PREFEASIBILITY REPORT

FOR

MODIFICATION - MANUFACTURING OF BULK DRUGS & INTERMEDIATES FACILITY

AT

PLOT NO. 23-B,

KIADB KOLHAR INDUSTRIAL AREA,

BIDAR TALUK & DISTRICT, KARNATAKA

PROMOTER:

M/S. CHORUS LABS LIMITED

BIDAR

For Chorus Labs Ltd.,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

1. EXECUTIVE SUMMARY

M/s. **Chorus Labs Limited** is situated in **Kolhar Industrial area, Kolhar** in **Bidar** district of **Karnataka State**. It is a progressive company engaged in the Manufacturing of API's & Intermediates and is professionally managed by people who have vast experience in the field of bulk drugs. The company is promoted by technically qualified and professionally experienced technocrats who crave for innovation and value addition. We recognize that our ability to excel in our core competences depends on the skill, knowledge, creativity and hard work of our employees. A high standard of ethics, integrity and responsibility towards our customers remains our top priority. The company's competitiveness is displayed not only in cost-effectiveness and fast time frames but also in dependability, quality and respect for intellectual property rights and strict procedural norms ensuring clients and associates absolute confidentiality. We have a well established and highly motivated R&D team working relentlessly to develop new molecules and to improve the quality and process of the existing products. Manufacturing with effective quality management is of paramount importance to our success. Our manufacturing sites are regularly evaluated internally and inspected by regulatory authorities to ensure that finished product have the identity, strength, quality and purity they are required to have. Our line of products is vast and varied. With a strong emphasis on innovative and efficient process development our products conform to the highest standards of quality that we have set for ourselves. Apart from our core competence in standard unit operations, process innovation and development to achieve higher yields, we see ourselves as our customers long term and faithful partners, motivated by the understanding that the customers success is our success.

Chorus Labs was incepted in 2009, with a clear vision to master API manufacturing. The company is foraying aggressively in to the pharma market in developing and commercializing products while catering to a variety of therapeutic categories. True to its mission that epitomizes team work and strong expertise, the company is making its presence felt, both nationally and internationally towards creating a healthy society.

Coupled with an insight in to its core competencies and a strong foresight on the current trends, Chorus Labs is raring to become a reliable and strong player by investing in its Research and

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development, Manufacturing Capabilities, Human Resources and well established quality management systems.

Mr. B. Narasa Reddy, the soul and heart behind Chorus Labs, is a person who comes in with loads of expertise. Also the brain behind Chorus Labs, he started the company basing it on his immense strength gained from the experience of running a laboratory that was instrumental in developing and commercializing processes for several APIs.

Started with a strong passion to drive the company to be recognized as an aggressive company, he has built a cultre that exemplifies this vision in the company's strength of R&D and manufacturing. He started a company with definite advantages in terms of cost and chemistry with a strong emphasis on quality of the products. His undying attitude to excel has seen the company develop processes for several products at relatively low cost, thus making several life saving drugs affordable.

For the company, he is a true inspiration and motivation. The company looks up to this leader in working towards achieving the organizational goals.

Vision & Values

Chorus Labs values its position in the pharma industry as an aggressive player at a global level and looks at solidifying its position in supplying generics, combining intellectual property and strong human resource inputs. The company values social responsibilities associated with companies in the pharma industry and its importance in reaching higher altars.

Customer-focus, understanding the requirements of the eco-system and delivering the products at the right pace is a core value of the company. Chorus Labs values its people and considers it as the core of all its success. This company continuously invests in their capabilities and believes in honing the skills of its employees to reach the pinnacle of success.

The company believes in continuous evaluation and improvement that results in transforming the organization into a global force to reckon with. Chorus envisions itself a process driven company with a passion to develop products that are eco-friendly. The company makes a conscious efforts to ensure that none of its processes disturb the ecological harmony.

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Mission

Chorus's mission is to be a global player in the pharma world by deploying processes that are in accordance with the requirements of healthcare. Imbibing the philosophy of being conscious to both, its stakeholder and the social community, the company is driven by its zeal to better its research and manufacturing capabilities.

Today, it's a name which epitomizes hard work, experience and success. A young company that is making its presence felt and making its presence in nationally and internationally. Involved in the manufacturing of active pharmaceutical ingredients, Chorus Labs is one of its kinds of the very few companies which have been able to carve a niche in the pharmaceutical industry given the present scenario where it requires a right blend of intellectual strength, core competencies and a precise foresight for the future.

Profile of Directors

Mr. P.Subba Reddy has a Post Graduation in Economies with 23 years Experience in Purchase & Procurements.

Mr. B. Narasa Reddy has a Post Graduation in Chemistry with 30 years overall in Manufacturing Bulk Products and 15 years of experience as Operational Head of Hetero Group of Companies and also Director of Hetero Drugs Limited & Hetero Labs Limited.

Mrs. B. Baby with a Graduation in Chemistry with 20 years overall Experience in Bulk Products Quality.

All directors have experience in the field of drug manufacturing and different lines of activities in Pharma Industry, and as well as worked for major leading pharmaceuticals in the industry.

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2. INTRODUCTION OF THE PROJECT/BACKGROUND INFORMATION

i. Identification of project and project proponent. In case of mining project, a copy of mining lease/letter of intent should be given

The proposed project is Modification for change in product and product mix in the existing product without changing load. 5 products are substitute in the existing 17 products.
The modification of Bulk drugs manufacturing industry is located at Plot No. 23-B, KIADB Kolhar Industrial Area, Bidar Taluk & District, Karnataka.

ii. Brief description of nature of the project

The project area comes under notified Industrial Area. Hence the project falls under item no-5(f) of schedule to EIA notification, dated 14th September 2006 and can be classified as **Category B.**

iii. Need for the project and its importance to the country or region

India with its large talented manpower, cost effective chemical synthesis, legal & financial framework is poised to become sourcing destination of bulk drugs to the global market.
M/s. Chorus Labs Limited is positioned to become one of leading Pharmaceuticals and Specialty Chemicals Manufacturing and Exporting Company in India.

The pharmaceutical industry in India ranks third in the world in terms of volume and contributes 10% to the global pharmaceutical production. According to the Department of Pharmaceuticals, the Indian pharmaceutical industry is pegged at Rs 810 bn, which includes domestic sales and exports. The industry is the fourteenth-largest in the world in terms of value and accounted for 1.5% of the global pharmaceutical market. The industry has a lower share in the global market because Indian products are available at a price that is 5-50% lower than that in the developed countries. According to the Department of Pharmaceuticals, the sector employs about 340,000 persons and an estimated 400,000 doctors and 300,000 chemists are serving its 1 bn-plus market.

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iv. Demand and supply gap

The Indian Pharmaceutical Industry today is in the front rank of India's science-based industries with wide ranging capabilities in the complex field of drug manufacture and technology. A highly organized sector, the Indian Pharma Industry is estimated to be worth $ 4.5 billion, growing at about 8 to 9 percent annually. It ranks very high in the third world, in terms of technology, quality and range of medicines manufactured. From simple pain killers to sophisticated antibiotics and complex cardiac compounds, almost every type of medicine is now made indigenously. Indian Pharmaceutical Industry boasts of quality producers, and many units approved by regulatory authorities in USA and UK. International companies associated with this sector have stimulated, assisted and spearheaded this dynamic development in the past 53 years and helped to put India on the pharmaceutical map of the world.

The domestic pharmaceutical industry is quite fragmented with the top five companies constituting only 22% of the market share. Unlike the global pharmaceutical industry, where the top 10 companies account for 40% of the global pharmaceutical sales, in India, the top 20 companies account for 57% of the domestic market share. The Indian pharmaceutical industry comprises around 250 large units and about 80,000 small scale units that operate across the pharmaceutical value chain ranging from new drug discovery to marketing and distribution.

India's pharmaceutical industry is now the third largest in the world in terms of volume and stands 14th in terms of value. According to data published by the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, the total turnover of India's pharmaceuticals industry between September 2008 and September 2009 was US$ 21.04 billion. Of this the domestic market was worth US$ 12.26 billion.

The Indian pharmaceuticals market is expected to reach US$ 55 billion in 2020 from US$ 12.6 billion in 2009. The market has the further potential to reach US$ 70 billion by 2020 in an aggressive growth scenario.

Moreover, the increasing population of the higher-income group in the country, will open a potential US$ 8 billion market for multinational companies selling costly drugs by 2015. Besides, the domestic pharma market is estimated to touch US$ 20 billion by 2015, making India a lucrative destination for clinical trials for global giants.

Further estimates the healthcare market in India to reach US$ 31.59 billion by 2020. The market size is expected to grow at higher percentages in future years with more and more international companies depending on India to meet their bulk-drug supply needs.

During the market survey, it was found, that the following drugs are active and high potential demand both locally and in European Market. Hence, the management has opted to manufacture the same by adopting latest technology available in India. The company has decided to manufacture the following drugs like Etodolac, Oxalamine citrate etc., by discontinue manufacturing of existing Drugs. For convenience the products are identified as groups and will be produced a specified group in particular when the demand arise. This report gives detailed manufacturing process present and proposed drugs. This report also discusses the treatment proposal for controlling the water pollution, air pollution and handling of solid waste.

v. Imports v/s. Indigenous production

Active Pharmaceutical ingredients (APIs) play a pivotal role in any strategy designed to rise the standard of living of the people. The consumption level of the medicines is a barometer for measuring the growth of the country's health and present Indian population has recognized the importance of Healthcare and Health-care products. The API industry has shown good results in the last decade accepting the challenges on import substitution, meeting and fulfilling the input needs of the pharmaceutical industry through indigenous production.

India is well known for technically qualified manpower and good English speaking population. During the last few decades a large number of professionals entered the field of APIs with a high degree of motivation based on the promises and prospect evident in the demand projection of various APIs. These technocrats have done well not only in producing quality APIs but also in bringing down the prices of wide range of APIs, which are being imported in large quantities.

As a result of constant and considerable progress, the present production covers a wide range of APIs including antibiotics, vitamins, hormones, sulpha drugs, besides practically the entire range of pharmaceuticals, required by the medical profession. The technology adopted for the production of different bulk drugs and drug intermediates covers intricate and sophisticated

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fermentation technology, synthetic operations and extraction and purification of the active principles contained in the plant and animal kingdom.

M/s Chorus Labs Limited has reasonably sound base to overcome the technological barrier to meet the challenges of the industry. The demand for the bulk drugs is on increase, the industry is poised for substantial growth in the coming years.

vi. Export Possibility

The company has plans to export its products to outside the countries. The company has a long list of satisfied regular customers across the globe.

vii. Domestic/ Export Markets

Over 60 per cent of India's bulk drug production is exported. India's pharmaceutical exports are to the tune of Rs 87 billion, of which formulations contribute nearly 55 per cent and the rest 45 per cent comes from bulk drugs.

In financial year 2005, exports grew by 21 per cent. The Indian pharmaceutical market has been forecasted to grow to as much as US$ 25 billion by 2010 as per Organization of Pharmaceutical Producers of India (OPPI) estimates. However, Espicom's market projections forecast more modest but stable annual market growth of around 7.2 per cent, putting the market at US$ 11.6 billion by 2009.

Domestic pharmaceutical exports, growing at 30 per cent per annum, touched a new height of US$4.8 billion in the financial year 2006-07. The Year's exports will push the drug sectors contribution to India's Forex earnings to 7.75 per cent from the current 5 per cent.

viii. Employment generation (direct and indirect) due to the project

The total strength of the M/s Chorus Labs Limited plant facilities is 35 people it included both on roll and off roll, with a staggered weekly off.

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3. PROJECT DESCRIPTION

i. Type of project including interlinked and interdependent project if any

To cater the needs of the market & it is proposed to modify its production capacity in the existing unit at Plot No. 23-B, KIADB Kolhar Industrial Area, Bidar Taluk & District, Karnataka.
All the required concrete structures for the manufacture of the proposed change with its capacity are already available with additional few machineries/equipments to be erected.

ii. Location (map showing general location, specific location, and project boundary & project site layout) with coordinates

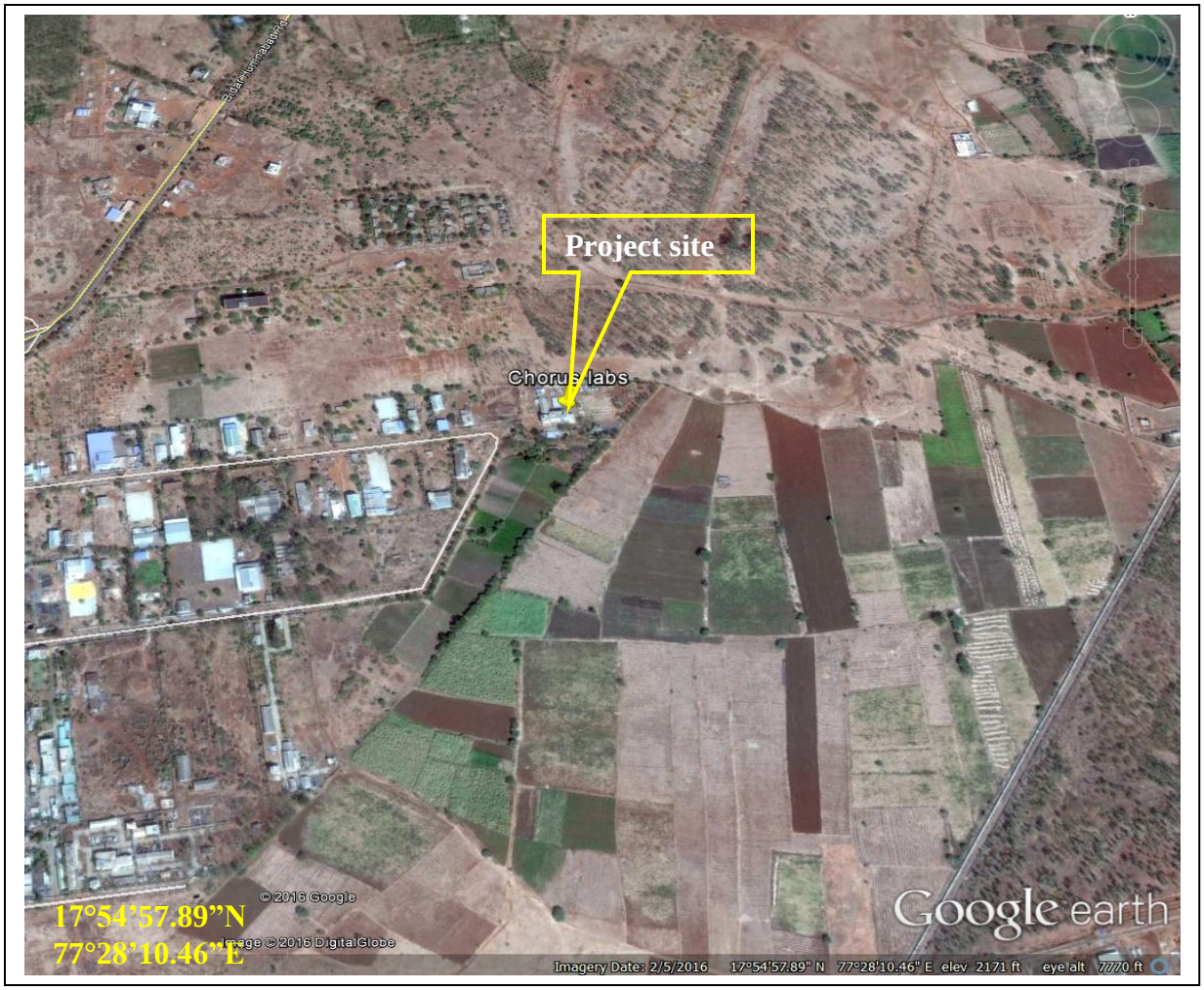

FIGURE: GOOGLE VIEW OF THE PROJECT SITE

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iii. Details of alternate sites considered and the basis of selecting the proposed site, particularly the environmental considerations gone into should be highlighted

There is no any alternate site as the proposed site is acquired.

Table 3.1 DETAILS OF ENVIRONMENTAL SETTINGS

Sl.No.	Particulars	Details
1	Plant site latitude	17°54'57.89"N
2	Plant site longitude	77°28'10.46"E
3	Temperature Max. Min.	42° C 28° C
4	Present land use	Industrial area
5	Nearest Highway	SH- 105 – 1km.
6	Nearest railway Station	Bidar railway station – 4.8 Km
7	Nearest Airport	Hyderabad – 115 Km
8	Nearest village	Kohlar -1.1 Km
9	Nearest major city	Bidar – 5.2 Km
10	Nearest river	Papnash river – 3.7 Km.(NE) Janwada kere – 8.6 Km (N)
11	Type of soil	Red Soil
12	Nearest forest	Honnikere Reserved forest – 2.0 Km (N) Chitta Reserved forest – 2.5 Km (SE) Kamthana Reserved forest – 4.1 Km (N) Kaplapur protected forest – 5.8Km (NW)
13	Defence installation	Bidar Air Force – 850m (S)
14	State boundary	Karnataka – Telangana state boundary – 11.5 Km (E)

iv. Size or magnitude of operation

M/s. Chorus Labs Limited, is presently planning to modify the manufacturing of chemical product at proposed unit at plot No. 23-B, Kolhar Industrial Area, Bidar Taluk & District.

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The details of the manufacturing chemical drug products are given in below table.

TABLE 3.4.1: LIST OF PRODUCTS

S. No.	Existing consented products	Substitution of products in place of existing products	Production capacity after expansion Kg/day
1	Capecitabine		1000
2	Cefpodoxime	Etodolac	1000
3	Diclofinac Sodium		600
4	Efavirenz		1000
5	Leviteracitam		1000
6	Moxifloxacin		750
7	Cefixime	Oxalamine citrate	250
8	Nebivolal		750
9	Neverapine		1000
10	Saquinavir Mesylate		200
11	Stavudine		300
12	Telmisartan	Dothiepin	150
13	Torsimide	Oxalamine Phosphate	325
14	Zindovudine		300
15	Valsatran	Diacerein	400
16	Terbinafine HCL		200
17	Ezitimibe		1000
Total			**10,225**

Note: Only five new products will be substituted to the existing facility and quantity & pollution load will not be changed after substitution of new products.

v. Project description with process details (a schematic diagram/ flow chart showing the project layout, components of the project etc, should be given)

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Description of the proposed change in product

1. ETODOLAC:

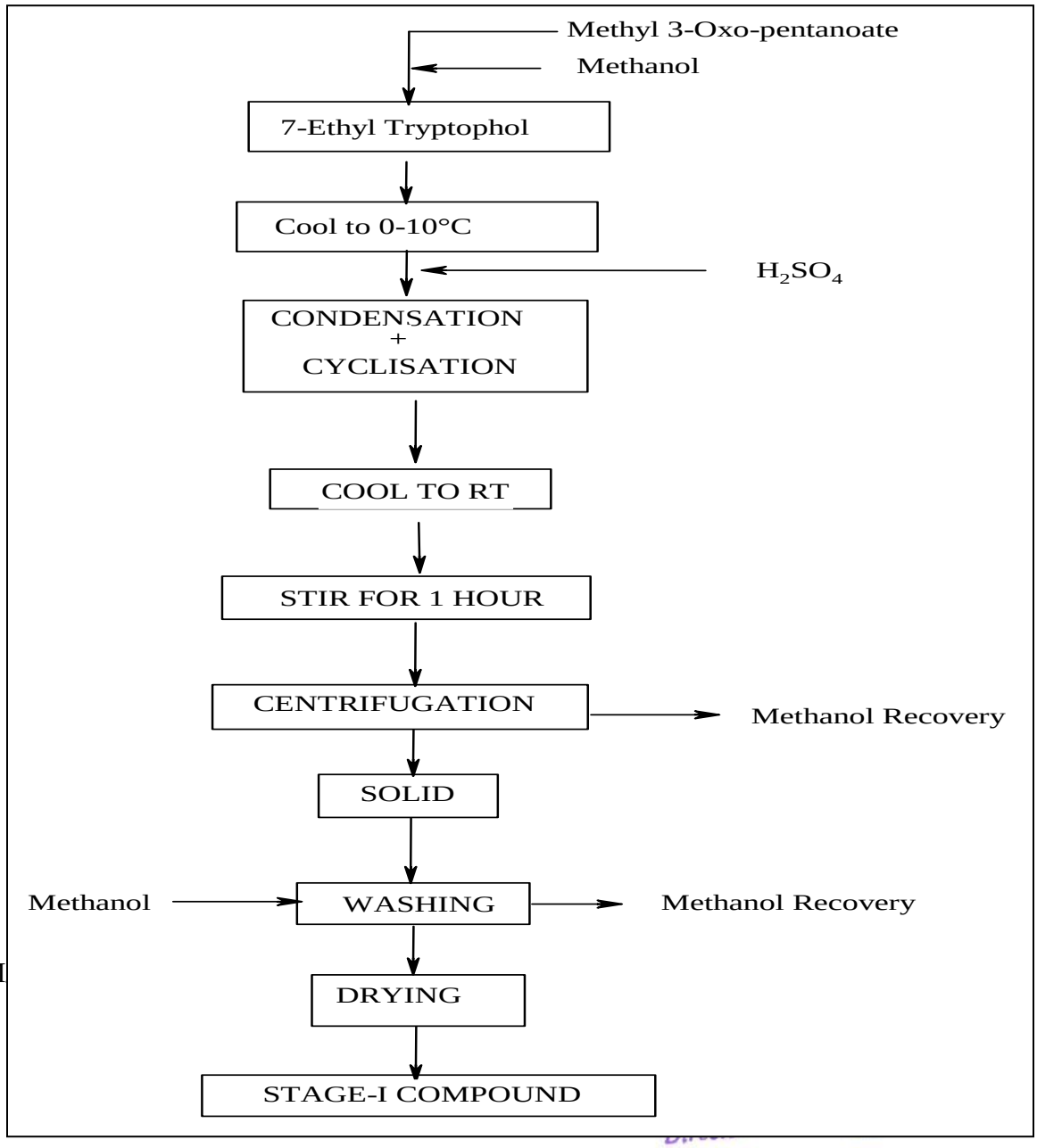
Description:

STAGE-I: 7-Ethyl Tryptophol is treated with Methyl 3-Oxopentanoate in the presence of Sulphuric acid and Methanol to give the intermediate Stage-I (Etodolac Methyl Ester).

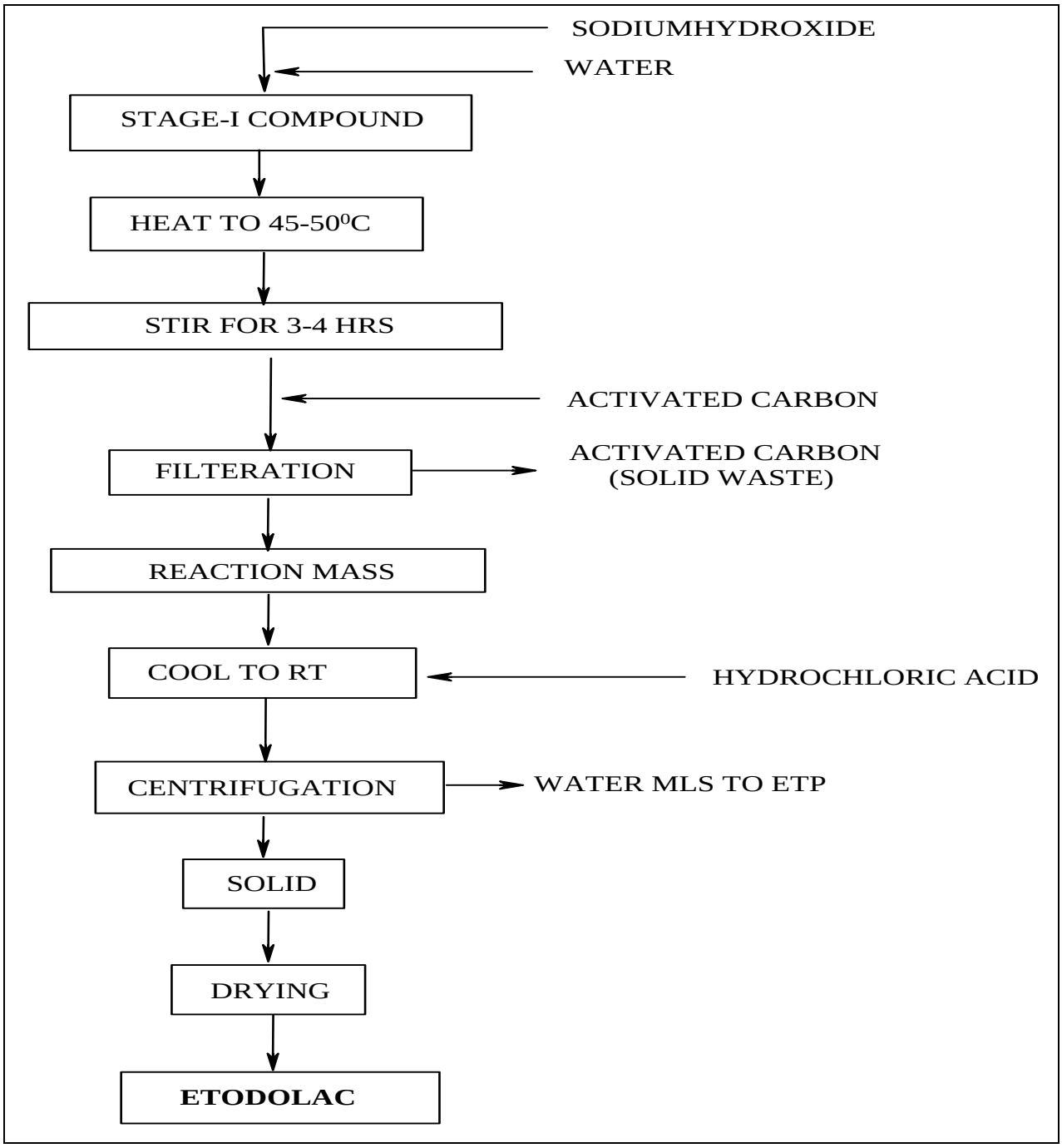
STAGE-II: Stage-I(Etodolac Methyl Ester) is treated with Sodium hydroxide and Hydrochloric acid in the presence of Water and Methanol to give the Product ETODOLAC.

Flow chart:

STAGE-I:



STAGE-II:



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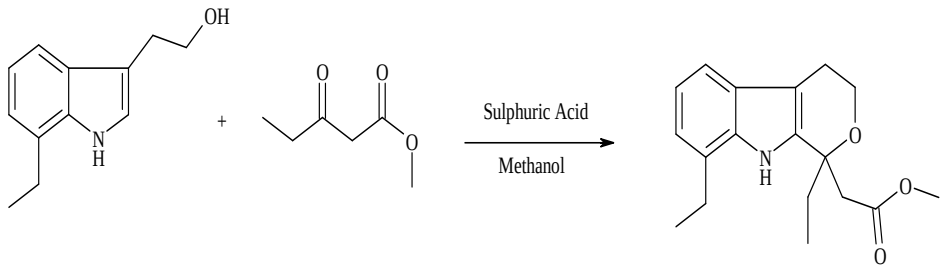
Route of synthesis of product:

STAGE-I

Yield - 89.5%



7-Ethyl Tryptophol
Molecular Weight =189.26
Molecular Formula =C12H15NO

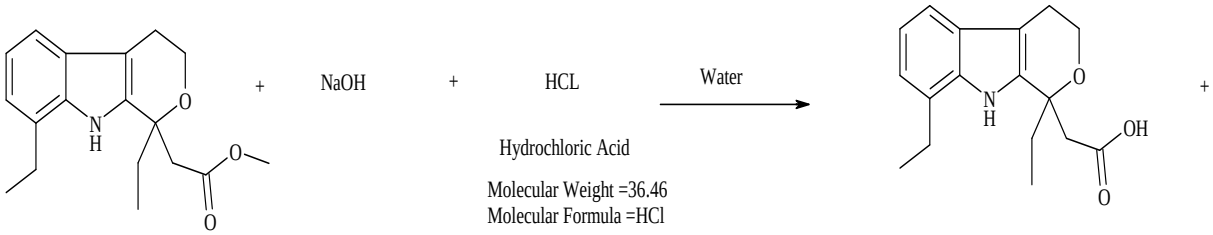
Methyl-3-Oxo-pentanoate
Molecular Weight =130.14
Molecular Formula =C6H10O3

Etodolac Methyl Ester
Molecular Weight =301.39
Molecular Formula =C18H23NO3

Molecular Weight =18.02
Molecular Formula =H2O

STAGE-II

Yield- 91.2 %



Etodolac Methyl Ester
Molecular Weight =301.39
Molecular Formula =C18H23NO3

Sodium Hydroxide
Molecular Weight =40.00
Molecular Formula =NaOH

Molecular Weight =36.46
Molecular Formula =HCl

ETODOLAC
Molecular Weight =287.36
Molecular Formula =C17H21NO3

CH_3OH + NaCl

Methanol — Sodium Chloride

Molecular Weight =32.04
Molecular Formula =CH4O

Molecular Weight =58.44
Molecular Formula =NaCl

Material Balance:

STAGE-I:

SL No:	Input	Kg	Output	Kg	Remarks
1	7-Ethyl Tryptophol	189.3	Stage –I compound	270.1	Stage –I compound
2	Methyl 3-Oxopentanoate	145.3			
3	Sulphuric Acid	46.6			

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4	Methanol	450	Methanol Recovery	440	Reuse
5			Unreacted Organic 1.7-Ethyl Tryptophol (20.5) 2. Methyl 3-Oxopentanoate (17.1)	37.6	
6			Solvent loss	10	loss
7			Sulphuric Acid (46.6) –water (18)	64.6	
8			Reside	9	
	Total input	**831.2**	**Total output**	**831.2**	

STAGE-II:

SL No:	**Input**	**Kg**	**Output**	**Kg**	**Remarks**
1	Stage –I compound	270.1	Etodolac	234.1	Final compound
2	Sodium hydroxide	48.5			
3	Hydrochloric Acid	146			
4	Water	800	Waste water-water	780	
5	Activated Carbon	3	Activated Carbon	3	Solid Waste
6			Unreacted Organic 1. Stage –I compound (1.1) Unreacted inorganic 1. Hydrochloric Acid	1.1 55.0	To waste water To waste water
7			Byproduct Sodium Chloride Methanol	52.1 28.8	To waste water
8			Waste Water	113.5	
	Total Input	**1264.6**	**Total Output**	**1264.6**	

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2. OXOLAMINE CITRATE

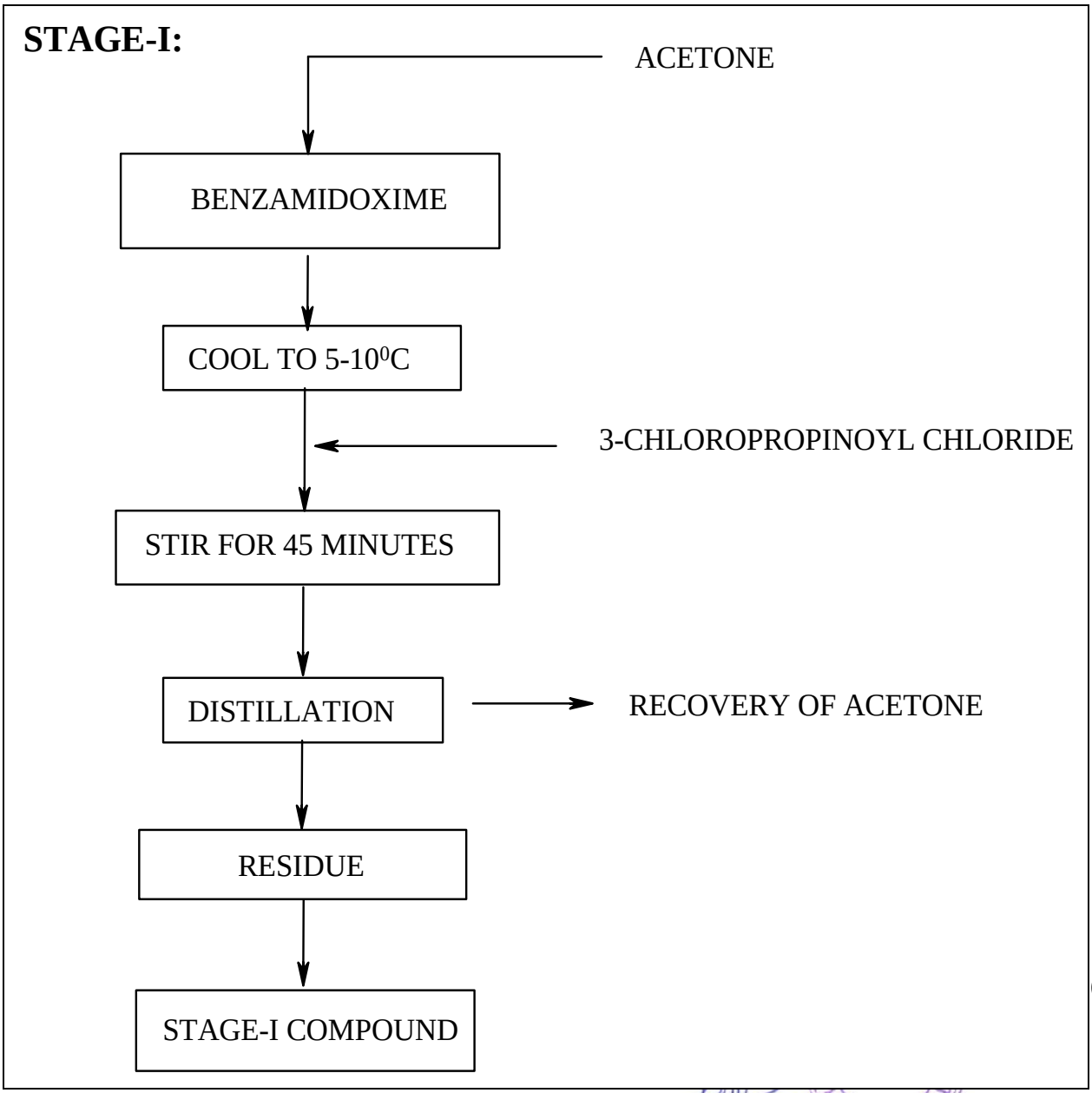
Description:

Stage-1: Benzamidoxime is treated with 3-chloropropinoyl chloride in the presence of Acetone gives the intermediate O-(3-Chioropropionyl) benzamidoxime (Stage-I Compound).

