Andhra Pradesh- Karnataka Inter State Boundary– 0.5 Km (S)

LIST OF ENCLOSURES

S. No	Particulars	Enclosure No
1.	APIIC Provisional Land Allotment Orders	Enclosure 1
2.	Plant Lay out	Enclosure 2

//By R.P.A.D //

A.P. Industrial Infrastructure Corporation Limited
(An undertaking of Government of Andhra Pradesh)
Zonal Office, Industrial Park, Anantapur - 515 004
Tel: 08554-270973 Cell: +91 98481 75457

APIIC
The Future is Here

L.V.V.R.K. Ranjit
Zonal Manager

Lr.No. ZO-ATP/IP-Gollapuram/UDL/PBC/2015/ Dt:02.01.2015

To

M/s. PENN BIO CHEMICALS INDIA PVT. LTD.,
Director: Sri G. Ravindra Reddy,
141/B, IDA,
Road No.14,
Mallapur,
Uppal,
R.R.District - 500 076,
Telangana.

Sir,

Sub: APIIC Ltd. - Zonal Office, Anantapuramu - Industrial Park, Gollapuram Application of **M/s. Penn Bio Chemicals India Pvt. Ltd. - Plot No.34** measuring **Acs.9.47 (or) 38338.58 Sq.Mtrs** on outright sale basis - **Provisional Allotment Orders** - Issued.

Ref: 1. Your Application dt:07.06.2014.
2. Minutes of SLAC Meeting held on 11.11.2014 at Head Office.

****

It is to state that basing on your application cited and relying on your assurance to implement the project / industry, you are provisionally allotted **Plot No.34** in Industrial Park, Gollapuram situated in Survey No.**270(pt), 271(pt), 278(pt) & 279(pt)** of Gollapuram village, with the Hindupur Revenue Mandal, Anantapuramu District (AP), measuring about **9.47 Acres (or) 38338.58 Sq.Mtrs** for setting up of an industry manufacturing of bulk drugs i.e., **"1. Abacavir, 2. Aliskiran, 3. Darunavir, 4. Entecavir & 5. Val acyclovir"** on outright sale basis subject to the following terms and conditions.

The plot is allotted to you on 'as is where is' basis subject to final approach by themselves to rear plots in Sy.Nos.270(pt), 271(pt), 278(pt) & 279(pt) and it is for you to develop the plot/land allotted to you i.e., leveling, cleaning etc. and set up the specified industry within the stipulated time

1. The **Plot No.34** is allotted at a tentative cost of Rs.**640.00** per sq.mtr. The total tentative cost of the plot works out **Rs.2,45,36,691/-.**

2. a) You should pay the tentative total cost of the plot cost, which works out to **Rs. 2,45,36,691/-** within 90 ninety days from the date of receipt of this allotment order less EMD of Rs.23,06,789/- already paid.

3. You should execute the sale agreement with appropriate stamp duty on full plot/ land cost at your own expenses within one month from the date of final allotment orders. The sale agreement should be registered within (21) days from the date of execution of sale agreement. You are also bound to take over possession of the plot within 15 days of the registration of the sale agreement.

(Contd...2)

4. a) You should commence construction of factory building, duly obtaining building approval plans from the competent authorities within 6 months of being put in possession and you should go into regular commercial production, duly erecting machinery and obtaining regular power supply connection within two years of being put in possession of the allotted plot/land.

   b) Any extensions of time, for project implementation shall as per the APIIC Allotment Regulations-2012 as amended from time to time.

5. You should implement the project the industry in the plot, for the purpose for which it is allotted, within **2 (two) years** of the taking possession and go into commercial production before seeking registration of the plot in your favour.

6. All payments against this allotment shall be made to the Zonal Manager by way of a crossed demand draft drawn in favour of APIIC Ltd.

7. You should submit _____ (any documents that are to be obtained) from the allottee along with payments stipulated at para (3) above. *(only if applicable/required)*

8. If payment as stipulated in condition (3) above is not made within 90 days of receipt of this allotment letter, this allotment letter shall stands cancelled automatically and the EMD paid shall remain forfeited.

9. You should bear the cost of sewer lines passing through the area and pay property tax also as and when demanded and also furnish an undertaking to that effect on Rs. 100/- Non Judicial Stamp paper.

10 You shall be responsible for getting power supply to your unit and shall not claim any rebate/ reduction in the cost from the APIIC Limited for any delay in getting power supply from the APTRANSCO or for any other purpose.

11. Please note that the Provisional allotment will stand automatically cancelled and the Corporation forfeits all amounts paid by the allottee, if any of the terms and conditions stipulated in the allotment letter are not complied by you.

12. The allotted land/plot shall not be transferred or conveyed to any person(s) without the prior written permission of the Corporation and approved by it. Any change in the constitution/ ownership of the allottee concern shall be informed to the Corporation and prior necessary approval obtained from the Corporation.

13. You shall pay property tax to the concerned local authority/local body or maintenance charges to the Corporation as prescribed from time to time. You shall be responsible to pay and clear the property tax, other taxes, cess, charges, levies to the competent authority from the date of taking possession.

14. You should install water meter at your own cost including other incidental charges.

15. You should pay water charges that will be charged separately for which you have to enter into an agreement with APIIC Limited.

(Contd...3)

16. This allotment and occupancy of the plot/land is subject to adherence to the directives issued by the State Board for Prevention and Control of Water and Air Pollution. You should undertake for the treatment and disposal of effluents as prescribed by the AP Pollution Control Board. An undertaking to this effect should be given in the proforma prescribed on Rs. 100/- non-judicial stamp paper.

17. Possession of the plot/land has been taken under the provisions of the Land Acquisition Act by the APIIC Limited and as such the land acquisition cost has not been finalized. In the event of Civil Courts ordering enhanced compensation at the instance of the persons affected in the land acquisition at a later date, enhanced compensation will be apportioned to all the allottees in respect of the plots/land allotted to them and the said proportionate cost shall be paid by you. You should furnish an undertaking to his effect on Rs.100/- Non-judicial stamp paper in the prescribed format enclosed to make the payments.

18. You should implement the project envisaged and commence commercial production within **(2) two** years of taking possession of the plot/land. If within **2** years from the date of final allotment and taking possession of the plot/land the project is not implemented, the allotment made shall remain cancelled and the Corporation shall have a right to resume possession of the subject plot/land.

19. Registration of the sale deed will be made in your favour only after implementation of your unit in full in the allotted plot/land.

20. The Corporation reserves the right to appropriate the money paid by you or standing to your credit towards any out-standing dues payable by you on any account whatsoever. Payments made by you shall be adjusted first towards (penal) interest and balance, if any towards principal outstanding on any account.

21. The Corporation is not responsible for payment of electricity charges or other dues, if any payable to APSEB in respect of the Plots allotted/resumed by the Corporation.

22. The allottee shall obtain Consent for Establishment (CFE), Consent for Operation (CFE), from Andhra Pradesh Pollution Control Board (APPCB) under the /Air (Prevention and Control Pollution) Act1981 as well as Water (Prevention & Control of pollution) Act, 1974.

23. Allottee shall comply all the time with applicable environmental standards stipulated by statutory authorities and shall aware of any new modifications in the standards/notifications etc. In case of non-compliances, APIIC shall have the right to close the operations of the industries. Allottee shall document all environmental activities with proper attestation all the time.

24. Allottee shall keep copies of all the environmental regulations, EIA report, EC Clearance, MOEF/PCB investigation reports and all other relevant Environmental documents in place all the time for inspection by APIIC at any time.

(Contd...4)

25. Allottee shall abide by the country fly ash utilization regulations Possibilities of utilization of fly ash for bricks and other uses during the construction stages shall be explored. Ready mixed concrete must be used in the building construction.

26. Allottee shall provide copies of environmental compliance reports submitted to APPCB and/or MOEF to the APIIC as well.

27. The ground water shall not be drawn at any stage in the Industrial Parks/IDP/Special Economic Zones (SEZs), without prior written consent of the competent authorities and the APIIC.

28. Allottee shall adopt water reuse and water recycling methods for water conservation. Fixtures for showers, toilet flushing and drinking should be of low flow either by use of aerators or pressure reducing devices of sensor based control.

29. For storm water collection, the allottee shall provide drainage system within their premises. It is mandatory for industries to provide rainwater harvesting pits within the industry premises for harvesting rain water. Before reaching the roof/surface run off to the pit, pre-treatment must be done to remove the suspended matter, oil and grease. The excess storm water should be discharged into the common storm water drainage of the Industrial Park/Special Economic Zone (SEZ).

30. Allottee shall minimize waste generation by adopting suitable techniques and the details of such measures are to be provided to the APIIC from time to time.

31. Allottee shall adopt energy conservation measures and use renewable energy in all possible ways and such application of techniques shall be provided to the APIIC from time to time.

32. Allottee should make all arrangements for proper disposal of garbage/waste at regular intervals and keep the premises inside and outside of the unit as clean and hygienic.

33. The allottee shall provide proper fire, safety and hazard management facility within their premises. A first-aid room shall be provided in the project both during construction and operation of the project.

34. Construction spoils including bituminous material and other hazardous materials must not be allowed to contaminate watercourses and the dump sites for such material must be secured so that they should not leach into the ground water.

35. The allottee shall have arrangements for effective hazardous and non hazardous waste collection, segregation, and storage and management system. The allottee shall have temporary storage facility for 30 days detention and hazardous wastes shall be periodically disposed off to nearby approved treatment, storage and disposal facility (TSDF). Industries having hazardous waste shall obtain necessary authorization from A.P.Pollution Control Board (APPCB) for handling/storage/treatment/disposal.

(Contd...5)

36. APIIC authorities have the right to enter into unit premises for checking and inspection of unit at any time. The allottee shall not withhold any information pertaining to Environmental Management of their units. In case of non compliance or not submitting the desired information to APIIC, necessary action for cancellation of allotments or closure of unit, as deemed fit, would be initiated.

37. The Allottee shall not take up any activities, due to which the property of APIIC such as roads, green belt, and drainages, street lights etc., may be damaged. In case of non compliance, APIIC may revoke the allotment orders or collect the fine from the allottee as deemed fit.

38. Allottee shall adhere to the provisions for Water (Prevention and Control of Pollution), Act 1974 the Air (Prevention and Control of Pollution) Act 1981, the Environment (Protection) Act 1986, the Public Liability (Insurance) Act 1991 and EIA notification 2006 including the amendments and rules made thereafter.

39. Allottee shall provide on-site parking for trucks within their premises. No trucks shall be parked on the internal roads of Industrial Park/Special Economic Zone (SEZs).

40. Allottee shall monitor the emissions, effluents, wastes, stack emissions and their ambient air quality and water quality within their premises periodically after commissioning of project.

41. The allottee has to provide sufficient budget for environmental protection measures as directed by the Pollution Control Board.

42. All top soil excavated during construction activities should be stored for use in horticulture/landscape development within the project site.

43. Use of glass should not be more than 40% of building envelope to reduce the electricity consumption and load on air conditioning. If necessary, use high quality double glass with special reflective coating in window.

44. Roof should meet perspective requirement as per Energy Conservation Building Code by using appropriate thermal insulation to fulfill requirement.

45. The green belt design along the periphery of the plot shall achieve attenuation factor conforming to the day and night noise standards prescribed for residential land use. The open space inside the plot should be suitably landscaped and covered with vegetation of indigenous variety.

46. The D.G. sets shall be provided within adequate stack height as per norms.

47. The allottee has to spend funds for Corporate Social Responsibility as per "Companies Act 2013" and rules framed there-under.

(Contd...6)

48. The allottee has to provide employment to the land ousters/locals to the maximum extent based on their qualification/skills subject to minimum 20% of total requirement.

49. Allottee has to establish their own Effluent Treatment Plant (ETP) in their premises to treat the effluent of their units and the discharge standards strictly as per the guidelines of APPCB, in case the CETP is not established by APIIC. Guard pond with five compartments for 5 days storage capacity shall be constructed by the allottee so as to test the treated waste water before utilizing the same for flushing, washing, gardening etc. Quality of treated effluent reaching the guard pond shall be continuously monitored and in case the treatment is not adequate there shall be arrangement to recycle the effluent from the guard pond through the CETP. In case the CETP is established at Park level by APIIC/co-developer, pre-treatment has to be done by the allottee himself to meet the inlet standards of CETP.

50. Allottee has to make their own arrangements to manage/treat the domestic sewage by constructing septic tank or sewage treatment plant (STP) in their premises as per norms, the quantity of sewage, in case no sewage disposal system is provided by APIIC at Park level. No waste water shall be discharged outside the premises.

51. There will be no recharge of ground water by industrial effluent.

52. That in case of any doubt with regard to the allotment or this indenture/letter the decision of the VC& MD of the corporation shall be final and binding.

53. The allotment will be confirmed in your favour through a final allotment letter after payment of the total cost tentatively fixed and you will confirm to be liable and be bound by the terms and conditions set-forth herein even after the final allotment letter, sale agreement and/or sale deed.

Yours faithfully,

ZONAL MANAGER

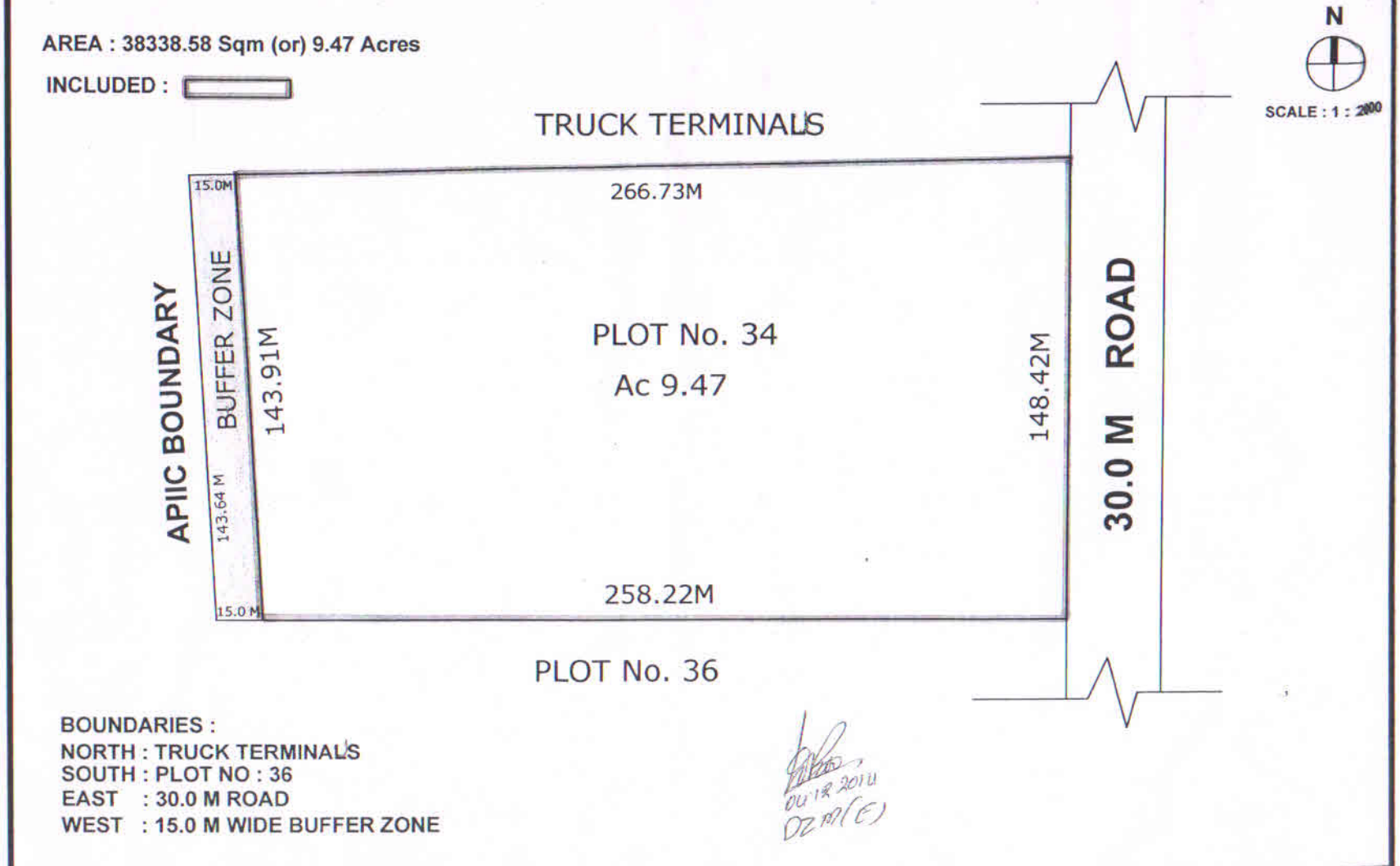
Encl: Site Plan dt:04.12.2014

Copy submitted to the Vice Chairman & Managing Director, APIIC Ltd, Hyderabad for favour of information.

SITE PLAN OF PLOT No. 34 AT I.P. GOLLAPURAM (V),HINDUPUR (M), ANANTAPURAMU DIST.

AREA : 38338.58 Sqm (or) 9.47 Acres

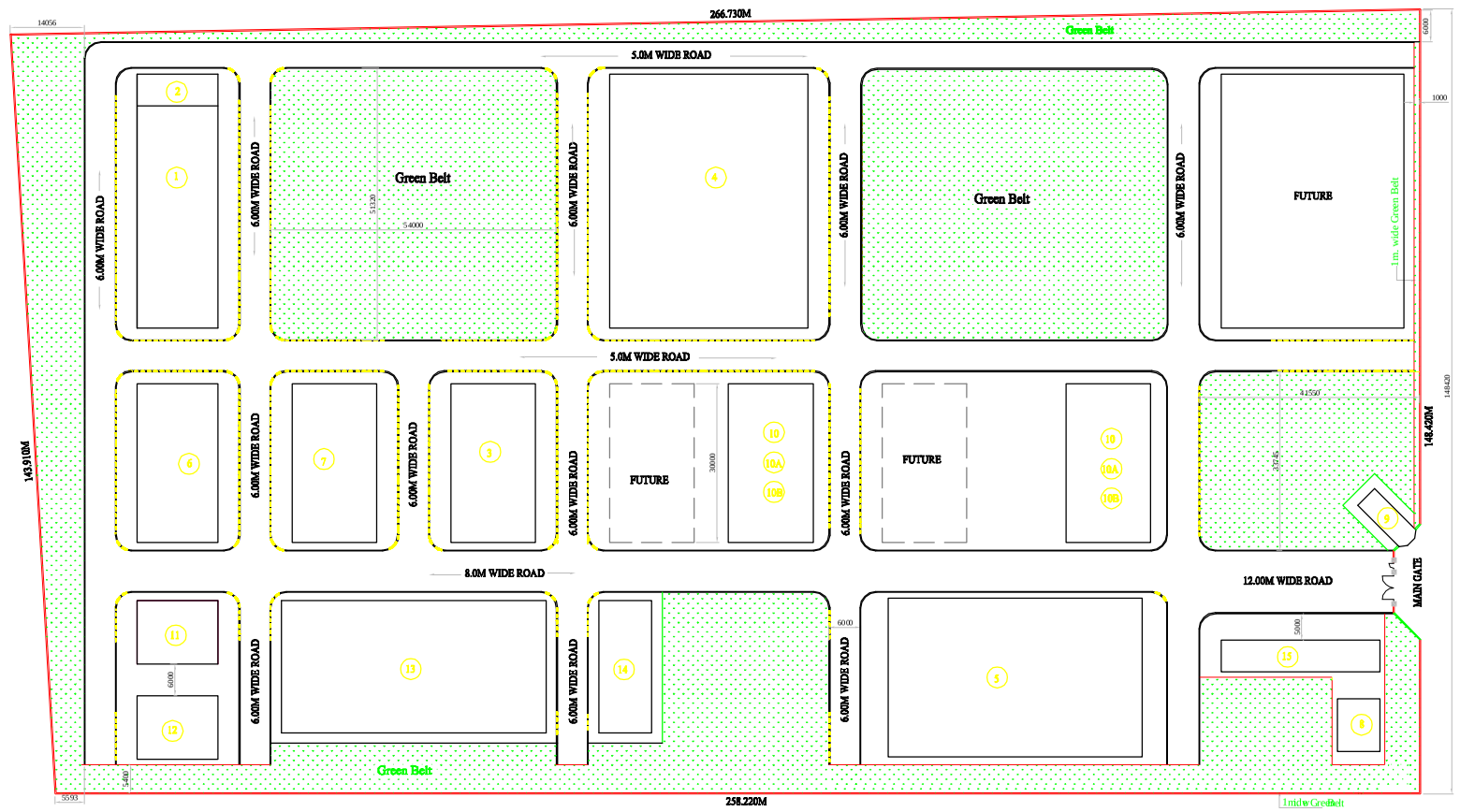
INCLUDED :



BOUNDARIES :

NORTH : TRUCK TERMINALS
SOUTH : PLOT NO : 36
EAST : 30.0 M ROAD
WEST : 15.0 M WIDE BUFFER ZONE

DC 18.2011
DZ M(E)



SITE LAYOUT

PROPOSED BUILDING DETAILS						no. of floors	Plinth area
Sr. no.	Description	L	B	H	Roof		in sqm
1	PRODUCTION BLOCK -I	48.00	15.25	10.00	RCC	2	732.00
2	SRS TOWER	6.00	15.25	20.00	RCC	5	457.50
3	PHARMA	30.00	15.25	10.00	RCC	2	457.50
4	STORES	48.00	37.50	4.20	RCC	1	1800.00
5	UNDER GROUND STORAGE TANKS	48.00	30.00	---	---	---	---
6	PILOT PLANT	30.00	15.25	10.00	RCC	2	1220.00
7	UTILITY	30.00	15.25	4.50	RCC	1	610.00
8	UG SUMP	100 KL CAPACITY			RCC	1	---
9	SECURITY	12.00	4.50	3.20	RCC	1	54.00
10	QC, QA (GF)	40.00	15.25	3.60	RCC	1	610.00
10A	R&D (FF)	40.00	15.25	3.60	RCC	1	610.00
10B	ADMIN (SF)	40.00	15.25	3.60	RCC	1	610.00
11	ELECTRICAL D.G & PCC	12.00	15.25	4.50	RCC	1	183.00
12	BOILER	12.00	15.25	6.50	RCC	1	183.00
13	EFFLUENT TREATMENT & ME SYSTEM	25.00	50.00	2.50	---	1	1250.00
14	DRUM YARD	25.00	10.00	---	RCC	1	250.00
15	TRANSFORMER	30.00	6.00	---	---	---	---
TOTEL CONSTRUCTION AREA							9026.00

LOCATION

PLOT NO. : 34.

GOLLAPURAM (V), HINDUPUR(M.), ANANTAPURAMU DISRTICT.

AREA STATEMENT

1) TOTAL PLOT AREA	:	38338.58 SQ.MTS.(9.47 ACRES)
2) TOTAL BUILTUP AREA	:	9026.00 SQ.MTS.
3) TOTAL ROADS AREA	:	11437.581 SQ.MTS.
4) TOTAL GREEN BELT AREA	:	13091.70 SQ.MTS.
5) OPEN PLOT AREA	:	4783.299SQ.MTS.

GENERAL NOTES

ALL DIMENSIONS ARE IN MM & MTS

CLIENT:

M/S. PENN BIO CHEMICAL INDIA PVT LTD

PROJECT:

GOLLAPURAM, ANAMTHAPUR DISRTICT

TITLE:

SITE LAYOUT

AA AASHRITHA ASSOCIATES
ARCHITECTS, ENGINEERS & INDUSTRIAL CONSULTANTS
FLAT NO.102, SAI SRILAKSHMI RESIDENCY, BALKAMPET ROAD
S.R.NAGAR, HYDERABED – 500 038, INDIA

SCALE	DRAWN	DATE	CHEKED	APPROVED
1:100	SUDHEER	09.01.15	D.K.R	D.K.R
SHEET	DWG. NO.			REV
1 OF 1	AA-12085-GEN-LAYOUT-1001			0

LIST OF ANNEXURE

S. No	Particulars	Annexure No
1.	List Of Products	Annexure 1
2.	List of By- Products	Annexure 2
3.	Manufacturing Process	Annexure 3
4.	Water Requirement Details and Waste Water Details & HTDs & LTDs Details	Annexure 4
5.	Solid Waste Details	Annexure 5
6.	Stack Emissions For Boiler & DG Sets	Annexure 6
7.	Process Emission Details	Annexure 7

M/s. Penn Bio Chemicals India Pvt. Ltd.

