A PROCESS TO SYNTHESIZE (ARYL)(HETEROARYL)METHANOLS

IITM Technology Available for Licensing

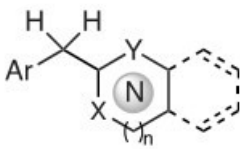
Problem Statement

- The **(aryl)(heteroaryl)methanol derivatives** are basic core in many drug molecules.
- Several efficient procedures were reported for the **synthesis of aryl heteroaryl ketones** by direct oxidation of **C(sp3)–H bonds**.
- Certain drawbacks are utilization of precious metal catalysts, pre-modified raw materials, sensitive chemical reagents.
- Moreover, **no catalytic procedure** is reported for the preparation of (aryl)(heteroaryl) methanols by a controlled oxidation of C(sp3)–H bonds of (aryl)(heteroaryl)methanes.
- So, it is of particular interest to develop an **alternative** and straight forward approach to **synthesize (aryl)(heteroaryl)methanols**.

Technology

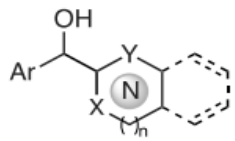
The present invention relates to a **transition-metal-free process method to synthesize** (aryl)(heteroaryl)methanol derivatives **I** from (aryl)(heteroaryl)methanes **II** through halogen bond-assisted **C(sp³)-H bond** activation strategy.

A process to synthesize (aryl) (heteroaryl) methanol derivatives comprising the steps of:



II

Reacting an (aryl) (heteroaryl) methane represented by formula II in the presence of catalyst (III) and one or more additives (IV, V, VII, VIII) in an aprotic solvent (VI) at room temperature,



I

heating the reaction mixture between 80-120oC for a period between 5 mins to 20 hours to obtain the (aryl)(heteroaryl) methanol having formula I

Wherein **Ar** represents one of the groups independently selected from group comprising of:

2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 3-methoxyphenyl, 4-ethylphenyl, 2-iodophenyl, phenyl, 4-methoxyphenyl, 4-(methylthio) phenyl, 3,5-dimethylphenyl, 4-tertbutylphenyl, 1-napthyl, 2-hydroxyphenyl, 4-chlorophenyl, 4-fluorophenyl, 2-thiophenyl, 1,1'-biphenyl, 4-bromophenyl, or 2-chlorophenyl

- **catalyst** is molecular iodine (III), One/more **additives** is selected from triphenylsilylchloride (IV), hydroiodic acid (V), trimethylsilylchloride (VII), triethylsilylchloride (VIII) and **aprotic solvent** is dimethylsulfoxide (VI).
- **'N' (nitrogen)** embedded ring independently represents a **heterocyclic ring** selected from a group comprising of 2-pyridyl 4-pyridyl, and 2-benzo[d]thiazole, wherein **X** is **methine group** and **Y** is a **heteroatom** selected from **'N' or 'S' or 'O' and 'n'** is an independent integer **0 or 1**.
- The reaction stoichiometry the ratio between formula II, III, IV, V is **1:0.1:0.6: 0.2**.

Technology Category/ Market

Category: Chemistry & chemical Analysis, Drugs & Pharmaceutical Engineering

Industry: Catalysts and Chemical Manufacturing, Drugs & Pharmaceutical manufacturing

Applications: Drug Manufacturing

Market: The global methanol market is projected to grow from **$28.74 B** to **$39.18 B** at **4.5% CAGR** during forecast period, **2021-2028**.

Intellectual Property

IITM IDF Number: 2215
IP Patent Number: 406714 (**Granted**)

TRL (Technology Readiness Level)

TRL – 3; Proof of Concept

Key Features / Value Proposition

- This methodology particularly relates to an advantages preparation of wide range of **medicinally important (aryl)(heteroaryl) methanol derivatives**.
- The (aryl)(heteroaryl)methanol derivatives are basic core in many **drug molecules** like phenyl(pyridin-2-yl)methanol which is an **anticonvulsant**, (4- chlorophenyl) (pyridin-2-yl) methanol is an **antihistamine** intermediate of **carbinoxamine** & **doxylamine** & also serves as a key **intermediate** in **chloropheniramine synthesis** known for **antirhinitis**.
- It is derived by using **polyaromatic group-substituted methane** as a raw material, **iodine** as **catalyst**, **silylchloride** as **additive** and **dimethyl sulfoxide** as **source of oxygen atom** and a **reaction medium** in **high yields & purity.**

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