

Match Maker/ Pharmaceutical Process Innovations/ 20 March 2025

Process for the preparation of Sacubitril Intermediates

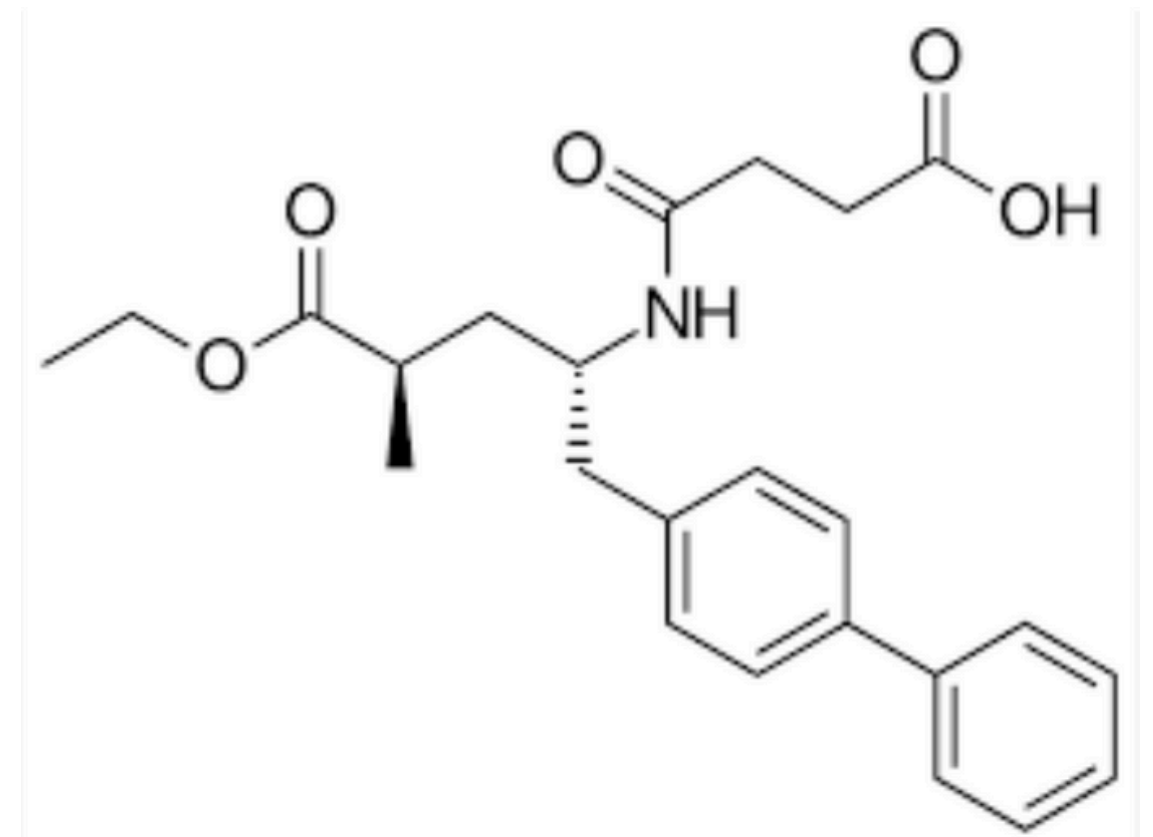
Lead Inventor: Dr. Ravindar Kontham

Organization: CSIR-NCL

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What is Sacubitril ?

- Sacubitril and valsartan combination is used to treat chronic heart failure in adults to help reduce the risk of death and hospitalization. This medicine is also used to treat children with symptomatic heart failure.
- Valsartan is an angiotensin II receptor blocker (ARB). It works by blocking a substance in the body that causes blood vessels to tighten. As a result, valsartan relaxes the blood vessels. This lowers blood pressure and increases the supply of blood and oxygen to the heart.