Annexure-1

LIST OF PRODUCTS

S.No	Product Name	Therapeutic Category	CAS No's	Quantity Kg/Month	Quantity Kg/Day
1	Abacavir Sulphate	Antiretroviral	188062-50-2	2500.00	83.33
2	Aliskiren Hemifumarate	Antihypertensive agent	173334-58-2	1500.00	50.00
3	Darunavir ethanolate	Antiretroviral	635728-49-3	2000.00	66.67
4	Duloxetine Hydrochloride	Antidepressant	136434-34-9	2000.00	66.67
5	Entecavir Monohydrate	Antiviral agent	209216-23-9	3000.00	100.00
6	Febuxostat	Xanthine oxidase inhibitor	144060-53-7	2500.00	83.33
7	Fosamprenavir	Antiretroviral Agent	226700-81-8	1000.00	33.33
8	Montelukast Sodium	Antiasthmatic	151767-02-1	2000.00	66.67
9	Pregabalin	Neuropathic Pain Agent	148553-50-8	10000.00	333.33
10	Sevelamer Hydrochloride	Phosphate binder	152751-57-0	3000.00	100.00
11	Tadalafil	Anti-erectile dysfunction agent	171596-29-5	5000.00	166.67
12	Tizanidine hydrochloride	Skeletal muscle relaxant	64461-82-1	5000.00	166.67
13	Valacyclovir hydrochloride Monohydrate	Antiviral	124832-27-5	1500.00	50.00
	Total			**41000.00**	**1366.67**

Annexure-2

LIST OF BY-PRODUCTS

S.No	Name of the Product	Name of the By-Product	Quantity in Kg/Day
1	Darunavir Ethanolate	Isobutene	7.67

Annexure-3

MANUFACTURING PROCESS

1. ABACAVIR SULPHATE

Process Description:

Stage-1

N-(2-Amino-4, 6-dichloro pyrimidin-5-yl)formamide reacts with (1S,4R)-4-Amino cyclopent-2-enyl methanol tartaric acid salt in the presence of Triethylorthoformate and IPA as a solvent media to give stage-1 as product.

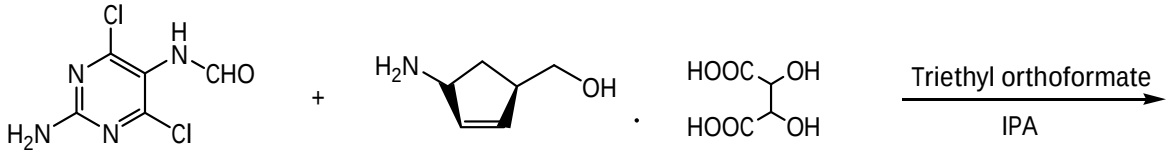
Stage-2

Stage-1 reacts with Cyclopropyl amine and sulphuric acid in the presence of IPA as a solvent media to give Abacavir Sulfate as product.

ABACAVIR SULPHATE

Route of synthesis:

Stage-1:



N-(2-Amino-4,6-dichloro-pyrimidin-5-yl)-formamide

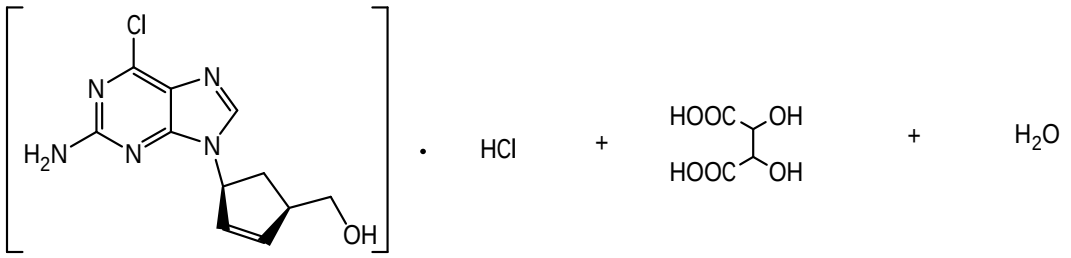
$C_5H_4Cl_2N_4O$

207.02

(4-Amino-cyclopent-2-enyl)-methanol Tartaric acid salt

$C_{10}H_{17}NO_7$

263.24



[4-(2-Amino-6-chloro-purin-9-yl) -cyclopent-2-enyl]-methanol

$C_{11}H_{12}ClN_5O.HCl$

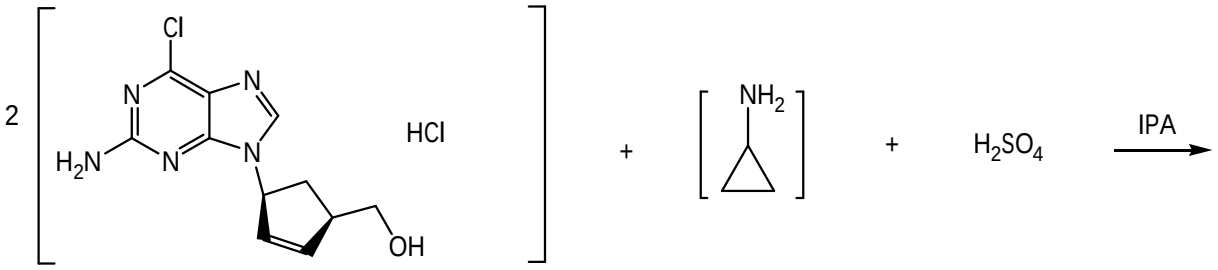
302.16

Tartaric acid

150.09

18.00

Stage-2:



[4-(2-Amino-6-chloro-purin-9-yl)
-cyclopent-2-enyl]-methanol

$C_{11}H_{12}ClN_5O.HCl$

302.16

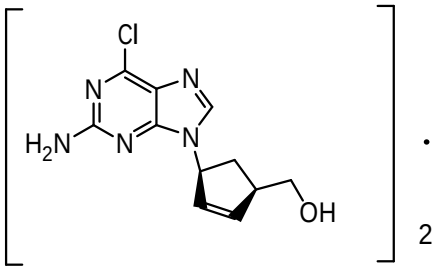
Cyclopropylamine

C_3H_7N

2X57.09=114.18

Sulphuric acid

98.06



$\cdot\ H_2SO_4$ + 4 HCl

Abacavir Sulphate

$C_{11}H_{12}ClN_5O.H_2SO_4$

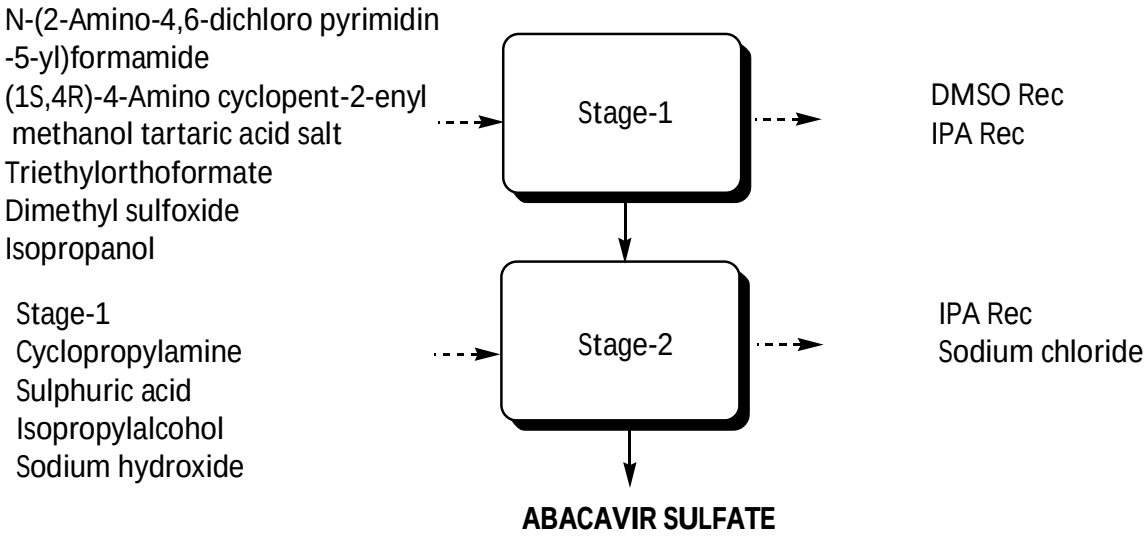
670.66

Hydrochloric acid

4X36.5=146.00

ABACAVIR SULPHATE

Flow Chart:



ABACAVIR SULPHATE

Material Balance:

Material Balance of Abacavir Sulphate Stage-1 Batch Size: 100.0 Kgs				
Name of the input	**Quantity in Kg**		**Name of the out put**	**Quantity in Kg**
N-(2-Amino-4,6-dichloro pyrimidin-5-yl)formamide	62.00		Stage-1	74.00
(1S,4R)-4-Aminocyclopent-2 enyl methanol tartaric acid salt	79.00		DMSO Recovery	518.40
Triethylorthoformate	230.00		DMSO Loss	21.60
Dimethyl sulfoxide	540.00		Triethylorthoformate Recovery	220.80
Isopropanol	460.00		Triethylorthoformate Loss	9.20
Water	800.00		Isopropanol Recovery	440.60
			Isopropanol Loss	18.40
			Effluent water	851.43
			(Water-800,Tartaric acid-45.04, Generated water-5.39,IPA-1)	
			Organic Residue	16.57
Total	2171.00		Total	2171.00

Material Balance of Abacavir Sulphate Stage-2 Batch Size: 100.0 Kgs				
Name of the input	**Quantity in Kg**		**Name of the out put**	**Quantity in Kg**
Stage-1	74.00		Abacavir Sulphate	100.00
Cyclopropyl amine	30.00		Isopropyl alcohol Recovery	844.00
Sulfuric acid	25.00		Isopropyl alcohol Loss	44.00
Isopropyl alcohol	890.00		Effluent water	1058.33
Sodium Hydroxide	30.00		(Water-1000,Sodium chloride-43.83,Generated water-13.5, IPA-1)	
Activated Carbon	10.00		Spent carbon	10.00
Water	1000.00		Organic Residue	2.67
			(Organic impurities-1.67,IPA-1)	
Total	2059.00		Total	2059.00

ALISKIREN HEMIFUMARATE

Process Description:

Stage-1

4-(2-Chloromethyl-3-methyl-butyl)-1-methoxy-2-(3-methoxy-propoxyl-benzene) reacts with 5-Chloro-2-isopropyl-pent-4-enoic acid and Magnesium in presence of Toluene as a solvent media to give Stage-1 as a product.

Stage-2

Stage-1 product reacts with 3-Hydroxy-4-isopropyl-oxazolidin-2-one in presence of Tetrahydrofuran as a solvent media to give Stage-2 as a product.

Stage-3

Stage-2 product reacts with Sodium azide in presence of methanol as a solvent media to give Stage-3 as aproduct.

Stage-4

Stage-3 product reacts with 3-Amino-2, 2-dimethyl-propionamide and 2-Hydroxy pyridine to give Stage-4 as aproduct.

Stage-5

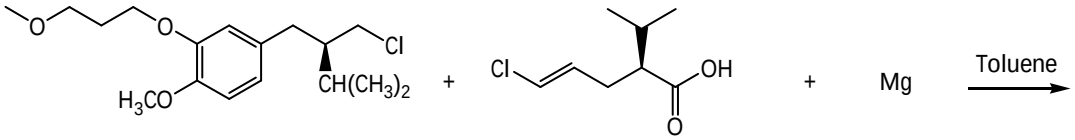
Stage-4 product reacts with Fumaric acid and palladium carbon in presence of Ethanol and Acetone as asolvent media to give Aliskirenhemifumarate as a product.

ALISKIREN HEMIFUMARATE

Route of Synthesis:

Stage-1:

Step-A:



4-(2-Chloromethyl-3-methyl-butyl)
-1-methoxy-2-(3-methoxy-propoxy)
-benzene

$C_{17}H_{27}ClO_3$

314.85

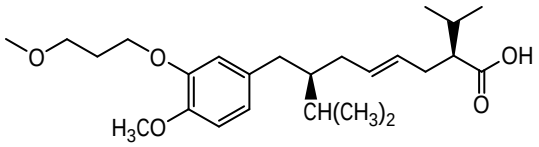
5-Chloro-2-isopropyl-pent
-4-enoic acid

$C_8H_{13}ClO_2$

176.64

Magnesium

24.31



\+ $MgCl_2$

2-Isopropyl-7-[4-methoxy-3-(3-methoxy-propoxy)
-benzyl]-8-methyl-non-4-enoic acid

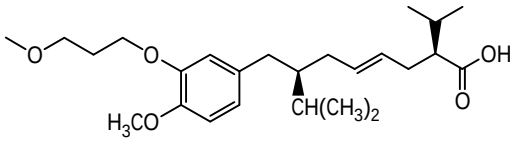
$C_{25}H_{40}O_5$

420.58

Magnesium chloride

95.21

Step-B

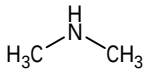


2-Isopropyl-7-[4-methoxy-3-(3-methoxy-propoxy)
-benzyl]-8-methyl-non-4-enoic acid

$C_{25}H_{40}O_5$

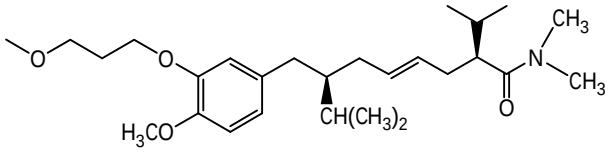
420.58

\+



Dimethylamine

45.08



2-Isopropyl-7-[4-methoxy-3-(3-methoxy-propoxy)-
benzyl]-8-methyl-non-4-enoic acid dimethylamide

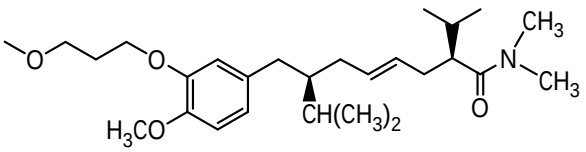
$C_{27}H_{45}NO_4$

447.65

\+ H_2O

18.00

Stage-2:

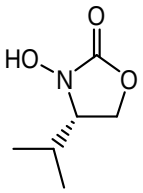


2-Isopropyl-7-[4-methoxy-3-(3-methoxy-propoxy)-benzyl]-8-methyl-non-4-enoic acid dimethylamide

$C_{27}H_{45}NO_4$

447.65

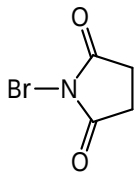
+



3-Hydroxy-4-isopropyl-oxazolidin-2-one

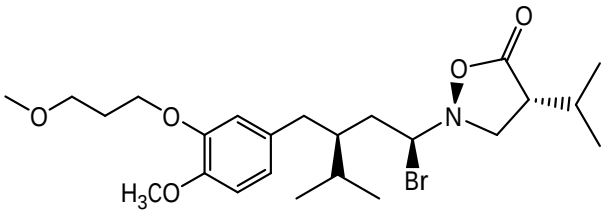
$C_6H_{11}NO_3$

145.16



n-Bromo succinimide

177.98

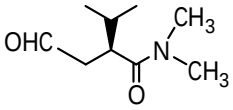


2-{1-Bromo-3-[4-methoxy-3-(3-methoxy-propoxy)-benzyl]-4-methyl-pentyl}-4-isopropyl-isoxazolidin-5-one

$C_{24}H_{38}BrNO_5$

500.47

+

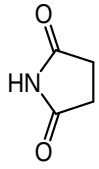


3,N,N-Trimethyl-2-(2-oxo-ethyl)-butyramide

$C_9H_{17}NO_2$

171.24

+

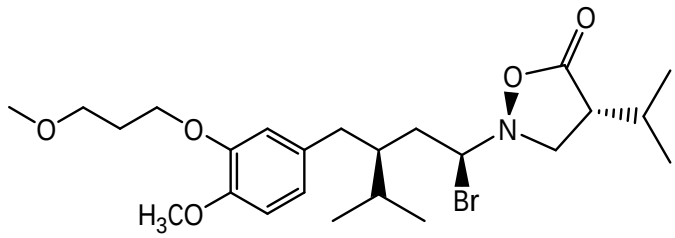


Pyrrolidine-2,5-dione

$C_4H_5NO_2$

99.09

Stage-3:



2-{1-Bromo-3-[4-methoxy-3-(3-methoxy-propoxy)-benzyl]-4-methyl-pentyl}-4-isopropyl-isoxazolidin-5-one

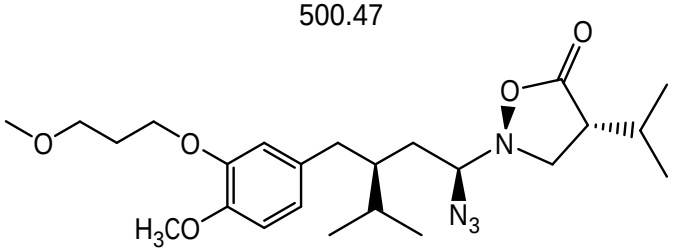
$C_{24}H_{38}BrNO_5$

500.47

\+ NaN_3

Sodium azide

65.01



2-{1-Azido-3-[4-methoxy-3-(3-methoxy-propoxy)-benzyl]-4-methyl-pentyl}-4-isopropyl-isoxazolidin-5-one

$C_{24}H_{38}N_4O_5$

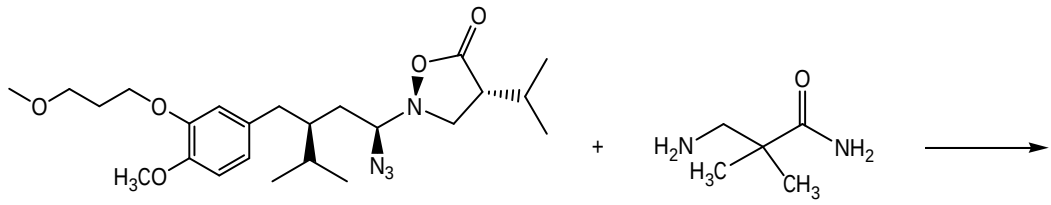
462.58

\+ NaBr

Sodium bromide

102.89

Stage-4:



2-{1-Azido-3-[4-methoxy-3-(3-methoxy-propoxy)-benzyl]-4-methyl-pentyl}-4-isopropyl-isoxazolidin-5-one

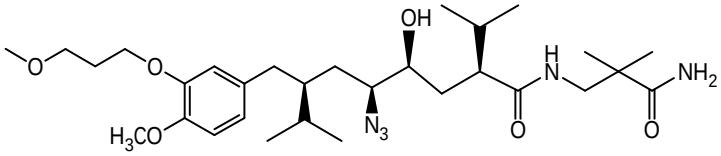
$C_{24}H_{38}N_4O_5$

462.58

3-Amino-2,2-dimethyl-propionamide

$C_5H_{12}N_2O$

116.16



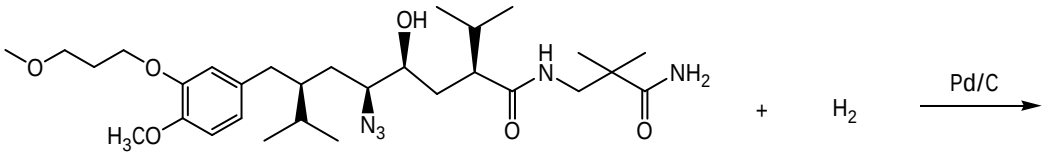
5-Azido-4-hydroxy-2-isopropyl-7-[4-methoxy-3-(3-methoxy-propoxy) -benzyl]-8-methyl-nonanoic acid (2-carbamoyl-2-methyl-propyl)-amide

$C_{30}H_{51}N_5O_6$

577.76

Stage-5:

Step-A



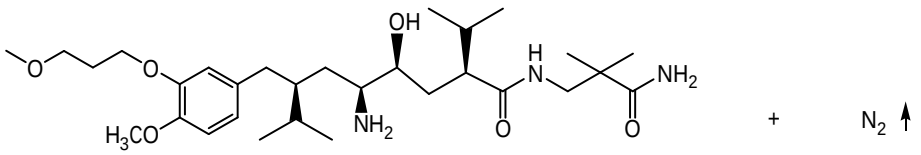
5-Azido-4-hydroxy-2-isopropyl-7-[4-methoxy-3-(3-methoxy-propoxy) -benzyl]-8-methyl-nonanoic acid (2-carbamoyl-2-methyl-propyl)-amide

$C_{30}H_{51}N_5O_6$

577.76

Hydrogen

2.00



Aliskiren

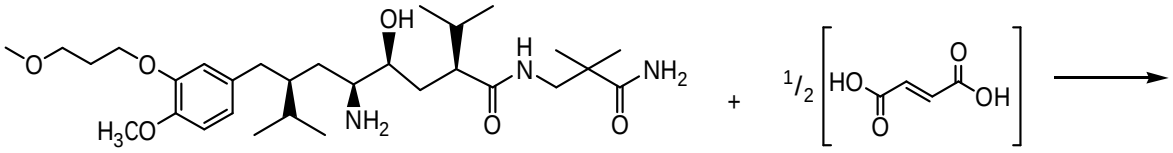
$C_{30}H_{53}N_3O_6$

551.76

Nitrogen

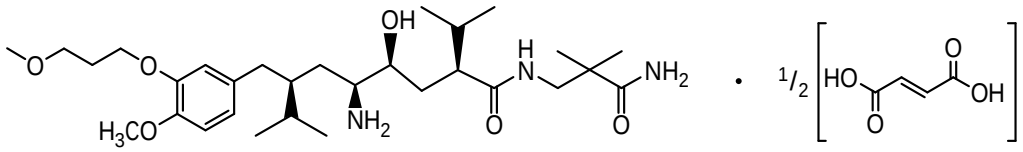
2X14=28.0

Step-B



Aliskiren
$C_{30}H_{53}N_3O_6$
551.76

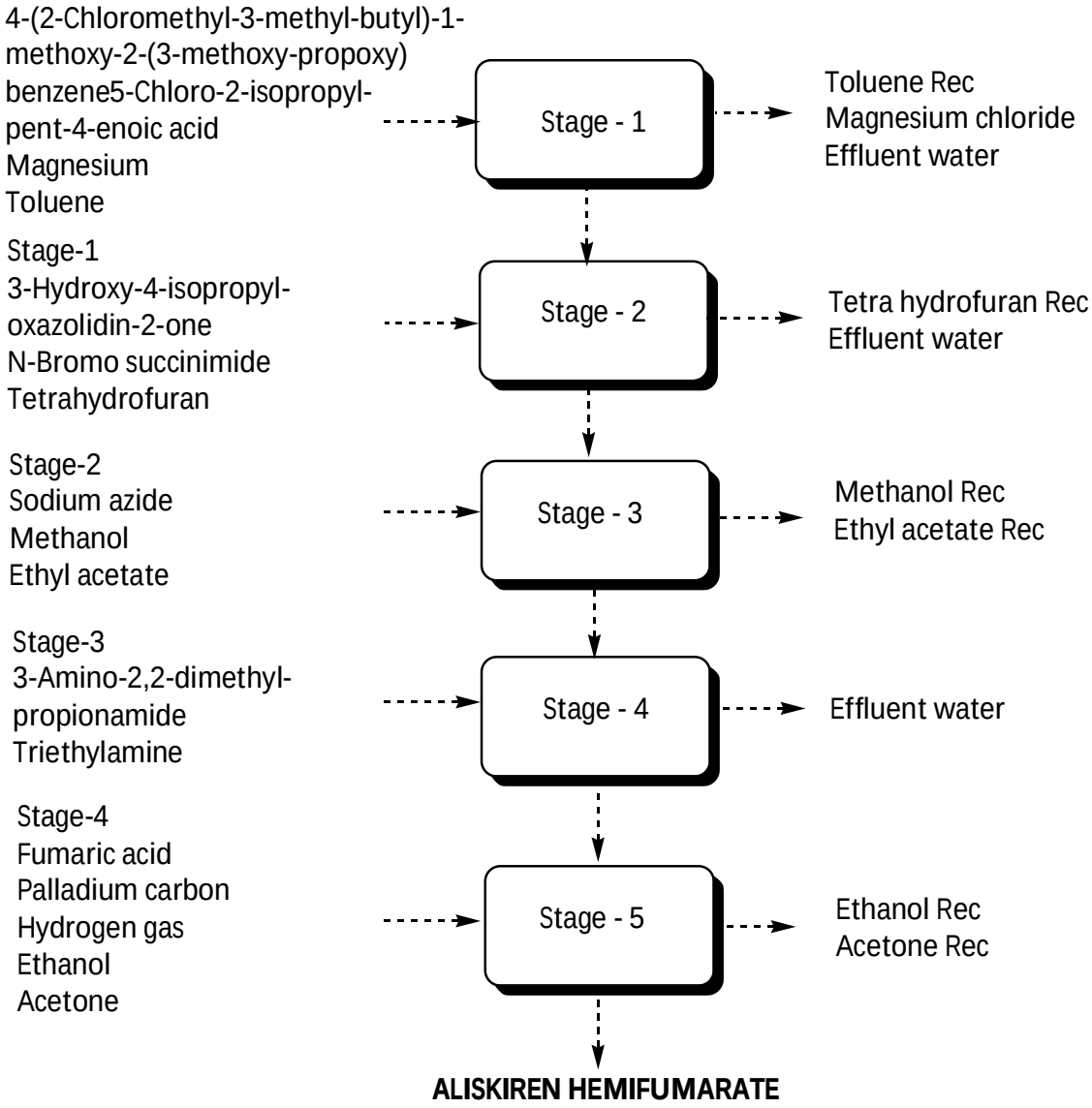
Fumaric acid
$C_4H_4O_4$
$^1/_2$X116.07=58.03



Aliskiren Hemifumarate
$C_{30}H_{53}N_3O_6.C_4H_4O_4$
609.79

ALISKIREN HEMIFUMARATE

Flow Chart



ALISKIREN HEMIFUMARATE

Material Balance:

Material Balance of Aliskiren Hemifumarate Stage-1 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
4-(2-Chloromethyl-3-methyl-butyl)-1-methoxy-2-(3-methoxy-propoxy)benzene	56.50		Stage-1	75.00
5-Chloro-2-isopropyl-pent-4-enoic acid	32.00		Toluene Recovery	284.00
Magnesium	4.50		Toluene Loss	15.00
Dimethylamine	8.00		Effluent water	721.82
Toluene	300.00		(Water-700,Magnesium chloride-17.62,Generated water-3.2,Toluene-1)	0
Water	700.00		Organic Residue	5.18
Total	1101.00		Total	1101.00

Material Balance of Aliskiren Hemifumarate Stage-2 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-1	75.00		Stage-2	83.50
3-Hydroxy-4-isopropyl-oxazolidin-2-one	24.50		Tetrahydrofuran Recovery	236.50
N-Bromo succinimide	30.00		Tetrahydrofuran Loss	12.50
Tetrahydrofuran	250.00		Hexane Recovery	284.00
Hexane	300.00		Hexane Loss	15.00
Water	500.00		Effluent water	529.68
			(Water-500,3-N,N-Trimethyl-2-(2-oxo-ethyl)-butyramide-28.68,Hexane-1)	
			Organic Residue	18.32
			(Organic impurities-17.32, THF-1)	
Total	1179.50		Total	1179.50

Material Balance of AliskirenHemifumarate Stage-3 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-2	83.50		Stage-3	77.00
Sodium azide	11.00		Methanol Recovery	189.00
Methanol	200.00		Methanol Loss	10.00
Ethyl acetate	250.00		Ethyl acetate Recovery	237.50
Sodium bicarbonate	10.00		Ethyl acetate Loss	12.50
Hydrochloric acid	5.00		Effluent water	277.25
Water	250.00		(Water-250,Sodium bromide-17.16,Sodium chloride-6.95,Generated water-2.14,Methanol-1)	
			Process Emission	5.23
			(Carbon dioxide)	
			Organic Residue	1.02
Total	809.50		Total	809.50

Material Balance of AliskirenHemifumarate Stage-4 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-3	77.00		Stage-4	96.00
3-Amino-2,2-dimethyl-propionamide	21.00		Effluent water	225.00
Triethylamine	20.00		(Water-200,Triethylamine-20, 2-Hydroxy pyridine-5)	
2-Hydroxy pyridine	5.00		Organic Residue	2.00
Water	200.00			
Total	323.00		Total	323.00

Material Balance of AliskirenHemifumarate Stage-5 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-4	96.00		AliskirenHemifumarate	100.00
Fumaric acid	11.00		Ethanol Recovery	237.50
Palladium carbon	10.00		Ethanol Loss	12.50
Hydrogen gas	2.00		Acetone Recovery	285.00
Ethanol	250.00		Acetone Loss	15.00
Acetone	300.00		Spent Catalyst	10.00
			(Palladium carbon)	
			Process Emission	4.65
			(Nitrogen)	
			Organic Residue	4.35
Total	669.00		Total	669.00

DARUNAVIR ETHANOLATE

Process Description:

Stage-1

(2S,3S)-1,2-epoxy-(BOC amino)-4-Phenyl butane reacts with isobutyl amine in the presence of IPA as solvent media to get as Stage-1 as product.

