple and cost efficient process for the preparation of 4,6-dialkoxy 2-(alkylsulfonyl)pyrimidine.

Yet another object of the present disclosure is to provide a high yielding process for the preparation of 4,6-dialkoxy 2-(alkylsulfonyl)pyrimidine.

A further object of the present disclosure is to provide a process for the preparation of 4,6-dialkoxy 2-(alkylsulfonyl)pyrimidine of high purity.

It is another object of the present disclosure to provide a process for the preparation of 2, 6-dihydroxybenzoic acid.

It is another object of the present disclosure to provide a process for the preparation of 2, 6-dihydroxybenzoic acid, which is high yielding.

It is yet another object of the present disclosure to provide a process for the preparation of 2, 6-dihydroxybenzoic acid, which is environment-friendly.

It is still another object of the present disclosure to provide a process for the preparation of 2, 6-dihydroxybenzoic acid, which is economical.

Other objects and advantages of the present disclosure will be more apparent from the following description when read in conjunction with the accompanying figures, which are not intended to limit the scope of the present disclosure.

Summary:

In accordance with the present disclosure there is provided a process for the preparation of Bispyribac sodium; said process comprises condensing 2,6-dihydroxy benzoic acid with 2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine at a temperature ranging between 20 and 80^0C in the presence of at least one base and at least one solvent.

Typically, the base is selected from the group consisting of sodium hydride, potassium hydride, lithium and calcium hydride

Typically, the solvent is selected from the group consisting of tetrahydrofuran, dimethylsulfoxide, dimethylformamide, dimethyl acetamide, N-methyl pyrrolidone, sulfolane, monoglyme and diglyme.

Typically, 2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine is 2-(methyl sulfonyl)-4,6-dimethoxy pyrimidine.

In another aspect of the present disclosure there is provided a process for the preparation 4,6-dialkoxy-2-(alkylsulfonyl)pyrimidine, said process comprising the following steps:

i. reacting dialkyl malonate and thiourea in the presence of sodium alkoxide and an alcohol to obtain a sodium salt of thiobarbituric acid;

ii. alkylating said salt of thiobarbituric acid with alkyl chloride to obtain 2-alkyl thio-4,6-dihydroxypyrimidine;

iii. chlorinating said 2-alkylthio-4,6-dihydroxypyrimidine with phosphoryl chloride ($POCl_3$) to obtain 2-alkylthio-4,6-dichloropyrimidine;

iv. alkoxylating said 2-alkyl thio-4,6-dichloropyrimidine with sodium alkoxide to obtain 4,6-dialkoxy-2-(alkylthio) pyrimidine; and

v. oxidizing said 4,6-dialkoxy-2-(alkylthio) pyrimidine in the presence of hydrogen peroxide, acetic acid and a catalyst and to obtain 4,6-dialkoxy-2-(alkylsulfonyl) pyrimidine.

Typically, wherein dialkyl malonate is selected from the group consisting of dimethyl malonate, diethyl malonate, di-n-propyl malonate and di-n-butyl malonate, preferably, dialkyl malonate is dimethyl malonate.

Typically, sodium alkoxide is sodium methoxide.
Typically, alkyl chloride is methyl chloride.

Typically, 2-alkyl thio-4,6-dihydroxypyrimidine is 2-methyl thio-4,6-dihydroxypyrimidine.
Typically, 2-alkyl thio-4,6-dichloropyrimidine is 2-methyl thio-4,6-dichloropyrimidine.
Typically, 4,6-dialkoxy-2-(alkylthio) pyrimidine is 4,6-dimethoxy-2-(methylthio) pyrimidine.
Typically, 4,6-dialkoxy-2-(alkylsulfonyl) pyrimidine is 4,6-dimethoxy-2-(methylsulfonyl) pyrimidine.

Typically, the alcohol is selected from the group consisting of methanol, ethanol, n-propyl alcohol and n-butyl alcohol.

In one embodiment the step (i) comprises adding dimethyl malonate and thiourea to methanol to obtain a mass, heating the mass to a temperature ranging between 50 and 70^0C, incorporating a methanolic solution of sodium methoxide to said mass to obtain a mixture, maintaining said mixture at a temperature ranging between 50 and 70^0C for a period of 1 to 5 hours, removing methanol from said mixture by distillation to obtain a second mass, cooling said mass to obtain a cooled mass, filtering said mass to obtain a cake; and washing said cake with methanol followed by drying to obtain a sodium salt of thiobarbituric acid.

In one embodiment the step (ii) comprises mixing sodium salt of thiobarbituric acid with sodium hydroxide solution and methanol obtain a mass, adding methyl chloride to said mass and stirring to obtain 2-methylthio-4,6-dihydroxypyrimidine.

In one embodiment the step (iii) comprises mixing 2-methylthio-4,6-dihydroxypyrimidine, $POCl_3$, at least one aromatic hydrocarbon and at least one base to obtain a mixture, heating said mixture to a temperature ranging between 40 to 90^0C to obtain a heated mixture, and adding $POCl_3$ and chlorine into said heated mixture followed by stirring at a temperature of 40 to 60^0 to obtain 2-methylthio-4,6-dichloropyrimidine.

In one embodiment the step (iv) comprises mixing an alcoholic solution of sodium methoxide, cuprous chloride and sodium iodide to obtain a mixture, cooling said mixture followed by adding 2- methylthio-4,6-dichloropyrimidine at a temperature ranging between 15 and 25^0C to obtain a mass, and heating said mass at a temperature ranging between 30 and 50 ^{0}C to obtain 4,6-dimethoxy-2-(methylthio) pyrimidine.

In one embodiment the step (v) comprises mixing 4,6-dimethoxy-2-(methylthio) pyrimidine, sodium tungstate and acetic acid to obtain a mixture, heating said mixture and adding hydrogen peroxide (H_2O_2) to obtain 4,6-dimethoxy-2-(methylsulfonyl) pyrimidine.

In one embodiment the catalyst is sodium tungstate.

Typically, the aromatic hydrocarbon is selected from the group consisting of monochlorobenzene, o-dichlorobenzene and combination thereof.

Typically, the base is selected from the group consisting of triethylamine, tripropylamine, tributylamine and combinations thereof.

