PROCESS FOR PREPARATION OF SUBSTITUTED TETRAHYDROQUINOLIN-4-ONE COMPOUNDS

IITM Technology Available for Licensing

Problem Statement

- Tetrahydroquinolin-4-one compounds are important because they act as the core structure in many medicines, including anticancer, antiviral, and neurological drugs.
- Traditional methods use multicomponent reactions or metal-mediated cyclisation that require high temperatures and toxic catalysts. These approaches are expensive, generate harmful waste, and make purification difficult.
- Modern catalytic techniques like hydrogenation, Michael addition, and domino reactions can produce these compounds. However, they still depend on costly ligands, toxic metals, or complex multi-step processes that limit industrial use.
- There is a demand for a greener, cheaper, and more efficient synthesis method that avoids toxic byproducts. This invention meets that need by using Lewis acid–catalyzed ring-opening of cyclopropanes, giving high yields under mild, eco-friendly conditions.

TRL (Technology Readiness Level)

TRL 3, Experimental proof of concept

Technology Category/ Market

Category- Chemistry & Chemical Analysis
Industry:
Pharmaceutical Industry, Medicinal Chemistry & Drug Discovery, **Fine Chemicals & Specialty Chemicals,** Agrochemical Industry,
Applications:
medicinal chemistry for designing and optimizing new therapeutic molecules, pesticides, herbicides, and fungicides, anticancer drugs, CNS disorder treatments, hormone receptor agonists, antitumor agents.

Market report: The global 1,2,3,4-Tetrahydroquinoline reagent market size was estimated **at USD 1.2 billion in 2023** and is projected to reach **USD 2.3 billion by 2032**, growing at a compound annual growth **rate (CAGR) of 7.2% during the forecast period.**

Intellectual Property

- **IITM IDF Ref 3407**
- **IN 202541074805 Patent Application**

Research Lab

Prof. GOVINDASAMY SEKAR
Dept of Chemistry

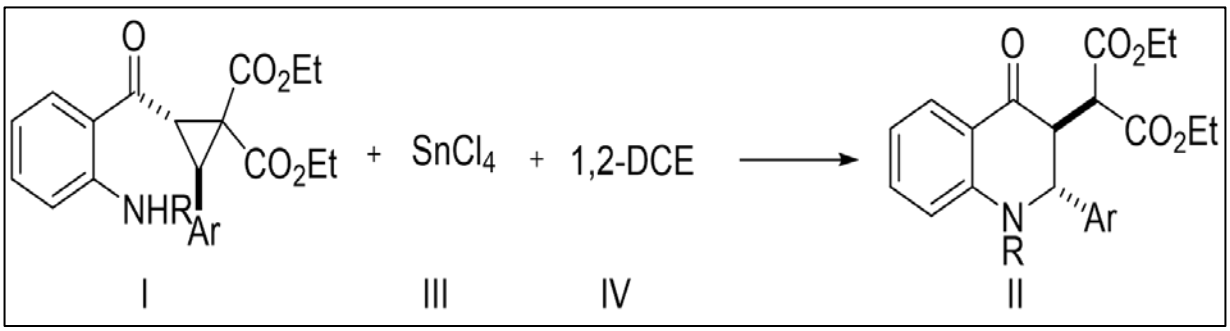

Figure: Lewis acid-**catalyzed ring-opening of 2′-o-aminoarene cyclopropane (Formula I)** in 1,2-DCE **using $SnCl_4$, followed by extraction and purification**, yields 2,3-disubstituted **tetrahydroquinolin-4-one derivatives (Formula II).**

CONTACT US
Dr. Dara Ajay, Head TTO
Technology Transfer Office,
IPM Cell- IC&SR, IIT Madras
Email: headtto-icsr@icsrpis.iitm.ac.in
ttooffice@icsrpis.iitm.ac.in
Phone: +91-44-2257 9756/ 9843

Technology

The compound called **2'-o-aminoarene cyclopropane**. This small, strained ring molecule is chosen because it can easily be opened and rearranged into more complex structures.

A **Lewis acid catalyst** such as stannic chloride ($SnCl_4$) is added to trigger the reaction. The catalyst helps break open the cyclopropane ring and guides it into forming the desired product.

The reaction is carried out in solvents like dichloroethane or dichloromethane. It takes place at **moderate temperatures (25–55 °C)** avoiding the need for extreme heating.

Under stirring, the cyclopropane ring opens and rearranges into a **tetrahydroquinolin-4-one structure.** This step is efficient and produces mainly one stable form of the molecule.

After the reaction, the solvent is removed, and the product is extracted with an organic solvent such as ethyl acetate. The compound is then dried and purified, yielding the final **drug-building block** in high yield.

Key Features / Value Proposition

The process uses Lewis acid catalysts such as **$SnCl_4$, $TiCl_4$, or $Cu(OTf)_2$ in 5–15 mol%** amounts, ensuring efficient ring-opening without toxic heavy metals.

The reaction runs in common solvents like **1,2-dichloroethane (DCE) at 25–55 °C**, avoiding extreme heating and making it energy-efficient.

The catalyst, solvent, and starting material are **used in a ratio of 1 : 0.05–0.2 : 1–2,** which balances cost and efficiency.

The reaction time is short, **only 20–60 minutes, and yields up to 90%** product with a single diastereomer (high purity).

Workup is simple: extraction with ethyl acetate**, drying with anhydrous sodium sulfate, and purification** by column chromatography, making it industrially scalable.

CONTACT US
Dr. Dara Ajay, Head TTO
Technology Transfer Office,
IPM Cell- IC&SR, IIT Madras
Email: headtto-icsr@icsrpis.iitm.ac.in
ttooffice@icsrpis.iitm.ac.in
Phone: +91-44-2257 9756/ 9843