



(51) International Patent Classification:

C07C 25/10 (2006.01)

(21) International Application Number:

PCT/IB2021/050485

(22) International Filing Date:

22 January 2021 (22.01.2021)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

202021003568 27 January 2020 (27.01.2020) IN

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

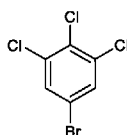
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ,

UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: PROCESS FOR PREPARATION OF 5-BROMO-1, 2, 3-TRICHLOROBENZENE



(I)

(57) Abstract: The present invention relates to a process for preparation of 5-bromo-1,2,3-trichlorobenzene of formula (I) in simple, economical manner with high yield. The 5-bromo-1,2,3-trichlorobenzene of formula (I) is used in preparation of 1-(3,4,5-trichloro-phenyl)-2,2,2-trifluoro-ethanone which is a key intermediate of isoxazoline derivatives. (I)

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**PROCESS FOR PREPARATION OF 5-BROMO-1, 2, 3-  
TRICHLOROBENZENE**

**RELATED APPLICATION**

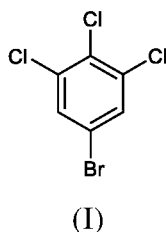
10 This application claims the benefit of Indian Provisional Application No IN202021003568, filed on January 27, 2020 the contents of which are incorporated by reference herein.

**FIELD OF THE INVENTION**

15

The present invention relates to a process for preparation of 5-bromo-1, 2, 3-trichlorobenzene of Formula (I) in simple, economical manner with high yield. The 5-bromo-1, 2, 3-trichlorobenzene of formula (I) is used in preparation of 1-(3, 4, 5-trichloro-phenyl)-2, 2, 2-trifluoro-ethanone which is a key intermediate of isoxazoline derivatives.

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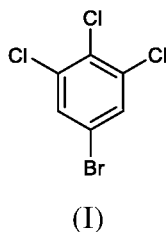


**BACKGROUND OF THE INVENTION**

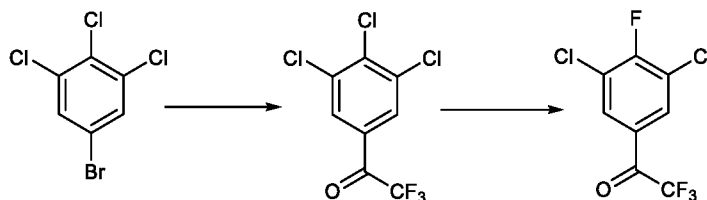
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The 5-bromo-1,2,3-trichlorobenzene of formula (I) is building block for the preparation of halo-substituted-1-aryl-2,2,2-trifluoro-ethanone such as 1-(3,5-dichloro-4-fluoro-phenyl)-2,2,2-trifluoro-ethanone, 1-(3,4,5-trichloro-phenyl)-2,2,2-trifluoro-ethanone which are key intermediates in preparation of various veterinary active ingredients for example Sarolaner, Lotilaner.

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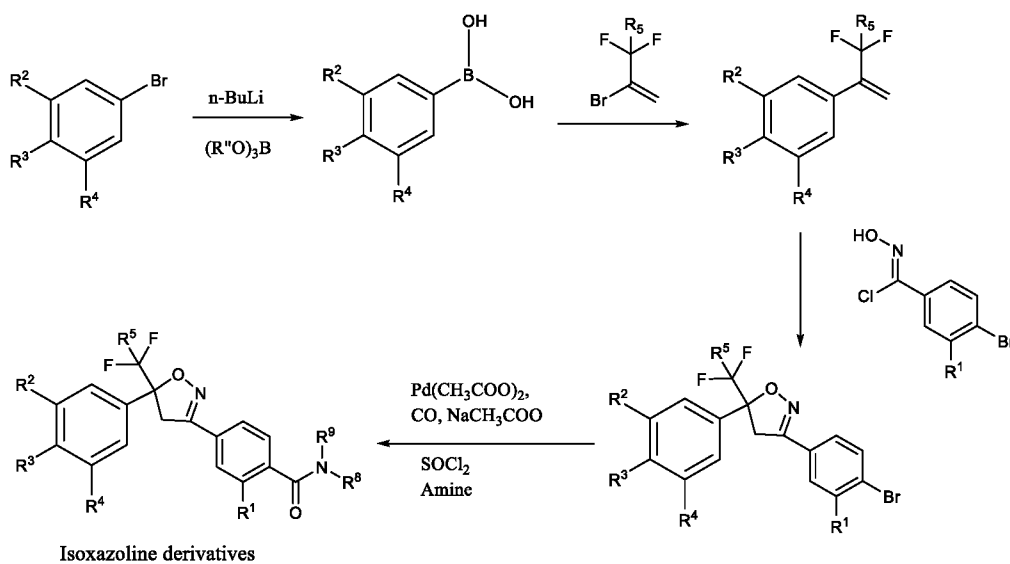


- 5 The U.S. patent no.9, 809,524B1 discloses the key intermediates of Sarolaner, Lotilaner and its synthesis using 5-bromo-1,2,3-trichlorobenzene as shown herein.



