



FORM I
{FOR AMENDMENT IN
ENVIRONMENT CLEARANCE}

Bulk Drug Manufacturing [API (65 TPA) and Steroid (5 TPA)] Plant At Plot No. C-24 & 25, RIICO Industrial Area, Village Sotanala, Tehsil Behror, District Alwar (Rajasthan) Reg. amendment in Environment Clearance Letter	Form 1/ Appendix-I
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APPENDIX - I

(See paragraph – 6)

FORM 1

(For Amendment in Environment Clearance)

(I) Basic Information

S. No.	Item	Details																				
1.	Name of the Project	Bulk Drug Manufacturing [API (65 TPA) and Steroid (5 TPA)] Plant at Plot No. C-25, RIICO Industrial Area, Village Sotanala, Tehsil Behror, District Alwar (Rajasthan) by M/s. Shree Jee Laboratory Pvt. Ltd.																				
2.	S. No. in the schedule	<ul style="list-style-type: none"> ❖ As per EIA Notification dated 14.09.2006, the project falls in Category 'A', S. No. - 5(f). ❖ GC is applicable on the project 																				
3.	Proposed capacity / area/ length/ tonnage to be handled/ command area/ lease area/ number of wells to be drilled	<p>Amendment in Environmental Clearance EC Letter {File no. J-11011/176/2014-IA II (I)} issued by MoEFCC, New Delhi dated 25th June, 2015 (enclosed herewith as Annexure-1)</p> <p>Product – Synthetic Drugs API : 65 TPA Steroid : 5 TPA</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: center;">S. No.</th> <th style="text-align: center;">Particular</th> <th style="text-align: center;">As per EC Letter dated 25th June, 2015</th> <th style="text-align: center;">Proposed Amendment</th> </tr> </thead> <tbody> <tr> <td style="text-align: center;">1.</td> <td>Plot No. & Area</td> <td></td> <td></td> </tr> <tr> <td></td> <td>Plot No.</td> <td style="text-align: center;">C- 25</td> <td style="text-align: center;">C- 24 & 25</td> </tr> <tr> <td></td> <td>Plot Area</td> <td style="text-align: center;">9,478 sq. m</td> <td style="text-align: center;">17,680 sq. m</td> </tr> </tbody> </table> <p>Land Allotment letter by RIICO Industrial Area is enclosed herewith as Annexure-2.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tbody> <tr> <td style="text-align: center;">2.</td> <td>Change in Product Range*</td> <td style="text-align: center;">12 API & 5 Steroids Products</td> <td style="text-align: center;">12+29 API & 5+ 2 Steroid Products</td> </tr> </tbody> </table> <p>* Keeping the total manufacturing capacity same as per the earlier granted EC</p> <p>List of Products is enclosed herewith as Annexure-3</p>	S. No.	Particular	As per EC Letter dated 25 th June, 2015	Proposed Amendment	1.	Plot No. & Area				Plot No.	C- 25	C- 24 & 25		Plot Area	9,478 sq. m	17,680 sq. m	2.	Change in Product Range*	12 API & 5 Steroids Products	12+29 API & 5+ 2 Steroid Products
S. No.	Particular	As per EC Letter dated 25 th June, 2015	Proposed Amendment																			
1.	Plot No. & Area																					
	Plot No.	C- 25	C- 24 & 25																			
	Plot Area	9,478 sq. m	17,680 sq. m																			
2.	Change in Product Range*	12 API & 5 Steroids Products	12+29 API & 5+ 2 Steroid Products																			

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4.	New/ Expansion / modernization	Amendment in earlier EC granted by MoEF&CC, dated 25 th June, 2015
5.	Existing Capacity / area etc.	Existing Capacity - Synthetic Drugs API 65 TPA & Steroid 5 TPA and Existing Area - 9478 sqm Application for EC amendment only.
6.	Category of Project i.e. 'A' or 'B'	As per EIA Notification dated 14.09.2006, the project falls in Category 'A', S. No. - 5(f). GC is applicable on the project.
7.	Does it attract the general condition? If yes, please specify	Yes, it attracts the General Condition {Interstate Boundary of Haryana – Rajasthan} within 5 km from the Proposed Unit boundary.
8.	Does it attract the specific condition? If yes please specify	No, it does not attract the specific condition.
9.	Location	
	Plot/Survey/Khasra No.	C- 24 & 25
	Village	Sotanala, RIICO Industrial Area
	Tehsil	Behror
	District	Alwar
	State	Rajasthan
10.	Nearest Railway Station / airport along with distance in KMs	❖ Narnaul Railway Station (~30 km in NW direction) ❖ New Delhi Airport (~120 km in NNE direction)
11.	Nearest Town, city, District headquarters along with distance in Kms	❖ Behror Town (~6.5 km in NNE direction)
12.	Village panchayats, Zilla parishad, municipal Corporation, local body (complete postal address with telephone nos. to be given)	Village Jainpurwas, Panchayat Bhavan, Tehsil Behror, District Alwar (Rajasthan)
13.	Name of the Applicant	Shree Jee Laboratory Pvt. Ltd.
14.	Registered address	C-25, RIICO Industrial Area, Sotanala, Behror, District Alwar (Rajasthan)
15.	Address for correspondence:	Project Proponent
	Name	Dr. Anil Kumar
	Designation (Owner/ Partner/CEO)	Chief Scientific Officer
	Address	Mankind Research Centre, 191-E, Sector 4-II, IMT Manesar, Haryana

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	Pin Code	122050
	E-mail	dranil@mankindpharma.com contact@mankindpharma.com
	Telephone No.	0124-2873900
16.	Details of Alternate Sites examined, if any. Location of these sites should be shown on a topo sheet	No, EC Amendment Only.
17.	Interlinked Projects	There are no interlinked projects related to this project.
18.	Whether separate application of interlinked project has been submitted?	Not Applicable
19.	If yes, date of submission	Not Applicable
20.	If no, reason	Not Applicable
21.	Whether the proposal involves approval/ clearance under : if yes, details of the same and their status to be given (a) The forest (Conservation) Act, 1980 (b) The wildlife (Protection) Act, 1972 (c) The C. R.Z Notification, 1991	The proposal does not involve any approval /clearance under any act as mentioned in the condition. No No No
22.	Whether there is any Government order/ policy relevant / relating to the site?	The Project falls under RIICO (Rajasthan State Industrial Development and Investment Corporation) Industrial Area.
23.	Forest land involved (hectares)	No forest land is involved in the proposed project.
24.	Whether there is any litigation pending against the project and/ or land in which the project is propose to be set up? (a) Name of the Court (b) Case No. (c) Orders/ directions of the court, if any and its relevance with the proposed project	No litigation is pending against the project.

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(II) Activity

- Construction, operation or decommissioning of the Project involving actions, which will cause physical changes in the locality (topography, land use, changes in water bodies, etc.)

S. No.	Information/Checklist confirmation	Yes/ No	Details there of (with approximate quantities /rates, wherever possible) with source of information data
1.1	Permanent or temporary change in land use, land cover or topography including increase in intensity of land use (with respect to local land use plan)	No	This land comes under RIICO Industrial Area. Plot no 24 & 25 has been acquired by the company. After Amendment total plant area will be 17,680 Sq. meter.
1.2	Clearance of existing land, vegetation and buildings?	No	There will be no clearance of buildings and vegetation required for the project activity.
1.3	Creation of new land uses?	No	The land is located within the RIICO Industrial Area, Sotanala, Behror, District Alwar (Rajasthan) and meant for Industrial purpose only. Thus no new land use will be created.
1.4	Pre-construction investigations e.g. bore houses, soil testing?	No	No heavy construction activities needed therefore bore house and soil testing is not required.
1.5	Construction works?	No	The existing infrastructure will be adequate as per previous EC.
1.6	Demolition works?	No	Not Applicable
1.7	Temporary sites used for construction works or housing of construction workers?	No	Not Applicable
1.8	Above ground buildings, structures or earthworks including linear structures, cut and fill or excavations	No	No cut and fill or excavations are required.
1.9	Underground works including mining or tunneling?	No	Not Applicable
1.10	Reclamation works?	No	Not Applicable
1.11	Dredging?	No	Not Applicable
1.12	Offshore structures?	No	Not Applicable
1.13	Production and manufacturing	Yes	There is no change in production quantity.

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	processes?		The list of raw material details is enclosed herewith as Annexure - 4. Manufacturing Process of each proposed Product with Chemical Reaction is enclosed herewith as Annexure - 5.
1.14	Facilities for storage of goods or materials?	Yes	Raw material storage area, Tank farm area & finished products area will be developed as per amendment.
1.15	Facilities for treatment or disposal of solid waste or liquid effluents?	No	There will be no change in existing effluent treatment or disposal of solid waste/ liquid effluent.
1.16	Facilities for long term housing of operational workers?	No	Local labors are employed and thus no permanent housing facility is provided.
1.17	New road, rail or sea traffic during construction or operation?	No	The development did not have any major impact on traffic pattern. Internal roads are well constructed to manage traffic.
1.18	New road, rail, air waterborne or other transport infrastructure including new or altered routes and stations, ports, airports etc?	No	No any new road, rail, air, waterborne or other transport infrastructure is proposed. The project site has good road, rail & air connectivity. All these are being used suitably during operation phase.
1.19	Closure or diversion of existing transport routes or infrastructure leading to changes in traffic movements?	No	There is no diversion or closure of the existing transport routes and infrastructure.
1.20	New or diverted transmission lines or pipelines?	No	Not Applicable
1.21	Impoundment, damming, converting, realignment or other changes to the hydrology of watercourses or aquifers?	No	Not Applicable
1.22	Stream crossings?	No	No stream crossing the site.
1.23	Abstraction or transfers of water form ground or surface waters?	No	Source of water supply from Supplied by RIICO & Ground water will not change.
1.24	Changes in water bodies or the land surface affecting drainage or run-off?	No	No change on water bodies or the land surface affecting drainage or run-off
1.25	Transport of personnel or	No	No increase traffic load due to amendment.

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	materials for construction, operation or decommissioning?		
1.26	Long-term dismantling or decommissioning or restoration works?	No	No long term dismantling/ decommissioning is proposed.
1.27	Ongoing activity during decommissioning which could have an impact on the environment?	No	No decommissioning is involved.
1.28	Influx of people to an area in either temporarily or permanently?	Yes	There will be influx of people during the operational phase.
1.29	Introduction of alien species?	No	Not Applicable
1.30	Loss of native species or genetic diversity?	No	Not Applicable
1.31	Any other actions?	No	Not Applicable

2. Use of Natural resources for construction or operation of the Project (such as land, water, materials or energy, especially any resources which are non-renewable or in short supply):

S. No.	Information/checklist confirmation	Yes/ No	Details thereof (with approximate quantities/ rates, wherever possible) with source of information data
2.1	Land especially undeveloped or agricultural land (ha)	No	This land comes under RIICO Industrial Area. The total project area is 9478 Sq. meter. Existing Plant and the area has been in RIICO Industrial Area and Plot No. 24 & 25 has been acquired by the company with appropriate NOC.
2.2	Water (expected source & competing users) unit: KLD	No	Total Water consumption (50 m ³ /day) will not be changed as per earlier EC granted by MoEFCC. Water Balance is enclosed herewith as Annexure - 6 . EC Letter {File no. J-11011/176/2014-IA II (I)} issued by MoEFCC, New Delhi dated 25 th June, 2015
2.3	Minerals (MT)	No	Not Applicable
2.4	Construction material – stone, aggregates, sand / soil (expected source – MT)	No	Not Applicable

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2.5	Forests and timber (source – MT)	No	Not Applicable
2.6	Energy including electricity and fuels (source, competing users) Unit: fuel (MT), energy (MW)	No	Electricity (1.5 MW) will not be changed as per previous EC obtained. Source - RIICO/ Rajasthan Rajya Vidyut Utpadan Nigam Limited & DG sets (2x500 KV & 250 KVA) will be provided as standby power back up
2.7	Any other natural resources (Use appropriate standard units)	No	Not Applicable

3. Use, storage, transport, handling or production of substances or materials, which could be harmful to human health or the environment or raise concerns about actual or perceived risks to human health.

S. No.	Information/Checklist confirmation	Yes/ No	Details thereof (with approximate quantities/rates, wherever possible) with source of information data
3.1	Use of substances or materials, which are hazardous (as per MSIHC rules) to human health or the environment (flora, fauna, and water supplies)	No	Hazardous substance used in the process will not be changed as per previous EC obtained. EC Letter issued by MoEFCC, New Delhi dated 25 th June, 2015
3.2	Changes in occurrence of disease or affect disease vectors (e.g. insect or water borne diseases)	No	No change in occurrence of disease or affect disease vectors.
3.3	Affect the welfare of people e.g. by changing living conditions?	Yes	Positive impact will be created. The project will provide employment and there will be increase in per capita income.
3.4	Vulnerable groups of people who could be affected by the project e.g. hospital patients, children, the elderly etc.,	No	No vulnerable group of people who could be affected by the project.
3.5	Any other causes	No	Not Applicable

4. Production of solid wastes during construction or operation or decommissioning (MT/month)

S. No.	Information/Checklist confirmation	Yes/ No	Details thereof (with approximate quantities/ rates, wherever possible) with source of information data
4.1	Spoil, overburden or mine wastes	No	Not Applicable

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4.2	Municipal waste (domestic and or commercial wastes)	No	Disposal of Municipal waste will not be changed as per previous EC obtained.
4.3	Hazardous wastes (as per Hazardous Waste Management Rules)	No	Generation and disposal of Hazardous waste will not be changed as per previous EC obtained. Hazardous waste management details is enclosed herewith as Annexure - 7 .
4.4	Other industrial process wastes	No	Other discarded containers, barrels etc. and used oil will be sold to registered recyclers.
4.5	Surplus product	No	Not Applicable
4.6	Sewage sludge or other sludge from effluent treatment	No	Treatment of Sewage will not be changed as per previous EC obtained.
4.7	Construction or demolition wastes	No	Not Applicable
4.8	Redundant machinery or equipment	No	Not Applicable
4.9	Contaminated soils or other materials	No	Not Applicable
4.10	Agricultural wastes	No	Not Applicable
4.11	Other solid wastes	No	Not Applicable

5. Release of pollutants or any hazardous, toxic or noxious substances to air (Kg/hr)

S. No.	Information/Checklist confirmation	Yes/ No	Details thereof (with approximate quantities/rates, wherever possible) with source of information data
5.1	Emissions from combustion of fossil fuels from stationary or mobile sources.	No	There is no change from the previous EC obtained.
5.2	Emissions from production processes.	No	There is no change from the previous EC obtained.
5.3	Emissions from materials handling including storage or transport.	No	Material transfer takes place in closed pipeline systems using pumps with mechanical seals..
5.4	Emissions from construction activities including plant and equipment.	No	There would not be any emission from the construction activities.
5.5	Dust or Odor from handling of materials including construction materials, sewage and waste.	No	There is no change from the previous EC obtained.
5.6	Emissions from incineration of waste	No	No such activity will be carried out by the unit.
5.7	Emissions from burning of waste in open air (e.g. slash materials,	No	Not applicable as there will be no burning of waste in open air.

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	construction debris)		
5.8	Emissions from any other sources	No	Not Applicable

6. Generation of Noise and Vibration, and Emissions of Light and Heat:

S. No.	Information/Checklist confirmation	Yes/ No	Details thereof (with approximate quantities/rates, wherever possible) with source of information data with source of information data
6.1	From operation of equipment e.g. engines, ventilation plant, crushers	No	There is no change from the previous EC obtained.
6.2	From industrial or similar processes	No	Not Applicable
6.3	From construction or demolition	No	Not Applicable
6.4	From blasting or piling	No	Not Applicable
6.5	From construction or operational traffic	No	No change in existing traffic pattern.
6.6	From lighting or cooling systems	No	Not Applicable
6.7	From any other sources	No	Not Applicable

7. Risks of contamination of land or water from releases of pollutants into the ground or into sewers, surface waters, groundwater, coastal waters or the sea:

S. No.	Information/Checklist confirmation	Yes/ No	Details thereof (with approximate quantities/rates, wherever possible) with source of information data
7.1	From handling, storage, use or spillage of hazardous materials	No	There is no change from the previous EC obtained.
7.2	From discharge of sewage or other effluents to water or the land (expected mode and place of discharge)	No	Industrial effluent will be treated as per previous EC obtained. Effluent treatment plant description and flowchart is enclosed herewith as Annexure - 8 .
7.3	By deposition of pollutants emitted to air into the land or into water	No	Not Applicable
7.4	From any other sources	No	Not Applicable
7.5	Is there a risk of long term build up of pollutants in the environment from these sources?	No	Not Applicable

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8. Risk of accidents during construction or operation of the Project, which could affect human health or the environment

S. No.	Information/Checklist confirmation	Yes/ No	Details thereof (with approximate quantities/rates, wherever possible) with source of information data
8.1	From explosions, spillages, fires etc from storage, handling, use or production of hazardous substances	No	There is no change from the previous EC obtained. All safety precautions are taken by the industry to avoid such accident.
8.2	From any other causes	No	Not Applicable
8.3	Could the project be affected by natural disasters causing environmental damage (e.g. floods, earthquakes, landslides, cloudburst etc)?	No	Not Applicable

9. Factors which should be considered (such as consequential development) which could lead to environmental effects or the potential for cumulative impacts with other existing or planned activities in the locality

S. No.	Information/Checklist confirmation	Yes/ No	Details thereof (with approximate quantities/ rates, wherever possible) with source of information data
9.1	Lead to development of supporting utilities, ancillary development or development stimulated by the project which could have impact on the environment e.g.: <ul style="list-style-type: none"> • Supporting infrastructure (roads, power supply, waste or waste water treatment, etc.) • housing development • extractive industries • supply industries • other 	No	This is applied for amendment in Environmental Clearance for adding additional Plot no & area and product range.
9.2	Lead to after-use of the site, which could have an impact on the environment	No	Not Applicable

Bulk Drug Manufacturing [API (65 TPA) and Steroid (5 TPA)] Plant At Plot No. C-24 & 25, RIICO Industrial Area, Village Sotanala, Tehsil Behror, District Alwar (Rajasthan) Reg. amendment in Environment Clearance Letter	Form 1/ Appendix-I
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9.3	Set a precedent for later developments	No	Not Applicable
9.4	Have cumulative effects due to proximity to other existing or planned projects with similar effects	No	Not Applicable

(III) Environmental Sensitivity

S. No.	Areas	Name/ Identity	Aerial distance (within 15 km.) Proposed project location boundary
1	Areas protected under international conventions, national or local legislation for their ecological, landscape, cultural or other related value	No	Not Applicable
2	Areas which are important or sensitive for ecological reasons-Wetlands, watercourses or other water bodies, coastal zone, biospheres, mountains, forests	Yes	❖ Sota Nadi (~0.5 km in North direction) ❖ Sabi Nadi (~3.2km in SSE direction) (Both are seasonal rivers)
3	Areas used by protected, important or sensitive species of flora or fauna for breeding, nesting, foraging, resting, overwintering, migration	No	Not Applicable
4	Inland, coastal, marine or underground waters	No	Not Applicable
5	State, National boundaries	Yes	State Boundaries (Haryana – Rajasthan) approx. 4.0 km in West direction from the plant site.
6	Routes or facilities used by the public for access to recreation or other tourist, pilgrim areas	No	-
7	Defense installations	No	Nil
8	Densely populated or built-up area	Yes	Behror town, approx. 6.5 km in NNE direction from the plant site.

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9	Areas occupied by sensitive man-made land uses (<i>hospitals, schools, places of worship, community facilities</i>)	Yes	Primary schools, middle school, high schools, Colleges, Health centres, public health sub centres, dispensaries, Hospital, Temples, Community centres, other facilities exist within 15 km radius.
10	Areas containing important, high quality or scarce resources (<i>ground water resources, surface resources, forestry, agriculture, fisheries, tourism, minerals</i>)	No	Not Applicable
11	Areas already subjected to pollution or environmental damage. (<i>those where existing legal environmental standards are exceeded</i>)	No	Not Applicable
12	Areas susceptible to natural hazard which could cause the project to present environmental problems (<i>earthquakes, subsidence, landslides, erosion, flooding or extreme or adverse climatic conditions</i>)	No	The proposed project site falls in Zone-II as per IS 1893 (Part-I): 2002.



SHREE JEE LABORATORY PVT. LTD.

C-24-25, RIICO Indl. Area, Sotanala, Behror-301701 Distt. Alwar (Raj.)
Phone No:+91-124-2873900-901-902 to 923 • E-mail: shrijeelaboratory@gmail.com

UNDERTAKING

"I hereby given undertaking that the data and information given in the application and enclosures are true to the best of my knowledge and belief and I am aware that if any part of the data and information submitted is found to be false or misleading at any stage, the project will be rejected and clearance given if any to the project will be revoked at our risk and cost.

Date: 19/06/2017

Place: Behror

for Shree Jee Laboratory Pvt. Ltd.

Anil Kumar
Authorised Signatory

Signature of the applicant

For Shree Jee Laboratory Limited
Dr. Anil Kumar

Chief Scientific Officer (CSO)
(Project proponent/Authorized Signatory)

Note:

1. The projects involving clearance under Coastal Regulation Zone Notification, 1991 will submit with the application a C.R.Z. map duly demarcated by one of the authorized agencies, showing the project activities, w.r.t. C.R.Z. (at the stage of ToR) and the recommendations of the State Coastal Zone Management Authority (at the stage of EC). Simultaneous action will also be taken to obtain the requisite clearance under the provisions of the C.R.Z. Notification, 1991 for the activities to be located in the CRZ.
2. The projects to be located within 10 km of the National Parks, Sanctuaries, Biosphere Reserves, Migratory Corridors of Wild Animals, the project proponent will submit the map duly authenticated by Chief Wildlife Warden showing these features vis-à-vis the project location and the recommendations or comments of the Chief Wildlife Warden thereon (at the stage of EC).
3. All correspondence with the Ministry of Environment & Forests including submission of application for ToR/Environmental Clearance, subsequent clarifications, as may be required from time to time, participation in the EAC Meeting on behalf of the project proponent will be made by the authorized signatory only. The authorized signatory should also submit a document in support of his claim of being an authorized signatory for the specific project.



ANNEXURE-1

**ENVIRONMENTAL CLEARANCE LETTER
ISSUED BY MOEFCC, NEW DELHI DATED
25TH JUNE, 2015**

J-11011/176/2014-IA II (I)
Government of India
Ministry of Environment, Forest and Climate Change
(I.A. Division)

Indira Paryavaran Bhawan
Aliganj, Jorbagh Road,
New Delhi -110003

E-mail : lk.bokolia@nic.in
Telefax : 011-24695313
Dated 25th June, 2015

To,
Dr. Anil Kumar
Chief Scientific Officer
M/s Shree Jee Pvt. Ltd.
Mankind Research Centre .
191-E, Sector 4-II IMT, Manesar
(Haryana)

Email.: dranil@mankindpharma.com / contact@mankindpharma.com / imenviron@hotmail.com Fax.: 0124-4141029

Subject: Bulk Drug Manufacturing [API(65 TPA) and Steroid (5 TPA)] Plant at Plot No.C-25, RIICO Industrial Area, Village Sotanala, Tehsil Behror, District Alwar, Rajasthan by M/s Shri Jee Laboratory Pvt. Ltd.- Environment Clearance reg.

Ref.: Your letter no nil dated 30.01.2015.

Sir,

This has reference to your letter dated 30th January, 2015 alongwith project documents including Form I, Terms of References, Pre-feasibility Report, EIA/EMP Report regarding above mentioned project.

2.0 The Ministry of Environment, Forest and Climate Change has examined the application. It is noted that proposal is for setting up of Bulk Drugs API(65 TPA) and Steroid (5 TPA) Plant at Plot No.C-25, RIICO Industrial Area, Village Sotanala, Tehsil Behror, District Alwar, Rajasthan by M/s Shri Jee Laboratory Pvt. Ltd. Plot area is 9478 Sqm. (2.34 Acre) (0.947 ha) of which area earmarked for greenbelt is 0.77 acre. Cost of the project is Rs. 35 Crore. It is reported that no national park/wildlife sanctuary/RF/PF is located within 10 km distance. Sota Nadi and Sabi Nadi is flowing at a distance of 0.5 km and 3.2 km respectively. Following products will be manufactured:

S.N.	Products	Quantity (MTPA)
1	Moxifloxacin Hydrochloride	20.3
2	Cilnidipine	1.0
3	Silodosin	0.5
4	Montelukast Sodium	5.0
5	Fexofinadine hydrochloride	6.0
6	Linezolid	20.0
7	Escitalopram	1.0
8	Etizolam	0.1
9	FlupentixolDihydrochloride	0.5
10	Besifloxacin Hydrochloride	0.5
11	Granisetron Hydrochloride	0.1
12	AzilsartanMedoxomil Potassium	10.0
	TOTAL	65.0

B	Steroid	
1	Finasteride	0.6
2	LoteprednolEtabonate	0.35
3	Mefipristone	3.0
4	Deflazacort	0.8
5	Ulipristal Acetate	0.25
	TOTAL	5.0

3.0 Bagfilter will be provided to the pet coke/bio-briquette/husk fired boiler to control particulate emissions. Fresh water requirement from RICCO Industrial Area will be 50 m³/day. Industrial effluent and domestic effluent generation will be 44 m³/day and treated in the effluent treatment plant (ETP) followed by reverse osmosis (RO). RO rejects will be evaporated in the Multiple Effect Evaporator (MEE). RO permeate and Condensate will be recycled/reused for process/cooling tower make up. No effluent will be discharged outside the plant premises. Spent solvent will be sent to the authorized recyclers. ETP sludge and MEE salt will be sent to TSDf. Spent oil will be sent to the authorized recycler/re-processors.

4.0 Public hearing as per Section 7 (i), III Stage (3), Para (i) (b) of EIA Notification 2006 as project is located in the notified industrial area.

5.0 All the synthetic organic chemicals industry (Bulk Drugs Manufacturing Unit) located inside the notified industrial area are listed at S.N. 5(f) under Category 'B'. However, due to applicability of general condition i.e. interstate boundary within 5 km (i.e. 4 Km Rajasthan-Haryana), project is treated as Category 'A' project and appraised at the Central level.

6.0 The proposal was considered by the Expert Appraisal Committee (Industry-2) in its 21st and 36th meetings held during 30th July, 2014 - 1st August, 2014 and 16th -17th March, 2015 respectively. Project Proponent and the EIA Consultant (M/s J.M EnviroNet Pvt. Ltd.) have presented EIA / EMP report as per the TOR. EAC has found the EIA Study / EMP Report to be adequate and in full consonance with the presented TORs. The Committee recommended the proposal for environmental clearance.

7.0 Based on the information submitted by the project proponent, the Ministry of Environment and Forests hereby accords environmental clearance to above project under the provisions of EIA Notification dated 14th September 2006, subject to the compliance of the following Specific and General Conditions:

A. SPECIFIC CONDITIONS

- i) National Emission Standards for Organic Chemicals Manufacturing Industry issued by the Ministry vide G.S.R. 608(E) dated 21st July, 2010 and amended time to time shall be followed by the unit.
- ii) As proposed, bagfilter shall be provided to the pet coke/bio-briquette/husk fired boiler to control particulate emissions within permissible limit. The gaseous emissions shall be dispersed through stack of adequate height as per CPCB/GPCB guidelines. If petcoke is used, limestone powder shall be fed alongwith pet coke to control the SO₂ emission.
- iii) Ambient air quality data shall be collected as per NAAEQS standards notified by the Ministry vide G.S.R. No. 826(E) dated 16th September, 2009. The levels of PM_{2.5}, PM₁₀, SO₂, NO_x, VOC and CO shall be monitored in the ambient air and emissions from the stacks and displayed at a convenient location near the main gate of the company and at important public places. The company shall upload the results of monitored data on its website and shall update the same periodically. It shall simultaneously be sent to the Regional office of MOEF, the respective Zonal office of CPCB and the Rajasthan State Pollution Control Board (RSPCB).

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- iv) In plant control measures for checking fugitive emissions from all the vulnerable sources shall be provided. Fugitive emissions shall be controlled by providing closed storage, closed handling & conveyance of chemicals/materials, multi cyclone separator and water sprinkling system. Dust suppression system including water sprinkling system shall be provided at loading and unloading areas to control dust emissions. Fugitive emissions in the work zone environment, product, raw materials storage area etc. shall be regularly monitored. The emissions shall conform to the limits stipulated by the RSPCB.
- v) For further control of fugitive emissions, following steps shall be followed :
1. Closed handling system shall be provided for chemicals.
 2. Reflux condenser shall be provided over reactor.
 3. System of leak detection and repair of pump/pipeline based on preventive maintenance.
 4. The acids shall be taken from storage tanks to reactors through closed pipeline. Storage tanks shall be vented through trap receiver and condenser operated on chilled water.
 5. Cathodic protection shall be provided to the underground solvent storage tanks.
- vi) The gaseous emissions from DG set shall be dispersed through adequate stack height as per CPCB standards. Acoustic enclosure shall be provided to the DG sets to mitigate the noise pollution.
- vii) Solvent management shall be carried out as follows :
- i. Reactor shall be connected to chilled brine condenser system
 - ii. Reactor and solvent handling pump shall have mechanical seals to prevent leakages.
 - iii. The condensers shall be provided with sufficient HTA and residence time so as to achieve more than 95% recovery.
 - iv. Solvents shall be stored in a separate space specified with all safety measures.
 - v. Proper earthing shall be provided in all the electrical equipment wherever solvent handling is done.
 - vi. Entire plant shall be flame proof. The solvent storage tanks shall be provided with breather valve to prevent losses.
 - vii. All the solvent storage tanks shall be connected with vent condensers with chilled brine circulation.
- viii) Total fresh water requirement from RICCO Industrial Area water supply shall not exceed 50 m³/day.
- ix) As proposed, industrial effluent generation shall not exceed 44 m³/day. Effluent shall be treated in ETP followed by RO. RO rejects shall be concentrated in the MEE. MEE condensate shall be recycled for cooling tower make up. Water quality of treated effluent shall be monitored regularly.
- x) 'Zero' effluent discharge should be adopted and no effluent will be discharged outside the premises.
- xi) Automatic /online monitoring system (24 x 7 monitoring devices) for flow measurement and relevant pollutants in the treatment system to be installed. The data to be made available to the respective SPCB and in the Company's website.
- xii) Hazardous chemicals shall be stored in tanks, tank farms, drums, carboys etc. Flame arresters shall be provided on tank farm. Solvent transfer shall be by pumps.

