



IIT MADRAS

Indian Institute of Technology Madras

Technology Transfer Office
TTO - IPM Cell



Industrial Consultancy & Sponsored Research (IC&SR)

Synthesis Of Trisubstituted 1H-pyrrole-3-carbaldehyde Compounds

IITM Technology Available for Licensing

PROBLEM STATEMENT

- **Poly-substituted 1H-pyrroles** are valuable in organic synthesis, bioactive molecules, and catalysis due to their unique structural features and potential biological activities.
- They are used in **drug discovery for antitumor**, antibacterial, antiviral, anti-inflammatory, and anticancer agents.
- **Synthesis methods** include multicomponent reactions, metal mediated cyclization, and 1,3-dipolar cycloaddition using metals.
- Examples include **Oroidin, Porphobilinogen, Sunitinib malate, Pentabromopseudilin, and Pyoluteorin.**
- Researchers have also developed metal-catalyzed oxidative dehydrogenation/aromatization reactions and **copper-catalyzed** three-component reactions for polysubstituted pyrroles from α -diazo ketones, nitroalkenes, and amines.

TECHNOLOGY CATEGORY/MARKET

Technology: Synthesis Of Trisubstituted 1H-pyrrole-3-carbaldehyde Compounds

Category: Chemistry & Chemical Synthesis

Industry: Medicinal Industries

Application: Active Pharmaceutical Ingredient

Market: The global market size of aldehyde, including carbaldehyde, was valued at USD 6.3 billion in 2022 and is projected to reach USD 8.5 billion by 2031, with a CAGR of 39% during the forecast period 2023-2031.

INTELLECTUAL PROPERTY

IITM IDF Ref. - 2999

Patent No: IN - 562780

TRL (Technology Readiness Level)

TRL-3, Experimental Proof of Concept;

Research Lab

Prof. G. Sekar,
Department of Chemistry, IIT Madras

TECHNOLOGY

Organic Synthesis and Catalysis

- The process involves organic synthesis, using chemical reagents and catalysts to build complex molecules. The key step involves using a racemic diphenylprolinol trimethylsilyl ether (IV) as a chiral catalyst, which facilitates the reaction by enabling selective formation of the desired product.
- Cinnamaldehyde (I) reacts with thiazolium salts (II), along with a DMAP (V), which helps in facilitating nucleophilic addition and controlling reaction mechanisms.
- This is an example of heterocyclic chemistry, where 1H-pyrrole, an important heterocyclic compound, is synthesized with functional groups like aldehyde (-CHO) attached at specific positions.

Reagents and Solvents

- Ethanol (EtOH) is used as the solvent for the reaction, and various other reagents such as EtOAc (ethyl acetate) for extraction and Na_2SO_4 for drying are involved.
- Column chromatography using silica gel is employed to purify the products. The elution process (petroleum ether/ethyl acetate mixture) is optimized to separate the different compounds based on their polarities.

Analytical Techniques

- Thin Layer Chromatography (TLC) is used to monitor reaction progress.
- Melting Point Analysis, IR spectroscopy, NMR spectroscopy, and High-Resolution Mass Spectrometry (HRMS) are used to characterize the final products and ensure their purity and structure.

CONTACT US

Dr. Dara Ajay, Head TTO

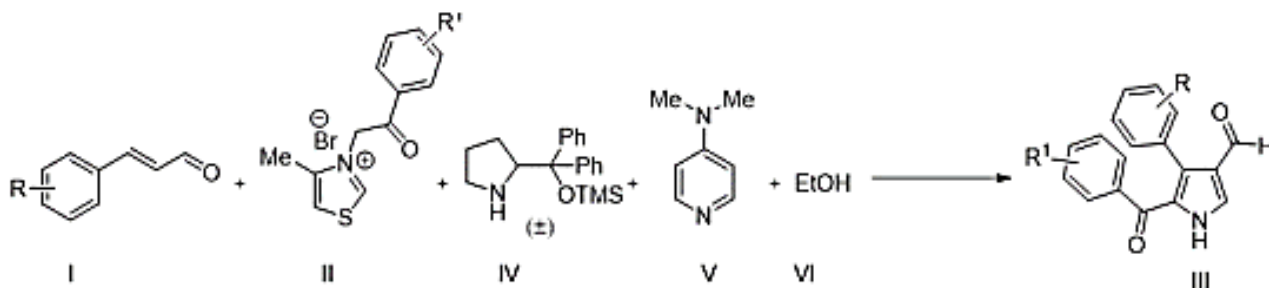
Technology Transfer Office,
IPM Cell- IC&SR, IIT Madras

Email: headtto-icsr@icsrpis.iitm.ac.in

ttooffice@icsrpis.iitm.ac.in

Phone: +91-44-2257 9843

Preparation of Trisubstituted 1H-pyrrole-3- Carbaldehyde Compounds



Formula I - Unsaturated Aldehyde(Cinnamaldehyde)

Formula II - substituted or unsubstituted 4-Methyl thiazolium salt

Formula IV- diphenylprolinol trimethylsilyl ether

Formula V- DMAP

Formula VI – Ethanol

Formula III - Trisubstituted 1H-pyrrole-3- Carbaldehyde

Crystallography

The synthesis employs single crystal X-ray diffraction (XRD), a powerful tool for determining the three-dimensional structure of the compounds at the molecular level.

Purification and Separation

Column chromatography is crucial for isolating pure products from the crude reaction mixtures, which is a common technique in synthetic organic chemistry for separating compounds based on their different solubilities.

Key Features / Value Proposition

Innovative and Efficient Synthesis

Racemic catalysts combined with thiazolium salts offer an efficient method for synthesizing functionalized pyrrole derivatives, enabling the production of complex, highly specific molecules in simple reaction steps.

Scalability and Purity

The purification methods and reaction conditions ensure that the products can be obtained with high purity and yield, making them suitable for scale-up and industrial applications. This process also demonstrates scalability, which is crucial for mass production in pharmaceuticals or chemical industries.

High-Value Chemical Compounds

Trisubstituted 1H-pyrrole-3-carbaldehyde, a valuable intermediate in medicinal chemistry, organic electronics, and materials science, is derived from the pyrrole backbone found in biologically active molecules.

Environmental and Process Efficiency

Using ethanol as a solvent and employing drying agents like anhydrous Na₂SO₄, the process appears relatively eco-friendly compared to processes that use toxic or hazardous solvents. The high yields (often 70% or higher) suggest an efficient process with minimal waste generation.

Pharmaceutical Applications

Many pyrrole derivatives are potential candidates for drug development due to their pharmacological properties. For instance, compounds with aldehyde groups may show activity in fields like cancer research, neurodegenerative diseases, and antimicrobial therapies.

Application in Material Science

The synthesized pyrrole derivatives might have applications in organic electronic materials, such as conducting polymers or materials used in sensors, displays, and solar cells.

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Phone: +91-44-2257 9843