Stage-2: Stage-I Compound, which on treatment with Diethyl amine in the presence of toluene gives the product Oxolamine.

Stage-3: Stage-II is salt formation with Citric acid in the presence of Methanol gives the product OXOLAMINE CITRATE.

Flow chart:



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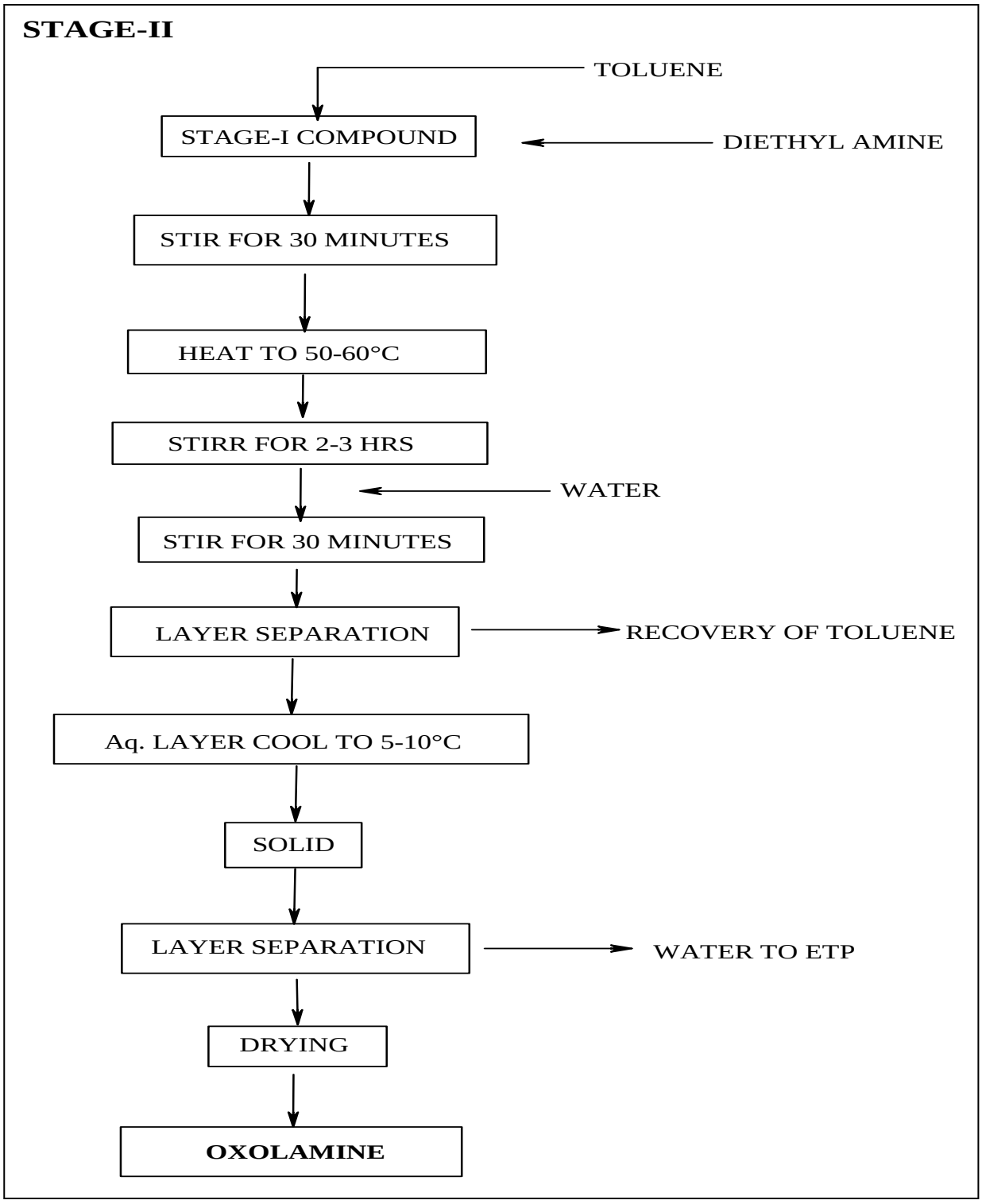

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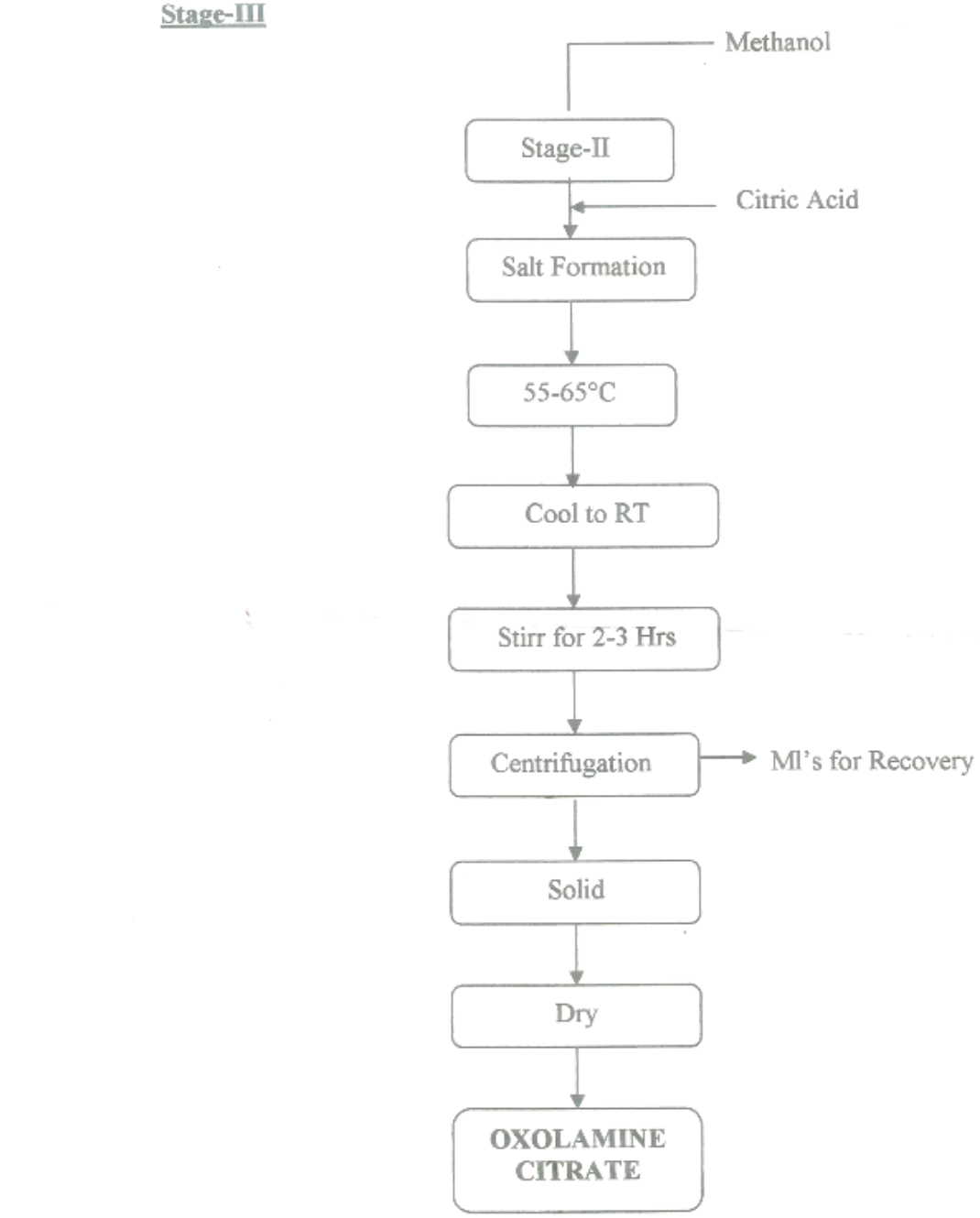
FLOW CHART FOR OXOLAMINE CITRATE

Stage-III



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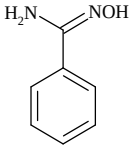
Route of synthesis of product:

STAGE-I:



BENZAMIDOXIME

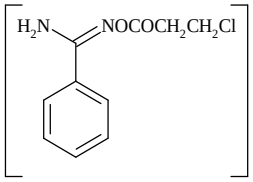
Molecular Weight =136.15
Molecular Formula =C7H8N2O

+ $ClCOCH_2CH_2Cl$

3-CHLOROPROPIONYL CHLORIDE

Molecular Weight =126.97
Molecular Formula =C3H4Cl2O

ACETONE →



O-(3-Chioropropionyl)benzamidoxime

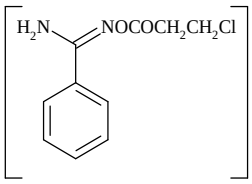
Molecular Weight =226.67
Molecular Formula =C10H11ClO2N2

+ HCL

Hydrochloric acid

Molecular Weight =36.46
Molecular Formula =HCl

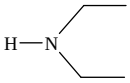
STAGE-II:



O-(3-Chioropropionyl)benzamidoxime

Molecular Weight =226.67
Molecular Formula =C10H11ClO2N2

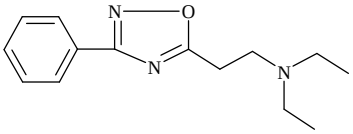
+



DI-ETHYLAMINE

Molecular Weight =73.14
Molecular Formula =C4H11N

TOLUENE
WATER →



OXOLAMINE

Molecular Weight =245.33
Molecular Formula =C14H19N3O

+ HCL

Hydrochloric acid

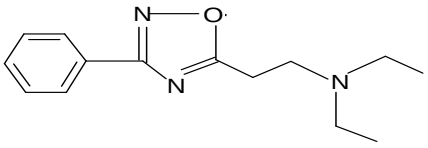
Molecular Weight =36.46
Molecular Formula =HCl

+

Water (H2O)

Molecular Weight =18.02
Molecular Formula =H2O

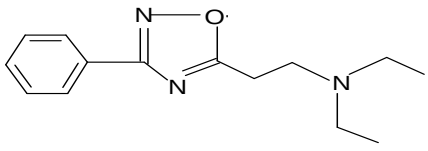
STAGE-III

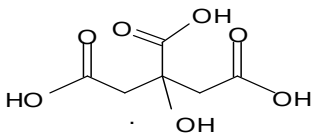


N,N-diethyl-2-(3-phenyl-1,2,4-oxadiazol-5-yl) ethanamine

Molecular Weight=245.32
Molecular Formula=$C_{14}H_{19}N_3O$

Citric Acid
Methanol →





N,N-diethyl-2-(3-phenyl-1,2,4-oxadiazol-5-yl)ethanamine; 2-hydroxypropane-1,2,3-tricarboxylic acid

Molecular Weight=437.50
Molecular Formula=$C_{14}H_{19}N_3O.C_6H_8O_7$

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Director

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Material Balance:

Stage-I:

Sl No:	Input	Kg	Output	Kg	Remarks
1	Benzamidoxime	100.0	Stage-I compound.	150.0	Stage-I compound
2	3-chloropropinoyl chloride	100.0	Hydrochloric acid	26.7	To scrubber
3	Acetone	180	Acetone	165 15	For Recovery Loss
4			Unreacted organics: 1. Benzamidoxime (8.6) 2. 3-chloropropinoyl chloride (14.7)	23.3	Recovery and reuse
	Total input	**380.0**	**Total output**	**380.0**	

Stage-II:

Sl No:	Input	Kg	Output	Kg	Remarks
1	Stage-I compound.	150.0	Stage-II compound.	140.0	Oxolamine
2	Diethyl amine	120.0	Hydrochloric acid	22.5	
3	Toluene	565	Toluene	510 55	For Recovery Loss
4	Water	300	Water-waste water	311.5	
5			Unreacted organics: 1. Stage-I compound (5.3) 2. Diethyl amine (75.5)	80.8	Recovery and reuse
6			Residue	15	
	Total input	**1135.0**	**Total output**	**1135.0**	

Stage-III:

SL NO.	INPUT	Kg	OUTPUT	Kg	REMARKS
1	Stage-II Compound.	140	Stage-III Compound.	183	Oxolamine Citrate

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2	Citric Acid	110			
3	Methanol	500	Methanol	480 20	For Recovery Loss
4			Unreacted Organics: 1. Stage-II Compound	37	Recovery and Reuse
5			Residue	30	
	Total Input	**750**	**Total Output**	**750**	

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Director

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3. DOTHIEPIN (DOSULEPIN) HCL

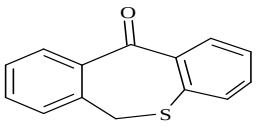
Description:

Stage-I: 11H-10-Thia-dibenzo[a, d]cyclohepten-5-one is treated with 3-chloropropyl dimethyl amine in the presence of Mg Toluene and Tetrahydrofuran to give 5-(3-Dimethylamino-propyl)-5,11-dihydro-10-thia-dibenzo[a,d]cyclohepten-5-ol (Stage-I) compound.

Stage-2: 5-(3-Dimethylamino-propyl)-5,11-dihydro-10-thia-dibenzo[a,d]cyclohepten-5-ol (Stage-I) is treated with Hydrochloric acid to give **Dothiepin (Dosulepin)Hydrochloride.**

Route of synthesis of product:

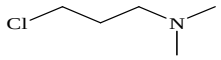
Stage-I:



11H-10-Thia-dibenzo[a,d]cyclohepten-5-one

Molecular Weight =226.30
Molecular Formula =C14H10OS

+



(3-Chloro-propyl)-dimethyl-amine

Molecular Weight =121.61
Molecular Formula =C5H12ClN

+ Mg

Magnesium

Molecular Weight =24.87

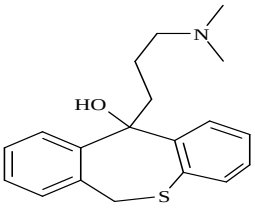
+ HCL

Hydrochloric Acid

Molecular Weight =36.46
Molecular Formula =HCl

TOLUENE + THF

WATER
METHANOL



5-(3-Dimethylamino-propyl)-5,11-dihydro-10-thia-dibenzo[a,d]cyclohepten-5-ol

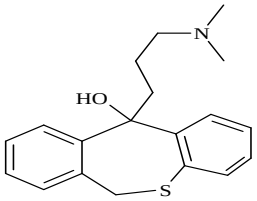
Molecular Weight =313.47
Molecular Formula =C19H23NOS

+ $MgCl_2$

Magnesium chloride

Molecular Weight =95.21

Stage-II:



5-(3-Dimethylamino-propyl)-5,11-dihydro-10-thia-dibenzo[a,d]cyclohepten-5-ol

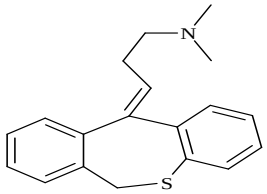
Molecular Weight =313.47
Molecular Formula =C19H23NOS

+ HCL

Hydrochloric Acid

Molecular Weight =36.46
Molecular Formula =HCl

Dichloromethane
ACETONE



. HCl

DOSULEPIN (DOTHIEPIN) HYDROCHLORIDE

Molecular Formula: C19H21NS. HCl
Molecular Weight: 331.90.

+

Water (H2O)

Molecular Weight =18.02
Molecular Formula =H2O

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Director

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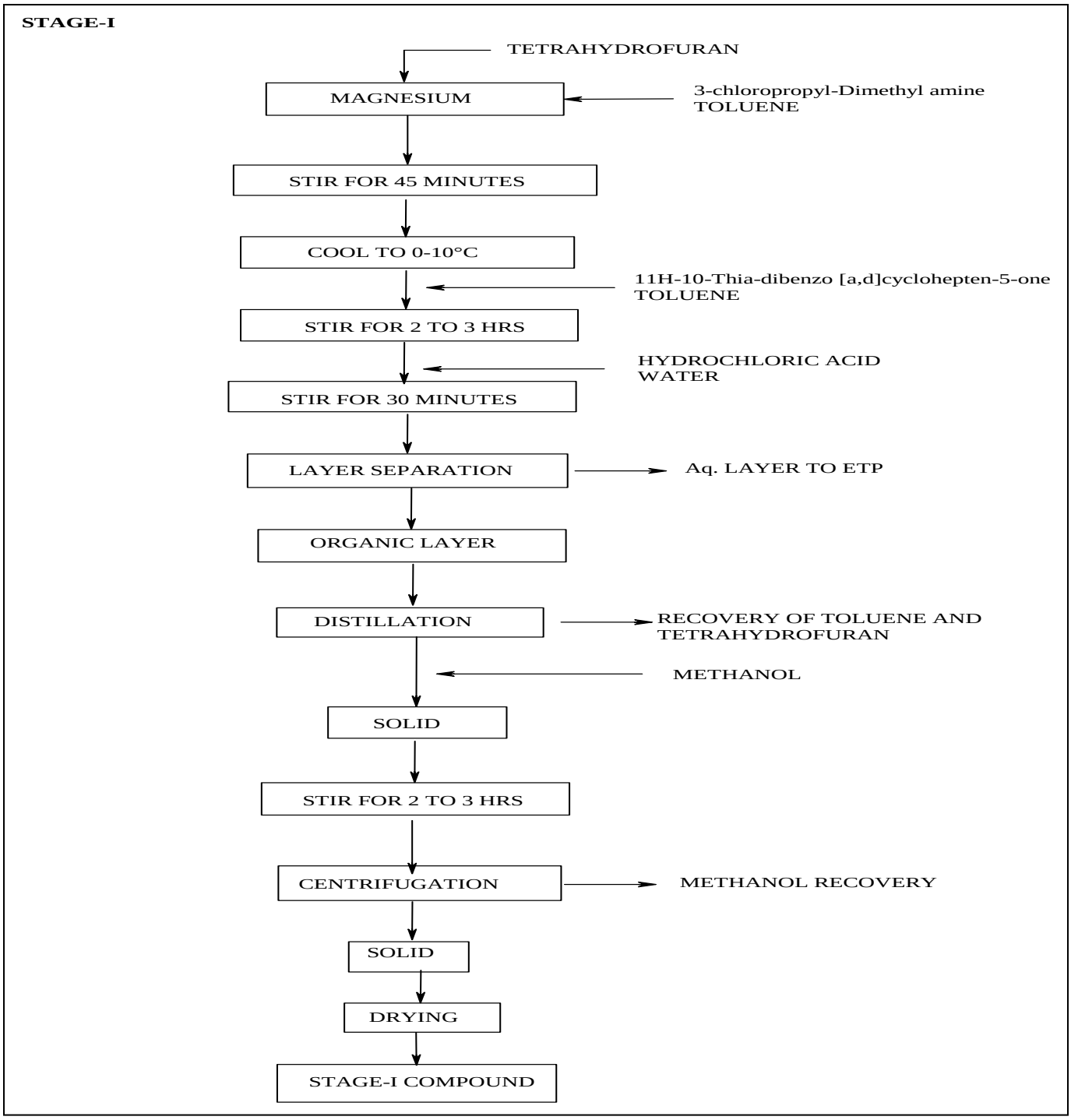
Flow Chart:



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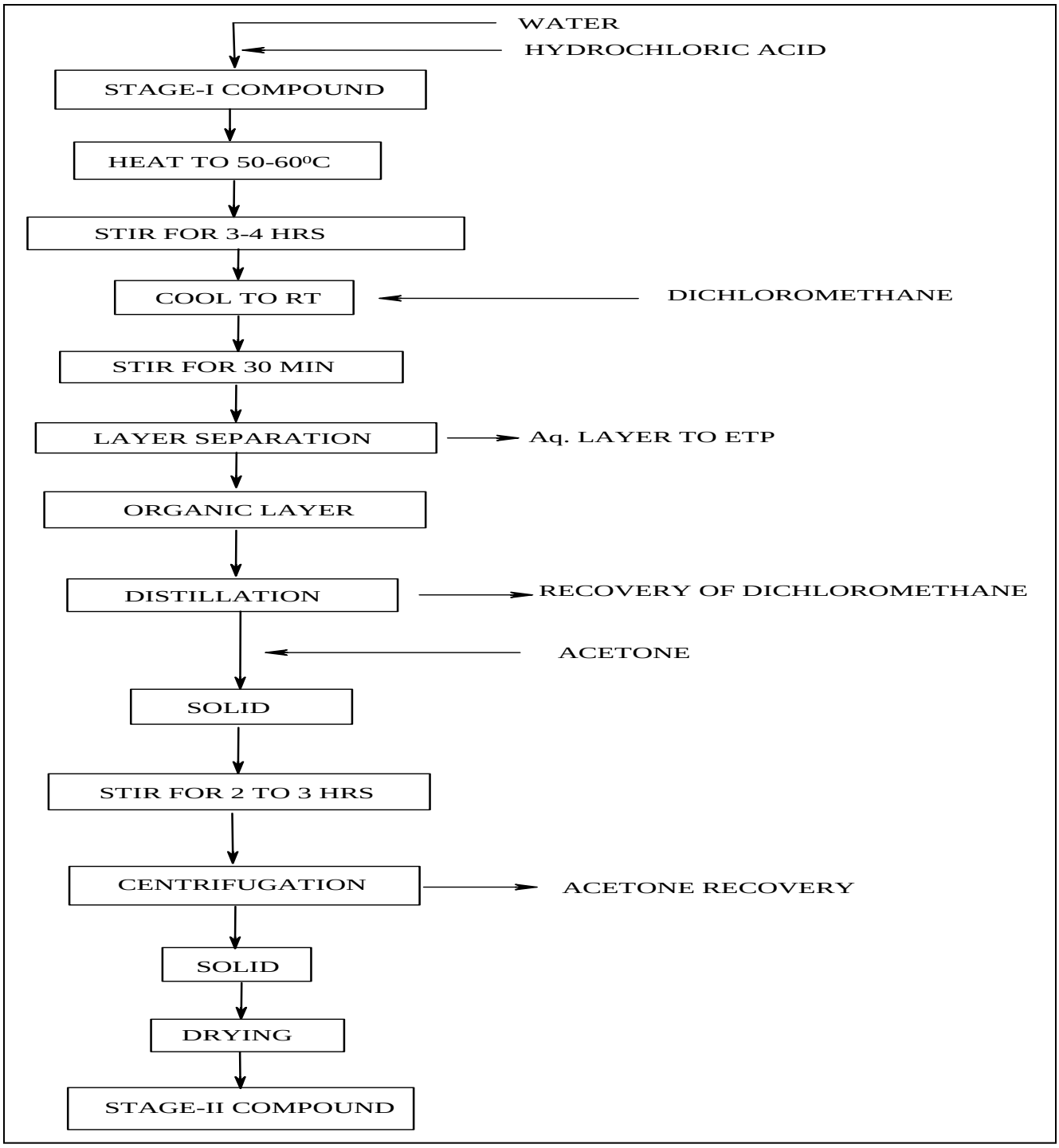
Stage-II:



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Material Balance:

Stage-I:

S.No:	Input	Kg	Output	Kg	Remarks
1	11H-10-Thia-dibenzo [a,d]cyclohepten-5-one	100.0	Stage-I compound.	110.0	Stage-I compound
2	3-chloropropyl-Dimethyl amine	95.0	Waste water + Unreacted Hydrochloric acid	270	To waste water
3	Magnesium	18.3	Toluene+ Tetrahydrofuran	490	For Recovery
4	Toluene	370	Toluene+ Tetrahydrofuran	60	Loss
5	Tetrahydrofuran	180			
4	Hydrochloric Acid	80			
5	Water	200	Residue	20	
6			Unreacted organics: 1. 211H-10-Thia-dibenzo[a,d]cyclohepten-5-one (7.3) 2. 3-chloropropyl-Dimethylamine (42.7) Unreacted Inorganic: Magnesium (1.2)	51.2	To waste water To waste water
			$MgCl_2$	42.1	Solid Waste
	Total input	**1143.3**	**Total output**	**1143.3**	

Stage-II:

SL No:	Input	Kg	Output	Kg	Remarks
1	Stage-I compound	110.0	Stage-I compound.	100.0	Stage-I compound
2	Hydrochloric Acid	30 kg	Waste water + Unreacted Hydrochloric acid	220	To waste water
3	Dichloromethane	665	Dichloromethane	530 135	For Recovery Loss
4	Acetone	475	Acetone	430 45	For Recovery Loss
5	Water	200	Residue	18	
6	Methanol	200	Methanol	180 20	For Recovery Loss
7			Unreacted organics: Stage-I compound (2.0)	2.0	To waste water To waste water
	Total input	**1680**	**Total output**	**1680**	

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4. OXOLAMINE PHOSPHATE

Description:

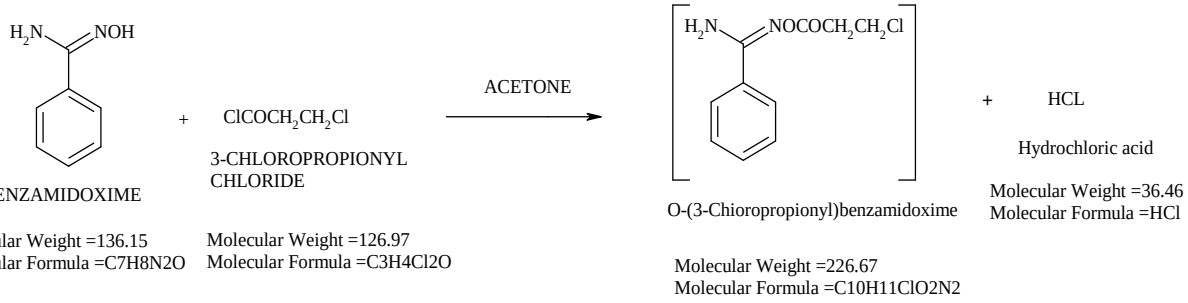
Stage-1: Benzamidoxime is treated with 3-chloropropinoyl chloride in the presence of Acetone gives the intermediate O-(3-Chioropropionyl) benzamidoxime (Stage-I Compound).

Stage-2: Stage-I Compound, which on treatment with Diethyl amine in the presence of toluene gives the product Oxolamine.

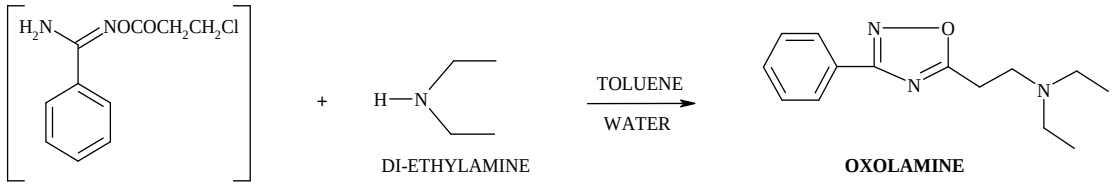
Stage-3: Stage-II is salt formation with Phosphoric Acid in the presence of Acetone gives the product **OXOLAMINE PHOSPHATE.**

Route of synthesis of product:

STAGE-I:



STAGE-II:



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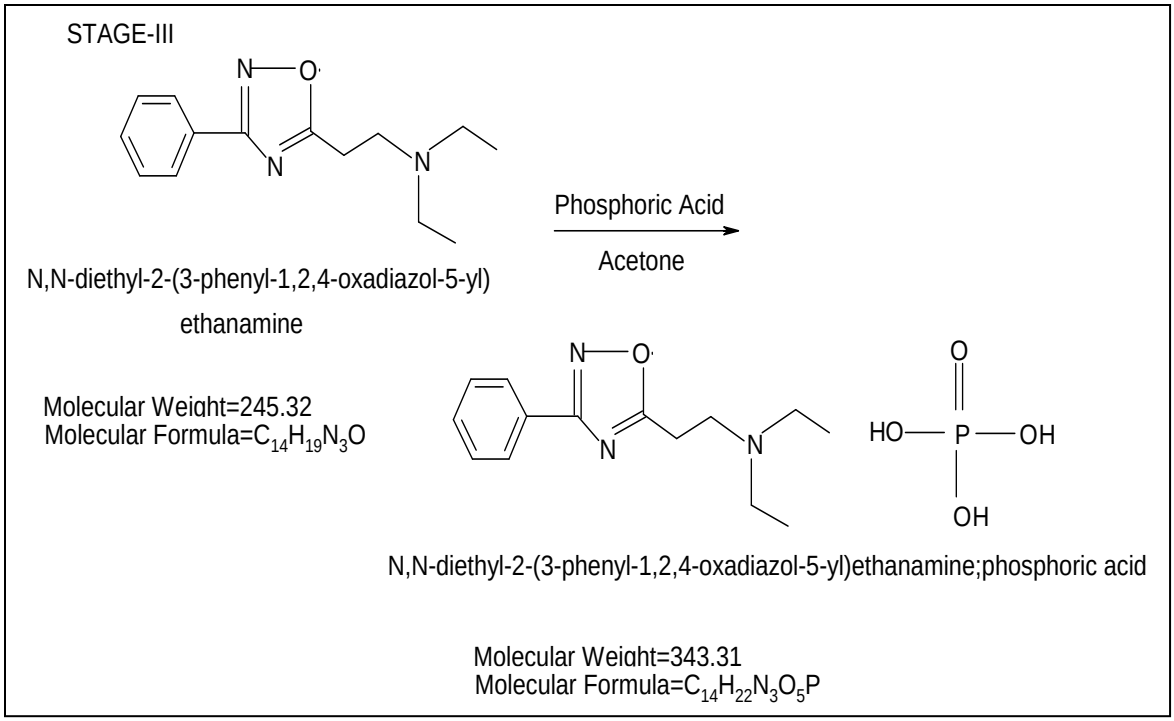

Material Balance:

SL No:	Input (Stage-1)	Kg	Output	Kg	Remarks
1	Benzamidoxime	100.0	Stage-I compound.	150.0	Stage-I compound
2	3-chloropropinoyl chloride	100.0	Hydrochloric acid	26.7	To scrubber
3	Acetone	180	Acetone	165 15	For Recovery Loss
4			Unreacted organics: 1. Benzamidoxime (8.6) 2. 3-chloropropinoyl chloride (14.7)	23.3	Recovery and reuse
	Total input	**380.0**	**Total output**	**380.0**	

Stage-II:

Sl. No:	Input	Kg	Output	Kg	Remarks
1	Stage-I compound	150.0	Stage-II compound.	140.0	Oxolamine
2	Diethyl amine	120.0	Hydrochloric acid	22.5	
3	Toluene	565	Toluene	510 55	For Recovery Loss
4	Water	300	Water-waste water	311.5	
5			Unreacted organics: 1. Stage-I compound (5.3) 2. Diethyl amine (75.5)	80.8	Recovery and reuse
6			Residue	15	
	Total input	**1135.0**	**Total output**	**1135.0**	

Stage-III:

SL NO.	INPUT	Kg	OUTPUT	Kg	REMARKS
1	Stage-II Compound	140	Stage-III Compound.	165	Oxolamine Phosphate
2	Phosphoric Acid	56			
3	Acetone	500	Acetone	475 25	For Recovery Loss
4			Unreacted Organics: 1. Stage-II Compound	16	Recovery and Reuse
5			Residue	15	
	Total Input	**696**	**Total Output**	**696**	

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5. DIACEREIN

Description:

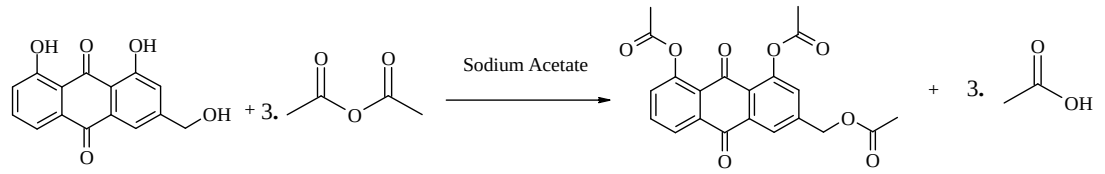
Stage-1: Aloe-emodin is treated with acetic anhydride in the presence of Sodium acetate gives the intermediate product

Stage-2: Tri acetyl aloe emodine which upon treatment with CrO_3 in the presence of acetic acid gives product Stage-I (Diacerein Crude).

Stage-3: (Diacerein Crude) is treated purified in DMA to give the product Diacerein.