In accordance with another aspect of the present disclosure there is provided a process for the preparation of 2, 6-dihydroxybenzoic acid, said process comprising the following steps:

- carboxylating resorcinol in the presence of carbon dioxide and at least one base in at least one solvent at a temperature ranging between 100 and 200 °C to obtain a mixture containing 2, 6-dihydroxybenzoic acid, 2, 4-dihydroxybenzoic acid and 4, 6-dihydroxyisophthalic acid; and

- acidifying said mixture with at least one acid to obtain 2, 6-dihydroxybenzoic acid of purity> 95 %, wherein the acidifying step comprises adjusting the pH of said mixture ≤ 1.

In one embodiment 2, 6-dihydroxybenzoic acid is prepared by the following process:

- carboxylating resorcinol in the presence of carbon dioxide and at least one base in at least one solvent at a temperature ranging between 100 and 200 °C to obtain a mixture containing 2, 6-dihydroxybenzoic acid, 2, 4-dihydroxybenzoic acid and 4, 6-dihydroxyisophthalic acid;

- maintaining said mixture at a temperature of 140 °C to 180^{0}C for a period of 1 to 10 hours;

- cooling the mixture to obtain a cooled mixture;

- acidifying said cooled mixture to a pH 5.5 to 6 with an acid followed by maintaining at 90-110 °C for a period of 1 to 20 hours to obtain an acidified mass and cooling said mass;

- adjusting the pH of said mass to 2 to 3 with an acid followed by filtering, washing and drying to obtain a solid mass and a filtrate; and

- adding an acid to said filtrate to adjust the pH to 0.8 to 1 followed by stirring, cooling, filtering, washing and drying to obtain 2, 6-dihydroxybenzoic acid having purity > 95 %.

Typically, the step of carboxylation is carried out at a temperature ranging between 140 and 180 °C.

Typically, said acid is selected from the group consisting of hydrochloric acid, sulphuric acid and acetic acid.

Typically, said base is selected from the group consisting of potassium carbonate, potassium hydroxide, sodium carbonate and combinations thereof.

Typically, the solvent is selected from the group consisting of toluene, N, N-dimethylformamide, N, N-diethylformamide, ethanol, methanol, acetone, water and combinations thereof.

Typically, the step of carboxylation is carried out in a reactor having a pressure ranging between 5 kg/cm^2 and 45 kg/cm^2.

Typically, the drying is carried out at a temperature ranging between 40 to 70^0C.

In one embodiment the purity of 2, 6-dihydroxybenzoic acid is > 99%.
In one embodiment the process for the preparation of 2, 6-dihydroxybenzoic acid include the step of decarboxylation of 2, 4- dihydroxy benzoic acid and 4, 6-dihydroxyisophthalic acid to obtain resorcinol and recycling of said resorcinol.

Brief description of the accompanying drawings

Figure 1 illustrates a reaction scheme for the preparation of Bispyribac-sodium in accordance with the present disclosure; and
Figure 2 illustrates a reaction scheme for the preparation of 2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine.

Detailed description

In accordance with the present disclosure there is provided a process for the preparation of Bispyribac-sodium. The process involves condensing 2,6-dihydroxy benzoic acid with 2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine at a temperature ranging between 20 and 80^0C in the presence of at least one base selected from the group consisting of sodium hydride, potassium hydride, lithium and calcium hydride and at least one solvent selected from the group consisting of tetrahydrofuran, dimethylsulfoxide, dimethylformamide, dimethyl acetamide, N-methyl pyrrolidone, sulfolane, monoglyme and diglyme to obtain Bispyribac- sodium. In accordance with the present disclosure 2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine employed is 2-(methyl sulfonyl)-4,6-dimethoxy pyrimidine.

In another aspect there is provided a process for the preparation of 4,6-dialkoxy-2-(alkylsulfonyl)pyrimidine.

In the first step, dialkyl malonate is reacted with thiourea in the presence of sodium alkoxide and an alcohol to obtain a sodium salt of thiobarbituric acid.
In accordance with the present disclosure dialkyl malonate is selected from the group consisting of dimethyl malonate, diethyl malonate, di-n-propyl malonate and di-n-butyl malonate. In one embodiment dialkyl malonate is dimethyl malonate. The alcohol is selected from the group consisting of methanol, ethanol, n-propyl alcohol and n-butyl alcohol.

The obtained salt of thiobarbituric acid is alkylated with alkyl chloride to obtain 2-alkyl thio-4,6-dihydroxypyrimidine.
In the next step, 2-alkylthio-4,6-dihydroxypyrimidine is subjected to chlorination using phosphoryl chloride ($POCl_3$) to obtain 2-alkylthio-4,6-dichloropyrimidine which is then alkoxylated with sodium alkoxide to obtain 4,6-dialkoxy-2-(alkylthio) pyrimidine.

Finally, the obtained 4,6-dialkoxy-2-(alkylthio) pyrimidine is oxidized in the presence of hydrogen peroxide, acetic acid and a catalyst and to obtain 4,6-dialkoxy-2-(alkylsulfonyl) pyrimidine. The catalyst employed in oxidation step is sodium tungstate.

The present disclosure particularly provides preparation of 4,6-dimethoxy-2-(methylsulfonyl)pyrimidine.
In the first step, dimethyl malonate is reacted with thiourea in the presence of sodium methoxide and methanol to obtain a sodium salt of thiobarbituric acid. The obtained salt of thiobarbituric acid is alkylated with methyl chloride to obtain 2-methyl thio-4,6-dihydroxypyrimidine.

In the next step, 2-methylthio-4,6-dihydroxypyrimidine is subjected to chlorination using phosphoryl chloride ($POCl_3$) to obtain 2-methylthio-4,6-dichloropyrimidine which is then alkoxylated with sodium methoxide to obtain 4,6-dimethoxy-2-(methylthio) pyrimidine.
Finally, the obtained 4,6-dimethoxy-2-(methylthio) pyrimidine is oxidized in the presence of hydrogen peroxide, acetic acid and a catalyst and to obtain 4,6-dimethoxy-2-(methylsulfonyl) pyrimidine.

In one exemplary embodiment the preparation of a sodium salt of thiobarbituric acid involves the following steps:

- adding dimethyl malonate and thiourea to methanol to obtain a mass, heating the mass to a temperature ranging between 50 and 70^{0}C,
- incorporating a methanolic solution of sodium methoxide to said mass over a period of 2 hours to obtain a mixture, maintaining said mixture at a temperature ranging between 50 and 70^{0}C for a period of 1 to 5 hours,
- removing methanol from said mixture by distillation to obtain a second mass, cooling said mass to obtain a cooled mass, filtering said mass to obtain a cake; and
- washing said cake with methanol followed by drying to obtain a sodium salt of thiobarbituric acid.