- xiii) As proposed, process organic residue and spent carbon shall be sent to cement industries. ETP sludge, MEE salt and process inorganic shall be disposed off to the TSDF.
- xiv) The company shall obtain Authorization for collection, storage and disposal of hazardous waste under the Hazardous Waste (Management, Handling and Trans-Boundary Movement) Rules, 2008 and amended as on date for management of Hazardous wastes and prior permission from RSPCB shall be obtained for disposal of solid / hazardous waste in the TSDF. Measures shall be taken for fire fighting facilities in case of emergency.
- xv) The Company shall strictly comply with the rules and guidelines under Manufacture, Storage and Import of Hazardous Chemicals (MSIHC) Rules, 1989 as amended time to time. All Transportation of Hazardous Chemicals shall be *as per* the Motor Vehicle Act (MVA), 1989.
- xvi) The unit shall make the arrangement for protection of possible fire hazards during manufacturing process in material handling. Fire fighting system shall be as per the norms.
- xvii) Occupational health surveillance of the workers shall be done on a regular basis and records maintained as per the Factories Act.
- xviii) At least 2.5 % of the total cost of the project shall be earmarked towards the Enterprise social responsibility based on Public Hearing issues and item-wise details along with time bound action plan shall be prepared and submitted to the Ministry's Regional Office Bhopal. Implementation of such program shall be ensured accordingly in a time bound manner.
- xix) Green belt should be developed at least in 0.77 acre in and around the plant premises to mitigate the effects of fugitive emissions all around the plant as per the CPCB guidelines in consultation with DFO.
- xx) The Company shall submit within three months their policy towards Corporate Environment Responsibility which should inter-alia address (i) Standard operating process/procedure to being into focus any infringement/deviation/ violation of environmental or forest norms/conditions, (ii) Hierarchical system or Administrative order of the Company to deal with environmental issues and ensuring compliance to the environmental clearance conditions and (iii) System of reporting of non compliance/violation environmental norms to the Board of Directors of the company and/or stakeholders or shareholders.
- xxi) Provision shall be made for the housing for the construction labour within the site with all necessary infrastructure and facilities such as fuel for cooking, mobile toilets, safe drinking water, medical health care, crèche etc. The housing may be in the form of temporary structure to be removed after the completion of the project. All the construction wastes shall be managed so that there is no impact on the surrounding environment.

B. GENERAL CONDITIONS:

- i. The project authorities shall strictly adhere to the stipulations made by the State Government and Rajasthan State Pollution Control Board (RSPCB).
- ii. No further expansion or modifications in the plant shall be carried out without prior approval of the Ministry of Environment and Forests. In case of deviations or alterations in the project proposal from those submitted to this Ministry for clearance, a fresh reference shall be made to the Ministry to assess the adequacy of conditions imposed and to add additional environmental protection measures required, if any.
- iii. The locations of ambient air quality monitoring stations shall be decided in consultation with the RSPCB and it shall be ensured that at least one station is installed in the upwind and downwind direction as well as where maximum ground level concentrations are anticipated.
- iv. The overall noise levels in and around the plant area shall be kept well within the standards by providing noise control measures including acoustic hoods, silencers,

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enclosures etc. on all sources of noise generation. The ambient noise levels shall conform to the standards prescribed under Environment (Protection) Act, 1986 Rules, 1989 viz. 75 dBA (day time) and 70 dBA (night time).

- v. The Company shall harvest rainwater from the roof-tops of the buildings and storm water drains to recharge the ground water and use the same water for the process activities of the project to conserve fresh water.
- vi. During transfer of materials, spillages shall be avoided and garland drains be constructed to avoid mixing of accidental spillages with domestic wastewater and storm water drains.
- vii. Usage of Personnel Protection Equipments by all employees/ workers shall be ensured.
- viii. Training shall be imparted to all employees on safety and health aspects of chemicals handling. Pre-employment and routine periodical medical examinations for all employees shall be undertaken on regular basis. Training to all employees on handling of chemicals shall be imparted.
- ix. The company shall also comply with all the environmental protection measures and safeguards proposed in the project report submitted to the Ministry. All the recommendations made in the EIA/EMP in respect of environmental management, risk mitigation measures and public hearing relating to the project shall be implemented.
- x. The company shall undertake CSR activities and all relevant measures for improving the socio-economic conditions of the surrounding area.
- xi. The company shall undertake eco-developmental measures including community welfare measures in the project area for the overall improvement of the environment.
- xii. A separate Environmental Management Cell equipped with full fledged laboratory facilities shall be set up to carry out the Environmental Management and Monitoring functions.
- xiii. The company shall earmark sufficient funds for recurring cost per annum to implement the conditions stipulated by the Ministry of Environment and Forests as well as the State Government along with the implementation schedule for all the conditions stipulated herein. The funds so earmarked for environment management/ pollution control measures shall not be diverted for any other purpose.
- xiv. A copy of the clearance letter shall be sent by the project proponent to concerned Panchayat, Zila Parisad/Municipal Corporation, Urban local Body and the local NGO, if any, from who suggestions/ representations, if any, were received while processing the proposal.
- xv. The project proponent shall also submit six monthly reports on the status of compliance of the stipulated Environmental Clearance conditions including results of monitored data (both in hard copies as well as by e-mail) to the respective Regional Office of MoEF, the respective Zonal Office of CPCB and the Rajasthan State Pollution Control Board. A copy of Environmental Clearance and six monthly compliance status report shall be posted on the website of the company.
- xvi. The environmental statement for each financial year ending 31st March in Form-V as is mandated shall be submitted to the Rajasthan State Pollution Control Board as prescribed under the Environment (Protection) Rules, 1986, as amended subsequently, shall also be put on the website of the company along with the status of compliance of

environmental clearance conditions and shall also be sent to the Lucknow Regional Offices of MoEF by e-mail.

- xvii. The project proponent shall inform the public that the project has been accorded environmental clearance by the Ministry and copies of the clearance letter are available with the SPCB/Committee and may also be seen at Website of the Ministry at www.moef.nic.in. This shall be advertised within seven days from the date of issue of the clearance letter, at least in two local newspapers that are widely circulated in the region of which one shall be in the vernacular language of the locality concerned and a copy of the same shall be forwarded to the concerned Regional Office of the Ministry.
- xviii. The project authorities shall inform the Regional Office as well as the Ministry, the date of financial closure and final approval of the project by the concerned authorities and the date of start of the project.

8.0 The Ministry may revoke or suspend the clearance, if implementation of any of the above conditions is not satisfactory.

9.0 The Ministry reserves the right to stipulate additional conditions, if found necessary. The company in a time bound manner will implement these conditions.

10.0 The above conditions will be enforced, inter-alia under the provisions of the Water (Prevention & Control of Pollution) Act, 1974, Air (Prevention & Control of Water Pollution) Act, 1981, the Environment (Protection) Act, 1986 Hazardous Waste (Management, Handling and Trans-boundary Movement) Rules, 2008 and the Public Liability Insurance Act, 1991 along with their amendments and rules.

11.0 Environmental Clearance is issued to M/s Shri Jee Laboratory Pvt. Ltd. Bulk drug manufacturing [API(65 TPA) and Steroid (5 TPA)] Plant at Plot No.C-25, RIICO Industrial Area, Village Sotanala, Tehsil Behror, District Alwar, Rajasthan.



(Lalit Bokolia)
Additional Director

Copy to :-

1. Secretary, Department of Environment and Forests, Government of Rajasthan, Jaipur, Rajasthan.
2. Chairman, Central Pollution Control Board, Parivesh Bhavan, CBD-cum-Office Complex, East Arjun Nagar, Delhi -110032.
3. Chairman, Rajasthan State Pollution Control Board, 4, Institutional area, Jhalana, Doongri, Jaipur, Rajasthan.
4. Chief Conservator of Forests (Central), Ministry of Environment and Forests, Region Office (Central), Kendriya Bhawan, 5th Floor, Sector-H, Aliganj, Lucknow – 226 024, U.P.
5. Monitoring Cell, Ministry of Environment, Forest and Climate Change, Indira Paryavaran Bhavan, Jorbagh, New Delhi.
6. Guard File/Monitoring File/Record File.



(Lalit Bokolia)
Additional Director

ANNEXURE-2

LAND ALLOTMENT LETTER BY RIICO

(Speed Post/E-mail)

No:..9249

Date:..12.12.16

M/s Aromatic Alloys & Allied Pvt. Ltd.
G-2, Vikas Apartments,
34/1, East Punjabi Bagh,
New Delhi-110026

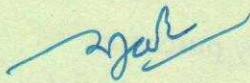
Sub:- Permission for transfer of lease hold right of Plot No. C-24 & merger of plot
No. C-24 & C-25 Industrial Area Sotanala in favour of M/s Shree Jee
Laboratory Pvt. Ltd.

Ref:- M/s Shree Jee Laboratory Pvt. Ltd. letter dated 20.01.2016.

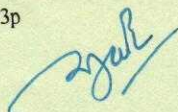
Dear Sir,

In reference to above cited letter and sale deed registered on 14.01.2016 between your company M/s Aromatic Alloys & Allied Private Limited (CIN: U74899DL1995PTC064931) and M/s Shree Jee Laboratory Private Limited (CIN:U24232DL2011PTC272907) and other documents submitted by both the companies, the permission for transfer of lease hold right of Plot No. C-24 measuring 8,202 sqm & merger of plot no. C-24 with plot no. C-25 measuring 9,478 sqm, the lease hold right of which was transfred to M/s Shree Jee Laboratory Private Limited vide this office letter no. 8033 dated 15.02.2012 at Industrial Area Sotanala for the remaining period of lease deed executed between RIICO and M/s A.D. Textiles Private Limited is granted in favour of M/s Shree Jee Laboratory Private Limited on following terms & conditions:-

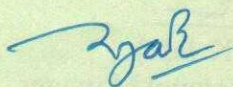
1. That your company shall be named as "seller" & M/s Shree Jee Laboratory Pvt. Ltd. as "purchaser" in all future correspondence.
2. That transfer Charges @ 18.75% of prevailing value of land amounting to Rs. 30,75,750/- has been deposited vide CR No. 18227/91 dated 05.02.2016 The purchaser company shall set up unit of "Bulk Drugs/Synthetic Drugs API & Steroids" with an investment of Rs. 5,000.00 lacs by completing minimum 20% built up area of the plot area on ground or FAR (Built up area would mean a building with roof and having side walls/covering as required for the nature of product/activity). Purchaser will be start commercial production on the combined plots up to 30.11.2016.
3. The details of plot are as under:-
 - a) Whereas the plot no. C-24 measuring 8,202 sqm at Industrial area Sotanala was allotted to M/s A.D. Textiles (Proprietorship Firm) for establishing a unit for Mfg. of "Textile Products" vide RIICO Ltd. letter No. 2206 dated 02.08.2006.
 - b) Whereas permission for change of constitution of firm from Proprietorship to Private Limited and name of company as M/s A.D. Textiles Private Limited granted vide office order No. 50 dated 01.04.2010.



- c) Whereas **M/s A.D. Textiles Pvt. Ltd.** had executed the lease deed for the plot No. C-24 Industrial area Sotanala measuring 8,202 sqm on 13.05.2010 and got it registered in the record of Sub-Registrar Behror on 17.05.2010 at Book No. 01 Volume No. 380 S.No. 2010000961 Page No. 196 & additional Book No. 1 Volume No. 867 Page No. 211 to 215.
- d) Whereas **M/s A.D. Textiles Pvt. Ltd.** through its Director Shri Jitender Kumar Sharma S/o Shri V.P. Sharma has sold the plot No. C-24, measuring 8202 sqm to **M/s Artomatic Alloys Allied Pvt. Ltd.** on dated 10.05.2011 by way of registered sale deed and got it registered in the record of Sub-Registrar Bhiwadi on dated 10.05.2011 at Book No. 01 Volume No. 347 S.No. 2011001577 Page No. 177 & additional Book No. 1 Volume No. 1137 Page No. 225 to 233.
- e) Whereas the Corporation has transferred lease hold rights of plot on the request of lessee, vide letter No. 4169 dated 23.08.2011 in favour of **M/s Artomatic Alloys Allied Pvt. Ltd.** on deposition of transfer charges Rs. 15,37,875/- vide CR No. 14805/60 dated 21.07.2011.
- f) Whereas **M/s Artomatic Alloys Allied Pvt. Ltd.** had executed the correction deed and got it registered in the record of Sub-Registrar Behror on 28.12.2015 at Book No 01 Volume No. 508 S.No. 2015004020 Page No. 105 & additional Book No. 01 Volume No. 1378 Page No. 17 to 20.
- g) Whereas the Corporation issued an office order for correction in name of the company from **M/s Artomatic Alloys Allied Pvt. Ltd.** to **M/s Aromatic Alloys & Allied Pvt. Ltd.** on the request of lessee, vide letter No. 8117-19 dated 01.01.2016.
- h) Whereas **M/s Aromatic Alloys & Allied Pvt. Ltd.** had executed amended deed on 04.01.2016 and registered in the record of Sub-Registrar Neemrana on dated 04.01.2016 at Book No 01 Volume No. 509 S.No. 2016000017 Page No. 3 & additional Book No. 01 Volume No. 1380 Page No. 13 to 18.
- i) Whereas **M/s Artomatic Alloys & Allied Pvt. Ltd.** has sold the plot No. C-24, measuring 8202 sqm to **M/s Shree Jee Laboratory Pvt. Ltd.** on 14.01.2016 by way of registered sale deed and got it registered in the record of Sub-Registrar Behror on dated 14.01.2016 at Book No. 01 Volume No. 509 S.No. 2016000132 Page No. 118 & additional Book No. 1 Volume No. 1382 Page No. 71 to 84.
4. The possession of the land of Plot No. C-24 at Industrial Area Sotanala has already been given to the purchaser.
5. The purchaser will deposit the annual Economic Rent and Service Charges & Service Tax in advance by 1ST April of each year at the rate decided by the Corporation from time to time.
6. All the dues pertaining to water supply shall be paid by Purchaser.
7. The terms & condition of original allotment letter dated 02.08.2006 and lease deed executed on 13.05.2010 will be binding upon purchaser.
8. If dues of RIICO are further worked out towards the old allottees of this plot during audit observations then purchaser i.e. **M/s Shree Jee Laboratory Pvt. Ltd.** is liable to deposit the same as and when demanded by RIICO.
9. The Purchaser will not dig/bore/drill the open well/hand pump/tube well in the plot.
10. The Purchaser will plant at least one row of trees in the plot at a reasonable distance along the boundary wall.
11. Other taxes as applicable shall be paid by purchaser.
12. The transfer of plot is made exclusively on the risk of the purchaser.



13. The Purchaser would install a dust controller in industry to avoid dust, nuisance in the area (applicable in case of dust producing industries.)
14. The purchaser shall have to pay the cost of power line & other charges as and when demanded by JVVNL for release of power Connection.
15. In case power/Telephone line is passing through the plot, the Corporation does not undertake any responsibility for its removal. The purchaser would be required to plan construction leaving prescribed set back applicable for the plot.
16. RIICO shall not be liable for any dues of Govt. department/Organization/ Companies or Financial Institution towards the seller firm. The Purchaser would be fully responsible for such liability.
17. This letter shall also be treated as N.O.Cs of the corporation for taking power/water connection in the allotted plot from JVVNL/RIICO in favour of the purchaser.
18. The purchaser shall abide by the provision of Indian Electricity Act. 1948 and Rules made there under.
19. Stamp duty payable under the stamp law Rajasthan, will be borne by the purchaser for all changes made from time to time from the date of allotment till now.
20. That purchaser shall obtain NOC & abide by rule/regulation of local authorities Administrations police, Fire fighting authority, Airport authority, pollution Control Board & other Central/ State Govt. Department as per their rules applicable to your unit/project.
21. Lease deed executed between RIICO and M/s A.D. Textiles Pvt. Ltd. on 13.05.2010, sale deed registered on 10.05.2011 between M/s A.D. Textiles Pvt. Ltd. & M/s Artomatic Alloyes & Allied Pvt. Ltd., Correction deed dated 28.12.2015 and sale deed registered on 14.01.2016 between M/s Aromatic Alloyes & Allied Pvt. Ltd. & M/s Shree Jee Laboratory Pvt. Ltd. will be treated as one document. All the clause of original lease agreement will be complied by the purchaser party.
22. The lease hold rights are being transferred for a period of 99 years period which shall be counted from the date of land allotment to the original allottee. (i.e. 02.08.2006). As such the transferee will have the status of an allottee/leasee of the Corporation and all the rules and regulations of the Corporation will apply to the transferee "Mutatis-Mutandis". The transferee will be holding the land for the remaining lease period available in balance to him.
23. The transfer permission is subject to condition that the effluent & sludge will have to be pretreated to the satisfaction of Rajasthan State Pollution Control & Prevention Board/Central Pollution Control & Prevention Board and purchaser firm will obtain consent to establish & consent to operate from the board before starting the unit. **However no disposal of effluent shall be allowed in the storm water drain constructed by RIICO in the industrial area. The purchaser shall have to maintain the status of Zero discharge from your unit.**
24. The orders/notifications if any; issued by MOEF; Govt. of India regarding EIA clearances for compliance of corporation; then all those orders/notifications would be binding upon the purchaser also and same have to abide by them.



25. The purchaser firm shall setup the industrial project on the allotted plot which is not covered under the category A & B of the notification issued by ministry of environment & Forest Govt. of India on dated 14TH September 2006 & would not require any Environment impact assessment clearance from the Govt. of India under this Notification.
26. The purchaser shall abide by all terms and conditions as may be laid down in RIICO Disposal of Land Rules, 1979 and its amendments made from time to time.
27. The allottee shall commence the activities after completion of minimum requisite construction (built up area) for which land use has been allowed up to 30.11.2016. The minimum requisite construction for the purpose of considering utilization of the allotted plot shall be 20% of the standard/prescribed FAR. The built up area would mean a building with roof and having side walls/covering as required for the nature of product/activity.
28. The allottee shall intimate by registered letter to the Corporation about the activities after utilization of the plot as per above. Utilization of the plot will be recorded by the Unit Head as per rule 21 of RIICO Disposal of Land Rules, 1979 as amended from time to time.
29. For water conservation and increasing of level of ground water, all plot allottees having more than or equal to 500 sqm shall have to construct Rain Water Harvesting Structures (RWHS) in their premises to recharge the ground water so as to ensure that all rain water is effectively harvested and recharged within stipulated time period of commencement of production activity. Plot allottee is required to intimate concern unit office in writing about completion of RWHS. The allotted plot will be treated as utilized without completion of RWHS. However, the allottee will be required to pay lump-sum penalty for delay in completion of RWHS as per norms.
30. If the documents submitted by the applicant are not found correct, the permission for transfer of lease hold right may be treated as withdrawn.
31. The purchaser company shall execute amended lease deed at his cost within 30 days from the issue of this letter.

Thanking You,

Yours faithfully,

(Sudhir Lohiya)

Sr. Regional Manager

Enc.- Site plan of merged plot no. C-24 & C-25.

Copy to:-

- ✓ 1. M/s Shree Jee Laboratory Pvt. Ltd., R/o 208, Okhla Industrial Estate, Phase-III, New Delhi-110020, Email:- shrijeelaboratory@gmail.com

Copy also to:-

1. General Manager, DIC, Bhiwadi
2. Branch Manager, RFC, Bhiwadi (Alwar)
3. Sub Registrar, Behror (Alwar)
4. RM(VKJ) RIICO Ltd. Neemrana.
5. RM (SIH) RIICO Ltd., Neemrana.

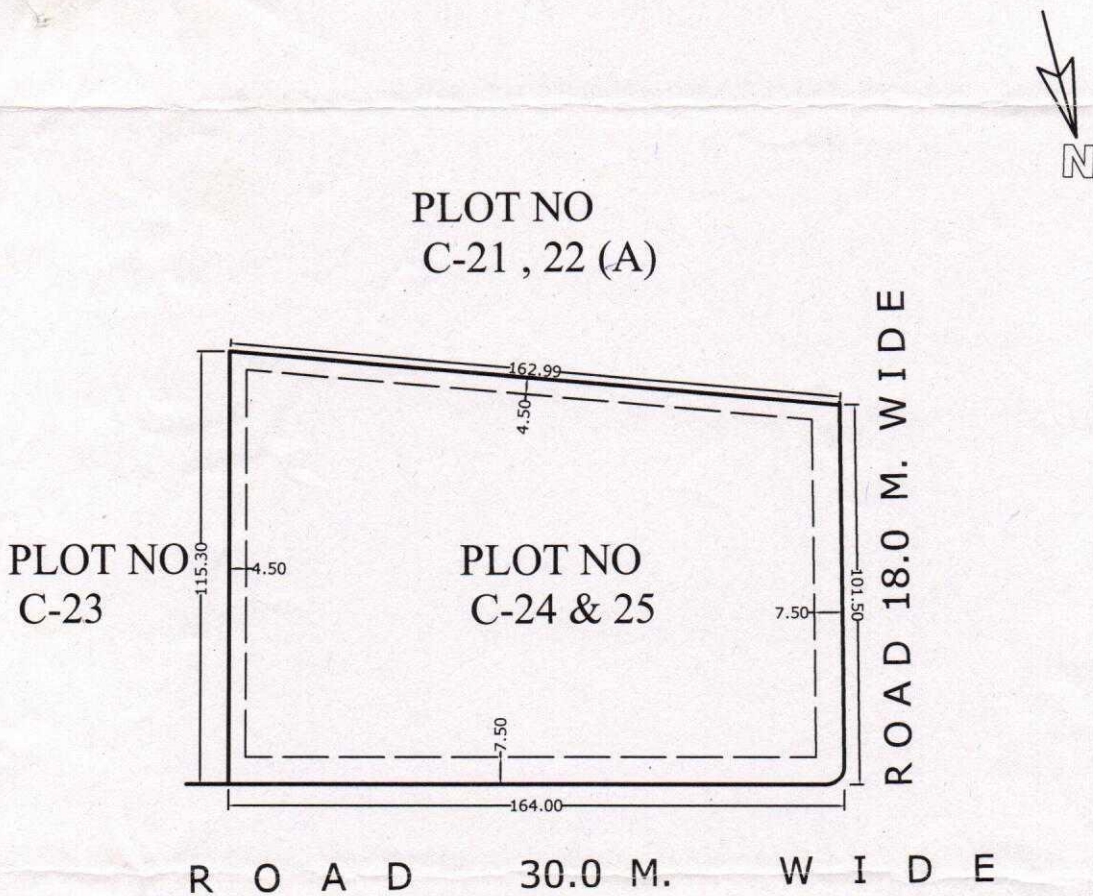
(V.K. Jain)
Regional Manager

SITE PLAN OF PLOT NO. C-24 & 25 AT
INDUSTRIAL AREA SOTANALA DISTT, ALWAR (RAJASTHAN)

ALLOTTED TO M/S
SCALE - 1CM. = 20.0 M.

PLOT AREA - 17680 SQM

NOTE
1- ALL DIMENSION ARE IN MRTERS
2- RIICO BUILDING REGULATION RIICO DISPOSAL OF LAND RULES, 1979 AND AMANDED FROM TIME
TIME AND LEASE CONDITIONS OF SET BACKS SHOULD BE FOLLOWED STRICTLY BY THE ALLOTTEES



[Signature]
SR D/MAN

[Signature]
R.M.

RIICO

NEEMRANA



ANNEXURE-3

LIST OF CHANGED PRODUCT RANGE

LIST OF PRODUCTS WITH QUANTITY

Name of The Product		Quantity per year with Unit(No Change)	
Bulk Drugs API		Existing as per Previous EC Letter No. J-11011/176/2014-IA II (I) dated 25th June, 2015	After addition of Proposed Products range
S. No.	EXISTING	65 MTPA	65 MTPA
1.	Moxifloxacin Hydrochloride		
2.	Cilnidipine		
3.	Silodosin		
4.	Montelukast Sodium		
5.	Fexofenadine Hydrochloride		
6.	Linezolid		
7.	Escitalopram Oxalate		
8.	Etizolam		
9.	Flupentixol Dihydrochloride		
10.	Besifloxacin Hydrochloride		
11.	Granisetron Hydrochloride		
12.	Azilsartan Medoxomil Potassium		
PROPOSED			
1.	Amitriptyline hydrochloride		
2.	Teneligliptin hemipentahydrobromide hydrate		
3.	Nitrofurantoin monohydrate		
4.	Nitrofurantoin macrocrystals		
5.	Ranolazine		
6.	Clomipramine hydrochloride		
7.	Sitagliptin Phosphate/Hydrochloride		
8.	Leuprolide Acetate		
9.	Terbinafine Hydrochloride		
10.	Levosulpiride		
11.	Rifaximin		
12.	Telmisartan		
13.	Valsartan+Sacubitril complex		
14.	Sacubitril Sodium		
15.	Methylcobalamin		
16.	Etoricoxib		
17.	Efonidipine Hydrochloride ethanolate		
18.	Azelnidipine		

19.	Nadifloxacin		
20.	Bromopride		
21.	Seratrodast		
22.	Fenticonazole nitrate		
23.	Folic acid		
24.	Clindamycin Hydrochloride		
25.	Haloperidol/ Haloperidol decanoate		
26.	Sugammadex Sodium		
27.	Verapamil Hydrochloride		
28.	Lifitegrast		
29.	Varenicline Tartrate		
STEROID			
Sr. No.	EXISTING	5 MTPA	5 MTPA
1.	Finasteride		
2.	Loteprednol Etabonate		
3.	Mifepristone		
4.	Deflazacort		
5.	Ulipristal Acetate		
PROPOSED			
1.	Dydrogesterone		
2.	Progesterone		



ANNEXURE-4
LIST OF RAW MATERIAL DETAILS

Raw material requirement for the project
(For Existing & Proposed Product)

Sr. No.	Key Raw Materials	Required Quantity (MTPA)	Nature (Solid, Liquid, Gas)
EXISTING			
1.	4-fluoro bromo benzene	2.0	Liquid
2.	Magnesium metal	0.5	Solid
3.	Dimethyl amino propylchloride	0.7	Liquid
4.	Aq. Ammonia	1.0	Liquid
5.	Phosphorous oxy chloride	20.0	Liquid
6.	Pyridine	2.0	Liquid
7.	Indoline	4.0	Solid
8.	1-Bromo-3-chloro propane	8.0	Liquid
9.	Nitroethane	4.0	Liquid
10.	Sodium Borohydride	13.0	Solid
11.	Hydroxyl amine hydrochloride	25.0	Solid
12.	Benzoic acid	4.45	Solid
13.	L(+)- Tartaric acid	3.7	Solid
14.	Hydrogen peroxide (30%)	1.0	Liquid
15.	2,2,2-Trifluoroethanol	0.9	Liquid
16.	2-Methoxy phenol	1.0	Liquid
17.	2-Bromo ethanol	0.7	Liquid
18.	P-Toluene sulphonyl chloride	5.0	Solid
19.	Methane sulphonyl Chloride	2.5	Liquid
20.	3,4 – difluoro nitrobenzene	20.0	Liquid
21.	Epichlorohydrin	15.0	Liquid
22.	Carbonyl diimidazole	15.0	Solid
23.	Acetic anhydride	20.0	Liquid
24.	Hydrazine hydrate	6.0	Liquid
25.	Morpholine.	10.0	Liquid
26.	Oleum (20%)	6.0	Liquid
27.	Citric acid	1.0	Solid
28.	Gutaraldehyde(25%)	1.3	Liquid
29.	Benzaldehyde	0.3	Liquid
30.	Phenyl hydrazine	0.33	Liquid
31.	Dimethyl sulphate	1.21	Liquid
32.	Disodium hydrogen phosphate	0.22	Solid
33.	2- mercapto benzoic acid	0.917	Solid

34.	2-chlorobenzotrifluoride	1.2	Liquid
35.	Allayl chloride	0.35	Liquid
36.	Acetyl chloride	0.1	Liquid
37.	2-hydroxy ethyl piperazine	0.87	Liquid
38.	3-chloro-2-methyl-1-propene	4.8	Solid
39.	Benzene	4.0	Liquid
40.	Potassium acetate	2.0	Solid
41.	4-chloro- butyryl chloride	6.9	Liquid
42.	Azacyclonol	4.3	Solid
43.	2- Chlorobenzonitrile	0.5	Solid
44.	Sodium metal	0.2	Solid
45.	Sulpher powder	0.091	Solid
46.	N-Phthaloyl glycine	0.4	Solid
47.	Phosphorous pentasulphide	0.18	Solid
48.	Trimethylorthoacetate	0.14	Liquid
49.	Triethylorthoformate	0.14	Liquid
50.	Triethyl aniline	1.0	Liquid
51.	(11b,16b)-11-hydroxy-2'-methyl-5'-H-Pregna-1,4-dieno[17,16-d]oxazole-3,20-dione	0.6	Solid
52.	Iodine	0.8	Liquid
53.	Calcium Oxide	0.5	Solid
54.	Acetic Acid	1.0	Liquid
55.	Triethyl Amine	5.0	Liquid
56.	NaHCO ₃	5.0	Solid
57.	Ethyl aceto acetate	1.2	Liquid
58.	2-methoxy ethanol	0.6	Liquid
59.	m-nitro benzaldehyde	0.65	Solid
60.	Trans Cinamaldehyde	0.46	Liquid
61.	BOC anhydride	0.5	Liquid
62.	19-Norpragna-5(10), 9(11)-diene-3, 20-dione,17-hydroxy-,cyclic 3, 20. Bis (1,2-ethanediylacetal), (5a,10a)	0.25	Solid
63.	m-Chloroperbenzoic acid	1.5	Solid
64.	p-Bromo-N,N,-dimethyl aniline	2.0	Solid
65.	Amonium chloride	1.0	Solid
66.	Ethylene dltanone(K.S.M)	3.0	Solid
67.	Pottasiumtert. Butoxide	1.5	Solid
68.	Trifluoroacetophenone	0.5	Liquid

69.	Sodium thiosulphate	0.5	Solid
70.	Cuprous chloride	1.0	Solid
71.	4-Bromo-N,NS-dmethyl aniline	0.2	Solid
72.	Prednisolone [(11 β)-11,17,21-trihydroxy pregna-1,4-diene-3,20-dione]	0.216	Solid
73.	Sodium Metaperiodate	0.28	Solid
74.	Ethyl chloformate	5.9	Liquid
75.	Potassium carbonate	1.0	Solid
76.	Sodium thiosulphate	0.05	Solid
77.	Chloriodomethane	0.1	Liquid
78.	DDQ	0.41	Solid
79.	BSTFA	2.1	Solid
80.	N-(1,1-dimethylethyl)-3-oxo-(5 α ,17 β)-4-azaandrost-17-carboxamide	0.63	Solid
81.	p-Toluene sulphonic acid	0.5	Solid
82.	Methyl orthobutyrate	0.5	Liquid
83.	Oxalic acid	0.5	Solid
84.	Caprolactam	3.5	Liquid
85.	Triethanolamine	2.5	Liquid
86.	SodiumAzide	2.5	Solid
87.	BF ₃ THF	15.0	Liquid
88.	1-Cyclo propyl-6,7-difluoro-4 oxoquinolone-3-carboxylic acid	0.85	Solid
89.	Sulfuryal chloride	0.75	Liquid
90.	7-Chloroquinilidine	9.3	Solid
91.	Isophthalaldehyde	15.0	Solid
92.	Vinyl magnesium bromide	5.0	Liquid
93.	Methyl-2-iodobenzoate	10.0	Solid
94.	DIP Chloride	13.0	Liquid
95.	Methyl magnesium chloride	13.0	Liquid
96.	1-mercapto methyl cyclo propane acetic acid	2.7	Solid
97.	Dicyclohexylamine	2.99	Solid
98.	Sodium methoxide	0.5	Solid
99.	2,3 Pyridine dicarboxylic acid	26.0	Solid
100.	Benzyl amine	19.0	Liquid
101.	D(-) Tartric Acid	15.0	Solid
102.	Gati Acid	15.0	Solid