Market Opportunities

The global sacubitril valsartan sodium market size in 2023 was estimated to be USD 2.9 billion

Factors driving the growth:

- Increasing prevalence of heart failure
- Growing demand for effective treatments to manage chronic debilitating condition

Major players in India:

- Novartis India Ltd. : Vymada
- Lupin Limited: Valentas and Arnipin
- Dr. Reddy's Laboratories: CIDMUS
- Cipla Ltd. : Arnicor
- JB Chemicals & Pharmaceuticals: Azmarda



4.1 % CAGR

Cardiovascular Drugs Market to grow at a CAGR of 4.1 % during 2023-2030

Cardiovascular Drugs Market

2023	2030
US\$ 148.65	US\$ 196.93

Market Size in billion

<https://www.maximizemarketresearch.com/market-report/global-cardiovascular-drugs-market/26071/>

Comparison to existing innovations

Merck has patents related to the production of Sacubitril. Novartis has patents related to Sacubitril and Valsartan to be used together for chronic heart failure

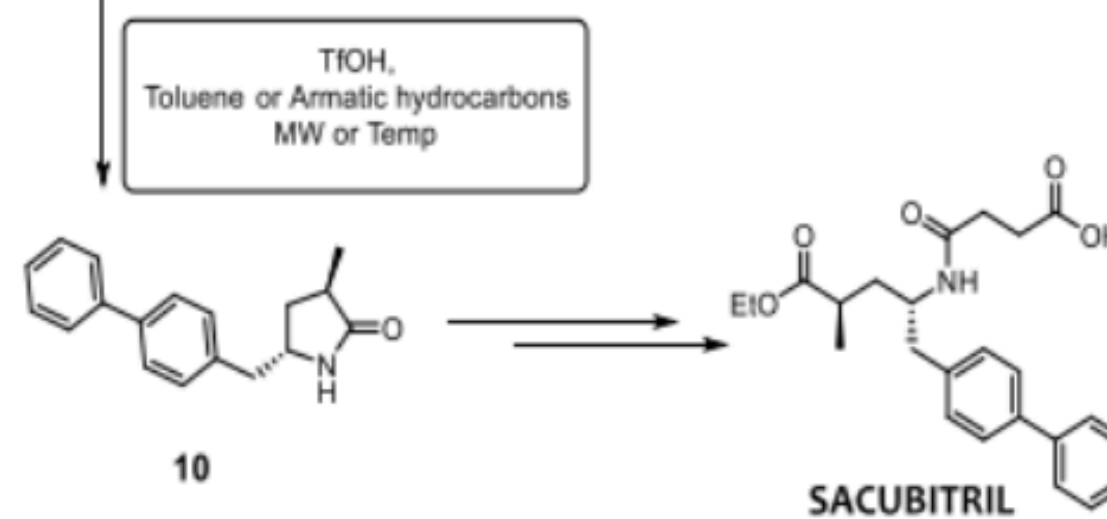
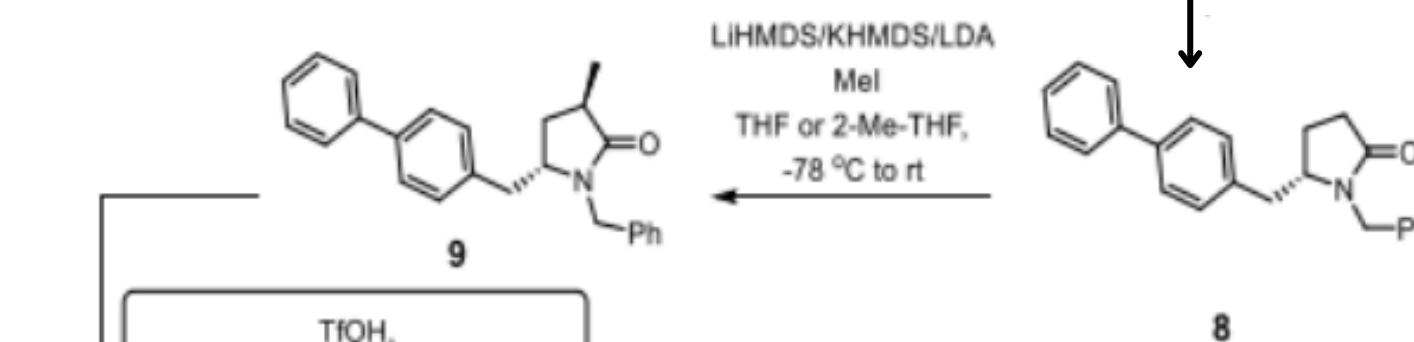
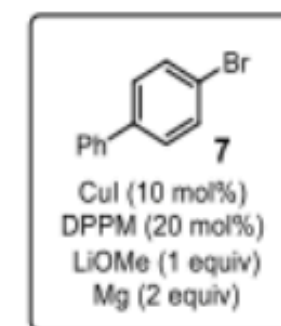
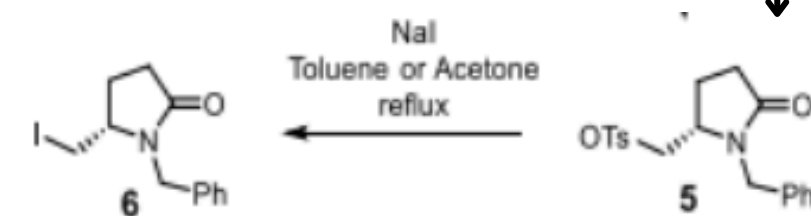
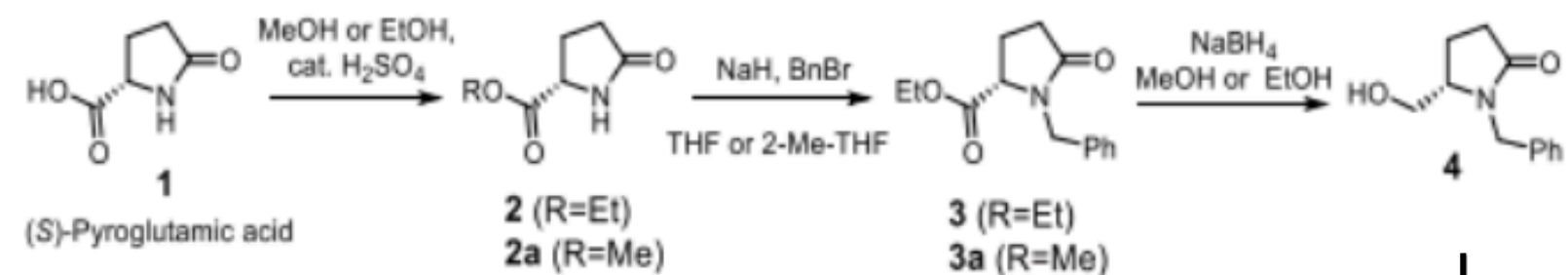
In 2022, Novartis sold its India marketing rights of Sacubitril Valsartan to JB Pharma, under the brand name Azmarda

