Applicant: National Chemicals Limited [NCL]

CEO: Sidhant Thalor(221055)

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Chemical Formula: $C_{13}H_{19}N_2OBr_2Cl$

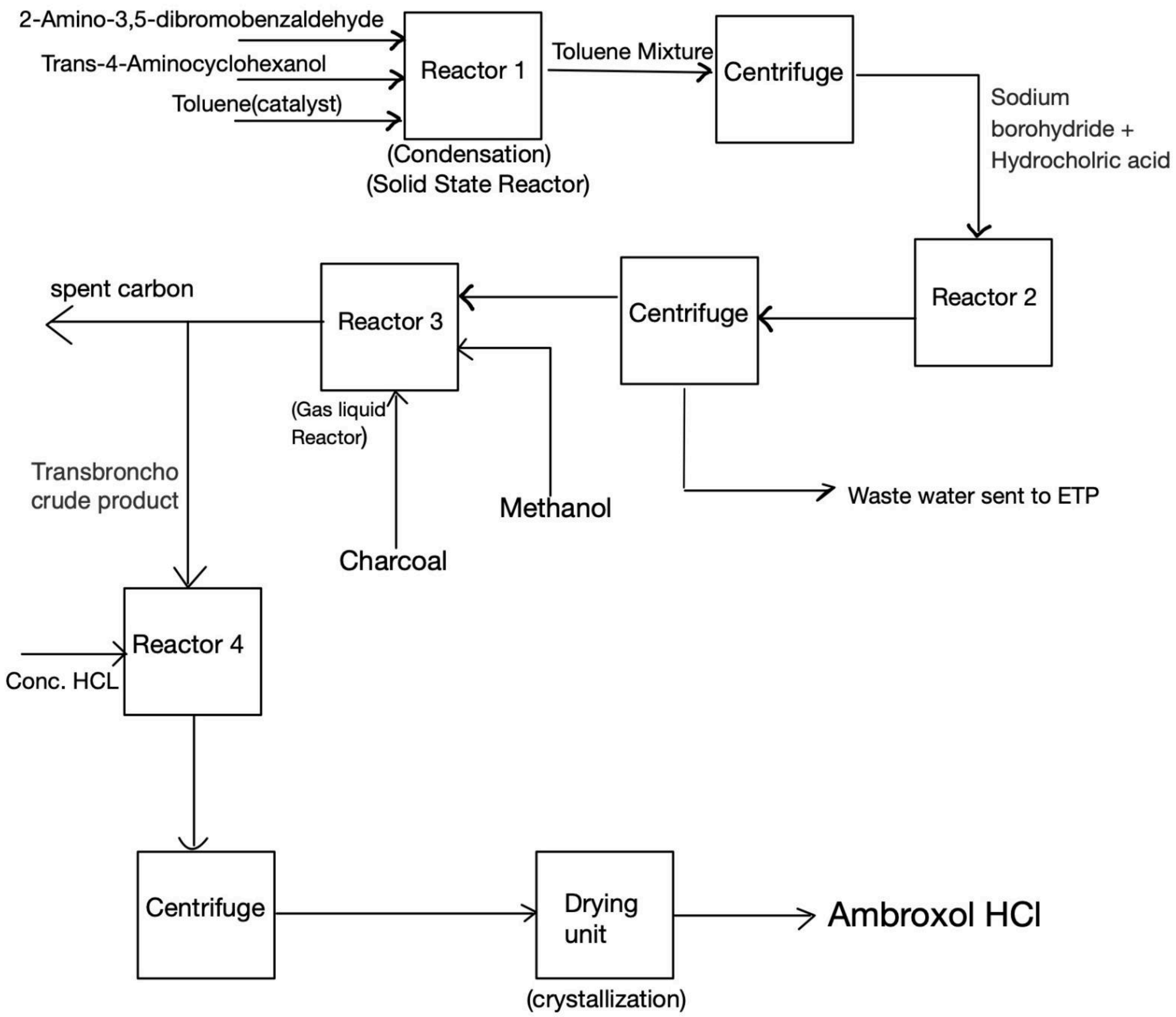
Chemical Name: Ambroxol

Process Title: Production of Ambroxol using Toluene

Process Description: Reaction is happening in the following 3 steps:-

- Condensation: In this step, we use 2-amino-3,5-dibromo benzaldehyde and Trans-4-Aminocyclohexanol, stir in a solvent, and get Schiff bases solution.
- Reduction: In The Schiff bases solution add sodium borohydride or lithium aluminium hydride (we are using sodium borohydride) to get the Trans broncho alkaline solution.
- Salify: With the Trans broncho alkaline solution cooling that step b obtains, regulate pH value with the hydrochloric acid solution under the agitation condition, the temperature control reaction is filtered, and washes and drying gets Ambroxol HCl. The yield of the step-1 reaction is 90.16% The yield of the step-2 reaction is 71.17% The final purity is 83%.