103.	Boric Acid	5.0	Solid
104.	3-Nitro-Phthalic acid	20.0	Solid
105.	Tetraethyl orthocarbonate	13.0	Liquid
106.	Medoxomil chloride	6.0	Solid
107.	Ortho tolylbenzotrile	15.0	Solid
108.	Thionyl chloride	5.0	Liquid
109.	Palladium Carbon(10%	0.1	Solid
110.	THF	6.0	Liquid
111.	Hydrochloric acid	40.0	Liquid
112.	Sodium hydroxide	15.0	Solid
113. S	Ethyl acetate	10.0	Liquid
114.	Methanol	30.0	Liquid
115.	Acetone	30.0	Liquid
116.	Toluene	30.0	Liquid
117.	Methylene chloride	20.0	Liquid
118.	Isopropanol	10.0	Liquid
119.	Dimethyl formamide	3.0	Liquid
120.	Sulfuric acid	2.0	Liquid
121.	Caustic lye (47%)	5.0	Liquid
122.	Dimethyl sulfoxide	2.0	Liquid
123.	NMP	3.0	Liquid
124.	6-Predoxy-6perbromo-gama-cycloextrin	0.892	Solid
125.	3-Mercaptopropionate	0.715	Liquid
126.	Dibenzosuberone:	3.2	Solid
127.	N,N-dimethylaminopropyl chloride hydrochloride	9.2	Liquid
128.	Phenyl acetic acid	4.6	Solid
129.	Phthalic anhydride	4.8	Solid
130.	(2S)-4-oxo-2-(3-thiazolidinylcarbonyl)-1-pyrrolidinecarboxylic acid tert-butyl ester	1.0	Solid
131.	1-(3-Methyl-1-phenyl-1H-pyrazol-5-yl)piperazine	0.807	Solid
132.	Sodium triacetoxyborohydride	1.42	Solid
133.	Progesterone	20.0	Solid
134.	Ethanol	76.0	Liquid

135.	Collidine	35.0	Liquid
136.	Leutidine	1.0	Liquid
137.	Urea	1.124	Solid
138.	Hydrazine hydrate	0.750	Liquid
139.	Acetone semicarbazone	1.013	Solid
140.	Ethyl chloroacetate	1.443	Liquid
141.	5-Nitrofurfuraldiacetate	1.428	Solid
142.	2-methoxy phenol	7.0	Liquid
143.	1,4-dioxane	3.5	Liquid
144.	Epichlorohydrin	6.3	Liquid
145.	2,6- dimethyl aniline	6.3	Liquid
146.	Chloro-acetyl chloride	8.2	Liquid
147.	Piperazine	22.0	Solid
148.	N,N-Dimethylaminopropyl chloride Hydrochloride	0.639	Liquid
149.	3-Chloroiminodibenzyl	0.270	Solid
150.	(3R)-3-[(tert-butoxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)butanoic acid	7.0	Solid
151.	3-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrazine HCl	1.25	Solid
152.	Hydroxybenzotriazole	3.36	Solid
153.	1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride	4.76	Solid
154.	N,N-Diisopropylethylamine	7.70	Liquid
155.	Orthophosphoric Acid/Hydrochloric acid	2.10	Liquid
156.	N-alpha-(9-Fluorenylmethoxycarbonyl)-N'-2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl-L-arginine	0.023	Solid
157.	N-(9-Fluorenylmethoxycarbonyl)-L-leucine	0.006	Solid
158.	N-[(9H-Fluorén-9-ylméthoxy)carbonyl]leucine	0.004	Solid
159.	N-(9-Fluorenylmethoxycarbonyl)-O-tert-butyl-L-tyrosine	0.0058	Solid
160.	N-alpha-(9-Fluorenylmethoxycarbonyl)-O-t-butyl-L-serine	0.0048	Solid

161.	N-alpha-(9-Fluorenylmethyloxycarbonyl)-N-in-t-butylloxycarbonyl-L-tryptophan	0.0066	Solid
162.	N α -[(9H-Fluoren-9-ylmethoxy)carbonyl]- τ -(triphenylmethyl)-L-histidine	0.006	Solid
163.	L-Pyroglytamic acid	0.0016	Solid
164.	Trifluoroacetic acid	0.1	Liquid
165.	Piperidine	0.054	Liquid
166.	2-CTC Resin	0.018	Solid
167.	N-Methyl-1-naphthylmethyl) methyl amine hydrochloride	1.93	Solid
168.	1-chloro-6,6 dimethylhept-2-en-4-yne	1.33	Solid
169.	6,6-dimethyl hep-1-en-4-yne-3-ol	1.33	Solid
170.	Phosphorous oxychloride	0.53	Liquid
171.	Methyl-2-methoxy-5-sulphonamido-benzoate	1.755	Solid
172.	(S)-1-ethyl-2-aminomethyl pyrrolidine	0.10	Liquid
173.	L-proline	2.05	Solid
174.	Ethyl bromide	2.89	Liquid
175.	Rifamycin S	0.77	Solid
176.	Rifamycin O	0.85	Solid
177.	Ascorbic acid	0.20	Solid
178.	2-Amino-4-methylpyridine	0.46	Solid
179.	1,7'-Dimethyl-2'-propyl-2,5'-bi-benzimidazole	1.31	Solid
180.	2-(4-Bromomethylphenyl)benzoic acid methyl ester	1.58	Solid
181.	Valsartan	0.55	Solid
182.	Sacubitril	0.60	Solid
183.	tert-butyl [(1R)-2-biphenyl-4-yl-1-(hydroxymethyl)ethyl]carbamate	1.60	Solid
184.	Ethyl 2-(triphenylphosphoranylidene) propanoate	1.70	Solid
185.	Succinic anhydride	3.50	Solid
186.	(2R,4S)-5-(Biphenyl-4-yl)-4-[(tert-butoxycarbonyl)amino]-2-methylpentanoic acid	1.20	Solid
187.	Cyanocobalamin	0.22	Solid

188.	Cobalt chloride	0.005	Solid
189.	Ketosulphone	2.20	Solid
190.	Chloro acetyl chloride	1.82	Liquid
191.	Benzyl chloride	0.25	Liquid
192.	Aniline	0.06	Liquid
193.	Neopentyl glycol	0.59	Liquid
194.	Propargyl alcohol	0.23	Liquid
195.	Benzophenone	0.50	Solid
196.	m-nitrobenzaldehyde	0.30	Solid
197.	8,9-difluoro-5-methyl-1-oxo-6,7-dihydro-1 <i>H</i> ,5 <i>H</i> -pyrido[3,2,1- <i>ij</i>]quinoline-2-carboxylic acid	0.24	Solid
198.	4-amino salicylic acid	0.445	Solid
199.	<i>N,N</i> -diethylethylenediamine	0.840	Liquid
200.	Cyclohexanone	0.50	Liquid
201.	Benzoyl chloride	0.725	Liquid
202.	2,3,5-trimethyl hydroquinone	0.262	Solid
203.	2,2,4-trichloroacetophenone	0.625	Solid
204.	1-Chloromethyl phenylthiobenzene	0.420	Solid
205.	2,4,5 triamino-6-hydroxypyrimidine sulphate	5.4	Solid
206.	2-[(4-aminobenzoyl)amino] pentanedioic acid	5.4	Solid
207.	Lincomycin Hydrochloride	0.91	Solid
208.	Pregnenolone	8.5	Solid
209.	4-(4-chlorophenyl)-4-hydroxy piperidine	0.213	Solid
210.	4-Chloro-4'-fluoro butyrophenone	0.242	Liquid
211.	Decanoyl chloride	0.215	Liquid
212.	6-Predoxo-6perbromo-gama-cycloextrin	0.892	Solid
213.	3-Mercaptopropionate	0.715	Liquid
214.	Gamma-cyclodextrin	1.0	Solid



ANNEXURE-5

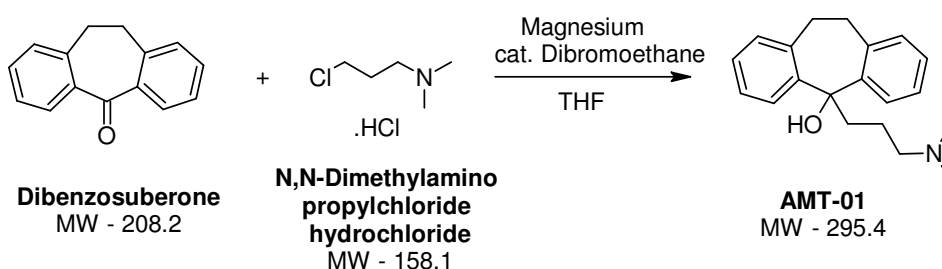
MANUFACTURING PROCESS OF EACH
PROPOSED PRODUCT WITH CHEMICAL
REACTION



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Amitriptyline hydrochloride:

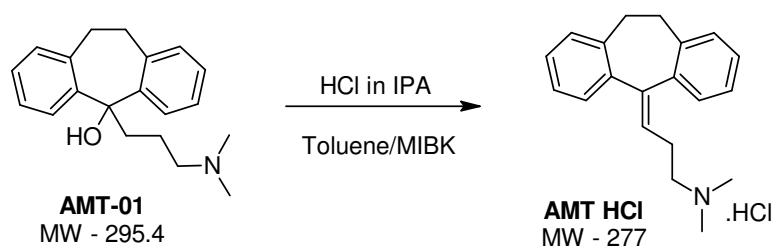
Step-01:



Extraction of Dimethylamino propyl chloride:

Charge Dimethyl amino propyl chloride hydrochloride 60-65% aq. solution (2.0 m.Eq.) and add 50% Aq. NaOH solution Add toluene, stir and separate layers. Dry Toluene layer .Charge magnesium turnings in THF. Heat reaction mass 65°C. Add Dibromoethane (*Cat.*). Add above toluene layer drop wise maintaining temp.60-65°C.Stir reaction mass. Cool reaction mass at RT. Add solution of Dibenzosuberone in toluene. Stir reaction mass for 2 h .Cool the reaction mass 5-10°C. Add water and add 10% sulfuric acid aqueous solution (5V). Stir and separate layer. Distil organic layer under vacuum at 50-55°C to get white colour crystal of AMT/01.

Step-02:



Add Methanol and ~10-15% methanol.HCl to above residual white crystal of AMT/01. Heat reaction mass to 70-75°C.

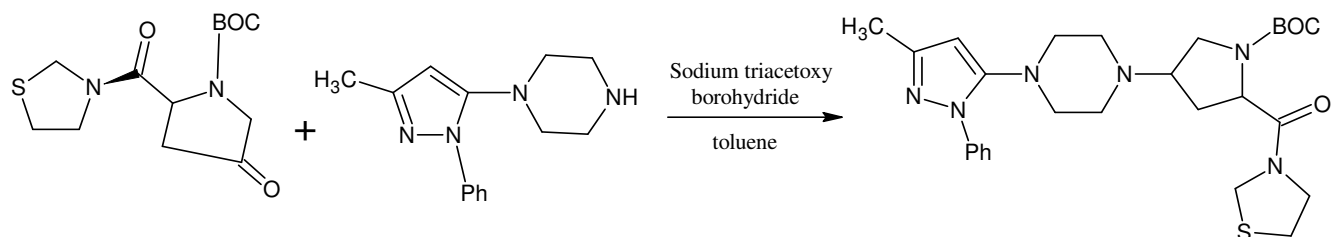
Add activated charcoal. Stir and filter through hyflo bed. Distil out methanol completely under vacuum. Add toluene (1 V) and distill out residual solvent under vacuum. Add Methyl isobutyl ketone. Stir 1-2 h and filter. Dry the solid under vacuum at 50-55°C.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Teneligliptin hemipentahydrobromide hydrate:

Step-01



(2*S*)-4-oxo-2-(3-thiazolidinyl carbonyl)-1-pyrrolidine carboxylic acid tert butyl ester [Intermediate-A]

1-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)piperazine [Intermediate-B]

1-pyrrolidine carboxylic acid, 4-[4-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)-1-piperazinyl]-2-(3-thiazolidinyl carbonyl)-1,1-dimethylethyl ester, (2*S*,4*R*) [Step-01]

CAS No.: [401564-36-1]

CAS No.: [401566-79-8]

CAS No.: [1404559-22-3]

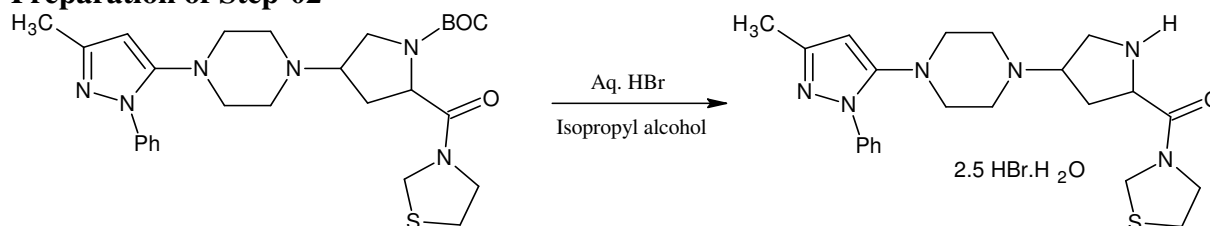
Molecular Formula : C₁₃H₂₀N₂O₄S
 Mol.Wt.: 300.37

Molecular Formula: C₁₄H₁₈N₄
 Mol. Wt.: 242.32

Molecular Formula: C₂₇H₃₈N₆O₃S
 Mol. Wt.: 526.69

(2*S*)-4-oxo-2-(3-thiazolidinyl carbonyl)-1-pyrrolidine carboxylic acid tert butyl ester [Intermediate-A] on reaction with 1-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)piperazine [Intermediate-B] in the presence of Sodium triacetoxy borohydride and toluene to form 1-pyrrolidine carboxylic acid, 4-[4-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)-1-piperazinyl]-2-(3-thiazolidinyl carbonyl)-1,1-dimethylethyl ester, (2*S*,4*R*) [Step-01]

Preparation of Step-02



1-pyrrolidine carboxylic acid, 4-[4-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)-1-piperazinyl]-2-(3-thiazolidinyl carbonyl)-1,1-dimethylethyl ester, (2*S*,4*R*) [Step-01]

Teneligliptin hemipenta hydrobromide hydrate [Step-02]

CAS No.: [1404559-22-3]

CAS No. [906093-29-6]

Molecular Formula: C₂₇H₃₈N₆O₃S
 Mol. Wt.: 526.69

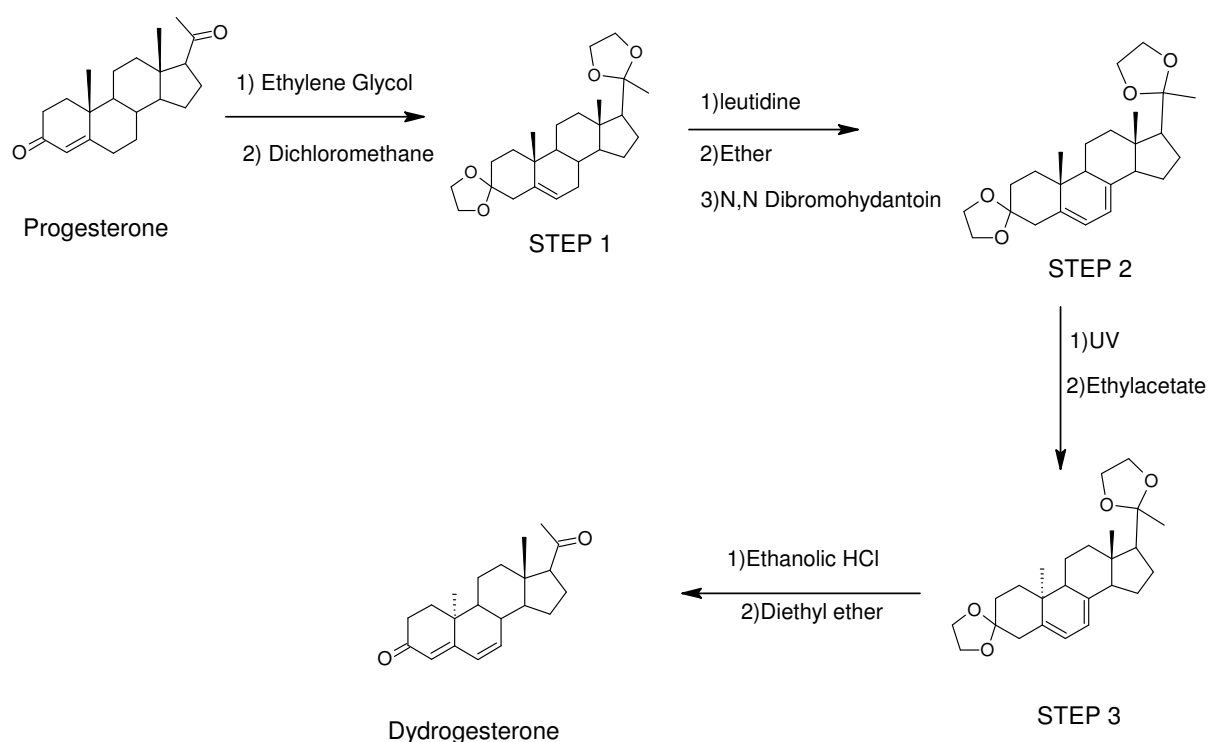
Molecular Formula: C₂₂H₃₀NO₂S2.5HBr.H₂O
 Mol. Wt :628.69



MANUFACTURING PROCESS OF PROPOSED PRODUCT

1-pyrrolidine carboxylic acid, 4-[4-(3-methyl-1-phenyl-1*H*-pyrazol-5-yl)-1-piperazinyl]-2-(3-thiazolidinyl carbonyl)-1,1-dimethylethyl ester, (2*S*,4*R*) [Step-01] on reaction with aqueous hydrobromide in isopropyl alcohol to form Teneligliptin hemipenta hydrobromide hydrate [Step-02]

Dydrogesterone:



Progesterone on reaction with ethylene glycol in dichloromethane gives step-1 which on reaction with leutidine, ether and *N,N*-dibromohydantoin to give step-2.

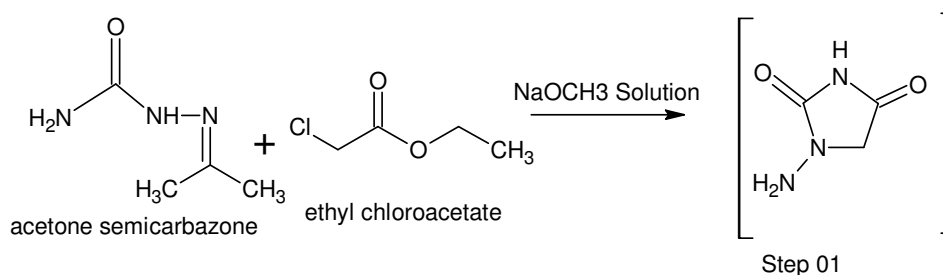
Step-2, expose with UV light in ethyl acetate to give step-3 which on further reaction with ethanolic HCl in diethyl ether to give Dydrogesterone.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

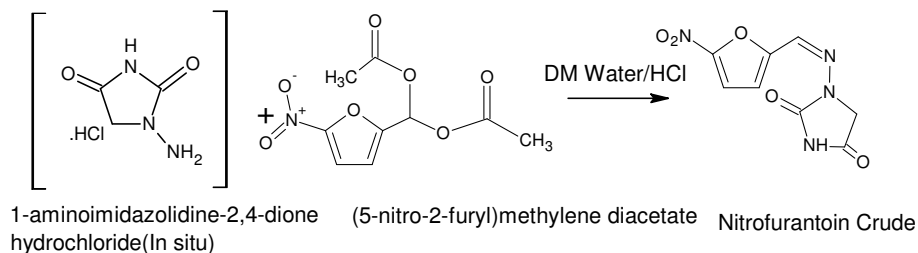
Nitrofurantoin monohydrate:

Stage 01



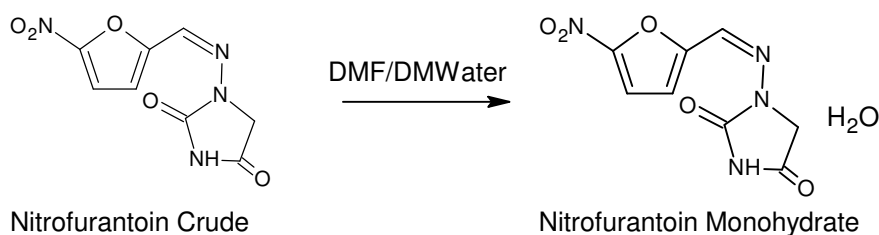
Charge acetone semicarbazone, ethylchloroacetate in sodium methoxide solution in RBF. Heat the reaction mass for 2 hr at 55-60°C. After completion of reaction, to get the compound.

Stage 02



Charge Step 01 and (5-nitro-2-furyl)methylenediacetate and DM Water in RBF. Heat the reaction mass for 2 hr at 70 to 75°C After completion of reaction to get the Nitrofurantoin Crude.

Stage 03



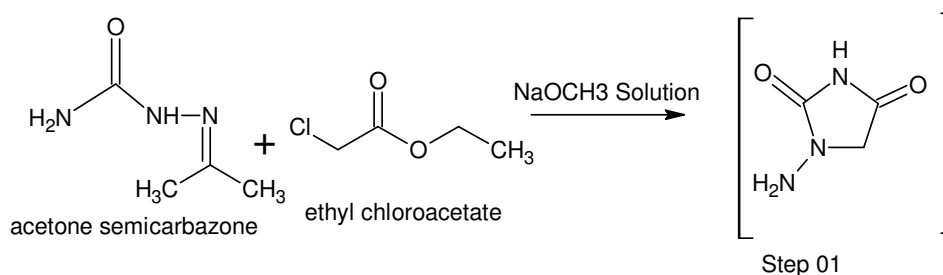
Charge nitrofurantoin Crude in Dimethyl formamide, DM water in round bottom flask to get the Nitrofurantoin Monohydrate.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

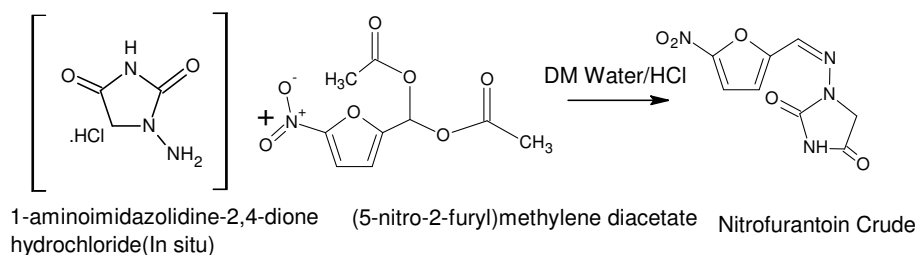
Nitrofurantoin Macrocrystal:

Stage 01



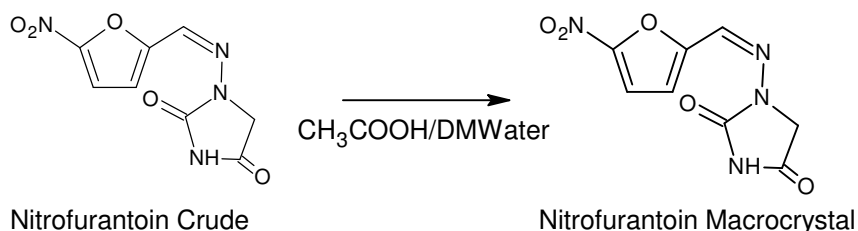
Charge acetone semicarbazone, ethylchloroacetate in sodium methoxide solution in RBF. Heat the reaction mass for 2 hr at 55-60°C. After completion of reaction, to get the compound.

Stage 02



Charge Step 01 and (5-nitro-2-furyl)methylenediacetate and DM Water in round bottom flask. Heat reaction mass for 2 hr at 70 to 75°C. After completion of reaction to get the Nitrofurantoin Crude.

Stage 03



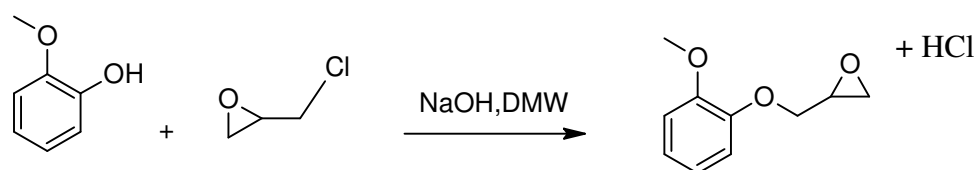
Charge Nitrofurantoin Crude in Acetic Acid and DM water in round bottom flask to get Nitrofurantoin Macrocrystal.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Ranolazine:

RNZ-01:



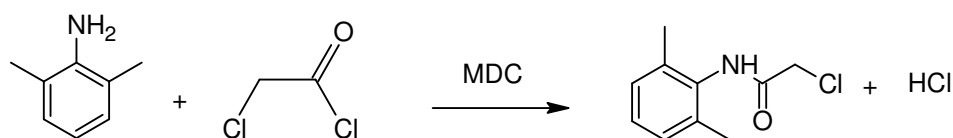
Guaiacol
M.W. 124.14

Epichlorohydrine
M.W. 92.6

RNZ-01
M.W. 180.14

2-methoxy phenol (Guaiacol) reacts with Epichlorohydrine in the presence of sodium Hydroxide as a base and water as reaction medium. After reaction, water removes by separating layers then isolate the compound {1-methoxy-2-(oxiranylmethoxy) benzene (RNZ01)} by distillation.

RNZ-02:



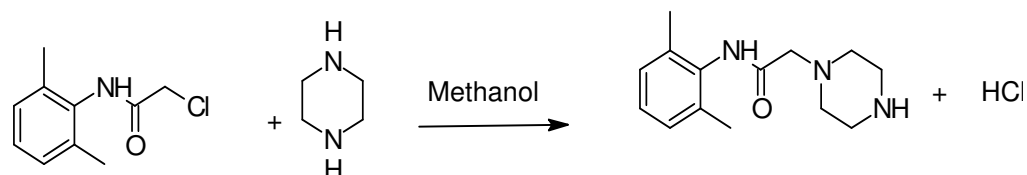
2,6-Dimethyl aniline
M.W.121.2

Chloro-acetyl chloride
M.W.112.94

RNZ-02
M.W. 197.6

2, 6-dichloroaniLine reacts with Chloroacetyl chloride in Dichloromethane. After completion of the reaction excess HCl neutralize with NaOH solution and distil MDC then the compound isolate with Cyclohexane.

RNZ-03:



RNZ-02
M.W. 197.6

Piperazine
M.W.86.13

RNZ03
M.W. 247.3

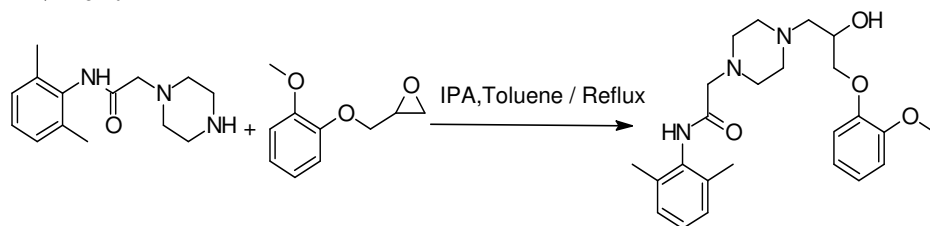
Shree Jee Laboratory Pvt. Ltd.
 C- 24 &25, RIICO Industrial Area Sotanala
 Behror, Alwar, Rajasthan - 301701
 India



MANUFACTURING PROCESS OF PROPOSED PRODUCT

2-chloro-N-(2,6-dimethylphenyl)-acetamide reacts with Piperazine in methanol. After completion of the reaction added DM water into the reaction mass and filter unwanted residue through hyflow bed then extract the compound with MDC.

RNZ-04:



RNZ-03RNZ-01

M.W. 247.3

M.W.180.2

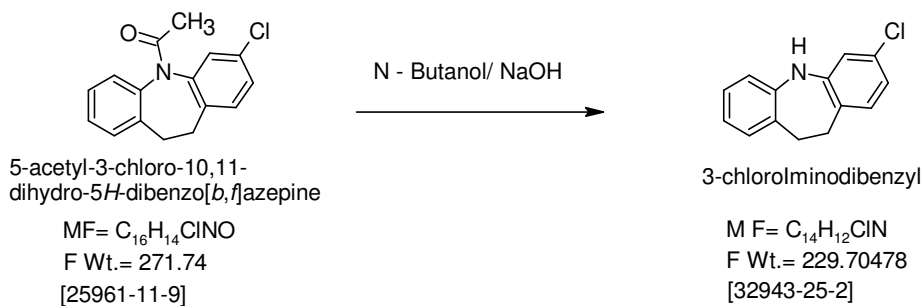
RNZ-04 (Ranolazine)

M.W. 427.5

N-(2,6-dimethylphenyl)-I-piperazineacetamide reacts with 1-Methoxy-2-(oxiranylmethoxy)benzene in toluene and IPA solvents mixture at heating. After reaction completion cool the reaction and isolate Ranolazine by filtering. Purify the compound by crystallization in methanol.

Clomipramine Hydrochloride:

Stage-01

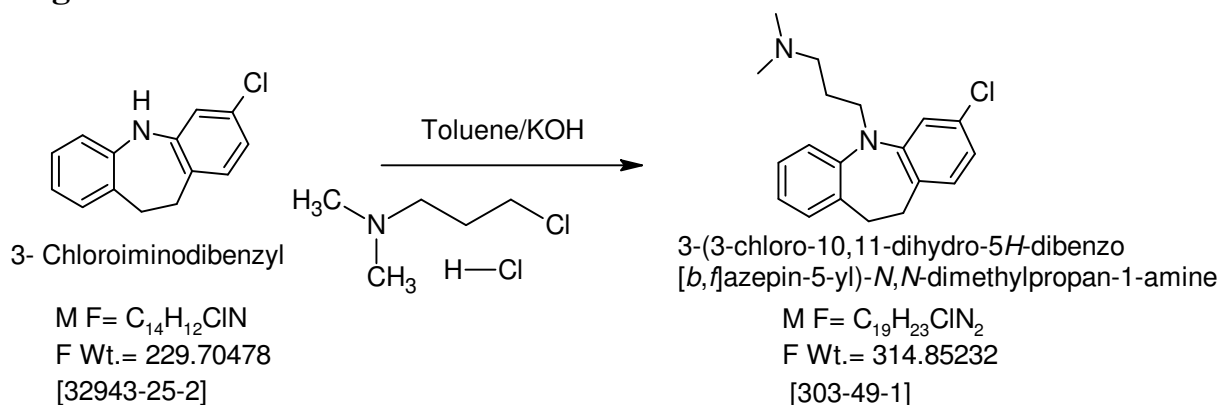


Charge 5-acetyl-3-chloro-10,11-dihydro-5H-dibenzo[b,f]azepine, sodium hydroxide and Butanol in RBF. Heat reaction mass for 4.0 hr at 90 to 95°C. After completion of reaction cool reaction mass followed by crystallisation with Hexane.