Merck Patents

- 1. US9061973B2: Processes for producing NEP inhibitors or prodrugs thereof (Priority date: 11 Nov 2013)**
- 2. US9206116B2: Process for preparing 5-biphenyl-4-amino-2-methyl pentanoic acid (Priority date: 20/2/2015)**

U.S. Patent		Expiration
8,101,659	combinations of sacubitril and valsartan	July 15, 2025
11,096,918	amorphous forms of sacubitril and valsartan	November 8, 2026
9,388,134	crystalline forms of sacubitril and valsartan	May 8, 2027
8,877,938	crystalline forms of sacubitril and valsartan	November 27, 2027
11,058,667	dosage regimen for treating chronic heart failure	May 9, 2036

Dr. Kontham's Process



Compound 10	43,754	1kg	RMC(in INR)
	502.9	1kg	RMC(in USD)
Sacubitril	96,033.28	1kg	RMC (in INR)
	1103.83	1kg	RMC (in USD)

Value Proposition

- Stoichiometry of reagents and products is significantly improved
- Raw material: Chiral starting material; easy to work with
- Starting material: standard easily available building block
- Reduced purification steps and cost
- Reduced quantities of catalyst and other materials thus reduced costs

Current Status

- Status of the technology - TRL 4 (Lab level results shown)
- Intermediates at 10g scale
- Sacubitril final product at 1g scale

- Patent information : Granted
- Indian Patent No. 439945

- Publications : Studies on the Stereoselective Synthesis of Sacubitril via a Chiral Amine Transfer Approach, Chemistry–An Asian Journal, e202401223 (2024)

Production of Sacubitril and the Intermediates are included in PLI Scheme from the Government of India.

