TRANSITION METAL-FREE DENITRATIVE C-S CROSS COUPLING OF 2'- NITROCHALCONES FOR THE SYNTHESIS OF THIOCHROMANONES

IITM Technology Available for Licensing

Problem Statement

- Conventional methods for synthesizing thioflavanones have several drawbacks:
  - Expensive and **toxic metal-catalysts**.
  - **Sensitive ligands** are required.
  - Smelly sulfur sources are utilized.
  - High-temperature conditions are necessary.
  - Unavoidable by-products are generated.
  - **Multistep synthesis** is involved.
  - Air-sensitive starting materials are used.
- These limitations make existing protocols less suitable for industrial production.
- The inventors devised a new protocol to address these issues and make the process more useful for industrial production.

Technology Category/ Market

Category-Chemicals, Pharmaceuticals & Drugs
Applications - Pharmaceuticals, Thioflavanones with antifungal, antibacterial, and antioxidant properties can be explored for their therapeutic potential in Medicine, and has applications in Biotechnology, Chemicals Industry.
Industry - Pharmaceuticals and Healthcare, Drug Development, Biotechnology

Market - The global industrial Catalyst market size was USD 20.4 Billion in 2022 and is expected to reach USD 34.6 Billion in 2032, and register a revenue **CAGR of 5.3%.**

TRL (Technology Readiness Level)

TRL - 3, Proof of concept stage.

Research Lab

Prof. Govindasamy Sekar, Dept. of Chemistry

Intellectual Property

- IITM IDF Ref. **2280**
- **IN 408736 - Patent Granted**

Technology

- The present disclosure relates to **a transition-metal free synthesis of thiochromanone and its derivatives from 2'-nitrochalcones** as starting material, iodine as a catalyst, sodium acetate as base and xanthate as an odorless sulfur surrogate.

- The main aspect of the present disclosure provides **a process for synthesizing thiochromanones**, wherein the process comprising the steps of:

a. **Adding 2'-nitrochalcone, potassium ethyl xanthate, iodine and sodium acetate base to oven-dried reaction tube to form a reaction mixture;**
b. **Adding DMSO in the reaction mixture of step (a);**
c. **Keeping the reaction mixture of step (b) in pre-heated oil bath having a temperature of 80 oC for a time ranging from 3 to 8 hours to obtain a reaction mixture of thiochromanone;**
d. **Decreasing the temperature of thiochromanone reaction mixture of step (c) to room temperature and extracting the crude product with organic solvents;**
e. **Brine wash the extracted crude product of step (d) and drying over anhydrous Na2SO4;**
f. **Removing the solvents and separation of crude product using organic solvents to obtain the final product.**

CONTACT US
Dr. Dara Ajay, Head
Technology Transfer Office,
IPM Cell- IC&SR, IIT Madras

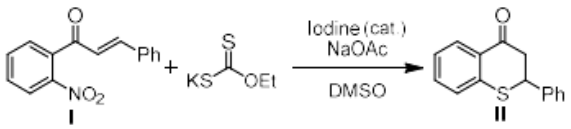
IITM TTO Website:
https://ipm.icsr.in/ipm/

Email: smipm-icsr@icsrpis.iitm.ac.in
sm-marketing@imail.iitm.ac.in
Phone: +91-44-2257 9756/ 9719

Industrial Consultancy & Sponsored Research (IC&SR)

Key Features / Value Proposition

1. Having the initial result in hand, the reaction condition was systematically optimized by screening all the parameters.
2. After extensive optimization, the best result was obtained with 3 equiv. of xanthate, 1 equiv. of sodium acetate and 20 mol% iodine in DMSO solvent at 80 oC to yield the desired 2- arylthiochromanones.



3. Thiochromanones were observed in moderate to good yield from 65% to 90%.
4. Developed methodology can be used without any modification.
5. Easily accessible and inexpensive raw materials such as 2'-nitrochalcones have been utilized as starting material.
6. The protocol evades the use of toxic transition metals as catalyst.
7. Environmentally friendly and safer process.

Areas of Application

1. The methodology can be utilized to attain 3'-hydroxythioflavanone with a hydroxyl group at the 3'-position. The molecule is known to exhibit high antioxidant activity as well as potent inhibition of NO production in LPS-induced macrophage cells.
2. Various other thioflavanones can be prepared which display biological properties such as antifungal, antibacterial and antioxidant properties.
3. Hydrazone derivatives of thiochromanones can be prepared by post synthetic modification of these thiochromanones which show enhanced antileishmanial activity.
4. The thiochromanones can be oxidized to thiochromenones very easily on reacting with catalytic amount of iodine and DMSO as solvent.
5. Thiochromenones also tend to various show biological properties.

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IITM TTO Website:
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Email: smipm-icsr@icsrpis.iitm.ac.in
sm-marketing@imail.iitm.ac.in
Phone: +91-44-2257 9756/ 9719