Stage-2

Stage-1 reacts with 4-acetylaminobenzene sulfonyl chloride in the presence of sodium bicarbonate and acidified with Sulfuric acid to get Stage-2 as product.

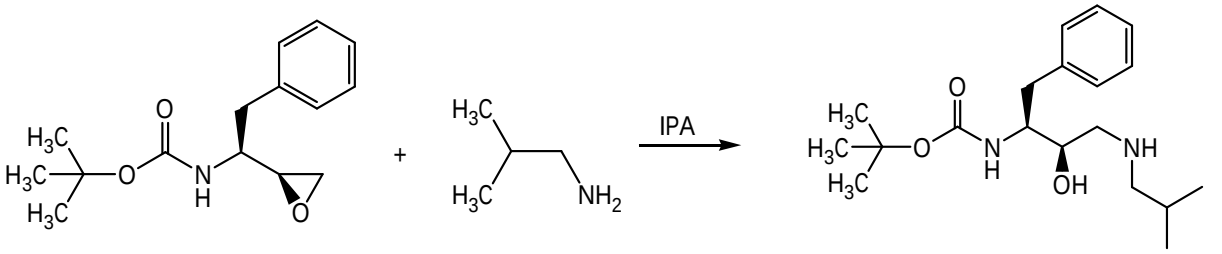
Stage-3

Stage-2 product reacts with 1-([[(3R,3As,6Ar)-Hexahydrofuro[2,3-b]furan-3-yloxy]carbonyl]oxy)-2,5-pyrrolidinedione in the presence of Ethyl acetate as solvent media to get Darunavir as product.

DARUNAVIR ETHANOLATE

Route of Synthesis:

Stage-1:



(2S,3S)-1,2-Epoxy-(BOC Amino) -4-Phenyl butane

$C_{15}H_{21}NO_3$

263.33

Isobutylamine

$C_4H_{11}N$

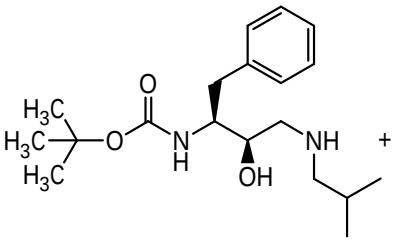
73.14

N-[2R,3S)-3-Tert butoxycrbonyl amino-2-hydroxy-4-phenyl butyl]-isobutylamine

$C_{19}H_{32}N_2O_3$

336.47

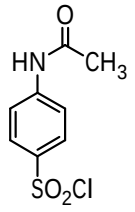
Stage-2:



N-[2R,3S)-3-Tert butoxycrbonyl amino-2-hydroxy-4-phenyl butyl] -isobutylamine

$C_{19}H_{32}N_2O_3$

336.47



4-Acetylamino-benzene sulfonyl chloride

$C_8H_8ClNO_3S$

233.67

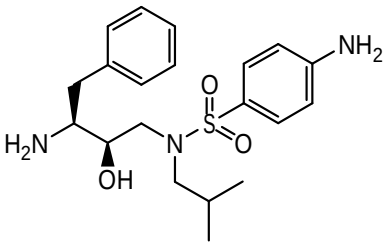
+ $NaHCO_3$ + $5H_2SO_4$ + 7.5NaOH + $2.5NH_4OH$

Sodium bicarbonate 84.01

Sulphuric acid 5X98.08=490.4

Sodium hydroxide 7.5X40=300

2.5X35.05=87.62



N-[(2R,3S)-3-Tert butoxycarbonylamino-2-hydroxy-4-phenyl butyl]-isobutylamine

$C_{20}H_{29}N_3O_3S$

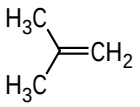
391.53

+ NaCl + 10 H_2O + $3.75Na_2SO_4$

Sodium chloride 58.44

10X18=180.0

Sodium sulphate 3.75X142.04=532.65

+  + CH_3COOH + 1.25 $(NH_4)_2SO_4$ + 2 CO_2 ↑

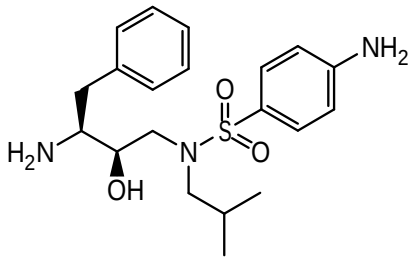
Isobutene 56.11

Acetic acid 60.05

Ammonium sulphate 1.25X132.14=165.17

Carbon dioxide 2X44=88.0

Stage-3:

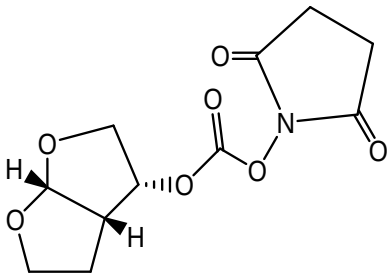


N-[(2R,3S)-3-Tert butoxycarbonylamino-2-hydroxy-4-phenyl butyl]-isobutylamine

$C_{20}H_{29}N_3O_3S$

391.53

+



1-([[3R,3aS,6aR)-hexahydrofuro[2,3-b] furan-3-yloxy]carbonyl]-oxy)-2,5-pyrrolidinedione

$C_{11}H_{13}NO_7$

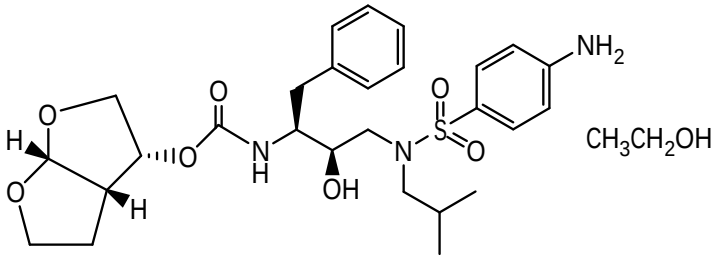
271.22

+

CH_3CH_2OH

Ethanol

46.07



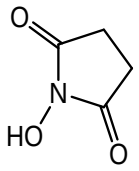
Darunavir

$C_{27}H_{37}N_3O_7S.C_2H_6O$

593.70

CH_3CH_2OH

+



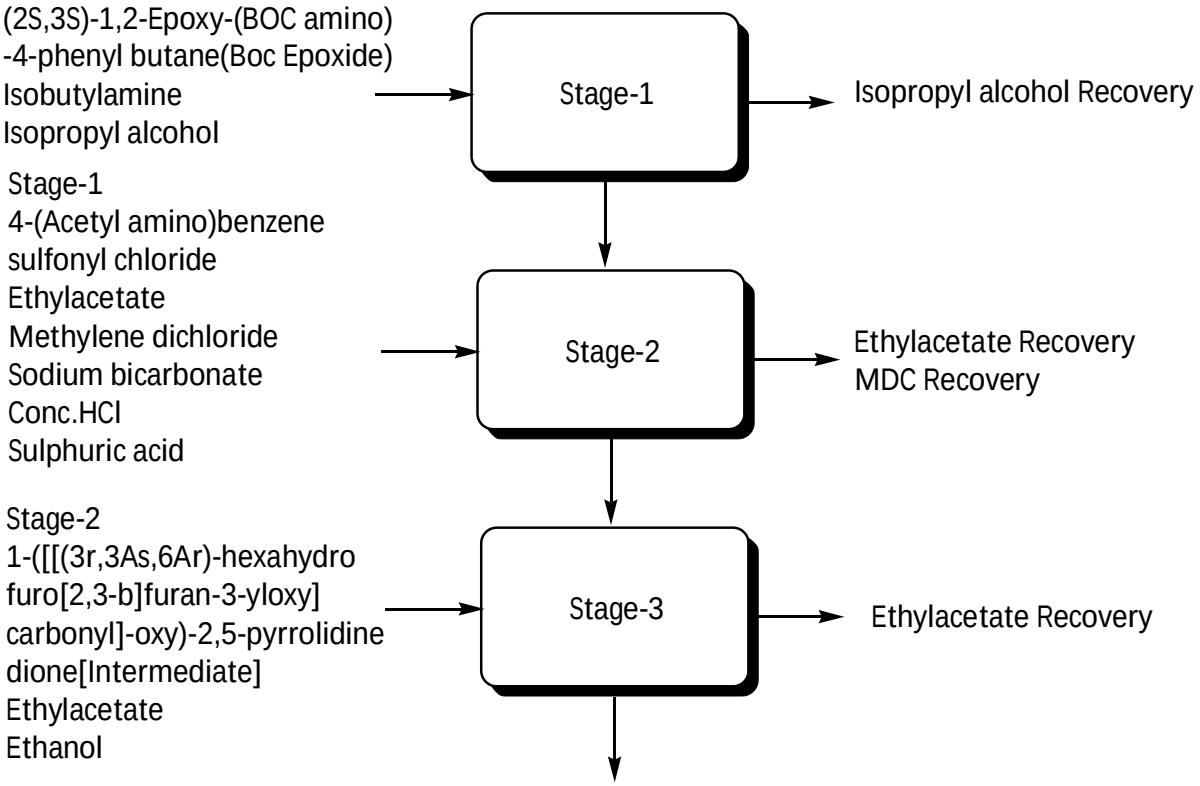
1-Hydroxy-pyrrolidine -2,5-dione

$C_4H_5NO_3$

115.10

DARUNAVIR ETHANOATE

Flow Chart:



DARUNAVIR ETHANOLATE

DARUNAVIR ETHANOATE

Material Balance:

Material Balance of Darunavir Ethanoate Stage-1 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
(2S,3S)-1,2-Epoxy-(BOC amino)-4-phenyl butane (**Boc Epoxide)**	56.00		Stage-1	69.00
Isobutylamine	20.00		Isopropyl alcohol Recovery	235.50
Isopropyl alcohol	250.00		Isopropyl alcohol Loss	12.50
Water	800.00		Effluent water	802.00
			(Water-800,IPA-2)	
			Organic Residue	7.00
Total	1126.00		Total	1126.00

Material Balance of Darunavir Ethanoate Stage-2 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-1	69.00		Stage-2	80.00
4-(Acetyl amino)benzene sulfonyl chloride	48.00		Ethyl acetate Recovery	237.50
Ethyl acetate	250.00		Ethyl acetate Loss	12.50
Methylene dichloride	300.00		Methylene dichloride Recovery	285.00
Toluene	600.00		Methylene dichloride Loss	15.00
Methanol	300.00		Methanol Recovery	284.00
Sodium hydroxide	25.00		Methanol Loss	15.00
Sodium bicarbonate	30.00		Toluene Recovery	569.00
Ammonium hydroxide	15.00		Toluene Loss	30.00
Conc.HCl	10.00		Effluent water	1564.53
Sulphuric acid	25.00		(Water-1500,Sodium chloride-4.87, Generated water-36.91,Acetic acid-12.33,Ammonium sulphate-8.42, Toluene-1,Methanol-1)	
Activated carbon	5.00		Spent carbon & Hyflow	11.00
Hyflow	6.00		Byproduct	11.50
Water	1500.00		(Isobutene)	
			Process Emission	31.42
			(carbon dioxide)	
			Inorganic Residue	27.15
			((Sodium sulphate)	
			Organic Residue	9.40
Total	3183.00		Total	3183.00

Material Balance of Darunavir Ethanoate Stage-3 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-2	80.00		Darunavir Ethanoate	100.00
1-([[(3r,3As,6Ar)-hexahydrofuro [2,3-b]furan-3-yloxy] carbonyl]-oxy)-2,5-pyrrolidine dione[Intermediate]	56.00		Ethyl acetate Recovery	285.00
Ethylacetate	300.00		Ethyl acetate Loss	15.00
Ethanol	75.00		Effluent water	1782.50
Sodium bisulphate	38.50		(Water-1550,Ethanol-75, Sodium bisulphate-38.5, Sodium chloride-65, Potassium carbonate-30, 1-Hydroxy-pyrrolidine-2,5-dione-24)	0
Sodium chloride	65.00		Organic Residue	12.00
Potassium carbonate	30.00			
Water	1550.00			
Total	2194.50		Total	2194.50

DULOXETINE HYDROCHLORIDE

Process Description:

Stage-1

N-Methyl N-Acetylamine-1-thiophen-2-naphthoxy propan Hydrochloride reacts with Sodium Hydroxide in presence of Dimethyl Sulfoxide and Ethyl acetate as a solvent media to give Stage-1 as a product.

Stage-2

Stage-1 undergoes Racemisation with Di-P-Tolyl-L-Tartaric acid in presence of Methanol and acetone as a solvent media to give Stage-2 as a product.

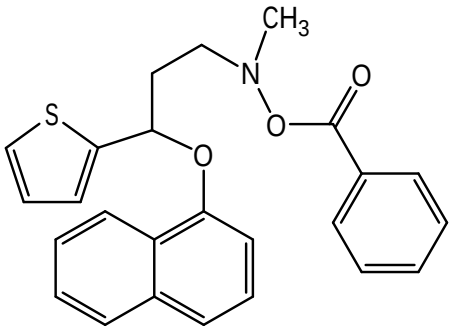
Stage-3

Stage-2 reacts with Sodium Hydroxide in presence of MDC to give S-Duloxetine.This is further reacts with Isopropyl Alcohol Hydrochloride in presence of Acetone as a solvent media to give Duloxetine Hydrochloride as a product.

DULOXETINE HYDROCHLORIDE

Route of synthesis:

Stage-1

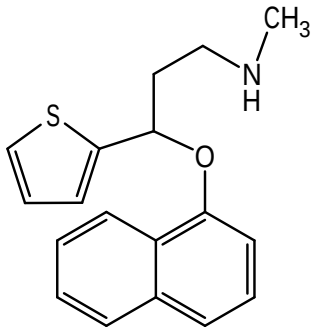


. HCl + 2 NaOH

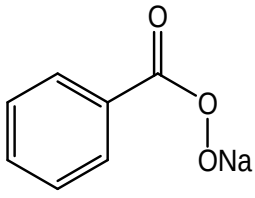
N-Methyl N-Acetylamine-1-thiophen
-2-naphthoxy propan Hydrochloride
$C_{25}H_{24}ClNO_3S$
453.98

Sodium hydroxide
2X40=80.00

Ethyl acetate | DMSO



+



+ NaCl + H_2O

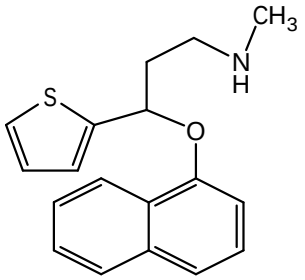
R,S-Duloxetine
$C_{18}H_{19}NOS$
297.41

Sodium Perbonzoate
$C_7H_5NaO_3$
160.10

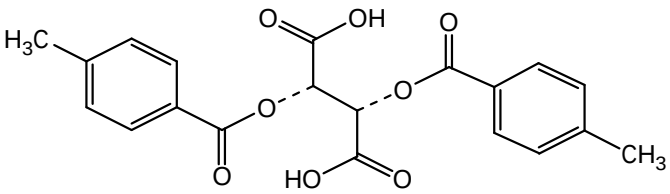
Sodium chloride
58.44

18.00

Stage-2



+



R,S-Duloxetine

$C_{18}H_{19}NOS$

297.41

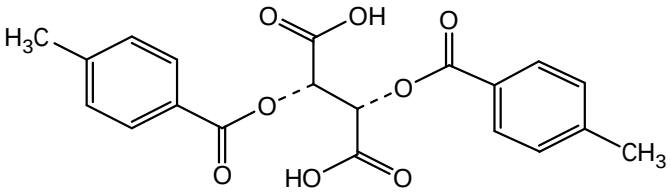
Di-P-Tolyl-L-Tartaric acid

$C_{20}H_{18}O_8$

386.35

Methanol

1/2 ·



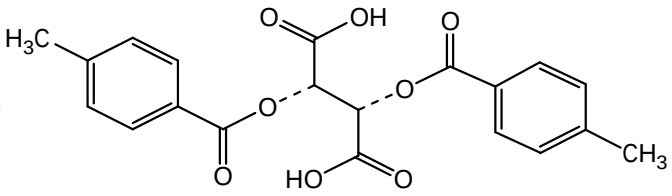
+

S-Duloxetine DPTTA Salt

$C_3H_{37}NO_9S$

1/2X683.77=341.88

1/2 ·



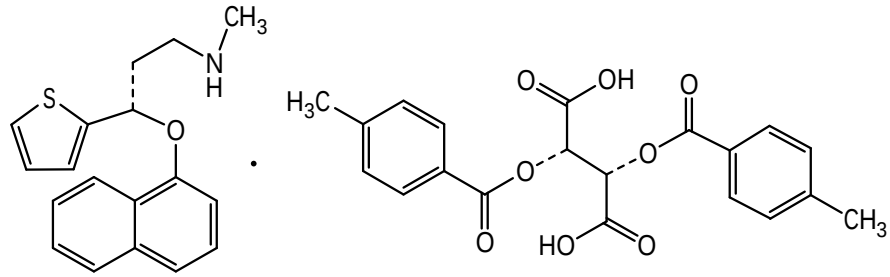
R-Duloxetine DPTTA Salt

$C_3H_{37}NO_9S$

1/2X683.77=341.88

Stage-3

Step-A



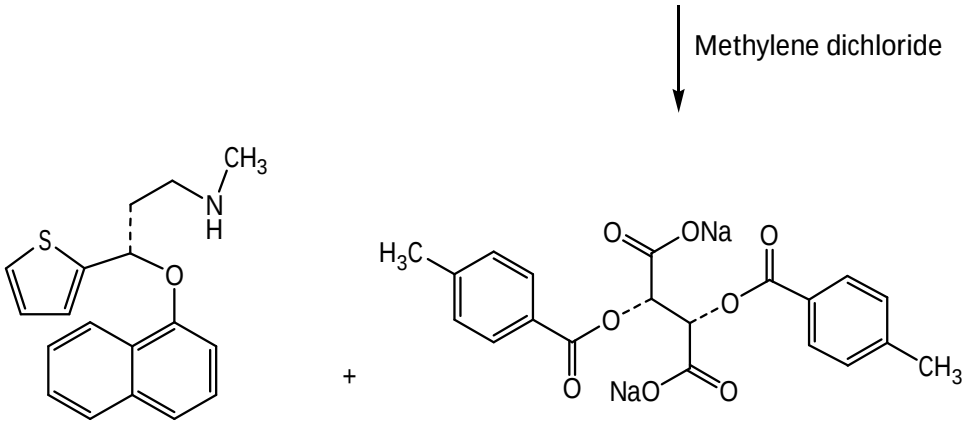
S-Duloxetine DPTTA Salt

$C_3H_{37}NO_9S$

683.77

Sodium hydroxide

2X40=80.00



S-Duloxetine

$C_{18}H_{19}NOS$

297.41

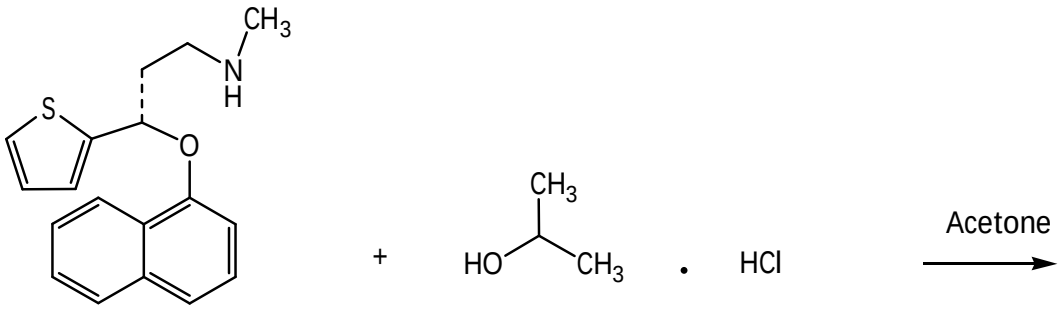
Di-P-Tolyl Tartarate Sodium

$C_{20}H_{16}Na_2O_8$

430.32

2X18=36.00

Step-B



S-Duloxetine

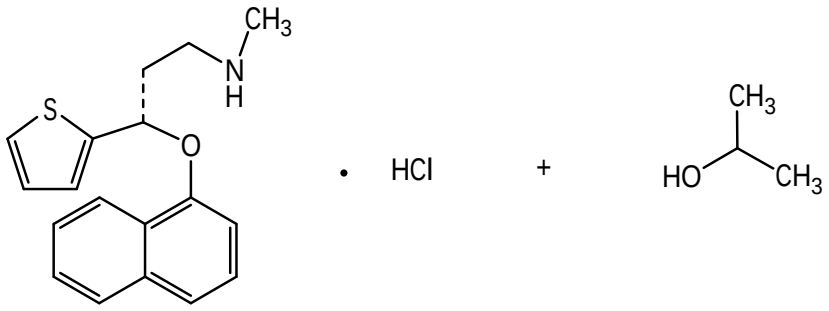
$C_{18}H_{19}NOS$

297.41

Isopropyl alcohol Hydrochloride

C_3H_9ClO

96.56



Duloxetine Hydrochloride

$C_{18}H_{20}ClNOS$

333.88

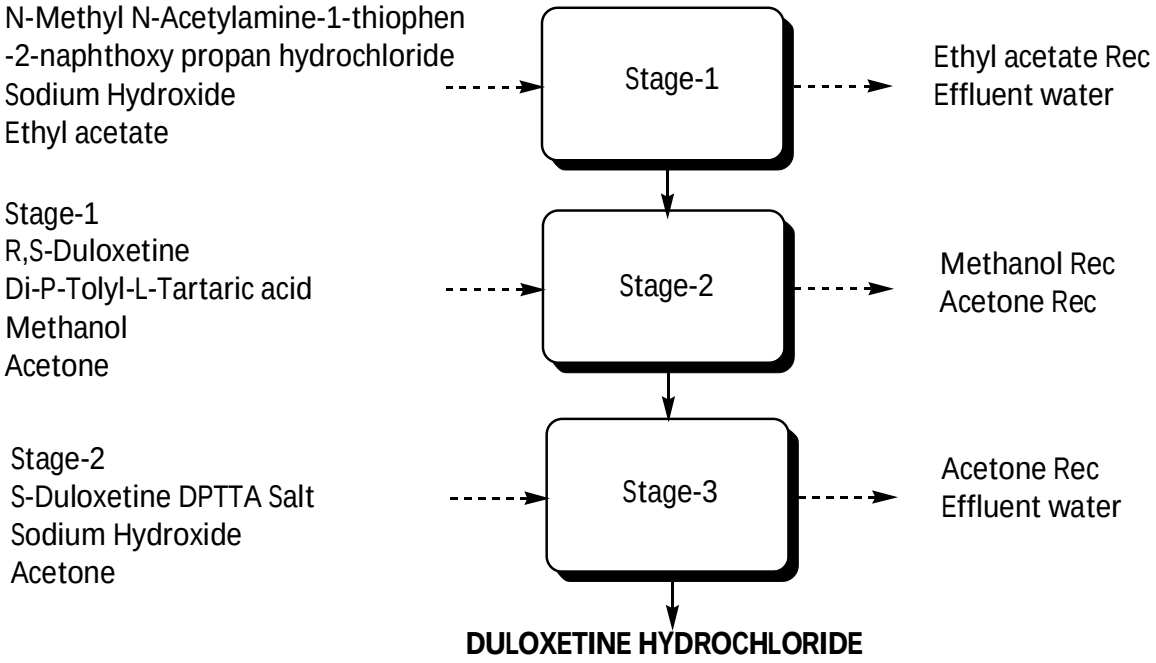
Isopropyl alcohol

C_3H_8O

60.10

DULOXETINE HYDROCHLORIDE

Flow chart



DULOXETINE HYDROCHLORIDE

Material Balance:

Material Balance of Duloxetine Hydrochloride Stage-1 Batch Size: 100.0Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
N-Methyl N-Acetylamine-1-thiophen-2-naphthoxy propane Hydrochloride	450.00		Stage-1	262.00
Sodium hydroxide Solution (48%)	180.00		Di methyl Sulfoxide Recovery	940.00
Dimethyl Sulfoxide	1000.00		Di methyl sulfoxide Loss	40.00
Ethyl Acetate	600.00		Ethyl acetate Recovery	570.00
Water	2250.00		Ethyl acetate Loss	30.00
			Effluent water	2605.29
			(Water-2250,Water from sodium hdyroxide-93.6,generated water-17.86, Sodium chloride-58.05, Sodium hydroxide-7.02, Sodium prebenzoate-158.76, DMSO-20)	
			Organic Residue	32.71
			(Organic Impurities-32.71)	
Total	4480.00		Total	4480.00

Material Balance of Duloxetine Hydrochloride Stage-2 Batch Size: 100.0Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-1	262.00		Stage-2	285.00
Di-P-Tolyl-L-Tartaric acid	340.50		Methanol Recovery	475.00
Methanol	500.00		Methanol Loss	25.00
Acetone	600.00		Acetone Recovery	569.00
			Acetone Loss	30.00
			(R)-Duloxetine DPTTA Salt Recovered for reuse	285.00
			Organic Residue	33.50
			(Organic Impurities-32.5, Acetone-1)	
Total	1702.50		Total	1702.50

Material Balance of Duloxetine Hydrochloride Stage-3 Batch Size: 100.0Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-2	285.00		Duloxetine Hydrochloride	100.00
Sodium Hydroxide	41.50		MDC Recovery	469.00
Methylene Dichloride	500.00		MDC Loss	30.00
Acetone	1000.00		Acetone Recovery	930.00
Isopropyl Alcohol Hydrochloride	90.00		Acetone Loss	50.00
Carbon	10.00		IPA Recovery	67.00
Water	3420.00		IPA Loss	3.50
			Effluent water	3640.50
			(Water-3420,Generated water-15,Di-p-Tolyl tartarate sodium-179.4,Sodium hydroxide-8.1, Acetone-18)	
			Spent carbon	10.00
			Process Emission	2.80
			(Hydrogen chloride)	
			Organic Residue	43.70
			(Organic Impurities-39.2,MDC-1,Acetone-2,IPA-1.5)	
Total	5346.50		Total	5346.50

ENTECAVIR MONOHYDRATE

Process Description:

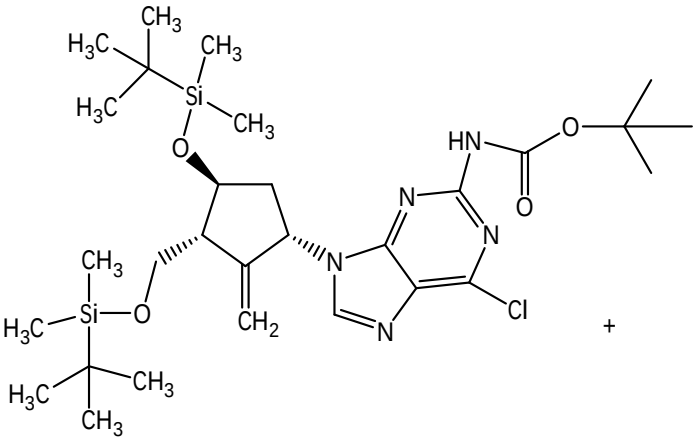
Stage-1

[6-Chloro-9-[(1S, 3R, 4S)-4-[[1, 1-dimethylethyl) dimethyl silyl]oxy]-3-[[[(1,1-dimethylethylsilyl]oxy]methyl]-2-methylene cyclo-pentyl 9H-purin-2-yl]-carbamic acid tert-butyl ester reacts with hydrochloric acid and Sodium hydroxide in the presence of Toluene and Methanol as a solvent media to give Entecavir Monohydrate as a product.

ENTECAVIR MONOHYDRATE

Route of synthesis:

Stage-1:



{9-[4-(*tert*-Butyl-dimethyl-silanyloxy)-3-(*tert*-butyl-dimethyl-silanyloxymethyl)-2-methylene-cyclopentyl]-6-chloro-9*H*-purin-2-yl}-carbamic acid *tert*-butyl ester

$C_{29}H_{50}ClN_5O_4Si_2$

624.36

+ 3HCl + NaOH + H_2O

Hydrochloric acid

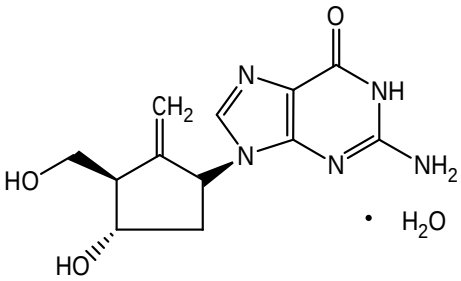
3X36.45=109.35

Sodium hydroxide

40.00

18.00

THF

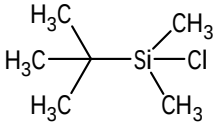


Entecavir Monohydrate

$C_{12}H_{15}N_5O_3.H_2O$

295.29

+ 2



tert-Butyl-chloro-dimethyl-silane

$C_6H_{15}ClSi$

2X150.72=301.44

+ $(CH_3)_3CCl$

tert-Butyl-chloronium

92.56

+ CO_2 ↑ + NaCl

Carbon dioxide

44.00

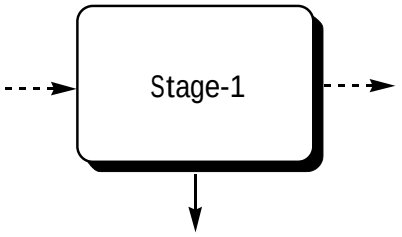
Sodium chloride

58.44

ENTECAVIR MONOHYDRATE

Flow Chart:

[6-Chloro-9-[(1S,3R,4S)-4-[[1,1-dimethyl ethyl)dimethyl silyl]oxy]-3-[[[(1,1-dimethyl ethylsilyl]oxy]methyl]-2-methylene cyclo-pentyl 9H-purin-2-yl]-carbamic acid tert-butyl ester.
Sodium hydroxide
Methanol
Toluene



Toluene Rec
Methanol Rec

ENTECAVIR MONOHYDRATE

ENTECAVIR MONOHYDRATE

Material Balance:

Material Balance of Entecavir Monohydrate Stage-1 Batch Size:100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
[6-Chloro-9-[(1S,3R,4S)-4-[[1,1-Dimethylethyl)dimethysilyl]oxy]-3-[[[(1,1-dimethyl ethyl)dimethylsilyl]oxy]methyl]-2-methylenecyclopentyl]-9H-Purin-2-yl]-carbamic acid tert butyl ester	212.00		Entecavir Monohydrate	100.00
Conc. Hydrochloric acid	37.50		THF Recovery	284.00
Sodium hydroxide	30.00		THF Loss	15.00
Toluene	500.00		Toluene Recovery	475.00
Activated carbon	10.00		Toluene Loss	25.00
THF	300.00		N,N-Dimethyl formamide Recovery	190.00
N,N-Dimethyl formamide	200.00		N,N-Dimethyl formamide Loss	10.00
Methanol	300.00		Methanol Recovery	285.00
Hyflow	5.00		Methanol Loss	15.00
Water	1500.00		Effluent water	1654.81
			(Water-1500,Tertbutyl chloro dimethyl silane-102.35,2-Chloro-2-methyl propane-31.42,Sodium chloride20.04,THF-1)	
			Spent carbon &hyflow	15.00
			Process Emission	15.00
			(Carbon dioxide)	
			Organic Residue	10.69
Total	3094.50		Total	3094.50

FEBUXOSTAT

Process Description:

Stage-1

4-Hydroxy benzaldehyde reacts with Bromine in the presence of methanol as solvent media to give Stage-1A as product.

Stage-2

Stage-1 A product reacts with Hydroxylamine Hydrochloride and Sodium formate in the presence of water to give Stage-1 as product.

Stage-3

Stage-1 product reacts with thio acetamide and Hydrochloric acid in the presence of IPA as solvent media to give Stage-2A as product.

Stage-4

Stage-2A product undergoes cyclisation with 2-Chloroacetoacetic acid ethyl ester in the presence of IPA as solvent media to give Stage-2 as product.

Stage-5

Stage-2 product reacts with Isobutyl bromide in the presence of IPA as solvent media to give Stage-3 as product.

Stage-6

Stage-3 product reacts with Copper cyanide and Hydrochloric acid in the presence of Copper iodide as catalyst in the presence of DMF as solvent media to give Stage-4 as product.

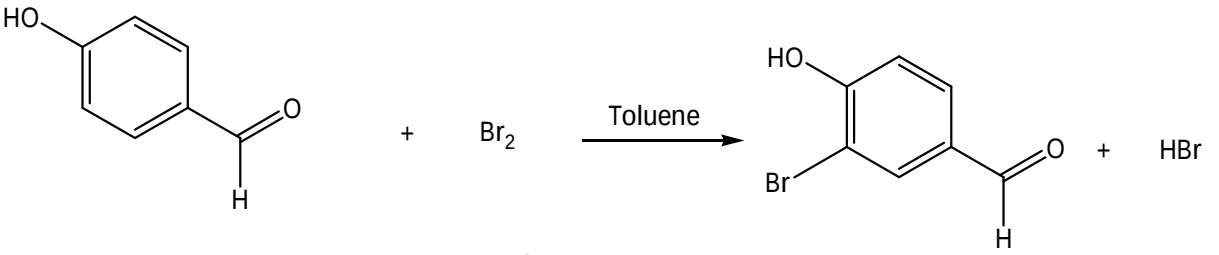
Stage-7

Stage-4 product reacts with sodium hydroxide in the presence of THF as solvent media to give Febuxostat as product.

FEBUXOSTAT

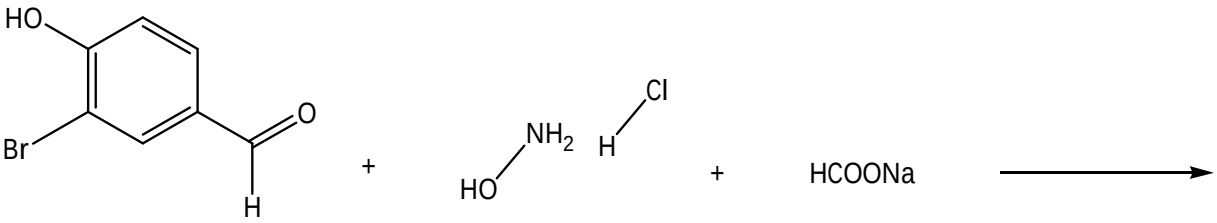
Route of Synthesis:

Stage-1:

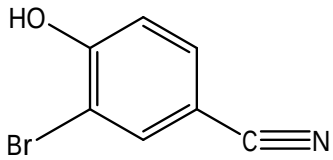


4-Hydroxy-benzaldehyde	Bromine	3-Bromo-4-hydroxy-benzaldehyde	80.91
$C_7H_6O_2$	159.81	$C_7H_5BrO_2$	
122.12		201.02	

Stage-2:

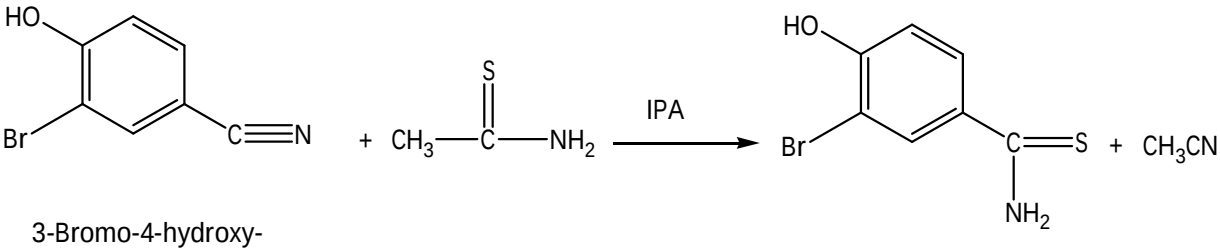


3-Bromo-4-hydroxy-benzaldehyde	Hydroxyl amine Hydrochloride	Sodium formate
$C_7H_5BrO_2$	69.49	68.01
201.02		



+	HCOOH	+	NaCl	+	$2H_2O$
3-Bromo-4-hydroxy-benzonitrile	46.03		58.50		2X18=36.0
C_7H_4BrNO					
198.02					

Stage-3:



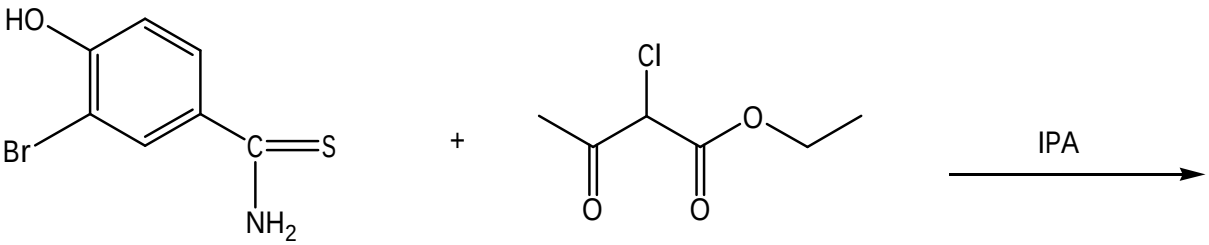
3-Bromo-4-hydroxy-benzonitrile
C_7H_4BrNO
198.02

Thio acetamide
C_2H_5NS
75.13

3-Bromo-4-hydroxy-thiobenzamide
C_7H_6BrNOS
232.10

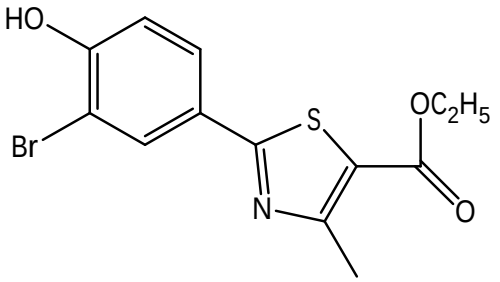
41.05

Stage-4:



3-Bromo-4-hydroxy-thiobenzamide
C_7H_6BrNOS
232.10

2-Chloroacetoacetic acid ethyl ester
$C_6H_9ClO_3$
164.59



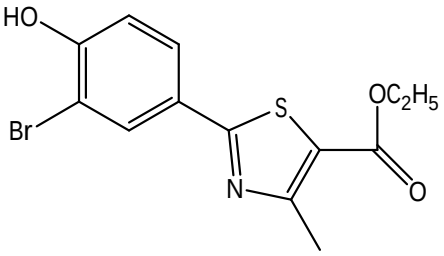
+ HCl + H_2O

2-(3-Bromo-4-hydroxyphenyl)-4-methyl thiazole-5-carboxylic acid ethyl ester
$C_{13}H_{12}BrNO_3S$
342.21

36.46

18.0

Stage-5:

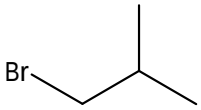


2-(3-Bromo-4-hydroxyphenyl)-4-methyl thiazole-5-carboxylic acid ethyl ester

$C_{13}H_{12}BrNO_3S$

342.21

\+



Isobutyl bromide

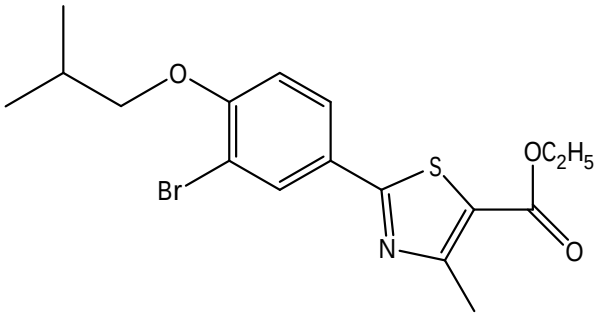
C_4H_9Br

137.02

\+ $1/2K_2CO_3$ —IPA→

Potassium carbonate

1/2X138.21=69.10



2-(3-Bromo-4-isobutoxy-phenyl)-4-methyl-thiazole-5-carboxylic acid ethyl ester

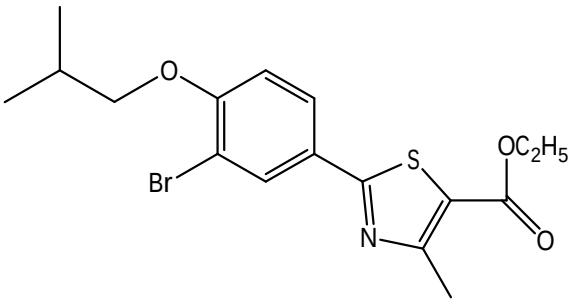
$C_{17}H_{20}BrNO_3S$

398.31

\+ KBr + $1/2CO_2\uparrow$ + $1/_2H_2O$

119.0 22.0 9.0

Stage-6:



2-(3-Bromo-4-isobutoxy-phenyl)-4-methyl-thiazole-5-carboxylic acid ethyl ester

$C_{17}H_{20}BrNO_3S$

398.31

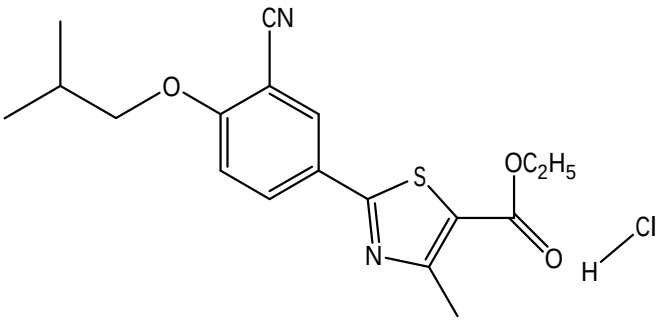
\+ CuCN + HCl —DMF→

Copper Cyanide

89.56

Hydrochloric acid

36.46



2-(3-Cyano-4-isobutoxy-phenyl)-4-methyl-thiazole-5-carboxylic acid ethyl ester Hydrochloride

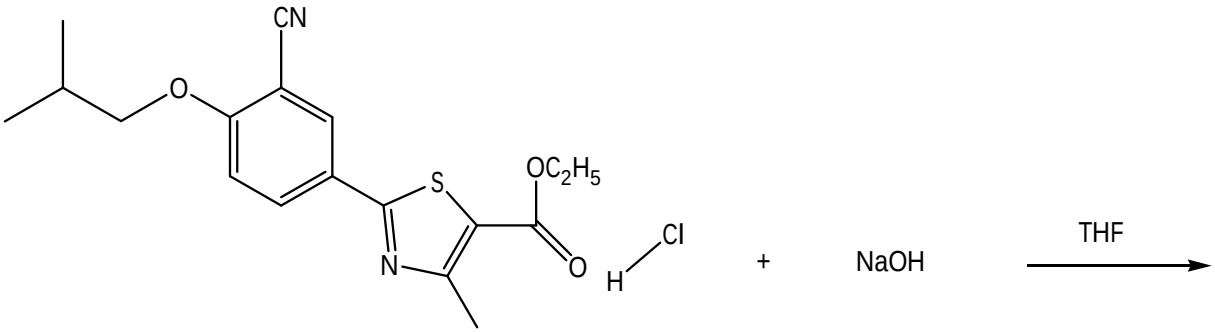
$C_{18}H_{21}ClN_2O_3S$

380.93

\+ CuBr

143.45

Stage-7:



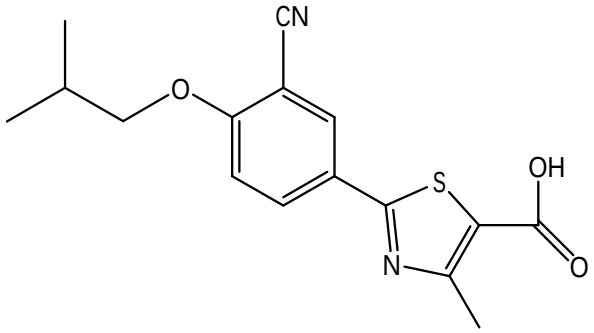
2-(3-Cyano-4-isobutoxy-phenyl)-4-methyl-thiazole-5-carboxylic acid ethyl ester Hydrochloride

$C_{18}H_{21}ClN_2O_3S$

380.93

Sodium Hydroxide

40.0



+ NaCl + C_2H_5OH

Febuxostat

$C_{16}H_{16}N_2O_3S$

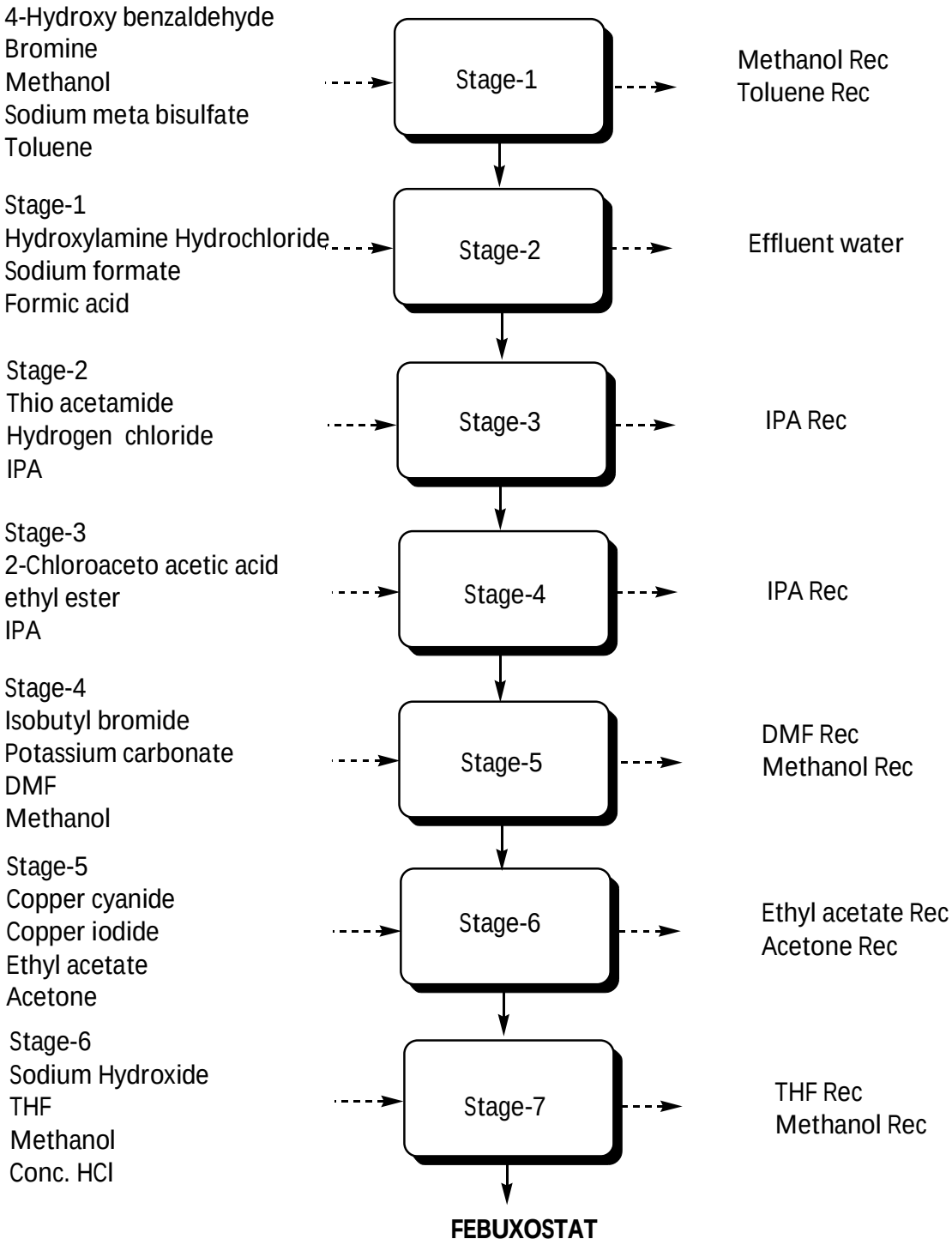
316.37

58.5

46.07

FEBUXOSTAT

Flow Chart:



FEBUXOSTAT

Material Balance:

Material Balance of Febuxostat Stage-1 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
4-Hydroxy benzaldehyde	72.00		Stage-1	110.00
Bromine	87.00		Methanol Recovery	474.50
Methanol	500.00		Methanol Loss	25.00
Sodium meta bisulfate	20.00		Toluene Recovery	284.00
Toluene	300.00		Toluene Loss	15.00
Water	1180.00		Effluent water	1245.04
			(Water-1180,Hydrobromic acid-44.04,Sodium metabisulfate-20,Toluene-1)	
			Organic Residue	5.46
			(Organic Impurities-4.96, Toluene-0.5)	
Total	2159.00		Total	2159.00

Material Balance of Febuxostat Stage-2 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-1	110.00		Stage-2	108.00
Hydroxylamine Hydrochloride	38.00		Formic acid Recovery	297.90
Sodium formate	37.50		Formic acid Loss	15.00
Formic acid	350.00		Effluent water	827.13
Water	750.00		(Water-750,Generated water-19.7, Sodium chloride-32.26, Formic acid-25.17)	
			Organic Residue	37.47
Total	1285.50		Total	1285.50

Material Balance of Febuxostat Stage-3 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-2	108.00		Stage-3	125.00
Thio acetamide	41.00		IPA Recovery	236.50
Hydrogen chloride gas	5.00		IPA Loss	12.50
IPA	250.00		Process Emission	5.00
			(Hydrogen chloride)	
			Organic Solid waste	25.00
			(Methyl cyanide-22.4,Organic Impurities-1.6,IPA-1)	
Total	404.00		Total	404.00

Material Balance of Febuxostat Stage-4 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-3	125.00		Stage-4	154.00
2-Chloroaceto acetic acid ethyl ester	75.00		IPA Recovery	237.00
IPA	250.00		IPA Loss	12.50
			Generated water	9.70
			Process Emission	16.60
			(Hydrogen chloride)	
			Organic Residue	20.20
			(Organic Impurities-19.7,IPA-0.5)	
Total	450.00		Total	450.00

Material Balance of Febuxostat Stage-5 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-4	154.00		Stage-5	155.00
Isobutyl bromide	54.00		DMF Recovery	474.50
Potassium carbonate	27.50		DMF Loss	25.00
DMF	500.00		Methanol Recovery	190.00
Methanol	200.00		Methanol Loss	10.00
			Generated water	3.52
			Inorganic solid waste	47.35
			(Potassium bromide)	
			Process Emission	8.75
			(Carbon dioxide)	
			Organic Residue	21.38
			(Organic Impurities-20.88,DMF-0.5)	
Total	935.50		Total	935.50

Material Balance of Febuxostat Stage-6 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-5	155.00		Stage-6	148.00
Copper cyanide	58.00		Ethyl acetate Recovery	950.00
Copper iodide	12.00		Ethyl acetate Loss	50.00
Conc. HCl	23.00		Acetone Recovery	283.00
Ethylene di amine	580.00		Acetone Loss	15.00
Ethyl acetate	1000.00		Ethylene di amine Recovery	551.00
Acetone	300.00		Ethylene Di amine Loss	29.00
Water	1000.00		Effluent water	1091.82
			(Water-1000,Copper bromide-55.82,Copper iodide-12, Conc.HCl-23,Acetone-1)	
			Organic Residue	10.18
			(Organic Impurities-8.18, Acetone-1)	
Total	3128.00		Total	3128.00

Material Balance of Febuxostat Stage-7 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-6	148.00		Febuxostat	100.00
Sodium Hydroxide	16.00		Methanol Recovery	284.00
THF	210.00		Methanol Loss	15.00
Methanol	300.00		THF Recovery	199.50
Activated carbon	7.00		THF Loss	10.50
Conc. HCl	15.00		Effluent water	556.30
Water	500.00		(Water-500,Sodium chloride-23.4,Ethanol-17.90,Conc.HCl-15)	
			Spent carbon	7.00
			Organic Residue	23.70
			(Organic Impurities-22.7, Methanol-1)	
Total	1196.00		Total	1196.00

FOSAMPRENAVIR

Process Description

Stage-1

(1-Benzyl-2-hydroxy-3-isobutylamino-propyl)-carbamic acid tert-butyl ester reacts with Benzyl chloro formate in presence of Toluene as a solvent media to give
Stage-1 as product.

Stage-2

Stage-1 product reacts with Sodium chloride in presence of Methanol as asolvent media to give Stage-2 as a product.

Stage-3

Stage-2 product reacts with Carbonic acid-3-oxo-isoxazolidin-2-yl ester tetrahydro-furan-3-yl ester in presence of Methanol as a solvent media to give Stage-3 as a product.

Stage-4

Satge-3 product reacts with Palladium carbon in presence of Toluene as asolvent media to give Stage-4 as a product.

Stage-5

Stage-4 product reacts with 4-Nitrobenzene sulfonyl chloride in presence of Methanol as a solvent media to give Stage-5 as a product.

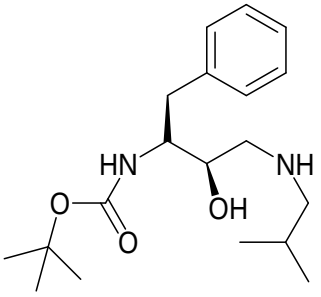
Stage-6

Stage-5 product reacts with Phosphoryl chloride in presence of Toluene as a solvent media to give Fosamprenavir

FOSAMPRENAVIR

Route of Synthesis:

Stage-1:

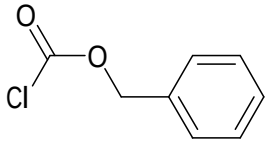


(1-Benzyl-2-hydroxy-3-isobutylamino-propyl)-carbamic acid *tert*-butyl ester

$C_{19}H_{32}N_2O_3$

336.47

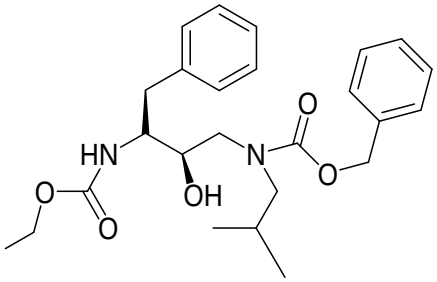
\+



Benzyl chloroformate

$C_8H_7ClO_2$

170.59

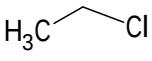


(3-Ethoxycarbonylamino-2-hydroxy-4-phenyl-butyl)-isobutyl-carbamic acid benzyl ester

$C_{25}H_{34}N_2O_5$

442.55

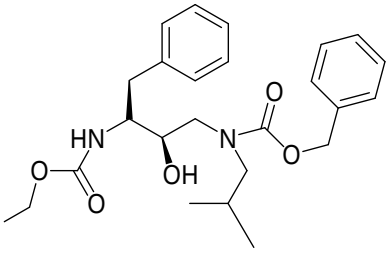
\+



Ethyl chloride

64.51

Stage-2:



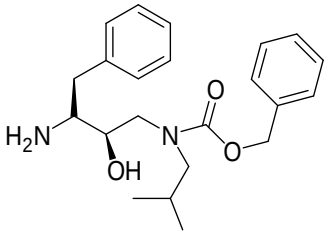
(3-Ethoxycarbonylamino-2-hydroxy-4-phenyl-butyl)-isobutyl-carbamic acid benzyl ester

$C_{25}H_{34}N_2O_5$

442.55

\+ H_2O

18.00



(3-Amino-2-hydroxy-4-phenyl-butyl)-isobutyl-carbamic acid benzyl ester

$C_{22}H_{30}N_2O_3$

370.49

\+ $CO_2\uparrow$ + CH_3CH_2OH

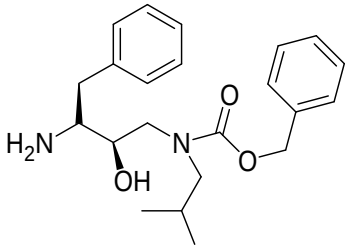
Carbondioxide

44.00

Ethanol

46.07

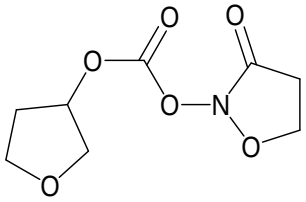
Stage-3:



(3-Amino-2-hydroxy-4-phenyl-butyl)-isobutyl-carbamic acid benzyl ester

$C_{22}H_{30}N_2O_3$

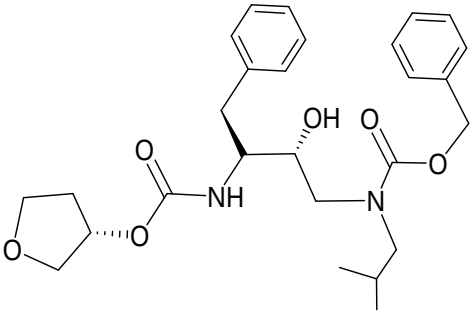
370.49



Carbonic acid 3-oxo-isoxazolidin-2-yl ester tetrahydro-furan-3-yl ester

$C_8H_{11}NO_6$

217.18

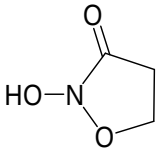


[1-Benzyl-3-(benzyloxycarbonyl-isobutyl-amino)-2-hydroxy-propyl]-carbamic acid tetrahydro-furan-3-yl ester

$C_{27}H_{36}N_2O_6$

484.58

+

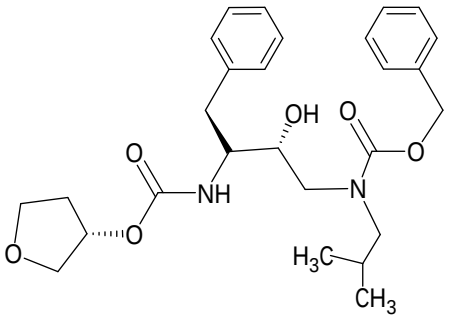


2-Hydroxy-isoxazolidin-3-one

$C_3H_5NO_3$

103.08

Stage-4:

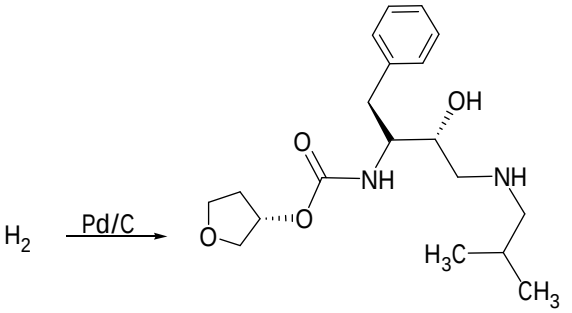


[1-Benzyl-3-(benzyloxycarbonyl-isobutyl-amino)-2-hydroxy-propyl]-carbamic acid tetrahydro-furan-3-yl ester

$C_{27}H_{36}N_2O_6$

484.58

\+



Hydrogen

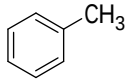
2.00

(1-Benzyl-2-hydroxy-3-isobutylamino-propyl)-carbamic acid tetrahydro-furan-3-yl ester

$C_{19}H_{30}N_2O_4$

350.45

\+



Toluene

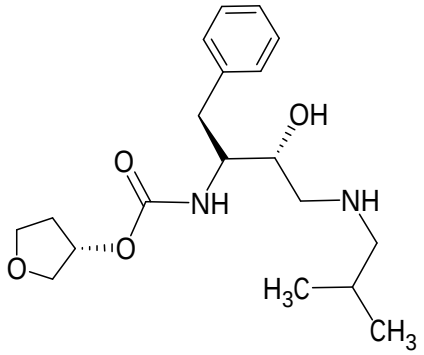
92.14

\+ CO_2 ↑

Carbondioxide

44.00

Stage-5:

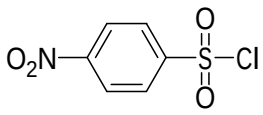


(1-Benzyl-2-hydroxy-3-isobutylamino -propyl)-carbamic acid tetrahydro -furan-3-yl ester

$C_{19}H_{30}N_2O_4$

350.45

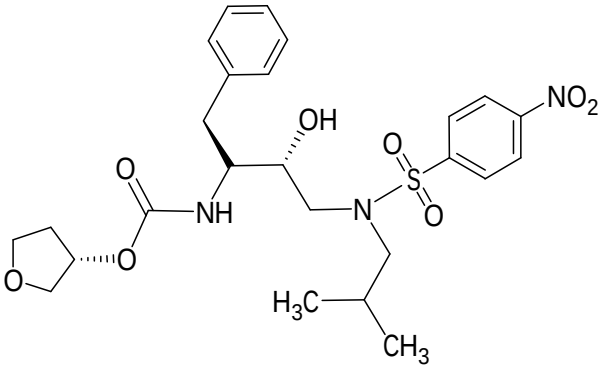
+



4-Nitro-benzenesulfonyl chloride

$C_6H_4ClNO_4S$

221.62



{1-Benzyl-2-hydroxy-3-[isobutyl-(4-nitro-benzenesulfonyl)-amino]-propyl}-carbamic acid tetrahydro-furan-3-yl ester

$C_{25}H_{33}N_3O_8S$

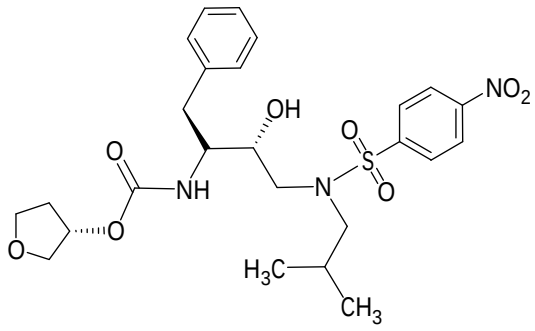
535.61

+ HCl

Hydrochloric acid

36.5

Stage-6:



{1-Benzyl-2-hydroxy-3-[isobutyl-(4-nitro-benzene sulfonyl)-amino]-propyl}-carbamic acid tetrahydro-furan-3-yl ester

$C_{25}H_{33}N_3O_8S$

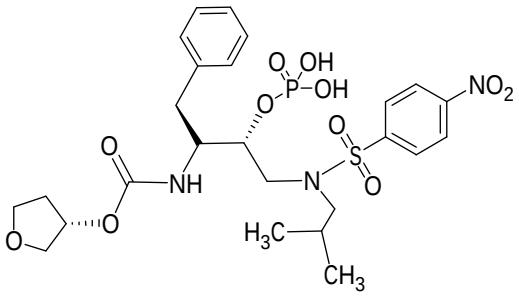
535.61

+ $POCl_3$ + $2H_2O$ ⟶

Phosphoryl chloride

153.33

2X18=36.0



Fosamprenavir

$C_{25}H_{34}N_3O_{11}PS$

615.59

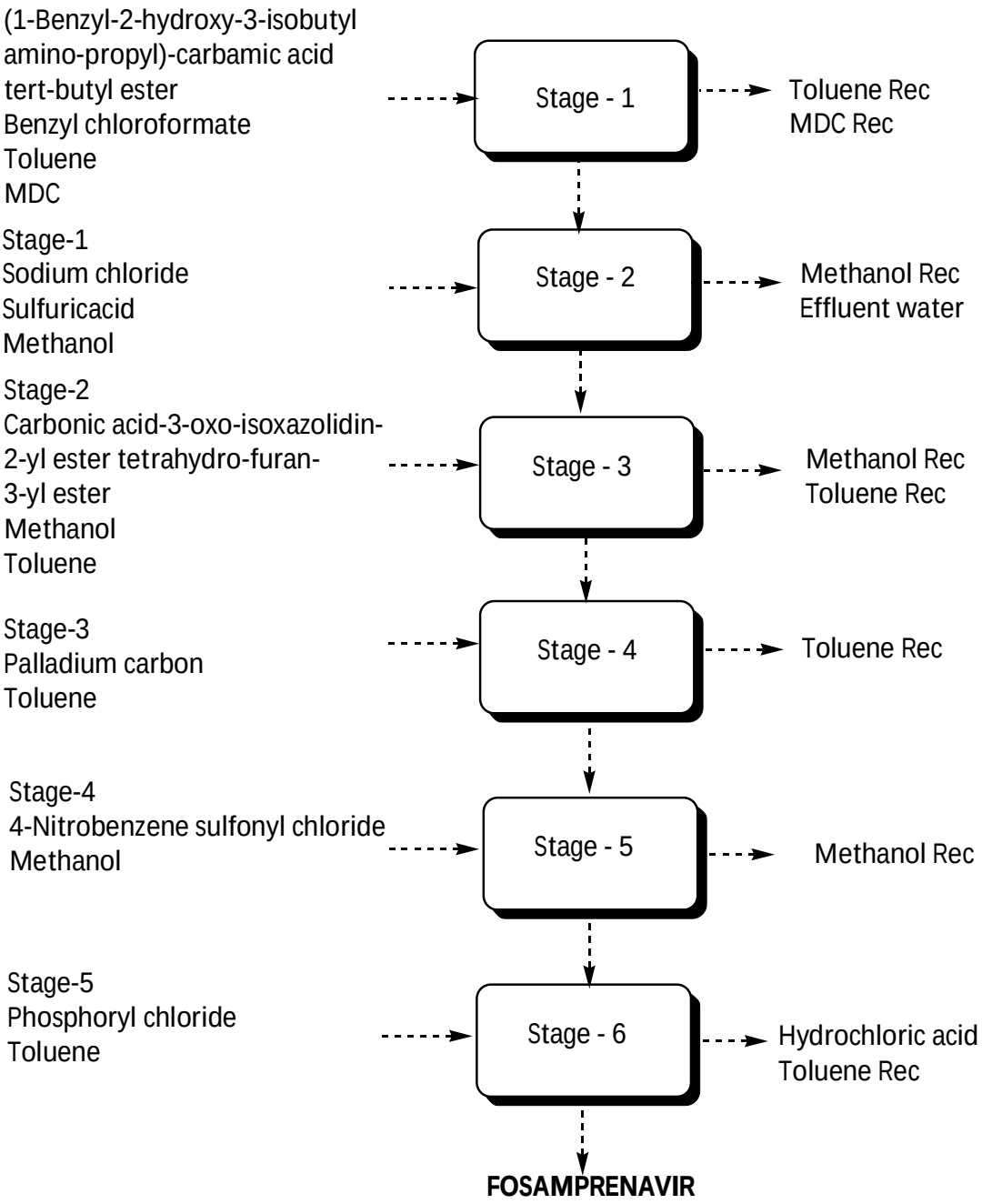
+ 3HCl

Hydrochloric acid

3X36.5=109.5

FOSAMPRENAVIR

Flow Chart



FOSAMPRENAVIR

Material Balance:

Material Balance of Fosamprenavir Stage-1 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
(1-Benzyl-2-hydroxy-3-isobutylamino-propyl)-carbamic acid tert-butyl ester	55.50		Stage-1	72.50
Benzyl chloroformate	28.50		Toluene Recovery	236.50
Toluene	250.00		Toluene Loss	12.50
MDC	200.00		MDC Recovery	190.00
Water	600.00		MDC Loss	10.00
			Effluent water	601.00
			(Water-600,Toluene-1)	
			Organic Residue	11.50
			(Organic impurities-0.72, Ethylchloride-10.78)	
Total	1134.00		Total	1134.00

Material Balance of Fosamprenavir Stage-2 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-1	72.50		Stage-2	60.50
Sodium chloride	10.00		Methanol Recovery	284.95
Sodium hydroxide	22.00		Methanol Loss	15.00
Sulfuricacid	19.00		Effluent water	524.29
Methanol	300.00		(Water-500,Generated water-6.75,Sodium chloride-10, Ethanol-7.54)	
Water	500.00		Inorganic Residue	27.53
			(Sodium sulphate)	
			Process Emission	7.20
			(Carbon dioxide)	
			Organic Residue	4.03
			(Organic impurities-1.98, Methanol-0.05)	
Total	923.50		Total	923.50

Material Balance of Fosamprenavir Stage-3 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-2	60.50		Stage-3	79.00
Carbonic acid-3-oxo-isoxazolidin-2-yl ester tetrahydro-furan-3-yl ester	35.50		Methanol Recovery	141.50
Methanol	150.00		Methanol Loss	7.50
Toluene	250.00		Toluene Recovery	237.50
Water	300.00		Toluene Loss	12.50
			Effluent water	317.83
			(Water-300,2-Hydroxyisooxazolidin-3-one-16.83,Methanol-1)	
			Organic Residue	0.17
Total	796.00		Total	796.00

Material Balance of Fosamprenavir Stage-4 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-3	79.00		Stage-4	57.00
Palladium carbon	10.00		Toluene Recovery	188.50
Toluene	200.00		Toluene Loss	10.00
Water	500.00		Effluent water	515.02
			(Water-500,Toluene-15.02)	
			Process Emission	7.17
			(carbon dioxide)	
			Organic Residue	11.31
			(Organic impurities-10.81, Toluene-0.5)	
Total	789.00		Total	789.00

Material Balance of Fosamprenavir Stage-5 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-4	57.00		Stage-5	87.00
4-Nitrobenzene sulfonyl chloride	55.00		Methanol Recovery	189.00
Methanol	200.00		Methanol Loss	10.00
Water	250.00		Effluent water	260.05
			(Water-250,Hydrochloric acid-9.05,Methanol-1)	
			Organic residue	15.95
Total	562.00		Total	562.00

Material Balance of Fosamprenavir Stage-6 Batch Size: 100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-5	87.00		Fosamprenavir	100.00
Phosphoryl chloride	25.00		Toluene Recovery	236.50
Toluene	250.00		Toluene Loss	12.50
Water	300.00		Effluent water	313.00
			(Water-294.15,Hydrochloric acid-17.85,Toluene-1)	
Total	662.00		Total	662.00

MONTELUKAST SODIUM

Process Description:

Stage-1:

7-Chloro Quinaldehyde is reacted with Isopthalaldehyde and acetic anhydride in the presence of methanol as solvent media to give stage-1 as product.

Stage-2:

Stage-1 is reacted with vinyl magnesium bromide in tetra hydrofuran in the presence of toluene as solvent media to give stage-2 as product.

Stage-3:

Stage-2 is reacted with methyl iodo benzoate in the presence of palladium acetate as a catalyst and Acetonitrile as solvent media to give stage-3 as product.

Stage-4:

Stage-3 is reacted with Dip chloride in the presence of Tetrahydrofuran to give Stage-4 as product.

Stage-5:

Stage-4 is reacted with Methyl magnesium chloride and hydrochloric acid in the presence of isopropylether to give Stage-5 as product.

Stage-6:

Stage-5 is reacted with Methane sulfonyl chloride in the presence of Diisopropylamine, Toluene as solvent media to give Stage-7 as product.

Stage-7:

Stage-6 is reacted with (1-Mercaptomethyl cyclopropyl) acetic acid in the presence of Tetrahydrofuran and ethyl acetate as solvent media to give Stage-7 as product.

Stage-8:

Stage-7 is reacted with Dicyclo hexyl amine in the presence of Ethyl acetate as solvent media to give stage-8 as product.

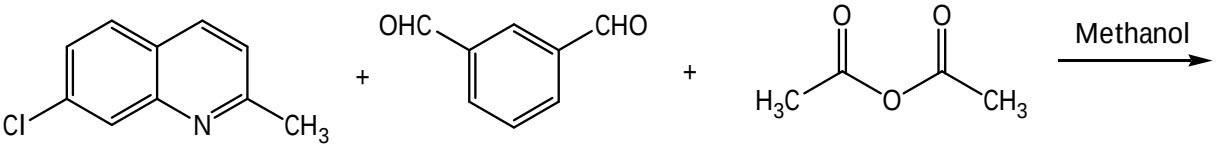
Stage-9:

Stage-8 is reacted with Sodium hydroxide in the presence of Toluene as solvent media to give stage-9 as product.

