Applicant: National Chemicals Limited [NCL]

CEO: Sidhant Thalor(221055)

Inventors: C Zoliansangi(220303), Prince Yadav (200725), Kushagra Tiwari (220574),Mohit Rajpoot(220665), Harshit Kumar (220440)

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

Chemical Name: Ambroxol

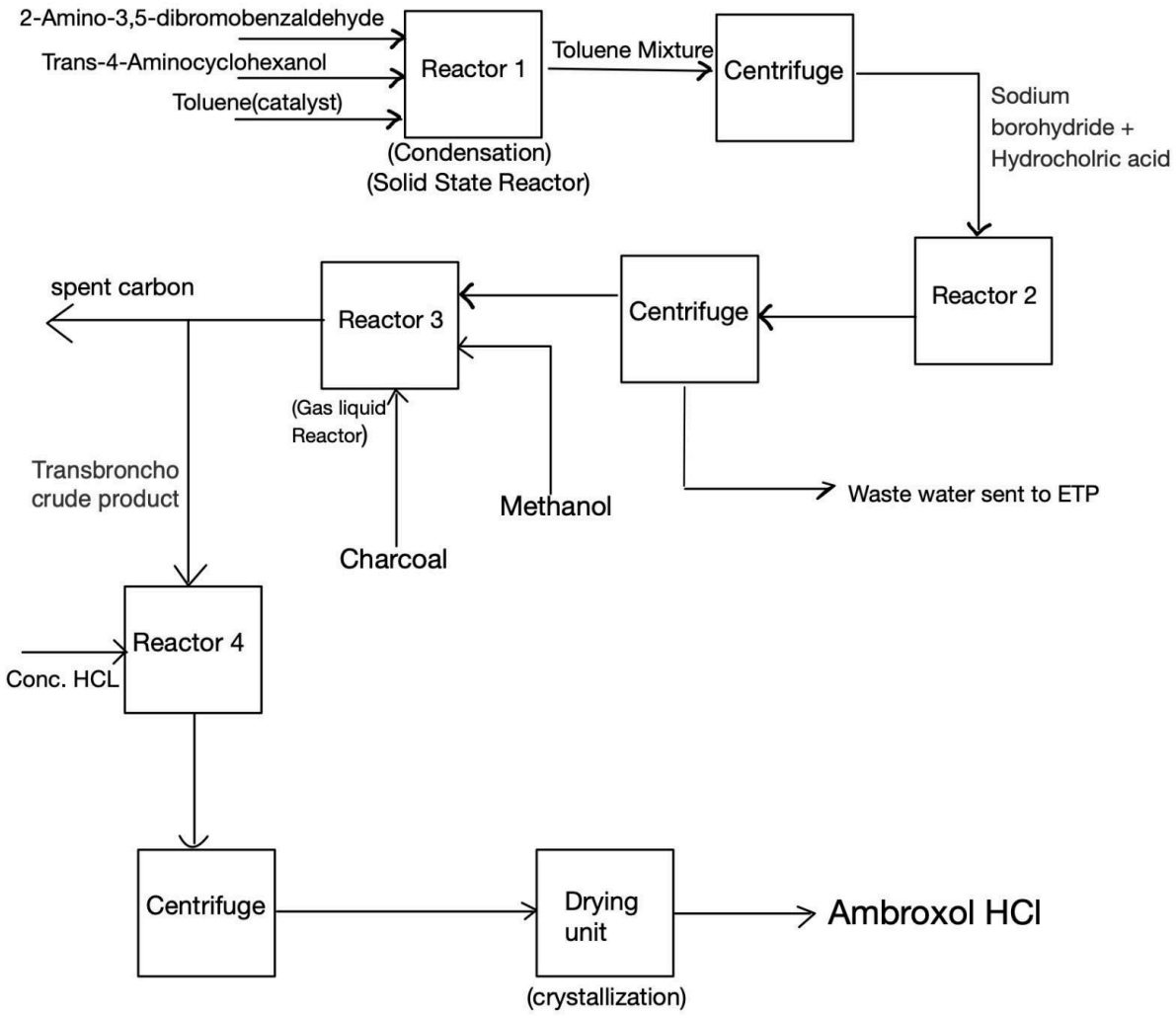
Process Title: Production of Ambroxol using Toluene

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 - liquid reactor (stirred tank reactor)
- **Operating Conditions**:
  - Temperature: 60 ℃-65 ℃
  - Pressure: Atmospheric pressure.
  - Catalysts: Toluene

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

2. **Centrifuge (Toluene mixture)-**

- **Unit Operation**: Centrifugation.
- **Operating Conditions**:
    - Rotation Speed: Sufficient to separate the desired product from the toluene mixture.
- **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.(jacketed and agitated reactor)

- **Operating Conditions**:
    - Temperature: 20 ℃-30 ℃
    - Reaction time -6 hr
    - 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:**

- **Unit Operation**: Reaction with methanol and charcoal. (Bubble column)
- **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. HCL):**

- **Unit Operation**: Concentration.