Who should be interested and why?

API Manufacturers

Sacubitril and the intermediates are imported from China at high cost. The several patents owned by Novartis make it difficult to manufacture using a variety of processes. Additionally, using a Grignard's reaction, the stoichiometries of the reagents make the resulting product expensive to produce. This new method, which has modified stoichiometries and reduced quantities of catalysts, is quite attractive.

Sacubitril and its intermediates are also included as part of the PLI Scheme from the Government of India

Lead inventor

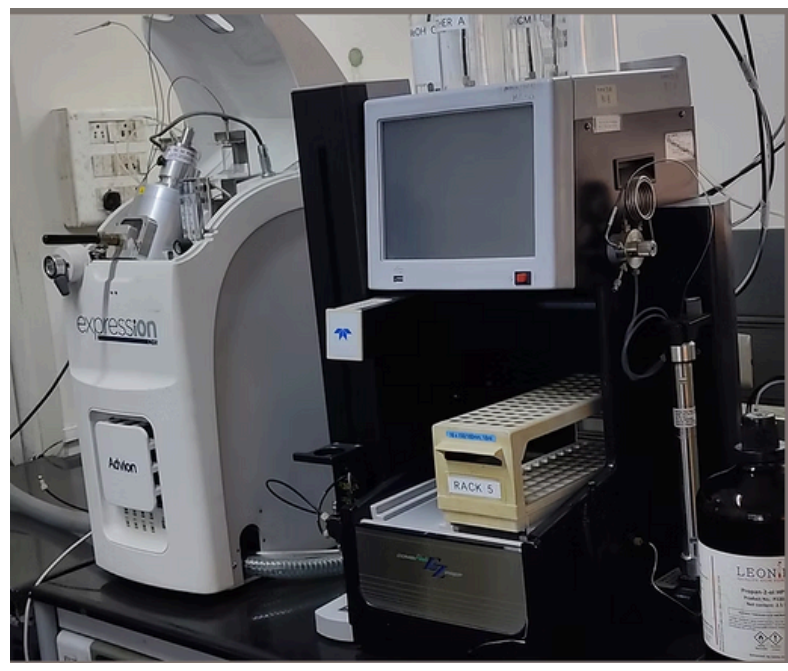


Dr. Ravindar Kontham
Principal Scientist, CSIR-NCL

CSIR-NCL is a science and knowledge-based research, development and consulting organization. It is internationally known for its excellence in scientific research in chemistry and chemical engineering as well as for its outstanding track record of industrial research involving partnerships with industry from concept to commercialization.

Research Interests: development of novel cascade/domino reactions; design and synthesis of new chemical entities for drug discovery applications; process development for APIs and API intermediates

State of the art laboratory and eager scientists ready for scale up



Next Steps

- a) The team has developed the background science, demonstrated lab scale processes and proof-of-concept. The team understands how the process can be modified to get desired products.
- b) The next phase will be to work closely with industry partners to
- Define techno-commercial specifications for the product and process of interest.
 - Optimize process to meet industry requirements
- c) Scale-up, further optimization to meet end-customer needs, testing & certifications.

Seeking

Industrial partners interested in technology licensing

Industrial partners interested in sponsoring further technology advancement and scale-up

Industrial partners interested in raising 3rd party funds for a collaborative project.

Industry interested in tapping scientist capabilities as an expert/consultant.

Startup founders who leverage the core capability to identify many more market opportunities in
a) Novel Drugs, b) Organic Synthesis



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