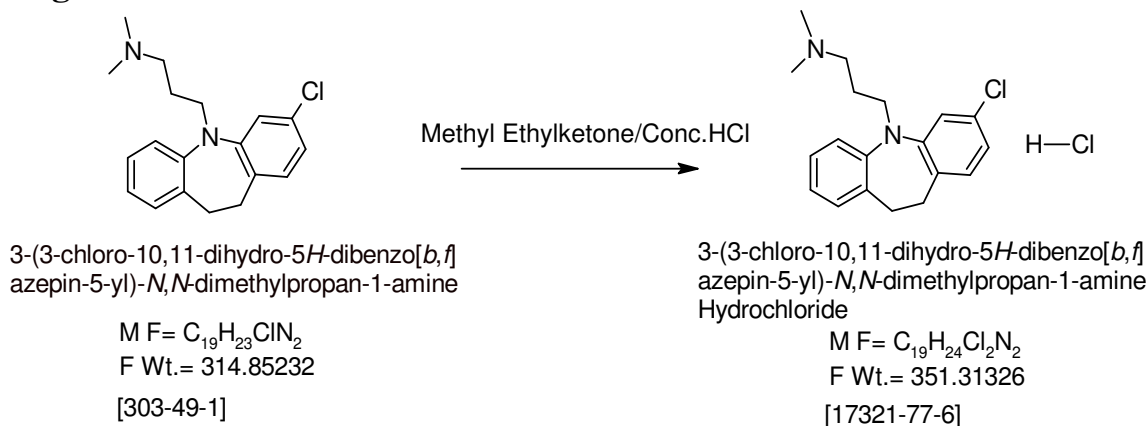
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Stage-02



Charge 3-chloro iminodibenzyl, potassium hydroxide and Toluene in RBF. Heat reaction mass for 1.0 hr at 90 to 95°C. Add dimethyl amine propyl chloride solution in reaction mass. Stir for 6.0 hr at 90 to 95°C. After completion of reaction distil out solvent completely under vacuum.

Stage-03



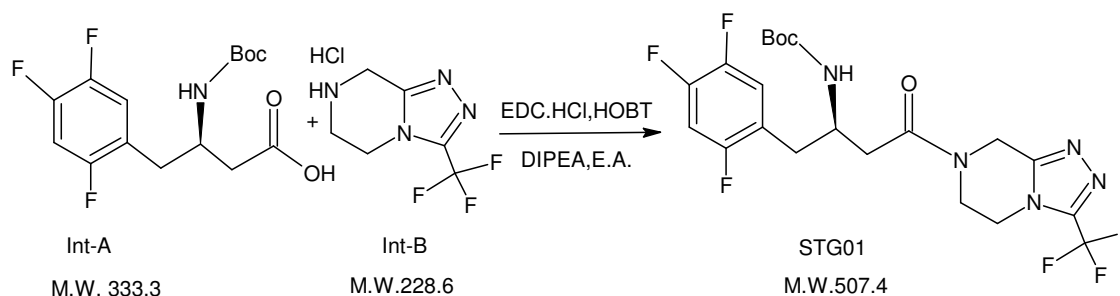
Charge CLP/01 in Methyl ethyl ketone in RBF. Adjusted pH using Aqueous HCl at 25 to 30°C. Stir the reaction mass for 2.0 hrs at 25 to 30°C. Filter reaction mass and wash with Methyl ethyl ketone followed by drying in air Oven at 50 to 55°C.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

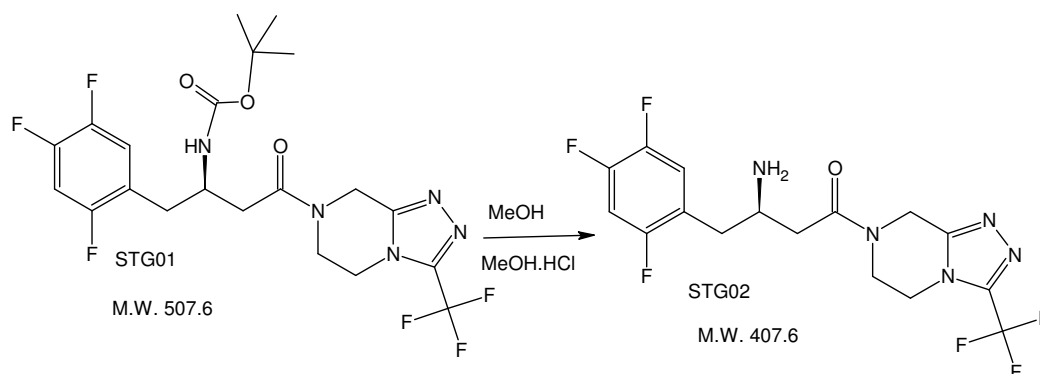
Sitagliptin phosphate/Hydrochloride:

STG-01



(3*R*)-3-[(*tert*-butoxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)butanoic acid (Int-A) reacts with 3-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-*a*]pyrazine hydrochloride in Ethyl acetate in presence of Di-isopropyl ethyl amine, EDC.HCl and HOBT. After reaction isolate the compound after solvent distillation.

STG-02

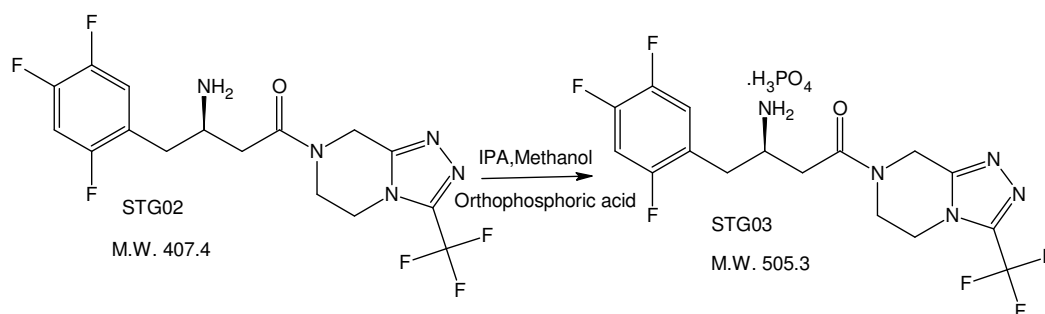


7-[(3*R*)-3-[(1,1-Dimethylethoxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)butanoyl]-3-(trifluoromethyl)-5,6,7,8-tetrahydro-1,2,4-triazolo[4,3- α]pyrazine (STG01) reacts with methanolic HCl in Methanol, form (3*R*)-3-amino-1-[3-(trifluoromethyl)-6,8-dihydro-5H-[1,2,4]triazolo[4,3-*a*]pyrazin-7-yl]-4-(2,4,5-trifluorophenyl)butan-1-one (STG02). After deprotection distills solvent and basify compound with sodium hydroxide in MDC and the compound crystallizes with MTBE.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

STG-03:



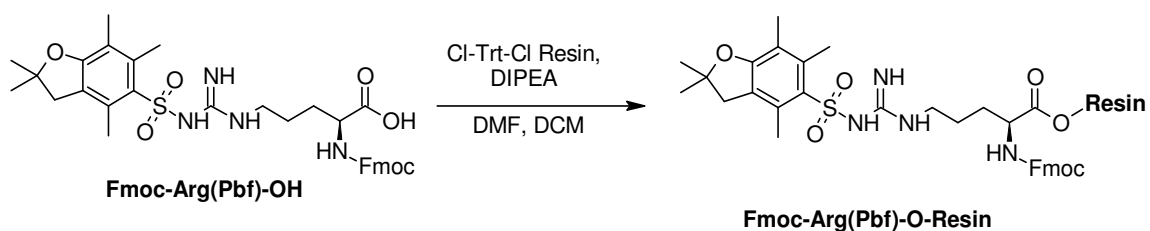
(3R)-3-amino-1-[3-(trifluoromethyl)-6,8-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl]-4-(2,4,5-trifluorophenyl)butan-1-one (STG02) reacts with orthophosphoric acid/Hydrochloric acid in Methanol/IPA to form (3R)-3-amino-1-[3-(trifluoromethyl)-6,8-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrazin-7-yl]-4-(2,4,5-trifluorophenyl)butan-1-one Phosphate.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Leuprolide Acetate:

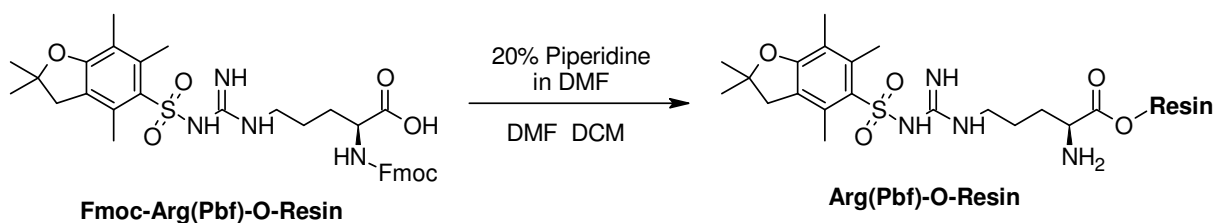
Step-01:



Charge **resin**. Add DCM. Allow resin to swell. Add **Fmoc-Arg(Pbf)-OH** and DIPEA in DCM and Stir at RT. Drain the solvent under nitrogen pressure. Wash the resin twice with DCM.

Add a mixture of DCM:Methanol:DIPEA and stir. Drain solvent under nitrogen pressure. Wash the resin with DMF and DCM alternatively.

Step-02:

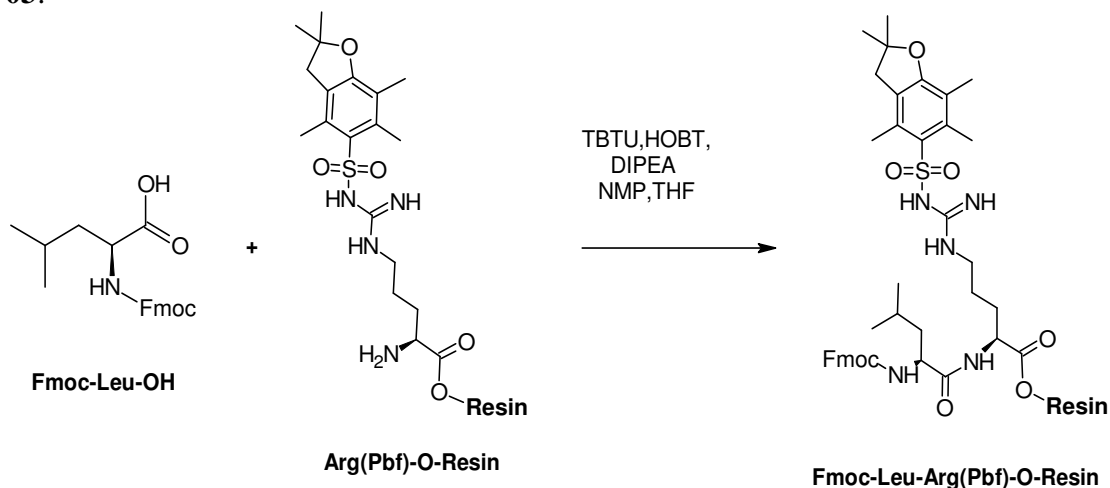


Add 20% piperidine in DMF and Stir. Analyze by HPLC. On confirmation of complete deprotection, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.



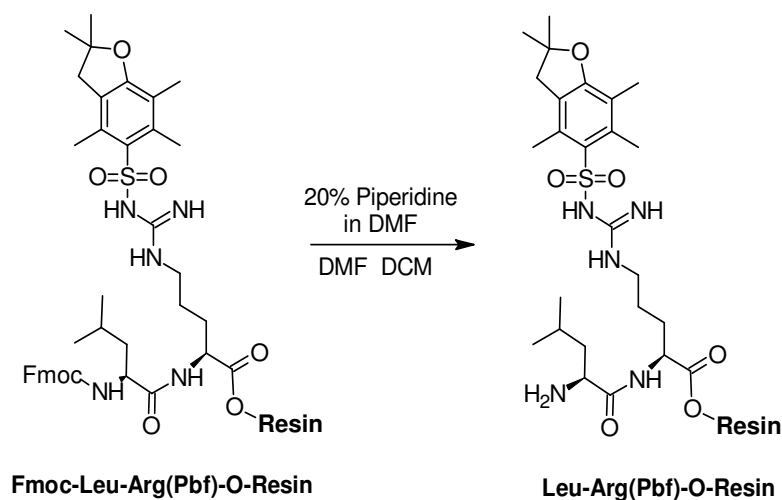
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-03:



Charge **Fmoc-Leu-OH**, TBTU, HOBT and DIPEA in the form of solution in NMP and THF and Stir. On confirmation of complete coupling by HPLC, drain the solvent under nitrogen pressure and wash the resin times with DCM and DMF alternatively.

Step-04:

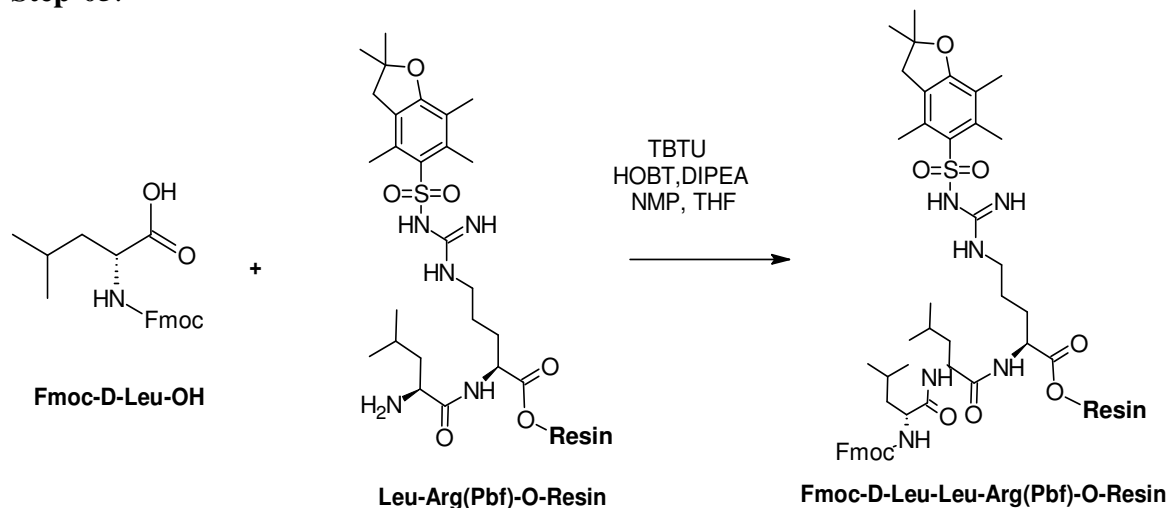


Add 20% piperidine in DMF and stir on confirmation of complete deprotection, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.



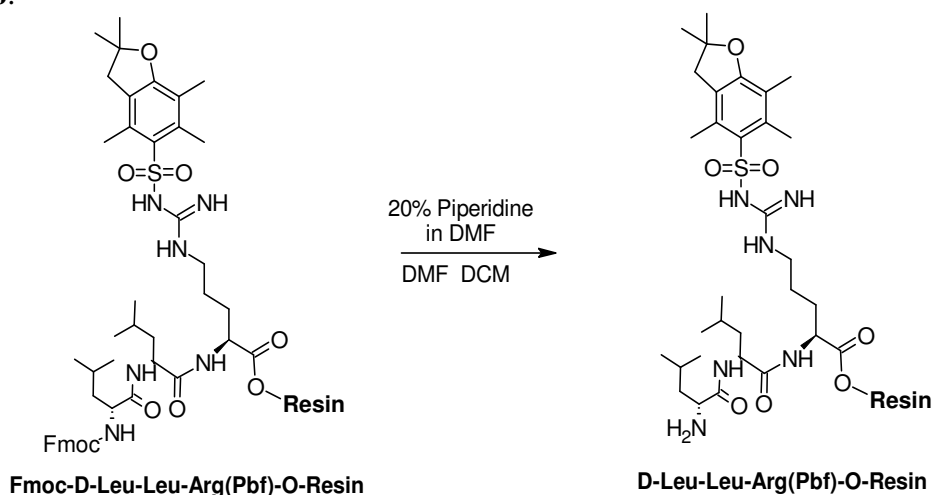
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-05:



Charge **Fmoc-D-Leu-OH** , TBTU , HOBT and DIPEA in the form of solution in NMP and THF and Stir. On confirmation of complete coupling by HPLC, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively

Step-06:



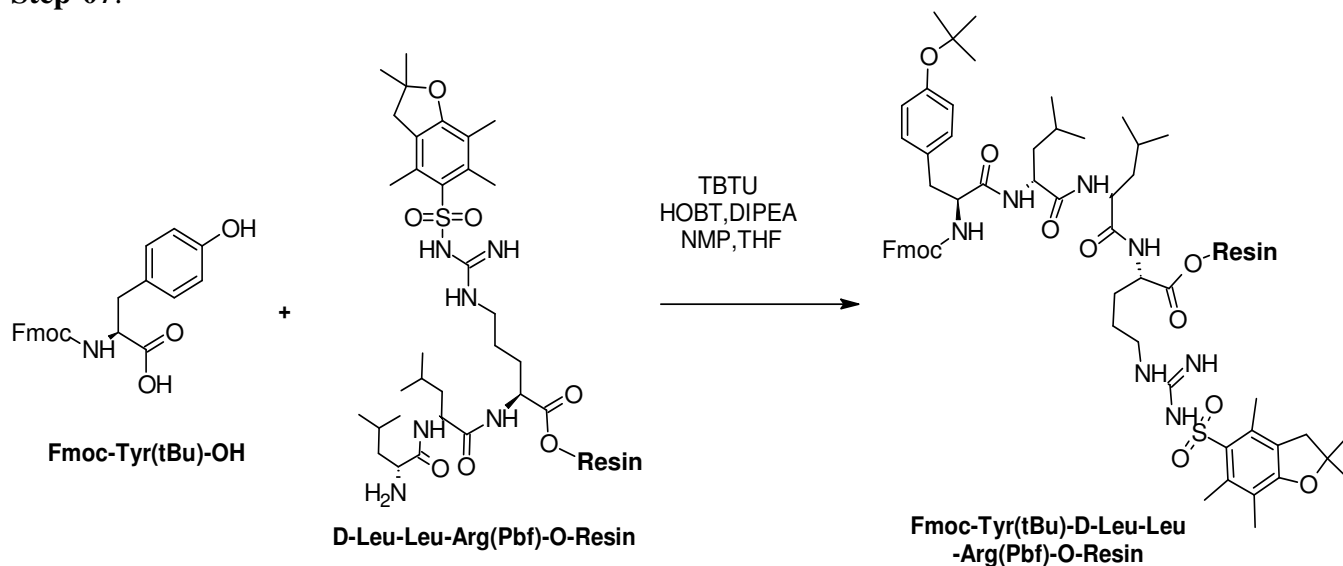
Add 20% piperidine in DMF and Stir. On confirmation of complete deprotection, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.

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MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-07:

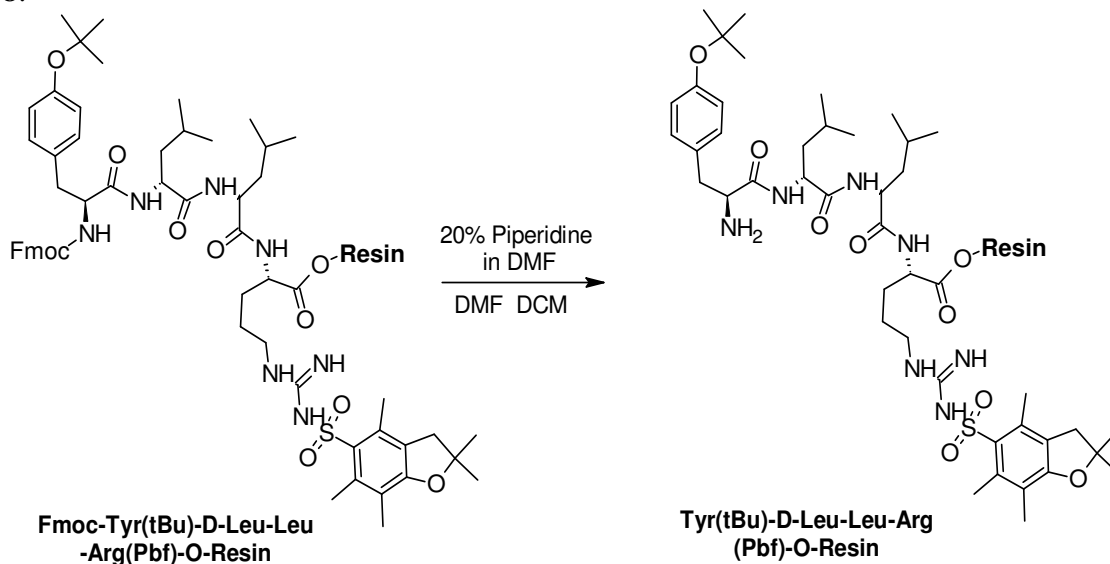


Charge **Fmoc-Tyr(tBu)-OH** , TBTU, HOBT and DIPEA in the form of solution in NMP and THF and Stir. On confirmation of complete coupling by HPLC, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-08:

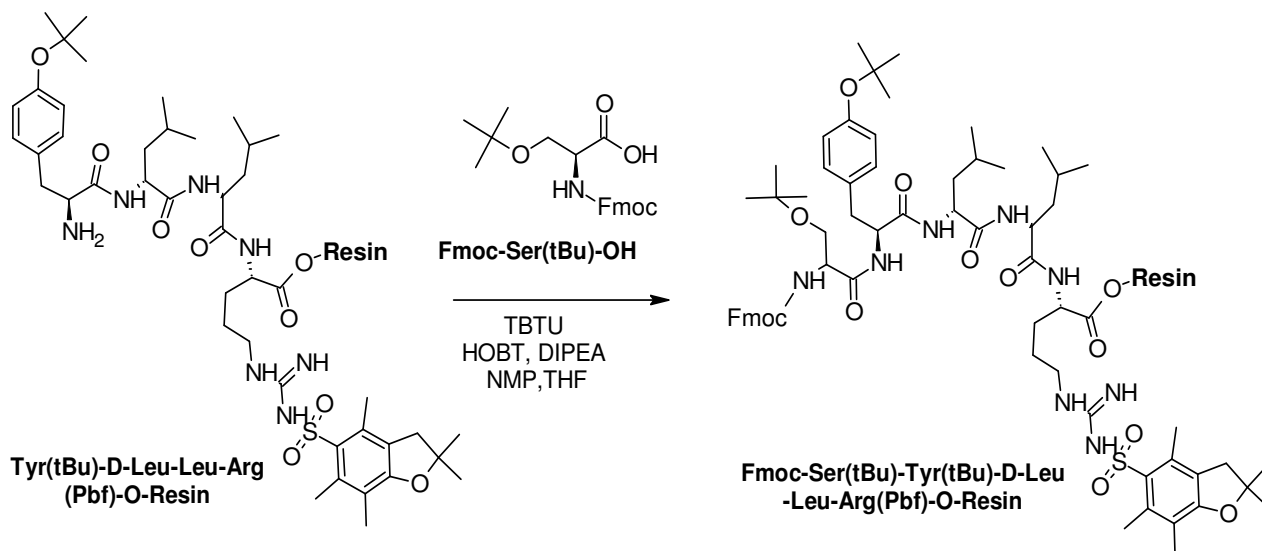


Add 20% piperidine in DMF and Stir. On confirmation of complete deprotection, drain the solvent under nitrogen pressure and wash the resin 5 times with DCM and DMF alternatively.



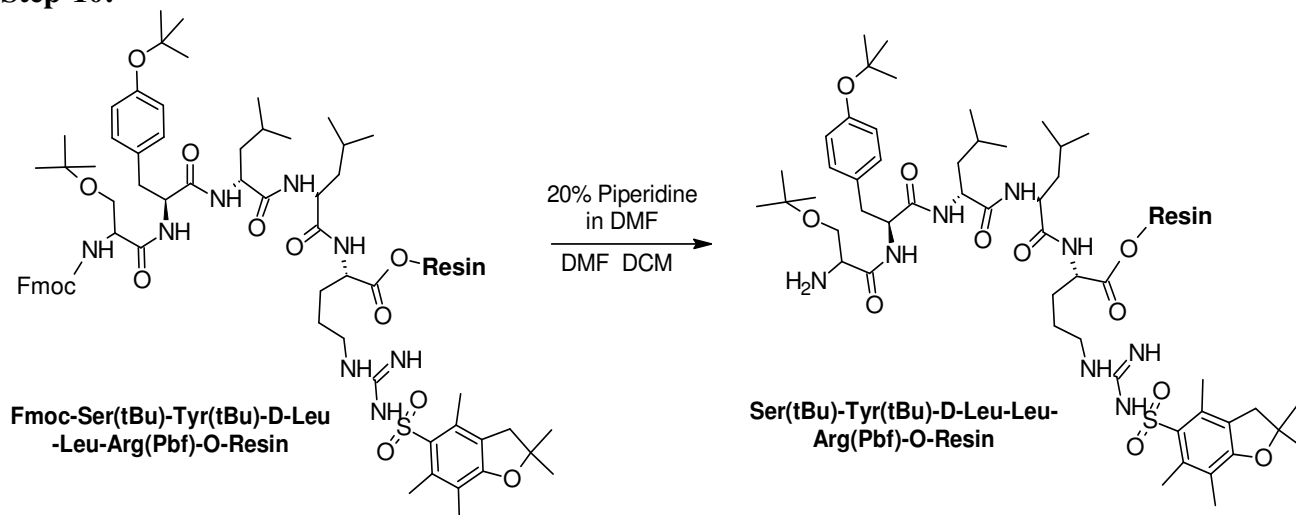
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-09:



Charge **Fmoc-Ser(tBu)-OH** , TBTU, HOBT and DIPEA in the form of solution in NMP and THF and Stir. On confirmation of complete coupling by HPLC, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.

Step-10:

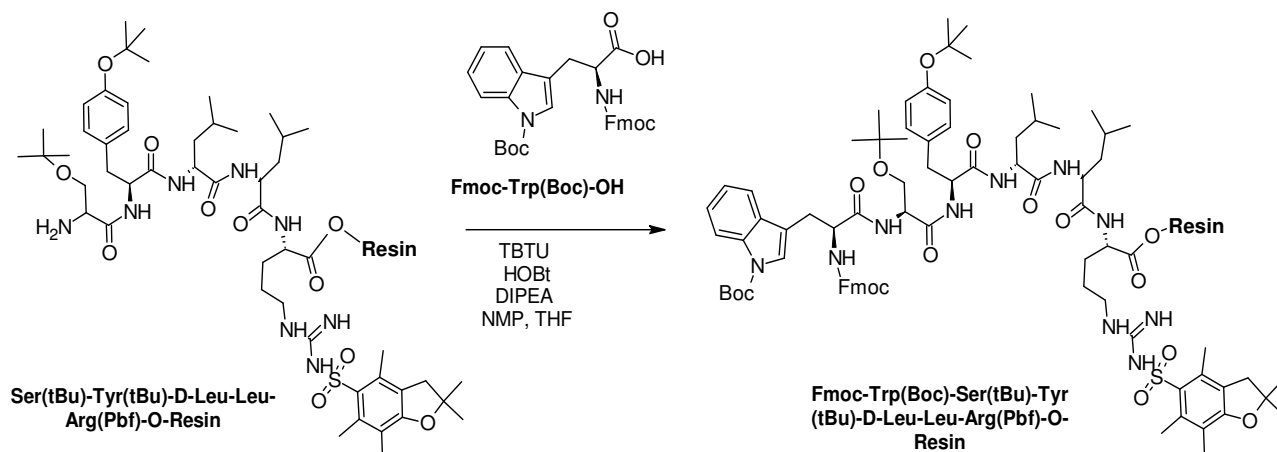


Add 20% piperidine in DMF and Stir. On confirmation of complete deprotection, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.



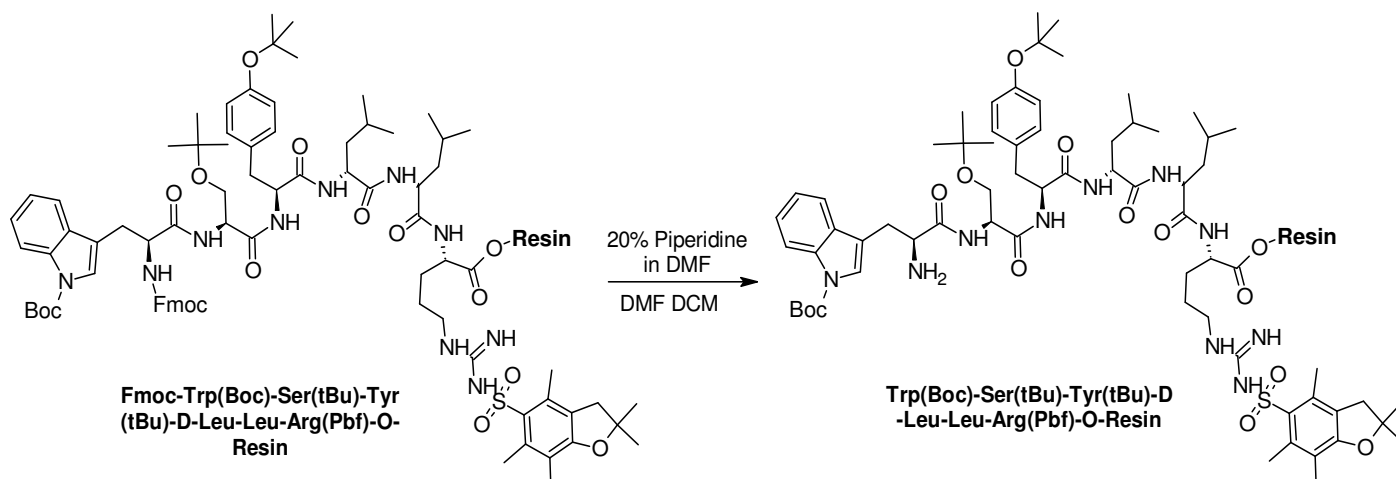
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-11:



Charge **Fmoc-Trp(Boc)-OH**, TBTU, HOBT and DIPEA in the form of solution in NMP and THF and Stir. On confirmation of complete coupling by HPLC, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.

Step-12:

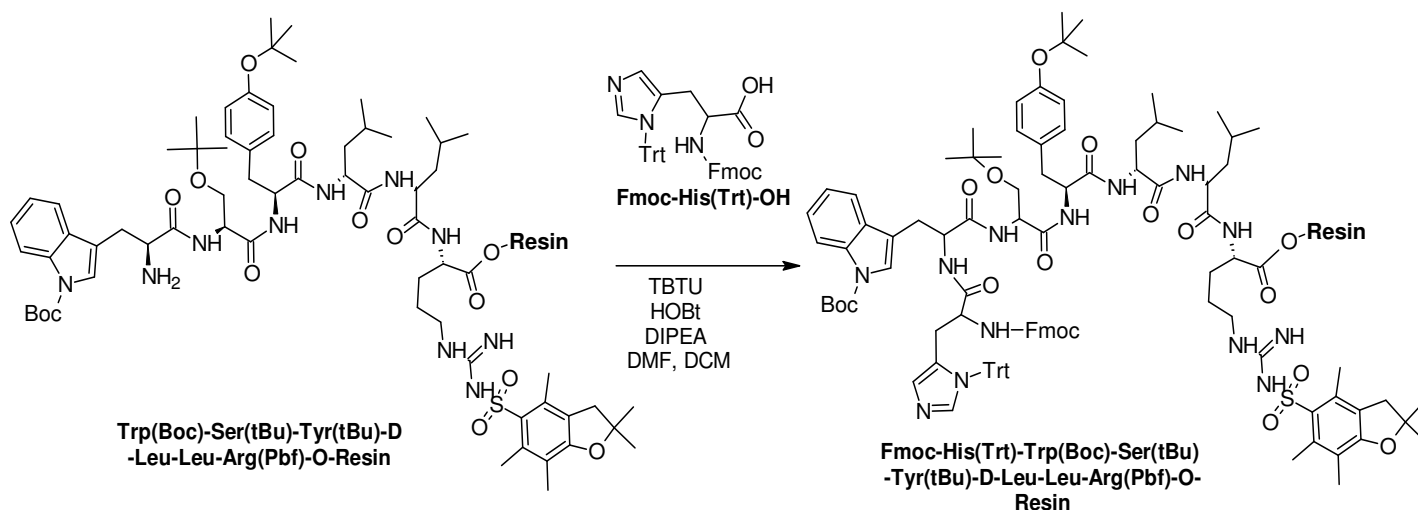


Add 20% piperidine in DMF and Stir. On confirmation of complete de-protection, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.