In one exemplary embodiment the preparation of 2-methylthio-4,6-dihydroxypyrimidine involves the following steps:

- mixing sodium salt of thiobarbituric acid with sodium hydroxide solution and methanol to obtain a mass,
- adding methyl chloride to said mass, and stirring said mass to obtain 2-methylthio-4,6-dihydroxypyrimidine.

In one exemplary embodiment the preparation of 2-methylthio-4,6-dichloropyrimidine involves the following steps:

- mixing 2-methylthio-4,6-dihydroxypyrimidine, $POCl_3$, at least one aromatic hydrocarbon and at least one base to obtain a mixture,
- heating said mixture to a temperature ranging between 40 to 90^{0}C to obtain a heated mixture, and
- adding $POCl_3$ and chlorine into the heated mixture followed by stirring at a temperature of 40 to 60^{0}C to obtain 2-methylthio-4,6-dichloropyrimidine.

The aromatic hydrocarbon is selected from the group consisting of monochlorobenzene, o-dichlorobenzene and combination thereof and the base is selected from the group consisting of triethylamine, tripropylamine, tributylamine and combinations thereof.

In one exemplary embodiment the preparation of 4,6-dimethoxy-2-(methylthio) pyrimidine involves the following steps:

- mixing an alcoholic solution of sodium methoxide, cuprous chloride and sodium iodide to obtain a mixture,

- cooling the mixture followed by adding 2-methylthio-4,6-dichloropyrimidine at a temperature ranging between 15 and 25^{0}C to obtain a mass, and
- heating said mass at a temperature ranging between 30 and 50 ^{0}C to obtain
- 4,6-dimethoxy-2-(methylthio) pyrimidine.

In one exemplary embodiment the preparation of 4,6-dimethoxy-2-(methylsulfonyl) pyrimidine involves the following steps:

- mixing 4,6-dimethoxy-2-(methylthio) pyrimidine, sodium tungstate and acetic acid to obtain a mixture, and
- adding hydrogen peroxide (H_2O_2) to the mixture to obtain 4,6-dimethoxy-2-(methylsulfonyl) pyrimidine.

In another aspect there is provided a process for the preparation of 2, 6-dihydroxybenzoic acid using resorcinol as the starting material.

The process involves the following steps:

In the first step, resorcinol is carboxylated in the presence of carbon dioxide and at least one base in at least one solvent at a temperature ranging between 100 and 200 °C to obtain a mixture containing 2, 6-dihydroxybenzoic acid, 2, 4-dihydroxybenzoic acid and 4, 6-dihydroxyisophthalic acid. The obtained mixture is acidified with at least one acid to obtain 2, 6-dihydroxybenzoic acid. The acidifying step involves adjusting the pH of the mixture ≤ 1. The purity of 2, 6-dihydroxybenzoic acid obtained by the process of the present disclosure is > 95 %, preferably greater than 99%. The acid is selected from the group consisting of hydrochloric acid, sulphuric acid and acetic acid, whereas the base is selected from the group consisting of potassium carbonate, potassium hydroxide, sodium carbonate and combinations thereof and the solvent is selected from the group consisting of toluene, N, N-dimethylformamide, N, N-diethylformamide, ethanol, methanol, acetone, water and combinations thereof. In accordance with the present disclosure the step of carboxylation is carried out at a temperature ranging between 140 and 180 °C. Typically, the step of carboxylation is carried out in a reactor having a pressure ranging between 5 kg/cm^2 and 45 kg/cm^2.

In one embodiment the process involves the following steps:

- carboxylating resorcinol in the presence of carbon dioxide and at least one base in at least one solvent at a temperature ranging between 100 and 200 °C to obtain a mixture containing 2, 6-dihydroxybenzoic acid, 2, 4-dihydroxybenzoic acid and 4, 6-dihydroxyisophthalic acid;

- maintaining said mixture at a temperature of 140 °C to 180^{0}C for a period of 1 to 10 hours;

- cooling the mixture to obtain a cooled mixture;
- acidifying said cooled mixture to a pH 5.5 to 6 with an acid followed by maintaining at 90-110 °C for a period of 1 to 20 hours to obtain an acidified mass and cooling said mass;

- adjusting the pH of said mass to 2 to 3 with an acid followed by filtering, washing and drying to obtain a solid mass and a filtrate; and

- adding an acid to said filtrate to adjust the pH to 0.8 to 1 followed by stirring, cooling, filtering, washing and drying to obtain 2, 6-dihydroxybenzoic acid having purity > 95 %.

The drying step is carried out at a temperature ranging between 40 and 70^{0}C.

In one embodiment the process include the step of decarboxylation of 2, 4- dihydroxy benzoic acid and 4, 6-dihydroxyisophthalic acid to obtain resorcinol and recycling of said resorcinol.

The disclosure is further illustrated by way of the following non limiting examples.

Preparation of Bispyribac sodium (Examples 1-5)

Example-1 :

A clear solution of 154 gm of 2,6-dihydroxy benzoic acid in 500 ml Dimethyl sulfoxide is added over 2-3 hr into a mixture of commercial available (60% emulsion in oil) 130 gm of Sodium hydride in 2 lit. of Dimethyl sulfoxide at 30-32°C . Mass is further stirred for 2 hr at 30-32°C and 480 gm of 4,6-Dimethoxy-2-(Methyl Sulfonyl)-pyrimidine is added into it over 2 hr. Reaction is maintained at 30-32^{0}C till completion to get Bispyribac sodium. The

reaction was monitored by HPLC. Mass is filtered, washed with DMSO. Wet solids were reslurried into 1000 ml of methanol & then in 1000 ml of 75% aq. Methanol. Wet solids were dried in oven to get 435 gm of Bispyribac sodium. This Bispyribac sodium is reslurried into 1200 ml of Toluene at reflux temperature, cooled, filtered & dried to give 385 gm of Bispyribac sodium (purity 98.7% HPLC).

Example-2 :

A clear solution of 154 gm of 2,6-dihydroxy benzoic acid in 500 ml. Dimethyl sulfoxide is added over 2-3 hr into a mixture of commercial available (60% emulsion in oil) 130 gm of Sodium hydride in 1500 ml of Dimethyl sulfoxide at 30-32°C . Mass is further stirred for 2 hr at 30-2°C and a slurry of 480 gm of 4,6-Dimethoxy-2-(Methyl Sulfonyl)-pyrimidine into 750 ml of DMSO is added into it over 2-3 hr. Reaction is maintained at 30-32^{0}C till completion to get Bispyribac sodium. The reaction was monitored by HPLC. Mass is filtered, washed with DMSO. Wet solids were reslurried into 1000 ml of methanol & then in 1000 ml of 75% aq. Methanol. Solids were dried in oven to get 430 gm of Bispyribac sodium. This Bispyribac sodium powder is reslurried into 1200 ml of Toluene at reflux temperature, cooled, filtered & dried to get 380 gm of Bispyribac sodium (purity 98.3% HPLC) .