MONTELUKAST SODIUM

Route of synthesis:

Stage-1:



2-Chloro-quinaldehyde

$C_{10}H_8ClN$

177.63

Isopthalaldehyde

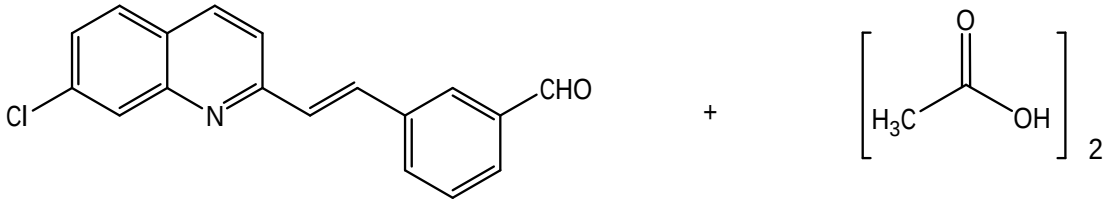
$C_8H_6O_2$

134.13

Acetic anhydride

$C_4H_6O_3$

102.08



3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-benzaldehyde

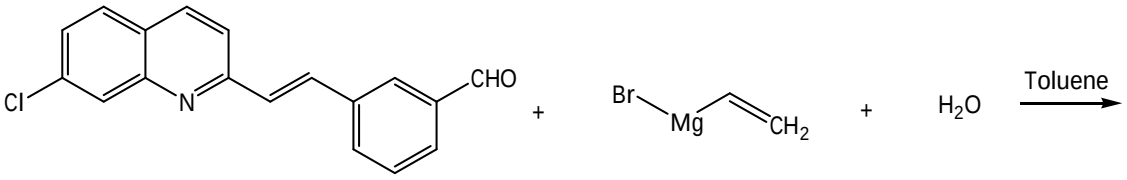
$C_{18}H_{12}ClNO$

293.74

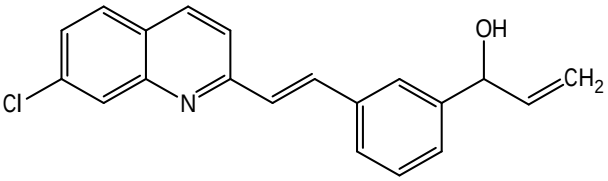
Acetic acid

2X60.05=120.10

Stage-2

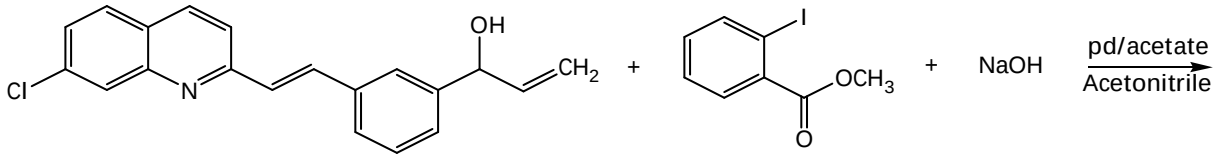


3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-benzaldehyde	Vinyl magnesium bromide	18.00
$C_{18}H_{12}ClNO$	C_2H_3BrMg	
293.74	131.25	

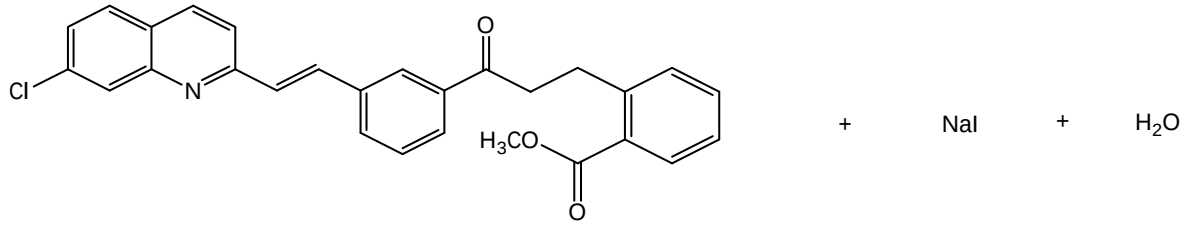


1-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-prop-2-en-1-ol	Magnesium hydroxy bromide
$C_{20}H_{16}ClNO$	121.21
321.80	

Stage-3:

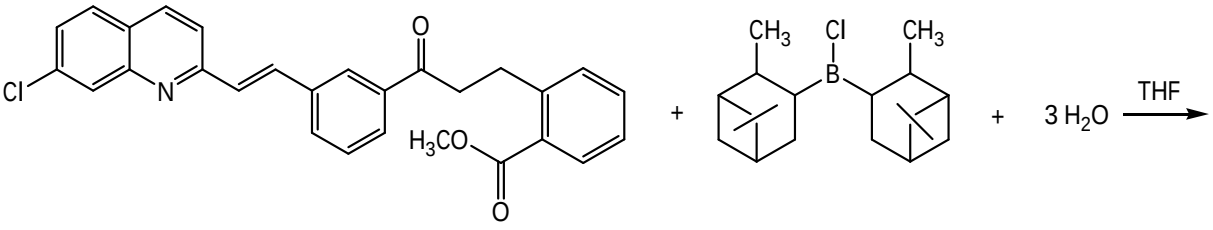


1-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-prop-2-en-1-ol	Methyl iodo benzoate	Sodium hydroxide
$C_{20}H_{16}ClNO$	$C_8H_7IO_2$	40.00
321.80	262.04	



2-(3-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-3-oxo-propyl)-benzoic acid methyl ester	Sodium iodide	18.00
$C_{28}H_{22}ClNO_3$	149.89	
455.93		

Stage-4:



2-(3-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-3-oxo-propyl)-benzoic acid methyl ester

$C_{28}H_{22}ClNO_3$

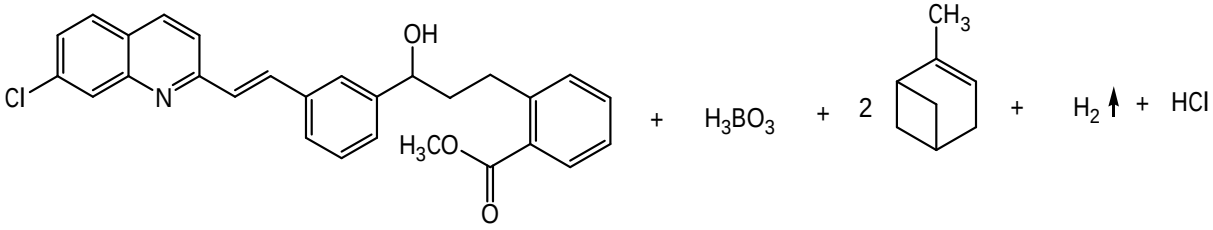
455.93

Dip chloride

$C_{20}H_{34}BCl$

320.74

3X18=54.00



2-(3-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-3-hydroxy-propyl)-benzoic acid methyl ester

$C_{28}H_{24}ClNO_3$

457.94

Boric acid

61.83

Alpha pinene

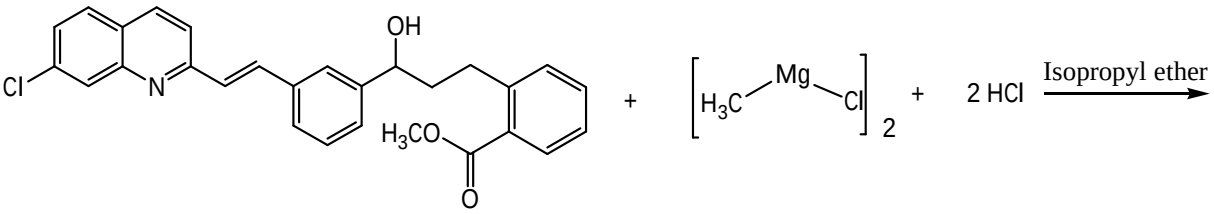
$C_{10}H_{16}$

2X136.23=272.46

2.00

36.5

Stage-5:



2-(3-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-3-hydroxy -propyl)-benzoic acid methyl ester

$C_{28}H_{24}ClNO_3$

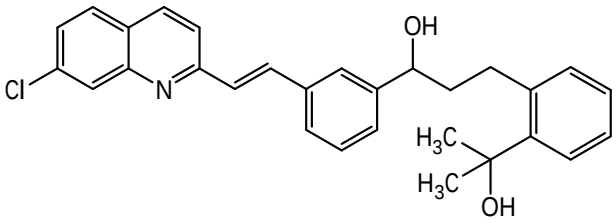
457.94

Methyl magnesium chloride

2X74.79=149.58

Hydrochloric acid

2X36.5=73.00



+ CH_3OH + 2 $MgCl_2$

1-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-3-[2-(1-hydroxy-1-methyl-ethyl)-phenyl]-propan-1-ol

$C_{29}H_{28}ClNO_2$

457.99

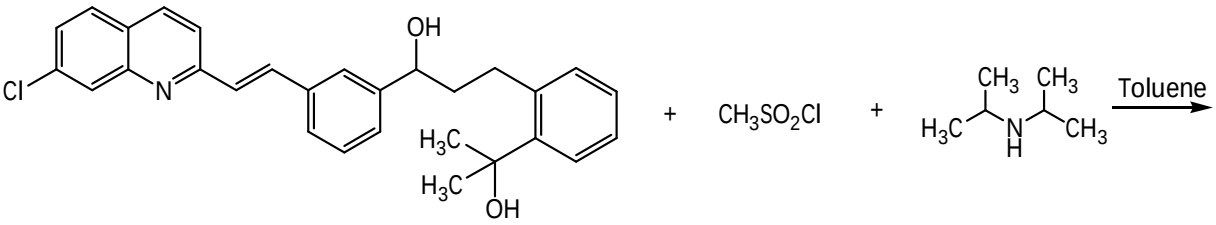
Methanol

32.04

Magnesium chloride

2X95.21=190.42

Stage-6:



1-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-3-[2-(1-hydroxy-1-methyl-ethyl)-phenyl]-propan-1-ol

$C_{29}H_{28}ClNO_2$

457.99

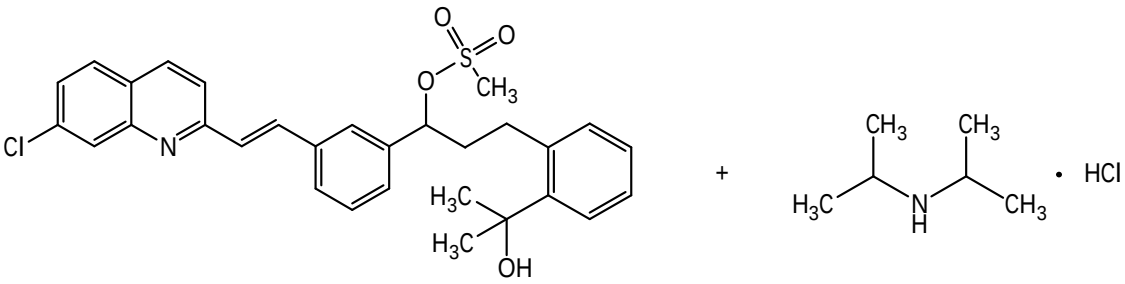
Methane sulfonyl chloride

114.55

Diisopropylamine

$C_6H_{15}N$

101.19



Methanesulfonic acid 1-{3-[2-(7-chloro-quinolin-2-yl)-vinyl]-phenyl}-3-[2-(1-hydroxy-1-methyl-ethyl)-phenyl]-propyl ester

$C_{30}H_{30}ClNO_4S$

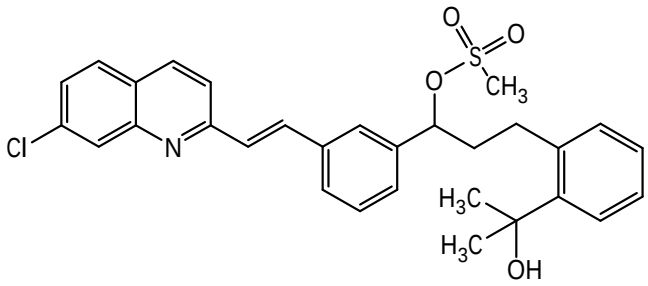
536.08

Diisopropylamine Hydrochloride

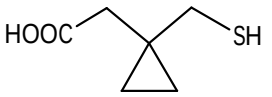
$C_6H_{14}N.HCl$

137.65

Stage-7:



\+



Ethyl acetate →

Methanesulfonic acid 1-{3-[2-(7-chloro-quinolin-2-yl)-vinyl]-phenyl}-3-[2-(1-hydroxy-1-methyl-ethyl)-phenyl]-propyl ester

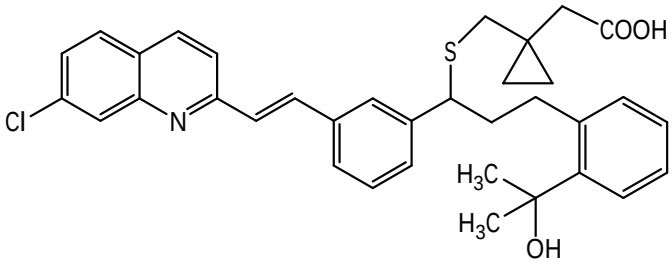
$C_{30}H_{30}ClNO_4S$

536.08

(1-Mercaptomethyl cyclopropyl) acetic acid

$C_6H_{10}O_2S$

146.20



\+ CH_3SO_3H

(1-{1-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-3-[2-(1-hydroxy-1-methyl-ethyl)-phenyl]-propylsulfanylmethyl}-cyclopropyl)-acetic acid

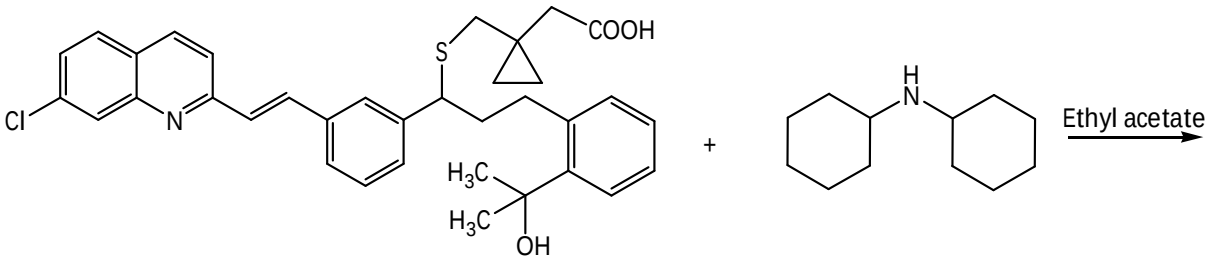
$C_{35}H_{36}ClNO_3S$

586.18

Methane sulfonic acid

96.10

Stage-8:



(1-{1-{3-[2-(7-Chloro-quinolin-2-yl)-vinyl]-phenyl}-3-[2-(1-hydroxy-1-methyl-ethyl)-phenyl]-propylsulfanylmethyl}-cyclopropyl)-acetic acid

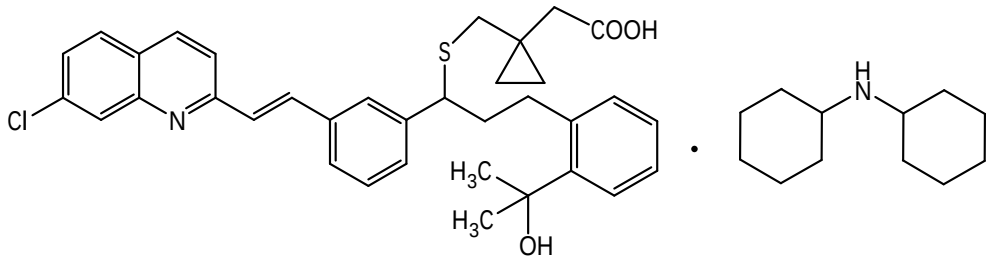
$C_{35}H_{36}ClNO_3S$

586.18

Dicyclohexylamine

$C_{12}H_{23}N$

181.31

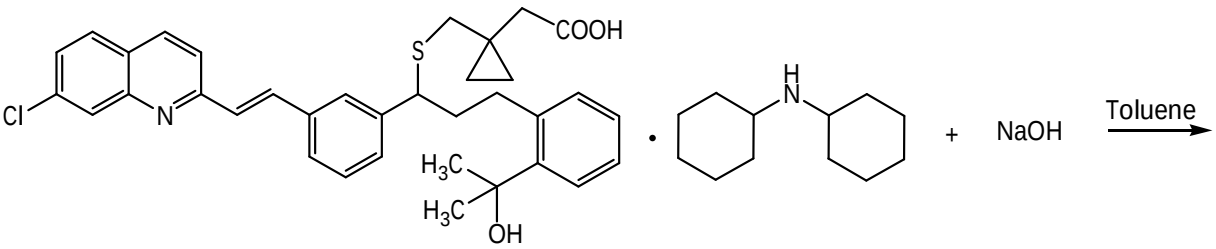


Montelukast Dicyclohexylamine

$C_{47}H_{59}ClN_2O_3S$

767.50

Stage-9:



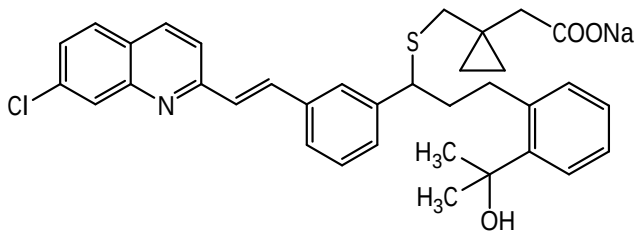
Montelukast Dicyclohexylamine

$C_{47}H_{59}ClN_2O_3S$

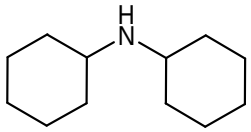
767.50

Sodium hydroxide

40.00



+



+ H_2O

Montelukast sodium

$C_{35}H_{35}ClNNaO_3S$

608.16

Dicyclohexylamine

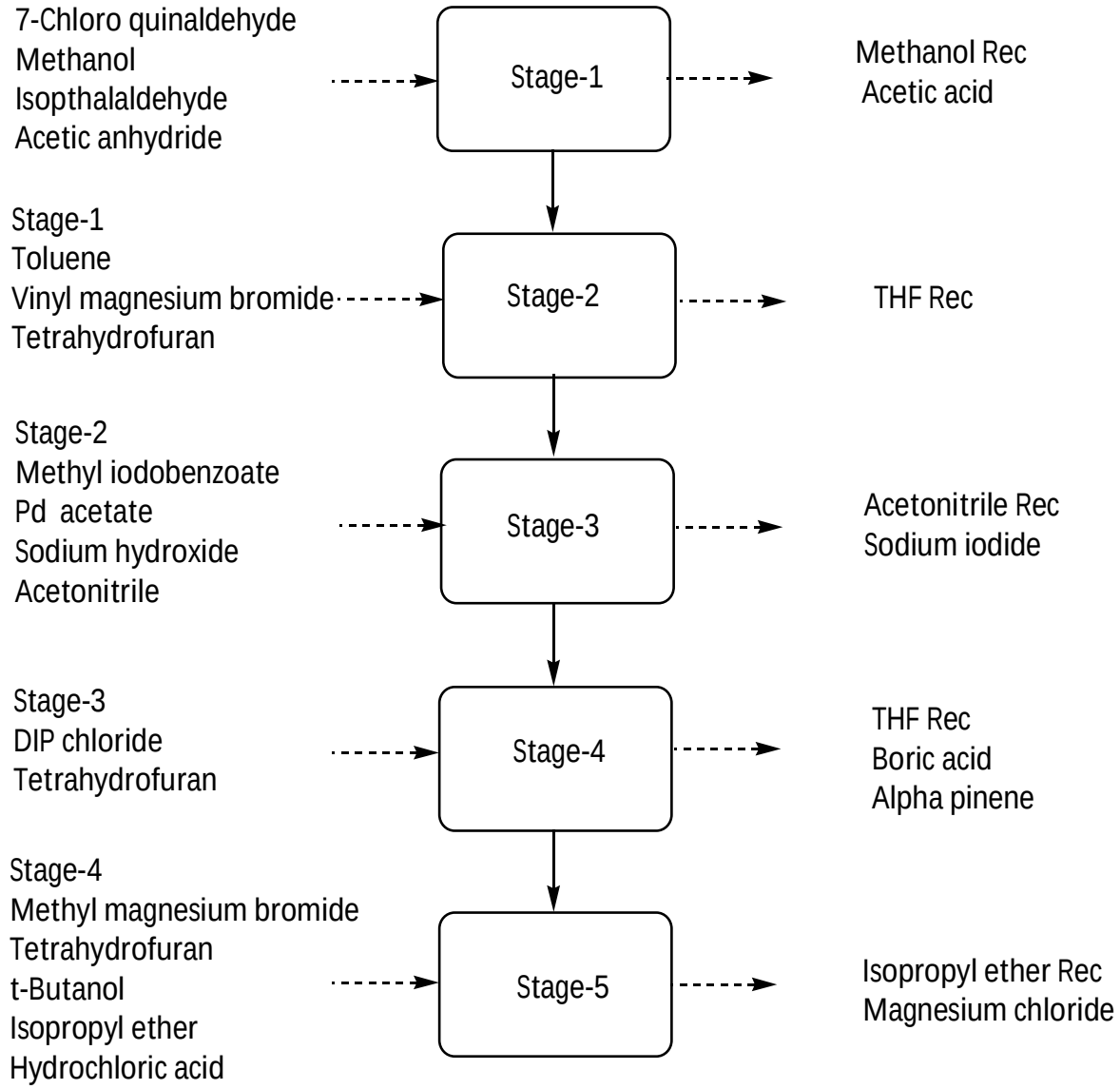
$C_{12}H_{23}N$

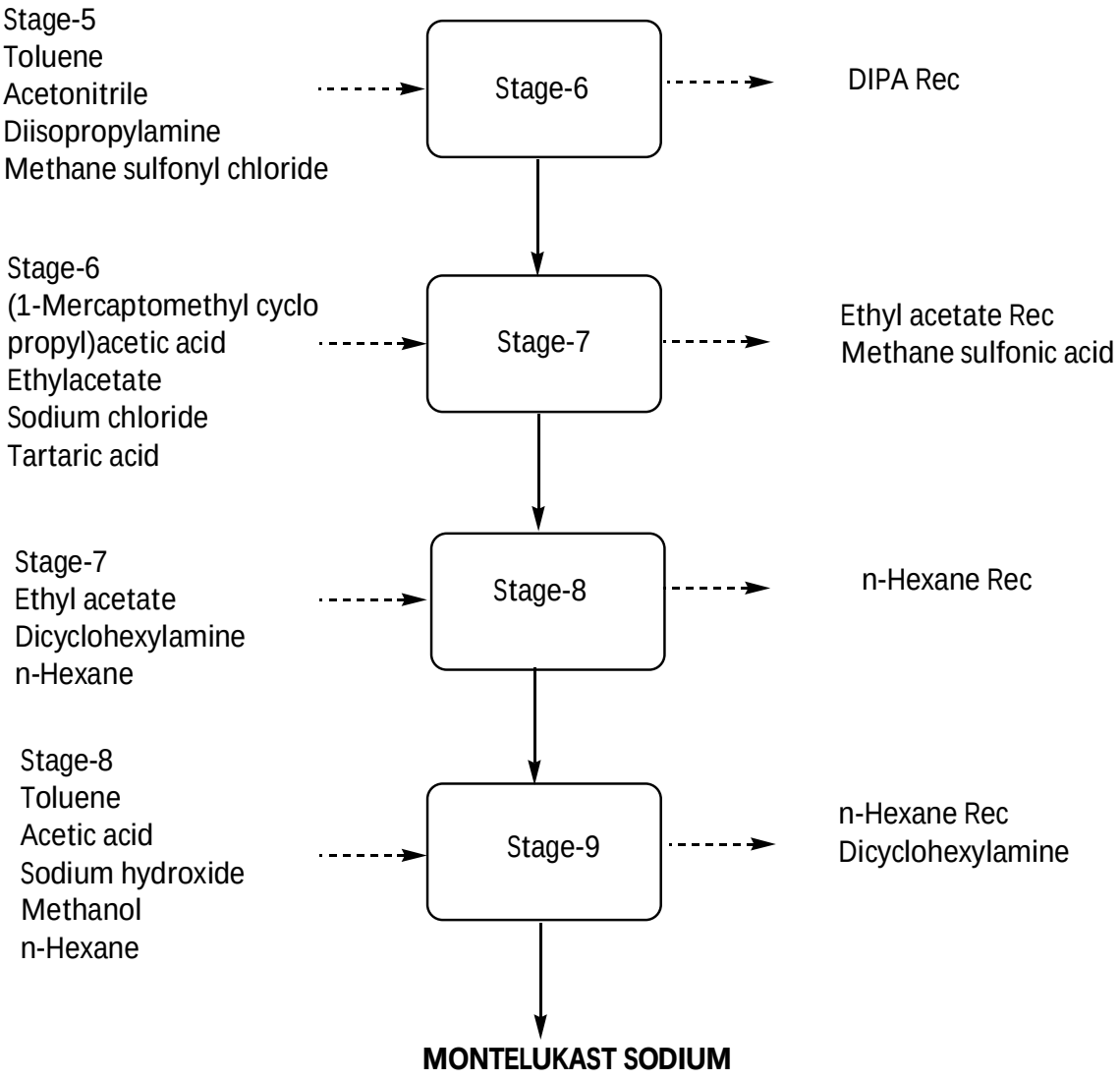
181.31

18.00

MONTELUKAST SODIUM

Flow Chart:




Stage-5
Toluene
Acetonitrile
Diisopropylamine
Methane sulfonyl chloride
Stage-6
DIPA Rec
Stage-6
(1-Mercaptomethyl cyclo propyl)acetic acid
Ethylacetate
Sodium chloride
Tartaric acid
Stage-7
Ethyl acetate Rec
Methane sulfonic acid
Stage-7
Ethyl acetate
Dicyclohexylamine
n-Hexane
Stage-8
n-Hexane Rec
Stage-8
Toluene
Acetic acid
Sodium hydroxide
Methanol
n-Hexane
Stage-9
n-Hexane Rec
Dicyclohexylamine
MONTELUKAST SODIUM

MONTELUKAST SODIUM

Material Balance:

Material Balance of Montelukast sodium Stage-1 Batch Size: 100.00Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
7-Chloro quinaldehyde	80.00		Stage-1	120.00
Iso pthalaldehyde	60.00		Methanol Recovery	186.00
Acetic anhydride	50.00		Methanol Loss	10.00
Methanol	200.00		Acetic acid Recovery	52.00
			Organic Residue	22.00
			(Organic impurities-16,Acetic acid-2,Methanol-4)	
Total	390		Total	390.00

Material Balance of Montelukast sodium Stage-2 Batch Size: 100.00 Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-1	120.00		Stage-2	120.00
Vinyl magnesium bromide in tetra hydrofuran	145.00		Toluene Recovery	282.00
Toluene	300.00		Toluene Loss	12.00
Water	600.00		Tetra hydrofuran Recovery	82.00
			Tetra hydrofuran Loss	3.00
			Effluent Water	644.00
			(Water-593,Magnesium hydroxyl bromide-49,Tetrahydrofuran-2)	
			Organic Residue	22.00
			(Organic Impurities-16,Toluene-6)	
Total	1165.00		Total	1165.00

Material Balance of Montelukast sodium Stage-3 Batch Size: 100.00Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-2	120.00		Stage-3	155.00
Methyl iodo benzoate	100.00		Acetonitrile recovery	225.00
Catalyst	1.00		Acetonitrile Loss	10.00
Sodium hydroxide	20.00		Catalyst Recovery	1.00
Acetonitrile	240.00		Effluent water	788.00
Water	720.00		(Water-720, gen.water-7,Sodium iodide-56,Sodium hydroxide-5)	
			Organic Residue	22.00
			(Organic impurities-17,Acetonitrile-5)	
Total	1201.00		Total	1201.00

Material Balance of Montelukast sodium Stage-4 Batch Size:100.00Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-3	155.00		Stage-4	140.00
DIP chloride	115.00		Alpha pinene(By product)	92.00
Tetra hydrofuran	235.00		Tetra hydrofuran Recovery	220.00
Water	465.00		Tetra hydrofuran Loss	10.00
			Effluent Water	471.00
			(Water-447,Boric acid-21, THF-3)	
			Organic Residue	24.00
			(Organic impurities-22, Tetrahydrofuran-2)	
			Process Emissions	13.00
			(Hydrogen chloride-12,Hydrogen-1)	
Total	970.00		Total	970.00

Material Balance of Montelukast sodium Stage-5 Batch Size:100.00 Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-4	140.00		Stage-5	125.00
Methyl magnesium chloride in Tetra hydrofuran	184.00		Tetra hydrofuran Recovery	130.00
t-Butanol	28.00		Tetra hydrofuran Loss	5.00
Isopropyl ether	280.00		t-Butanol Recovery	26.00
Hydrochloric acid	85.00		t-Butanol Loss	1.00
Water	700.00		Isopropyl ether Recovery	265.00
			Isopropyl ether Loss	10.00
			Effluent water	835.00
			(Water-700, Water from hydrochloric acid-55,Magnesium chloride-58, Hydrochloric acid-8, Tetrahydrofuran-3,t-Butanol-1, Methanol-10)	
			Organic Residue	20.00
			(Organic impurities-15,Isopropyl ether-5)	
Total	1417.00		Total	1417.00

Material Balance of Montelukast sodium Stage-6 Batch Size: 100.00 Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-5	125.00		Stage-6	125.00
Methane sulfonyl chloride	35.00		Toluene Recovery	360.00
Toluene	375.00		Toluene Loss	15.00
Acetonitrile	500.00		Acetonitrile Recovery	475.00
Diisopropyl amine	30.00		Acetonitrile Loss	25.00
			Organic Residue	65.00
			(Organic impurities-22.95, Di iso propyl amine Hydrochloride-42.05)	
Total	1065.00		Total	1065.00

Material Balance of Montelukast sodium Stage-7 Batch Size: 100.00Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-6	125.00		Stage-7	120.00
Tetra hydrofuran	500.00		Tetra hydrofuran Recovery	470.00
(1-Mercaptomethyl cyclo propyl)acetic acid	35.00		Tetra hydrofuran Loss	20.00
N-Butyl lithium in cyclohexane (15%)	250.00		Ethyl acetate Recovery	465.00
Ethyl acetate	500.00		Ethyl acetate Loss	25.00
Sodium chloride (10%)	1500.00		Cyclo hexane Recovery	212.50
Tartaric acid (5%)	1000.00		Effluent water	2569.50
			(Methane sulfonic acid-22,Sodium chloride-150,n-Butyl lithium - 37.5, Tetrahydrofuran-10,Tartaric acid-50,Water from sodium chloride-1350, water from Tartaric acid-950)	
			Organic Residue	28.00
			(Organic impurities-18, Ethylacetate-10)	
Total	3910.00		Total	3910.00

Material Balance of Montelukast sodium Stage-8 Batch Size: 100.00Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-7	120.00		Stage-8	145.00
Ethyl acetate	500.00		Ethyl acetate Recovery	465.00
Dicyclohexyl amine	50.00		Ethyl acetate Loss	25.00
n-Hexane	500.00		n-Hexane Recovery	465.00
			n-Hexane Loss	25.00
			Organic Residue	45.00
			(Organic impurities-25,Ethyl acetate-10,n-Hexane-10)	
Total	1170.00		Total	1170.00

Material Balance of Montelukast sodium Stage-9 Batch Size:100.00 Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-8	145.00		Montelukast sodium	100.00
Toluene	650.00		Toluene Recovery	612.50
Acetic acid	140.00		Toluene Loss	32.00
Sodium hydroxide in Methanol (50%)	20.00		n-Hexane Recovery	471.00
n-Hexane	500.00		n-Hexane Loss	25.00
Water	2610.00		Acetic acid Recovery	130.00
			Acetic acid Loss	7.00
			Effluent Water	2667.00
			(Water-2610,generated water-3, Acetic acid-3,Dicyclohexylamine-34,Methanol-10,Sodium hydroxide-3,Toluene-2,n-Hexane-2)	
			Organic Residue	20.50
			(Organic impurities-16.50,Toluene-2, n-Hexane-2)	
Total	4065.00		Total	4065.00

PREGABALIN

Process Description:

Stage-1

Isoveraldehyde reacts with diethyl malonate in the presence of n-hexane as solvent media to give stage–1 as product.

Stage-2

Stage-1 reacts with sodium cyanide and acetic acid in the presence of ethanol as solvent media to give stage–2 as product.

Stage-3

Stage –2 reacts with potassium hydroxide, water and acetic acid by passing hydrogen gas in the presence of raney nickel acting as catalyst to give stage –3 as product.

Stage-4

Stage –3 reacts with mandelic acid in the presence of isopropyl alcohol as solvent media to give Stage –4 as product.

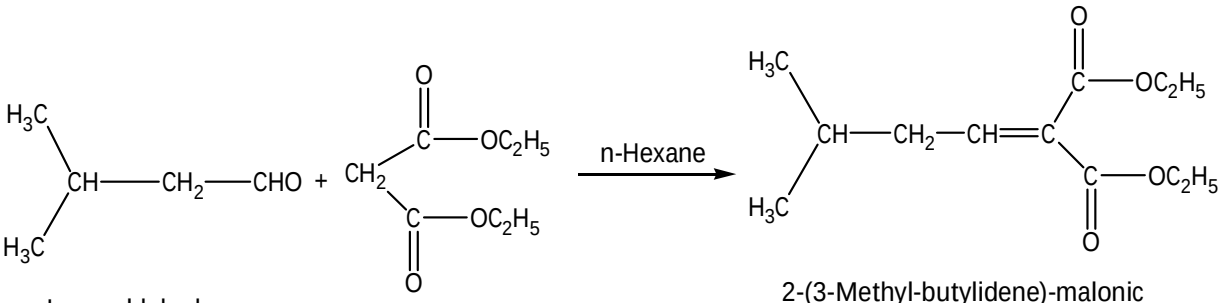
Stage-5

Stage –4 undergoes hydrolysis with tetrahydrofuran to give pregabalin as product.

PREGABALIN

Route of Synthesis:

Stage -1



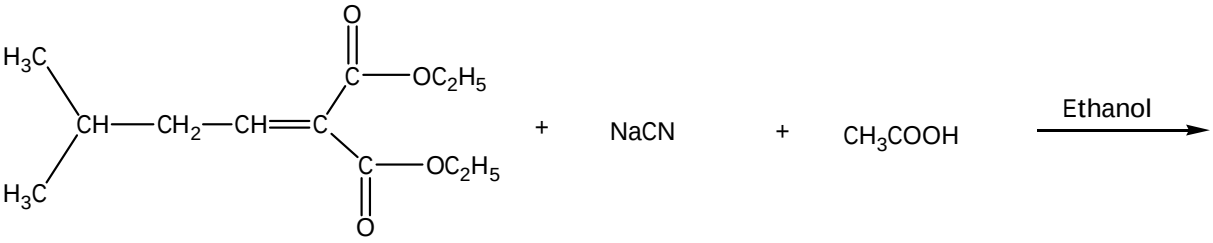
Isoveraldehyde
$C_5H_{10}O$
86.13

Diethyl malonate
$C_7H_{12}O_4$
160.17

2-(3-Methyl-butylidene)-malonic acid diethyl ester
$C_{12}H_{20}O_4$
228.28

+ H_2O
18.00

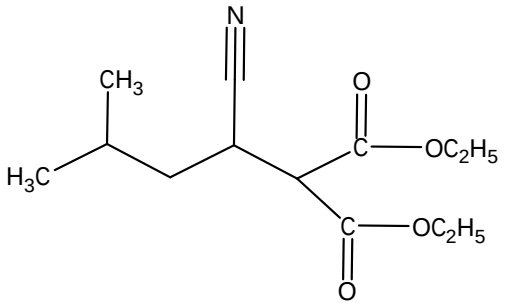
Stage - 2



2-(3-Methyl-butylidene)-malonic acid diethyl ester
$C_{12}H_{20}O_4$
228.28

Sodium cyanide
49.00

Acetic acid
60.05

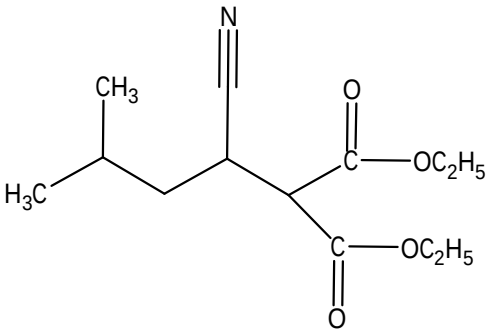


+ CH_3COONa

2-(1-Cyano-3-methyl-butyl)-malonic acid diethyl ester
$C_{13}H_{21}NO_4$
255.31

Sodium acetate
82.03

Stage - 3



+ $2H_2$ + KOH + CH_3COOH + H_2O

2-(1-Cyano-3-methyl-butyl)-malonic acid diethyl ester
$C_{13}H_{21}NO_4$
255.31

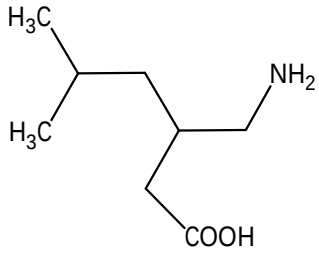
Hydrogen
2X2=4.0

Potassium hydroxide
56.11

Acetic aid
60.05

18.00

Raney Nickel



+ CH_3COOK + $2\ C_2H_5OH$ + CO_2 ↑

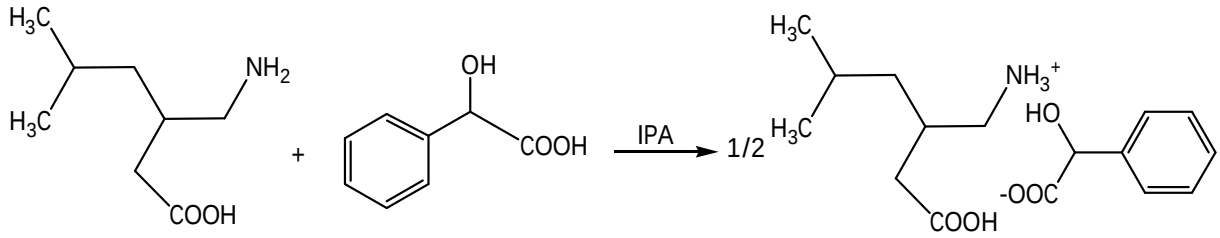
3-Aminomethyl 5 -methyl hexanoic acid
$C_8H_{17}NO_2$
159.23

98.14

2 X46.07=92.14

44.00

Stage -4



3-Aminomethyl 5 -methyl hexanoic acid
$C_8H_{17}NO_2$
159.23

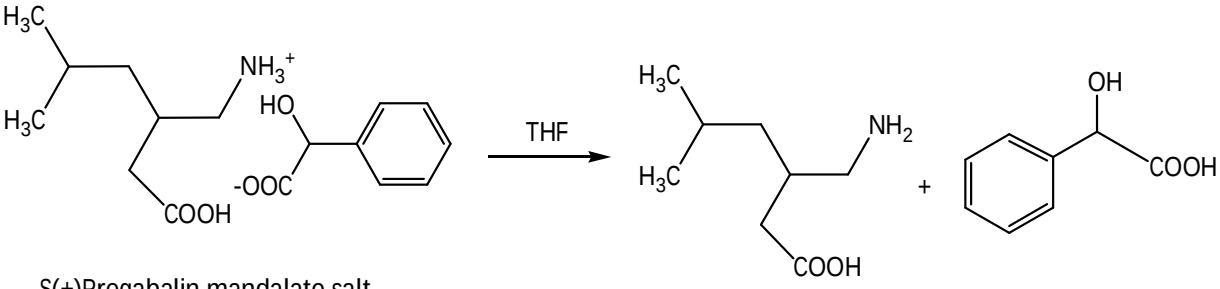
Mandelic acid
$C_8H_8O_3$
152.14

S(+)Pregabalin mandalate salt
$C_{16}H_{25}NO_5$
1/2X311.37=155.68

\+ 1/2 (R)-Isomer

1/2X311.37=155.68

Stage -5



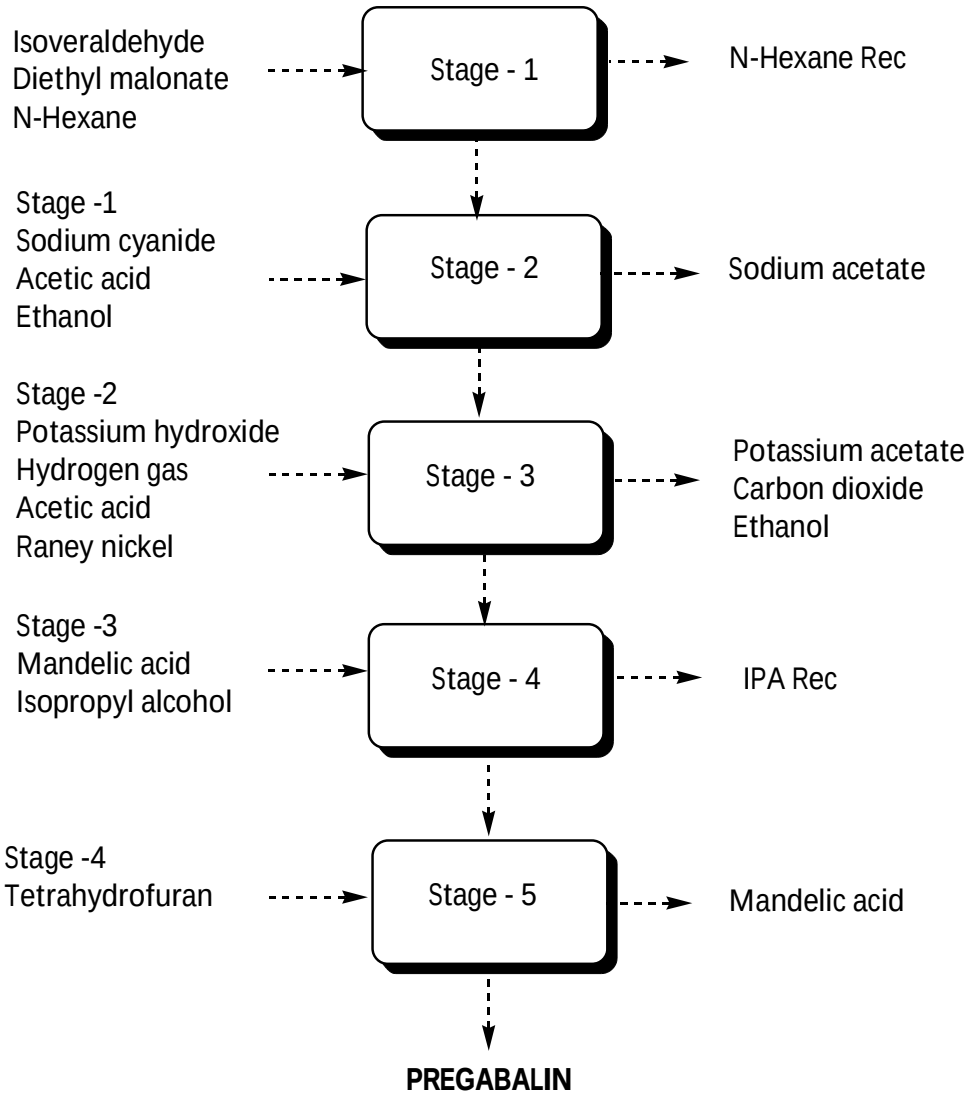
S(+)Pregabalin mandalate salt
$C_{16}H_{25}NO_5$
311.37

S(+)Pregabalin
$C_8H_{17}NO_2$
159.23

Mandelic acid
$C_8H_8O_3$
152.14

PREGABALIN

Flow Chart:



PREGABALIN

Material Balance:

Material Balance Of Pregabalin Stage-1 Batch Size: 50.0Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Isoveraldehyde	98.00		Stage –1	221.00
Diethyl malonate	185.00		n-Hexane Recovery	171.00
Acetic acid	13.00		n-Hexane Loss	9.00
Di isopropyl amine	10.00		Effluent Water	1781.18
n-Hexane	180.00		(Water-1735,generated water-20.5,Diisopropyl Amine-10,Acetic Acid-13,Diethyl Malonate-2.68)	
Water	1735.00		Organic Residue	38.82
			(Organic Impurities)	
Total	2221.00		Total	2221.00

Material Balance Of Pregabalin Stage-2 Batch Size: 50.0Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage –1	221.00		Stage-2	225.00
Sodium cyanide	47.50		Toluene Recovery	470.00
Ethanol	900.00		Toluene Loss	25.00
Toluene	500.00		Ethanol Recovery	855.00
Acetic acid	60.00		Ethanol Loss	45.00
Water	1000.00		Effluent Water	1084.30
			(Water-1000,Sodium Acetate-79.5,Acetic Acid-1.8,Toluene-3)	
			Organic Residue	24.20
			(Organic Impurities-22.2, Toluene-2)	
Total	2728.50		Total	2728.50

Material Balance Of Pregabalin Stage-3 Batch Size: 50.0Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-2	225.00		Stage-3	120.00
Methanol	220.00		Methanol Recovery	209.00
Potassium hydroxide	50.00		Methanol loss	11.00
Acetic acid	60.00		IPA Recovery	333.00
Raney nickel	30.00		IPA Loss	17.00
Ethanol	50.00		Ethanol Recovery	123.00
IPA	350.00		Raney Nickel Reuse	30.00
Hydrogen gas	5.00		Effluent water	1885.90
Water	1800.00		(Water-1784,Potassium Acetate-86.7,Ethanol-6.2, Acetic Acid-7,IPA-2)	
			Organic Residue	20.92
			Process Emission	40.18
			(Carbon dioxide-38.7, Hydrogen-1.48)	
Total	2790.00		Total	2790.00

Material Balance Of Pregabalin Stage-4 Batch Size: 50.0Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-3	120.00		Stage -4	110.00
(S)-Mandelic acid	118.00		IPA Recovery	908.00
Isopropyl alcohol	960.00		IPA Loss	48.00
Water	1300.00		Effluent water	1305.28
			(Water-1300,Mandelic acid-3.28,IPA-2)	
			R-Isomer Recycle	110.00
			Organic Residue	16.72
			(Organic Impurities-14.72, IPA-2)	
Total	2498.00		Total	2498.00

Material Balance Of Pregabalin Stage-5 Batch Size:50.0Kgs				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage -4	110.00		Pregabalin	50.00
Tetrahydrofuran	900.00		THF Recovery	852.00
Isopropyl alcohol	560.00		THF Loss	45.00
Water	1660.00		IPA Recovery	530.00
			IPA Loss	28.00
			Effluent water	1718.79
			(Water-1660,Mandelic acid-53.79,THF-3,Isopropyl alcohol-2)	
			Organic Residue	6.21
Total	3230.00		Total	3230.00

SEVELAMER HYDROCHLORIDE

Process Description

Stage-1

Ally amine Reacts with Hydrochloric acid in presence of Methanol as a solvent media to give Stage-1 as a product.

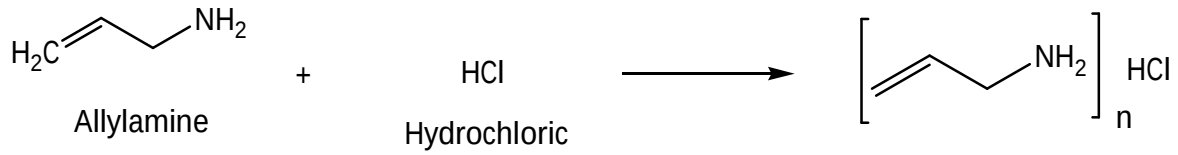
Satge-2

Sateg-1 product reacts with Epichloro hydrin in presence of Methanol as a solvent media to give Sevelamer Hydrochloride as a product.

SEVELAMER HYDROCHLORIDE

Route of synthesis

Stage-1

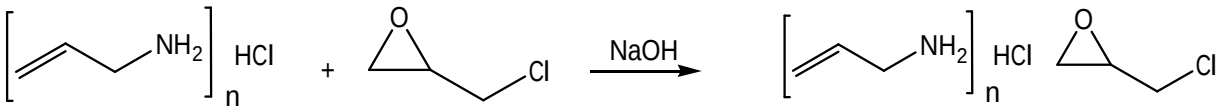


Allylamine
C_3H_7N
57.00

Hydrochloric acid
36.5

Poly allylamine Hydrochloride
C_3H_8ClN
93.56

Stage-2



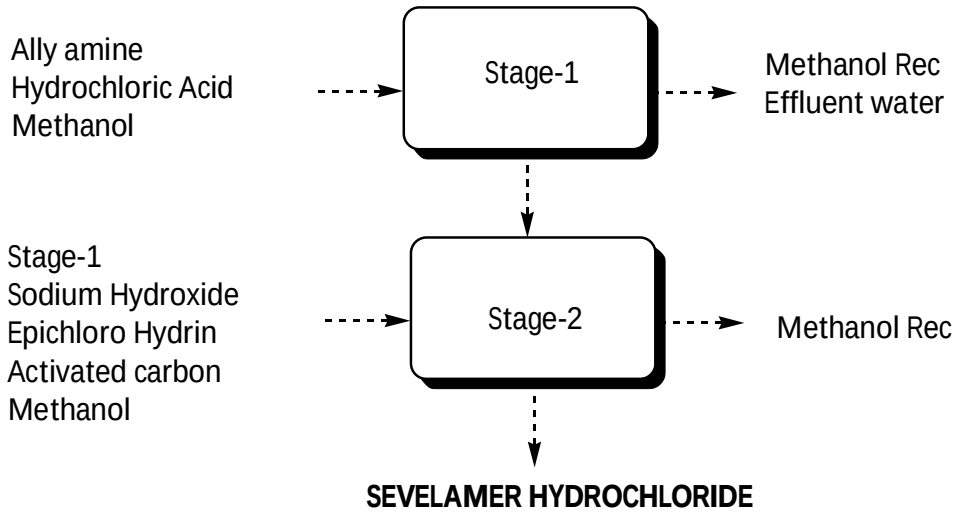
Poly allylamine Hydrochloride
$[C_3H_8ClN]_n$
93.56

2-Chloromethyl-oxirane
C_3H_5ClO
92.52

Sevelamer Hydrochloride
$[C_6H_{13}Cl_2NO]_n$
186.08

SEVELAMER HYDROCHLORIDE

Flow Chart



SEVELAMER HYDROCHLORIDE

Material Balance:

Material Balance of Sevelamer Hydrochloride Stage-1 Batch Size:100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Ally amine	33.50		Stage-1	55.00
Hydrochloric Acid	21.50		Methanol Recovery	285.00
Methanol	300.00		Methanol Loss	15.00
Total	355.00		Total	355.00

Material Balance of Sevelamer Hydrochloride Stage-2 Batch Size:100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-1	55.00		Sevelamer Hydrochloride	100.00
Sodium Hydroxide	20.00		Methanol Recovery	285.00
Epichloro Hydrin	54.00		Methanol Loss	15.00
Activated carbon	5.00		IPA Recovery	285.00
Methanol	300.00		IPA Loss	15.00
Isopropyl Alcohol	300.00		Effluent water	520.00
Water	500.00		(Water-500,Sodium hydroxide-20)	
			Spent carbon	5.00
			Organic Residue	9.00
Total	1234.00		Total	1234.00

TADALAFIL

Process Description:

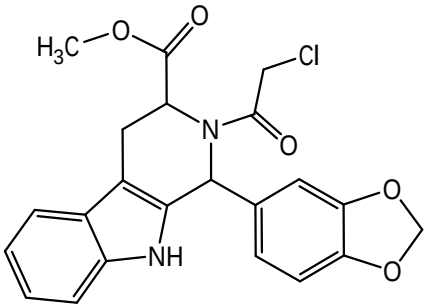
Stage-1

1-Benzo[1,3]dioxol-5-yl-9-(2-chloro-acetyl)-2,3,4,9-tetrahydro-1H-b-carboline-3-carboxylic acid methyl ester reacts with Methyl amine in the presence of Methanol as a solvent media to give Tadalafil as product.