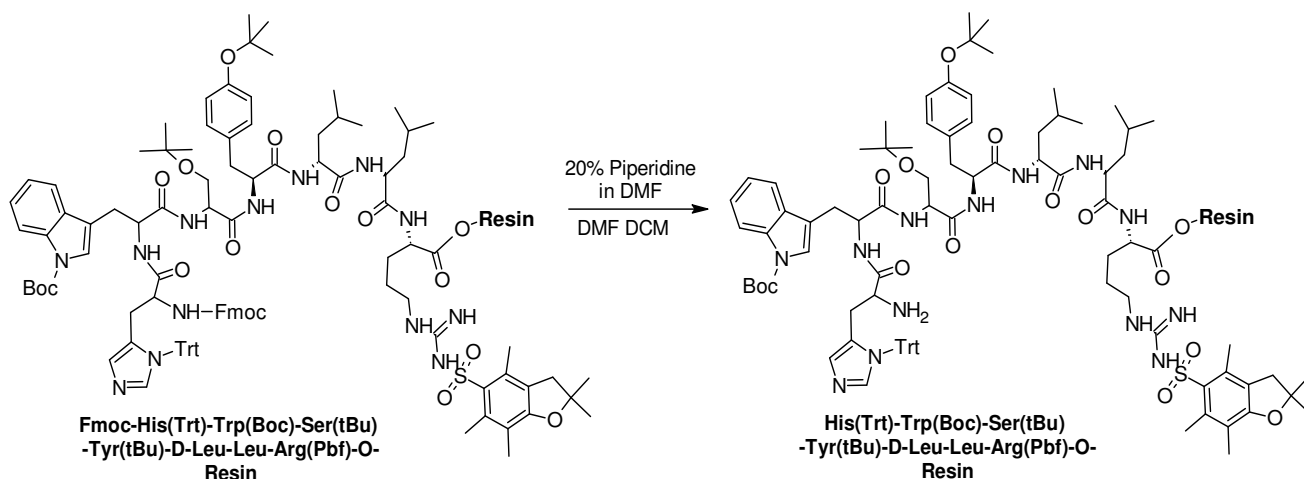
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-13:



Charge **Fmoc-His(Trt)-OH** , TBTU , HOBT and DIPEA in the form of solution in NMP and THF and Stir. On confirmation of complete coupling by HPLC, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.

Step-14:

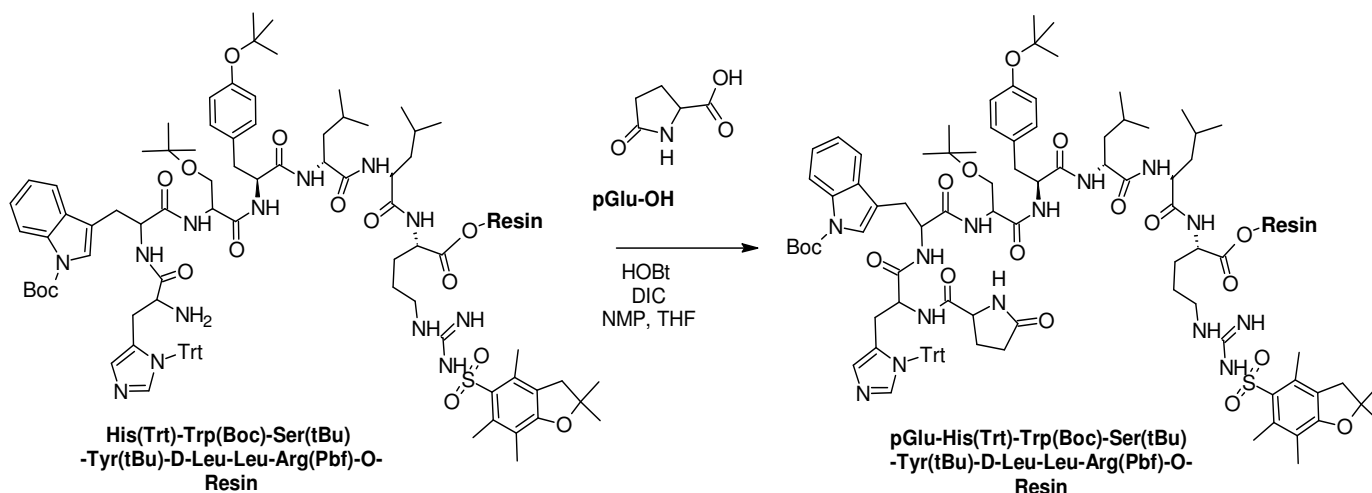


Add 20% piperidine in DMF and Stir. On confirmation of complete deprotection, drain the solvent under nitrogen pressure and wash the resin with DCM and DMF alternatively.



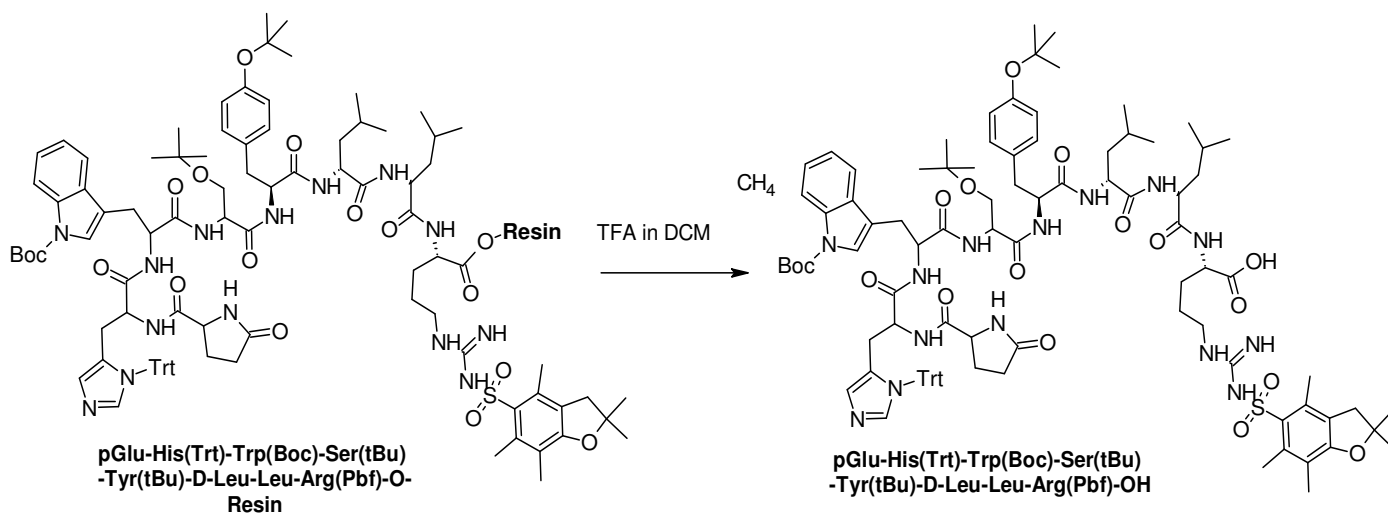
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-15:



Charge **pGlu-OH**, HOBt and DIC in the form of solution in NMP and THF and stir. On confirmation of complete coupling by HPLC, drain the solvent under nitrogen pressure and wash the resin with DMF and DCM respectively.

Step-16:

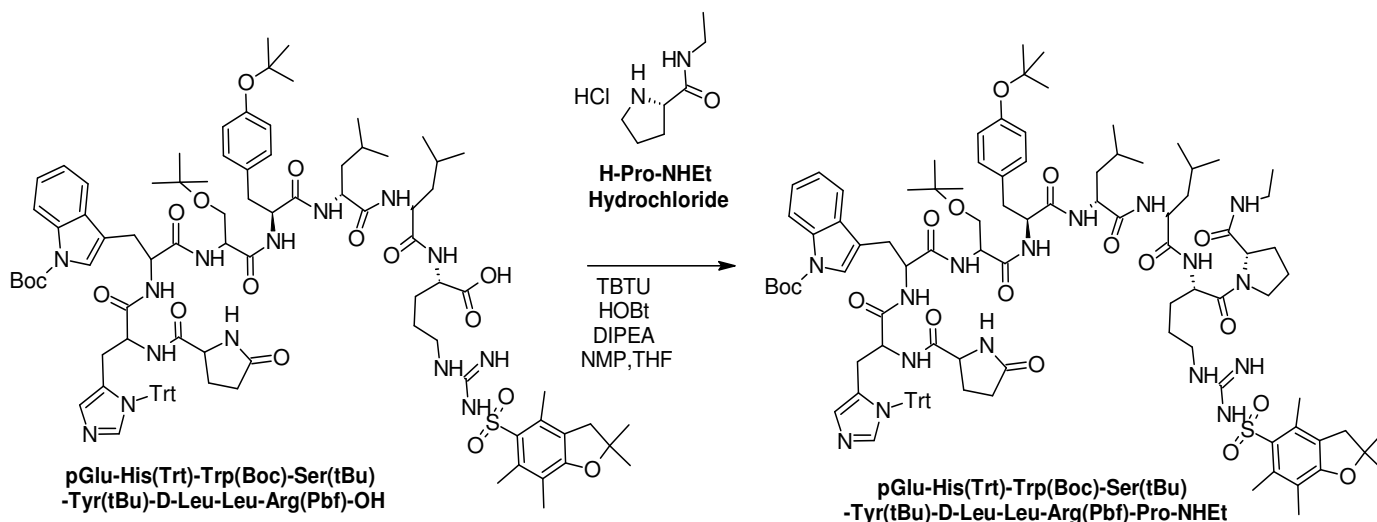


Add TFA solution in DCM and Stir. Drain and collect the filtrate and distil on Rotavap. Add water and stir. Filter and dry under nitrogen pressure.



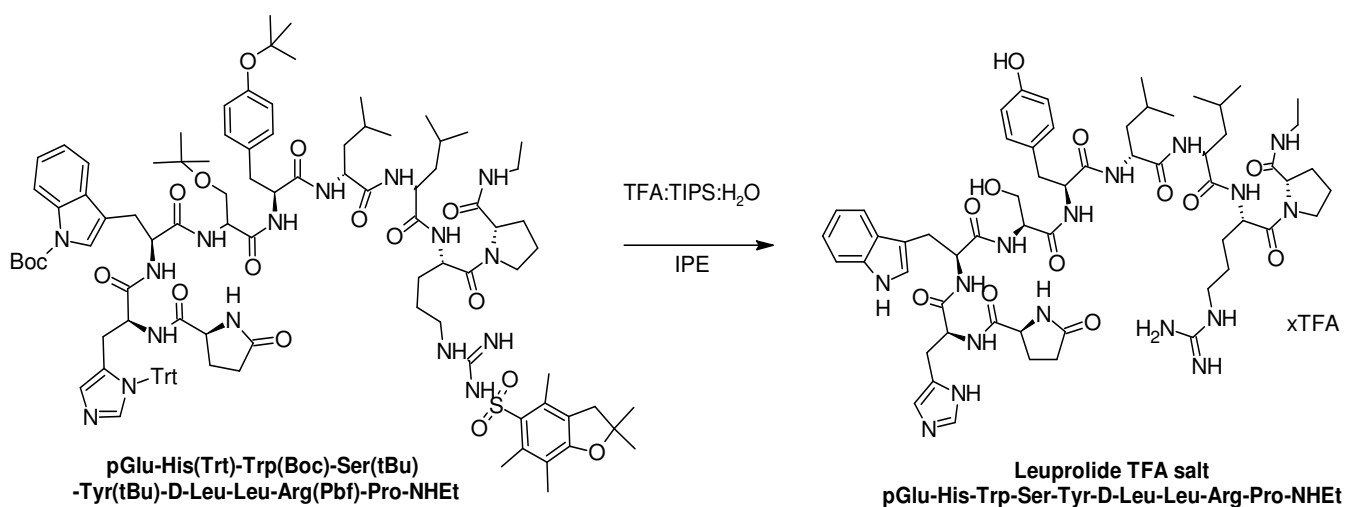
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-17:



Charge pGlu-His(Trt)-Trp(Boc)-Ser(tBu)-Tyr(tBu)-D-Leu-Leu-Arg(Pbf)-OH with ProNHEt.Hcl, HOBt and DIPEA in THF. Dissolve TBTU in NMP and add Dropwise. Stir and Distil out solvent under vacuum. Add chilled water, and filter the reaction mass. Charge wet cake in MDC and add water and stir and separate layers.

Step-18:



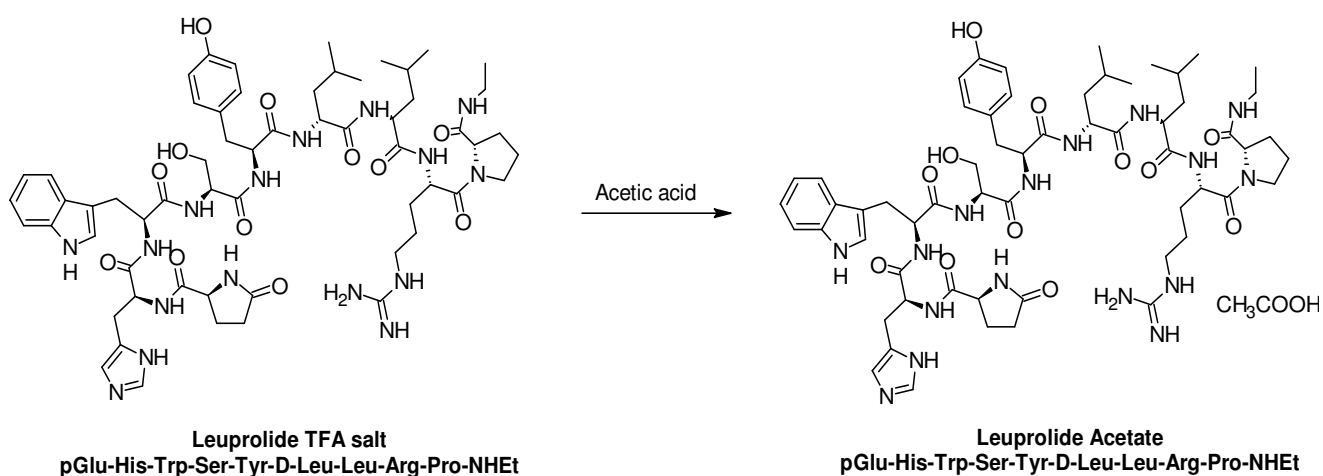
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MANUFACTURING PROCESS OF PROPOSED PRODUCT

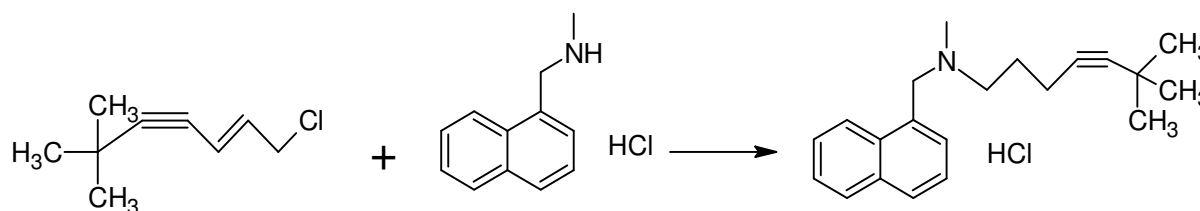
Charge **pGlu-His(Trt)-Trp(Boc)-Ser(tBu) -Tyr(tBu)-D-Leu-Leu-Arg(Pbf)-Pro-NHEt**
 Add mixture of TFA:TIPS:Water and stir at RT. Distil completely, Add IPE and triturate.
 Filter and wash with IPE and dry under nitrogen pressure.

Step-19:



Purification by prep HPLC.

Terbinafine Hydrochloride:



1-Chloro-6,6-dimethyl-hept-2-en-4-yne
 M.Wt.-156.0

N-methyl-(1-naphthylmethyl)amine hydrochloride.
 M.Wt.-195.0

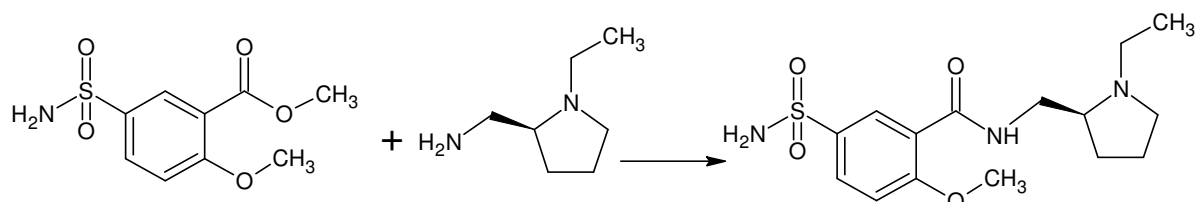
Step-01
 M.Wt.-351.0

1-Chloro-6,6-dimethyl-hept-2-en-4-yne is condensed with N-methyl-(1-naphthylmethyl)amine hydrochloride in the caustic solution to get terbinafine and the then treated with Conc. Hydrochloric acid to afford terbinafine hydrochloride.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Levosulpiride:



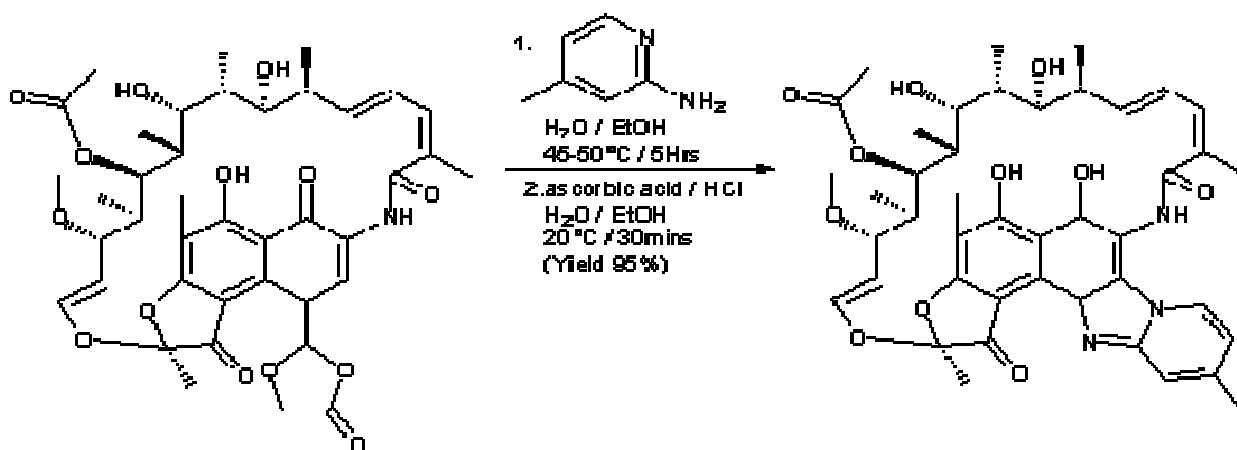
Methyl-2-methoxy-5-sulphonamido benzoate
 M.Wt.-245.22

(S)-(-)-2-Aminomethyl-1-ethyl pyrrolidine
 M.Wt.-128.22

Step-01
 M.Wt.-341.43

Methyl-2-methoxy-5-sulphonamido benzoate is condensed with (S)-(-)-2-Aminomethyl-1-ethyl pyrrolidine in ethylene glycol to yield Levosulpiride.

Rifaximin:



Rifamycin O/S
 CAS No. :-14487-05-9/13553-79-2

Rifaximin
 CAS No. :-80621-81-4

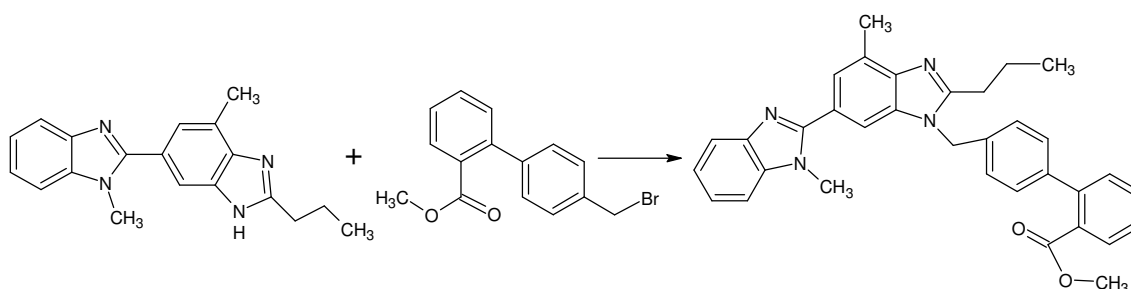
Rifamycin O/S reacts with 2-amino-4-methylpyridine to produce Rifaximin.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Telmisartan:

Step-01:



2-*N*-propyl-4-methyl-6-(1-methylbenzimidazole-2-yl)benzimidazole

M.wt.-304.4

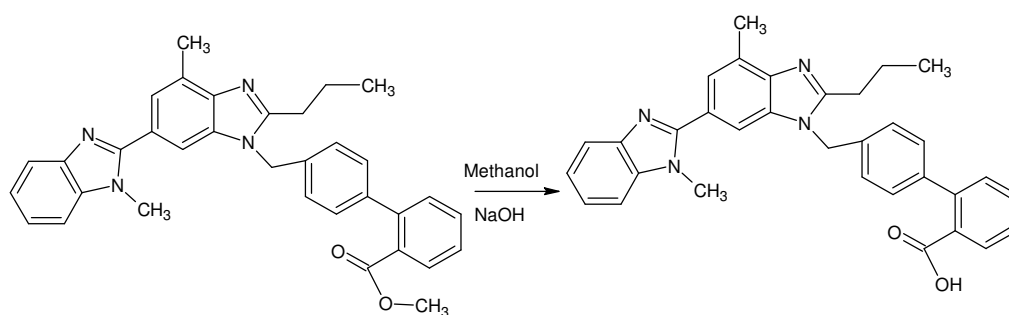
Methyl-4'-bromomethylbiphenyl-2-carboxylate

M.wt.-305.2

Methyl-4'-((1,4'-dimethyl-2'-propyl-2,6'-bi(1H-benzo[d]imidazol)-1'-yl)methyl)biphenyl-2-carboxylate
 M.wt.-528.6

2-*N*-propyl-4-methyl-6-(1-methylbenzimidazole-2-yl)benzimidazole reacts with Methyl-4'-bromomethylbiphenyl-2-carboxylate in the presence of sodium hydroxide in acetone to give step-01.

Step-02:



Methyl-4'-((1,4'-dimethyl-2'-propyl-2,6'-bi(1H-benzimidazol)-1'-yl)methyl)biphenyl-2-carboxylate
 M.wt.-528.6

4'-[(1,4'-dimethyl-2'-propyl-[2,6'-bi(1H-benzimidazol)-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid
 M.wt.-514.62

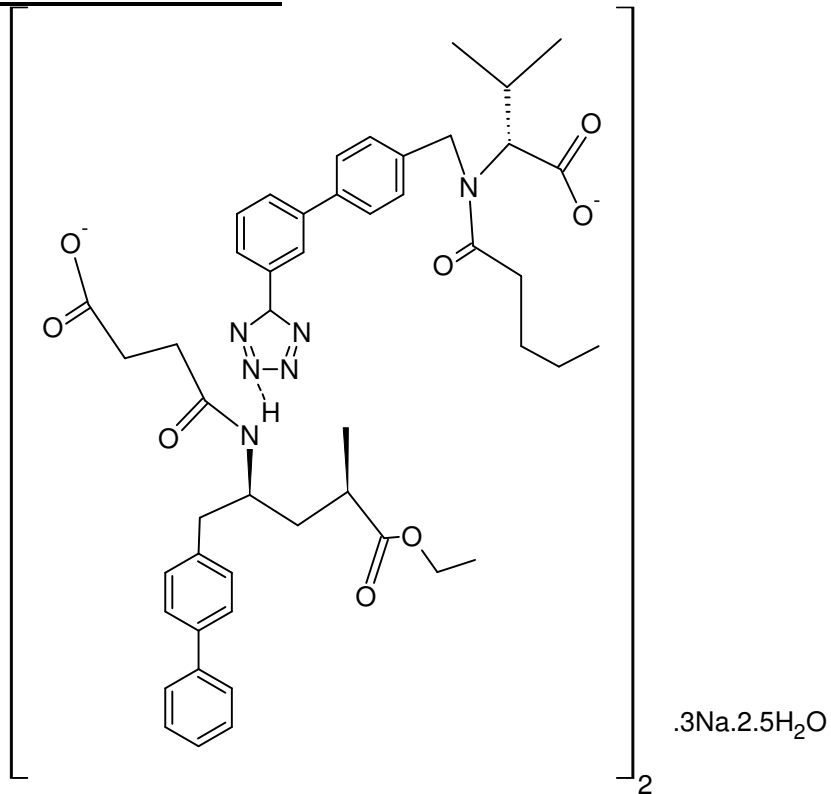
Telmisartan step-01 reacts with sodium hydroxide in the presence of methanol and DM water under reflux condition to give Telmisartan.

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MANUFACTURING PROCESS OF PROPOSED PRODUCT

Sacubitril/Valsartan Sodium Salt:



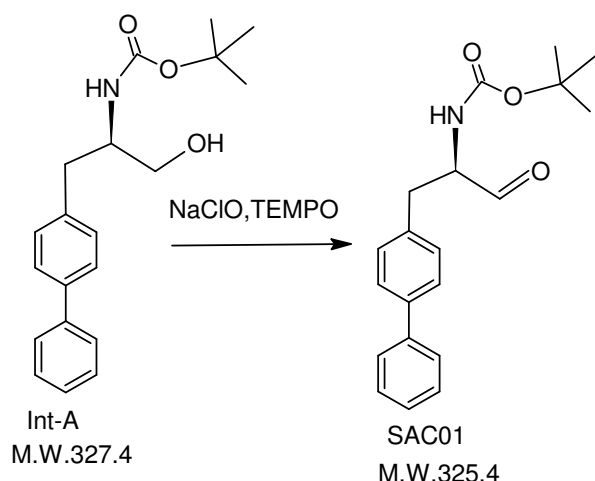
Valsartan and Sacubitril make salt together with NaOH in water and acetone.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

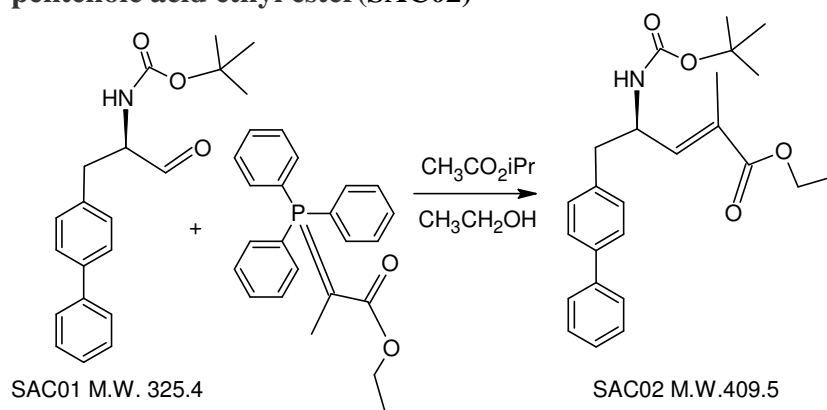
SacubitrilSodium:

tert-butyl [(1*R*)-2-biphenyl-4-yl-1-formylethyl]carbamate(SAC01)



tert-butyl [(1*R*)-2-biphenyl-4-yl-1-(hydroxymethyl)ethyl]carbamate(Int-A) reacts with Sodium hypochlorite and TEMPO in ethyl acetate, forms *tert*-butyl [(1*R*)-2-biphenyl-4-yl-1-formylethyl]carbamate (SAC01).

(4*R*)-5-[1,1'-Biphenyl]-4-yl-4-[[1,1-dimethylethoxy)carbonyl]amino]-2-methyl-2-pentenoic acid ethyl ester(SAC02)

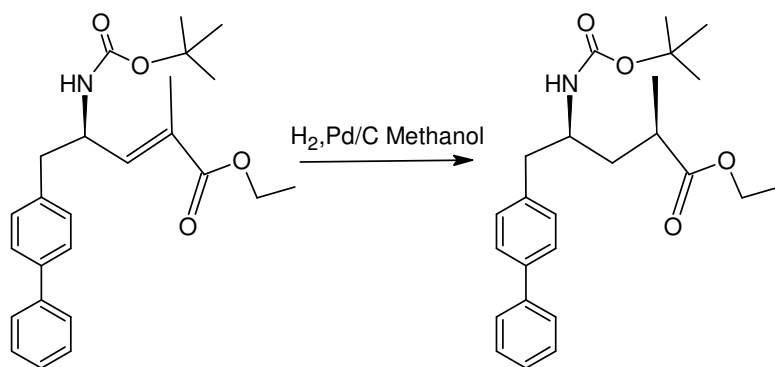


tert-butyl [(1*R*)-2-biphenyl-4-yl-1-formylethyl]carbamate (SAC01) reacts with ethyl 2-(triphenylphosphoranylidene) propanoate in presence of NaBr and NaOH in Isopropyl acetate and ethanol solvents, forms (4*R*)-5-[1,1'-Biphenyl]-4-yl-4-[[1,1-dimethylethoxy)carbonyl]amino]-2-methyl-2-pentenoic acid ethyl ester(SAC02).



MANUFACTURING PROCESS OF PROPOSED PRODUCT

SAC03

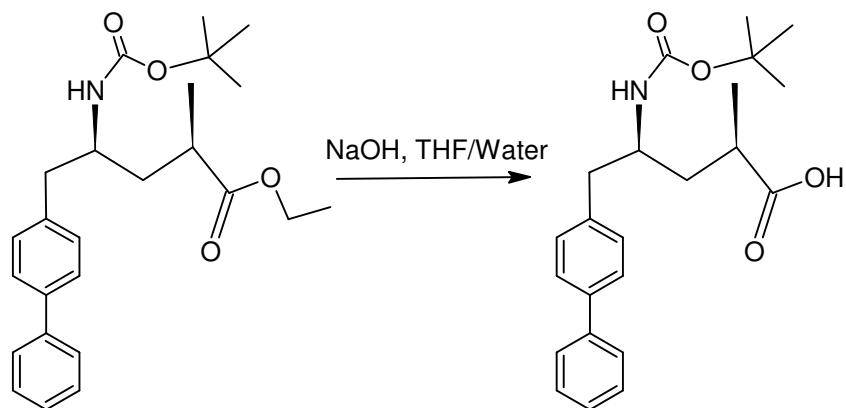


SAC02 M.W. 409.5

SAC03 M.W. 411.5

(4R)-5-[1,1'-Biphenyl]-4-yl-4-[[1,1-dimethylethoxy]carbonyl]amino]-2-methyl-2-pentenoic acid ethyl ester(SAC02) reduce with Hydrogen in the presence of palladium carbon catalyst to form SAC03.