Example-3 :

A clear solution of 154 gm of 2,6-dihydroxy benzoic acid in 500 ml of Dimethyl sulfoxide is added into a mixture of 130 gm of commercial available (60% emulsion in oil) Sodium hydride in 1500 ml of Dimethyl sulfoxide at 30-32°C . Mass is further stirred for 2 hr at 30°C and a slurry of 480 gm of 4,6-Dimethoxy-2-(Methyl Sulfonyl)-pyrimidine into 750 ml of DMSO is added into it. Reaction is maintained at 30-32^{0}C till completion to get Bispyribac sodium. Mass is filtered, washed with DMSO. Wet solids were reslurried into 1000 ml of methanol & then in 1000 ml of 75% aq. Methanol. Solids were dried in oven to get 440 gm of Bispyribac sodium. This Bispyribac sodium powder is reslurried into 1200 ml of Toluene at reflux temperature, cooled, filtered & dried to get 380 gm of Bispyribac sodium. (purity 98.5% HPLC).

Example-4 :

A clear solution of 154 gm of 2,6-dihydroxy benzoic acid in 500 ml of Dimethyl sulfoxide is added into a mixture of 130 gm of commercial available (60% emulsion in oil) Sodium hydride in 2 lit of Dimethyl sulfoxide at 30-32°C . Mass is further stirred for 2 hr at 30°C and

slurry of 480 gm of 4,6-Dimethoxy-2-(Methyl Sulfonyl)-pyrimidine into 750 ml of DMSO is added into it. Reaction is maintained at 30-32^{0}C till completion to get Bispyribac sodium. Mass is filtered, washed with DMSO. Wet solids were reslurried into 1000 ml of methanol & then in 1000 ml of 75% aq. Methanol. Solids were dried in oven to get 435 gm of Bispyribac sodium. This Bispyribac sodium powder is reslurried into 1200 ml of Toluene at reflux temperature, cooled, filtered & dried to get 385 gm of Bispyribac sodium (purity 98.6% HPLC).

Example-5 :

A clear solution of 154 gm of 2,6-dihydroxy benzoic acid in 500 ml of Dimethyl sulfoxide is added into a mixture of 130 gm of commercial available (60% emulsion in oil) Sodium hydride in 1500 ml of Dimethyl sulfoxide at 30-32°C . Mass is further stirred for 2 hr at 30°C and a clear solution of 480 gm of 4,6-Dimethoxy-2-(Methyl Sulfonyl)-pyrimidine into 1500 ml of DMSO is added into it. Reaction is maintained at 30-32^{0}C till completion to get Bispyribac sodium. Mass is filtered, washed with DMSO. Wet solids were reslurried into 1000 ml of methanol & then in 1000 ml of 75% aq. Methanol. Solids were dried in oven to get 400 gm of Bispyribac sodium. This Bispyribac sodium powder is reslurried into 1200 ml of Toluene at reflux temperature, cooled, filtered & dried to get 350 gm of Bispyribac sodium (purity 98.6% HPLC).

Preparation of 4, 6-dimethoxy-2-(methylsulfonyl) pyrimidine [Examples 6-10]

Example 6: Preparation of Thiobarbituric acid sodium salt

A solution of 1.10m thiourea and 1.0m dimethylmalonate in 280ml methanol was refluxed and a solution of 1.0m sodium methoxide in 150ml methanol was added over 15 to 45 minutes. Mass was refluxed for 4 hours and part of methanol was distilled. The resulting mass was cooled below 30°C, filtered and washed with methanol. The obtained cake was dried to obtain thiobarbituric acid sodium salt (yield: 90%).

Filtrate was concentrated to a level of 250- 280 ml. To this, 0.1m dimethyl malonate and 0.1m sodium methoxide solution were added. The obtained reaction mass was worked up as above. The yield of thiobarbituric acid sodium salt was 2%.

Example 7:

Preparation of 2-Methylthio-4, 6-dihydroxypyrimidine

1.0m thiobarbituric acid sodium salt was dissolved in 1.5m 1 N aqueous sodium hydroxide solution and 50 ml methanol in a SS autoclave to obtain a mixture. To this 0.5m methyl chloride was fed in 1 to 2 hours. The obtained reaction mass was stirred for 2 to 6 hours at 25-30°C, a second lot of 0.5m methyl chloride was fed in 1 to 2 hours and mass was stirred at 25-30°C for 6-8 hours. To this, 0.05m methyl chloride was fed and reaction mass was stirred for 2 to 6 hours. After the end of reaction HPLC indicated 85% 2-methylthio- 4, 6-dihydroxypyrimidine and 5% 2-methylthio-4-methoxy-6-hydroxypyrimidine.
Yield of product was 75-80 mole %.

Example 8:

Preparation of 2-methylthio-4, 6-dichloropyrimidine

To 4m monochlorobenzene, 1.0 m 2-methylthio-4,6-dihydoxypyrimidine was added. To this, 2.2m $POCl_3$ was added in 1 to 2 hours and 2.2 m triethylamine was added over 2 to 4 hours at 40-50°C.The obtained mixture was heated to 80°C which resulted in a clear solution and stirred for 4-8 hours to obtain a mass. The obtained mass was cooled to 60°C. To this 2.0m phosphorus trichloride was added. Then 2.0m chlorine was fed in 6-10 hours at 60°C and stirred at 60°C for 8 to 10 hours. Cl_2 feeding was carried out in absence of light to avoid side chain chlorination. $POCl_3$ was vacuum distilled and 200ml monochlorobenzene was added and continued the distillation to ensure complete removal of $POCl_3$. 4.0m to 4.3m $POCl_3$ was recovered; the residual mass was drowned in 200ml ice water and extracted with monochlorobenzene. To the monochlorobenzene layer, 100 ml water was added and neutralized with $NaHCO_3$. The layers were separated and monochlorobenzene layer was concentrated under vacuum. Yield of product was 85-87%.
Product was vacuum distilled and then crystallized using methanol to get 85 mole % with 99% purity.