Route of synthesis of product:

Stage-I



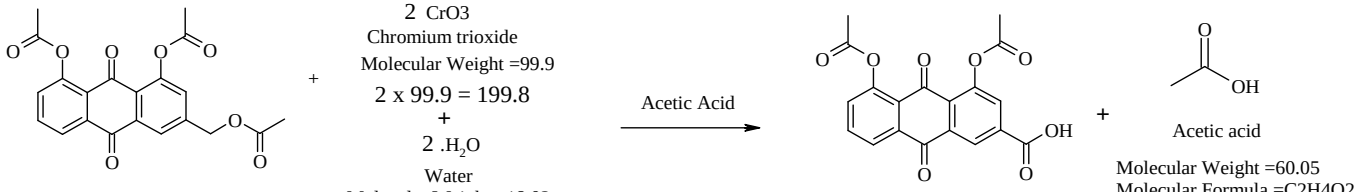
Aloe-emodin
Molecular Weight =270.24
Molecular Formula =C15H10O5

Acetic Anhydride
Molecular Weight =102.09
Molecular Formula =C4H6O3
3 x 102.09 = 306.27

Triacetyl Aloe-emodin
Molecular Weight =396.36
Molecular Formula =C21H16O8

Acetic acid
Molecular Weight =60.05
Molecular Formula =C2H4O2
3 x 60.05 = 180.15

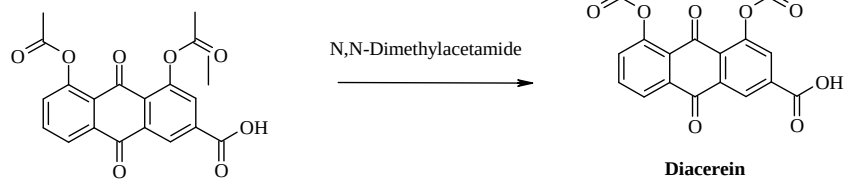
Stage-II



Triacetyl Aloe-emodin
Molecular Weight =396.36
Molecular Formula =C21H16O8

Diacerein Crude
Molecular Weight =368.30
Molecular Formula =C19H12O8

Stage-III



Diacerein Crude

Molecular Weight =368.30
Molecular Formula =C19H12O8

Diacerein

Molecular Weight =368.30
Molecular Formula =C19H12O8

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Material Balance:

Stage-I:

SL No:	Input	Kg	Output	Kg	Remarks
1	Aloe-emodin	100.0	Tri acetyl aloe emodine	142.0	Stage-I compound.
2	Acetic Anhydride	1000	Acetic Acid as byproduct	66.7	Recovery and Reuse
3	Sodium Acetate	100	Sodium Acetate	95	Recovery and Reuse
4			Unreacted organics: 1. Aloe-emodin (1.3) 2. Acetic anhydride (870)	871.3	Recovery and Reuse
5			Mixture of Acetic acid, acetic anhydride and sodium acetate	25	
	Total input	**1200**	**Total output**	**1200**	

Stage-II:

SL No:	Input	Kg	Output	Kg	Remarks
1	Tri acetyl aloe emodine	142.0	Diacerein Crude	122.0	Stage-II compound.
2	Acetic Acid	600	Acetic Acid	620	Recovery and Reuse
3	Water	60	Waste water Water	33	
4	Chromic anhydride (CrO_3)	200	Unreacted organics: Tri acetyl aloe emodine (2.5)	2.5	Recovery and Reuse
5			$CrO_3 H_2$	36.5	
			Unreacted Chromic anhydride (CrO_3) as Chromic acid	170	
			Residue	18	
	Total input	**1002**	**Total output**	**1200**	

Stage-III:

SL NO.	In put	Kg/d	Out put	Kg/d	Remarks
1.	Diacerein Crude	122.0	Diacerein	90	Final Product
2	N, N-Dimethylacetamide	600	N, N-Dimethylacetamide	580 20	Recovery Loss
3	Activated carbon	2	Activated carbon	2	Solid waste
			Unreacted Diacerein Crude	32	Recovery and reuse

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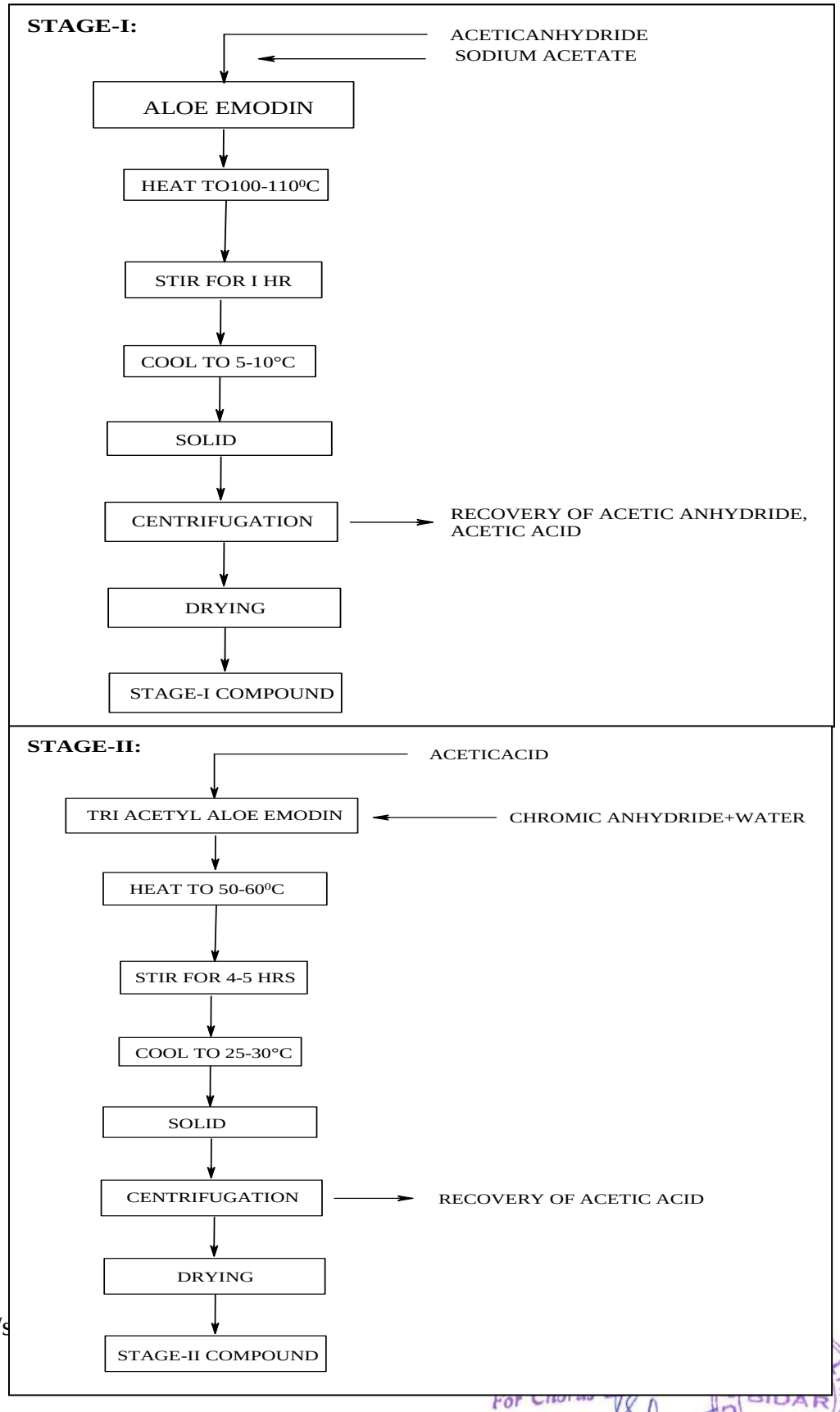
	Total input	**724**	**Total output**	**724**	

Flow Chart:



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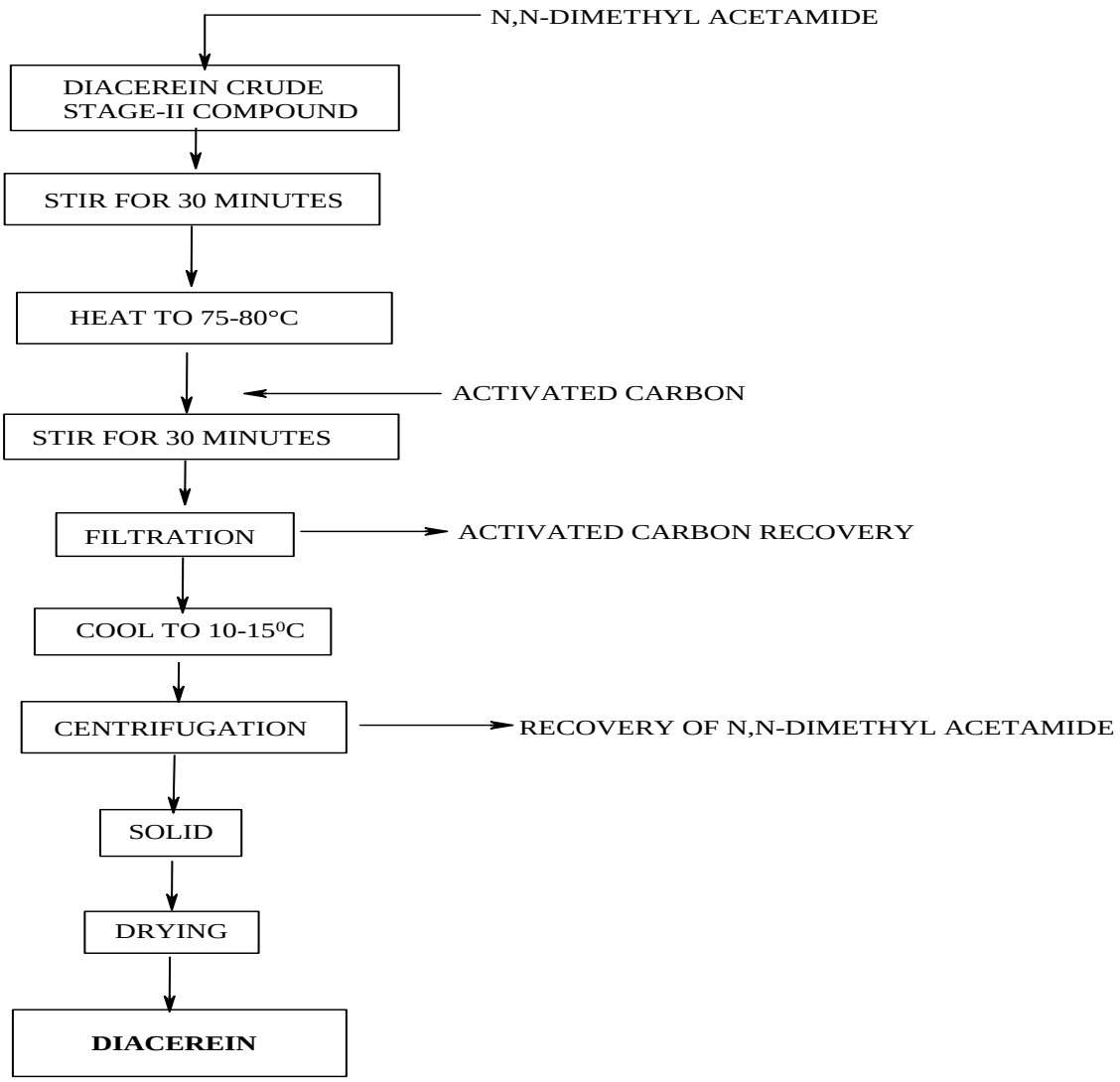
STAGE-III:



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Director

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Description of the existing product

1. CAPECITABINE

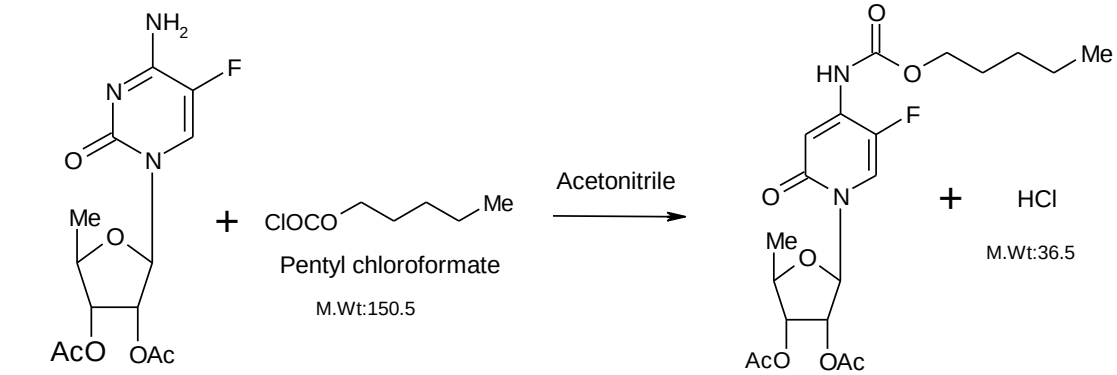
Description:

Stage-1: 5'-Deoxy-2',3'-di-O-acetyl-5-fluirocytiine is condensed with Pentylchloroformate in presence of Acetonitrile to give stage-I compound

Stage-2: Stage-I compound is treated with Sodium hydroxide (deprotected) in presence of Methanol to give CAPECITABINE

Route of synthesis of product:

Stage-I:



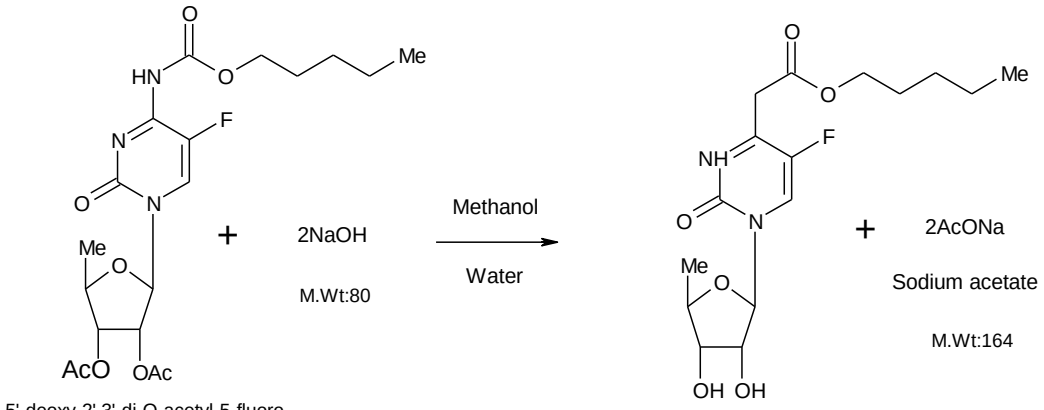
5'-deoxy-2',3'-di-O-acetyl -5-fluorocytidine

M.Wt:329

5-deoxy-2', 3-di-o-acetyl-5-fluoro -N-[(pentyloxy)carbonyl]cytidine

M.Wt:443

Stage-II:



5'-deoxy-2',3'-di-O-acetyl-5-fluoro-N-[(pentyloxy)carbonyl]cytidine

M.Wt:443

Capecitabine

M.Wt:359

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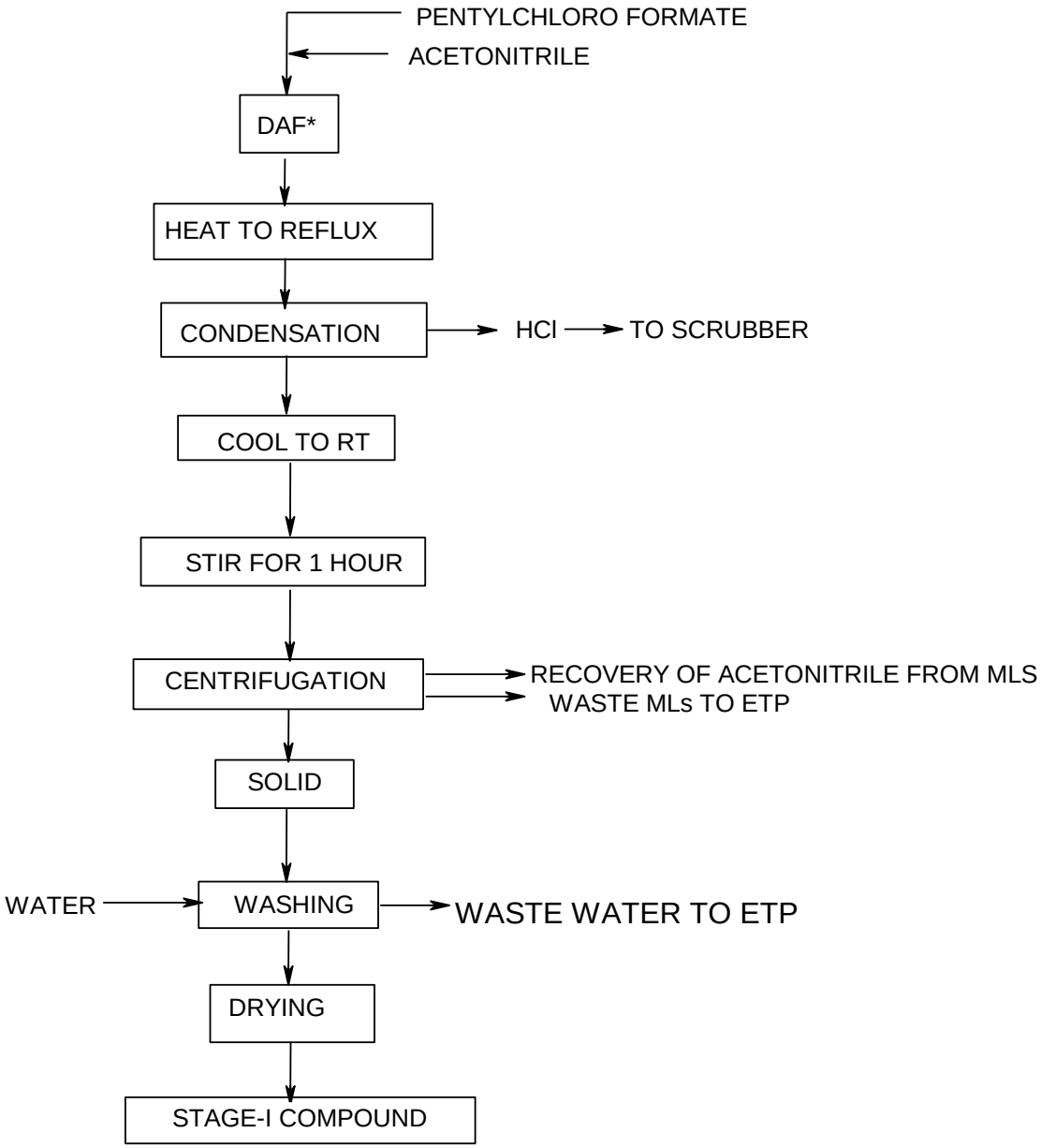
Flow Chart:

Stage-I:



DAF*: 5'-deoxy-2',3'-di-O-acetyl
-5-fluorocytidine

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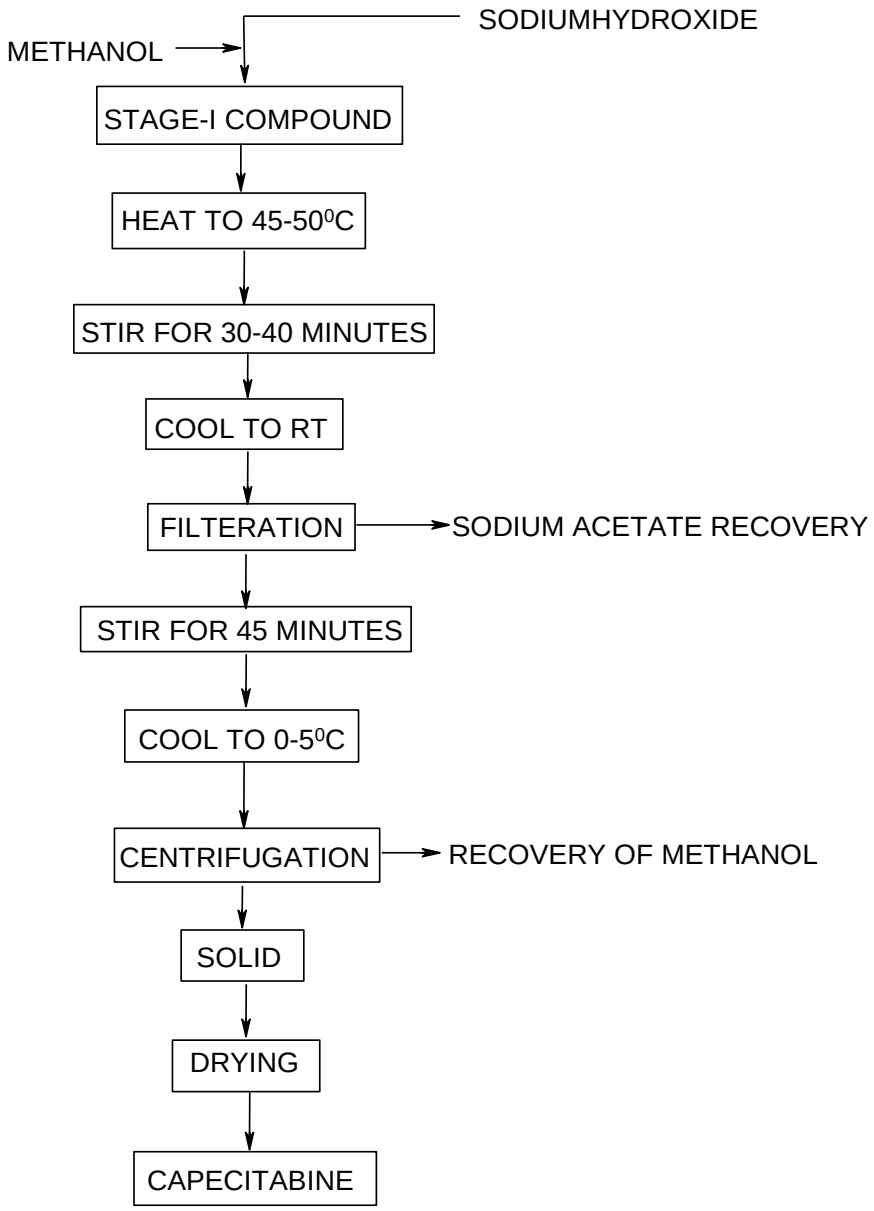
Stage-II:



Material Balance:

Stage-I:

S.No:	Input	Kg/d	Output	Kg/d	Remarks
1	5'-Deoxy-2',3'-di-O-acetyl-5-fluirocytiine	1552.6	Stage –I compound	1542.8	Stage –I compound
2	Pentylchloroformate	710.21			Reuse
3	Water	1200	Aq . mother liquor contains HCl	127.2	
4	Acetonitrile	1500	Acetonitrile Recovery	1470	Reuse

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5	Water	1200	Acetonitrile Loss	30	Loss
			Unreacted Organic 1. 5'-Deoxy-2',3'-di-O-acetyl-5-fluirocytiine (**400)** 2. Pentylchloroformate **(180)**	580	Recovery
			Waste water with organics 1. 5'-Deoxy-2',3'-di-O-acetyl-5-fluirocytiine **(7.631)** 2. Pentylchloroformate **(6.46)**	1200 +7.631+6.46	Forced Evaporation
	Total input	**4963.00**	**Total output**	**4963.00**	

Stage-II:

S.No:	Input	Kg/d	Output	Kg/d	Remarks
1	Stage –I compound	1542.78	Capecitabine	1000	Final compound
2	Sodium hydroxide	278.2	Methanol Recovered	960	Reuse
3	Methanol	1000	Solvent loss	40	Loss
4	Water	800	Waste water-water **with Inorganic** 1. Sodium hydroxide **(56)** **Organic** 1. Stage –I compound **(8.1)**	800 +56 +8.1	Forced Evaporation
5			**Unreacted Organic** 1. Stage –I compound (300)	300.0	Recovery
			Byproduct Sodium acetate	455.52	By Product
	Total Input	**3620.6**	**Total Output**	**3620.62**	

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2. DICLOFINAC SODIUM

Description:

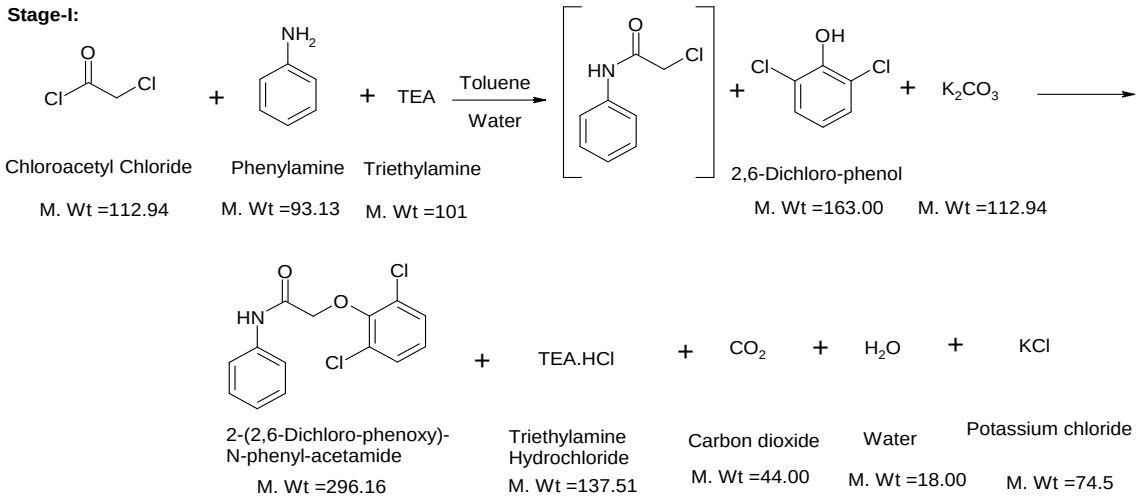
Stage-1: Aniline and chloroa- cetyl chloride is treated with 2,6-dichlorophenol in the presence of triethylamine and potassium carbonate to yield stage- I Compound.

Stage-2: Stage-I compound is reacted with sodium methoxide followed by treating with chloroacetyl chloride in the presence of triethylamine to yield stage-II compound.

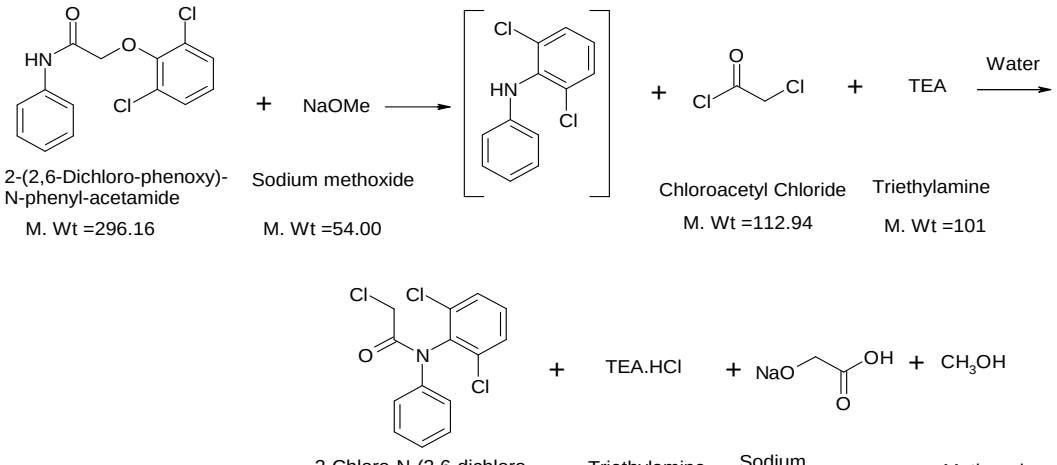
Stage-3: Stage-II compound is cycle zed with aluminum chloride followed by hydrolyzed with sodium hydroxide to yield Diclofenac Sodium.

Route of synthesis of product:

Stage-I:



Stage-II:



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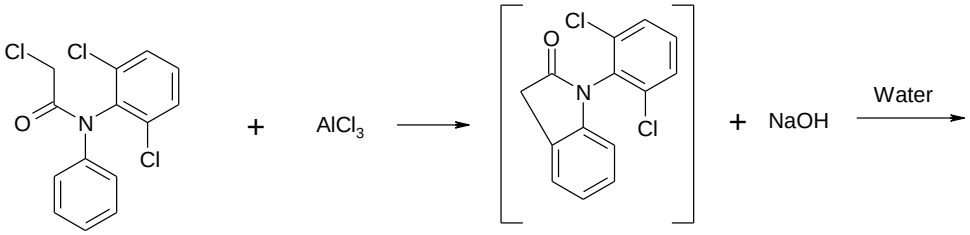
Stage-III:



2-Chloro-N-(2,6-dichloro-phenyl)-N-phenyl-acetamide

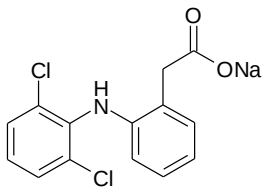
M. Wt =314.60

Aluminum chloride

M. Wt =133.34

Sodiumhydroxide

M. Wt =40.00



[2-(2,6-Dichloro-phenylamino)-phenyl]-acetic acid

Diclofenac Sodium

M. Wt =296.16

+ H_2O + $Al(OH)_3$ + HCl

Water

M. Wt =18.00

Aluminium hydroxides

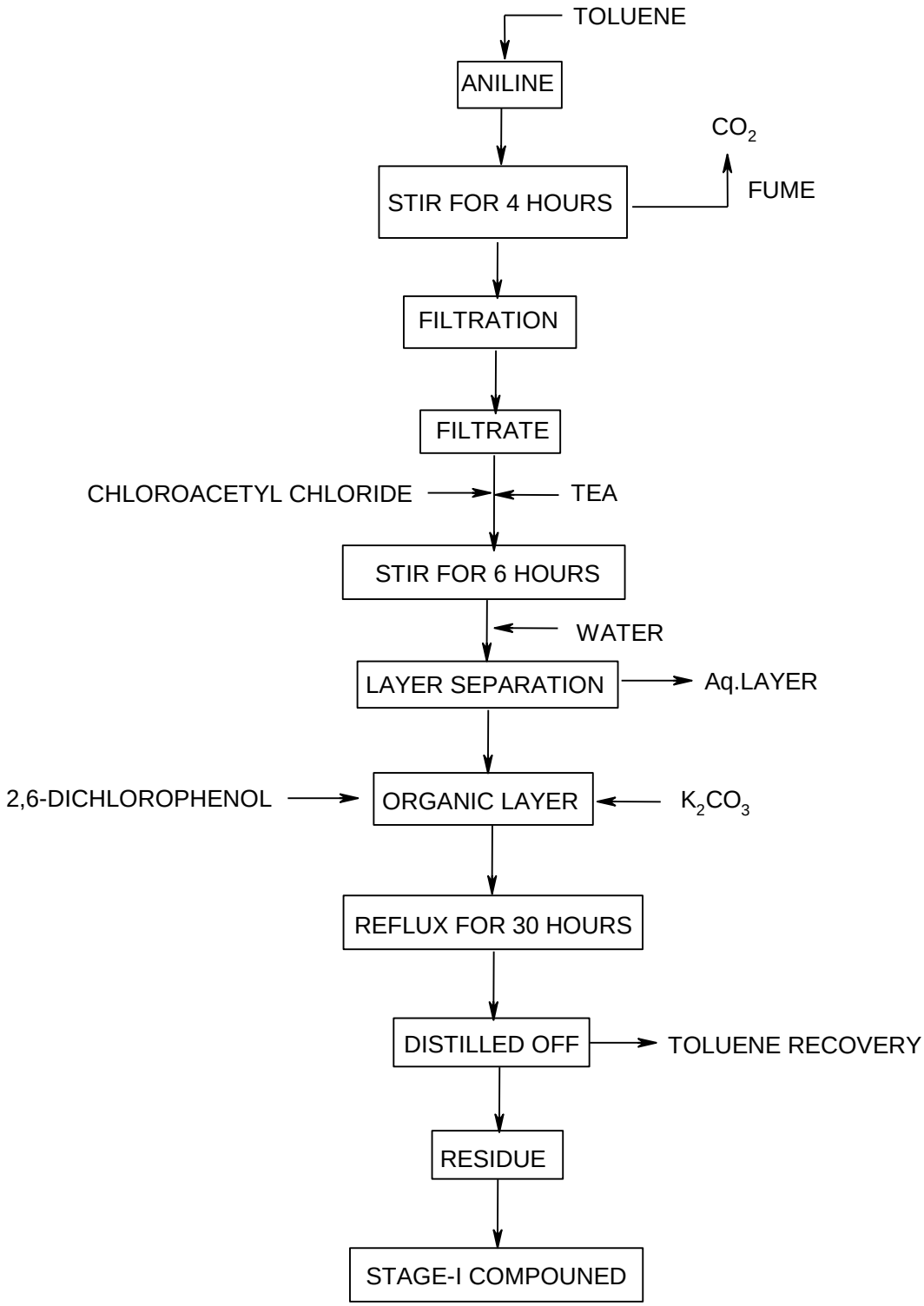
M. Wt =78.00

Hydrochloric acid

M. Wt =36.50

Flow Chart:

Stage-I:



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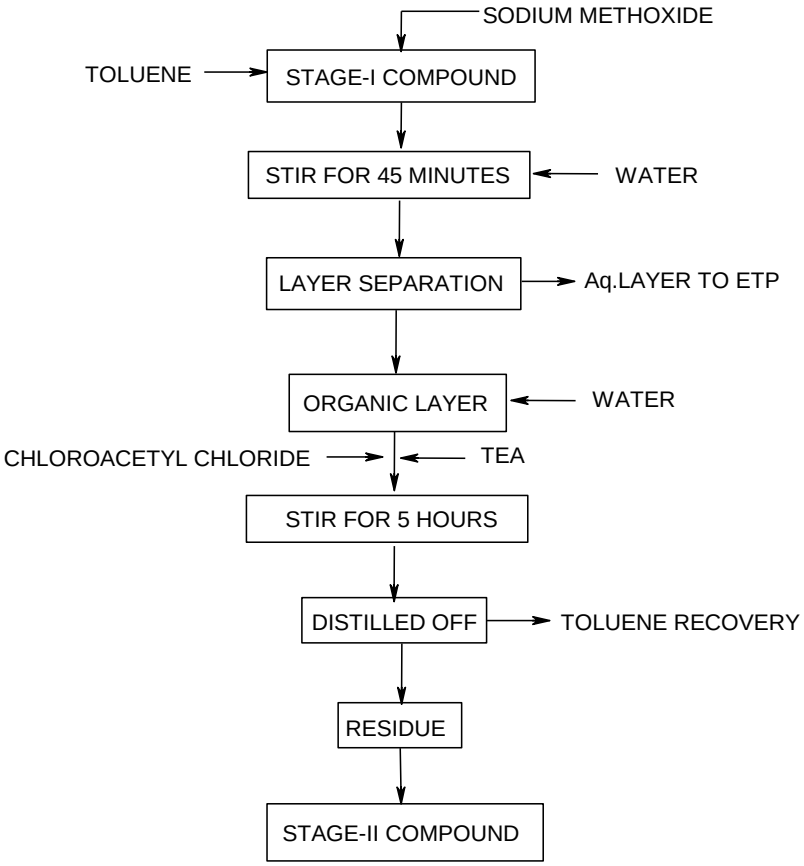
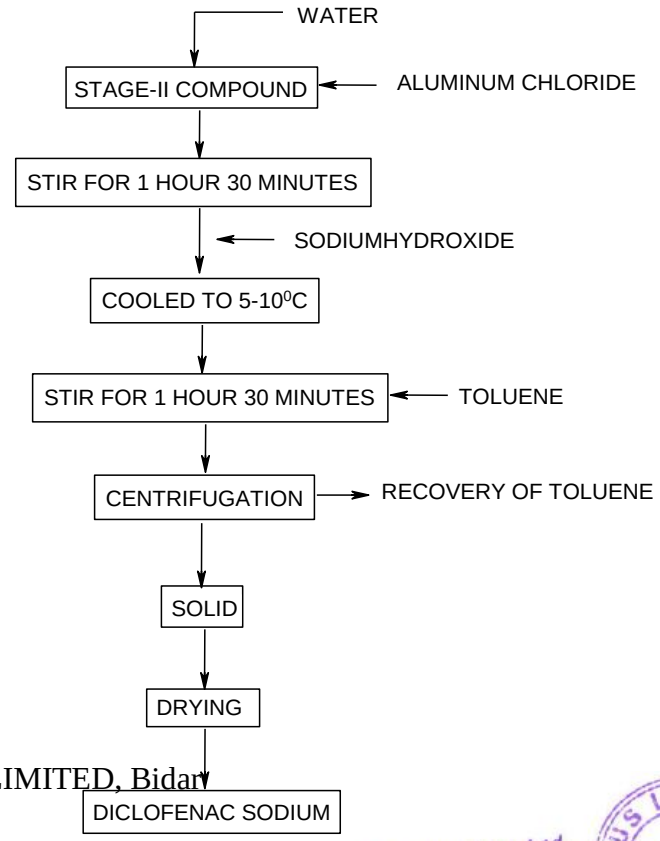
Stage-II:



Stage-III:



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Director

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Material Balance:

Stage-I:

S. No.	In put	kg/d	Out put	Kg/d	Remarks
1	Chloroacetyl Chloride	663.71	Stage-I product	1224.78	Stage-I product
2	2,6-Dichloro-phenol	981.03	Triethylamine HCl	1403.33	By product
3	Phenylamine	481.49	Carbon dioxide	228.48	emission
4	Triethylamine	607.87	Potassium chloride	1078.33	Solid waste
5	Water	1000.00	Water	1093.06	To waste water
6	Toluene	1034.78	Toluene	1034.78	To recovery & reuse
7	Potassium Carbonate	1293.99			
	Total input	**6062.87**	**Total output**	**6062.8**	

Stage-II:

S. No.	In put	kg/d	Out put	Kg/d	Remarks
1	Stage-I product	1224.78	Stage-II product	910.61	Stage-II product
2	Sodium methoxide	421.30	Triethylamine Hydrochloride	568.68	
3	Chloroacetyl Chloride	926.86	Sodium carboxymethanolate	405.41	
4	Triethylamine	815.52	Methanol	1429.16	recovery
5	Water	1000.00	Water	1074.60	To forced evaporation
6	Toluene	1600.00	Toluene recovery	1550.00	recovery
			Toluene loss	50.00	Loss- residue-40, to waste water -10
	Total input	**5988**	**Total output**	**5988**	

Stage-III:

S. No.	In put	kg/d	Out put	Kg/d	Remarks
1	Stage-II product	910.61	Diclofenac Sodium	600.00	product
2	Aluminum chloride	771.83	Aluminium hydroxides	514.33	
3	Sodiumhydroxide	455.30	Hydrochloric acid	682.76	Recovery and sold to vendors/for neutralization
4	Water	1000.00	Water +un reacted aluminium chloride and sodium hydroxide	1340.65	To forced evaporation

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S. No.	In put	kg/d	Out put	Kg/d	Remarks
	Total input	3137.74	**Total output**	3137.74	

For Chorus Labs Ltd,
P. Subba Reddy
Director

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3. EFAVERINZ

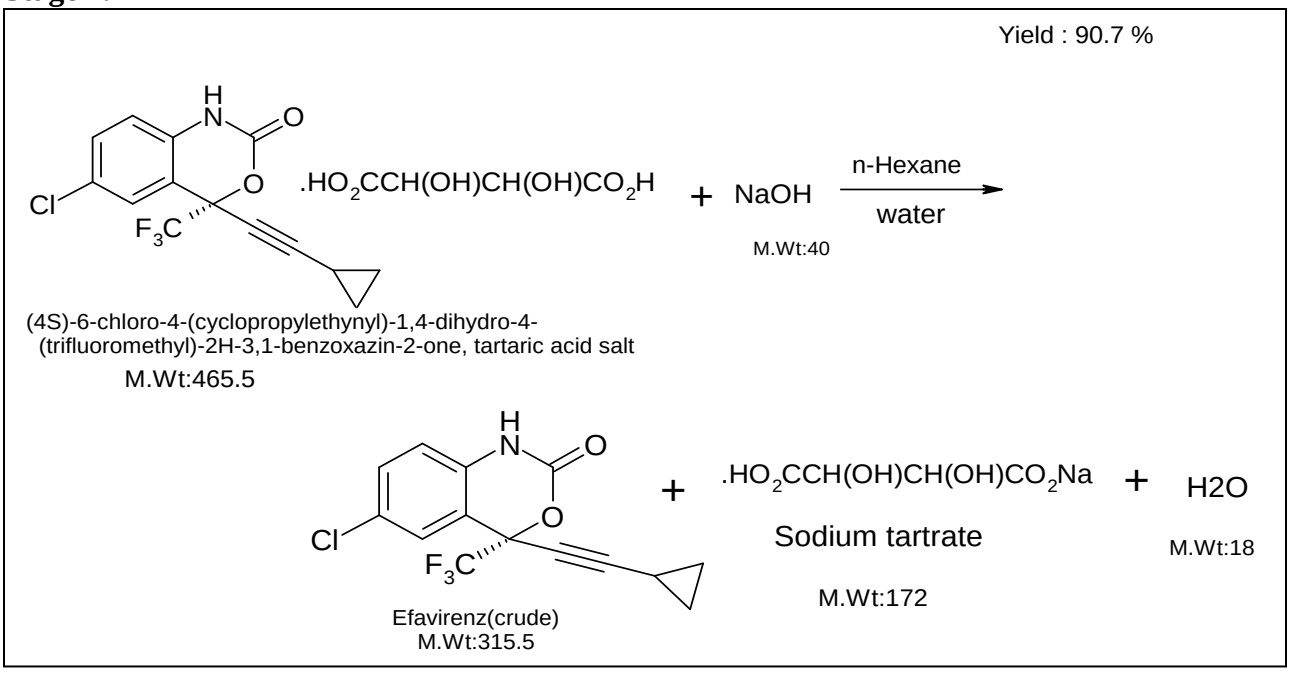
Description:

Stage-I: 4S-6 Chloro-4-(cyclopropylethynyl)-14-dihydro-4-trifiuoromethyl)-2H-3,1-benzoxazin-2-one,tartaricacid salt is treated with NaoH (desaltification) in presence of n-Hexane to yield Stage- I compound.

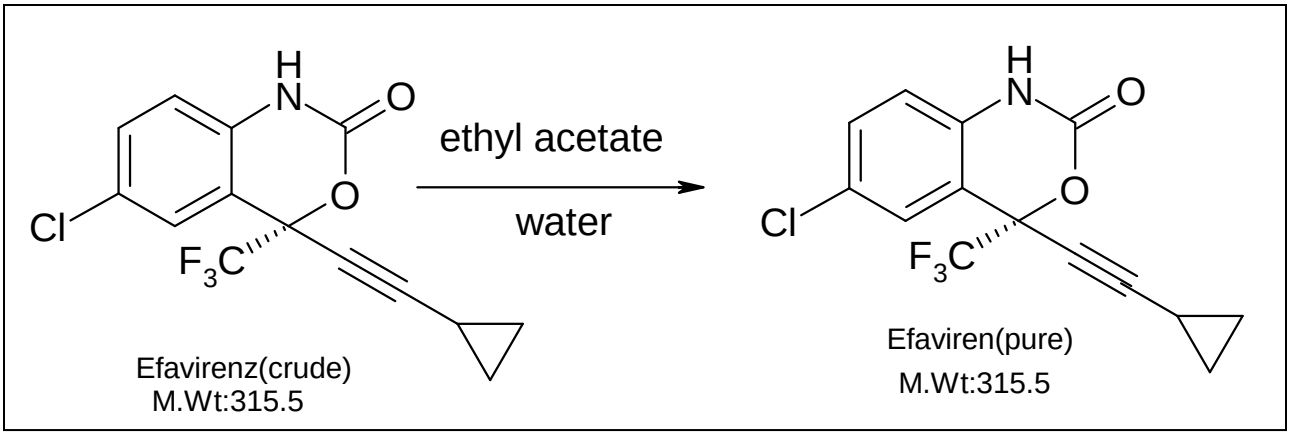
Stage-II: Stage-I compound is purified with ethyl acetate and water to yield Efaverenz.

Route of synthesis of product:

Stage-I:



Stage-II:



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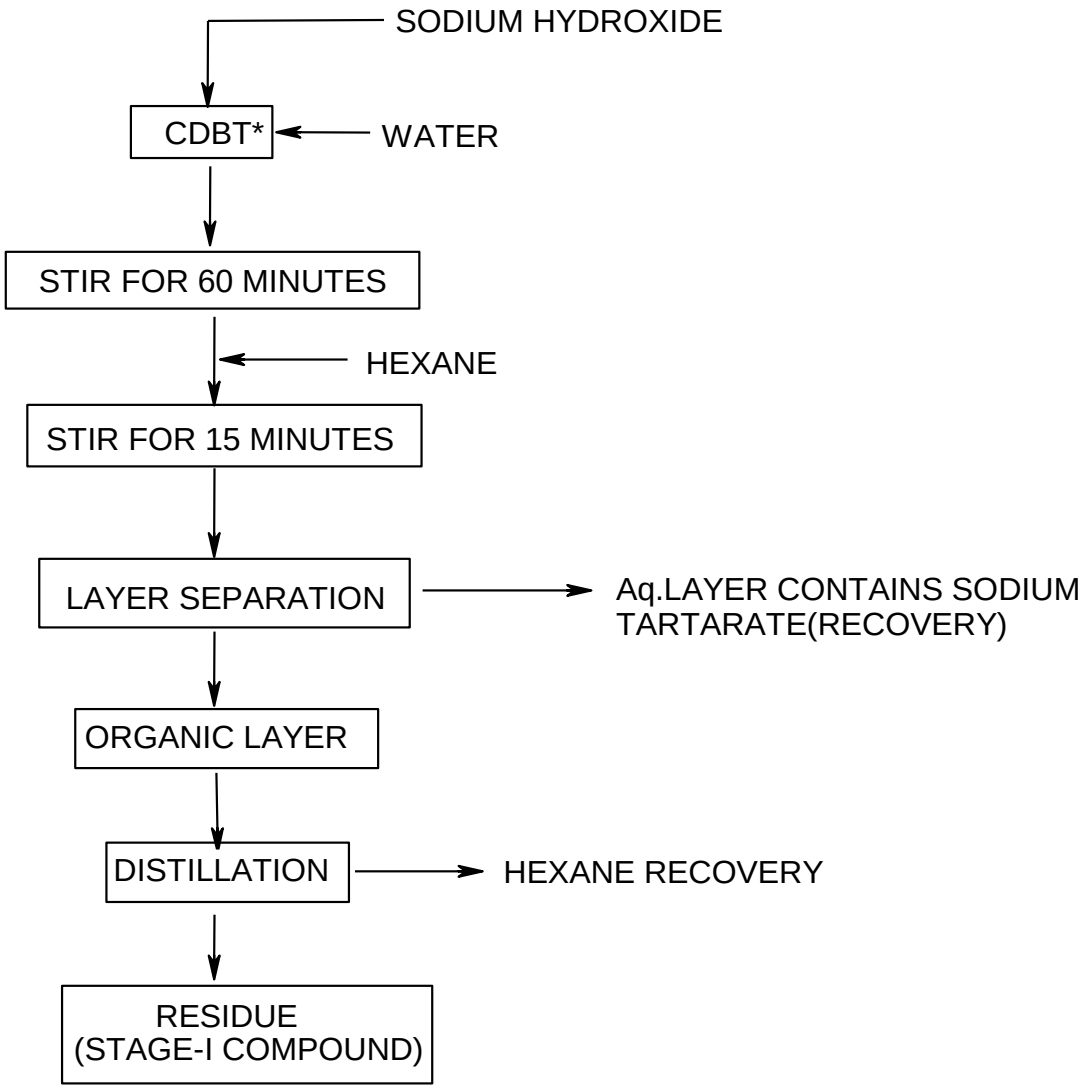
Flow Chart:

Stage-I:



CDBT*: (4S)-6-chloro-4-(cyclopropylethynyl)-1,4-dihydro-4-(trifluoromethyl)-2H-3,1-benzoxazin-2-one, tartaric acid salt

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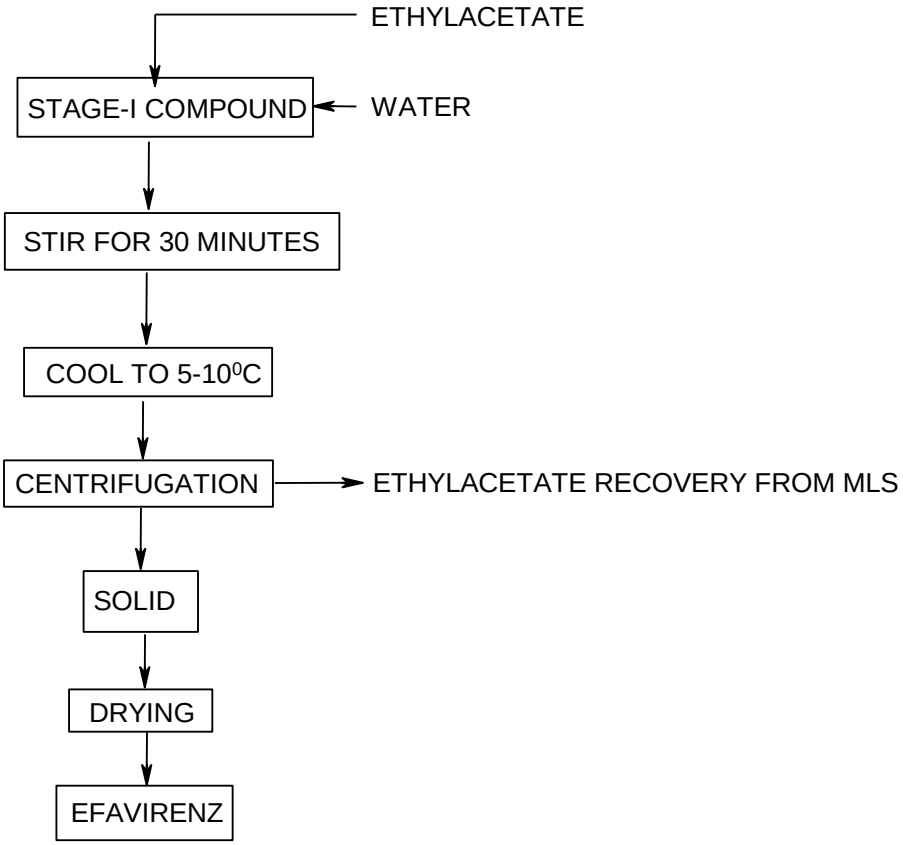
Stage-II:



Material Balance:

Stage-I:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	4S-6Chloro-4-(cyclopropyl ethynyl)-14-dihydro-4-trifiuoromethyl)-2H-3,1-benzoxazin-2-one,tartaricacid salt	758.615	Efavirenz crude	1081.08	Stage-I compound
2	n-Hexane	2000	By product-Sodium tartrate	589.358	Recovery and s0ld to vendors
3	NaOH	151.116	n-Hexane recover	1890	Recovery Reuse
4	Water	1000	Solvent loss	110	Residue -100 Loss- 10
			Unreacted Organics 1. 4S-6Chloro-4-(cyclopropyl ethynyl)-	160	Recovery Reuse

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			14-dihydro-4-trifiuoromethyl)-2H-3,1-benzoxazin-2-one,tartaricacid salt**(160)**		
			Waste water –Water 1. 4S-6Chloro-4-(cyclopropyl ethynyl)-14-dihydro-4-trifiuoromethyl)-2H-3,1-benzoxazin-2-one,tartaricacid salt **(3.5767)** NaOH **(14.056)**	1000 +**3.5767** +**14.056**	To forced evaporation
			Reaction water	61.677	To forced evaporation
	Total input	**4909.73**	**Total output**	**4909.73**	

Stage-II:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	Efavirenz crude	1081.08	Efavirenz	1000	
2	Ethyl acetate	1000	Ethyl acetate recovery	950	
3	Water	500	Solvent loss	50	Residue-40 Loss-10
			Waste water- with ethyl acetate solvent	500 +10	To forced Evaporation
			Unreacted Efavirenz crude	81.083	Recover & reuse
	Total input	**2581.08**	**Total output**	**2581.08**	

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4. Leviteracitam

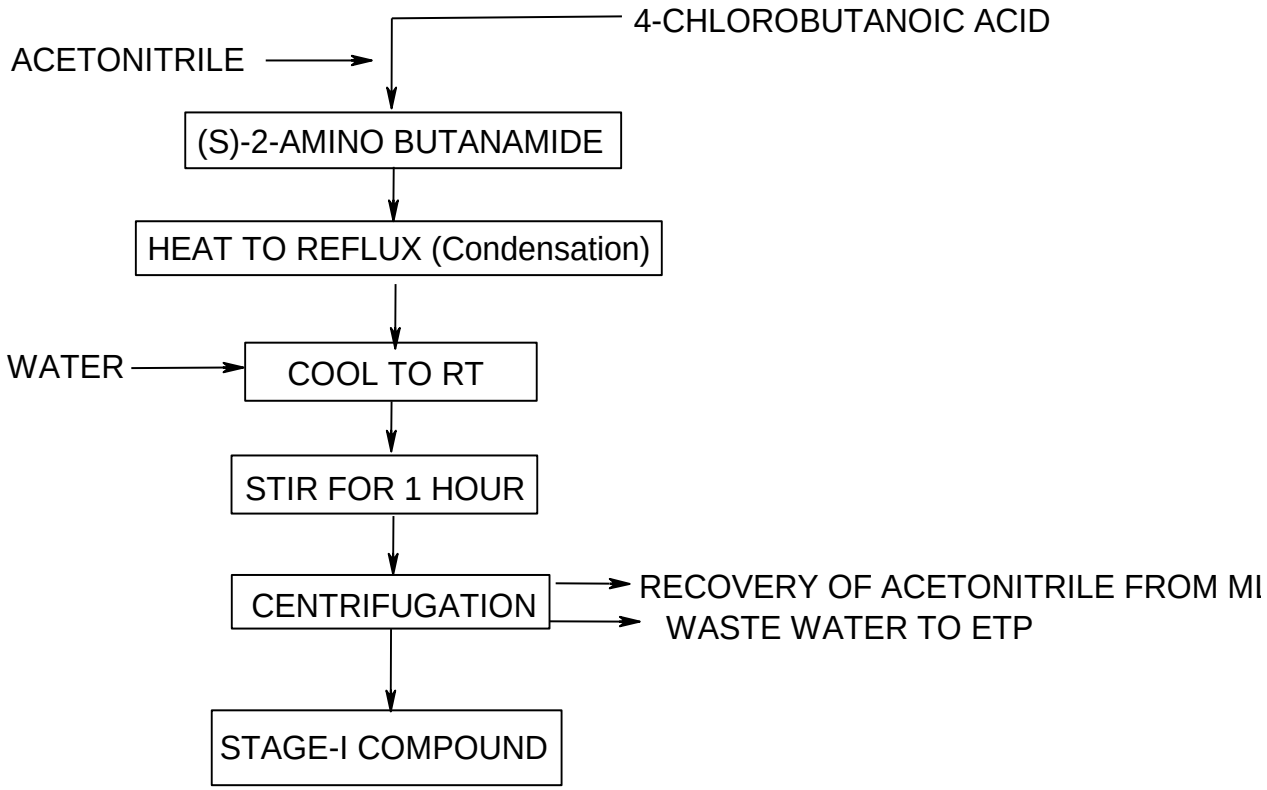
Description:

Stage-I: (S)-2-aminobutanamide is condensed with 4-chlorobutanoicacid in presence of Aceto nitrile to give stage-I compound

Stage-II: Stage-I compound is cyclised in presence of Sodium hydroxide and Ethyl acetate to give LEVETIRACETAM

Flow Chart:

Stage-I:



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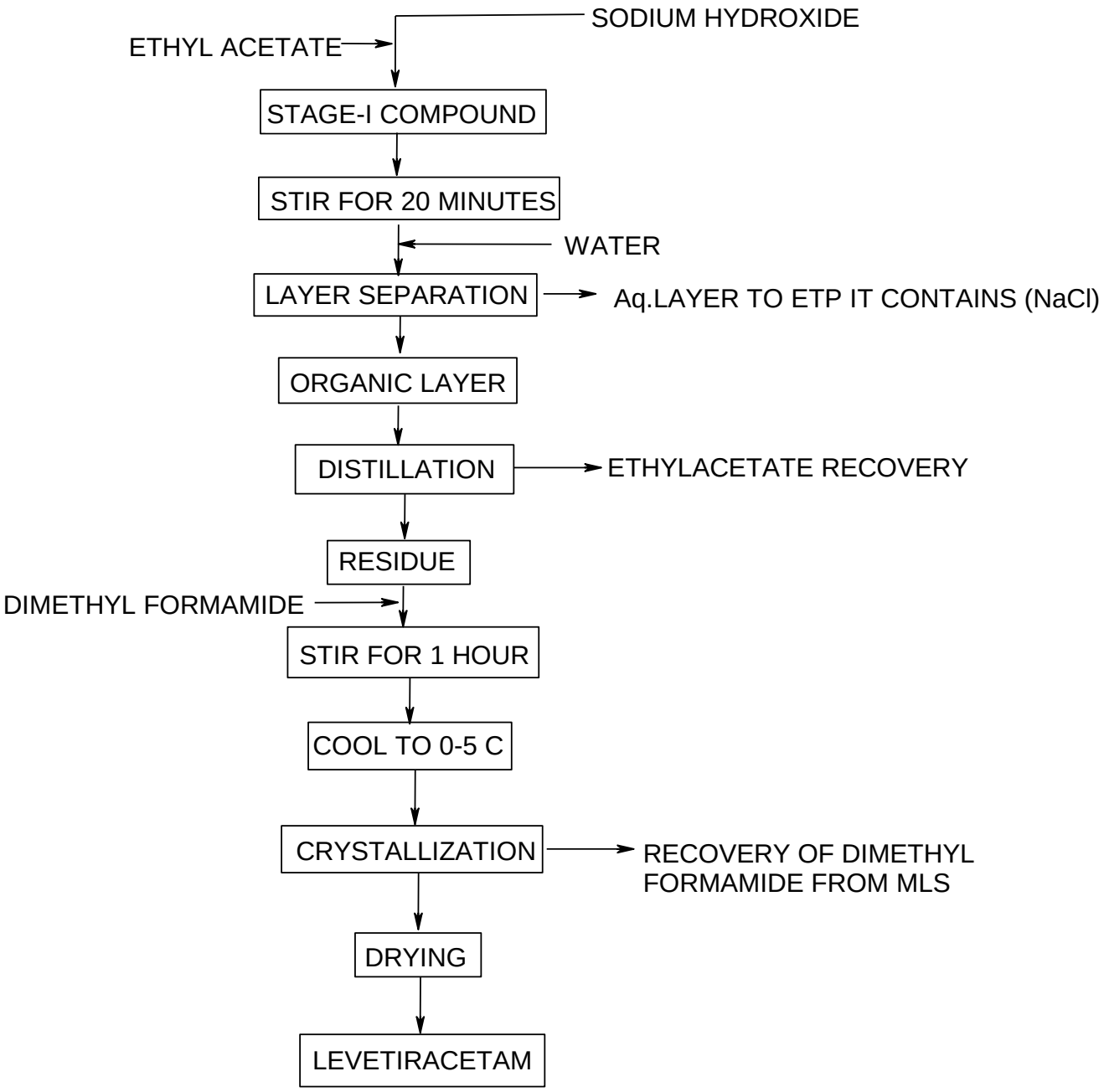
Stage-II:



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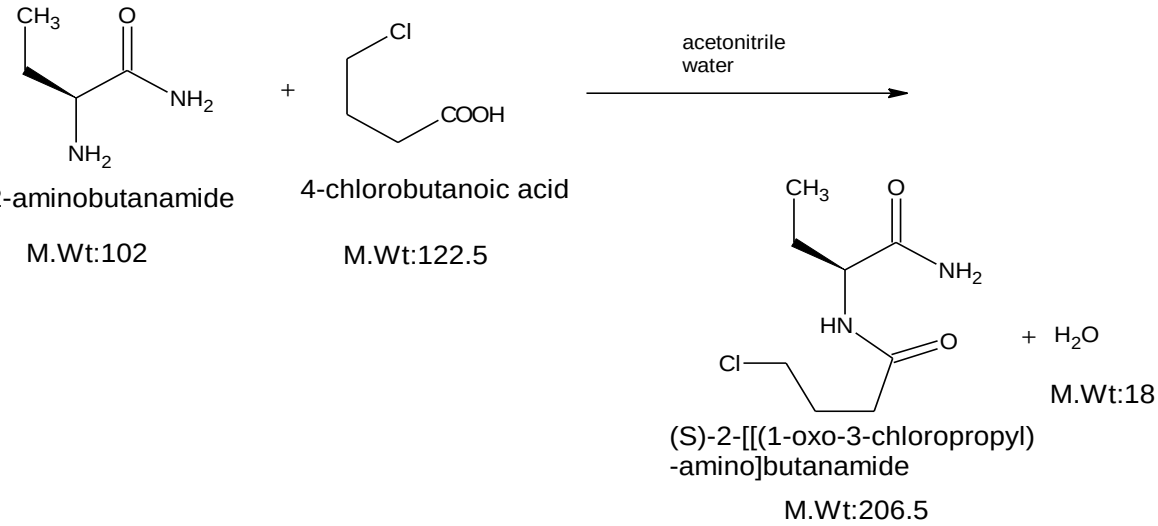
Route of synthesis of product:

LEVETIRACETAM

Stage-I

yield:75.1%



(S)-2-aminobutanamide

M.Wt:102

4-chlorobutanoic acid

M.Wt:122.5

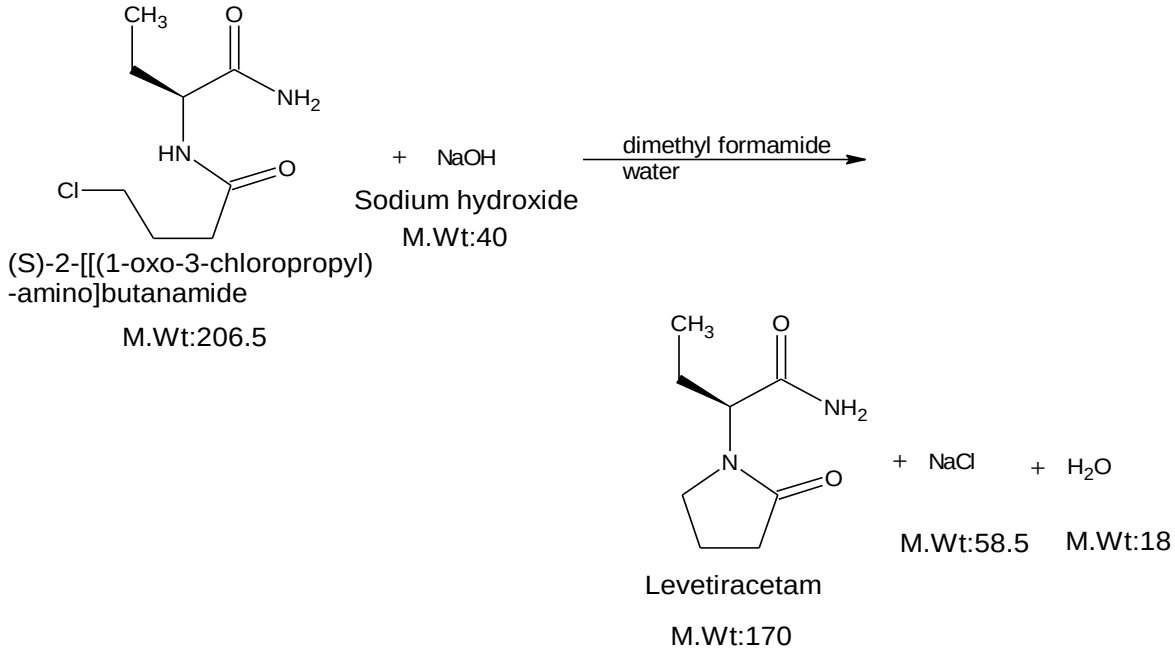
M.Wt:18

(S)-2-[[(1-oxo-3-chloropropyl)
-amino]butanamide

M.Wt:206.5

Stage-II

yield:83.4%



(S)-2-[[(1-oxo-3-chloropropyl)
-amino]butanamide

M.Wt:206.5

Sodium hydroxide

M.Wt:40

M.Wt:58.5

M.Wt:18

Levetiracetam

M.Wt:170

For Chorus Labs Ltd.,
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Director

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Material Balance:

Stage-I:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	(S)-2-aminobutanamide	957.954	Stage –I compound	1456.48	Stage –I compound
2	4-chlorobutanoicacid	1150.483	Acetonitrile recovery	1450	Recovery Reuse
3	Aceto nitrile	1500	Solvent loss	50	Loss Residue -40 Waste water-10
4	Water	1000	Waste water-water	1000 +8.54 +6.49	To forced evaporation
			Unreacted Organics (S)-2-aminobutanamide **(230.0)** 4-chlorobutanoicacid (**280. 0)**		Recovery Reuse
			Reaction water	126.954	To forced evaporation
	Total	**4608.43**	**Total**	**4608.47**	

Stage-II:

S.No:	Input	Kg/d	Output	Kg/d	Remarks
1	Stage –I compound	1456.48	Levetiracetam	1000	Final compound
2	Di methylformamide	1500	Di methylformamide Recovery	1450	Reuse
3	Sodium hydroxide	282.124	Di methylformamide loss	50	Loss Residue-40 Waste Water-10
4	Water	2000	Waste water- **Unreacted Inorganic** Sodium hydroxide **(46.92)** Stage –I compound **2.2245)**	2000 +46.92 +2.2254	Forced evaporation
5	Ethyl acetate	1500	**Unreacted Organic** 1. Stage –I compound **242.2245)**		Reuse
			NaCl	343.98	To waste water
			Reaction water	105.84	To waste water
			Ethyl acetate recovery	1460	Recovery & reuse
			Ethyl acetate loss	40	30-residue 10- waste water
	Total	**6738.604**	**Total**	**6738.9**	

For Chorus Labs Ltd.,
P. Subba Reddy
Director

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5. Moxifloxacin

Description:

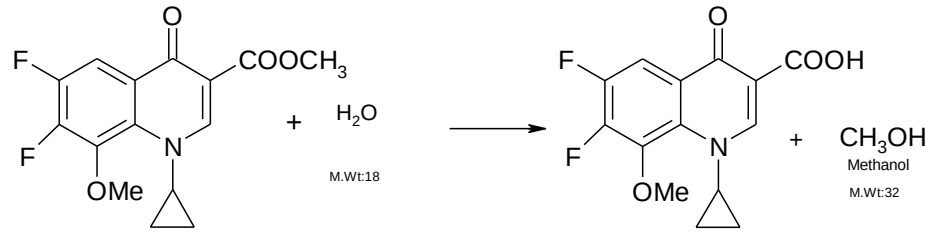
Stage-I: Methyl-1-cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinoline carboxylate is hydrolised with water, hydrochloric acid in presence of diisopropyl ether to yield stage-I compound.

Stage- II: Stage- I compound is condensed with ((S,S)-2,8-Diazobicyclo-[4,3,0]nonane to get Moxyfloxacin.