SAC04



SAC03 M.W. 411.5

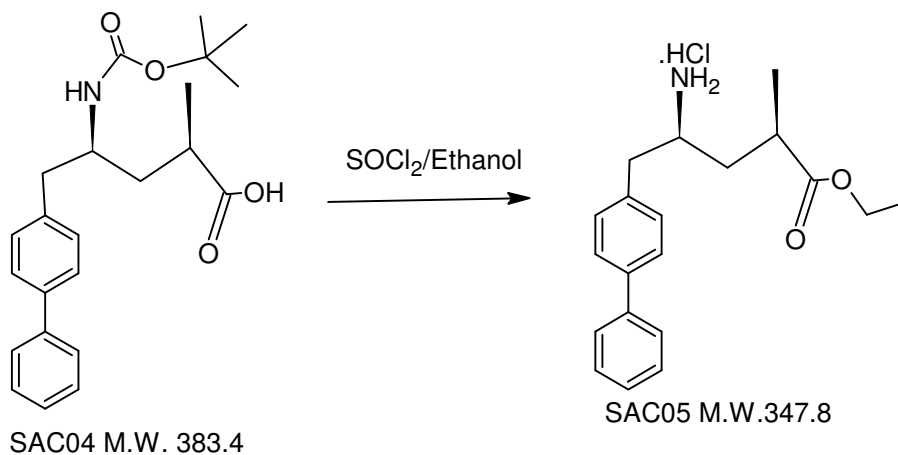
SAC04 M.W. 383.4

SAC03 hydrolyses with Sodium hydroxide in THF and Water solvents to form SAC04.



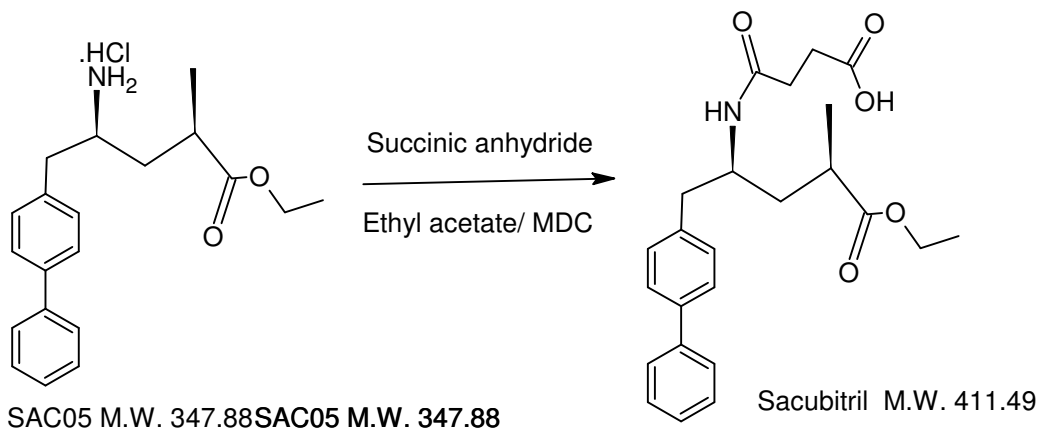
MANUFACTURING PROCESS OF PROPOSED PRODUCT

SAC05



SAC04 reacts with Thionyl chloride and ethanol to form SAC05

SAC06



SAC05 reacts with Succinic anhydride in Ethyl acetate and MDC, forms Sacubitril.

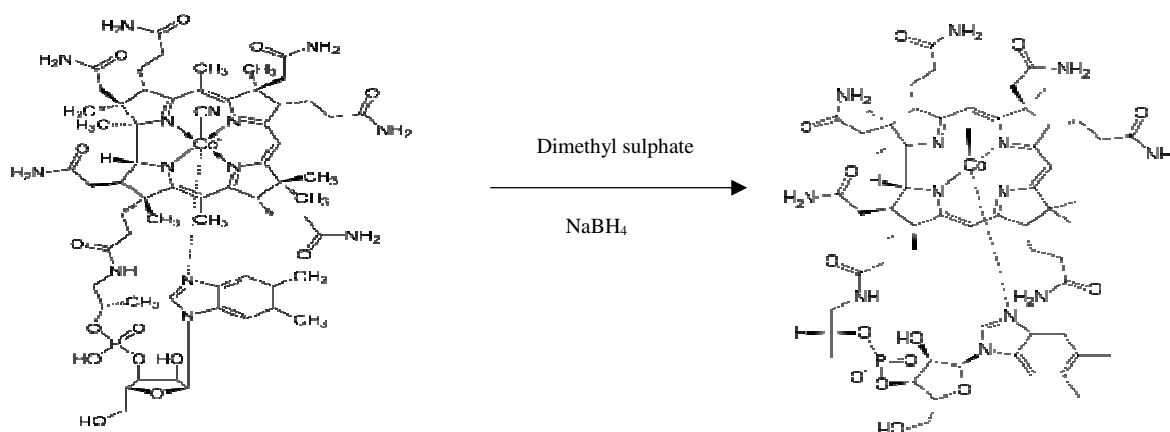
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MANUFACTURING PROCESS OF PROPOSED PRODUCT

Methylcobalamin:

Synthesis of step-01:



Co α -[α -(5,6-dimethyl-benzimidazolyl)]-Co β -
cyanocobamide. MCM-01 [Cyanocobalamin]
CAS No. [68-19-9]
Molecular Formula : C₆₃H₈₈CoN₁₄O₁₄P

Mol. Wt. : 1,355.3

Co α -[α -(5,6-dimethyl-benzimidazolyl)]-Co β -
methylcobamide MCM-02 [Methylcobalamin]
CAS No. [13422-55-4]
Molecular Formula : C₆₃H₉₁CoN₁₃O₁₄P

Mol. Wt. : 1,344.4

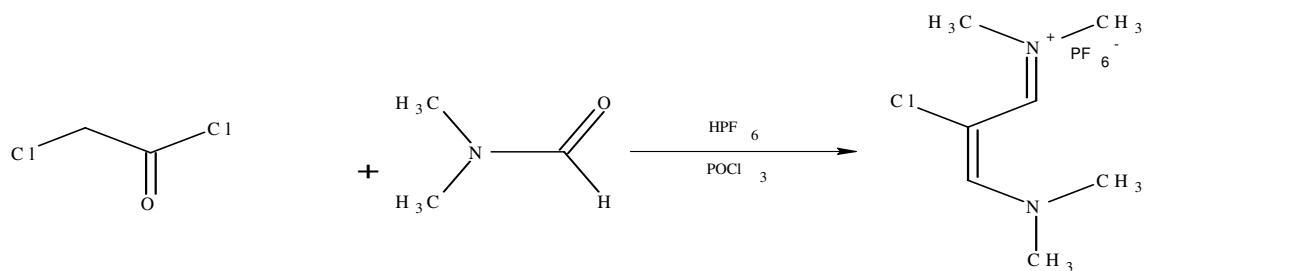
Co α -[α -(5,6-dimethyl-benzimidazolyl)]-Co β -methylcobamide [Methylcobalamin] is prepared by substitution of cyanide in cyanocobalamin [MCM01] with methyl group in the presence of sodium borohydride



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Etoricoxib:

Step-01:



Chloroacetyl chloride

N,N-dimethylformamide

2-chloro-1,3-bis
(dimethylamino)trimethinium
hexafluorophosphate [step-01]
CAS No.: [249561-98-6]
Molecular Formula: $C_7H_{14}ClN_2PF_6$
Mol. Wt.: 306.61

CAS No.: [79-04-9]

Molecular Formula : $C_2H_2Cl_2O$

Mol. Wt. :112.94

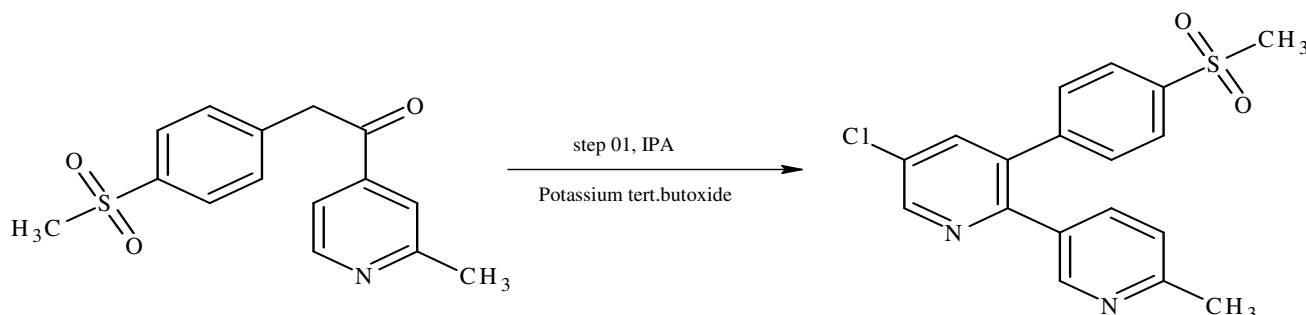
CAS No.: [68-12-2]

Molecular Formula : C_3H_7NO

Mol. Wt. :73.09

Chloroacetyl chloride on reaction with *N,N*-dimethylformamide in the presence of phosphorous oxy chloride and quenched with sodium hydroxide solution and hexafluoro phosphoric acid to give 2-chloro-1,3-bis(dimethylamino)trimethinium hexafluorophosphate [step-01].

Step-02:



2-(4-(mesitylphenyl)-1-(6-methylpyridin-3-yl)-
ethan-1-one [Ketosulphone]

CAS No. [221615-75-4]

Molecular Formula : $C_{15}H_{15}NO_3S$

Mol. Wt :289.34

5-chloro-6'-methyl-3-[4-(methyl
sulfonyl)phenyl]2,3'bipyridine[Etoricoxib]

CAS No.: [202409-33-4]

Molecular Formula: $C_{18}H_{15}ClN_2O_2S$

Mol. Wt.:358.84

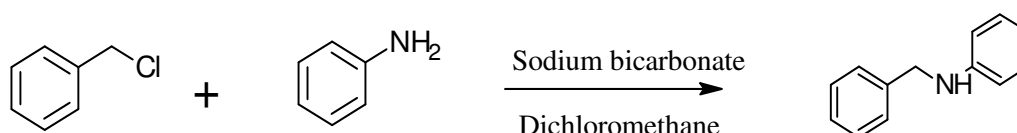
2-(4-(mesitylphenyl)-1-(6-methylpyridin-3-yl)-ethan-1-one [Ketosulphone] on reaction with step-01 in the presence of potassium tert butoxide in isopropyl alcohol to give Etoricoxib



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Efonidipine Hydrochloride ethanolate:

Step-01: Synthesis of Step-01 (A)



Benzyl Chloride
 CAS No. [100-44-7]

Molecular Formula : C₇H₇Cl
 Mol.Wt.: 126.58

Aniline
 CAS No. [62-53-3]

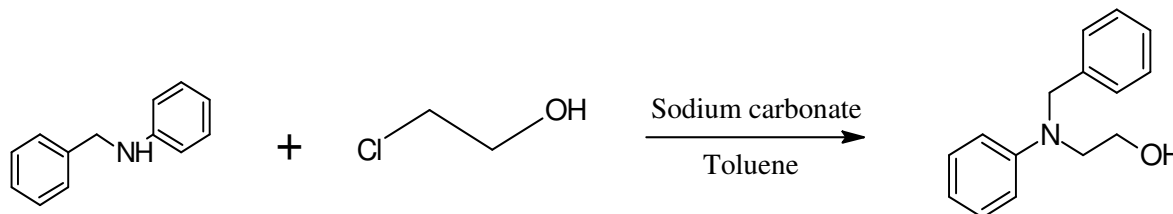
Molecular Formula : C₆H₅NH₂
 Mol.Wt.: 93.13

N-Benzyl aniline [Step-01(A)]
 CAS No. [103-32-2]

Molecular Formula : C₁₃H₁₃N
 Mol. Wt. :183.25

Benzyl Chloride on reaction with aniline in the presence of sodium bicarbonate to give *N*-Benzyl aniline [Step-01(A)]

Step-02: Synthesis of Step-02 (A)



N-Benzyl aniline [Step-01(A)]

CAS No. [103-32-2]

Molecular Formula : C₁₃H₁₃N
 Mol. Wt. :183.25

2-chloro ethanol

CAS No. [107-07-3]

Molecular Formula : C₂H₅ClO
 Mol.Wt.: 80.51

2-[phenyl(phenyl methyl)amino]-ethanol [Step-02 (A)]

CAS No. [33905-47-4]

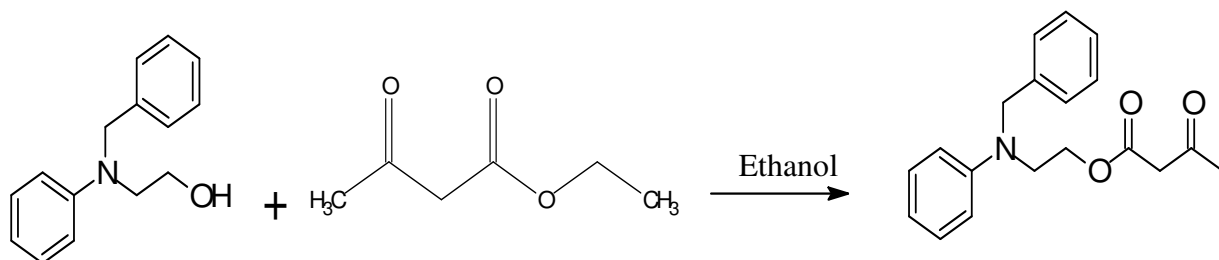
Molecular Formula : C₁₅H₁₇NO
 Mol. Wt. :227.30

N-Benzyl aniline [Step-01(A)] condensed with 2-chloro ethanol give 2-[phenyl(phenyl methyl) amino]-ethanol Step-02(A)



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-03: Synthesis of Step-03 (A)



2-[phenyl(phenyl methyl)amino]-ethanol [Step-02 (A)]
 CAS No. [33905-47-4]

Ethyl acetoacetate
 CAS No. [141-97-9]

2-[benzyl(phenyl)amino]ethyl 3-oxobutanoate [Step-03(A)]
 CAS No. [111011-83-7]

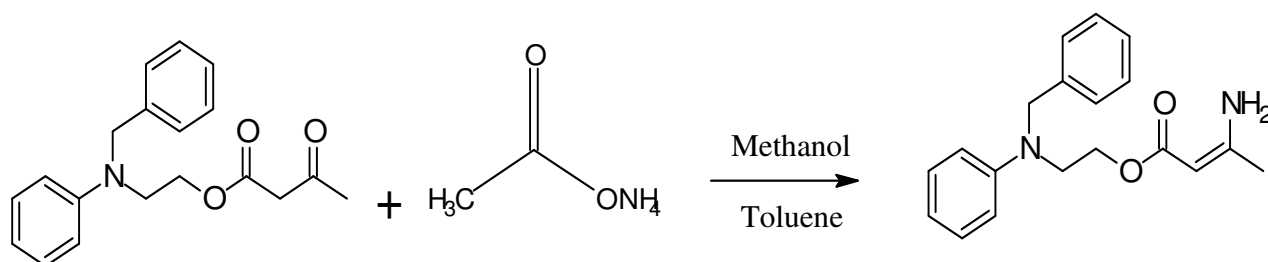
Molecular Formula : C₁₅H₁₇NO
 Mol. Wt. :227.30

Molecular Formula : C₆H₁₀O₃
 Mol.Wt.: 130.14

Molecular Formula : C₁₉H₂₁NO₃
 Mol. Wt. :311.37

2-[phenyl(phenyl methyl)amino]-ethanol Step-02(A) condense with ethyl acetoacetate to give 2-[benzyl(phenyl)amino]-ethyl-3-oxobutanoate [Step-03(A)]

Step-04: Synthesis of Step-04 (A)



2-[benzyl(phenyl)amino]ethyl-3-oxobutanoate [Step-03(A)]
 CAS No. [111011-83-7]

Ammonium acetate
 CAS No. [631-61-8]

3-Amino-but-2-enoic acid 2-(benzyl-phenyl-amino)-ethyl ester [Step-04(A)]
 CAS No. [111011-79-1]

Molecular Formula : C₁₉H₂₁NO₃
 Mol. Wt. :311.37

Molecular Formula : C₂H₇NO₂
 Mol.Wt.: 77.08

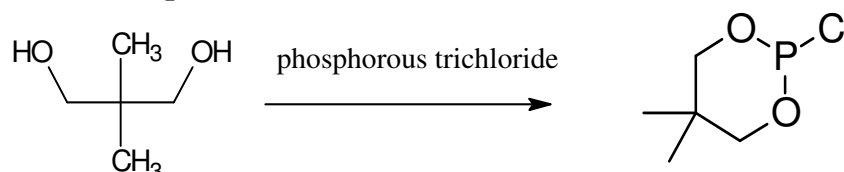
Molecular Formula : C₁₉H₂₂N₂O₂
 Mol. Wt. :310.39



MANUFACTURING PROCESS OF PROPOSED PRODUCT

2-[benzyl(phenyl)amino]-ethyl-3-oxobutanoate [Step-03(A)] on reaction with ammonium acetate to give 3-Amino-but-2-enoic acid 2-(benzyl-phenyl-amino)-ethyl ester [Step-04(A)]

Step-05: Synthesis of Step-01 (B)



Neopentyl glycol

CAS No. [126-30-7]

Molecular Formula : C₅H₁₂O₂

Mol. Wt. :104.14

2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane
 [Step-01(B)]

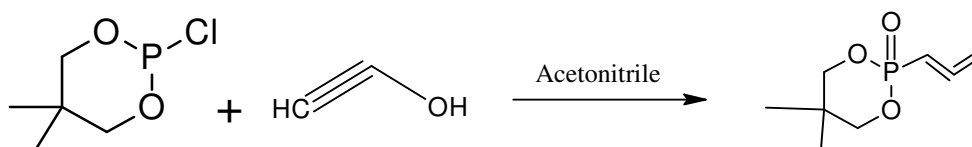
CAS No. [2428-06-0]

Molecular Formula : C₅H₁₀ClO₂P

Mol. Wt. :168.55

Neopentyl glycol is cyclized in the presence of phosphorous trichloride to give 2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane step-01(B)

Step-06: Synthesis of Step-02 (B)



2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane [Step-01(B)]
 CAS No. [2428-06-0]

Molecular Formula : C₅H₁₀ClO₂P
 Mol. Wt. :168.55

Propargyl alcohol

CAS No. [107-19-7]

Molecular Formula : C₃H₄O
 Mol.Wt.: 56.06

5,5-dimethyl-2-propadienyl-1,3,2-dioxaphosphorinane 2-oxide [Step-02(B)]
 CAS No. [119713-39-2]

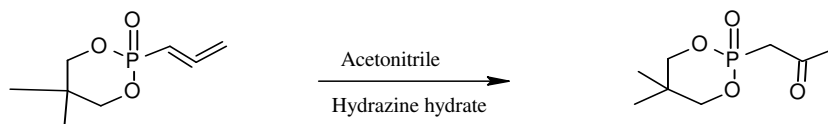
Molecular Formula : C₈H₁₃O₃P
 Mol. Wt. :188.16

2-chloro-5,5-dimethyl-1,3,2-dioxaphosphorinane [Step-01(B)] on reaction with Propargyl alcohol in the presence of triethylamine



MANUFACTURING PROCESS OF PROPOSED PRODUCT

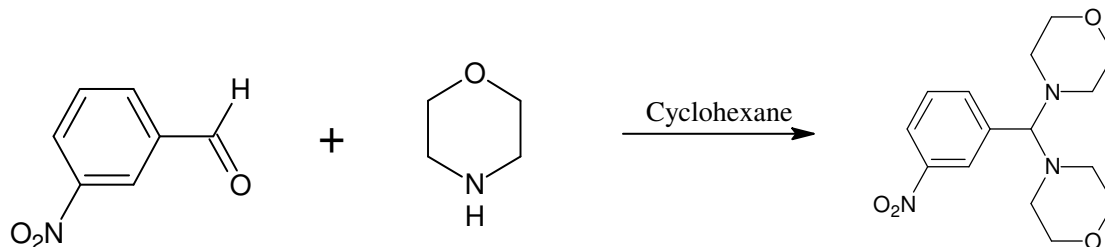
Step-07: Synthesis of Step-03 (B)



5,5-dimethyl-2-propadienyl-1,3,2-dioxaphosphorinane 2-oxide [Step-02(B)]
 CAS No. [119713-39-2]
 Molecular Formula : C₈H₁₃O₃P
 Mol. Wt. :188.16

1-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinane-2-yl)acetone [Step-03(B)]
 CAS No. [111011-80-4]
 Molecular Formula : C₈H₁₅O₄P
 Mol. Wt. :206.18

5,5-dimethyl-2-propadienyl-1,3,2-dioxaphosphorinane 2-oxide [Step-02(B)] on reaction with hydrazine hydrate and concentrated Hydrochloric acid to give 1-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinane-2-yl)acetone [Step-03(Step-07: Synthesis of Step-01 (C))



3-nitrobenzaldehyde

CAS No. [99-61-6]

Molecular Formula : C₇H₅NO₃

Mol. Wt. :151.12

Morpholine

CAS No: [110-91-8]

Molecular Formula: C₄H₉NO

Mol. Wt.: 87.12

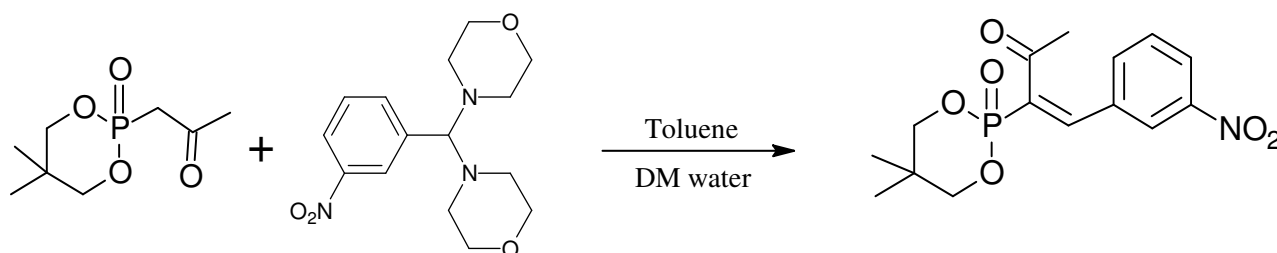
4,4'-((3-nitrophenyl)methylene)dimorpholine [Step-01(C)]

CAS No: [40891-03-0]

Molecular Formula: C₁₅H₂₁N₃O₄

Mol. Wt.: 307.34

Step-08: Synthesis of Step-04 (B)



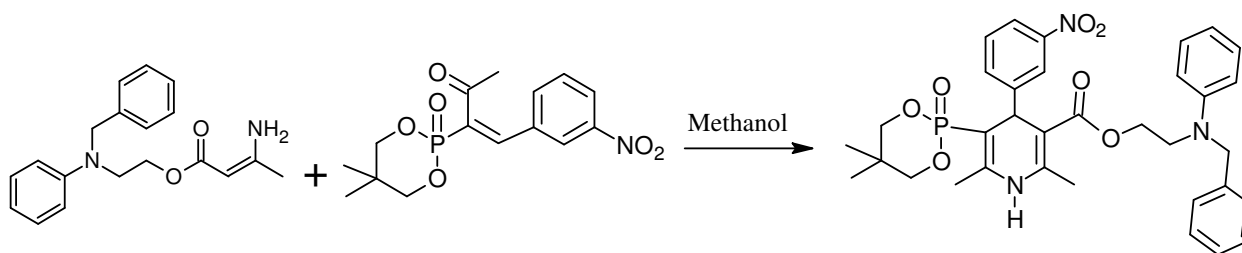


MANUFACTURING PROCESS OF PROPOSED PRODUCT

1-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)acetone [Step-03(B)]	4,4'-((3-nitrophenyl)Methylene) Dimorpholine [Step-01(C)]	3-Buten-2-one, 3-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)-4-(3-nitrophenyl)[Step-04(B)]
CAS No. [111011-80-4] Molecular Formula : C ₈ H ₁₅ O ₄ P Mol. Wt. :206.18	CAS No: [40891-03-0] Molecular Formula: C ₁₅ H ₂₁ N ₃ O ₄ Mol. Wt.: 307.34	CAS No: [111011-78-0] Molecular Formula: C ₁₅ H ₁₈ NO ₆ P Mol. Wt.: 339.28

1-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)acetone [Step-03(B)] is condensed with 4,4'-((3-nitrophenyl) Methylene) Dimorpholine [Step-01(C)] in the presence of mono chloro acetic acid to give 3-Buten-2-one, 3-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)-4-(3-nitrophenyl) [Step-04(B)]

Step-09: Synthesis of Step-01



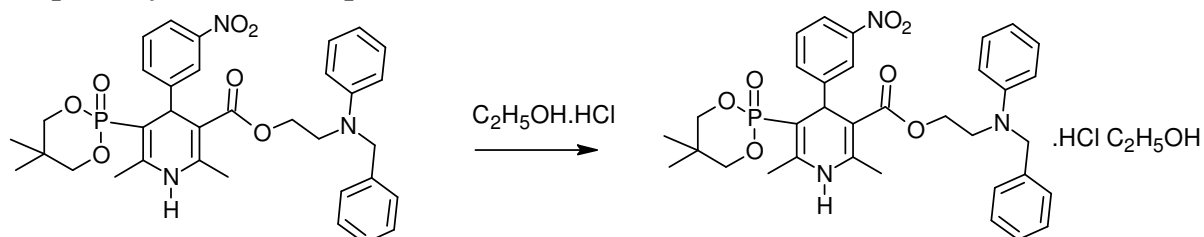
3-Amino-but-2-enoic acid 2-(benzyl-phenyl-amino)-ethyl ester [Step-04(A)]	3-Buten-2-one, 3-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)-4-(3-nitrophenyl) [Step-04(B)]	2-(phenyl-(phenylmethyl)amino)ethyl 5-(5,5-dimethyl-2-oxo-1,3-dioxo-2λ5-phosphacyclohex-2-yl)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylate [Step-01]
CAS No. [111011-79-1] Molecular Formula : C ₁₉ H ₂₂ N ₂ O ₂ Mol. Wt. :310.39	CAS No: [111011-78-0] Molecular Formula: C ₁₅ H ₁₈ NO ₆ P Mol. Wt.: 339.28	CAS No: [111011-63-3] Molecular Formula: C ₃₄ H ₃₈ N ₃ O ₇ P Mol. Wt.: 631.65

3-Amino-but-2-enoic acid 2-(benzyl-phenyl-amino)-ethyl ester [Step-04(A)] is condensed with 3-Buten-2-one, 3-(5,5-dimethyl-2-oxido-1,3,2-dioxaphosphorinan-2-yl)-4-(3-nitrophenyl) [Step-04(B)] in methanol to give 2-(phenyl-(phenylmethyl)amino)ethyl 5-(5,5-dimethyl-2-oxo-1,3-dioxo-2λ5-phosphacyclohex-2-yl)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylate [Step-01]



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-10: Synthesis of Step-02



henyl-(phenylmethyl)amino)ethyl 5-(5,5-dimethyl-2-oxo-1,3-dioxo-2λ5-phosphacyclohex-2-yl)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylate [Step-01]

CAS No: [111011-63-3]

Molecular Formula: $C_{34}H_{38}N_3O_7P$

Mol. Wt.: 631.65

2-(phenyl-(phenylmethyl)amino)ethyl-5-(5,5-dimethyl-2-oxo-1,3-dioxo-2λ5-phosphacyclohex-2-yl)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylate hydrochloride ethanolate [Step-02]

CAS No: [111011-76-8]

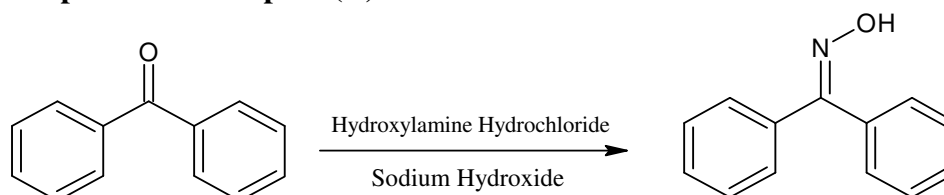
Molecular Formula: $C_{36}H_{45}ClN_3O_8P$

Mol. Wt.: 714.18

2-(phenyl-(phenylmethyl)amino)ethyl 5-(5,5-dimethyl-2-oxo-1,3-dioxo-2λ5-phosphacyclohex-2-yl)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylate [Step-01] on treatment with ethanolic Hydrochloric acid in ethanol to get 2-(phenyl-(phenylmethyl)amino)ethyl 5-(5,5-dimethyl-2-oxo-1,3-dioxo-2λ5-phosphacyclohex-2-yl)-2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3-carboxylate hydrochloride ethanolate [Step-02]

Azelnidipine:

Step-01: Preparation of Step-01 (A)



Benzophenone

CAS No. [119-61-9]

Molecular Formula : $C_{13}H_{10}O$

Mol.Wt.: 182.21

Benzophenone Oxime [Step-01(A)]

CAS No. [574-66-3]

Molecular Formula : $C_{13}H_{11}NO$

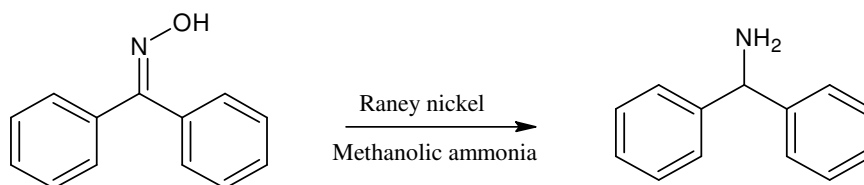
Mol. Wt. :197.23

Benzophenone on reaction with hydroxylamine hydrochloride in the presence of sodium hydroxide to form Benzophenone oxime.