Example 9:

Preparation of 4, 6-dimethoxy-2-(methylthio)pyrimidine

To 2.2 m 3 N sodium methoxide solution in methanol was added 2m% **cuprous chloride** and 2m% **sodium iodide** to obtain a mixture which was then cooled to 20°C. 1.0m 2-methyl thio-4,6-dichloropyrimidine was dissolved in 400ml **methanol** and was added to the mixture over 3-6 hours and stirred for 1 hour at 20°C to obtain a reaction mass. The temperature of mass was raised to 30°C and then to 40°C, and stirred at 40°c for 6-12 hours, HPLC indicate 95-96% 2-methylthio-4,6-dimethoxypyrimidine and 0.5% 2-methylthio-4-methoxy-6-

chloropyrimidine. The mass was cooled and sodium chloride was filtered off. From the filtrate, methanol was distilled, water was added to residual mass and extracted with toluene. Toluene layer was washed with water and then concentrated. Yield of product was 90%.

Example 10: Preparation of 4, 6-dimethoxy-2-(methylsulfonyl) pyrimidine

To 200ml acetic acid was added 3m% sodium tungstate. To this, 1.0m 2-methylthio-4,6-dimethoxypyrimidine was added to obtain a mass (clear solution). The mass was heated to 40°C. To the heated mass 2.1m 30% H_2O_2 was added in 4-8 hours and stirred at 40°c for 3-5 hours. Further, 0.05m 30 % H_2O_2 was added and stirred at 40°C till complete conversion. Reaction was carried out at 40°c. Reaction mixture was cooled and solids were filtered. The obtained cake was washed with aqueous acetic acid followed by water. The cake was then dried. Yield = 83%.

The filtrate was extracted with ethylene dichloride. The obtained ethylene dichloride layer was concentrated. wt = 42g, yield of product was about 1-1.5%.

Preparation of 2,6-dihydroxybenzoic acid [Examples 11-15]

Example 11: Preparation of 2,6-dihydroxybenzoic acid:

A mixture of resorcinol (110 grams, 1.0 mole), toluene (250 ml) and potassium hydroxide (65.1 grams of 86 %, 1.0 mole) was stirred in a reactor to which a Dean & Stark apparatus was installed to obtain a mass. The obtained mass was dehydrated by removing water from side arm of the Dean and Stark apparatus. After no more water was observed in the side arm of the Dean and Stark apparatus, toluene was completely distilled and N,N-dimethylformamide (330 ml) was added to obtain a solution.

The resultant solution was transferred to a dry stainless steel pressure reactor, pressurized using a carbon dioxide gas and heated to 150 °C to obtain a reaction mixture. The obtained reaction mixture was held at 150 °C for 6 hours under a carbon dioxide gas pressure of 9 kg/cm2.

The mixture was cooled to 50 °C, carbon dioxide pressure was released and carbon dioxide was vented into alkali scrubber. The mixture was then transferred to a glass reactor and N, N-dimethylformamide was distilled at 110°C liquid temperature and 10 mm Hg pressure to obtain a reaction mass. The resultant mass was cooled to ambient temperature and dissolved in water. The HPLC composition of the reaction mass was of 56.61 %-2,6-dihydroxybenzoic acid, 4.97 %-2,4-dihydroxybenzoic acid, 9.32 % resorcinol, 12.73% 4,6-dihydroxyisophthalic acid.

The aqueous mass was acidified to a pH value of 5.5 to 6 with concentrated hydrochloric acid and maintained at 100 °C for 6 hours. The reaction progress was monitored by HPLC.
The mass was cooled to 30 °C, acidified with conc. hydrochloric acid to pH 2.85, filtered, washed & dried at 60°C to get 15.35 g dry solids (HPLC comp = 95.2% 4,6-dihydroxyisophthalic acid, 2.97% 2,6-dihydroxybenzoic acid). Filtrate of 2.85 pH was neutralized to a pH value of 0.8 to 1 using concentrated hydrochloric acid, cooled to 10°C and filtered, washed with water. The wet solid was dried at 60°C to get 53.9 grams of solid with 96.1 % 2,6-dihydroxy benzoic acid by HPLC.

Example-12

A mixture of 220 grams resorcinol (2.0 mole), 1300 ml 50 % (v/v) aqueous ethanol and 276 grams (2.0 mole) potassium carbonate was added in a dry stainless steel high-pressure reactor. Reactor was pressurized to 5 kg using carbon dioxide and heated to 170 °C. The mixture was held at 170 °C for 5 hours keeping carbon dioxide pressure of 38 – 39 kg/cm^2.
The reaction mixture was cooled to ambient temperature and carbon dioxide was released and vented in alkali scrubber.
The mixture was then transferred to a glass reactor and analyzed by HPLC.
HPLC composition: 38.43 %-2,6-dihydroxybenzoic acid, 34.6 %-2,4-dihydroxybenzoic acid, 9.40 % resorcinol & 16.42 % 4,6-dihydroxyisophthalic acid.
The mixture was neutralized to pH = 5.5 to 6 by concentrated hydrochloric acid at 30 °C and ethanol/water was then distilled from the mixture at 100°C liquid temperature. The reaction mixture was further maintained at reflux for 12.5 hours with adding concentrated hydrochloric acid to maintain the pH value 5.5 to 6.
After 12.5 hours maintenance at 100 °C, the composition of the reaction mass by HPLC was 55.25 %-2,6-dihydroxybenzoic acid, 3.6 %-2,4-dihydroxybenzoic acid, 20.35% resorcinol & 19.90 % 4,6-dihydroxyisophthalic acid.
After completion of decomposition of 2,4-dihydroxybenzoic acid, concentrated hydrochloride acid was added to the mixture until the pH value reached to 2.83. The obtained solids were filtered and wet solid was further slurried in water. To this, concentrated hydrochloric acid was added until pH value of 0.90 was reached. Solids were filtered, washed and dried at 60 °C till constant weight to get 11.8 grams dry solids. (HPLC composition was 93.5 % of 4,6-dihydroxyisophthalic acid & 5.84 % 2,6-dihydroxy benzoic acid).
Filtrate of pH 2.83 was further acidified with concentrated hydrochloric acid until pH value reached 0.9 to 1.0 and stirred for 1 hr. The resultant slurry was cooled to 0 °C, stirred for 1

hour and filtered. The wet cake was further re-slurried in water, stirred at 55 – 60 °C for 1 hour, cooled to 0 °C and filtered. Solid was washed with chilled water and dried at 60 °C till constant weight to get 99.2 grams dry solid of 2,6-dihydroxybenzoic acid. (96.4 % purity by HPLC)

Example – 13

A mixture of 220 grams resorcinol (2 mole), 1300 ml of 50 % (v/v) aqueous ethanol, 138 grams (1.0 m) of potassium carbonate was added in a stainless steel high-pressure reactor. The mixture was pressurized to 5 kg using carbon dioxide and heated to 170 °C, the mixture was held at 170 °C for 5 hours with a carbon dioxide pressure of 23 – 25 kg/cm^2.

