Continuous flow process and apparatus for manufacture Of dl-2-nitro-1-butanol

IITM Technology Available for Licensing

Problem Statement

- An infectious death causing disease **Tuberculosis (TB)** that primarily affects lungs is **treatable** and **mendable** but **expensive** treatment.
- FDA approved first line anti TB drugs include **rifampicin, ethambutol, isoniazid, pyrazinamide**.
- Though India is one of the largest producers of **ethambutol, dl-2-amino-1-butanol;** the key intermediate for synthesis of ethambutol is mostly **imported** as there is no significant local production.
- Further, available **batch** processes for dl-2-amino-1-butanol synthesis suffer from **bottlenecks/challenges** including **safe handling** of raw materials, **excessive use** of reagents and its recovery, lack of **reaction control**, **low , etc.**

Hence there is a need to develop an improved method to overcome above-mentioned issues.

Technology Category/ Market

Chemical Engineering: Kinetics**,** Process design and reaction engineering
Industry: Pharmaceutical, Reactor Design
Applications: Bio-medical, Flow Reactors,
Market: The global flow reactor market was valued at **USD 1.60** billion in 2022 and is expected to grow at a **CAGR of 11.2%** over the forecast period.

Technology

Process Flow

A **continuous process** for preparation of **dl-2-nitro-1-butanol** comprises of the following steps:

Providing an aqueous solution of sodium hydroxide (A) and 1- nitro-propane (B) dissolved in an **alcohol (methanol or ethanol)**;

Pumping a predetermined first molar ratio of solution A and B to mix in a first tubular reactor for a first residence time to form intermediate product stream solution mixture;

Pumping formaldehyde aqueous solution to react with the intermediate product stream at a second predetermined molar ratio in a second tubular reactor for a second residence time to form a product stream;

Quenching the product stream in glacial acetic acid to obtain a quench liquor having dl-2-nitro-1-butanol, wherein the first and the second tubular reactors are maintained at temperature **≥ 35° C.**

Reactor Design

The **Continuous Flow Reactor** comprises:

- A first reservoir configured to store a solution of **1-nitropropane (starting material)** and connected to a first pump,
- A second reservoir for storing a solution of **NaOH** and connected to a second pump,
- Wherein the first pump and the second pump are connected with a **tubing** to join the first stream entering a first tubular reactor, and the first tubular reactor having a **first length** and is configured to output a mixture of solutions from first and second reservoir as **intermediate product stream**.
- A third reservoir is to store a solution of **formaldehyde** and connected to a third pump, wherein, the third pump is configured to pump the formaldehyde solution to **join** the intermediate product stream entering a second tubular reactor.
- Further, the second tubular reactor has a second length that is **3-8 times the first length** and configured to output an end product having dl-2- nitro-1-butanol.
- The equipment is further provided with a quench reservoir having glacial acetic acid wherein the dl-2-nitro-1-butanol is extracted from the quench liquor using a solvent (**dichloromethane**) from being converted to other products.

The first & second **tubular reactors** are configured to be maintained at a temperature **≥ 35° C.**

- The process have a following **properties**:
- The process cycle is completed in **≥30 minutes**;
- The predetermined first & second molar ratio= **1**.
- The conversion to dl-2-nitro-1-butanol is **≤89%.**
- The second residence time is **3-8 times** the first residence time.

A **continuous process** for preparation of dl-2-nitro-1-butanol from 1-nitropropane is shown in **FIG. 1** & **a continuous flow reactor** for producing dl-2-nitro-1-butanol from 1-nitropropane is shown in **FIG. 2**.

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Images

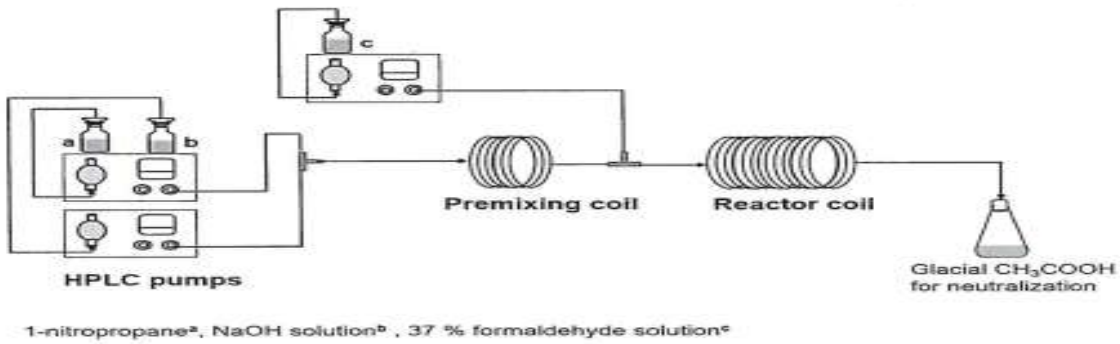

FIG. 1

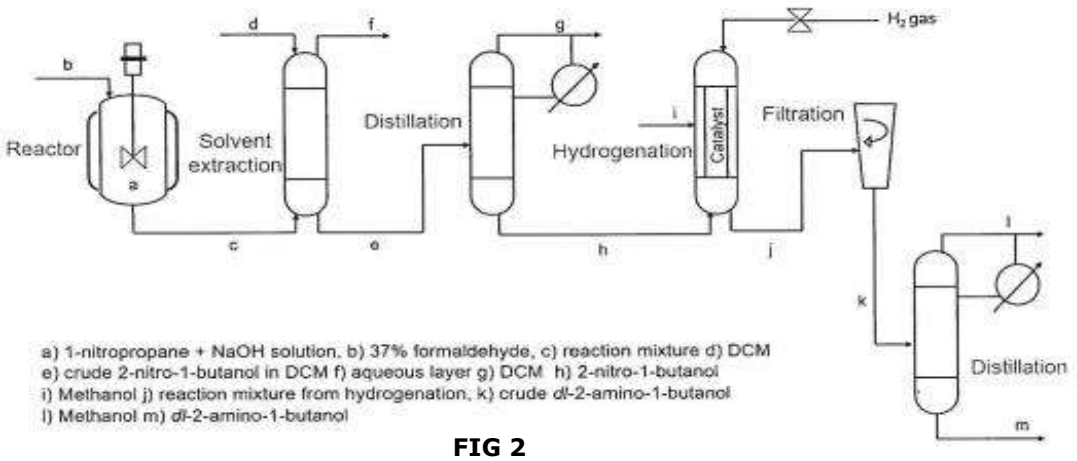

FIG 2

Key Features / Value Proposition

- **Optimal use** of reactants and reagents in flow reactor to produce dl-2-amino-1-butanol, making it a **cost effective process**.
- Facilitates **reduction of reaction time** using continuous flow process technology, grants **better temperature control** through high mass and heat transfers.
- Over **exposure** of raw materials to reagents is **avoided**, thereby reducing the **formation of undesired reaction products**.
- The continuous flow process is amenable to **online monitoring** and control of reaction progress using **spectroscopic techniques**.
- Process design and reaction engineering are **modifiable** to any scale of production.
- The technology used capacitates **optimization** of operation conditions and **study of intrinsic reaction kinetics**.

Research Lab

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Intellectual Property

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TRL (Technology Readiness Level)

TRL- **3/4** Proof of concept ready Stage

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