Step-02: Preparation of Step-02 (A)



MANUFACTURING PROCESS OF PROPOSED PRODUCT

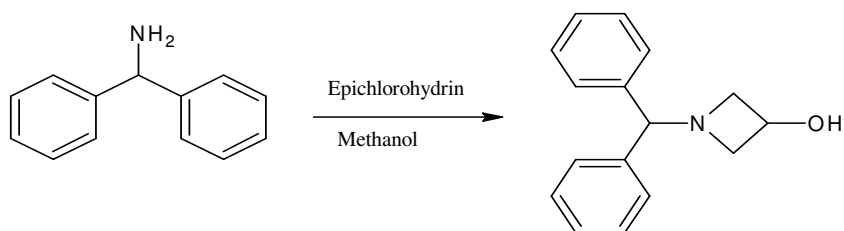


Benzophenone Oxime [Step-01(A)]
 CAS No.: [574-66-3]
 Molecular Formula: C₁₃H₁₁NO
 Mol. Wt. :197.23

Benzhydramine [Step-02(A)]
 CAS No. [91-00-9]
 Molecular Formula: C₁₃H₁₃N
 Mol. Wt. :183.24

Benzophenone Oxime [Step-01(A)] on reduction with raney nickel (catalyst) to form Benzhydramine [Step-02(A)]

Step-03: Preparation of Step-03 (A)

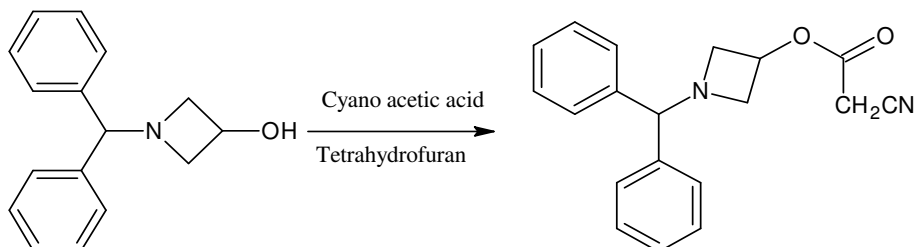


Benzhydramine [Step-02(A)]
 CAS No.: [91-00-9]
 Molecular Formula: C₁₃H₁₃N
 Mol. Wt. :183.24

1-(diphenylmethyl) azetidin-3-ol
 [Step-03(A)]
 CAS No.: NA
 Molecular Formula: C₁₆H₁₇NO
 Mol. Wt. :239.31

Benzhydramine [Step-02(A)] on reaction with epichlorohydrin to give 1-(diphenylmethyl) azetidin-3-ol [Step-03(A)]

Step-04: Preparation of Step-04 (A)



1-(diphenylmethyl)azetidin-3-ol [Step-03(A)]
 CAS No.: NA
 Molecular Formula: C₁₆H₁₇NO
 Mol. Wt.: 239.31

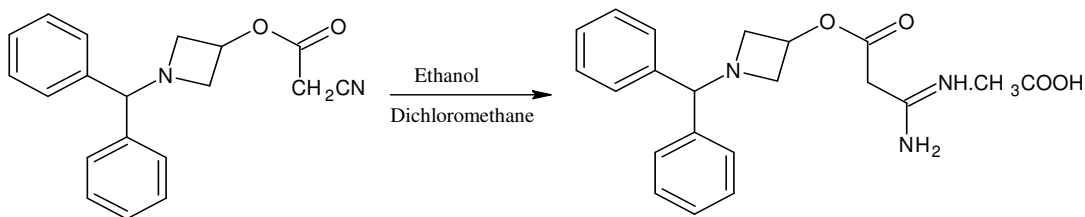
1-(diphenylmethyl) pyrrolidin-3-yl cyanoacetate [Step-04(A)]
 CAS No.: NA
 Molecular Formula: C₁₉H₁₈N₂O₂
 Mol. Wt.: 306.36



MANUFACTURING PROCESS OF PROPOSED PRODUCT

1-(diphenylmethyl)azetid-3-ol [Step-03(A)] react with cyano acetic acid to form 1-(diphenylmethyl) pyrrolidin-3-yl cyanoacetate [Step-04(A)]

Step-05: Preparation of Step-05(A)

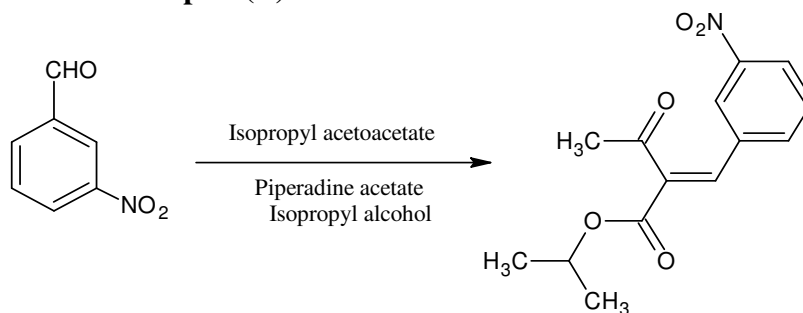


1-(diphenylmethyl) pyrrolidin-3-yl-
 cyanoacetate
 CAS No.: NA
 Molecular Formula: C₁₉H₁₈N₂O₂
 Mol. Wt.:306.35

Amidino acetic acid(1-benzhydryl-azetid-3-
 yl)ester [Step-05(A)]
 CAS No.: [170749-59-4]
 Molecular Formula: C₂₁H₂₅N₃O₄
 Mol. Wt.:383.44

1-(diphenylmethyl) pyrrolidin-3-yl-cyanoacetate react with ethanol to give Amidino acetic acid(1-benzhydryl-azetid-3-yl)ester [Step-05(A)]

Step-06: Preparation of Step-01(B)



3-nitrobenzaldehyde
 CAS No.: [99-61-6]
 Molecular Formula: C₇H₅NO₃
 Mol. Wt.:151.12

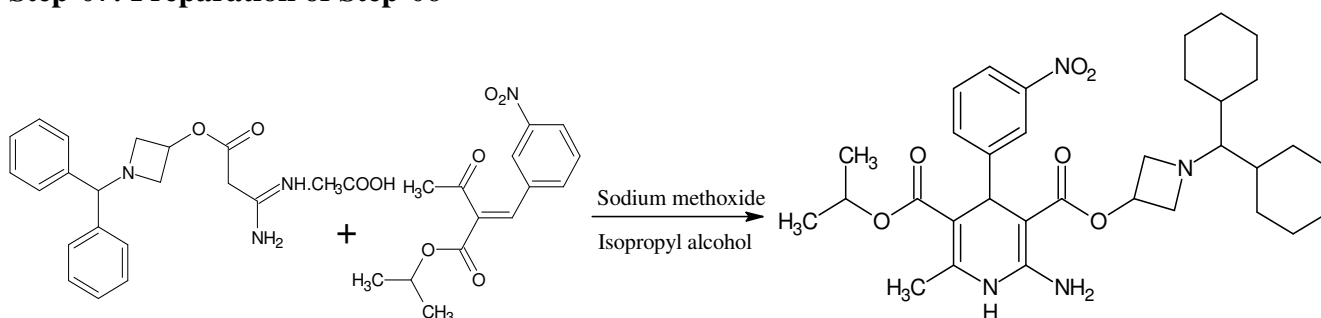
2-(3-nitrobenzylidene)isopropyl acetoacetate [Step-
 01(B)]
 CAS No.: [39562-25-9]
 Molecular Formula: C₁₄H₁₅NO₅
 Mol. Wt.: 277.27

3-nitrobenzaldehyde on reaction with isopropyl aceto acetate in the presence of piperidine acetate to form 2-(3-nitrobenzylidene)isopropyl acetoacetate [Step-01(B)]



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-07: Preparation of Step-06



Amidino acetic acid(1-benzhydryl-azetid-3-yl)ester [Step-05(A)]
 CAS No.: NA
 Molecular Formula: $C_{21}H_{25}N_3O_4$
 Mol. Wt.: 383.44

2-(3-nitrobenzylidene)isopropyl acetoacetate [Step-01(B)]
 CAS No.: [39562-25-9]
 Molecular Formula: $C_{14}H_{15}NO_5$
 Mol. Wt.: 277.27

3-1-Benzhydryl-3-azetidiny 5-isopropyl 2-amino-6-methyl-4-(*m*-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate [Step-06]
 CAS No.: [123524-52-7]
 Molecular Formula: $C_{33}H_{34}N_4O_6$
 Mol. Wt.: 582.64

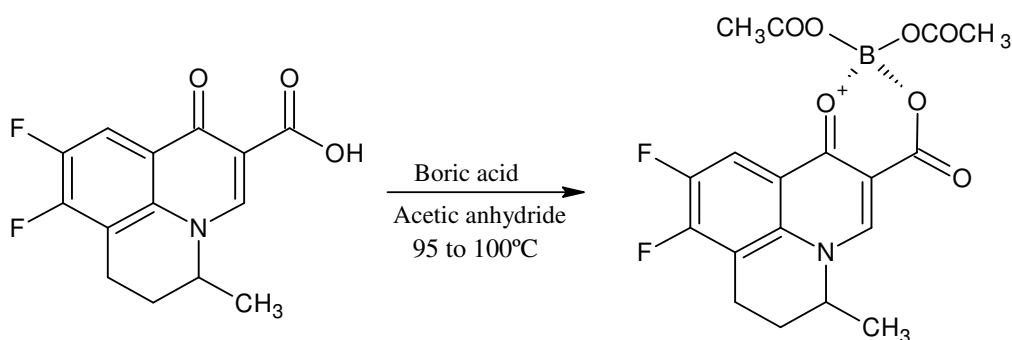
Amidino acetic acid(1-benzhydryl-azetid-3-yl)ester [Step-05(A)] on reaction with 2-(3-nitrobenzylidene)isopropyl acetoacetate [Step-01(B)] to form 3-1-Benzhydryl-3-azetidiny 5-isopropyl 2-amino-6-methyl-4-(*m*-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate [Step-06]



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Nadifloxacin:

Step-01: Preparation of NDF/S-01



8,9-difluoro-5-methyl-1-oxo-6,7-dihydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline-2-carboxylic acid
 [NDF/int./S-06]

CAS No. [80076-47-7]

Molecular Formula : C₁₄H₁₁F₂NO₃
 Mol.Wt.: 279.23

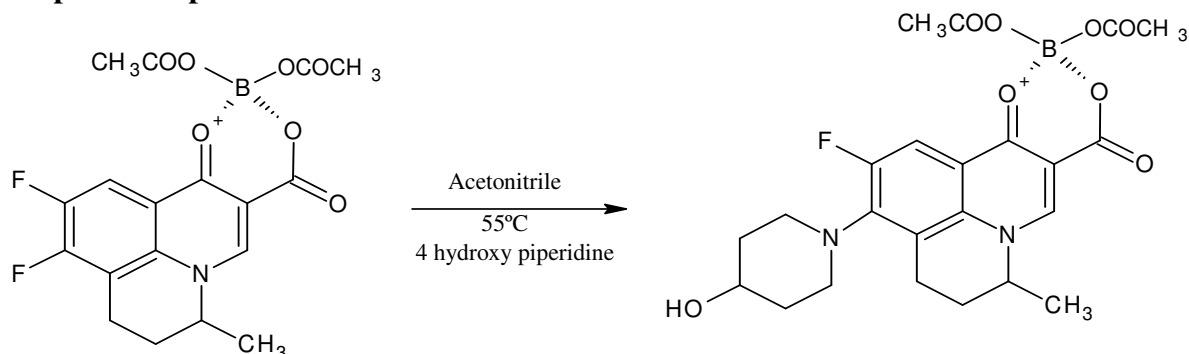
Diacetyl-(8,9-difluoro-5-methyl-6,7-dihydro-1-oxo-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid) borane
 [NDF/S-01]

CAS No. [130293-66-2]

Molecular Formula : C₁₈H₁₆BF₂NO₇
 Mol. Wt. :407.12

Add 8,9-difluoro-5-methyl-1-oxo-6,7-dihydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline-2-carboxylic acid [NDF/int./S-06] to the hot solution of acetic anhydride and boric acid. Wash the product with DM water to give diacetyl-(8,9-difluoro-5-methyl-6,7-dihydro-1-oxo-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid) borane [NDF/S-01]

Step-02: Preparation of NDF/S-02



Diacetyl-(8,9-difluoro-5-methyl-6,7-dihydro-1-oxo-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid) borane [NDF/S-01]

Diacetyl-9-fluoro-8-(4-hydroxy-1-piperidinyl)-5-methyl-6,7-dihydro-1-oxo-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid) borane [NDF/S-02]



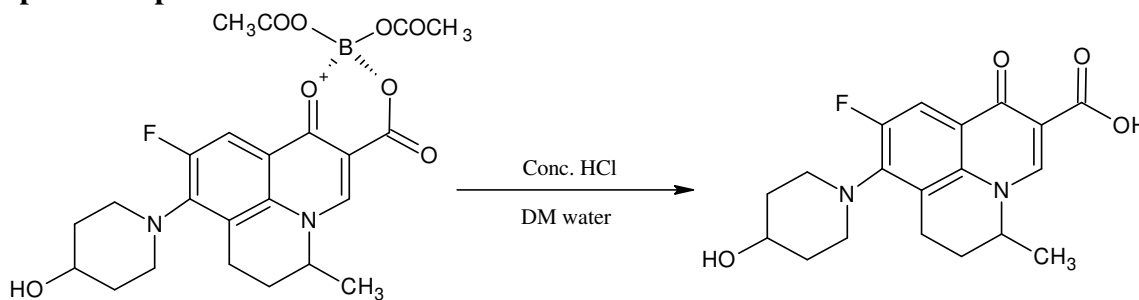
MANUFACTURING PROCESS OF PROPOSED PRODUCT

CAS No. [130293-66-2]
 Molecular Formula : C₁₈ H₁₆ B F₂ N O₇
 Mol. Wt. :407.12

CAS No. [NA]
 Molecular Formula: C₂₃ H₂₆ B F N₂ O₈
 Mol. Wt :488.27

Diacetyl-(8,9-difluoro-5-methyl-6,7-dihydro-1-oxo-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid) borane [NDF/S-01] reacts with 4-hydroxy piperidine and acetonitrile to give diacetyl-9-fluoro-8-(4-hydroxy-1-piperidinyl)-5-methyl-6,7-dihydro-1-oxo-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid) borane [NDF/S-02].

Step-03: Preparation of NDF/Final



Diacetyl-9-fluoro-8-(4-hydroxy-1-piperidinyl)-5-methyl-6,7-dihydro-1-oxo-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid) borane [NDF/S-02]

CAS No. [NA]
 Molecular Formula: C₂₃H₂₆BFN₂O₈
 Mol. Wt :488.27

9-fluoro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-6,7-dihydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline-2-carboxylic acid [NDF/FINAL]

CAS No: [124858-35-1]
 Molecular Formula: C₁₉H₂₁FN₂O₄
 Mol. Wt : 360.38

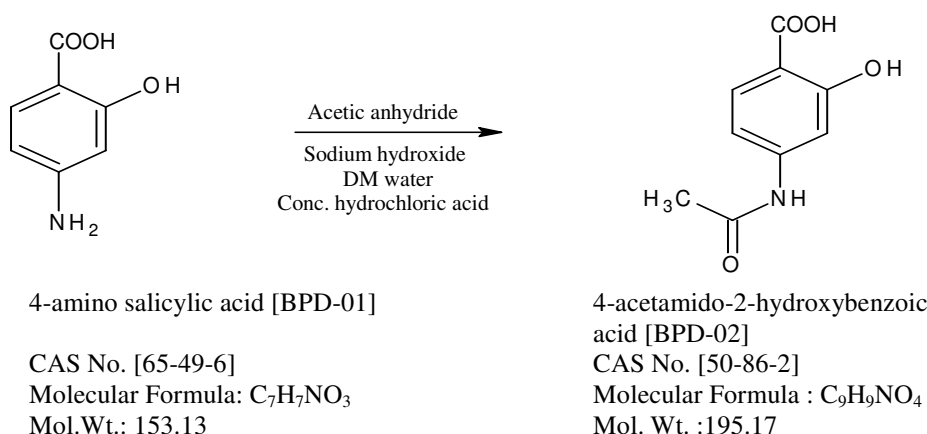
Diacetyl-9-fluoro-8-(4-hydroxy-1-piperidinyl)-5-methyl-6,7-dihydro-1-oxo-1*H*,5*H*-benzo[*ij*]quinolizine-2-carboxylic acid) borane [NDF/S-02] on reaction with concentrated hydrochloric acid and DM water to give 9-fluoro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-6,7-dihydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline-2-carboxylic acid [NDF/FINAL]



MANUFACTURING PROCESS OF PROPOSED PRODUCT

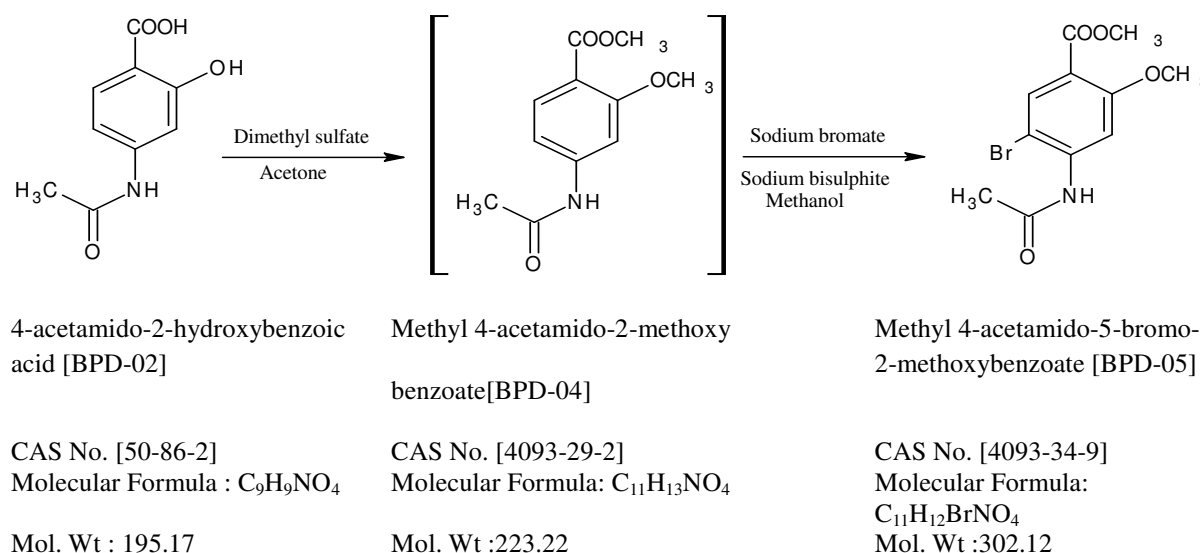
Bromopride:

Step-01: Preparation of 4-acetamido-2-hydroxybenzoic acid [BPD-02]



4-amino salicylic acid [BPD-01] is acetylated using acetic anhydride in presence of sodium hydroxide as base in DM water at 60-65°C to form 4-acetamido-2-hydroxybenzoic acid [BPD-02]

Step-02: Preparation of Methyl 4-acetamido-5-bromo-2-methoxybenzoate [BPD-05]

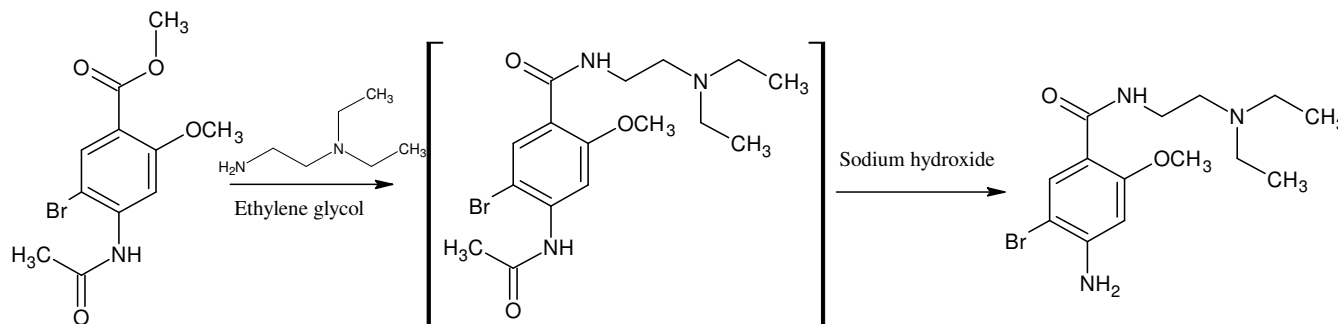


4-acetamido-2-hydroxybenzoic acid [BPD-02] is esterified and alkylated with dimethyl sulphate in acetone at reflux temperature to form Methyl 4-acetamido-2-methoxy benzoate [BPD-04]. BPD-04 is forwarded insitu to next step. BPD-04 is brominated with sodium bromate and sodium bisulphite at 15-20°C to form Methyl-4-acetamido-5-bromo-2-methoxybenzoate [BPD-05].



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-03: Preparation of 4-amino-5-bromo-*N*-[2-(diethylamino)ethyl]-2-methoxybenzamide [BPD-06]



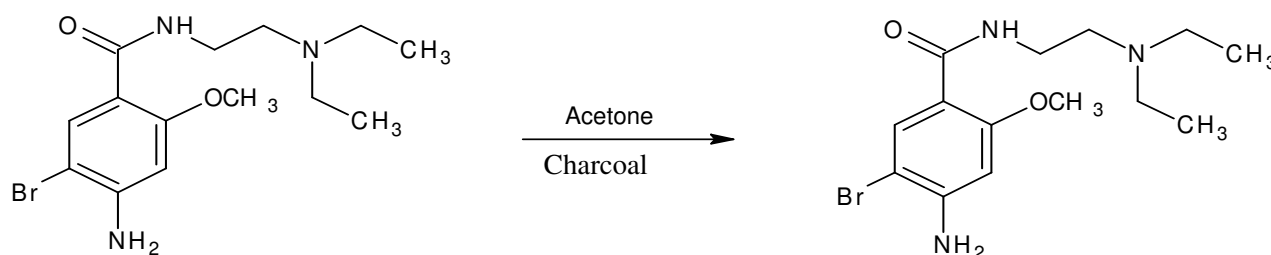
Methyl 4-acetamido-5-bromo-2-methoxybenzoate [BPD-05]
 CAS No. [4093-34-9]
 Molecular Formula:
 $C_{11}H_{12}BrNO_4$
 Mol. Wt :302.12

4-acet amido-5-bromo-*N*-[2-(diethylamino) ethyl]-2-methoxy benzamide [BPD-06-INT]
 CAS No. [NA]
 Molecular Formula:
 $C_{16}H_{24}BrN_3O_3$
 Mol. Wt :386.28

4-amino-5-bromo-*N*-[2-(diethyl amino)ethyl]-2-methoxybenzamide [BPD-06]
 CAS No: [4093-35-0]
 Molecular Formula: $C_{14}H_{22}BrN_3O_2$
 Mol. Wt :344.24

Methyl 4-acetamido-5-bromo-2-methoxybenzoate [BPD-05] on coupling with *N,N*-Diethylethylenediamine in ethylene glycol at 90-95°C which is hydrolyzed insitu with aqueous sodium hydroxide to give 4-amino-5-bromo-*N*-[2-(diethylamino)ethyl]-2-methoxybenzamide [BPD-06]

Step-04: Purification of 4-amino-5-bromo-*N*-[2-(diethylamino)ethyl]-2-methoxybenzamide [BPD-06]



4-amino-5-bromo-*N*-[2-(diethylamino)ethyl]-2-methoxy benzamide [BPD-06]
 CAS No: [4093-35-0]
 Molecular Formula: $C_{14}H_{22}BrN_3O_2$
 Mol. Wt :344.24

4-amino-5-bromo-*N*-[2-(diethylamino)ethyl]-2-methoxybenzamide [BPD-06]
 CAS No: [4093-35-0]
 Molecular Formula: $C_{14}H_{22}BrN_3O_2$
 Mol. Wt :344.24

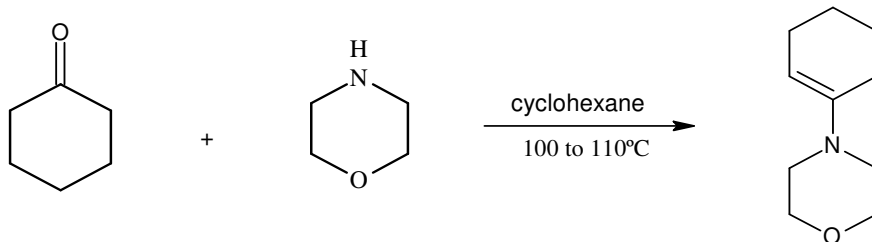
4-amino-5-bromo-*N*-[2-(diethylamino)ethyl]-2-methoxybenzamide [BPD-06] is charcolized and filtered over hyflo and crystallized with acetone to purify [BPD-06].



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Seratrodist:

Step-01: Synthesis of 4-cyclohex-1-en-1-ylmorpholine [Step-01]



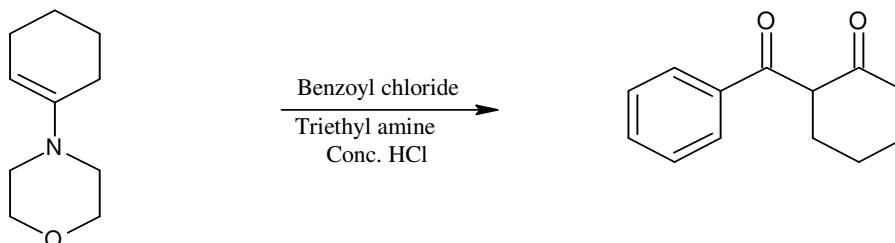
Cyclohexanone
CAS No. [108-94-1]
Molecular Formula: C₆H₁₀O
Mol. Wt.: 98.14

Morpholine
CAS No. [110-91-8]
Molecular Formula: C₄H₉NO
Mol. Wt.: 87.12

4-cyclohex-1-en-1-ylmorpholine [Step-01]
CAS No. [670-80-4]
Molecular Formula: C₁₀H₁₇NO
Mol. Wt.: 167.24

Cyclohexanone on reaction with morpholine with cyclohexane solvent at 100-110°C to give 4-cyclohex-1-en-1-ylmorpholine [Step-01]

Step 02: Synthesis of 2-benzoylcyclohexanone [Step-02]



4-cyclohex-1-en-1-ylmorpholine [Step-01]
CAS No. [670-80-4]
Molecular Formula : C₁₀H₁₇NO
Mol. Wt : 167.24

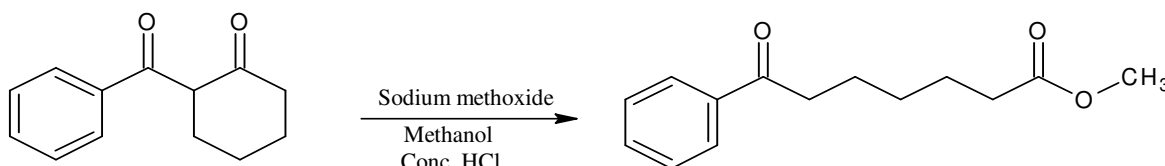
2-benzoylcyclohexanone [Step-02]
CAS No. [3580-38-9]
Molecular Formula: C₁₃H₁₄O₂
Mol. Wt : 202.24

4-cyclohex-1-en-1-ylmorpholine [Step-01] on reaction with benzoyl chloride in the presence of triethylamine as base to give 2-benzoylcyclohexanone [Step-02]



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step 03: Synthesis of Methyl-7-oxo-7-phenylheptanoate [Step-03]

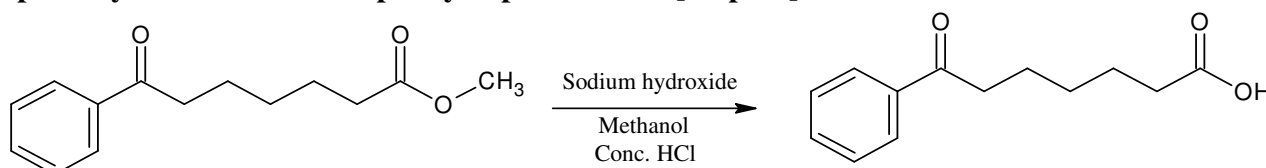


2-benzoylcyclohexanone [Step-02]
 CAS No. [3580-38-9]
 Molecular Formula: C₁₃H₁₄O₂
 Mol. Wt.: 202.24

Methyl-7-oxo-7-phenylheptanoate [Step-03]
 CAS No: [4124-81-6]
 Molecular Formula: C₁₄H₁₈O₃
 Mol. Wt :234.29

2-benzoylcyclohexanone [Step-02] on reaction with sodium methoxide with methanol as solvent to give Methyl-7-oxo-7-phenylheptanoate [Step-03]

Step 04: Synthesis of 7-oxo-7-phenylheptanoic acid [Step-04]

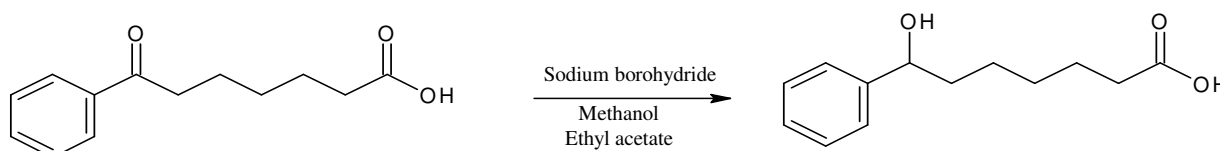


Methyl-7-oxo-7-phenylheptanoate [Step-03]
 CAS No. [4124-81-6]
 Molecular Formula: C₁₃H₁₄O₂
 Mol. Wt.: 202.24

7-oxo-7-phenylheptanoic acid [Step-04]
 CAS No: [7472-43-7]
 Molecular Formula: C₁₃H₁₆O₃
 Mol. Wt.:220.26

Methyl-7-oxo-7-phenylheptanoate [Step-03] hydrolyzed with sodium hydroxide and methanol as solvent to give 7-oxo-7-phenylheptanoic acid [Step-04]

Step 05: Synthesis of 7-hydroxy-7-phenylheptanoic acid [Step-05]



7-oxo-7-phenylheptanoic acid [Step-04]
 CAS No. [7472-43-7]
 Molecular Formula: C₁₃H₁₆O₃

7-hydroxy-7-phenylheptanoic acid [Step-05]
 CAS No. [103187-18-4]
 Molecular Formula: C₁₃H₁₈O₃



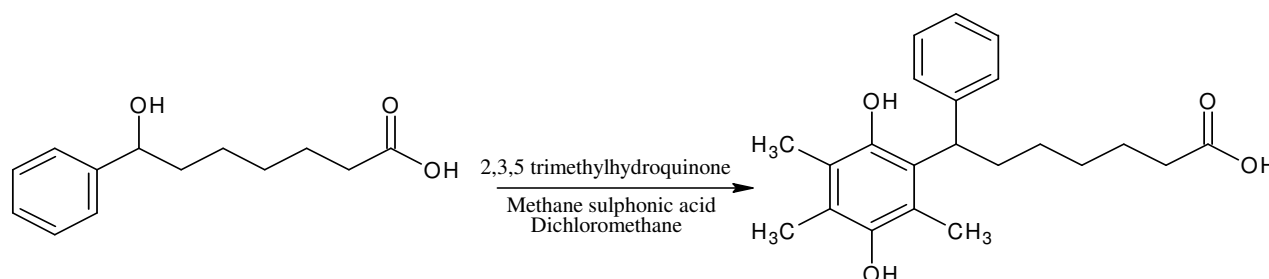
MANUFACTURING PROCESS OF PROPOSED PRODUCT

Mol. Wt.: 220.26

Mol. Wt.: 222.28

7-oxo-7-phenylheptanoic acid [Step-04] reduced with sodium borohydride in methanol as solvent to give 7-hydroxy-7-phenylheptanoic acid [Step-05]

Step 06: Synthesis of 7-phenyl-7-(2,4,5-trimethyl-3,6-dihydroxyphenyl)-heptanoic acid [Step-06]



7-hydroxy-7-phenylheptanoic acid [Step-05]

CAS No.: [103187-18-4]
 Molecular Formula: C₁₃H₁₈O₃
 Mol. Wt.: 222.26

7-phenyl-7-(2,4,5-trimethyl-3,6-dihydroxyphenyl)
 heptanoic acid [Step-06]
 CAS No.: [NA]
 Molecular Formula: C₂₂H₂₈O₄
 Mol. Wt.: 356.45

7-hydroxy-7-phenylheptanoic acid [Step-05] condensed with 2,3,5-trimethylhydroquinone with methane sulfonic acid and dichloromethane as solvent to give 7-phenyl-7-(2,4,5-trimethyl-3,6-dihydroxyphenyl)

Step 07: Synthesis of 7-phenyl-7-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-dien-1-yl)heptanoic acid [Step-07]

7-phenyl-7-(2,4,5-trimethyl-3,6-dihydroxyphenyl)
 heptanoic acid [Step-06]

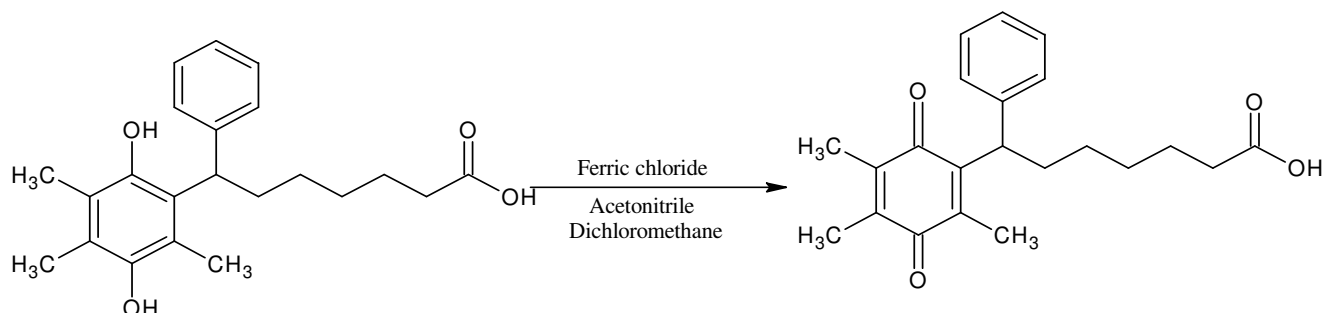
CAS No.: [NA]
 Molecular Formula: C₂₂H₂₈O₄
 Mol. Wt.: 356.45

7-phenyl-7-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4-
 dien-1-yl)heptanoic acid [Step-07]

CAS No.: [112665-43-7]
 Molecular Formula: C₂₂H₂₆O₄
 Mol. Wt.: 354.43



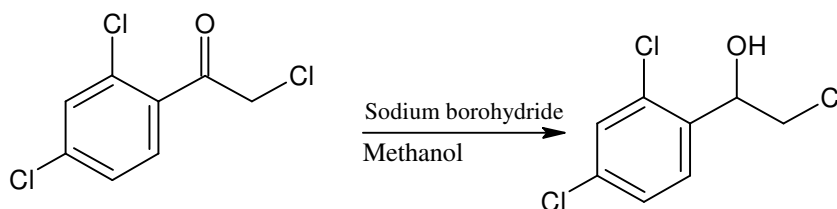
MANUFACTURING PROCESS OF PROPOSED PRODUCT



7-phenyl-7-(2,4,5-trimethyl-3,6-dihydroxyphenyl) heptanoic acid [Step-06] react with ferric chloride in acetonitrile to give 7-phenyl-7-(2,4,5-trimethyl-3,6-dioxocyclohexa-1,4dien-1-yl)heptanoic acid [Step-07].