The reaction mixture was cooled to ambient temperature, carbon dioxide was released, carbon dioxide was vented in alkali scrubber.

The mixture was neutralized to pH 5.5 to 6 using concentrated sulfuric acid at 30 °C. Ethanol/water was then distilled from the mixture to get 98 –100 °C liquid temperature. The reaction mixture was further maintained at reflux for 11 hours by adding concentrated sulfuric acid to the reaction mixture keeping pH value 5.5 to 6 during heating.

After 11 hours HPLC composition of the mass was 55.72 %-2,6-dihydroxybenzoic acid, 2.81 %-2,4-dihydroxybenzoic acid, 38.14 % resorcinol and 2.15 % 4,6-dihydroxyisophthalic acid as against initial value of 52.47 %-2,6-dihydroxybenzoic acid, 20.20 %-2,4-dihydroxybenzoic acid, 24.2 % resorcinol & 2.47 % 4,6-dihydroxyisophthalic acid).

The mass was cooled to ambient temperature and concentrated sulfuric acid was added to the mixture until the pH value reached 4. The mixture was filtered to remove potassium sulfate. Filtrate was further acidified using concentrated sulfuric acid until pH value reached 0.9 to 1.0. Stirred the mass for 1 hour. The resultant slurry was cooled to 10 °C and stirred for 1 hour & filtered. The wet solid was further reslurried in water, stirred at 55-60 °C for 1 hour, cooled to 25 °C and filtered. Solid was washed with water and dried at 60 °C till constant weight to get 110.4 grams dry solid of 2,6-dihydroxybenzoic acid. (99.1 % purity by HPLC)

The aqueous filtrate was mixed and extracted with methyl ethyl ketone several times. Combined methyl ethyl ketone extract was concentrated under reduced pressure to get 142 grams viscous mass having HPLC composition of 85.7 % resorcinol, 7.8 % -2,6-DHBA, 1.6 % 2,4-dihydroxybenzoic acid and 2.1 % 4,6-dihydroxybenzoic acid.

The residue post distillation of methyl ethyl ketone, which was rich in resorcinol, was recycled.

Example-14

The 142 grams of methyl ethyl ketone concentrated mass obtained from example – 13 (1.107 m resorcinol; 0.072 m 2,6-DHBA) was mixed with 90.3 grams fresh resorcinol (0.821 mole), to adjust the resorcinol quantity to 2 mole, 151.8 grams (1.10m) of potassium carbonate and 1300 ml of 50 % (v/v) aqueous ethanol.

The mixture was pressurized to 5 kg using carbon dioxide and heated to 170 °C, the mixture was kept at 170 °C for 5 hours with a carbon dioxide pressure of 23 – 25 kg/cm^2.

The reaction mixture was cooled to ambient temperature, carbon dioxide was released, carbon dioxide was vented in alkali scrubber.

The mixture was neutralized to pH 5.5 to 6 using concentrated sulfuric acid at 30 °C. Ethanol/water was then distilled from the mixture to get 98-100 °C liquid temperature. The reaction mixture was further maintained at reflux for 12 hours by adding concentrated sulfuric acid to the reaction mixture until pH value reached 5.5 to 6 during maintenance.

After 12 hours of maintenance the HPLC composition was 55.48 % -2,6-dihydroxybenzoic acid, 0.1 % 2,4-dihydroxybenzoic acid, 41.04 % resorcinol and 0.93 % 4,6-dihydroxyisophthalic acid as against initial value of 35.52 % -2,6-dihydroxybenzoic acid, 30.21 % 2,4-dihydroxybenzoic acid, 26.27 % resorcinol and 6.41 % 4,6-dihydroxyisophthalic acid. 4,6-dihydroisophtahlic acid shows complete decarboxyaltion at 100 °C using concentrated sulfuric acid.

Concentrated sulfuric acid was added to the mixture until the pH value reached 3.96. The slurry was equilibrated for 1 hour at 30 °C & filtered to remove potassium sulfate. Filtrate was further acidified using concentrated sulfuric acid until pH value is reached 0.9 to 1.0 and stirred for 1 hour. The resultant slurry was cooled to 10 °C & stirred for 1 hour. and filtered.

The wet solid was further reslurried in water, stirred at 55-60 °C for 1 hour, cooled to 25 °C & filtered. Solid was washed with water and dried at 60 °C till constant weight to get 76.5 grams dry cake of 2,6-dihydroxybenzoic acid. (99.0 % purity by HPLC).

Example-15

After performing the main reaction and isolation of 2,6-dihydroxy benzoic acid, as given in the example 13 and 14, aqueous filtrate was recycled.

Aqueous filtrate was neutralized to pH 7 using potassium carbonate & then it was treated with charcoal & filtered off charcoal. The content of resorcinol in aqueous filtrate was determined by HPLC and the shortfall of resorcinol for a batch size of 2.0 mole of resorcinol was compensated by adding fresh resorcinol and carboxylation was conducted as per the process given in the example 13 and 14.

The yield of 2,6-dihydroxy benzoic acid was 33 % (use of fresh resorcinol), 35 % after first recycle of aqueous filtrate and 32 % after second recycle of aqueous filtrate.

"Whenever a range of values is specified, a value up to 10 % below and above the lowest and highest numerical value respectively, of the specified range, is included in the scope of the disclosure".

While considerable emphasis has been placed herein on the preferred embodiments, it will be appreciated that many embodiments can be made and that many changes can be made in the preferred embodiments without departing from the principles of the disclosure. These and other changes in the preferred embodiments as well as other embodiments of the disclosure will be apparent to those skilled in the art from the disclosure herein, whereby it is to be distinctly understood that the forgoing descriptive matter to be implemented merely as illustrative of the disclosure and not as limitation.

Throughout this specification the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.
The use of the expression "at least" or "at least one" suggests the use of one or more elements or ingredients or quantities, as the use may be in the embodiment of the invention to achieve one or more of the desired objects or results.

Any discussion of documents, acts, materials, devices, articles or the like that has been included in this specification is solely for the purpose of providing a context for the invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the invention as it existed anywhere before the priority date of this application.