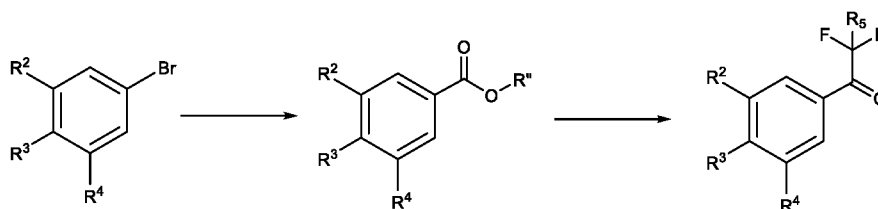
- The U.S. patent no. 8,853,410B2 discloses the preparation of isoxazoline derivatives using halogenated styrene and halo-substituted-1-aryl-2, 2, 2-trifluoroethanones as shown in scheme-1. The halogenated styrene and halo-substituted-1-aryl-2, 2, 2-trifluoroethanones are prepared by using 5-halo-1,2,3-halo-substituted-benzene as depicted in scheme-2 & 3.

### Scheme 1–



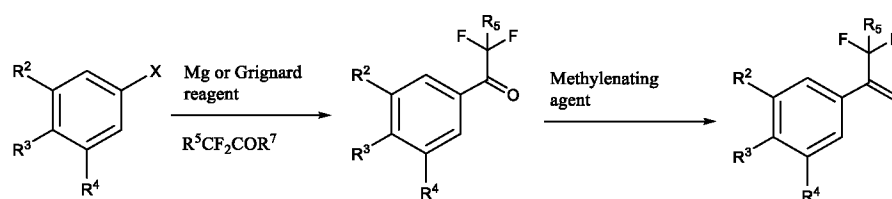
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### Scheme 2 –



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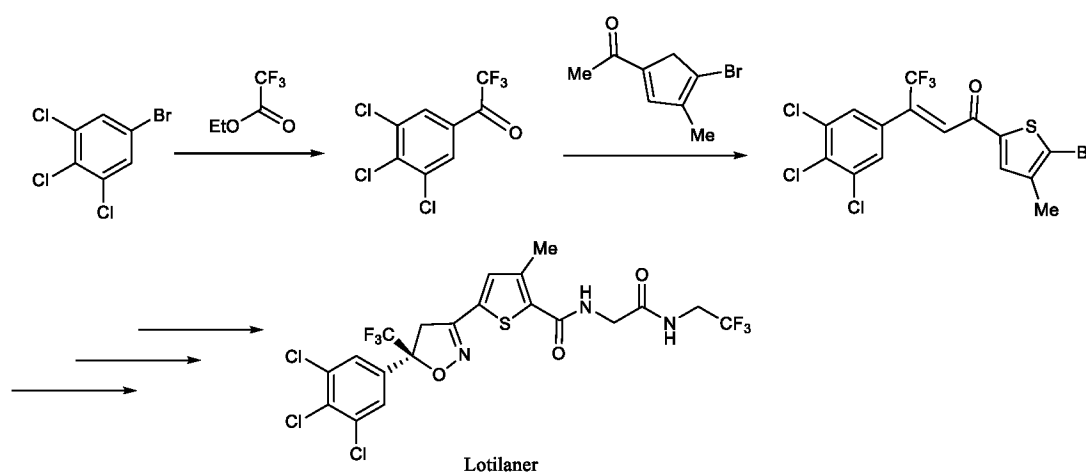
## 5 Scheme 3 –



The PCT patent application no. WO2014090918A1 discloses the preparation of Lotilaner using 5-bromo-1, 2, 3-trichlorobenzene as depicted below in scheme-4.

