A Process for the Preparation of the Core Structure in Quinolone and Naphthyridone Class of Antibiotics

IITM Technology Available for Licensing

Problem Statement

- The **existing method** to **synthesize quinolone and naphthyridone derivatives** are crucial in the **antibiotics development** and displaying potential in **anti-HIV** and other therapeutic applications, suffer from complexity, involvement of toxic reagents, low yields, and inefficiency.
- There is a pressing need for a more **streamlined**, **efficient and environmentally synthetic approach** to produce the derivatives, addressing challenges associated with current methods and **meeting the increasing demand** for these valuable compounds in pharmaceutical industry.
- Hence, there lies the need for the instant disclosure: **A Process for Preparation of Core Structure in Quinolone & Naphthyridone Class of Antibiotics.**

Technology Category/ Market

Chemistry & Chemical Analysis

Industry: Antibiotics, Pharmaceuticals, Materials Science, Chemicals, Catalysts

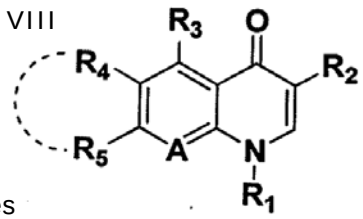
Applications: These compounds offer a wide range of potential applications, spanning drug development for novel therapeutics, material synthesis including coatings and polymers, and their use in various chemical processes such as catalysts, specialty chemicals, pharmaceuticals and materials science industries.

Market: The global antibiotics market size was estimated at **$50.91 Billion** in **2023;** is expected to grow at **4.2% CAGR** from **2024 to 2030.**

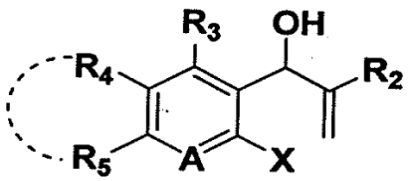
Technology

The invention relates to a process for the preparation of **Quinolone and Naphthyridone derivatives (Formula VII)** using Baylis-Hillman adducts and amines.

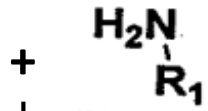
FIG 1: General Formula VIII
Where,
R1, R2, R3, R4, R5, & A are permissible substituents within the quinolone and naphthyridone molecules



VII

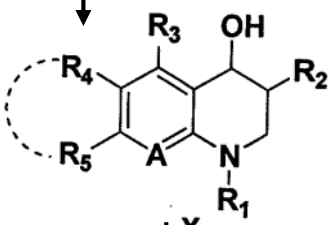


VIII



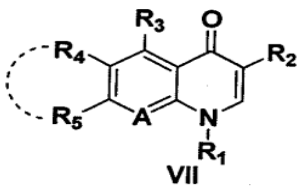
IX

Base, solvent



X

Δ Oxidation



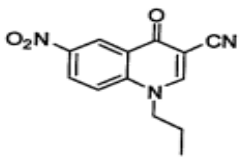
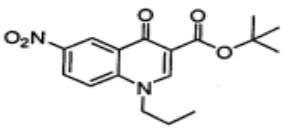
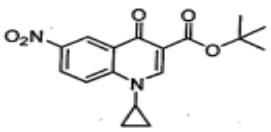
VII

After the **addition** of tandem Aza-Michael and **cyclization** of SNAr,

4-hydroxy-1,2,3,4-tetrahydroquinoline or **4-hydroxy-1,2,3,4-tetrahydro-1,8-naphthyridine** derivative is obtained as an **intermediate,**

which is then **oxidized** to get the **quinolone or naphthyridone** skeleton in single-step with excellent yield.

Given below is the list of synthesized quinolones & benzonaphthyridones, showing:
compound No. | Structure | Overall Yield (%)

VII-I		70
VII-J		90
VII-K		87

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Key Features / Value Proposition

User perspective:-

- The formula VII compounds offer a vast array of structural variations, providing users with a broad spectrum of potential applications.
- The compounds can be tailored with specific substituents, allowing users to fine-tune properties for desired functionalities. Its structural diversity indicates potential use various industries.

Industrial perspective:-

- The compounds' variability presents versatile opportunities, catering to multiple market segments.
- The wide range of chemical structures and synthesis methods offer market exclusivity for different product variations. With the ability to produce multiple variations, industries can expand their product lines to meet diverse market demands and explore new applications.

Technology perspective:-

- The synthesis process provides a route for generating a diverse library of compounds using a relatively flexible and controllable method, offering a clear and reproducible approach for synthesizing these compounds.
- The structural variations and the unique synthesis pathway could contribute to the development of novel compounds, potentially giving unique chemical properties or applications.

TRL (Technology Readiness Level)

TRL-4: Validated in Laboratory

Intellectual Property

IITM IDF No.: **852** | IP No.: **297020 (Granted)**

Research Lab

Prof. Muraleedharan K M; Department of Chemistry

The Invention Discloses:

The structural variations and permissible substituents (R1, R2, R3, R4, R5, and A) within the quinolone and naphthyridone molecules, encompassing a wide array of potential modifications.

- The process for synthesizing these derivatives, starting from a Baylis-Hillman adduct (formula VIII) and an amine compound (formula IX).

It involves a base-catalyzed reaction to yield 4-hydroxy-1,2,3,4-tetrahydroquinoline or 4-hydroxy-1,2,3,4-tetrahydro-1,8-naphthyridine derivative (formula X), followed by oxidation to produce the quinolone or naphthyridone derivative (formula VII).

- It cover specific aspects of the synthesis process, such as:
  - the intermediate obtained after step a) doesn't require chromatographic purification before proceeding to the next step.
  - specify the solvents suitable for steps a) and b) respectively, providing a broad range of temperature, the reaction time.
  - enumerates various bases suitable for the reaction in step a).
  - lists oxidizing agents that can be used in step b), offering a variety of choices.
  - reiterates that the amines used in step a) must possess the same R1 groups as defined in the previous claims.

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