The numerical values mentioned for the various physical parameters, dimensions or quantities are only approximations and it is envisaged that the values higher/lower than the numerical values assigned to the parameters, dimensions or quantities fall within the scope of the disclosure, unless there is a statement in the specification specific to the contrary.

CLAIMS:

1. A process for the preparation of Bispyribac sodium; said process comprises condensing 2,6-dihydroxy benzoic acid with 2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine at a temperature ranging between 20 and 80^0C in the presence of at least one base and at least one solvent.

2. The process as claimed in claim 1, wherein the base is selected from the group consisting of sodium hydride, potassium hydride, lithium and calcium hydride

3. The process as claimed in claim 1, wherein the solvent is selected from the group consisting of tetrahydrofuran, dimethylsulfoxide, dimethylformamide, dimethyl acetamide, N-methyl pyrrolidone, sulfolane, monoglyme and diglyme.

4. The process as claimed in claim 1, wherein 2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine is 2-(methyl sulfonyl)-4,6-dimethoxy pyrimidine.

5. The process as claimed in claim 1, wherein said 4,6-dialkoxy-2-(alkylsulfonyl)pyrimidine is prepared by the following steps:
    i. reacting dialkyl malonate and thiourea in the presence of sodium alkoxide and an alcohol to obtain a sodium salt of thiobarbituric acid;

    ii. alkylating said salt of thiobarbituric acid with alkyl chloride to obtain 2-alkyl thio-4,6-dihydroxypyrimidine;

    iii. chlorinating said 2-alkylthio-4,6-dihydroxypyrimidine with phosphoryl chloride ($POCl_3$) to obtain 2-alkylthio-4,6-dichloropyrimidine;

    iv. alkoxylating said 2-alkyl thio-4,6-dichloropyrimidine with sodium alkoxide to obtain 4,6-dialkoxy-2-(alkylthio) pyrimidine; and

    v. oxidizing said 4,6-dialkoxy-2-(alkylthio) pyrimidine in the presence of hydrogen peroxide, acetic acid and a catalyst and to obtain 4,6-dialkoxy-2-(alkylsulfonyl) pyrimidine.

6. The process as claimed in claim 5, wherein dialkyl malonate is selected from the group consisting of dimethyl malonate, diethyl malonate, di-n-propyl malonate and di-n-butyl malonate, preferably, dialkyl malonate is dimethyl malonate.

7. The process as claimed in claim 5, wherein sodium alkoxide is sodium methoxide.

8. The process as claimed in claim 5, wherein alkyl chloride is methyl chloride.

9. The process as claimed in claim 5, wherein 2-alkyl thio-4,6-dihydroxypyrimidine is 2-methyl thio-4,6-dihydroxypyrimidine.

10. The process as claimed in claim 5, wherein 2-alkyl thio-4,6-dichloropyrimidine is 2-methyl thio-4,6-dichloropyrimidine.

11. The process as claimed in claim 5, wherein 4,6-dialkoxy-2-(alkylthio) pyrimidine is 4,6-dimethoxy-2-(methylthio) pyrimidine.

12. The process as claimed in claim 5, wherein 4,6-dialkoxy-2-(alkylsulfonyl) pyrimidine is 4,6-dimethoxy-2-(methylsulfonyl) pyrimidine.

13. The process as claimed in claim 5, wherein the alcohol is selected from the group consisting of methanol, ethanol, n-propyl alcohol and n-butyl alcohol.

14. The process as claimed in claim 5, wherein the step (i) comprises adding dimethyl malonate and thiourea to methanol to obtain a mass, heating the mass to a temperature ranging between 50 and 70^0C, incorporating a methanolic solution of sodium methoxide to said mass to obtain a mixture, maintaining said mixture at a temperature ranging between 50 and 70^0C for a period of 1 to 5 hours, removing methanol from said mixture by distillation to obtain a second mass, cooling said mass to obtain a cooled mass, filtering said mass to obtain a cake; and washing said cake with methanol followed by drying to obtain a sodium salt of thiobarbituric acid.

15. The process as claimed in claim 5, wherein the step (ii) comprises mixing sodium salt of thiobarbituric acid with sodium hydroxide solution and methanol obtain a mass, adding

methyl chloride to said mass and stirring to obtain 2-methylthio-4,6-dihydroxypyrimidine.

16. The process as claimed in claim 5, wherein the step (iii) comprises mixing 2-methylthio-4,6-dihydroxypyrimidine, $POCl_3$, at least one aromatic hydrocarbon and at least one base to obtain a mixture, heating said mixture to a temperature ranging between 40 to 90^0C to obtain a heated mixture, and adding $POCl_3$ and chlorine into said heated mixture followed by stirring at a temperature of 40 to 60^0 to obtain 2-methylthio-4,6-dichloropyrimidine.

17. The process as claimed in claim 5, wherein the step (iv) comprises mixing an alcoholic solution of sodium methoxide, cuprous chloride and sodium iodide to obtain a mixture, cooling said mixture followed by adding 2- methylthio-4,6-dichloropyrimidine at a temperature ranging between 15 and 25^0C to obtain a mass, and heating said mass at a temperature ranging between 30 and 50 ^{0}C to obtain 4,6-dimethoxy-2-(methylthio) pyrimidine.

18. The process as claimed in claim 5, wherein the step (v) comprises mixing 4,6-dimethoxy-2-(methylthio) pyrimidine, sodium tungstate and acetic acid to obtain a mixture, heating said mixture and adding hydrogen peroxide (H_2O_2) to obtain 4,6-dimethoxy-2-(methylsulfonyl) pyrimidine.

19. The process as claimed in claim 5, wherein the catalyst is sodium tungstate.

20. The process as claimed in claim 16, wherein the aromatic hydrocarbon is selected from the group consisting of monochlorobenzene, o-dichlorobenzene and combination thereof.

21. The process as claimed in claim 16, wherein the base is selected from the group consisting of triethylamine, tripropylamine, tributylamine and combinations thereof.

22. The process as claimed in claim 1, wherein said 2, 6-dihydroxybenzoic acid is prepared by the following steps:

    i. carboxylating resorcinol in the presence of carbon dioxide and at least one base in at least one solvent at a temperature ranging between 100 and 200 ^{o}C

to obtain a mixture containing 2, 6-dihydroxybenzoic acid, 2, 4-dihydroxybenzoic acid and 4, 6-dihydroxyisophthalic acid; and

ii. acidifying said mixture with at least one acid to obtain 2, 6-dihydroxybenzoic acid of purity> 95 %, wherein the acidifying step comprises adjusting the pH of said mixture ≤ 1.