Route of synthesis of product:

MOXIFLOXACIN

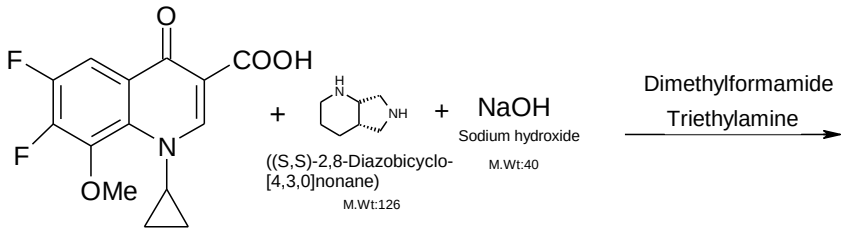
Stage-I yield :81.5 %



Methyl 1-Cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinoline carboxylate M.Wt:309

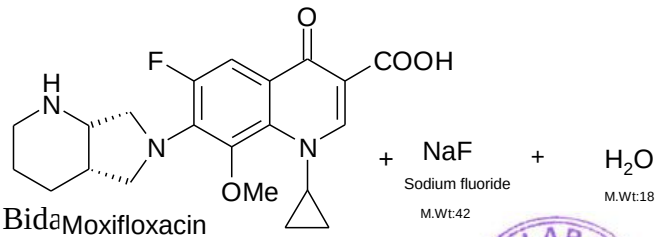
1-Cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinoline carboxylic acid M.Wt:295

Stage-II yield :72.5%



1-Cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinoline carboxylic acid M.Wt:295

((S,S)-2,8-Diazobicyclo-[4,3,0]nonane) M.Wt:126



Moxifloxacin M.Wt:401

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Director

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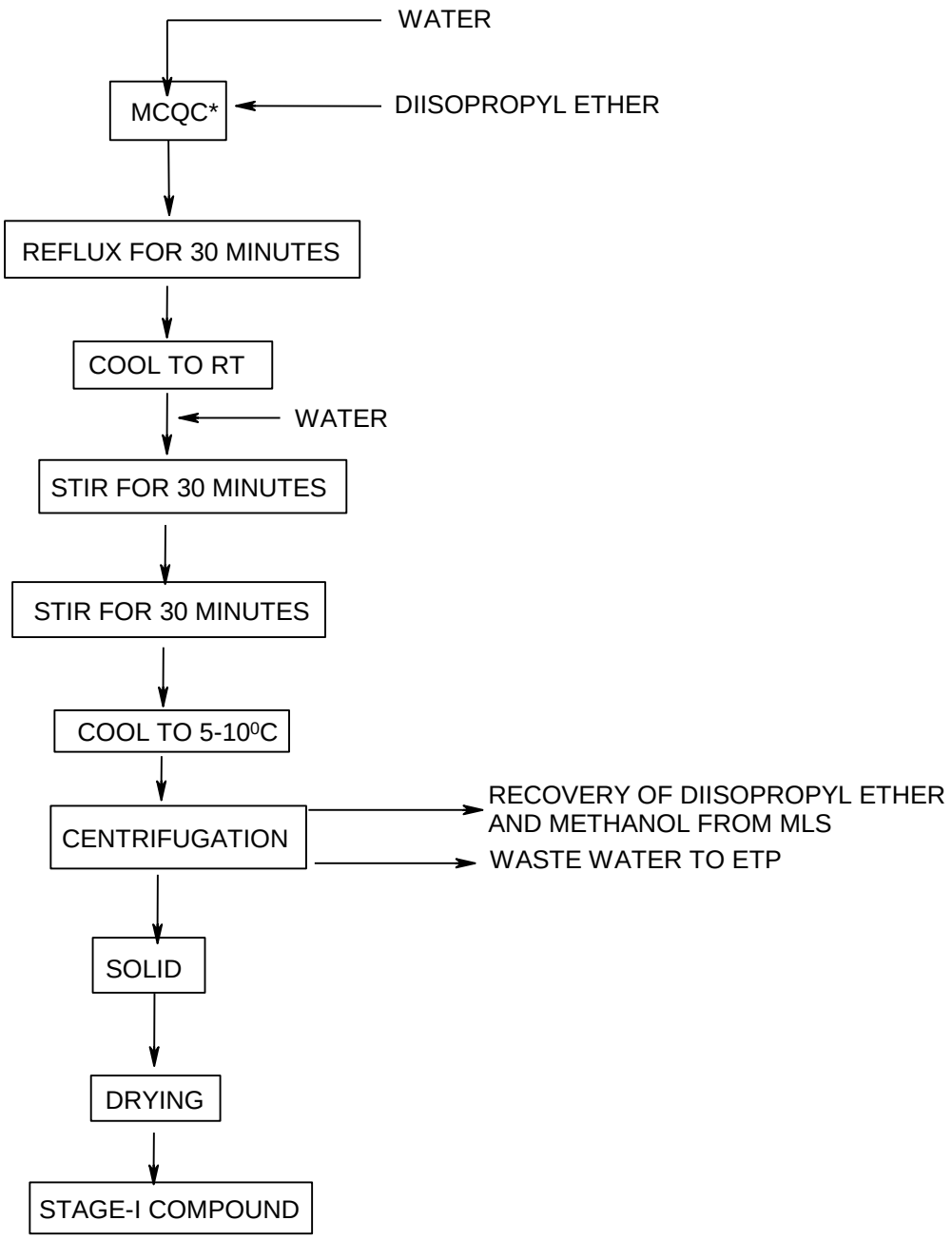
Flow Chart:

Stage-I:



MCQC*:METHYL-1-CYCLOPROPYL-6,7,DIFLUORO-1,4-DIHYDRO-8-METHOXY-4-OXOQUINOLINE CARBOXYLATE

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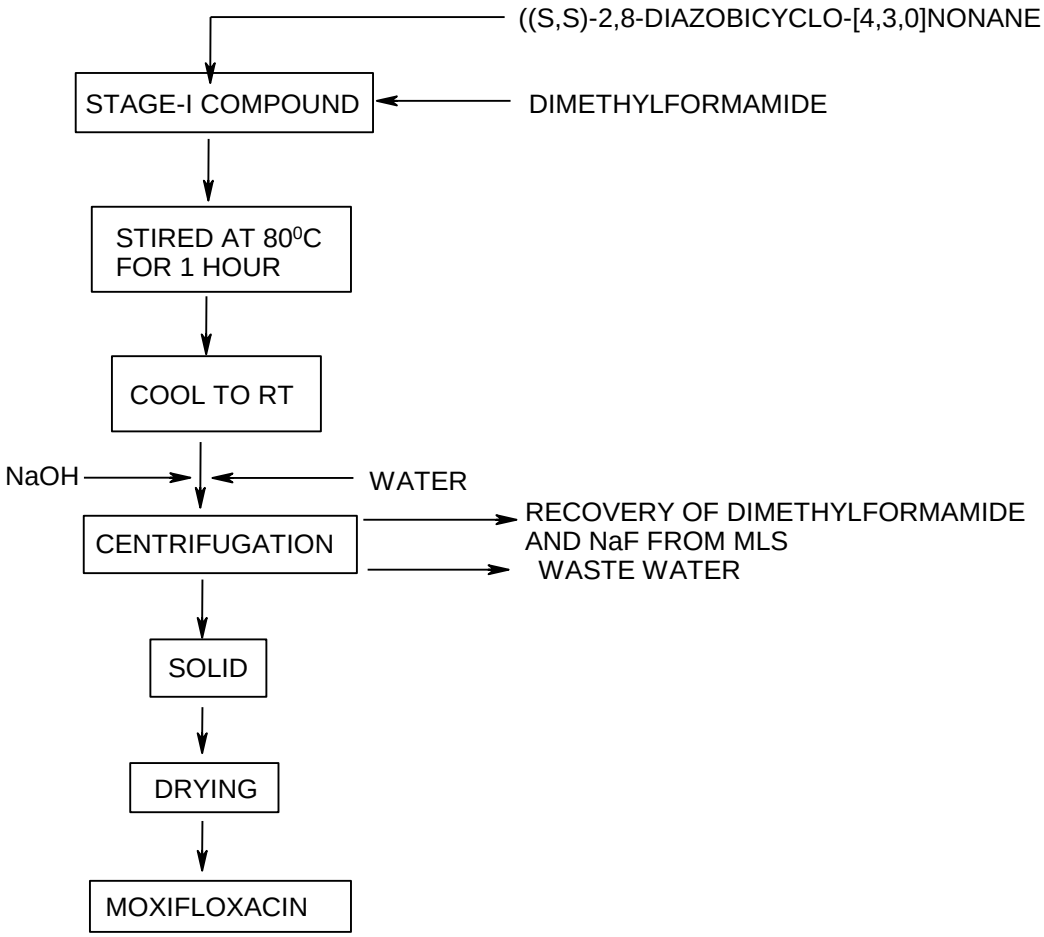
Stage-II:



Material Balance:

Stage-I:

S.NO.	In put	Kg/d	Out put	Kg/d	Remarks
1	Methyl-1-cyclopropyl-6, 7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinolinecarboxylate	978.09	1-cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinoline carboxylic acid	**761.028**	Stage-I compound
2	Water	56.97	Water-waste water including HCL	1055.5	Waste water
3	Diisopropylether	1000	**Un reacted Organics** 1. Methyl-1-cyclopropyl-6, 7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinolinecarboxylate **(181.074)**		To waste water As residue
4	Water	1000			

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Director
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5	Hydro chloric acid	45	Methanol	82.53	To waste water
			Diisopropylether recovery	980	Reuse
			Diisopropylether Loss	20	Loss
	Total input	**3080.1**	**Total output**	**3080.3**	

Stage-II:

S.NO.	In put	Kg/d	Out put	Kg/d	Remarks
1	1-cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinoline carboxylic acid	**761.028**	Moxofloxacin	**750**	Final Product
			Water-waste	1000 +9.45+ 9.46	Waste water
2	((S,S)-2,8-Diazobicyclo-[4,3,0]nonane	324.954	**Unreacted Organics** 1-cyclopropyl-6,7-difluoro-1,4-dihydro-8-methoxy-4-oxo-3-quinoline carboxylic acid **(200)** ((S,S)-2,8-Diazobicyclo-[4,3,0]nonane **(0)** **Unreacted Inorganics** Sodium hydroxide **(28.4)**		
3	Dimethylformamide	800	Sodium fluoride	78.54	Recovery and Reuse
4	Triethylamine	400	Dimethylformamide	770	Recovery and Reuse
5	Sodium hydroxide	103.16	Dimethylformamide	30	Loss Residue-20 Waste water-10
6	Water	1000	Triethylamine	370	Recovery and Reuse
			Triethylamine loss	30	Residue-20 Waste water-10
			Reaction water	33.66	To waste water
	Total input	**3389.14**	**Total output**	**3389.5**	

For Chorus Labs Ltd,
P. Subba Reddy
Director

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6. Nebivolal

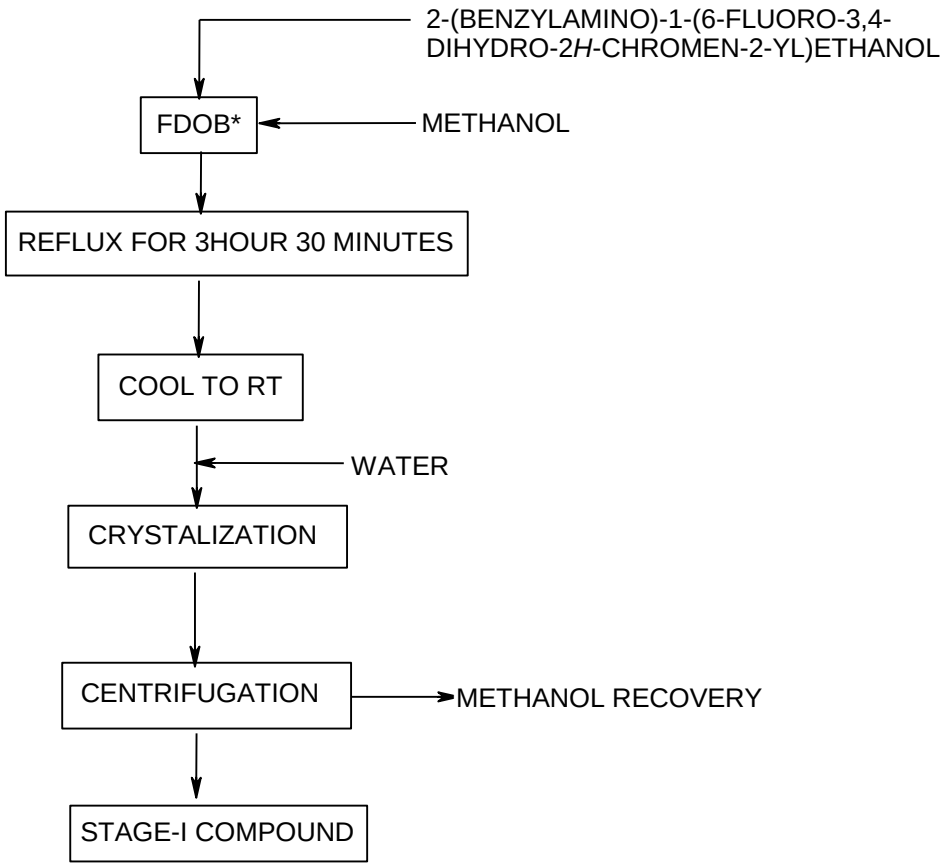
Description:

Stage-I: 6-Fluoro-3,4-dihydro-2-oxiranyl-2H-1-benzopyran is condensed with 2-(benzylamino)-1-(6-fluoro-3,4-dihydro-2H-chromen-2-yl)ethanol in presence of methanol to yield Stage- I Compound.

Stage-II: In presence of palladium carbon, Stage- I compound is hydrogenated and then reacted with HCl to yield Nebivolol Hydrochloride.

Flow Chart:

Stage-I:



FDOB*: 6-FLUORO-3,4-DIHYDRO-2-OXIRANYL-2H-1-BENZOPYRAN

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Director

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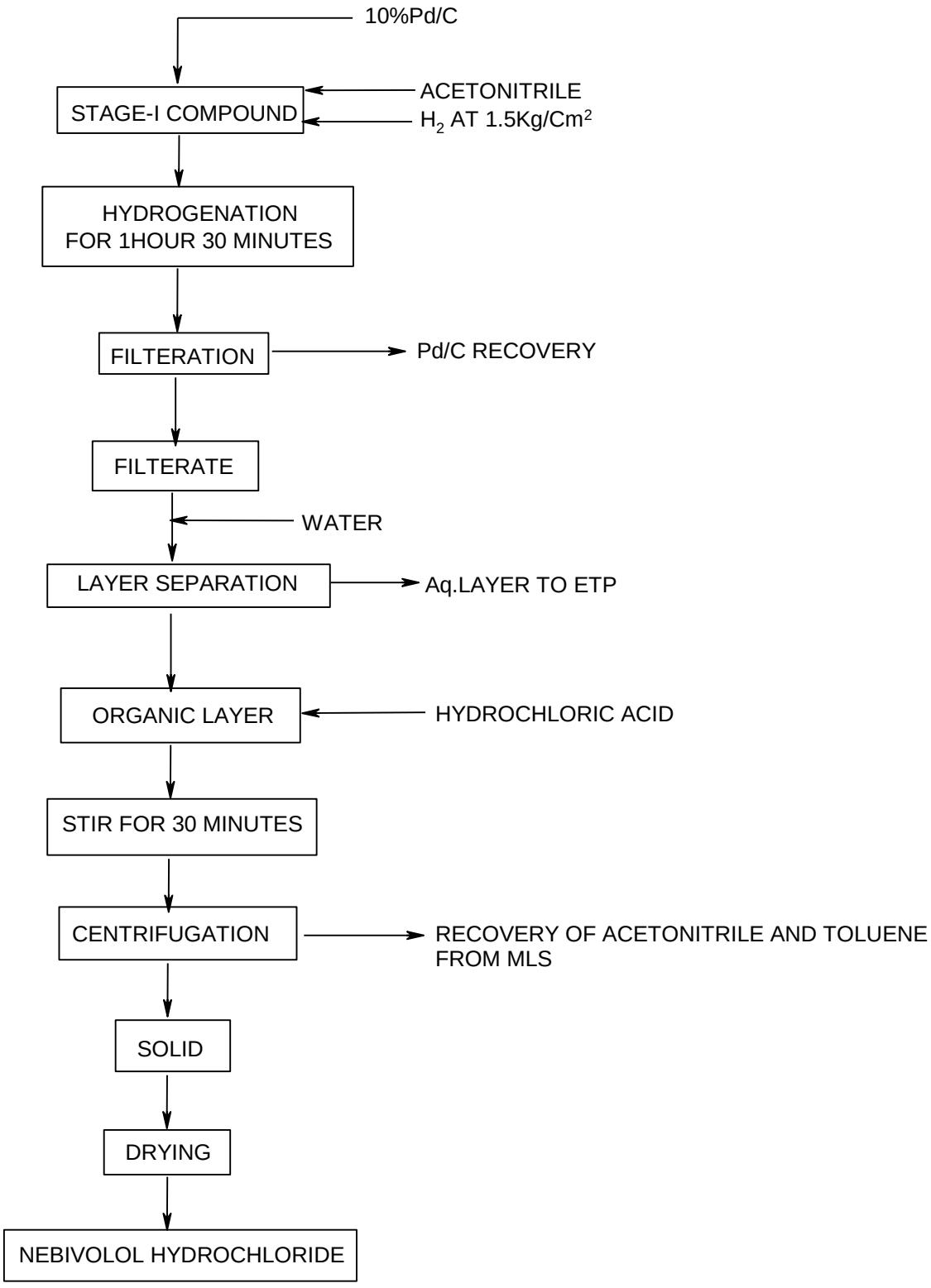
Stage-II:



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Director

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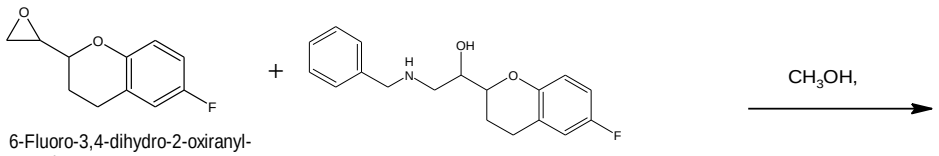
Route of synthesis of product:

NEBIVOLOL HYDROCHLORIC ACID

STAGE-I

Yield : 35 %

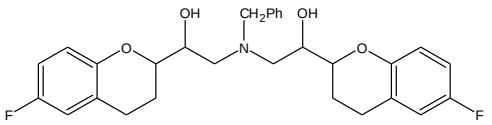


6-Fluoro-3,4-dihydro-2-oxiranyl-2H-1-benzopyran

M.Wt: 194.20

2-(benzylamino)-1-(6-fluoro-3,4-dihydro-2*H*-chromen-2-yl)ethanol

M.Wt: 301.35

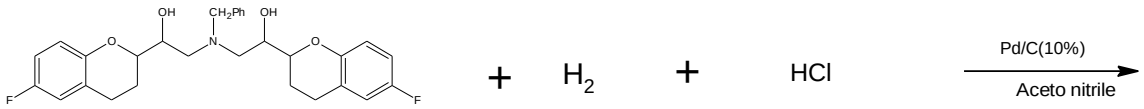


α,α'-[[(Phenylmethyl)imino]bismethylene]bis-[6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol]

M.Wt: 495.55

STAGE-II

yield :62.5 %

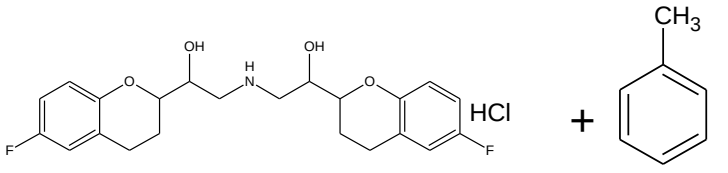


α,α'-[[(Phenylmethyl)imino]bismethylene]bis-[6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol]

M.Wt: 496.56

M.Wt: 2

M.Wt :36.5



NEBIVOLOL HYDRO CHLORIC ACID

M.Wt: 441.93

Toluene

M.Wt: 92.13

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Director

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Material Balance:

Stage-I:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	6-Fluoro-3,4-dihydro-2-oxiranyl-2H-1-benzopyran	1509.708	**Stage-I compound**	1348.34	Stage-I compound
2	2-(benzylamino)-1-(6-fluoro-3,4-dihydro-2*H*-chromen-2-yl)ethanol	2342.39	Methanol	1950	Recovery and Reuse
3	Methanol	2000	Methanol	50	Loss
4	Water	2000	Waste water-water	2000+ 1.29+2.72	Waste- water
			Unreacted Organics 1. 6-Fluoro-3,4-dihydro-2-oxiranyl-2H-1-benzopyran **(980)** 2**.** 2-(benzylamino)-1-(6-fluoro-3,4-dihydro-2*H*-chromen-2-yl)ethanol **(1520)**		
	Total	**7852.098**	**Total**	**7852.3**	

Stage-II:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	Stage-I compound	1348.34	Nebivolol Hydrochloric acid	750	Final compound
2	Water	2000	Pd.Carbon	50	Solid waste
3	Pd.Carbon	50	Acetonitrile	1450	Recovery and reuse
4	Acetonitrile	1500	Acetonitrile	50	Loss Residue-40 Waste water-10
			Waste water + Hydrochloric acid **(43.03)**	2000 +43.03	Forced Evaporation
5	Hydrogen gas	5.43	**Unreacted Organic** 1.Stage-I compound **501.448** 2.Hydrogen gas **(2.0358)**	**500** **2.0358**	Recovery and reuse Emission
6	Hydrochloric acid	99.0975			
			By product 1.Toluene	156.35	Waste water
			Waste water-water		
	Total	**5002.86**	**Total**	**5002.86**	

For Chorus Labs Ltd,
P. Subba Reddy
Director

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7. Neverapine

Description:

Stage-I: 3-Amino-2-chloro-4-methylpyridine is reacted with 2-ChloronicotinoylChloride (condensed) to give stage-I compound

Stage-II: Stage-I compound is reacted with Cyclopropyl amine (condensed) in presence of Methanol to give stage-II compound

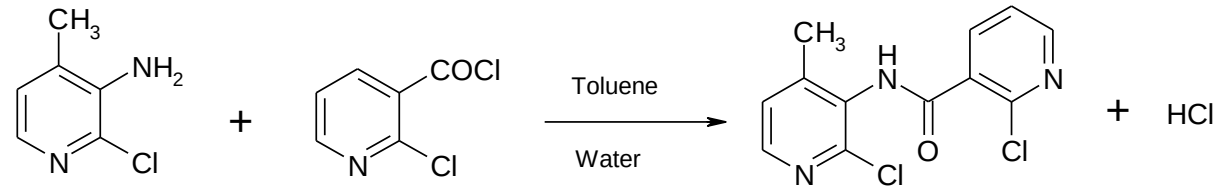
Stage-III: Stage-II compound is cyclised with Sodium hydroxide in the presence of O-Xylene to give the Stage-III compound

Stage-IV: Stage-III compound is purified with n-Heptane to give NEVIRAPINE

Route of synthesis of product:

Stage - I

Yield :76%



3-Amino-2-chloro-4-methylpyridine
M.Wt: 142.5

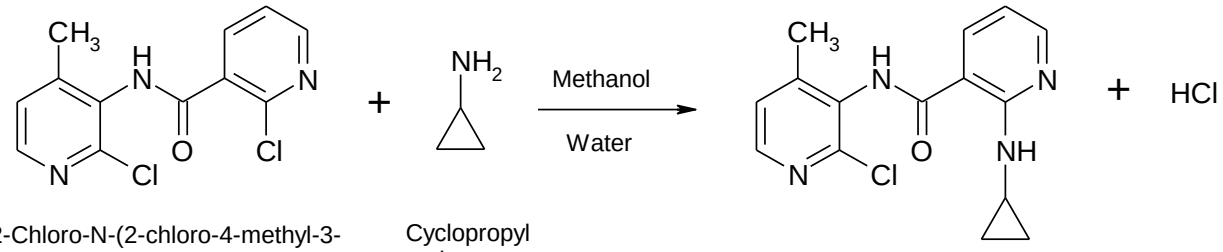
2-Chloronicotinoyl chloride
M.Wt: 176

2-Chloro-N-(2-chloro-4-methyl-3-pyridyl)-3-pyridinecarboxamide
M.Wt: 282

36.5

Stage - II

Yield:80 %



2-Chloro-N-(2-chloro-4-methyl-3-pyridyl)-3-pyridinecarboxamide
M.Wt: 282

Cyclopropyl amine
M.Wt: 57

N-(2-Chloro-4-methyl-3-pyridinyl)-2-(cyclopropylamino)-3-pyridine carboxamide
M.Wt: 302.5

36.5

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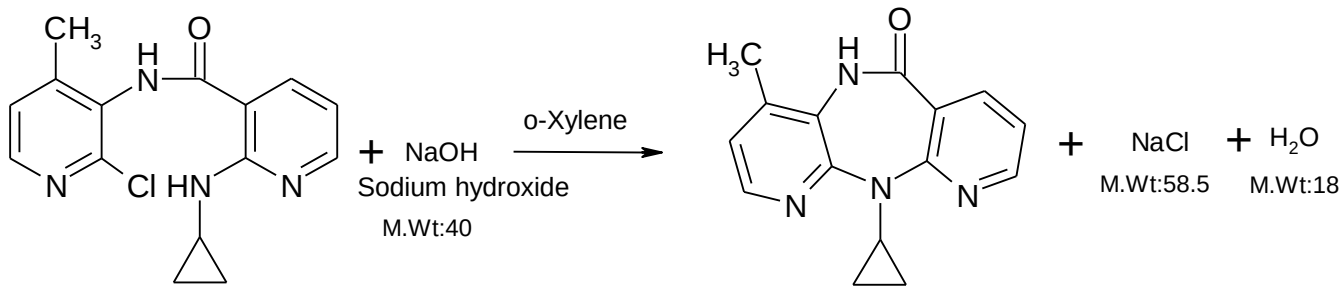
Stage-III:

yield : 71%



N-(2-Chloro-4-methyl-3-pyridinyl)-2-cyclopropylamino)-3-pyridine carboxamide

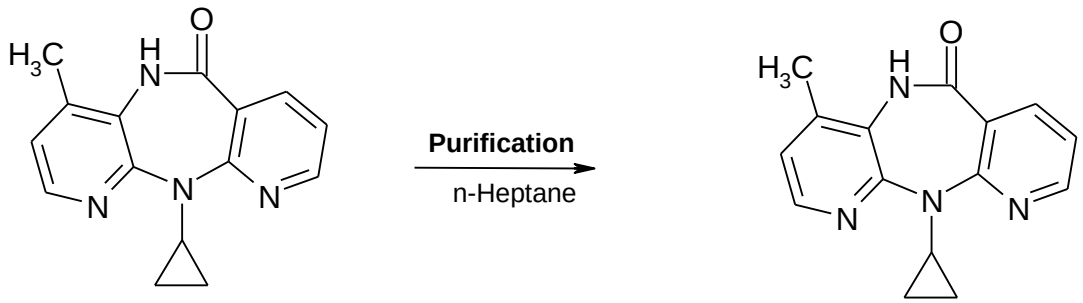
M.Wt:302.5

Nevirapine (crude)

M.Wt:266

Stage-IV:

yield : 95.1%



Nevirapine (crude)

M.Wt:266

Nevirapine

M.Wt:266

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Director

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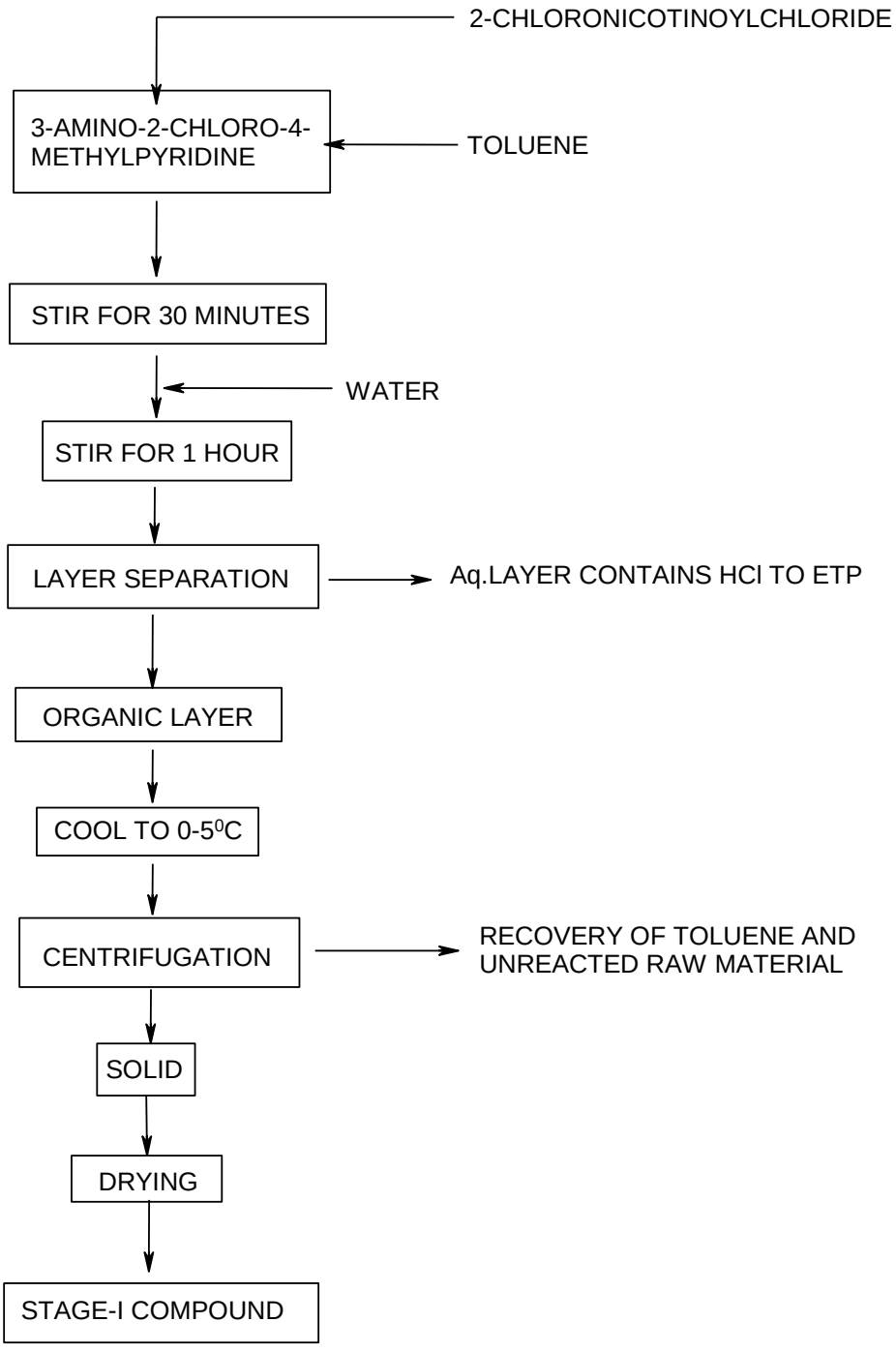
Flow Chart:

Stage-I:



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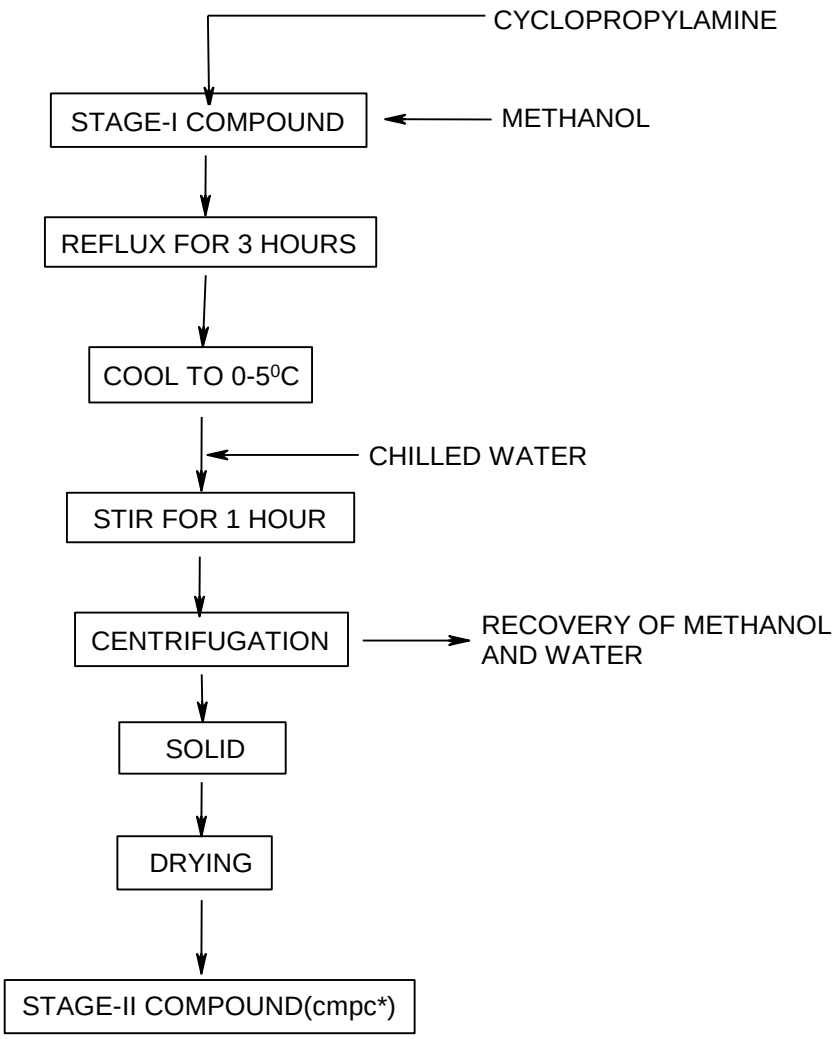
Stage-II:



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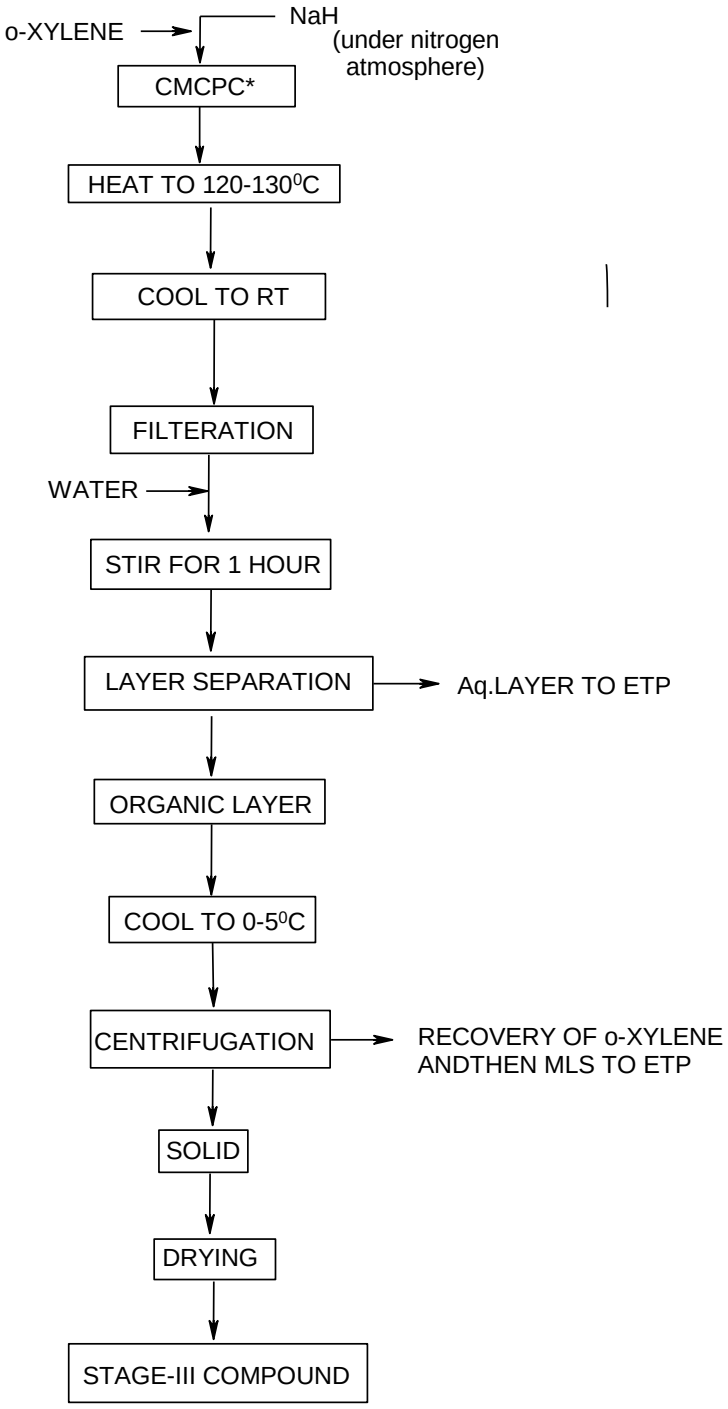
Stage-III:

STAGE-III



CMCPC*: N-(2-Chloro-4-methyl-3-pyridinyl)-2-cyclopropylamino)-3-pyridine carboxamide