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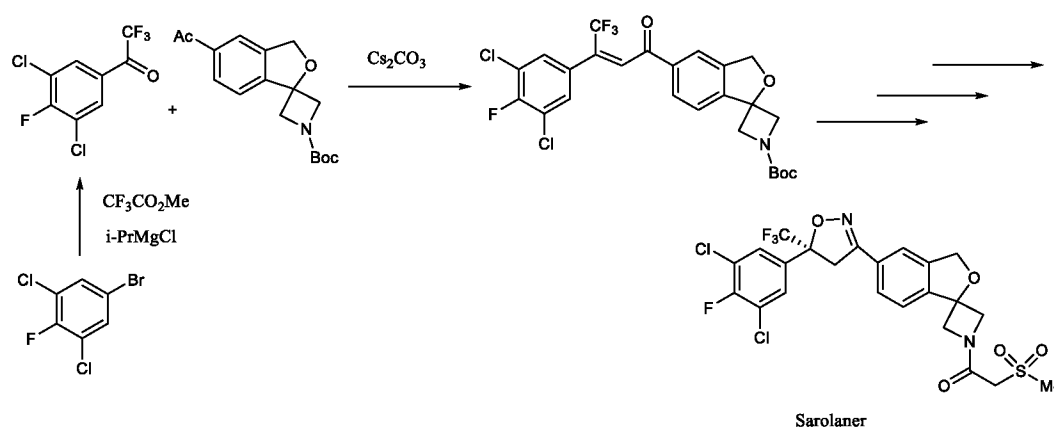
## Scheme 4–



The U.S. patent no.8, 466,115B2 discloses the preparation of Sarolaner using 5-bromo-1, 3-dichloro-2-fluorobenzene as depicted below in scheme-5.

15

## Scheme 5–



- 5 The 5-bromo-1, 2, 3-trichlorobenzene and its process of preparation is disclosed in various references. However, the process has one or more disadvantages and discussed herein below.

The bromination of aniline using N-bromosuccinimide (NBS) or potassium  
10 bromide (KBr), N,N-dimethyl-formamide (DMF), phosphorus oxychloride (POCl<sub>3</sub>) in solvent chloroform or dichloromethane (DCM) or solvent-free conditions (*Synthetic Communications*, 2009, 39(10), 1817-1824); using NBS in 1,4-dioxane (*Tetrahedron Letters*, 2010, 51(10), 1383-1385) or NBS in dichloroethane (*Catalysis Letters*, 2012, 142(3), 378-383) were disclosed in prior  
15 art. However, these processes are not industrially suitable.

The *J. Chem. Soc. Trans.* 1907, 91, 1543-1554 discloses the chlorination of 4-bromoaniline under heating using concentrated hydrochloric acid (conc. HCl), where product 2,6-dichloro-4-bromoaniline was contaminated with trichloro  
20 aniline and oxidative byproducts with dark color (quinones and azo-compounds) resulted in lower yield. Also, purification of 2,6-dichloro-4-bromoaniline became difficult and required additional steps.

The *Eur. J. Med. Chem.*, 2016, 124, 229-23 discloses the preparation of 4-amino-  
25 3,5-dichlorobenzenesulfonamide using sulfanilamide, 6N halogen acid, 30% hydrogen peroxide and recrystallization of the product from ethanol. This process involved large volume of solvent; thus, it is not industrially economical.

The *J. Chem. Soc. Trans.* 1917, 111, 41-50 discloses the preparation of  
30 tribromoaniline using 2,6-dibromosulphanilic acid, bromine, water. However, the document does not disclose the preparation of 4-amino-3,5-dichlorobenzene sulfonamide and 5-bromo-1,2,3-trichlorobenzene.

The U.S. patent no. 9,975,823B2 discloses the preparation of 1,2,3-trichloro-5-  
35 bromo-benzene by reacting 1,2,3-trichlorobenzene with a brominating agent in the presence of an acidic catalyst to obtain 1-bromo-2,3,4-trichlorobenzene which is then reacted with potassium tert-butoxide in tetrahydrofuran or 2-methyl-

- 5 tetrahydrofuran. The 1,2,3-trichlorobenzene is costly reactant which consequently leads to high production cost.

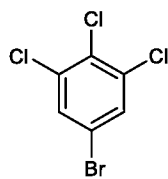
The prior art discloses the preparation of 2,6-dichloro-4-bromoaniline in two steps  
i) by treating 2,6-dichlorosulphonamide with concentrated Sulfuric acid (conc.  
10  $\text{H}_2\text{SO}_4$ ) at high temperature ( $165^\circ\text{C}$  to  $190^\circ\text{C}$ ) to obtain 2,6-dichloro aniline; ii)  
followed by bromination to obtain 2,6-dichloro-4-bromoaniline. The  
disadvantages of the prior art processes are; a) more number of reaction steps, b)  
high reaction temperature which is unsuitable and not economical.