-Operating Conditions:

- Temperature: 0 ℃-5 ℃
- -Reaction time- 2-6 hr
- Pressure: Atmospheric pressure.
- Evaporation Rate: Controlled as per concentration requirements.

- **Input**: Ambroxol HCl solution.

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).

Material Balances:

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.

Capital cost (only for the reactor):

Equipment	Design Capacity (L)	No. of units	Cost/unit ($ for year 2014)	Total Cost ($ for year 2014)
Reactor 1(Jacketed and agitated)	2500 L	1	37,700	37,700
Reactor 2(Jacketed and agitated)	2500L	1	37,700	37,700

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.

Name	Roll No	Signature
CEO - Sidhant Thalor	221055	Sidhant Thalor
First Author - Prince Yadav	200725	Prince Yadav
Second author -C Zoliansangi	220303	C Zoliansangi
Third author -Kushagra Tiwari	220574	Kushagra Tiwari
Fourth author -Mohit Rajpoot	220665	Mohit Rajpoot
Fifth author - Harshit Kumar	220440	Harshit Kumar

Nature of Invention: Process design

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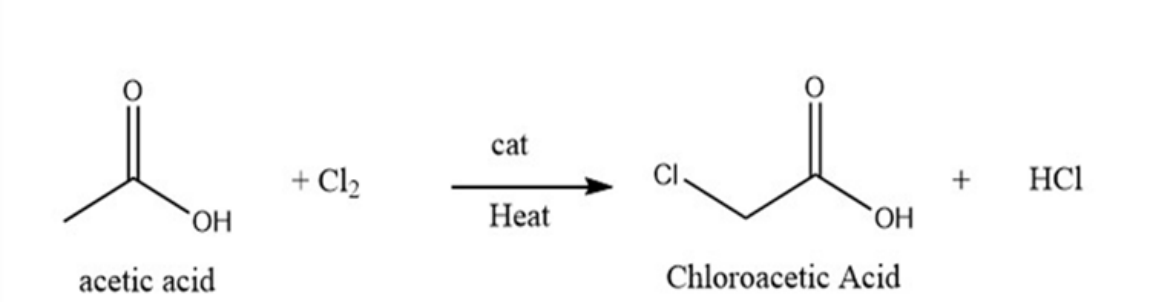
Chemical Formula: $C_2H_3O_2Cl$

Chemical Name: Mono-Chloro Acetic Acid (MCAA)

Process Title: Preparation of MCAA using Glacial Acetic acid

Process Description:

We are adding chlorine gas to Glacial acetic in the presence of strong acid as a catalyst to form MCAA. The reaction is Endothermic.