Block diagram



Unit operation and operation condition

1. **Solid-State Reaction (SSR Reaction):**

- **Unit Operation**: Solid-state reaction.
- **Operating Conditions**:

  - Temperature: Typically conducted at elevated temperatures suitable for solid-state reactions.
  - Pressure: Atmospheric pressure.
  - Catalysts: Not specified.

- **Input**:
    - 2-Amino-3,5-dibromobenzaldehyde
    - Trans-4-Aminocyclohexanol
    - Toluene
- **By-Product**: None

2. **Centrifuge (Toluene MLR)**:
- **Unit Operation**: Centrifugation.
- **Operating Conditions**:
    - Rotation Speed: Sufficient to separate the desired product from the toluene mixture.
    - Time: As required for complete separation.
- **Input**: Toluene mixture.
- **By-Product**: Toluene is sold to an authorised party.

3. **Sodium Borohydride and Water (Ambroxol stage I)**:
- **Unit Operation:** Reaction with sodium borohydride and water.
- **Operating Conditions**:
    - Temperature: Reaction temperature suitable for the specific chemistry involved.
    - Pressure: Atmospheric pressure.
- **Input**:
    - Sodium borohydride
    - Water
    - Intermediate compounds
- **By-Product**: None

4. **Centrifuge**
- **Unit operation** - For Separation
- **Input:** intermediate compound
- **By-Product**: Waste water sent to Effluent Treatment Plant (ETP).

5. **Methanol and Charcoal (GLR):**

- **Unit Operation**: Reaction with methanol and charcoal.

- **Operating Conditions**:
  - Temperature: Reaction temperature suitable for the specific chemistry involved.
  - Pressure: Atmospheric pressure.
- **Input**:
  - Methanol
  - Charcoal
  - Intermediate compounds
- By-product: Spent carbon (filtered charcoal).

6. **Concentration (Conc. Hel.):**

- **Unit Operation**: Concentration.
- **Operating Conditions**:
  - Temperature: Controlled temperature to evaporate solvent (if any) from the solution.
  - Pressure: Atmospheric pressure.
  - Evaporation Rate: Controlled as per concentration requirements.
- **Input**: Ambroxol HCl solution.
- **By-Product**: None.

7. **Drying**:

- **Unit Operation**: Drying.
- **Operating Conditions**:
  - Temperature: Controlled temperature suitable for drying the product.
  - Pressure: Atmospheric pressure.
- **Input**: Ambroxol HCl solution.
- **Product**: Ambroxol HCl (final product).

<u>Material Balances</u>:

The reaction takes place in 2 stages:

1. The yield of the step-1 reaction is 90.16% (in reference plant). For calculation, we will use 90%.
   For the production of 3.44kmol/day of intermediate production with 90% actual yield, we need 3.82kmol/day of ADBA i.e.1066.4kg/day of ADBA required.
   We need the 3.82 Kmol/day of TACH also, but in general industrial practices, it is taken in some extra amount, typically 1.5 times ADBA so we need 658.95kg/day of TACH.
   The amount of water generated is 3.44kmol/day, i.e. 61.92 litres/day.
2. The yield of the step-2 reaction is 71.17% (in reference plant). For calculations, we will use 70%.
   We need to produce 1000 kg/day of ambroxol, i.e. 2.41kmol/day with 70% actual yield we need 3.44kmol/day of intermediate.
   In industrial practices, $NABH_4$ is taken 3.5-4 times stage intermediate; we are taking 3.75 times, so for our plant production, we need 12.9kmol/day of $NaBH_{4,}$ i.e. 490.2kg/day required.
   In industrial practices, HCl is taken roughly the same quantity as stage intermediate, we need 125.56kg/day of HCl for our plant. $NaBH_2$ produced is 12.9kmol/day, i.e. 464.4kg/day. $NaBH_2$ produced is 12.9kmol/day, i.e. 464.4kg/day.

<u>Capital cost (only for the reactor): 20,500 $</u>

Equipment	Design Capacity (L)	No. of units	Cost/unit ($ for year 2014)	Total Cost ($ for year 2014)
Solid state reactor (Jacketed and non-agitated)	2470 L	1	20,500	20,500

References:

1. http://www.matche.com/equipcost/Reactor.html
2. https://patents.google.com/patent/CN103012167A/en
3. https://sphinxsai.com/Vol.3No.1/pharm_jan-mar11/pdf/JM11(PT=53)%20pp%20309-313.pdf
4. http://repository-tnmgrmu.ac.in/348/1/BALAJI%20%20P.pdf
5. https://www.researchgate.net/publication/266742851_Formulation_and_Characterization_of_Ambroxol_Hydrochloride_Loaded_Ethyl_Cellulose_Microparticles_for_Sustained_Release
6. https://doktori.bibl.u-szeged.hu/id/eprint/9882/1/Disszertacio_GYULAI%20ORSOLYA.pdf

List the contributions of each author:

- Kushagra has done material balance for a scaled-up process plant with a 1000 kg/day capacity.
- Prince Yadav has provided unit operation and operation conditions after getting information from the flow diagram.
- C Zoliansangi made the block diagram in accordance with the unit operation
- Mohit and Harshit calculated the design capacity of the reactor from the material balance and the capital cost.

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