- 15 The present invention provides process for preparation of 5-bromo-1,2,3-  
trichlorobenzene of formula (I) with high yield, minimum by-products formation  
and in economically viable manner. First time, the present invention provides a  
process for preparation of compound of formula (IV) using compound of formula  
(III) in a single step at mild reaction conditions avoiding extreme reaction  
20 conditions.

### **SUMMARY OF THE INVENTION**

- One aspect of the present invention is to provide a process for preparation of 5-  
25 bromo-1,2,3-trichlorobenzene of formula (I) using 4-bromo-2,6-dichloroaniline of  
formula (IV) which is simple, economical and commercially viable.

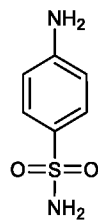
In one embodiment, the present invention provides a process for preparation of 5-  
bromo-1,2,3-trichlorobenzene of formula (I), which comprises the steps:



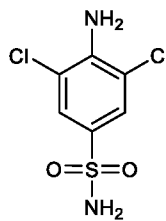
(I)

- 30 a) treating sulphanilamide of formula (II) with hydrogen peroxide,  
hydrochloric acid in dimethylformamide to obtain 4-amino-3,5-dichloro-  
benzenesulfonamide of formula (III);

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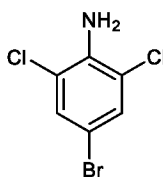
(II)



(III)

- b) treating 4-amino-3,5-dichlorobenzenesulfonamide of formula (III) with brominating agent in suitable solvent to obtain 4-bromo-2,6-dichloroaniline of formula (IV);

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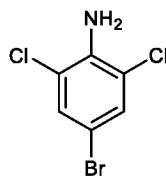


(IV)

- c) treating 4-bromo-2,6-dichloroaniline of formula (IV) with sodium nitrite, copper(I) chloride, hydrochloric acid to obtain 5-bromo-1,2,3-trichlorobenzene of formula (I).

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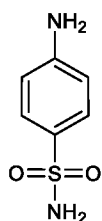
In another embodiment, the present invention provides a process for preparation of 4-bromo-2,6-dichloroaniline of formula (IV), which comprises the steps:



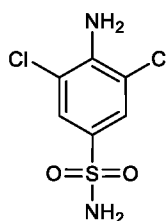
(IV)

- a) treating sulfanilamide of formula (II) with hydrogen peroxide, hydrochloric acid in dimethylformamide to obtain 4-amino-3,5-dichlorobenzenesulfonamide of formula (III);

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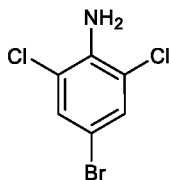
(II)



(III)

- 5      b) treating 4-amino-3,5-dichloro-benzenesulfonamide of formula (III) with  
brominating agent in suitable solvent to obtain a compound of formula (IV).

In another embodiment, the present invention provides a process for preparation  
of 4-bromo-2,6-dichloroaniline of formula (IV), which comprises the steps:



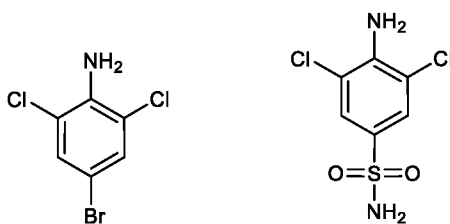
(IV)

- a) treating aniline with suitable brominating agent in dimethylformamide to  
obtain 4-bromoaniline;  
b) treating 4-bromoaniline with hydrogen peroxide, hydrochloric acid in  
15      dimethylformamide to obtain a compound of formula (IV).

In another embodiment, the present invention provides a process for preparation  
of 4-bromo-2,6-dichloroaniline of formula (IV) using 4-amino-3,5-dichloro-  
benzenesulfonamide of formula (III) in one step at mild reaction condition.

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In another embodiment, the present invention provides a process for preparation  
of 4-bromo-2,6-dichloroaniline of formula (IV), which comprises:



(IV)

(III)

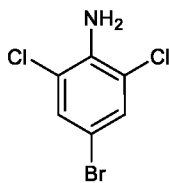
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treating 4-amino-3,5-dichloro-benzenesulfonamide of formula (III) with  
brominating agent in suitable solvent to obtain a compound of formula (IV).