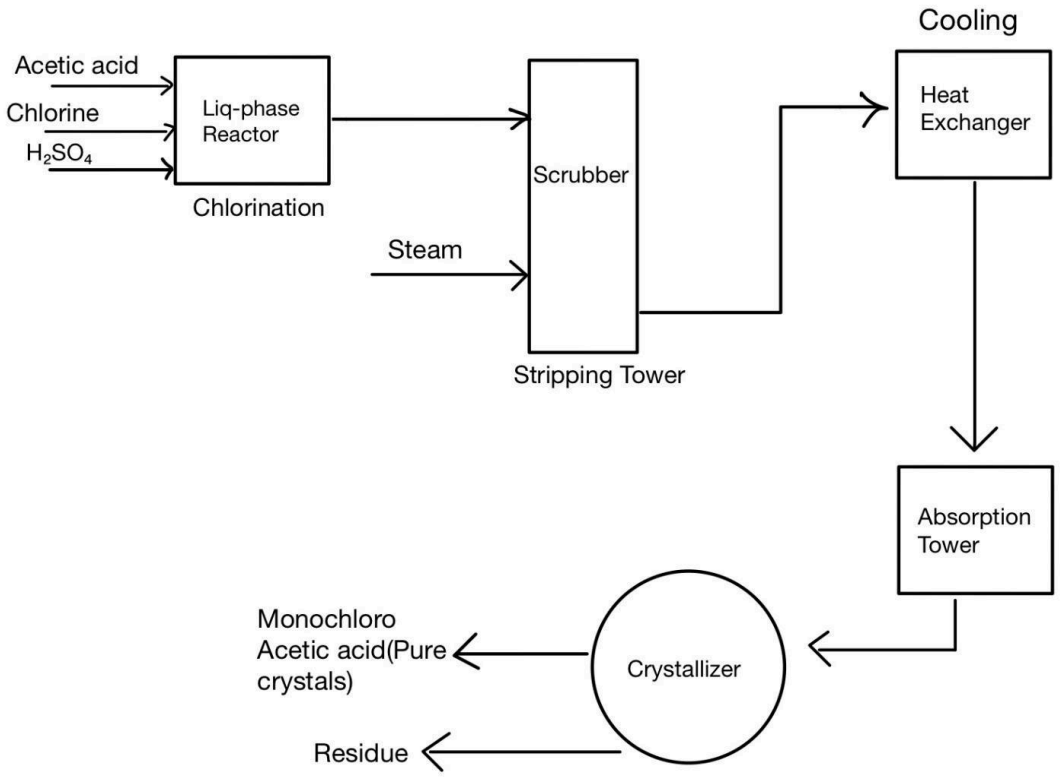
Reaction Temperature: 105℃ to 110℃

Reaction Time: 6 to 7 hrs

Yield: 89.5%

Purity: 93.8% (in product mixture) 97.5% to 99.1% (After crystallisation and separation).

Block Diagram



Unit operations and process conditions

1. Chlorination Reaction:

- **Unit Operation:** Reactor operation (liquid-phase reactor)
- **Operating Conditions:**

  -Temperature: Not explicitly provided, but typically within the range suitable for liquid phase reactions.

  - Pressure: 3-5 bar

  - Chlorine gas saturation in the liquid phase, under waterless conditions.

  - Endothermic reaction.

- **Type of Reactor:** Liquid-phase reactor

2. Stripping:

- Unit Operation: Stripping tower operation

- Operating Conditions:

- Temperature: Not explicitly provided, but typically between 120 and 180°C.

- Pressure: Between 1 and 7 bar

- Type of Reactor: Scrubber

3. Cooling:

- Unit Operation: Cooling process

- Operating Conditions:

- Temperature: Cooling to a temperature between 10 and 60°C (preferably around 35°C)

- Type of Equipment: Cooling system or heat exchanger

4. Absorption:

- Unit Operation: Absorption tower operation

- Operating Conditions:

- Temperature: Operating at the cooled temperature of the gaseous HCl stream.

- Type of Reactor: Absorption tower

5. Crystallization:

- Unit Operation: Crystallisation process

- Operating Conditions:

- Temperature: Dynamic behaviour analysis indicates a temperature of 273 K (0°C) as optimal.

- Type of Equipment: Crystallisation vessel or crystallizer

Specific Operating Conditions:

- The chlorination reaction occurs in a liquid-phase reactor under pressure, with chlorine gas saturation in the liquid phase, typically at temperatures suitable for liquid-phase reactions.

- Stripping of the liquid phase occurs at elevated temperatures and pressures to separate MCAA and DCAA.

- Cooling of the gaseous HCl stream occurs between 10 and 60°C before absorption.

- HCl gas is absorbed at the cooled temperature of the gaseous HCl stream.

- Crystallisation is carried out at a temperature of 273 K (0°C) for optimal separation of MCAA from the mother liquor.

Material Balances:

Yield: 89.5%

For 1000kg/day production of Mono chloro acetic acid production, i.e. 10.58kmol/day production, we need (10.58/0.895=11.82) 11.82 Kmol/day (709.2kg/day) of Acetic acid with 89.5% yield.

We need 11.82kmol/day (839.22kg/day) of Chlorine gas also, in this process, 431.43kg/day of HCl is produced.

Capital cost (only for the reactor):

Equipment	Design Capacity (L)	No. of units	Cost/unit ($ for year 2014)	Total Cost ($ for year 2014)
Reactor 1 Jacketed and Agitated(Liquid-phase reactor)	1850 L	1	44,900	44,900

Note :

1. **Design capacity is calculated by converting the mass required of the reactants into volume by using the density.**
   Density of liquid Acetone = **784 kg / m3**

   Density of saturated liquid chlorine = **1467 kg / m3**

References:

1. http://www.matche.com/equipcost/Reactor.html
2. US Patent for Method of industrially producing monochloroacetic acid Patent (Patent # 10,494,325) : https://patents.justia.com/patent/10494325
3. Mechanism of chlorination process: From acetic acid to monochloroacetic acid and byproducts using acetic anhydride as catalyst: http://web.icf.ro/rrch/
4. www.researchgate.net/publication/289269184_New_method_for_synthesizing_mono chloroacetic_acid Process for the preparation of monochloroacetic acid
5. https://patents.google.com/patent/US7135597B2/en
6. https://www.sciencemadness.org/smwiki/index.php/Chloroacetic_acid
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9. https://application.wiley-vch.de/books/sample/3527334777_c01.pdf

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