23. The process as claimed in claim 22, wherein said process comprising:

- carboxylating resorcinol in the presence of carbon dioxide and at least one base in at least one solvent at a temperature ranging between 100 and 200 °C to obtain a mixture containing 2, 6-dihydroxybenzoic acid, 2, 4-dihydroxybenzoic acid and 4, 6-dihydroxyisophthalic acid;
- maintaining said mixture at a temperature of 140 °C to 180°C for a period of 1 to 10 hours;
- cooling the mixture to obtain a cooled mixture;
- acidifying said cooled mixture to a pH 5.5 to 6 with an acid followed by maintaining at 90-110 °C for a period of 1 to 20 hours to obtain an acidified mass and cooling said mass;
- adjusting the pH of said mass to 2 to 3 with an acid followed by filtering, washing and drying to obtain a solid mass and a filtrate; and

a. adding an acid to said filtrate to adjust the pH to 0.8 to 1 followed by stirring, cooling, filtering, washing and drying to obtain 2, 6-dihydroxybenzoic acid having purity > 95 %.

24. The process as claimed in claim 22 or 23, wherein the step of carboxylation is carried out at a temperature ranging between 140 and 180 °C.

25. The process as claimed in claim 22 or 23, wherein said acid is selected from the group consisting of hydrochloric acid, sulphuric acid and acetic acid.

26. The process as claimed in claim 22 or 23, wherein said base is selected from the group consisting of potassium carbonate, potassium hydroxide, sodium carbonate and combinations thereof.

27. The process as claimed in claim 22 or 23, wherein the solvent is selected from the group consisting of toluene, N, N-dimethylformamide, N, N-diethylformamide, ethanol, methanol, acetone, water and combinations thereof.

28. The process as claimed in claim 22 or 23, wherein the step of carboxylation is carried out in a reactor having a pressure ranging between 5 kg/cm^2 and 45 kg/cm^2.

29. The process as claimed in claim 23, wherein the drying is carried out at a temperature ranging between 40 to 70^0C.

30. The process as claimed in claim 22 or 23, wherein the purity of 2, 6-dihydroxybenzoic acid is > 99%.

31. The process as claimed in claim 22 or 23, includes the step of decarboxylation of 2,4-dihydroxybenzoic acid and 4, 6-dihydroxyisophthalic acid to obtain resorcinol and recycling of said resorcinol.

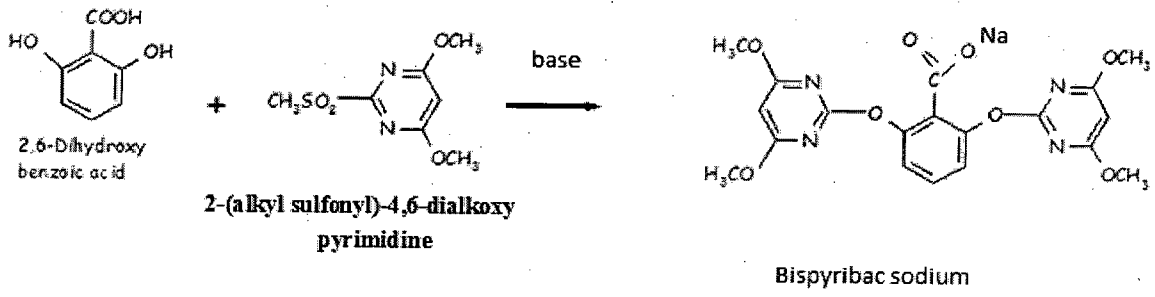
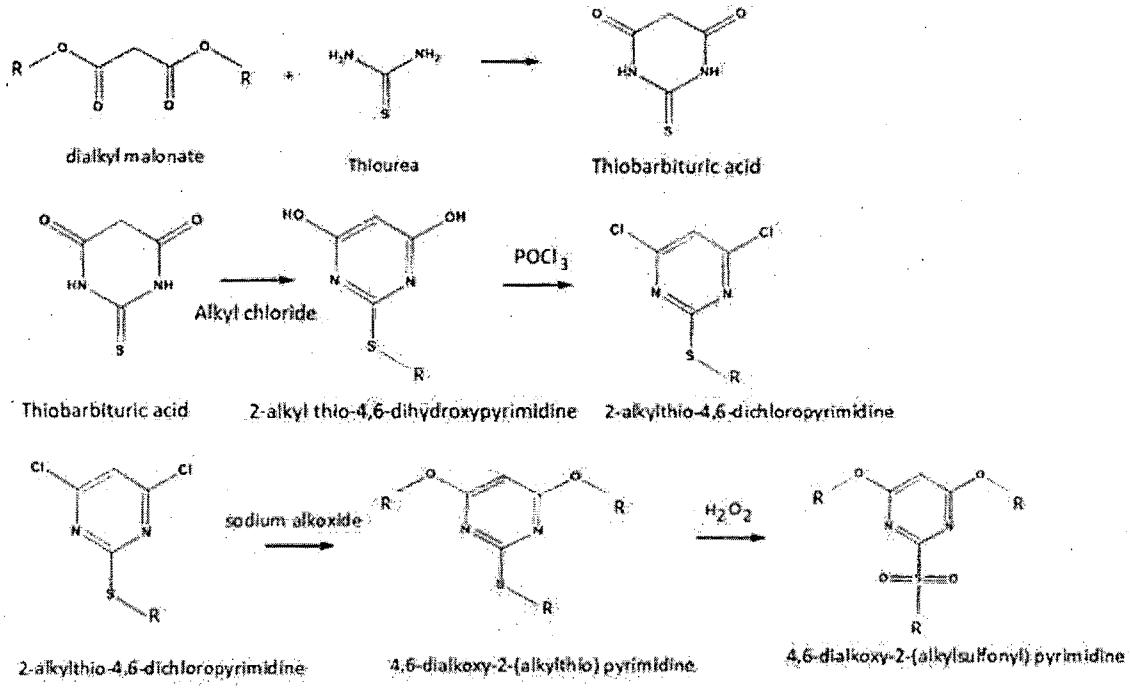

COOH
HO
OH
2,6-Dihydroxy benzoic acid
+
CH_3SO_2
OCH3
N
N
OCH3
2-(alkyl sulfonyl)-4,6-dialkoxy pyrimidine
base
H_3CO
N
N
H_3CO
O
O
Na
O
O
N
N
OCH3
OCH3
Bispyribac sodium

Figure 1



(*R= Alkyl group selected from the group consisting of methyl and ethyl)

Figure 2