In another embodiment, the present invention provides a process for preparation  
30      of 4-bromo-2,6-dichloroaniline of formula (IV), which comprises:



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(IV)

treating 4-bromoaniline with hydrogen peroxide, hydrochloric acid in dimethylformamide to obtain a compound of formula (IV).

## **DETAILED DESCRIPTION OF THE INVENTION**

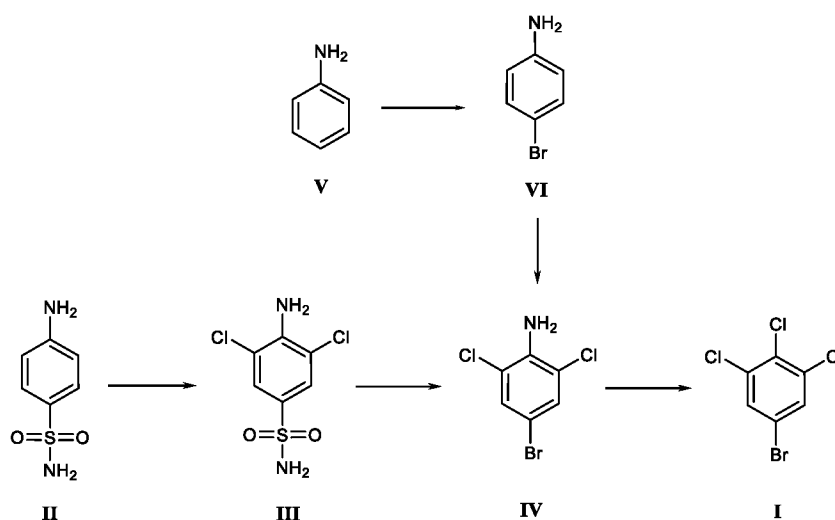
The present invention now will be described more detail hereinafter. The invention may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will satisfy applicable legal requirements. As used in the specification, and in the appended claims, the singular forms “a”, “an”, “the”, include plural referents unless the context clearly indicates otherwise.

The term ‘solvent’, as used herein refers to one or mixture of solvents.

The instant invention relates to a process for preparation of 5-bromo-1,2,3-trichlorobenzene of formula (I) using 4-bromo-2,6-dichloroaniline of formula (IV) which is simple, economical and commercially viable. Also, present invention further relates to a process for preparation of 4-bromo-2,6-dichloroaniline of formula (IV) using 4-amino-3,5-dichloro-benzenesulfonamide of formula (III) in one step at mild reaction condition. Alternatively, the present invention provides a process for preparation of 4-bromo-2,6-dichloroaniline of formula (IV), which comprises the steps: a) treating aniline with suitable brominating agent in dimethylformamide to obtain 4-bromoaniline; b) treating 4-bromoaniline with hydrogen peroxide, hydrochloric acid in dimethylformamide to obtain a compound of formula (IV).

The process of the present invention is illustrated in the following general synthetic scheme 6:

## 5 Scheme 6 –



In an embodiment of the present invention, wherein the brominating agent is selected from a group consisting of bromine, N-bromosuccinamide (NBS) and the like.

In another embodiment of the present invention, wherein the suitable solvent is selected from a group consisting of water, alcoholic solvents such as methanol, ethanol, isopropanol; dimethylformamide, dichloromethane, dichloroethane, acetonitrile, chloroform, carbon tetrachloride and the like.

In another embodiment of the present invention, wherein minimum volumes of dimethylformamide is used to obtain 4-amino-3,5-dichlorobenzenesulfonamide of formula (III) from sulfanilamide of formula (II), therefore, reducing from 20 volumes to 6 to 12 volumes of solvent with respect to sulfanilamide of formula (II), which reduces generation of excess effluent, thereby making process eco-friendly.

In another embodiment of the present invention, wherein 4-bromo-2,6-dichloroaniline of formula (IV) is prepared by using 4-amino-3,5-dichlorobenzenesulfonamide of formula (III), brominating agent and suitable solvent in one step at 25°C to 50°C.

5 In another embodiment of the present invention, wherein 4-bromo-2,6-dichloroaniline of formula (IV) is prepared by using 4-amino-3,5-dichlorobenzenesulfonamide of formula (III), brominating agent and suitable solvent in one step at 25°C to 50°C; thus avoiding i) use of conc. H<sub>2</sub>SO<sub>4</sub>, ii) high reaction temperature i.e. 165°C to 190°C, iii) extraction with organic solvent during  
10 isolation process and, iv) distillation operations.