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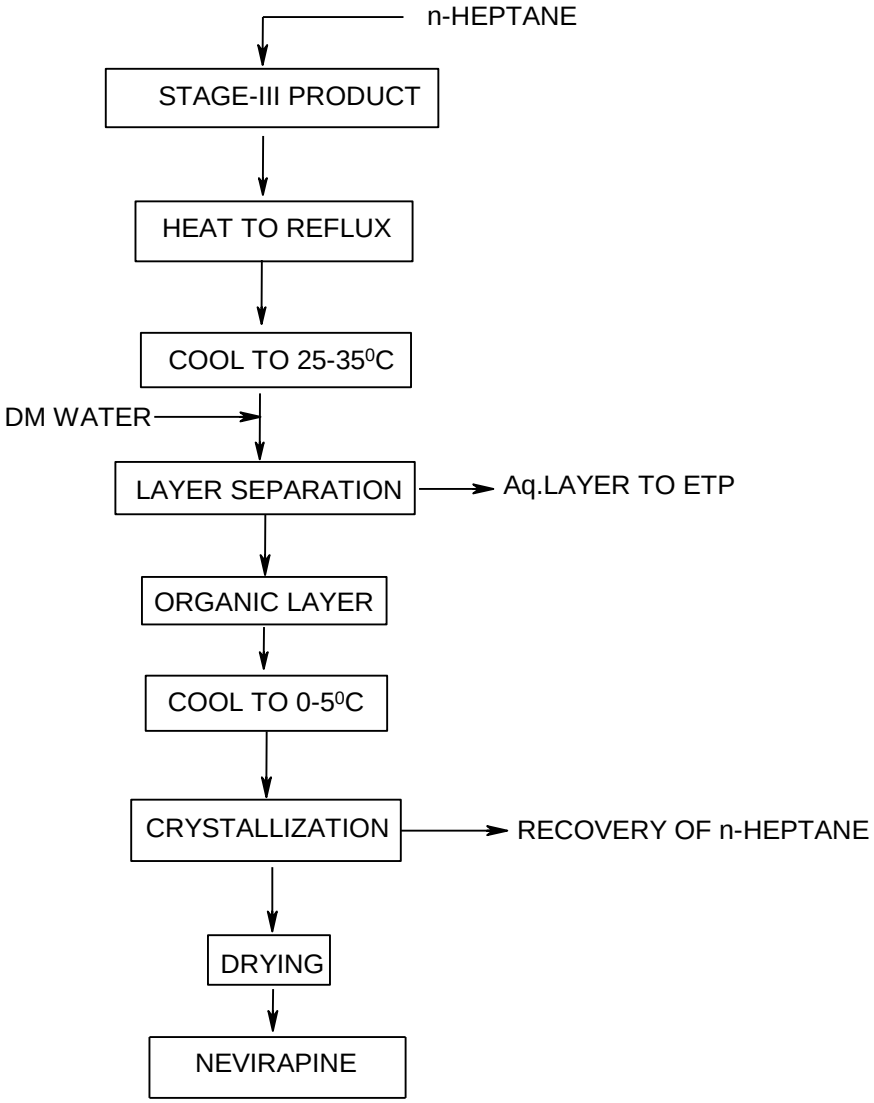
Stage-IV:



Material Balance:

Stage-I:

S.No	Input	Kg/day	Output	Kg/day
1	3-Amino-2-chloro-4-methylpyridine	1304.8	2-Chloro-N-(2-chloro-4-methyl-3-pyridyl)-3-pyridinecarboxamide	1962.602
2	2-Chloronicotinoyl chloride	1611.544	HCL	254.0
3	Toluene	1500	Unreacted organics: 3-Amino-2-chloro-4-methylpyridine **(310.0)** 2-Chloronicotinoyl Chloride **(380.0)**	
4	Water	1500	Wastewater	1500+3.143

				+6.776
5			Toluene- Rec Toluene-Loss	1450 50
	Total	**5916.344**		**5916.5**

Stage-II:

S.No	Input	Kg/day	Output	Kg/day	Remarks
1	2-Chloro-N-(2-chloro-4-methyl-3-pyridyl)-3pyridinecarboxamide	1962.602	N-(2-Chloro-4-methyl-3-pyridinyl) -2-(cyclopropylamino)-3-pyridine carboxamide	1684.219	
2	Cyclopropyl amine	396.663	HCL	202.94	recover
3			Unreacted: 2-Chloro-N-(2-chloro-4-methyl-3-pyridyl)-3pyridinecarboxamide **(390.0)** Cyclopropyl amine **(75.0)**	465	
4	Methanol	2000	Methanol -Rec Methanol- Loss	1950 50	Recover Loss
5	Water	1000	Wastewater	1000+ 2.518 +4.743	To forced evaporation
	Total	**5359.265**		**5359.42**	

Stage-III:

S. No.	In put	Qty Kgs	Out put	Qty Kgs	Remarks
1	N-(2-chloro-4-methyl-3-pyridinyl)-2-cyclopropylamino)-3-pyridinecarboxamide	1684.219	Nevirapine crude (Stage-III) compound	1051.51	Stage-III compound
2	O-Xylene	2000	O-Xylene recovery	1980	Reuse
3	Sodium hydroxide	222.68	Solvent loss	20	**Loss**
5	Water	1000	Waste water-Water	1000 +**8.235**	
			Unreacted Organics 1. N-(2-chloro-4-methyl-3-pyridinyl)-2-cyclopropylamino)-3 pyridinecarboxamide **(488.235)** 2. Sodium hydroxide **(64.56)**	**480**	Reused
			NaCl (231.25)		Into Waste

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			Reaction water	71.154	Into Waste
	Total input	**4906.899**	**Total output**	**4906.8**	

Stage-IV:

S. No.	In put	Qty Kgs	Out put	Qty Kgs	Remarks
1	Nevirapine crude	1051.51	**Nevirapine**	1000	Final product
2	n-Heptane	500	n-Heptane recovery	480	Reuse
3	Water	500	Solvent loss	20	Loss Residue 10 Waste water-10
			Waste water -Water	500+1.58	Forced Evaporation
			Unreacted Organics 1. Nevirapine crude	50	Recovered & reuse
	Total input	**2051.51**	**Total output**	**2051.58**	

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8. Saquinavir Mesylate

Description:

Stage-I: (S,S,S)-N-Tert-butyl-decahydro-3-isoquinolinecarboxamide is reacted with (S,S)-2-[1-[1-[(Benzyloxy)carbonyl]amino]-2-phenylethyl]oxirane (condensed) to give stage-I compound

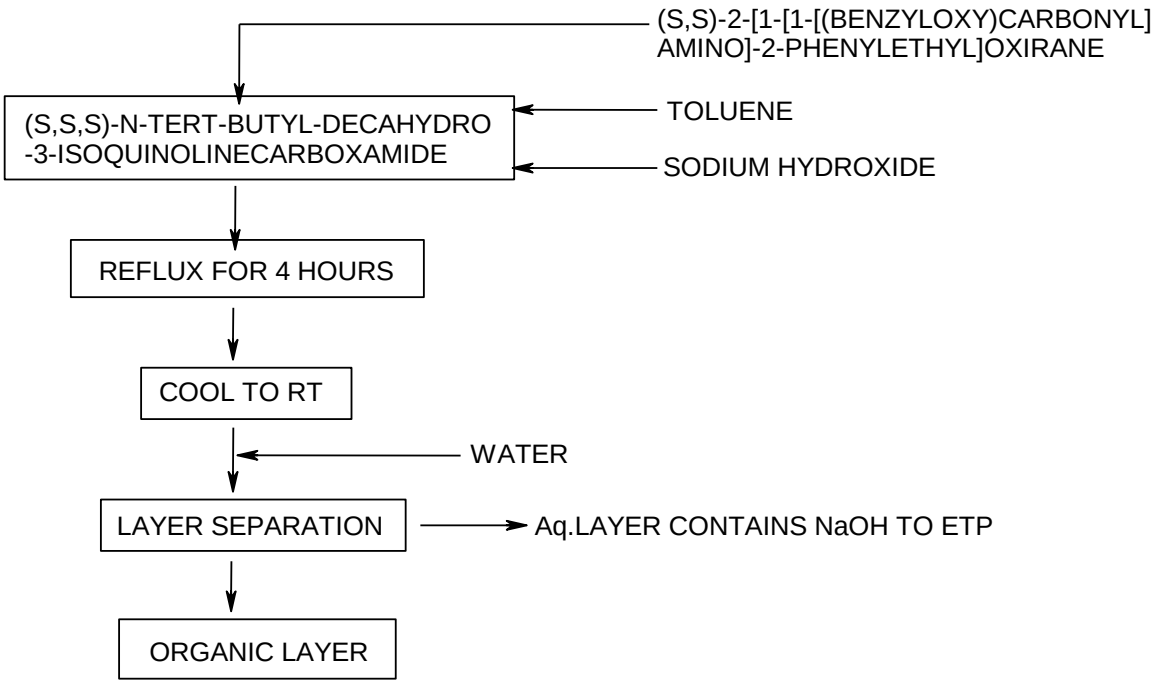
Stage-II: Stage-I compound is reduced in presence of ethanol to give stage-II compound

Stage-III: Stage-II compound is reacted with N-(2-quinolinylcarbonyl)-L-asparagine (condensed) in presence of Carbonyl diimidazole and THF to give the Stage-III compound

Stage-IV: Stage-III compound is salt formation with Methanesulfonic acid in presence of Methanol to give SAQUINAVIR MESYLATE

Flow Chart:

Stage-I:



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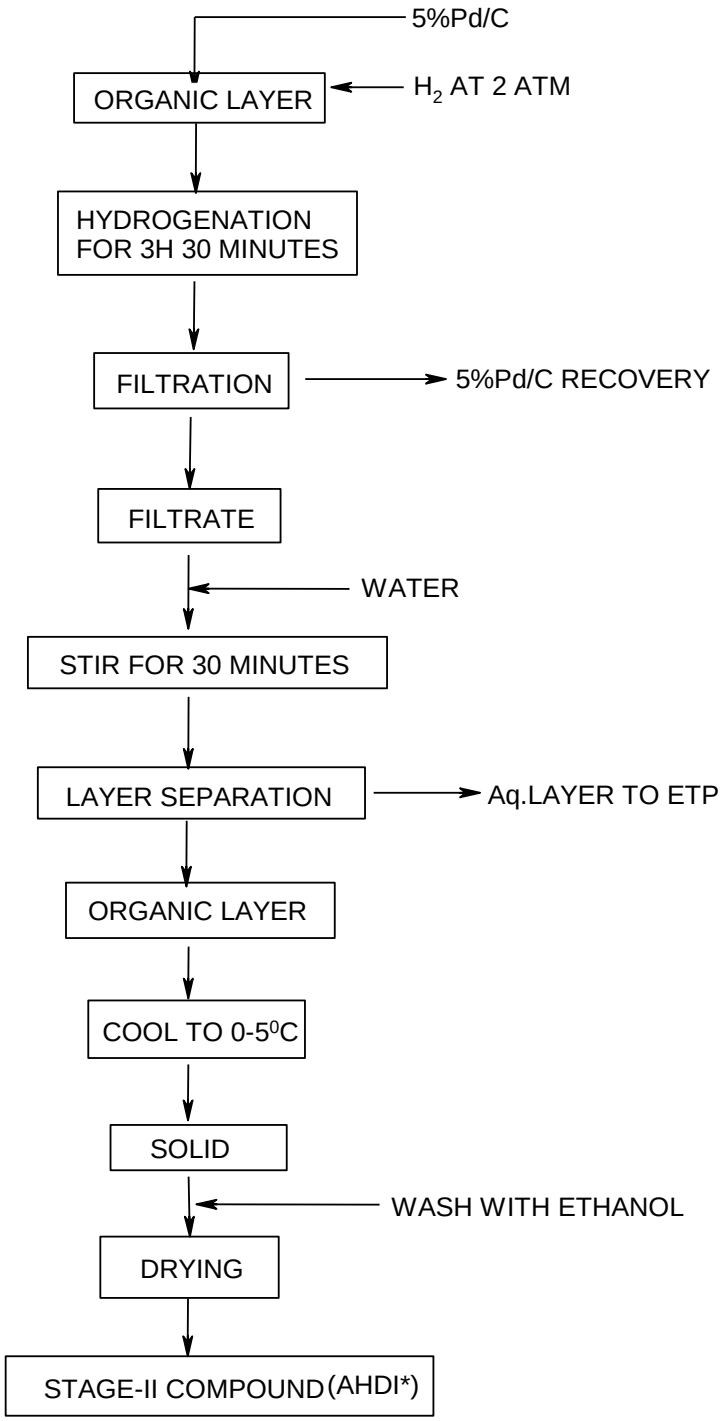
Stage-II:



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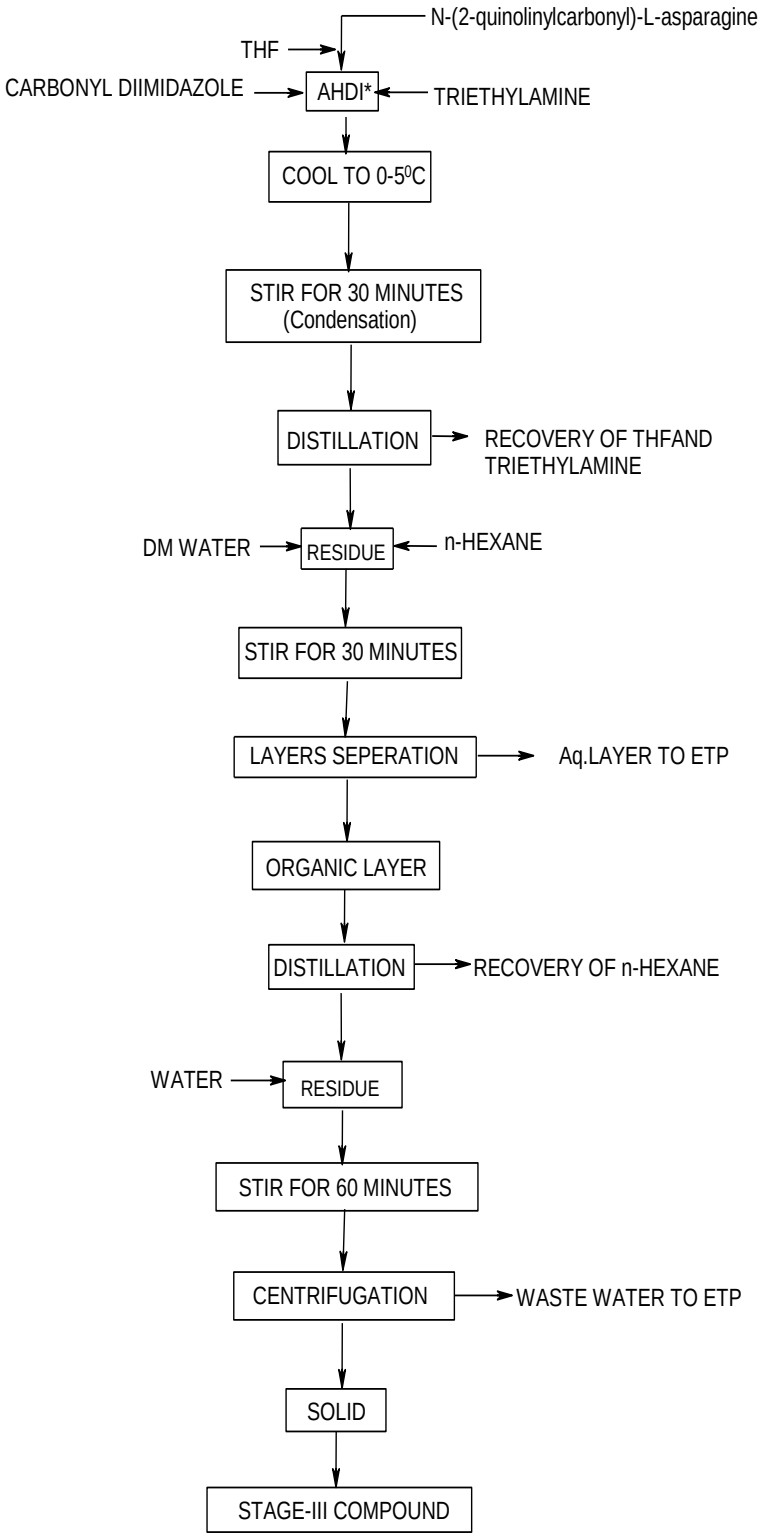
Stage-III:

STAGE-III



AHDI*; [3S[2R*[2S*[R*,S*]],4aβ,8aβ]]-2-[3-amino-2-hydroxy-4-phenylbutyl)-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide

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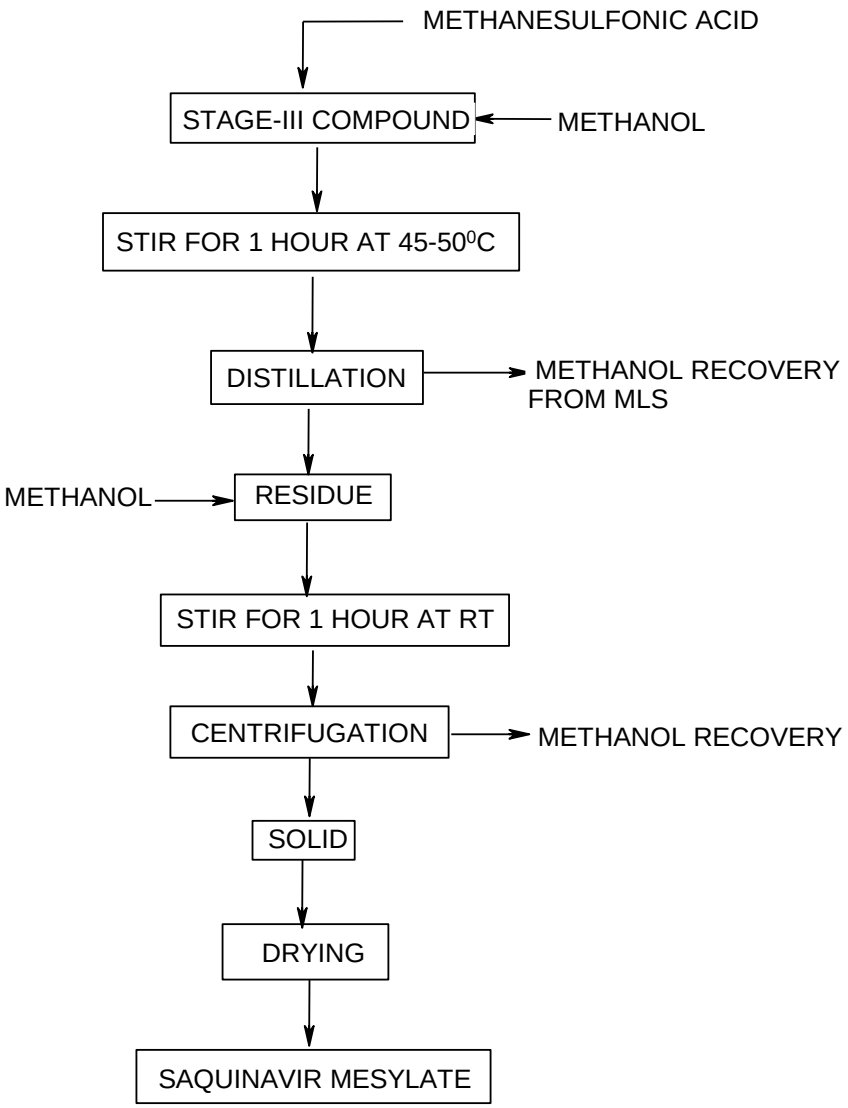
Stage-IV:

STAGE-IV



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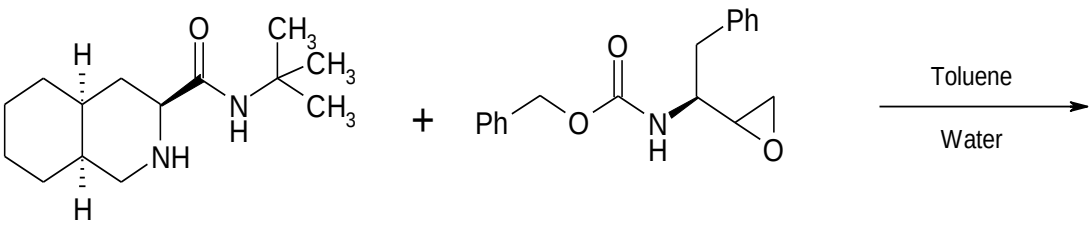
Route of synthesis of product:

Stage - I

Yield :72 %

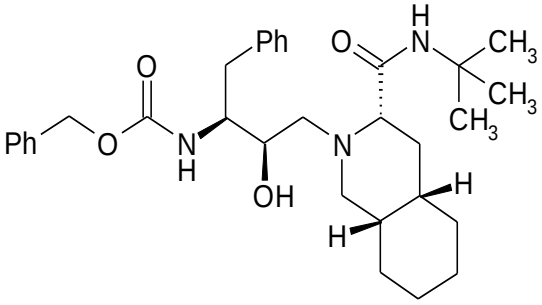


(S,S,S)-N-Tert-butyl-decahydro -3-isoquinolinecarboxamide

M.Wt: 238

(S,S)-2-[1-[1-[(Benzyloxy)carbonyl] amino]-2-phenylethyl]oxirane

M.Wt: 297

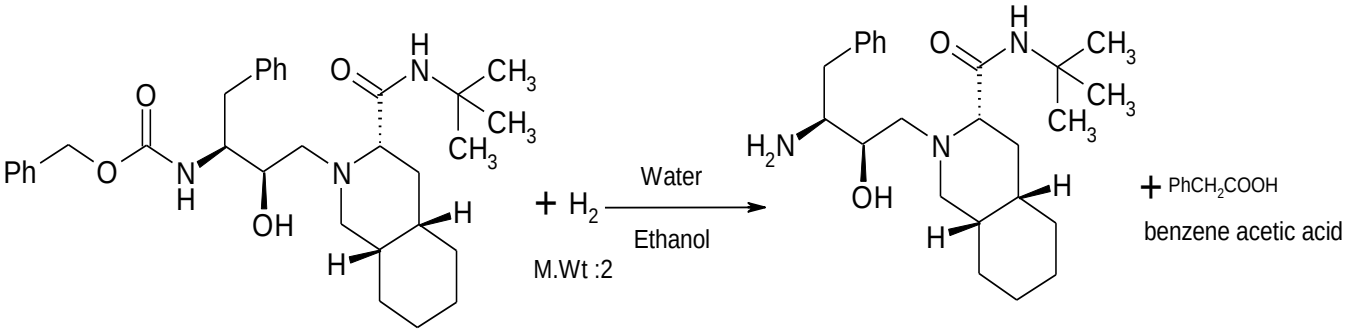


[3S-[2[1R*(R*),2S*],3alpha,4abeta,8abeta]]-2-[3-[(Phenyl methoxy)carbonyl]amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide

M.Wt: 535

Yield :78 %

Stage - II



[3S-[2[1R*(R*),2S*],3alpha,4abeta,8abeta]]-2-[3-[(Phenyl methoxy)carbonyl]amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide

M.Wt:535

M.Wt :2

[3S-[2(2S*,3S*)3alpha,4abeta,8abeta]]-2-(3-Amino-2-hydroxy-4-phenylbutyl)-N-(1,1-dimethylethyl)decahydro-3-isoquinoline carboxamide

M.Wt: 401

benzene acetic acid

M.Wt:136

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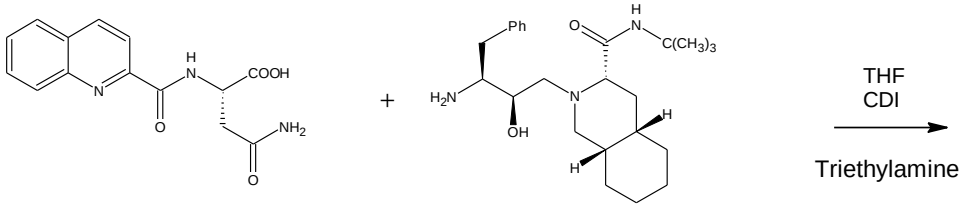
SAQUINAVIR MESYLATE

Stage-III

Yield :75.7%

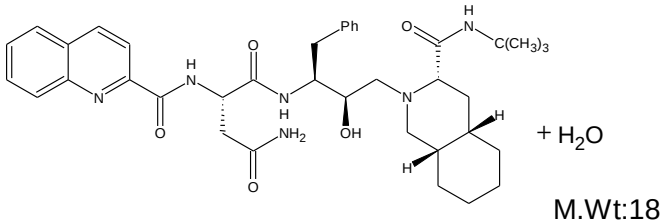


N-(2-quinolinylcarbonyl)-L-asparagine

M.Wt:287

[3S-[2[1R*(R*),2S*],3α ,4aβ ,8aβ]]-2-[3-amino-2-hydroxy-4-phenylbutyl)-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide

M.Wt:401



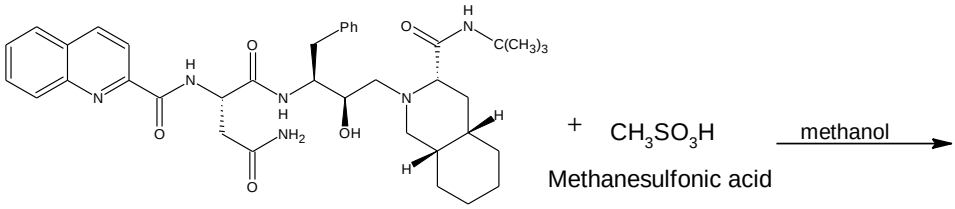
M.Wt:18

Saquinavir

M.Wt:670

Stage-IV

Yield :86.4%

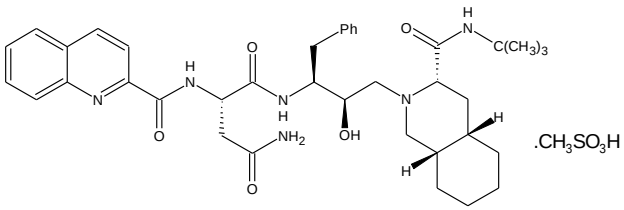


Methanesulfonic acid

M.Wt:96

Saquinavir

M.Wt:670



Saquinavir mesylate

M.Wt:766

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Material Balance:

Stage-I:

S.No	Input	Kg/day	Output	Kg/day	Remarks
1	(S,S,S)-N-Tert-butyl-decahydro -3-isoquinolinecarboxamide	121.045	[3S-[2[1R*(R*),2S*],3alpha,4abeta,8abeta]]-2-[3-[(Phenyl methoxy)carbonyl]amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide	195.91	
2	(S,S)-2-[1-[1-[(Benzyloxy)carbonyl] amino]-2-phenylethyl]oxirane	151.0245	1.(S,S,S)-N-Tert-butyl-decahydro -3-isoquinolinecarboxamide**) (33.8674)** 2. (S,S)-2-[1-[1-[(Benzyloxy)carbonyl] amino]-2-phenylethyl]oxirane **(42.2637)**	76.1305	Recovery & reuse
3	Water	500	Wastewater	500	Forced evaporation
4	Toluene	500	Toluene-Recovery Toluene -Loss	450 50	Recovery Loss+ residue
	Total	**1272.0**		**1272.0**	

Stage-II:

S.No	Input	Kg/day	Output	Kg/day	Remarks
1	[3S-[2[1R*(R*),2S*],3alpha,4abeta,8abeta]]-2-[3-[(Phenyl methoxy)carbonyl]amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide	195.91	[3S-[2(2S*,3S*)3alpha,4abeta,8abeta]]-2-(3-Amino-2-hydroxy-4-phenylbutyl)-N-(1,1-dimethylethyl)decahydro-3-isoquinoline carboxamide	114.5417	Stage-ii product
2	Hydrogen	0.7324	Benzene acetic acid recovery	38.84	Byproduct
3			**Unreacted organics:** [3S-[2[1R*(R*),2S*],3alpha,4abeta,8abeta]]-2-[3-[(Phenyl methoxy)carbonyl]amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide **(43.121)** Hydrogen Emission **(0.1612)**	**43.121** **0.1612**	Recover emission
4	Water	500	Wastewater	500	Waste water
5	Ethanol	500	Ethanol-Rec Ethanol-loss	480 20	Recovery Loss+ residue
	Total	**1196.64**	**Total**	**1196.66**	

Stage-III:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	[3S-[2[1R*(R*),2S*],3□ ,4a□ ,8a□]}2-[3-amino-2-	114.5417	**Saquinavir**	202.47	Stage-III compound

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	hydroxy-4-phenylbutyl)-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide				
2	**N-(2-quinolinylcarbonyl)-L-asparagine**	160.0391	THF Recover, **Triethylamine recovery**	360 450	Reuse
3	**THF**	400	Solvent loss	90	Loss
4	**Carbonyl diimidazole**	100	Waste water- water	600	Forced Evaporation
5	**Water**	600	**Unreacted Organic** 1. [3S-[2[1R*(R*),2S*],3□ ,4a□ ,8a□]]-2-[3-amino-2-hydroxy-4-phenylbutyl)-N-(1,1-dimethylethyl)-decahydro-3-isoquinolinecarboxamide **(27.839)** 2. N-(2-quinolinylcarbonyl)-L-asparagine **(38.897)**		Recover & reuse
6	**Triethylamine**	500	**Reaction water**	5.437	
			After the reaction is completed the reagent Carbonyl diimidazole is reacted with water and is converted in to Imidazole (recovery) and carbon dioxide	100	Reuse
	Total input	**1874.9**	**Total output**	**1874.7**	

Stage-IV:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	**Saquinavir**	202.470	Saquinavir mesylate	200	Final product
2	Methanesulfonic acid	29.00	Methanol recovery	450	Reuse
3	Methanol	500	Methanol loss	50	Loss
4	Water	500	Waste water-water	500	Forced evaporation
			Unreacted Organic 1. Saquinavir **(27.53)** 2. Methanesulfonic acid **(3.945)**	31.475	Recovery and reuse
	Total input	**1231.47**	**Total output**	**1231.47**	

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9. Stavudine

Description:

Stage-I: 5-Methyluridine is reacted with Acetyl bromide and Benzoylchloride (Benzoylation) in presence of Acetic acid to give stage-I compound

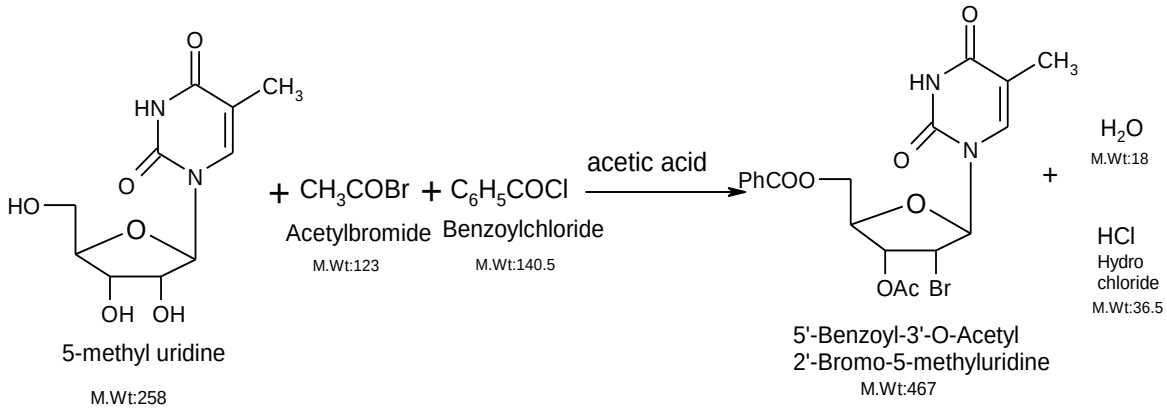
Stage-II: Stage-I compound is hydrogenation with Zn, Acetic acid in the presence of isopropyl alcohol to give the Stage-II compound

Stage-III: Stage-II compound is reacted with water (De Benzoylation) and followed by salt formation with NMPO to give stage-III compound

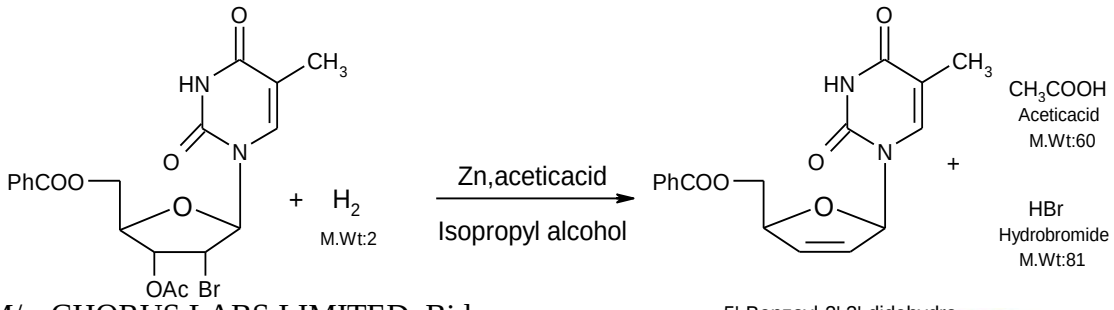
Stage-IV: Stage-III compound is Desalt formation with n-Hexane in presence of acetone to give STAVUDINE

Route of synthesis of product:

STAGE-I



STAGE-II



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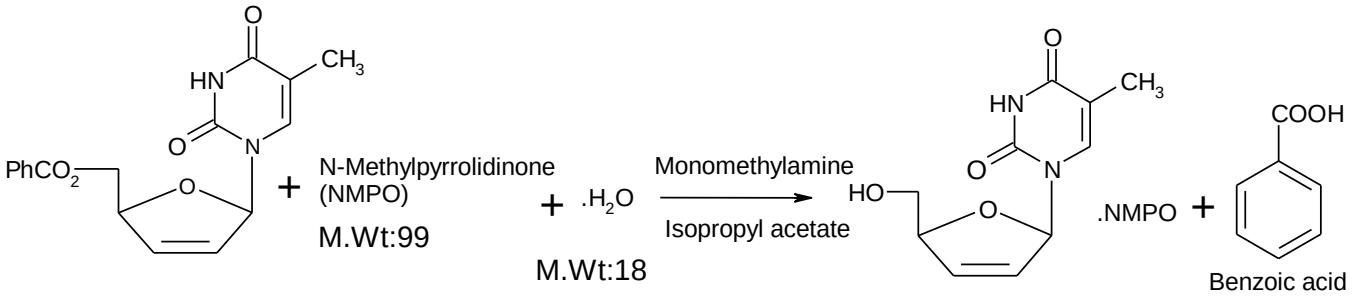
Stage-III:



5'-Benzoyl-2',3'-didehydro-3'-deoxythymidine

M.Wt:328

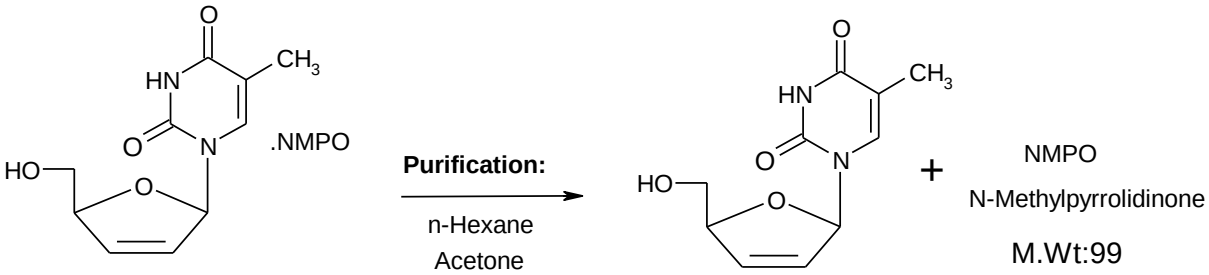
StavudineNMPO solvate

M.Wt:323

M.Wt:122

Stage-IV:

Yield :91.3%



StavudineNMPO solvate

M.Wt:323

Stavudine

M.Wt:224

Material Balance:

Stage-I:

S.No	Input	Kg/day	Output	Kg/day	Remarks
1	5-Methyluridine	1090.44	5'-Benzoyl-3'-O-Acetyl 2'-bromo-5-methyluridine.	1381.65	Ist stage product
2	Acetyl bromide	519.85	Reaction eater	53.253	To waste water
3	Benzoylchloride	593.823	Unreacted organics: 1) 5-Methyluridine (327.144) 2) Unreacted Acetyl bromide 155.964 3) Unreacted Benzoylchloride 178.154		Recovery & reuse

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4	Water	1000	Wastewater	1000	Forced evaporation
5	Acetic acid	500	Acetic acid recovery Acetic acid loss	400 100	Recovery & reuse Loss
			HCl	107.985	By product
	Total input	**3704.113**	**Total output**	**3704.15**	

Stage-II:

S.No	Input	Kg/day	Output	Kg/day	Remarks
1	5'-Benzoyl-3'-O-Acetyl 2'-bromo-5-methyluridine.	1381.65	5'-Benzoyl-2'.3'-didehydro-3'-deoxythymidine	679.138	Stage II compound
2	Zinc	16.9	Unreacted organics: i)5^{1}-Benzoyl-3'-O-Acetyl 2'-bromo-5-methyluridine (419.5092).		Recovery and reuse
3	Acetic acid	1500	Acetic acid- Recovery Acetic Acid Loss	1450 50	Recovery Loss
4	Water	500	Wastewater	500	Waste water
5	IPA	1000	**IPA- Recovery** IPA -Loss	960 40	Recovery Loss
5	Sodium Hydroxide	24	Byproducts: recovery I) Acetic acid (124.26) II) Hydrogen bromide (167.75) Sodium Hydroxide 24.0		By product
6	Hydrogen	5.7	Zinc	12.4	recovery
	Total	**4428.25**	**Total**	**4428.5**	

Stage-III:

S. No.	In put	Qty kgs	Out put	Qty Kgs	Remarks
1	5'-Benzoyl-2',3'-didehydro-3'-deoxythymidine	679.138	Stage-III compound	473.5	Stage-III compound
2	Monomethylamine	600	Isopropyl acetate-rec Isopropyl acetate-loss	760 40	Reuse
3	N-Methylpyrrolidinone	207.306	Monomethylamine recovery Loss	500 100	Reuse
4	Isopropyl acetate	800			Loss

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Director

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5	Reactant water	37.278	**Unreacted Organics** 1.5'-Benzoyl-2',3'-didehydro-3'-deoxythymidine **(200.4728)** 2. N-Methylpyrrolidinone **(59.9049)** 3. Reactant water **(10.89)**		Recovery &reuse
			By product Benzoic acid recovery	178.8398	Reuse
	Total input	**2323.7**	**Total output**	**2323.6**	

Stage-IV:

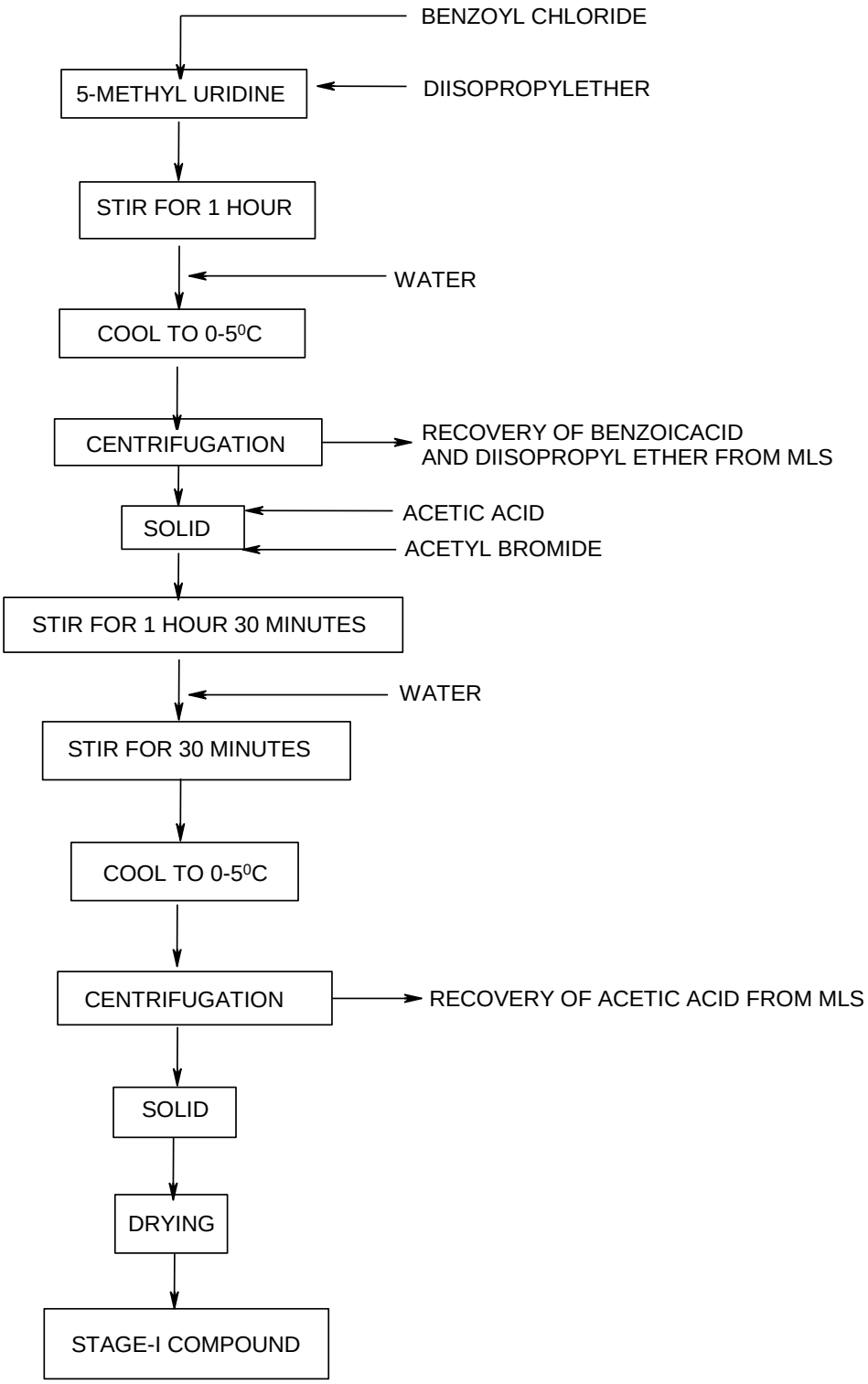
S. No.	In put	Qty kgs	Out put	Qty kgs	Remarks
1	**Stage-III compound**	473.5	**Stavudine**	300	Reuse
2	Acetone	600	Acetone recovery, n-Hexane recovery	550 370	Reuse
3	Activated Carbon	50	Activated Carbon recovery	50	Solid waste
4	n-Hexane	400	Solvent loss Acetone , n-Hexane	50 30	Loss-20-waste water Residue-60
5	water	500	**Unreacted Organic** 1. Stage-III compound	41.2477	Recovery & reuse
			By product N-Methylpyrrolidinone	132.5	By product
			Waste water	500	
	Total Input	**2023.5**	**Total output**	**1523.7**	

For Chorus Labs Ltd,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

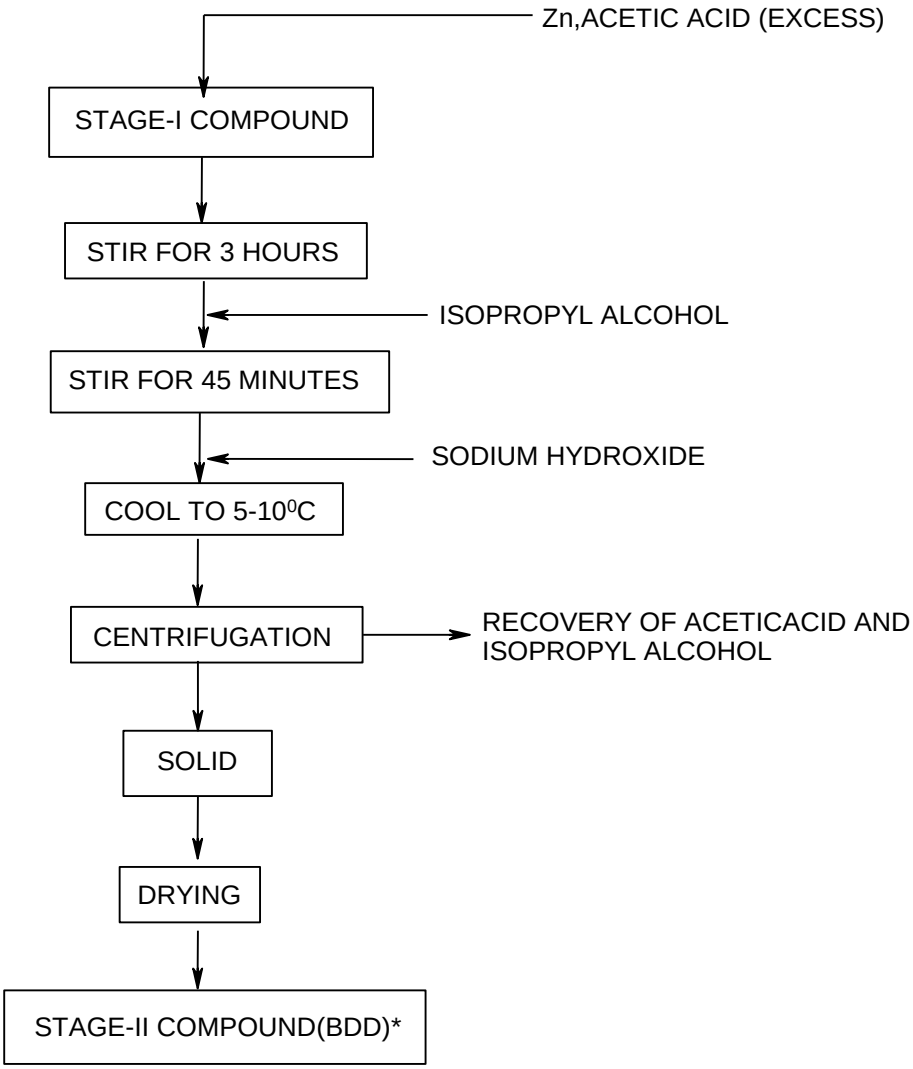
Flow Chart:

Stage-I:



For Chorus Labs Ltd.
P. Subba Reddy
Director
CHORUS LABS LIMITED BIDAR

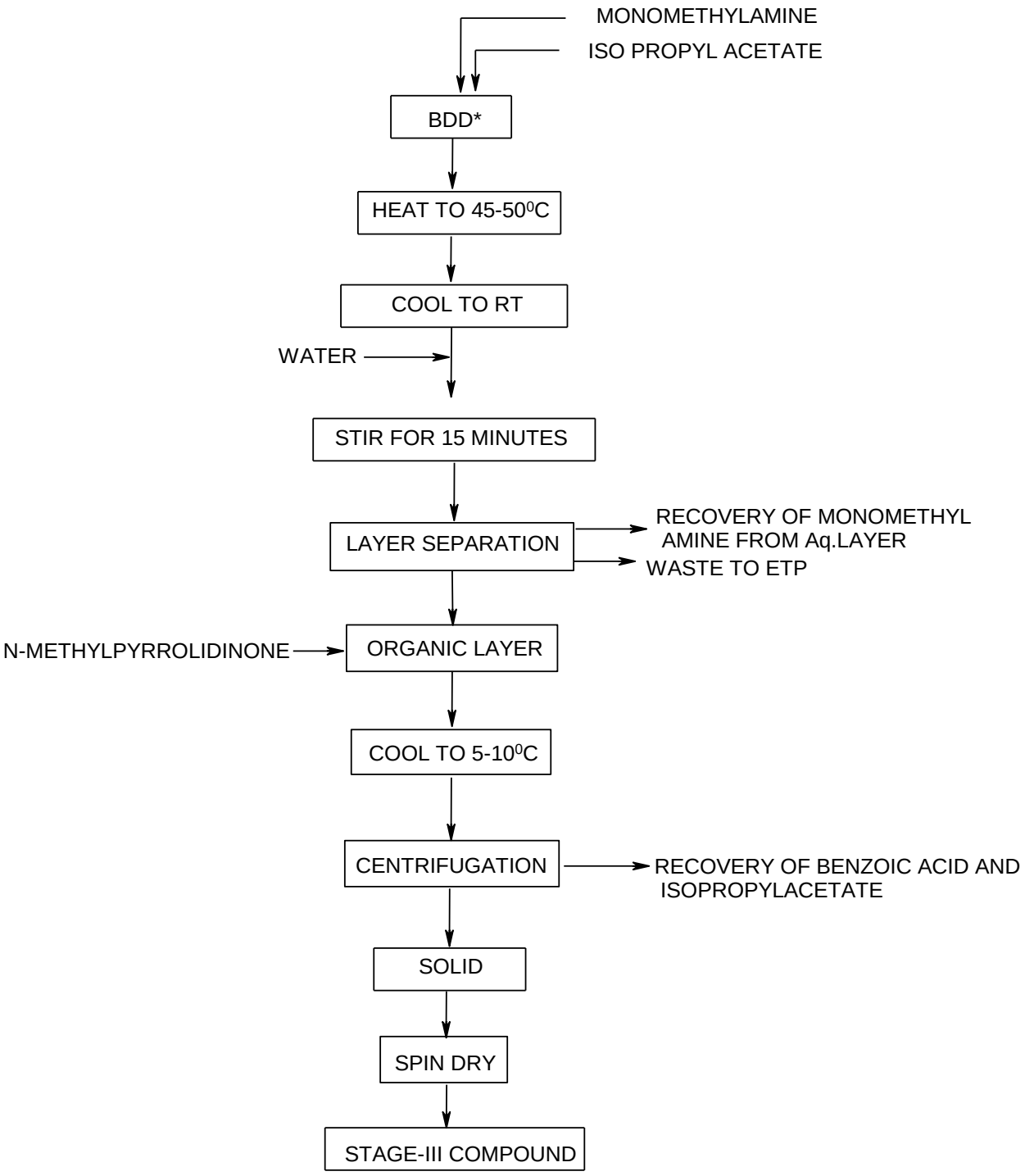
Stage-II:



For Chorus Labs Ltd.,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

STAGE-III



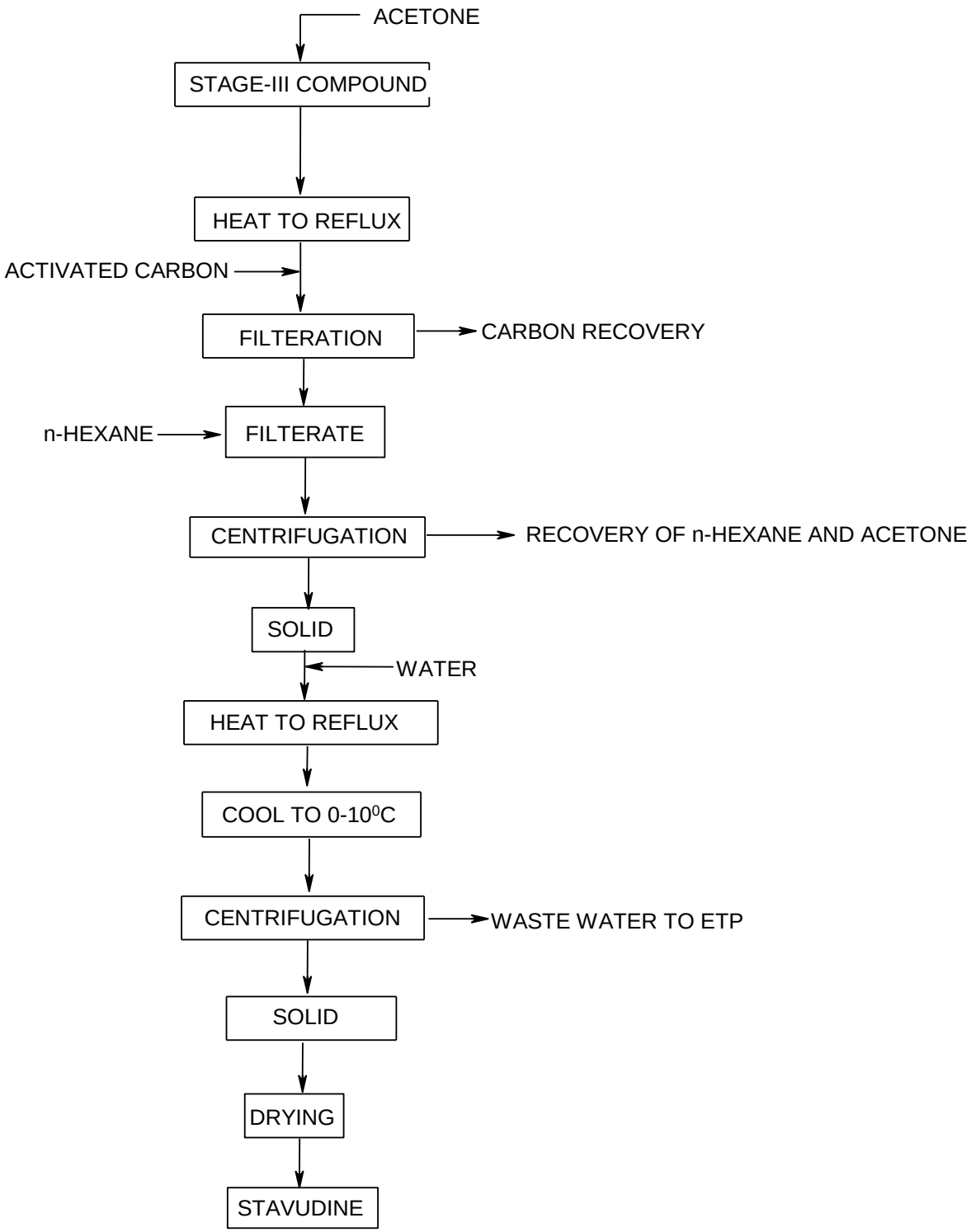
BDD*: 5'-Benzoyl-2',3'-didehydro-3'-deoxythymidine

For Chorus Labs Ltd.,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

10.

STAGE-IV



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Director

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Zindovudine

Description:

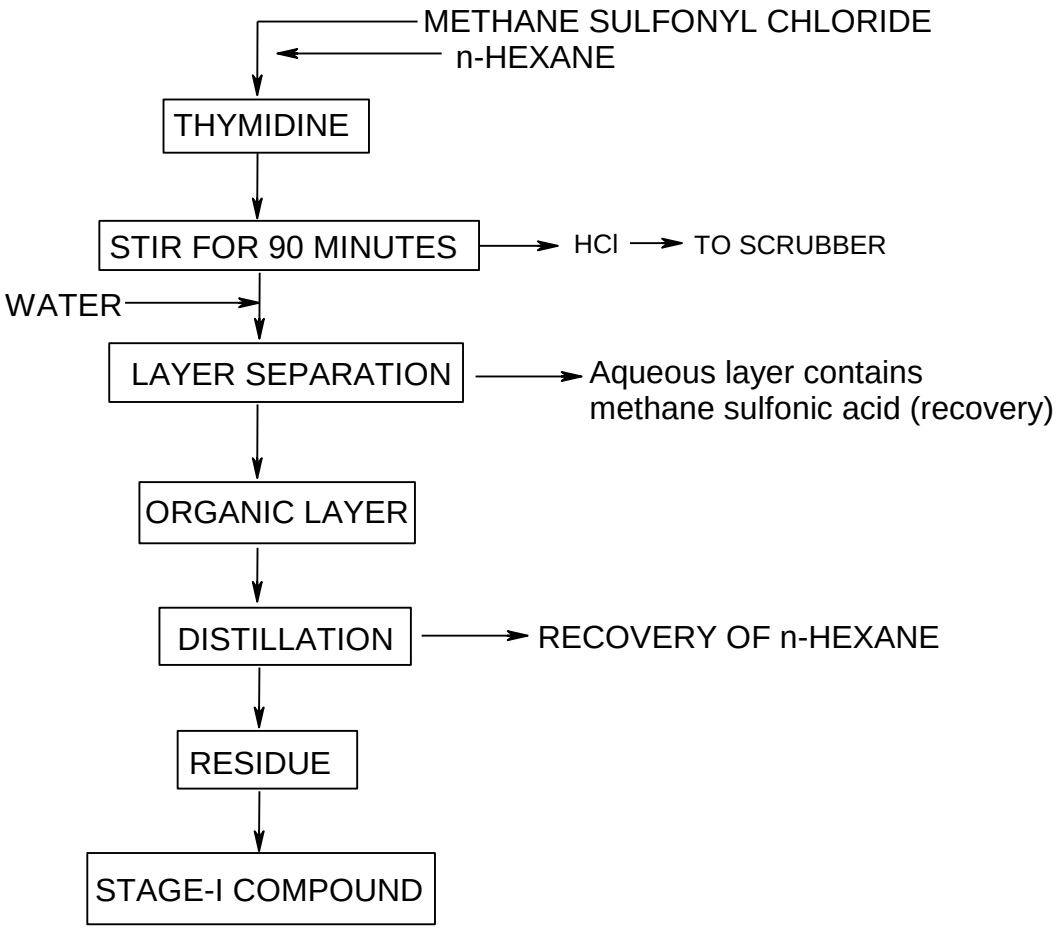
Stage- I: Thymidine is reacted with Methane sulfonyl chloride (protection) in presence of n-Hexane to give Stage-I compound

Stage-II: Stage-I compound is cyclised with Acetic anhydride to give Stage-II compound

Stage-III: Stage-II compound is reacted with Sodium azide in presence of HCl to give the final compound of ZIDOVUDINE.

Flow Chart:

Stage- I:



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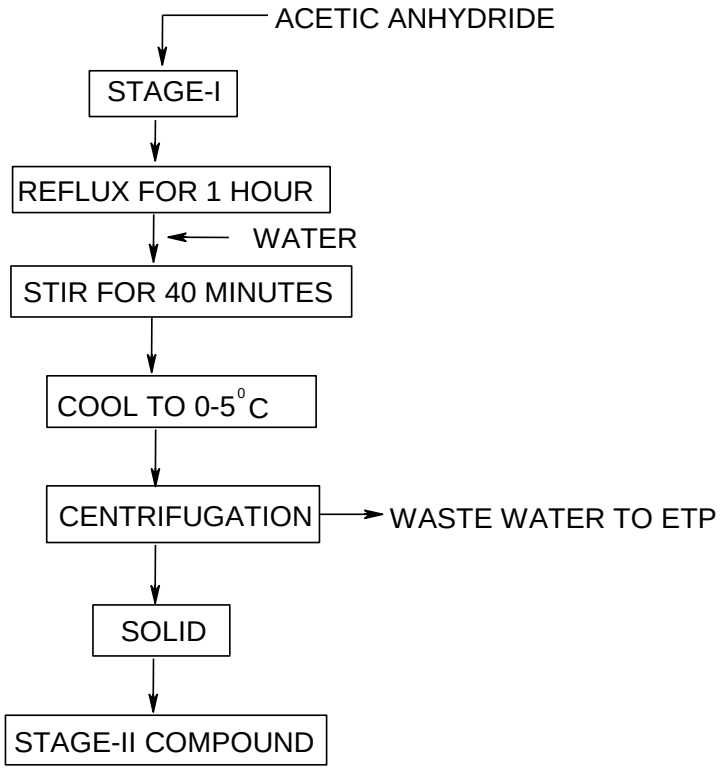
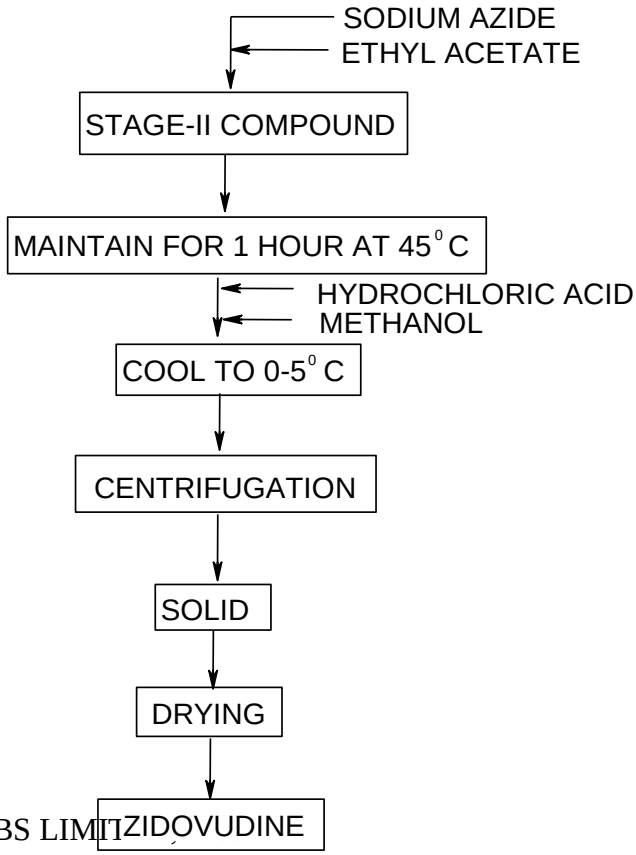
Stage- II:



Stage- III:



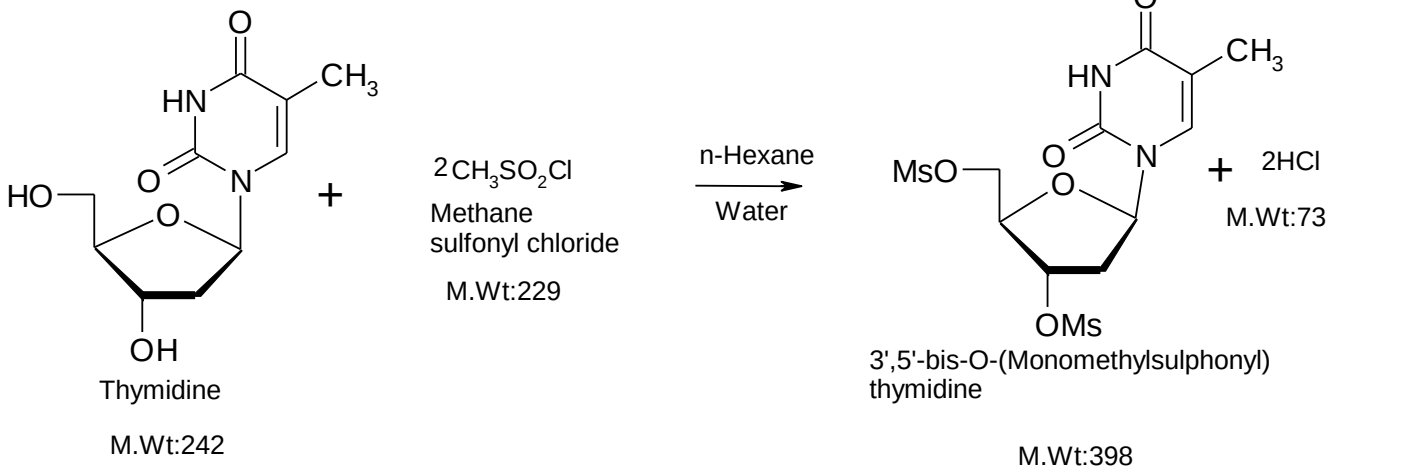
For Chorus Labs Ltd.,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

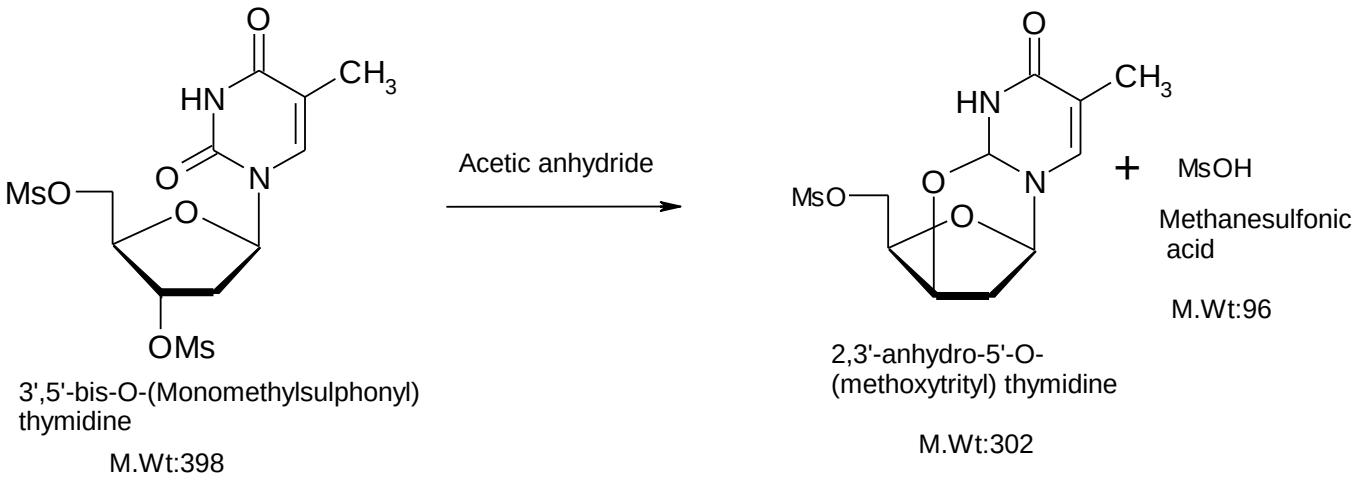
Route of synthesis of product:

Scheme:

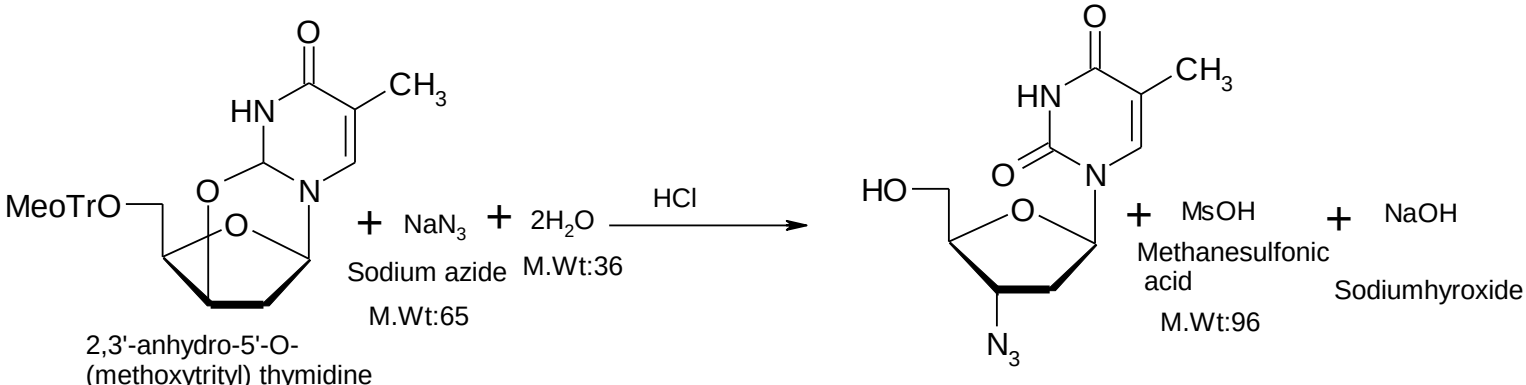
STAGE-I



STAGE-II



STAGE-III



M/s. CHORUS LABS LIMITED, Bidar

For Chorus Labs Ltd.
P. Subba Reddy
Director

Material Balance:

Stage-I:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	Thymidine	580.3	Stage-I compound	661.6	Stage-I compound
2	Methane sulfonyl chloride	549.2	n-Hexane recovery	980	Reuse
3	n-Hexane	1000	**Waste water-Water**	1000+5	Forced evaporation
4	Water	1000	Solvent loss	20	Loss-10 Residue-10
			Unreacted Organics 1. Thymidine **(173.1)** 2. Unreacted Methane sulfonyl chloride 168.7	341.8	
			Aqueous mls contain HCl	121.4	Waste water
	Total	**3129.5**	**Total**	**3129.8**	

Stage-II:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	Stage-I compound	661.86	Stage-II compound	398.26	Stage-II compound
2	Acetic anhydride	100	Acetic anhydride recovery	90	Reuse
3	Water	1000	**Solvent loss**	10	Loss
			Waste water-Water	1000	Forced evaporation
			Unreacted Organics 1. Stage-I compound	137	Reuse
			By product Methanesulfonic acid recovery	126.5	Reuse
	Total	1761.86	**Total**	1761.8	

For Chorus Labs Ltd,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

Stage-III:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	Stage-II compound	398.26	Zidovudine	300	Final compound
2	Sodium azide	85.7155	HCl	100	Reuse
3	HCl	100	**Solvent loss**		Loss
4	Water	147.81	Waste water-	107 +5	Forced Evaporation
			Unreacted Organic 1. Stage-II compound **(54.1014)** 2. Unreacted Sodium azide 12.72	66.8214	(recovery and reuse)
			Byproducts 1. Methanesulfonicacid **(107.8)** 2.Sodium hydroxide **(44.92)**	152.72	
	Total	731.7855	**Total**	731.67	

For Chorus Labs Ltd,
P. Subba Reddy
Director
CHORUS LABS LIMITED BIDAR

11. TERBINAFINE HCL

Description:

Stage-I: N-methyl-naphthalene methanamine is condensed with 1-bromo-6,6-dimethyl-2-hepten-4-yne in presence of Dimethyl sulfoxide to get Terbinafine (Stage- I product).