TADALAFIL

Route of Synthesis:

Stage-1:



1-Benzo[1,3]dioxol-5-yl-9-(2-chloro-acetyl)-2,3,4,9-tetrahydro-1*H*-b-carboline-3-carboxylic acid methyl ester

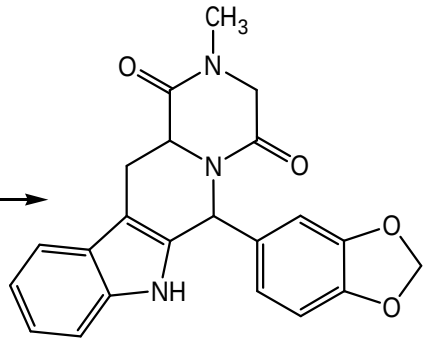
$C_{22}H_{19}ClN_2O_5$

426.84

+ CH_3NH_2

Methylamine

31.05



Tadalafil

$C_{22}H_{19}N_3O_4$

389.40

+ CH_3OH

Methanol

32.04

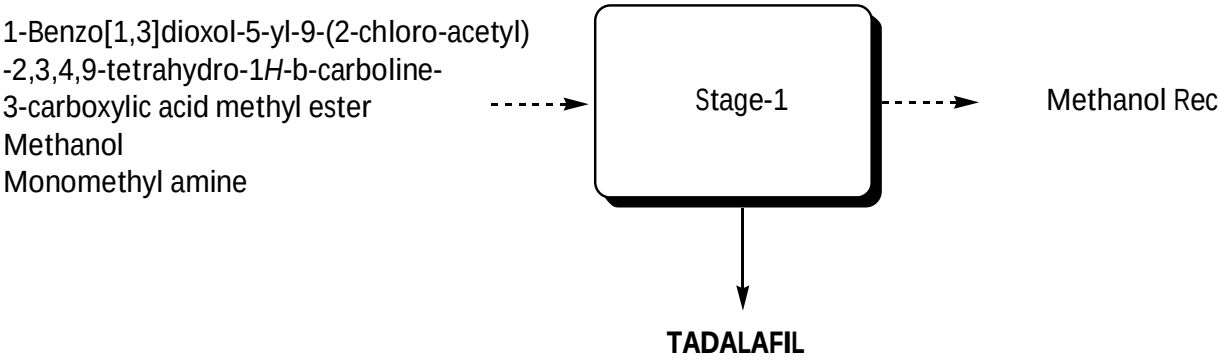
+ HCl

Hydrochloric acid

36.5

TADALAFIL

Flow Chart:



TADALAFIL

Material Balance:

Material balance of Tadalafil Stage-1 Batch Size:100.0Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity In Kg
(1R,3R)-Methyl-1-(benzo [d][1,3]dioxol-5-yl)-2-(2-chloro acetyl)-2,3,4,9-tetrahydro-1H- pyrido[3,4-b]indole-3-carboxylate (Tadalafil intermediate)	116.00		Tadalafil	100.00
Mono methylamine (40%)	206.00		Methanol Recovery	665.00
Methanol	700.00		Methanol Loss	35.00
Water	1000.00		Effluent water	1216.16
			(Water-1000,Water from Mono Methylamine-131.6, Monomethylamine-66.40, Methanol- 8.25, Hydrochloric acid-9.91)	
			Organic Residue	5.84
Total	2022.00		Total	2022.00

TIZANIDINE HYDROCHLORIDE

Process Description:

Stage-1

4-Amino-5-chloro-2, 1, 3-benzothiadiazole is condensed with 1-acetyl imidazolin-2-one reacts with phosphorous oxychloride and sodium hydroxide in water to give stage-1 as product.

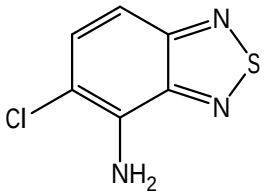
Stage-2

Stage-1 product reacts with Hydrochloric acid in methanol to give Tizianidine Hydrochloride as product.

TIZANIDINE HYDROCHLORIDE

Route of Synthesis:

Stage-1

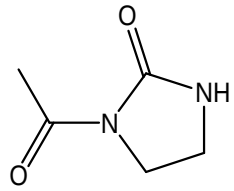


5-Chloro-benzo[1,2,5]thiadiazol-4-ylamine

$C_6H_4ClN_3S$

185.63

+



1-Acetyl-imidazolidin-2-one

$C_5H_8N_2O_2$

128.13

+ $POCl_3$

Phosphorous oxychloride

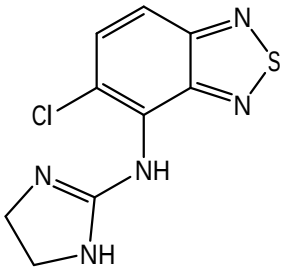
153.33

+ 4NaOH

Sodium hydroxide

4X40=160.0

Water



Tizianidine

$C_9H_8ClN_5S$

253.71

+ CH_3COOH

60.0

+ 3NaCl

3X58.5=175.5

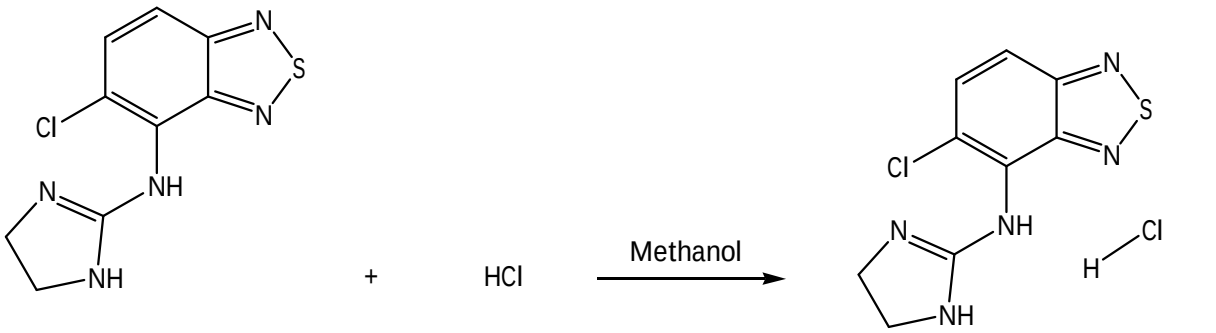
+ NaH_2PO_4

119.98

+ H_2O

18.0

Stage-2:



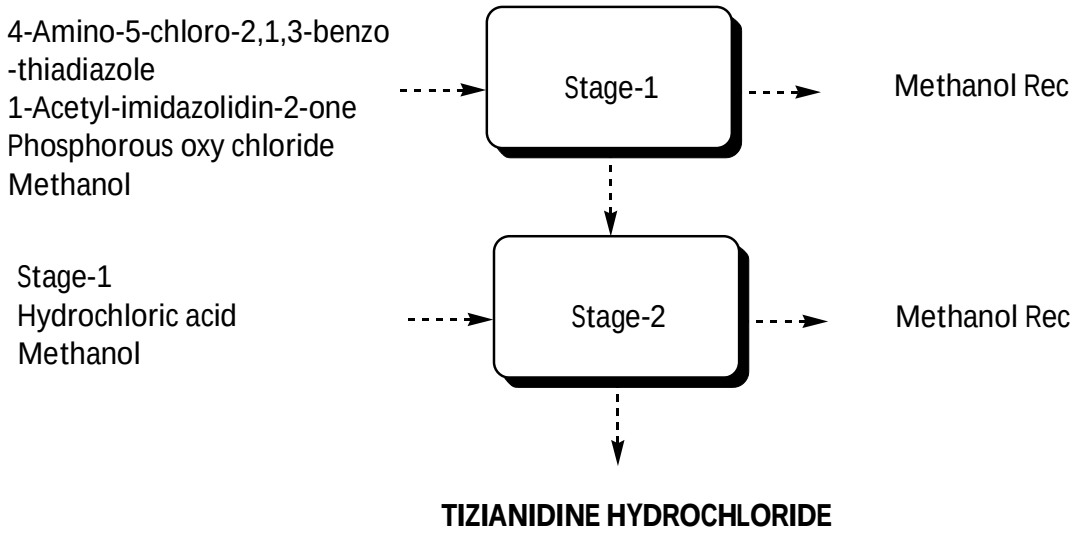
Tizianidine
$C_9H_8ClN_5S$
253.71

Hydrochloric acid
36.50

Tizianidine Hydrochloride (Crude)
$C_9H_9Cl_2N_5S$
290.21

TIZANIDINE HYDROCHLORIDE

Flow Chart:



TIZANIDINE HYDROCHLORIDE

Material Balance:

Material balance of Tizianidine Hydrochloride Stage-1 Batch Size:100.0 Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity In Kg
4-Amino-5-chloro-2,1,3-benzo-thiadiazole	68.00		Stage-1	93.00
1-Acetyl-imidazolidin-2-one	47.00		Effluent water	3305.73
Phosphorous oxy chloride	56.50		(Water-3200,Acetic acid-22.02, Sodium chloride-32.9,Sodium dihydrogen phosphate-44.21, Generated water-6.6)	
Sodium hydroxide	30.00		Organic Residue	2.77
Water	3200.00			
Total	3401.50		Total	3401.50

Material balance of Tizianidine Hydrochloride Stage-2 Batch Size:100.0 Kg				
Name of the input	Quantity in Kg		Name of the out put	Quantity In Kg
Stage-1	93.00		Tizianidine Hydrochloride	100.00
Hydrochloric acid	15.00		Methanol Recovery	475.00
Methanol	500.00		Methanol Loss	25.00
			Organic Residue	8.00
Total	608.00		Total	608.00

VALACYCLOVIR HYDROCHLORIDE MONOHYDRATE

Process Description:

Stage-1

2-(Acetylamine)-1,9-dihydro-9-[[2-(acetyloxy)ethoxy]methyl]-6h-purin-6-one condensed with carbobenzyloxy-L-valine in the presence of 40% Dimethylamine, Dimethylformamide, 4-Dimethylamine pyridine and 1,3-Dicyclohexyl carbodimide to yield 2-[(2-Amino-1,6-dihydro-6-oxo-9H-purin-9-yl)methoxy]ethyl N-[(benzyloxy) carbonyl] L-Valine(Stage-I Compound).

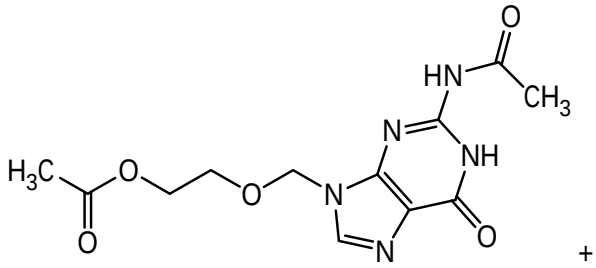
Stage-2

2-[(2-Amino--1,6-dihydro-6-oxo-9H-purin-9-yl)methoxy]ethyl N-[(benzyloxy)carbonyl] L-Valine is redused with H_2 Using palladium on carbon as catalysed and further Reacted with Hydrochloric acid and water to yield Valcyclovir Hydrochloride monohydrate.

VALACYCLOVIR HYDROCHLORIDE MONOHYDRATE

Route of Synthesis

Stage-1

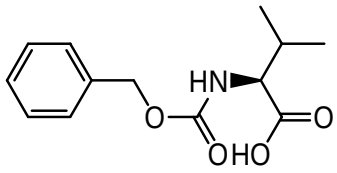


2-(Acetylamino)-1,9-dihydro-9-[[2-(acetyloxy) ethoxy]methyl]-6H-purin-6-one

$C_{12}H_{15}N_5O_5$

309.28

\+



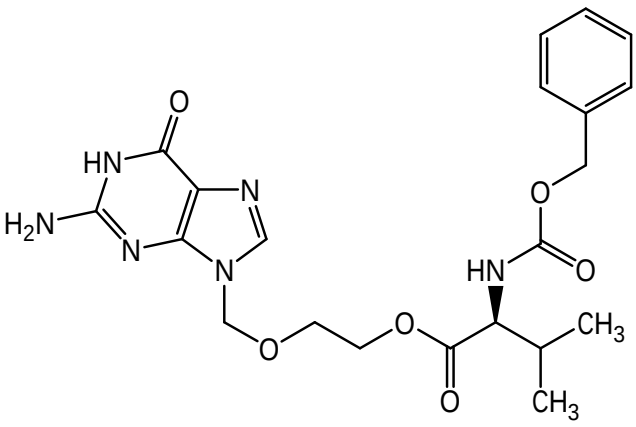
Carbobenzyloxy-L-Valine

$C_{13}H_{17}NO_4$

251.28

\+ H_2O

18.00



2-[(2-Amino-1,6-dihydro-6-oxo-9H-purin-9-yl) methoxy]ethyl N-[(benzyloxy)carbonyl] L-Valine

$C_{21}H_{26}N_6O_6$

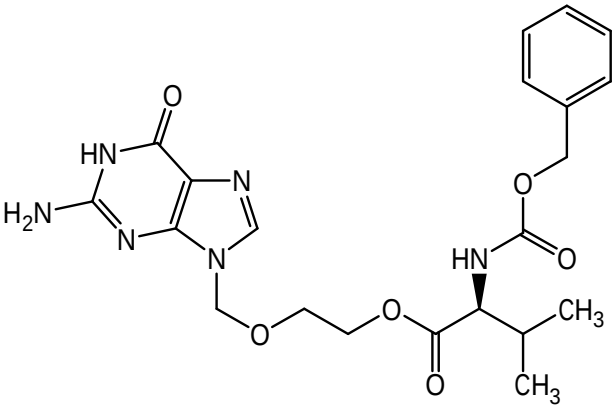
458.47

\+ 2 CH_3COOH

Acetic acid

120.0

Stage-2



2-[(2-Amino-1,6-dihydro-6-oxo-9H-purin-9-yl) methoxy]ethyl N-[(benzyloxy)carbonyl] L-Valine

$C_{21}H_{26}N_6O_6$

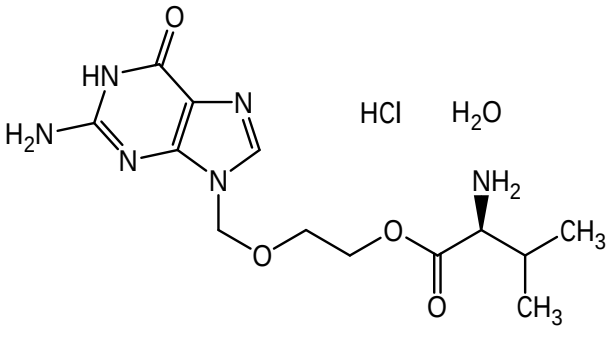
458.47

\+ HCl + H_2O + H_2

Hydrochloric acid 18.0 2.00

36.5

Pd/C

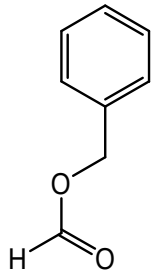


Valcyclovir Hydrochloride monohydrate

$C_{13}H_{23}ClN_6O_5$

378.81

\+



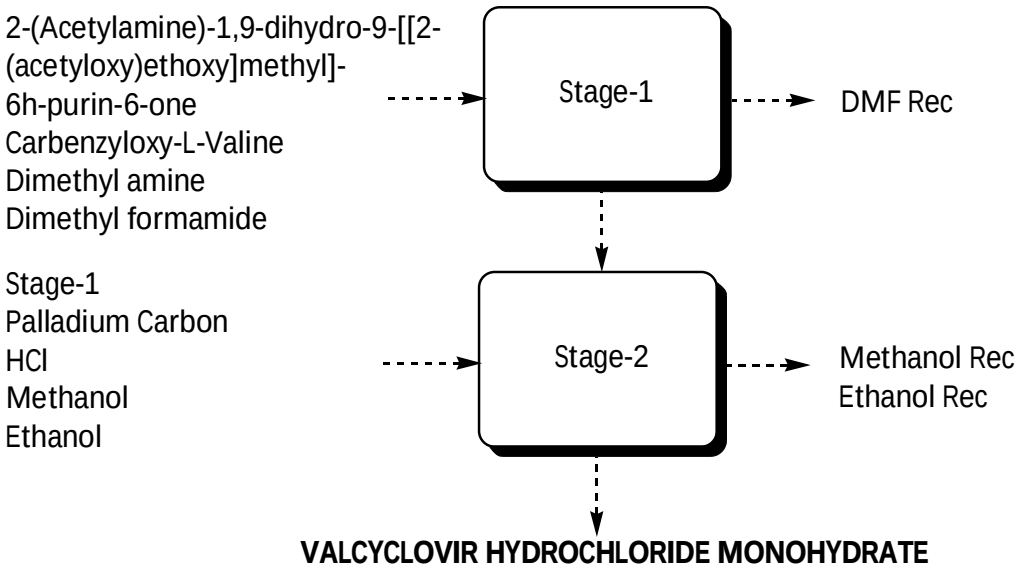
Phenylacetic acid

$C_8H_8O_2$

136.15

VALCYCLOVIR HYDROCHLORIDE MONOHYDRATE

Flow Chart



VALCYCLOVIR HYDROCHLORIDE MONOHYDRATE

Material Balance

Material Balance of Valcyclovir HCl Monohydrate Stage-1 Batch Size: 100.0Kg's				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
2-(Acetylamine)-1,9-dihydro-9-[[2-(acetyloxy)ethoxy]methyl]-6h-purin-6-one	102.00		Stage-I	150.00
Carbenzyloxy-L-Valine	83.00		Dimethyl amine Recovery	475.00
Dimethyl amine	500.00		Dimethyl amine Loss	25.00
Dimethyl formamide	800.00		DMF Recovery	760.00
4-Dimethylamino pyridine	5.00		DMF Loss	40.00
1,3-Dicyclohexyl carbodiamide	10.00		Acetone Recovery	570.00
Acetone	600.00		Acetone Loss	30.00
Activated carbon	5.00		Ethanol Recovery	660.00
Hyflo super cel	2.00		Ethanol Loss	40.00
Ethanol	700.00		Effluent Water	1064.91
Sodium hydroxide	26.30		(Water-994.06,Generated water-11.85,Sodium acetate-54, 4-Dimethylamino pyridine-5)	
Water	1000.00		Spent carbon & Hyflow	7.00
			1,3-Dicyclohexyl carbodiamide recovery	10.00
			Organic Residue	1.39
Total	3833.30		Total	3833.30

Material Balance of Valcyclovir HCl Monohydrate Stage-2 Batch Size: 100.0Kg's				
Name of the input	Quantity in Kg		Name of the out put	Quantity in Kg
Stage-I	150.00		Valcyclovir HCl Monohydrate	100.00
Palladium Carbon	10.47		Methanol Recovery	1143.00
Hydrochloric acid	11.95		Methanol Loss	55.00
Methanol	1200.00		Ethanol Recovery	1425.00
Ethanol	1500.00		Ethanol Loss	75.00
Hydrogen	2.00		Palladium Carbon Recovered for Reuse	10.47
Activated carbon	10.00		Effluent Water	1246.54
DM Water	1200.00		(Water-1200,Phenyl acetic acid-44.54, Methanol-2)	
			Spent Carbon	10.00
			Organic Solid waste	17.41
			Process Emission	
			(Hydrogen)	2.00
Total	4084.42		Total	4084.42

Annexure-4

WATER REQUIREMENT DETAILS

S.No	Purpose	Water Requirement In KLD
1	Process	76.00
2	Washings	2.00
3	Boiler make up	41.00
4	Cooling towers make up	130.00
5	DM Plant	2.00
6	Scrubbing system	2.00
7	Domestic	3.00
8	Gardening	4.00
	Total	**260.00**

Annexure-4

WASTE WATER DETAILS

S.No	Purpose	Effluent In KLD
1	Process	81.50
2	Washings	2.00
3	Boiler Blow down	6.00
4	Cooling towers Blow down	24.00
5	DM Plant	2.00
6	Scrubbing system	2.00
7	Domestic	2.50
	Total	**120.00**

Annexure-4

HTDS &LTDS DETAILS

Unit	HTDS In KLD	LTDS In KLD	Effluent Generation In KLD	Method of Disposal
Process	71.80	9.70	81.50	HTDS Sent to stripper followed by MEE and ATFD. Condensate will be send to ETP followed by RO. LTDS Effluents sent to ETP followed by RO system.RO Rejects sent to MEE system and RO Permeate to Reuse.
Washings	0.00	2.00	2.00	
Boiler Blow Down	6.00	0.00	6.00	
Cooling towers Blow Down	0.00	24.00	24.00	
DM Plant	2.00	0.00	2.00	
Scrubber System	2.00	0.00	2.00	
Domestic	0.00	2.50	2.50	Septic tank followed by soak pit
Total	**81.80**	**38.20**	**120.00**	

Annexure-5

SOLID WASTE DETAILS

S.No.	Name of the Solid Waste	Quantity In Kg/Day	Disposal Method
1	Organic Residue	1192.50	Sent to Cement Industries
2	Inorganic solid waste	27.50	Sent to TSDF
3	MEE salts	3354.00	Sent to TSDF
3	Spent carbon	57.00	Sent to Cement Industries
4	Coal ash from Boiler	8225.00	Sent to Brick manufacturers
5	ETP Sludge	200.00	Sent to TSDF
6	Solvent Distillation bottom Residue	1563.50	Sent to Cement Industries

Annexure-5

HAZARDOUS WASTE DETAILS

S.No	Description	Quantity	Mode of Disposal
1	Waste Oils & Grease	1000 Ltrs/Annum	APPCB Authorized Agencies for Reprocessing/Recycling
2	Detoxified Containers	300 No's/Month	After Detoxification sent back to suppliers/APPCB Authorized Parties
3	Used Lead Acid Batteries	6 No's/Annum	Send back to suppliers for buyback of New Batteries

Annexure-6

STACK EMISSION DETAILS FOR BOILER

Particulars	Units	2.0 TPH Coal fired Boiler	5.0 TPH Coal fired Boiler
Type of Fuel	--	Indian Coal	Indian Coal
Coal Consumption	TPD	5.0	12.5
Ash Content	%	47	47
Sulphur Content	%	0.8	0.8
Nitrogen Content	%	1.07	1.07
No. of Stacks	No	1	1
Height of stack	M	30	32
Diameter of Stack	M	0.60	0.60
Temperature of Flue Gas	^{o}C	95	110
Velocity of Flue Gas	m/s	6.5	8.5
Particulate Matter at outlet of Bag filter (Based on 115 mg/Nm3 at outlet)	gm/sec	0.21	0.27
Sulphur dioxide emission	gm/sec	0.46	1.15
Oxides of Nitrogen emission	gm/sec	0.57	1.54

Annexure-6

STACK EMISSION DETAILS FOR DG SET

Capacity In KVA	Emission of SPM in Mg/Nm^3	Emission Of SO_2 in Mg/Nm^3	Emission of NO_x in Mg/Nm^3	Stack dia. In m	Flue Gas Temp. in ^OC	Stack Height in (m)	Flue gas Velocity In m/sec.
250KVA	58.0	24.0	30.0	0.30	250	10	18.24
500 KVA	80.0	190.0	235.0	0.30	150	10	23.20

Annexure-7

PROCESS EMISSION DETAILS

S. No	Name of the Gas	Type of the Gas	Quantity In Kg/Day	Treatment Method
1	Carbon dioxide	Non polluting Gas	308.64	Dispersed into Atmosphere
2	Hydrogen	Non-Polluting Gas	11.53	Diffused by using Nitrogen through Flame arrestor
3	Nitrogen	Non-polluting	20.75	Dispersed into atmosphere
4	Hydrogen chloride	Polluting gas	432.00	Scrubbed by using Chilled water media