In another embodiment of the present invention, wherein brominating aniline with brominating agent in dimethylformamide at room temperature to obtain 4-bromoaniline with purity greater than 95%. In this embodiment 4-bromoaniline is  
15 isolated without work up and without extraction using organic solvent in high yield and greater chemical purity.

In another embodiment of the present invention, wherein 4-bromo-2,6-dichloroaniline of formula (IV) is prepared by using 4-bromoaniline of formula  
20 (VI) at room temperature without heating, avoiding organic solvent and distillation process. The 4-bromo-2,6-dichloroaniline of formula (IV) is isolated by filtration without work up and without extraction using organic solvents.

In another embodiment of the present invention, wherein 4-bromo-2,6-dichloroaniline of formula (IV) is prepared by using 4-bromoaniline of formula  
25 (VI) at 5°C to 35°C and compound (IV) is isolated without extraction.

In another embodiment of the present invention, wherein 5-bromo-1,2,3-trichlorobenzene of formula (I) is prepared by using 4-bromo-2,6-dichloroaniline  
30 of formula (IV) at 0°C to 20°C without heating.

The instant invention produces 5-bromo-1,2,3-trichlorobenzene of formula (I) and 4-bromo-2,6-dichloroaniline formula (IV) using low cost, readily available reactants and reagents.

35 In another embodiment of the present invention, wherein all the crude compound may be used as such or may be purified by distillation or crystallization or by different purification techniques well understood by person skilled in the art.

5

The preparation of the starting materials and reagents used in the present invention are well known in prior art.

The invention is further illustrated by the following examples, which should not  
10 be construed to limit the scope of the invention in anyway.

### **Experimental**

#### **Example 1: Preparation of 4-amino-3,5-dichloro-benzenesulfonamide (compound III)**

15 To a solution of sulfanilamide(II) (100 g, 0.58 mol) in conc. HCl (500 ml, 5V), DMF (500 ml, 5V) was charged in 20 to 40 min at 25°C to 45°C. The reaction mixture was cooled at 15°C to 25°C. Hydrogen peroxide (200 ml (30 %), 2V) was slowly added over 20 to 30 min under stirring. The reaction mixture was stirred for 3 to 5hrs at 20°C to 25°C. After completion of reaction, the reaction mixture  
20 was cooled at 0°C to 10°C, successively chilled water (1000 ml, 10V) was added and stirred for 2 to 4 hrs. The solid product was filtered, washed with chilled water and dried to get the compound of formula (III) (120 g, 85.64 % yield).  
<sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>), δ ppm: 7.62 (s, 2H), 7.25 (bs, 2H), 6.28(bs, 2H).  
<sup>13</sup>C NMR (400 MHz, DMSO-*d*<sub>6</sub>), δ ppm: 144.25, 131.36, 125.79, 117.05.  
25 GC-MS: 240, Base m/z: 124.

#### **Example 2a: Preparation of 4-bromo-2,6-dichloroaniline (compound IV)**

To a cooled solution of compound of formula (III) (50 g, 0.207 mol) in MeOH (250 ml, 5V) and DMF (75 ml, 1.5V), bromine (26.5 ml, 0.518 mol) was slowly  
30 added at 0°C to 10°C for 15 to 35 min. The reaction mixture was warmed at 40°C to 50°C and stirred for 3 to 5hrs. After completion of reaction, reaction mixture was quenched using 20% aqueous solution of sodium metabisulfite (500 ml, 10V). Their action mass was stirred for 3 to 5hrs at room temperature to precipitate out the solid. The solid was filtered, washed with chilled water (100  
35 ml, 2V), suck dried to obtain compound of formula (IV) (40 g, 80 % yield).  
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ ppm: 7.29 (s, 2H), 4.33 (bs, 2H).  
<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>), δ ppm: 139.35, 130.14, 119.91, 107.86.  
GC-MS: 239, 241, Base m/z: 241.

**5 Example 2b: Preparation of 4-bromo-2,6-dichloroaniline (compound IV)**

The mixture of 4-bromoaniline (100 g, 0.58 mol) in conc.HCl (1000 ml, 10V) and DMF (600 ml, 6V), was stirred till clear solution for 20 to 40 min at 25°C to 35°C. The reaction mixture was cooled at 0°C to 5°C. Hydrogen peroxide (30%, 200 ml, 2V) was drop wise added over 10 to 20 min. The reaction mixture was  
10 warmed to 20°C to 25°C and stirred for 3 to 5 hrs. After completion of reaction, the reaction mixture was cooled at 0°C to 5°C, successively chilled water (1000 ml, 10V) was added and stirred for 2 hrs. The solid was filtered, washed with chilled water (400 ml, 4V) and dried to obtain the compound of formula (IV) (124.5 g, 88.90 % yield).