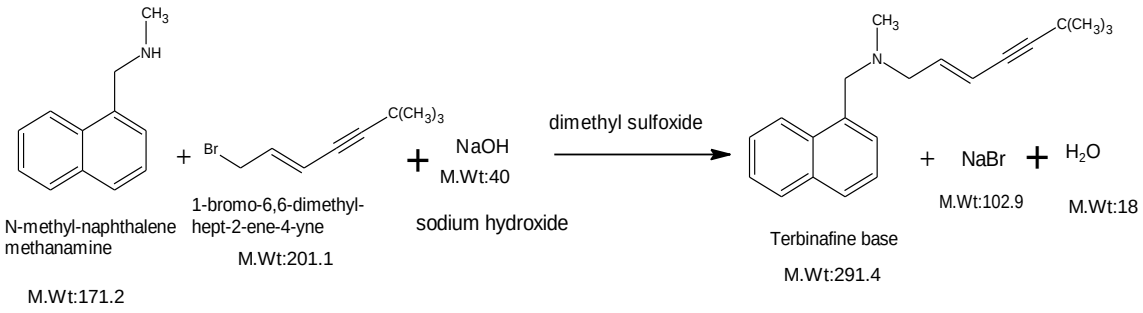
Stage-II: Terbinafine is reacted with HCl (Salt formation) in presence of NaoH and ethanol to yield Terbinafine HCl.

Route of synthesis of product:

TERBINAFINE HCl

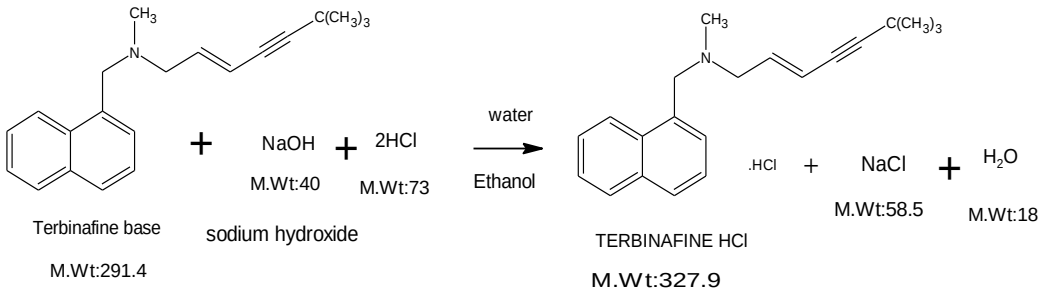
Stage-I

Yield : 58.2 %



Stage-II

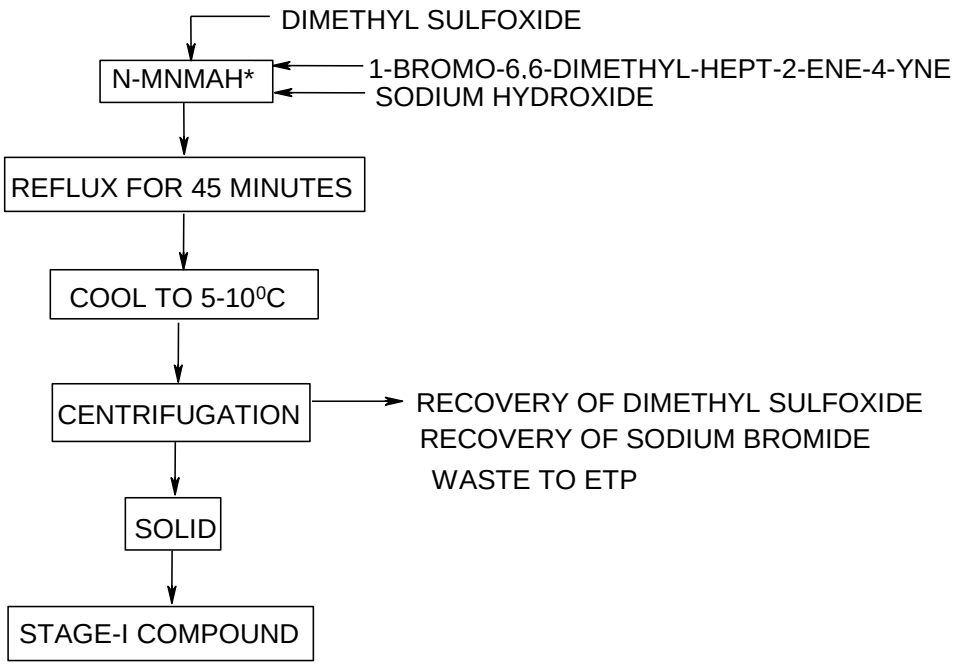
Yield :96.0 %



For Chorus Labs Ltd.,
P. Subba Reddy
Director
CHORUS LABS LIMITED BIDAR

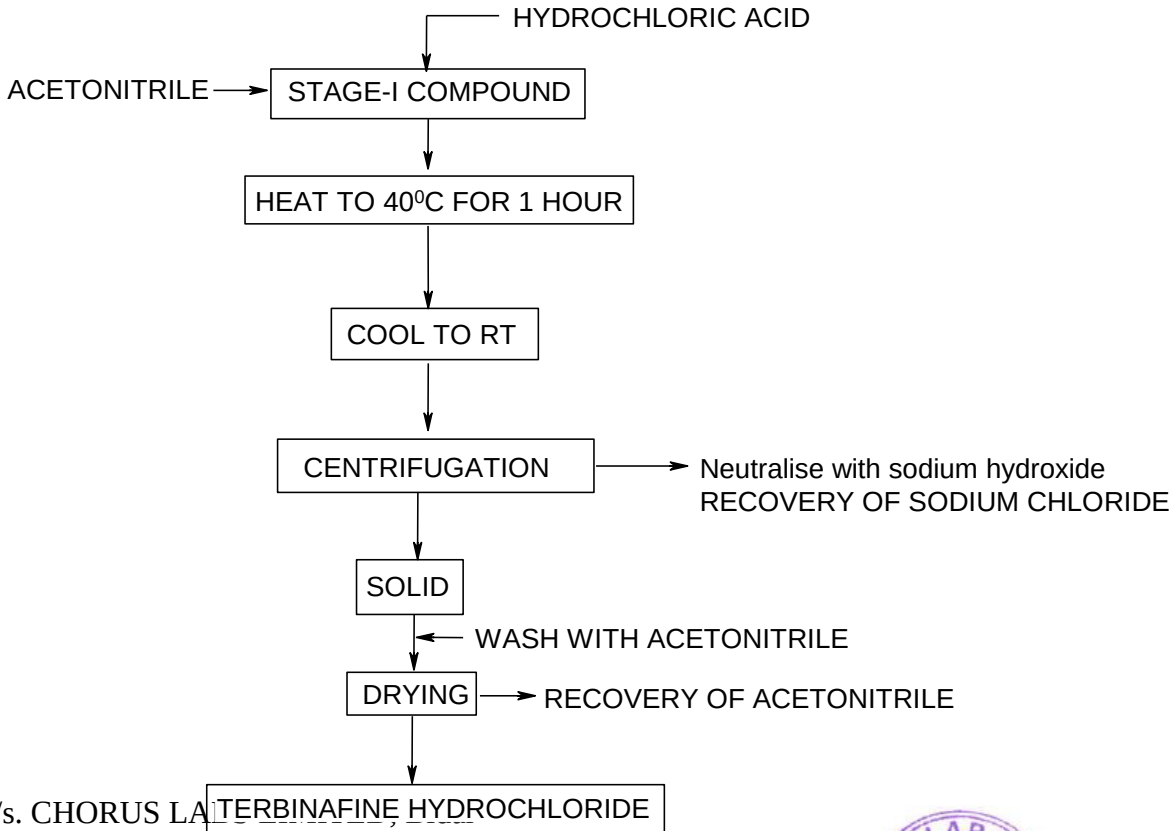
Flow Chart:

Stage- I:



N-MNMAH*: N-methyl-naphthalene methanamine

Stage- II:



For Chorus Labs Ltd.
P. Subba Reddy
Director

Material Balance:

Stage-I:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	N-methyl-naphthalene methanamine	186.872	Stage-I product	185.12	Stage-I product
2	1-bromo-6,6-dimethyl-2-hepten-4-yne	219.5	Dimethyl sulfoxide (Rec)	370	Reuse
3	Sodium hydroxide	43.66	Waste water-Water	500	Forced evaporation
4	Dimethyl sulfoxide	400	**Unreacted Organics-** 1. N-methyl-naphthalene methanamine **(78.118)** 2. 1-bromo-6,6-dimethyl-2-hepten-4-yne **(91.76)** **Unreacted Inorganics** 1. Sodium hydroxide **(18.252)**	188.13	ML's for reuse
5	DM Water	500	**Aqueous mother liquors contain Sodium bromide recovery**	65.37	By Product
			Reaction water	11.4336	Waste water
			Solvent loss	30	Residue-20 Waste water-10
	Total	**1350.03**	**Total**	**1350.05**	

Stage-II:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	Stage-I product	185.12	Terbinafine hydrochloride	200	Final product
2	Conc.Hydrochloric acid	46.3769	Waste water-	600	
3	Sodium hydroxide	25.412	Unreacted Organics- 1. Stage-I product **(10.256)** **Unreacted Inorganics** 1. Conc.Hydrochloric acid **(1.8542)** 2. Sodium hydroxide **(1.016)**	12.27	Reuse
4	Acetonitrile	500	**Acetonitrile recovery**	480	Reuse
			Acetonitrile loss	20	loss
5	Water	600	Aqueous mother liquors contain Sodium chloride	35.679	Waste water
			Reaction water	10.9782	Waste water
	Total	**1359. 0**	**Total**	**1359. 0**	

For Chorus Labs Ltd,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

12. EZITIMIBE

Description:

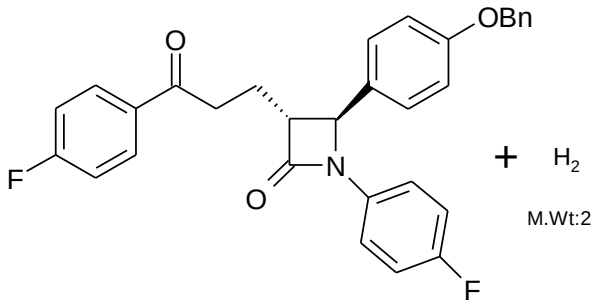
Stage- I: 3R-(3R*, 4S*)]-1-(4-fluorophenyl)-3-[3-(-4-fluorophenyl)-3-oxopropyl]-4-(phenylmethoxyl-2-azetidinone is reduced with Bistrimethylsilylurea in presence of Diisopropyl ether to give Stage-I compound

Stage-II: Stage-I compound is deprotected with Pd/C in presence of acetone to give EZETIMIBE

Route of synthesis of product:

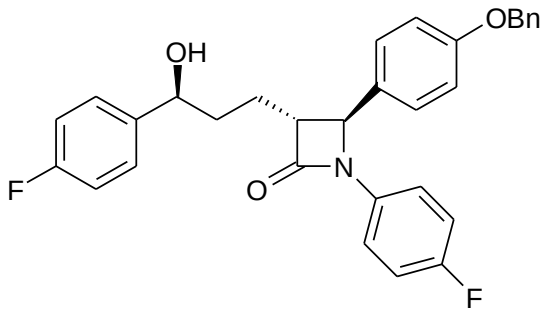
Stage- I:

Yield : 58.4 %



[3R-(3R*,4S*)]-1-(4-fluorophenyl)-3-[3-(-4-fluorophenyl)-3-oxopropyl]
-4-[4-(phenylmethoxy)phenyl-2-azetidinone

M.Wt:497



[3R-[3R*(S*),4S*]]-1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]
-4-[4-(phenylmethoxy)-2-azetidinone

M.Wt:499

For Chorus Labs Ltd,
P. Subba Reddy
Director

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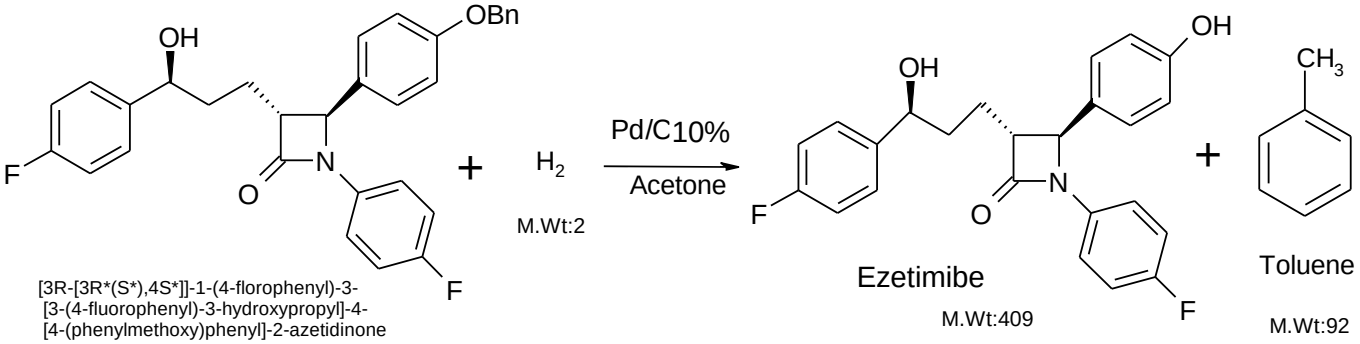
Stage- II:

Yield : 81.5 %

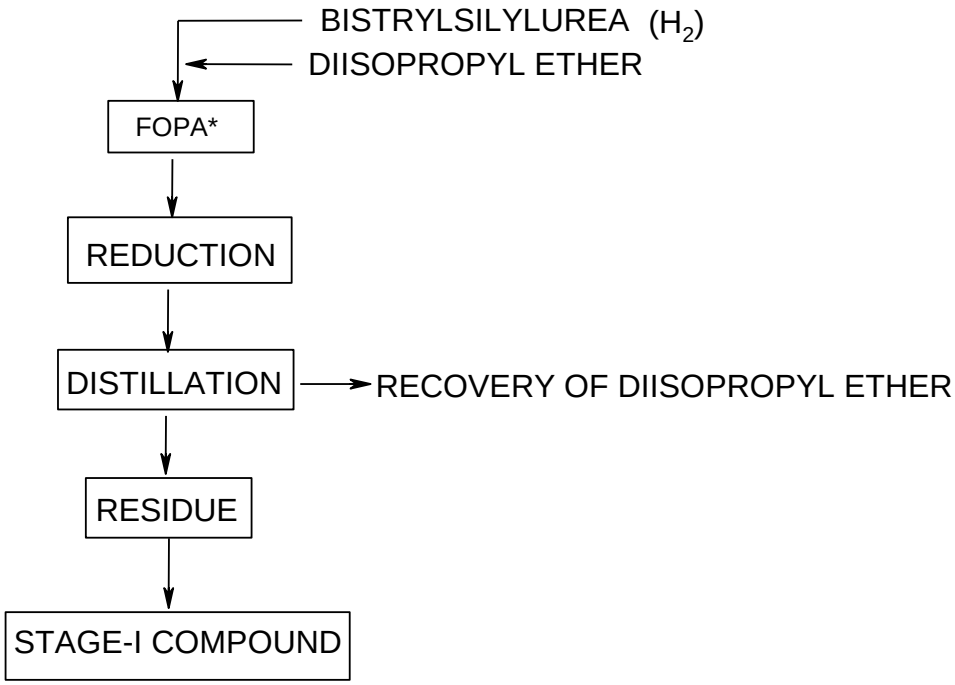


[3R-[3R*(S*),4S*]]-1-(4-florophenyl)-3-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-[4-(phenylmethoxy)phenyl]-2-azetidinone
M.Wt:499

Ezetimibe
M.Wt:409

Flow Chart:

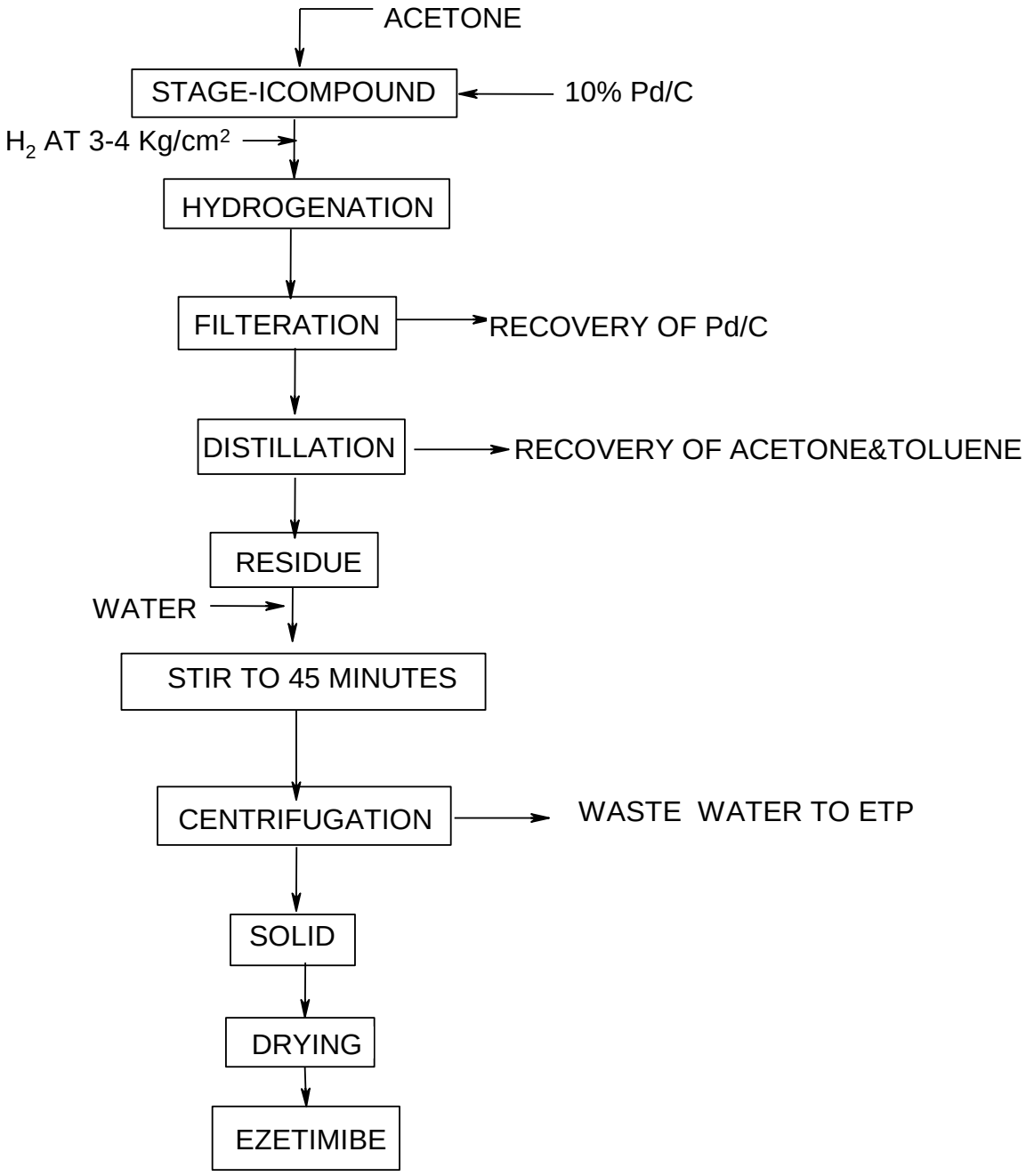
Stage- I:



FOPA*: [3R-[3R*(S*),4S*]]-1-(4-fluorophenyl)-3-[3-(4-fluorophenyl)-3-oxypropyl]-4-[4-(phenylmethoxy)phenyl]-2-azetidinone

For Chorus Labs Ltd.,
P. Subba Reddy
Director

Stage- II:



For Chorus Labs Ltd.
P. Subba Reddy
Director
CHORUS LABS LIMITED BIDAR

Material Balance:

Stage-I:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	3R-(3R*, 4S*)]-1-(4-fluorophenyl)-3-[3-(-4-fluorophenyl)-3-oxopropyl]-4-(phenylmethoxyl-2-azetidinone	2553.06	Stage-I compound	1496.99	Stage-I compound
2	Bistrimethylsilylurea	50	Bistrimethylsilylurea	50	To waste water
3	Water	2000	Solvent loss	100	Residue-90,to waste water-10
4	Hydrogen gas	10.273	**Unreacted Organic** 1. 3R-(3R*, 4S*)]-1-(4-fluorophenyl)-3-[3-(-4-fluorophenyl)-3-oxopropyl]-4-(phenylmethoxyl-2-azetidinone **(1052)** 2. Hydrogen gas **(4.2758)**	1052 4.2758	Recovery & reuse Emission
5	Diisopropyl ether	3000	Diisopropyl ether recovery	2900	Reuse
6			**Waste Water with** 3R-(3R*, 4S*)]-1-(4-fluorophenyl)-3-[3-(-4-fluorophenyl)-3-oxopropyl]-4-(phenylmethoxyl-2-azetidinone **(10. 53)**	2000 +**10. 53+10**	To waste water for forced evaporation
	Total input	**7613.4**	**Total output**	**7613.4**	

Stage-II:

S.No	Input	Kg/d	Output	Kg/d	Remarks
1	Stage-I compound	1496.99	Final compound	1000	Final compound
2	Pd.Carbon	25	Pd.Carbon	25	Solid waste
3	Hydrogen gas	5.988	Acetone recovery	1450	Reuse
4	Acetone	1500	Solvent loss	50	Loss(residue-40, Waste Water-10)
5	Water	1500	**Unreacted Organics** 1.Stage-I compound **(270)** 2. Hydrogen gas **(1.1082)**	270	Reuse Emission
			By product toluene recovery	224.93	Reuse
			Waste Water Stage-I compound **(7.4959)**	1500 +7.4959 +10	To forced evaporation
	Total input	**4527.978**	**Total output**	**4527.54**	

For Chorus Labs Ltd,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

vi. Raw material required along with estimated quantity likely source marketing area of final product/s, mode of transport of raw material and finished product

Details are provided in the previous item

vii. Resource optimization/recycling and reuse envisaged in the project if any should be briefly outlined

After the reaction is complete the solvents are recovered in a distillation unit. The distillation unit is Stainless Steel or Glass Lined Reactor. The residue from the distillation unit is collected in a container and sent to incinerator. The recovered solvents are collected in drums, labeled and analyzed. Then they are reused (recycled) for the process, mostly for the same product

viii. Availability of water its source, energy/power requirement and source should be given

Source of water is from KIADB and estimated as 31.5 KLD. Power requirement of the project is 200KVA from GESCOM.

ix. Quantity of wastes to be generated (liquid & solid) and scheme for their management/disposal

Trade waste water

The main sources of effluents are:

1. Process.
2. Floor wash
3. Boiler blow down
4. Coling tower blow down

Volume of Process waste water & Boiler blow down.

As already mentioned only two drugs are manufactured at a time during the colander month subject to the extent of maximum effluent load permitted by the KSPCB in the consent.

The volume of wastewater generated from process, per batch of Drug manufacture is furnished below.

Volume of wastewater generated from each Drug proposed to be manufactured

For Chorus Labs Ltd,
P. Subba Reddy
Director

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Treatment of Process waste water: MEE

Treatment of Other wastewater

The wastewater generated from Boiler blow down, cooling tower blow down will be drained to equalization cum neutralization tank followed by setting unit, and the treated clear effluents will be used for the greenbelt development and coal ash quenching.

Solvent residue

Sources of solid waste in the plant are (i) Solvent residue (ii) Process residue (iii) Forced evaporation salts and (iv) Coal ash.

Solid waste disposal

- The solid from the bottom of the neutralization tank will have a selling potentiality. In such case, this solid will be sold to the parties who have a license form handling the same, other it will be sent to Haz disposal yard established by Govt.
- The coal ash will be given to the brick manufactures by which we can be sure of safe disposal system.

Treatment & Disposal of Sewage as per IS: [Septic tank Dispersal system]

The domestic effluents will be treated in septic tank & disposed through dispersion trenches. No effluent will be discharged outside of the plant premises.

x. Schematic representations of the feasibility drawing which give information of EIA purpose

Attached site plan

For Chorus Labs Ltd,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

4. SITE ANALYSIS

(i) Connectivity:

Project site is well connected by an asphalted road which is located at a distance of about 5.2 Km from Bidar and near state highway SH-105 (Bidar-Humnabad road) just 1km away from the Factory entrance.

(ii) Land Form, Land use and Land ownership:

Land is owned by M/s Chorus Labs Limited of project proponent. This land has been allotted by KIADB in the Industrial area. The present land use is industrial.

(iii) Topography (along with map):

The project site is located at the western side from the Bidar town with the distance of 5.2 km. The elevation in the project site is 662 meter above mean sea level. An area covering 10 km radius, with project site as centre, is considered as the Study area.

(iv) Existing land use pattern (agriculture, non-agriculture, forest, water bodies (including area under CRZ)), shortest distances from the periphery of the project to periphery of the forests, national park, wild life sanctuary, eco sensitive areas, water bodies (distance from the HFL of the river), CRZ, In case of notified industrial area, a copy of the gazette:

It is bounded by Gulbarga district to the Southern portion, Andra Pradesh State towards Eastern side, Maharashtra state to the North and Western portion.

The project site is in the notified industrial area. There are no reserved forests, national parks, wild life sanctuary and CRZ regions within 10 km radius. There are no eco-sensitive locations within 10Km from the site.

(v) Existing Infrastructure:

M/s Chorus Labs Limited has the necessary concrete structures for the production. Only few types of equipment have to be installed.

PLANT LAYOUT

A copy of the Plant Layout is enclosed herewith. This details the entire plot area, position of all

For Chorus Labs Ltd.,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

the building structures within the plot

LAND

The Plant facilities are spread over 14,038 Sqmt KIADB of leveled land which is completely fortified and protected on all four sides by boundary walls.

BUILDINGS

Total built up area is divided into various sections like Production plant, Engineering, Quality Control/ and Administration, Canteen, toilets, There is adequate space & provision for present operations and future growth. Additional space is available for future storage requirements.

PLANT AND MACHINERY & UTILITIES

The plant facilities are spread over 6,890 Sqmt of leveled freehold land in developed KIADB Industrial Area at Bidar. The Plant Facilities have been designed and set up with the objective to carry out almost all critical chemical reactions and processes.

(vi) Soil Classification:

Geology: The entire district forms a part of the Deccan Plateau and is made up mostly of solidified lava. The northern part of the district is characterized by expanses of level and treeless surface punctuated here and there by flat and undulating hillocks, black soils and basaltic rocks. The southern half of the district is a high plateau about 715 m above mean sea level and is well drained. The average elevation of the district is between 580 to 610 m above mean sea level. Alluvial deposit is normally found along the banks of the Manjra river and its main tributaries.

The district is entirely covered by the Deccan trap flows of the tertiary period. The Deccan trap is composed of horizontal flows of basaltic lava. They generally form flat-topped hillocks and terrace-like features. The physical characteristics of individual flows show considerable variations. Some flows are hard and massive while others are weathered, soft and friable. This character has resulted in terraced landscape, suddenly ending in escarpments. The traps are seen generally 618 m above mean sea level. These are jointed and show the characteristics of spherical weathering leaving massive hard cores. Columnar jointing is predominantly developed in these rocks, besides horizontal joints, which impart to the rocks bedded appearance. The top layers of the Deccan trap in parts of Bidar and Humnabad Taluk are altered to reddish vesicular

laterite, forming and extensive undulating plateau.

The minerals found in the area are Bauxite, Kaolin and Red ochre. A deposit of highly siliceous bauxite clay has been located about three kilometers south of Basavakalyan. Similar deposits are noticed near Alwal and Kamthana Villages of Bidar Taluk. A large deposit of Kaolin is located near Kamthana village. Red ochre deposits are found near Sirsi and Aurad Village.

Soils: Two types of soils founds in the district are Lateritic red soil and black cotton soil. Aurad and Bhalki taluks have mainly black cotton soil. Bidar and Humnabad taluks have mainly lateritic red soil. Basavakalyan Taluk has both types of soils.

Soil samples from the following stations were collected & analyzed.

(vii) Climatic data from secondary sources:

The study area is characterized by general dryness except during the monsoon season. During summer the climate is hot. Rains during June to September are rare and occasionally heavy. Summer season observed during March to May, there is study increase in the temperature, with the maximum temperature of the year occurring in April and May.

The southwest monsoon season lasts from June to September, during which period humidity is high. October and November constitutes the Post monsoon season, when humidity decreases in this period to the minimum and the evening air begins to be chilly. Heavy fogs gather soon after sunset and continue towards the morning. For some time after sunrise, this reason is shrouded in thick mist.

The winter season lasts from December to February, Where the night temperature is at its minimum. The sky is generally clear or slightly cloudy.

(viii) Social Infrastructure available

As the proposed project brings employment generation, both skilled and unskilled, it is obvious to assume that, all the economic activities in the project area would induce considerable improvement in the socio-economic levels of people.

The impact of human settlement is expected to be positive, as apart from some people being directly employed, many others will get indirect employment.

For Chorus Labs Ltd,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

5. PLANNING BRIEF

i. Planning concept (type of industries, facilities, transportation etc) Town and Country Planning/Development authority Classification:

Industrial area.

ii. Population Projection:

Not applicable.

iii. Land use planning (breakup along with green belt etc):

Total land area = 14,038 Sqmt

iv. Assessment of Infrastructure Demand (Physical & Social):

As the entire infrastructure needed for modification is already available there is no demand of any further Infrastructure.

v. Amenities/Facilities:

All the facilities exist already. In the existing facility proposed products will be produced

For Chorus Labs Ltd.,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR

6. PROPOSED INFRASTRUCTURE

i. **Industrial Area**: The proposed project is coming in KIADB Industrial area.

ii. **Residential Area**: NA.

iii. **Greenbelt:** 4,934.35 Sqmt.

iv. **Social Infrastructure:** Necessary support infrastructure will be provided for the project.

v. **Connectivity:** Project site is well connected by an asphalted road which is located at a distance of about 5.2 Km from Bidar and near state highway SH-105 (Bidar-Humnabad road) just 1km away from the Factory entrance.

vi. **Drinking Water Management:** Separate drinking water will be provided.

vii. **Sewerage system:** The wastewater generated from Boiler blow down, cooling tower blow down will be drained to equalization cum neutralization tank followed by setting unit, and the treated clear effluents will be used for the greenbelt development and coal ash quenching.

viii. **Industrial waste management:**

a. Air Environment:

i. Sources:

- Boilers
- D.G. sets

ii. Mitigative measures:

1. Process emission will be connected to scrubber with a stack attached.
2. The vapours are been collected through exhaust system consisting of hood, duct and vacuum fan and then vented out.
3. Stack of 3mARL are provided to D.G. sets.
4. Boilers are connected with dust collector
5. Plantation of green trees around the factory building and premises to control the intensity of noise to the surrounding area.
6. Use of PPE's

b. Noise Environment:

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Director

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i. Sources:

- Generators
- Reactors
- Compressors
- Fans

ii. Mitigative measures:

1. Acoustic barriers or shields to the machineries.
2. Vibration free foundations for machineries
3. Acoustical walls and roofs to the building where such machineries are installed.
4. Segregation of machineries having high noise level in isolated buildings.
5. Sound control measures to steam vents.
6. Proper maintenance of machineries especially oiling and greasing of bearing and gears etc.
7. Avoiding vibration of machineries with proper design of machineries such as speed, balancing etc.
8. Use of personnel protective such as earmuff and ear fug for persons working in such locations.
9. Plantation of green trees around the factory building and premises to control the intensity of noise to the surrounding area.
10. Use of PPE's

c. Water Environment:

i. Sources:

- Process water
- Cooling tower blow down
- Floor wash
- Boiler blow down

ii. Mitigative measures:

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1. Effluents from the plant is been stored and neutralized in a collection tank and then sent to Forced Evaporation System
2. Rain water harvesting plan has been executed effectively & a storage reservoir of adequate capacity is provided to hold rainwater.
3. Domestic water will be treated in Septic tank followed by soak pit.
4. Recycle of process water including steam condensate and reuse of treated wastewater in the plant
5. Control of water taps, washings, leakages from pump glands and flanged joints.
6. Floor cleaning with water will be replaced with dry cleaning.

d. Solid & Hazardous waste:

i. Sources:

- Used oil
- Spent carbon
- Inorganic salts
- Polythene bags
- Used fiber drums

ii. Mitigative measures:

1. Used oil shall be collected in leak proof containers & disposed to Central Pollution Control Board / Karnataka State Pollution Control Board registered authorized recyclers.
2. The solid from the bottom of the neutralization tank will have a selling potentiality. In such case, this solid will be sold to the parties who have a license form handling the same, other it will be sent to Haz disposal yard established by Govt.
3. The coal ash will be given to the brick manufactures by which we can be sure of safe disposal system.

ix. Solid waste management: Oil soaked cotton wastes, discarded containers, etc are the solid wastes generated and it will be stored in secured manner & handed over to the Karnataka State Pollution Control Board authorized recyclers.

x. **Power Requirements and Supply and Source**: The total power requirement of the proposed plant is about 200KVA, which is being met from GESCOM. DG sets of about 200 KVA are available to meet the emergency power requirement.

7. REHABILITATION & RESETTLEMENT (R & R) PLAN

Rehabilitation and Resettlement is not applicable.

8. PROJECT SCHEDULE AND COST ESTIMATE

i. **Likely date of start of construction and likely date of completion (Time schedule for the project to be given)**

Not applicable as the plant is already exists and there is no additional infrastructure enhancement in the proposed expansion.

ii. **Estimated project cost along with analysis in terms of economic viability of the project.**

There is not much additional project cost as it is an existing unit. The gross value of existing infrastructure is Rs. 6.5 Crores. The infrastructure needed for the proposed modification is already in place except the additional equipments.

9. ANALYSIS OF PROPOSAL

i. **Financial and social benefits with special emphasis on the benefit to the local people including tribal population, if any, in the area**

The proposal will bring employment opportunities. It will also bring trade and export opportunities to the country.

For Chorus Labs Ltd.,
P. Subba Reddy
Director

CHORUS LABS LIMITED BIDAR