Fenticonazole nitrate:

Step-01: Synthesis of FNT-01



2,2,4-trichloroacetophenone

CAS No.: [4252-78-2]

Molecular Formula : C₈H₅Cl₃O

Mol. Wt.: 223.48

2-chloro-1-(2,4-dichlorophenyl)ethanol
 [FNT-01]

CAS No.: [13692-14-3]

Molecular Formula: C₈H₇Cl₃O

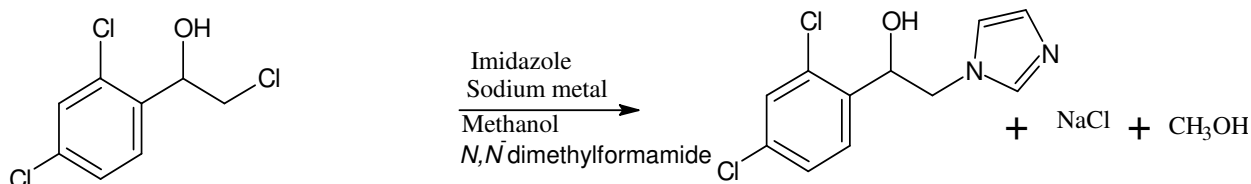
Mol. Wt.:225.49

2,2,4-trichloroacetophenone on reaction with sodium borohydride in methanol to get 2-chloro-1-(2,4-dichlorophenyl)ethanol.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-02: Synthesis of FNT-02



2-chloro-1-(2,4-dichlorophenyl)ethanol [FNT-01]

CAS No.: [13692-14-3]

Molecular Formula: C₈H₇Cl₃O

Mol. Wt.:225.49

1-(2,4-dichlorophenyl)-2-(1H-imidazol-1-yl)ethanol [FNT-02]

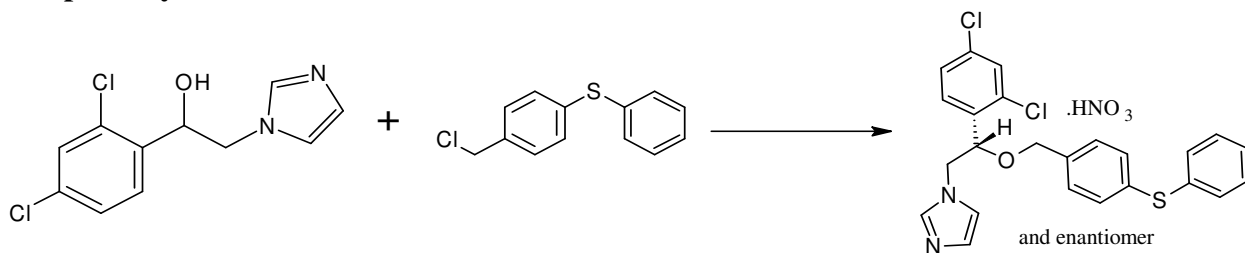
CAS No. [24155-42-8]

Molecular Formula : C₁₁H₁₀Cl₂N₂O

Mol. Wt.: 257.11

2-chloro-1-(2,4-dichlorophenyl)ethanol [FNT-01] on reaction with imidazole, methanol and sodium metal to give 1-(2,4-dichlorophenyl)-2-(1H-imidazol-1-yl)ethanol [FNT-02]

Step-03: Synthesis of FNT-03



1-(2,4-dichlorophenyl)-2-(1H-imidazol-1-yl)ethanol [Step-02]

CAS No. [24155-42-8]

Molecular Formula :
C₁₁H₁₀Cl₂N₂O

Mol. Wt.: 257.11

1-(chloromethyl)-4-(phenylthio)benzene

CAS No. [1208-87-3]

Molecular Formula: C₁₃H₁₁ClS

Mol. Wt.: 234.74

1-[2-(2,4-dichlorophenyl)-2-({[4-(phenylsulfanyl)phenyl]methoxy}ethyl)-1H-imidazole nitrate [Step-03]

CAS No. [73151-29-8]

Molecular Formula: C₂₄H₂₁Cl₂N₃O₄S

Mol. Wt.: 518.41

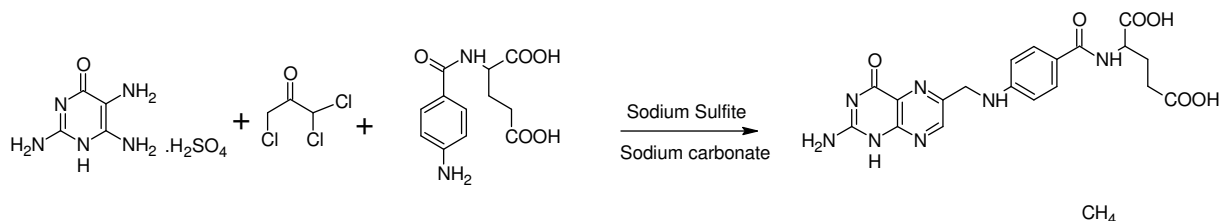


MANUFACTURING PROCESS OF PROPOSED PRODUCT

1-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-yl)ethanol [Step-02] on reaction with 1-(chloromethyl)-4-(phenylthio)benzene in dimethyl sulphoxide to give 1-[2-(2,4-dichlorophenyl)-2-{[4-(phenylsulfanyl)phenyl]methoxy}ethyl]1*H*-imidazole which upon reaction with nitric acid in isopropyl alcohol to give 1-[2-(2,4-dichlorophenyl)-2-{[4-(phenylsulfanyl)phenyl]methoxy}ethyl]-1*H*-imidazole nitrate [Step-03]

Folic acid:

Step-I: Preparation of Stage-04



2,4,5 triamino-6-hydroxypyrimidine sulfate [Stage-03]	1,1,3-trichloro Acetone [INT-01]	2-[(4-aminobenzoyl) amino]pentanedioic acid [INT-02]	(2 <i>S</i>)-2-[[4-[(2-Amino-4-oxo-1 <i>H</i> -pteridin-6-yl)methylamino]benzoyl]amino]pentanedioic acid
CAS No.: [35011-47-3]	CAS No.: [921-03-9]	CAS No.: [35011-47-3]	CAS No.: [59-30-3]
Molecular Formula: C ₄ H ₉ N ₅ O ₅ S	Molecular Formula: C ₃ H ₃ Cl ₃ O	Molecular Formula : C ₁₂ H ₁₄ N ₂ O ₅	Molecular Formula : C ₁₉ H ₁₉ N ₇ O ₆
Mol.Wt.: 239.20	Mol.Wt.:161.41	Mol.Wt.: 266.24	Mol.Wt.: 441.39

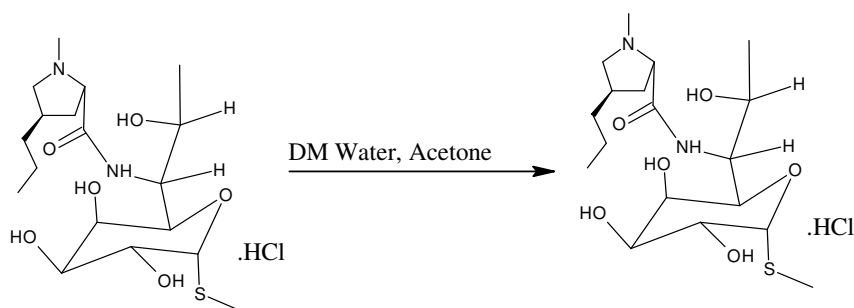
2,4,5 triamino-6-hydroxypyrimidine sulfate [Stage-03] on reaction with 1,1,3-trichloro Acetone [INT-01] and 2-[(4-aminobenzoyl) amino]pentanedioic acid in sodium sulfite and sodium carbonate to form (2*S*)-2-[[4-[(2-Amino-4-oxo-1*H*-pteridin-6-yl)methylamino]benzoyl]amino]pentanedioic acid.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Clindamycin Hydrochloride:

Step-01: Purification of Lincomycin hydrochloride

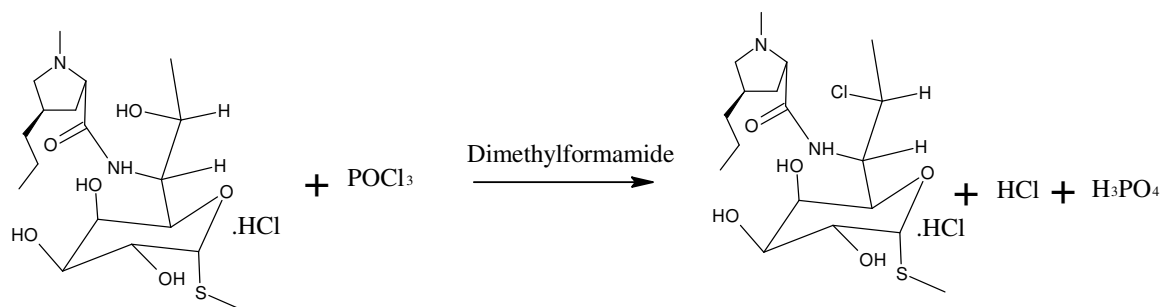


Lincomycin hydrochloride
 Mol. Wt.: 443.0
 Molecular formula: $C_{18}H_{35}ClN_2O_6S$

Lincomycin hydrochloride
 Mol. Wt.: 443.0
 Molecular formula: $C_{18}H_{35}ClN_2O_6S$

On treatment of lincomycin hydrochloride with DM water and acetone under heating condition followed by cooling results the clindamycin hydrochloride.

Step-02: Synthesis of Clindamycin hydrochloride



Lincomycin hydrochloride
 Mol. Wt.: 443.0
 Molecular formula: $C_{18}H_{35}ClN_2O_6S$

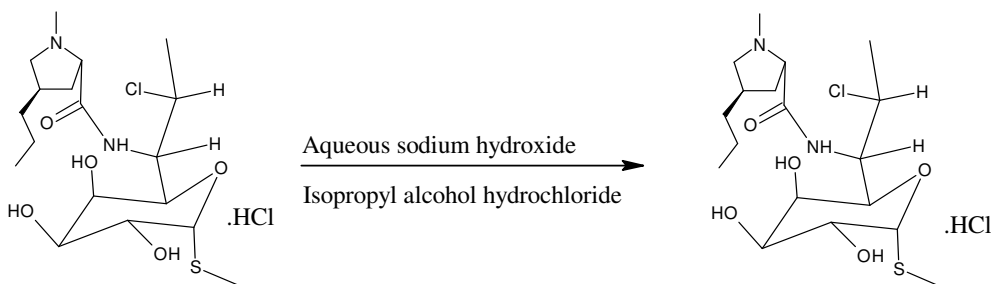
Clindamycinhydrochloride
 Mol. Wt.:461.44
 Molecular formula: $C_{18}H_{33}Cl N_2O_5S.HCl$

On treatment of Lincomycin hydrochloride with phosphoryl chloride in presence of dimethylformamide in 1,2-dichloroethane as a solvent results clindamycin free base which on acidifying with isopropyl alcohol hydrochloride leads to the formation of white solid clindamycin hydrochloride.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Step-03: Purification of Clindamycin hydrochloride

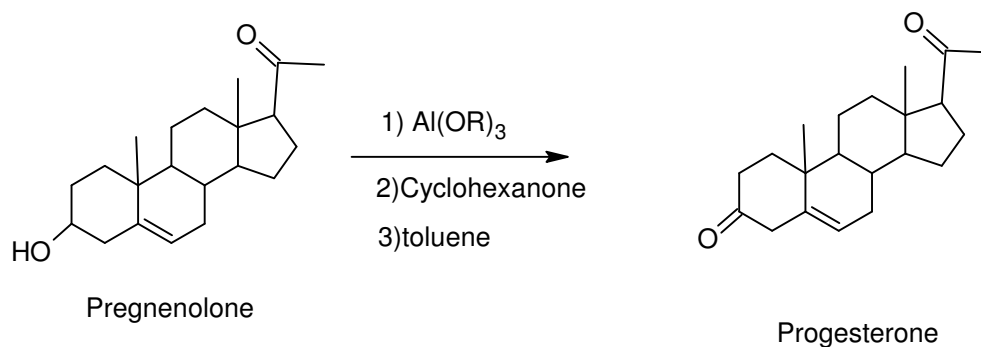


Clindamycin hydrochloride
CAS No.: [21462-39-5]
Mol. Wt.: 461.44
Molecular formula: $C_{18}H_{33}Cl N_2O_5S.HCl$

Clindamycin hydrochloride
CAS No.: [21462-39-5]
Mol. Wt.: 461.44
Molecular formula: $C_{18}H_{33}Cl N_2O_5S.HCl$

On basifying the crude clindamycin hydrochloride (obtained from the synthesis) by aqueous sodium hydroxide followed by its acidification using isopropyl alcohol hydrochloride leads to the pure clindamycin hydrochloride.

Progesterone:



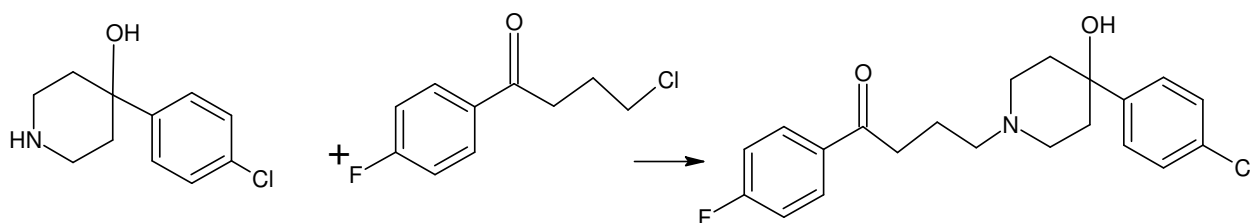
Progesterone is synthesized from Pregnenolone, cyclohexanone and toluene via oppenauer oxidation with aluminium isopropoxide at 110-115°C for 6 hours.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

Haloperidol /Haloperidol decanoate:

Step-01



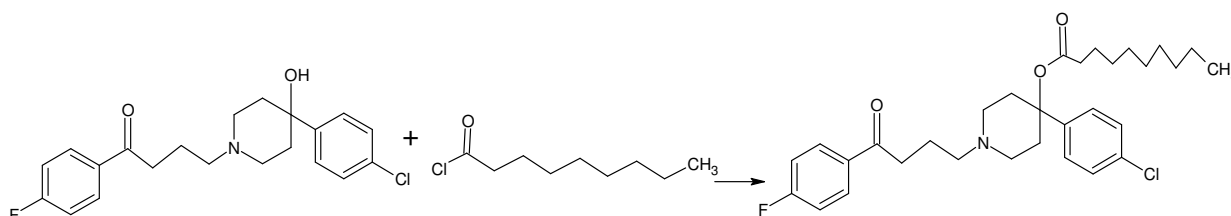
4-(4-chlorophenyl)-4-hydroxy
 piperidine
 M.Wt.-211.69

4-Chloro-4'-fluoro
 butyrophenone
 M.Wt.-200.63

1-(3-p-Fluorobenzoylpropyl)-4-p-
 chlorophenyl-4-hydroxypiperidine
 M.Wt.-375.86

4-(4-chlorophenyl)-4-hydroxy piperidine reacts with 4-Chloro-4'-fluoro butyrophenone in the presence of potassium iodide and potassium hydroxide in DM water at reflux temperature to get step-01.

Step-02



1-(3-p-Fluorobenzoylpropyl)-4-p-
 chlorophenyl-4-hydroxypiperidine

M.Wt.-375.86

Decanoyl chloride

M.Wt.-190.71

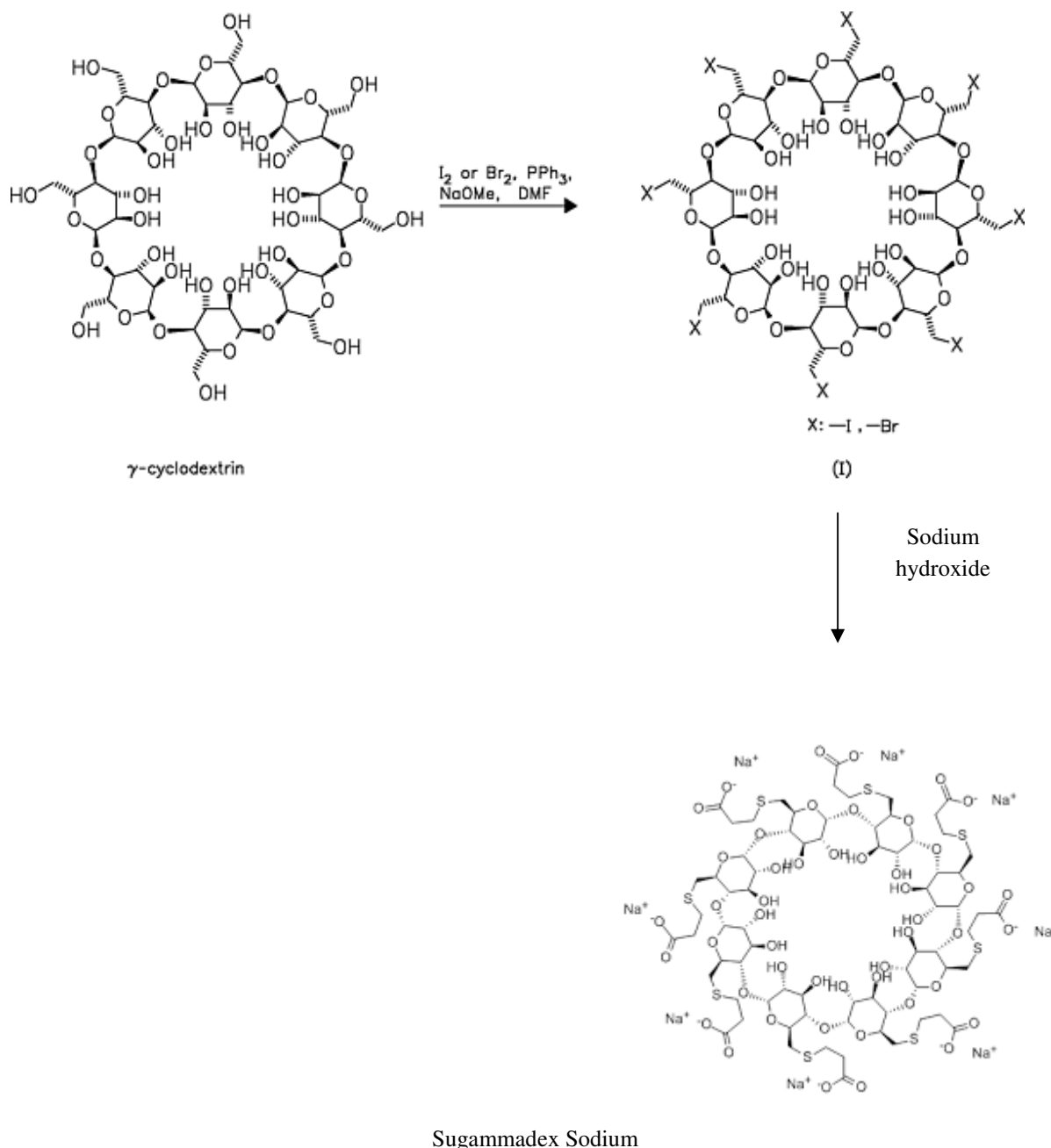
Decanoic Acid 4-(4-
 Chlorophenyl)-1-[4-(4-
 fluorophenyl)-4-oxobutyl]-4-
 piperidinyl Ester
 M.Wt.-530.11

1-(3-p-Fluorobenzoylpropyl)-4-p-chlorophenyl-4-hydroxypiperidine is condensed with decanoyl chloride in the presence of triethyl amine in Tetrahydrofuran to get haloperidol decanoate.



MANUFACTURING PROCESS OF PROPOSED PRODUCT

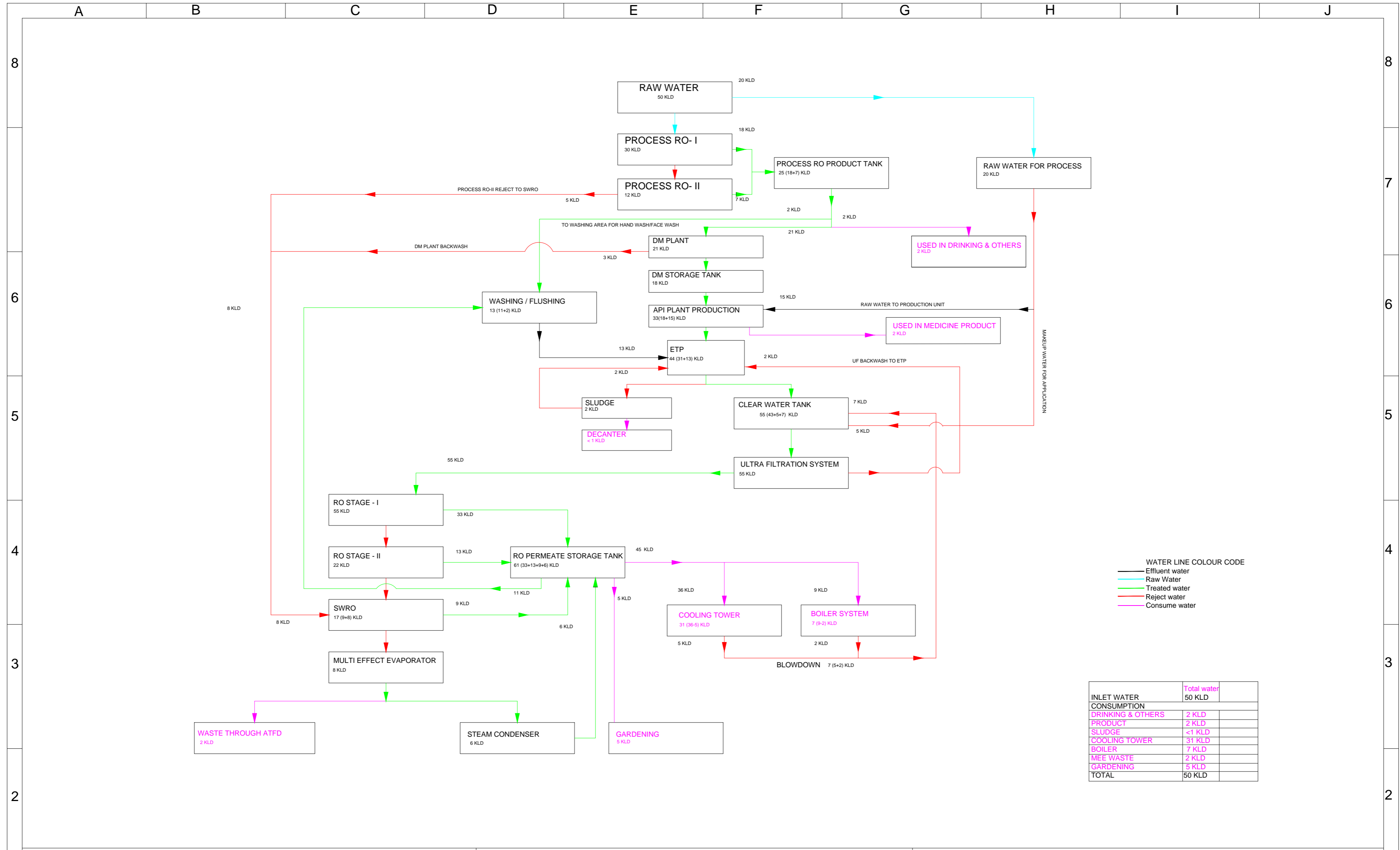
Sugammadex Sodium:



γ -cyclodextrin on reaction with methyl-3-mercaptopropionate in *N,N*-dimethyl formamide to give methyl ester intermediate followed with sodium hydroxide solution to get sugammadex sodium.



ANNEXURE-6
WATER BALANCE



CLIENT :- SHREE JEE LABORATORY PRIVATE LIMITED
SOTANALA (BEHROR) RAJASTHAN

ETP PLANT ZERO LIQUID DISCHARGE (80 KLD)

CONSULTANT:- INDIA- IPS INTERNATIONAL PRIVATE LIMITED

EXECUTED BY :-

 DEW ENVIROTECH PRIVATE LIMITED
K-47, UPSIDC SITE-V, KASNA
GREATER NOIDA

WATER BALANCE DRAWING

SCALE:-NTS	REVISION:00	DATE:- 22/02/2016	File No.
DRAWN BY:- ANJALI SINGH	CHECKED BY:- M.KUMAR	APPROVED BY:- SUBHASH BHARDUJ	Ref No.

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ANNEXURE-7
HAZARDOUS WASTE MANAGEMENT

Annexure 2

Hazardous Waste Management

S. No.	Hazardous Waste	Waste Category	Storage	Calorific value	Total	Mode of Disposal	Detailed Characteristic
					Rate of generation in MT / Year		
1.	Organic:- ETP Sludge through MBR	34.3	Closed Packed in leak-proof double liner and stored in dedicated HW storage area.	1500-5000 Kcal/Kg.	32	TSDF	Organic and in-organic substance/ Dry cake with 10-30% moisture content
	Inorganic:- ETP Sludge through RO-1, RO-2 and followed by MEE				175		
2.	Process residue and waste	28.1	Fiber Box/HDPE/MS/GI Drums	5000-7000 Kcal/Kg	300.0	TSDF	Organic solvents and unreacted substances / tarry or liquid Incinerable
3.	Used /Spent oil	5.1	HDPE/MS Drums	830-2000 Kcal/Kg	0.4	Approved recycler	Flammable Liquid, Incinerable
4.	Spent catalyst/Carbon	28.2	Closed Dry Container and away from strong oxidizer such as ozone, liquid oxygen chlorine.	2000-4000 Kcal/Kg.	2.2	TSDF	Organic and inorganic substances with flammable or aqueous solvent base/ wet cake, Incinerable
5.	Spent organic solvent/	28.5	HDPE/GI Drums	5000-7000 Kcal/Kg	3.65	Approved recycler	Organic solvents, un dissolved substances / liquid
6.	Date expired, discarded and off Specification products / medicine	28.4	Closed Packed Liner/ Cartoon	4000-5000 Kcal/Kg	1.5	TSDF	Organic and in-organic powder / dry powder or wet cake, Incinerable
7.	Discarded containers / barrels/Liners /Used PPE contaminated with Hazardous waste/Chemicals	33.3	Stored at dedicated hazardous waste storage area.	10-100 Kcal/Kg	2.0	TSDF	Solid Incinerable waste



ANNEXURE-8
**EFFLUENT TREATMENT PLANT
DESCRIPTION AND FLOWCHART**

Description of Effluent Treatment Plant cum ZLD
(Design Capacity = 80 KLD, Actual Generation = 44 KLD)

Shree Jee Laboratory Pvt. Ltd. has set up best industrial ZLD (Zero Liquid Discharge) system which has been provisioned for segregation of waste and for High COD stream it has been equipped with Stripper, MEE followed by ATFD & for Low COD stream it has been equipped with Effluent Treatment plant (Anaerobic & Biological) followed by UF, RO -I, RO-II & SWRO followed by MEE & ATFD.

Steroid Block has been equipped with advanced oxidation process followed by Stripper & MEE.

Effluent Treatment Plant has been setup by calculating the effluent generation from different stream and considering the quality of effluent. Our ZLD cum ETP system is able to treat the effluent perfectly and discharge water quality specification will be within permissible limit as specified by SPCB/CPCB/MOEF.

We will not exceed the water load/effluent generation load in future beyond the permissible capacity without getting evaluation of expansion and approval from MOEF/SPCB.

Following are the Process of Waste Water Stream:

S. No.	PROCESS	DETAILS
1.	Segregation of waste streams	<p>Standard Operation Procedure has been made for segregation, Storage, Treatment and Disposal of Waste.</p> <p>a.) High & Low COD effluent waste will be treated in ZLD cum ETP as per attached Flow Chart Annexure – I</p> <p>b.) Inorganic Waste:</p> <ul style="list-style-type: none"> - High COD effluent will be passed through stripper where solvents segregated and water will pass through MEE and ATFD. - Low COD stream will be treated in ETP (Anaerobic & Biological) followed by UF, RO- I, RO –II, SWRO, MEE & ATFD. <p>c.) Organic/mixed solvent waste: will be sent to approved recycler.</p> <p>d.) Hazardous solid waste: will be send to TSDF approved by SPCB.</p> <p>e.) Non Hazardous waste: will be reuse or sell out to recycler after decontamination (if any).</p>
2.	Detoxification and treatment of Steroid Stream	Steroid Stream will passed through AOP (Advanced Oxidation Process) followed by stripper, MEE and ATFD.

Shree Jee Laboratory Private Limited
 C -24 & 25, RIICO Industrial Area Sotanala
 Tehsil – Behror, Dist. – Alwar, Rajasthan
(ETP CUM ZLD BLOCK DIAGRAM)