15 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ ppm: 7.29 (s, 2H), 4.33 (bs, 2H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>), δ ppm: 139.35, 130.14, 119.91, 107.86.

**Example 3: Preparation of 4-Bromoaniline (compound VI)**

To a cooled solution of aniline (125 g, 1.34 mol) in a DMF (500 ml, 4V), N-bromosuccinamide (238.88g, 1.34 mol) was lot-wise charged at 0°C to 5°C for 30  
20 to 60 min. The reaction mixture was stirred at 0°C to 10°C for 1 to 3hrs. After completion of reaction, the reaction mixture was poured into chilled water (1250 ml, 10V) and stirred for 3hrs at 0°C to 5°C to precipitate out the solid. The solid was filtered, washed with chilled water and dried to obtain compound of formula  
25 (VI) (184.6 g, 79.94 % yield, purity by GC>95%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ ppm: 7.22 (dt, *J*<sub>1</sub>= 8.8 Hz, *J*<sub>2</sub>= 3.2 Hz, 2H), 6.53 (dt, *J*<sub>1</sub>= 8.8 Hz, *J*<sub>2</sub>= 3.2 Hz, 2H), 3.55 (bs, 2H).

<sup>13</sup>C NMR (400 MHz, CDCl<sub>3</sub>), δ ppm: 145.33, 131.86, 116.61, 109.99.

**30 Example 3: Preparation of 5-bromo-1,2,3-trichlorobenzene of formula (I)**

To a solution of 4-bromo-2,6-dichloroaniline of formula (IV) (100 g, 0.415 mol) in Conc.HCl (300 ml, 3V), drop wise aqueous solution of NaNO<sub>2</sub> (34.4 g, 0.498 mol) in water (100 ml, 1V) was charged at -5°C to 10°C and stirred for 1 hrs..  
Simultaneously, the solution of Cu(I)Cl (20.5 g, 0.207 mol) in conc.HCl (200 ml,  
35 2V) was prepared and stirred at 5°C to 15°C. To this solution, diazonium salt solution was added slowly at 5°C to 20°C and stirred for 1 hrs. After completion of reaction, water (700 ml, 7V) was added to the reaction mixture. The reaction

- 5 mass extracted with toluene, toluene layer washed with water and the crude product was purified by distillation to obtain compound of formula (I) as a white solid (75.6 g, 70% yield, purity by GC>97%).

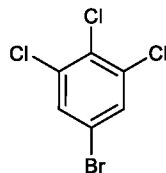
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ),  $\delta$  ppm: 7.49 (s, 2H).

$^{13}\text{C}$  NMR (400 MHz,  $\text{CDCl}_3$ ),  $\delta$  ppm: 134.90, 131.30, 130.85, 119.76.

- 10 GC-MS: 258, Base m/z: 260.

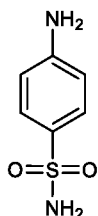
5 CLAIM:

1. A process for preparation of 5-bromo-1,2,3-trichlorobenzene of formula (I), which comprises the steps:

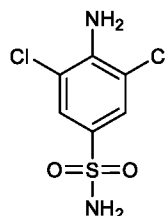


(I)

- a) treating sulfanilamide of formula (II) with hydrogen peroxide, hydrochloric acid in dimethylformamide to obtain 4-amino-3,5-dichloro-benzenesulfonamide of formula (III);

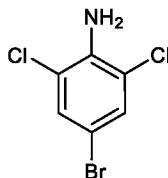


(II)



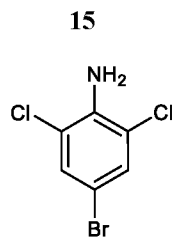
(III)

- b) treating 4-amino-3,5-dichloro-benzenesulfonamide of formula (III) with a brominating agent in a solvent to obtain 4-bromo-2,6-dichloroaniline of formula (IV);



(IV)

- c) treating 4-bromo-2,6-dichloroaniline of formula (IV) with sodium nitrite, copper(I) chloride, hydrochloric acid to obtain 5-bromo-1,2,3-trichlorobenzene of formula (I).
2. The process as claimed in claim 1 wherein, the process for preparation of 4-bromo-2,6-dichloroaniline of formula (IV) comprises the steps:



- a) treating aniline with a brominating agent in dimethylformamide to obtain 4-bromoaniline;
- b) treating 4-bromoaniline with hydrogen peroxide, hydrochloric acid in dimethylformamide to obtain a compound of formula (IV).

3. The process as claimed in claim 1 wherein, the process for preparation of 4-bromo-2,6-dichloroaniline of formula (IV) comprises:

treating 4-amino-3,5-dichloro-benzenesulfonamide of formula (III) with a brominating agent in a solvent to obtain a compound of formula (IV),

(OR)

treating 4-bromoaniline with hydrogen peroxide, hydrochloric acid in dimethylformamide to obtain a compound of formula (IV).

4. The process as claimed in claim 1 to 3 wherein, the brominating agent is selected from a group consisting of bromine and N-bromosuccinamide (NBS).

5. The process as claimed in claim 1 to 3 wherein, the solvent is selected from a group consisting of water, alcoholic solvents such as methanol, ethanol, isopropanol; dimethylformamide, dichloromethane, dichloroethane, acetonitrile, chloroform and carbon tetrachloride.

6. The process as claimed in claim 1 wherein, the dimethylformamide is used in 6 to 12 volumes.

7. The process as claimed in claim 1 to 3 wherein, 4-bromo-2,6-dichloroaniline of formula (IV) is prepared by using 4-amino-3,5-dichloro-benzenesulfonamide of formula (III), brominating agent and solvent in one step at 25°C to 50°C.

8. The process as claimed in claim 1 to 3 wherein, bromination of aniline with brominating agent in dimethylformamide is performed at room temperature to obtain 4-bromoaniline of



- 5 formula (VI) with purity greater than 95%; where 4-bromoaniline is isolated without work up and without extraction.
9. The process as claimed in claim 1 to 3 wherein, 4-bromo-2,6-dichloroaniline of formula (IV) is prepared by using 4-bromoaniline of formula (VI) at room temperature without  
10 heating, avoiding organic solvent and distillation process; where 4-bromo-2,6-dichloroaniline of formula (IV) is isolated by filtration without work up and without extraction.
10. The process as claimed in claim 1 to 3 wherein, 4-bromo-2,6-dichloroaniline of formula (IV) is prepared by using 4-bromoaniline of formula (VI) at 5°C to 35°C and isolated  
15 without extraction.
11. The process as claimed in claim 1 wherein, 5-bromo-1,2,3-trichlorobenzene of formula (I) is prepared by using 4-bromo-2,6-dichloroaniline of formula (IV) at 0°C to 20°C without  
20 heating.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2021/050485

## A. CLASSIFICATION OF SUBJECT MATTER

C07C25/10 Version=2021.01

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

TotalPatent One, IPO Internal Database

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Yun, Taikangxiang; Tan, Qin; Liu, Ying; Lai, Luhua (2016). Identification of acyl thiourea derivatives as potent Plk1 PBD inhibitors. European Journal of Medicinal Chemistry, (), S0223523416306869-. doi:10.1016/j.ejmech.2016.08.043 Page 5; para 1 and page 25; scheme 2 (x=C1)	1-11
Y	Qiu, M.-Y. & Lv, D.-J. (2005). Appl. Chem. Ind. 34, 115-116 See English translation of the abstract	1
Y	Rui Zhang; Lei Huang; Yanfang Zhang; Xiaorong Chen; Weihong Xing; Jun Huang (2012). Silver Catalyzed Bromination of Aromatics with N-bromosuccinimide. , 142(3), 378-383. doi:10.1007/s10562-011-0764-2 Page 383, Table 2, Ar-H = aniline	1-11
Y	Richard Sott; Christine Hawner; Jon E. Johansen (2008). Synthesis of dioxin-like monofluorinated PCBs: for the use as internal standards for PCB	1-11

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

\* Special categories of cited documents:

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

"D" document cited by the applicant in the international application

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

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

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

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

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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

27-04-2021

Date of mailing of the international search report

27-04-2021

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2021/050485

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>analysis. , 64(18), 4135-4142. doi:10.1016/j.tet.2008.01.003 See page 413, scheme 2; Compounds 7 and 8</p> <p>-----</p> <p>Sushil Kumar Sharma, Vol. 5(12), 54-73, December (2015). See page 56, Table 1, column 4</p>	2-11