海洋生物由来含硫アルカロイドImbricatineの合成研究

1995 Fiscal Year Final Research Report Summary

Synthetic Studies on Imbricatine, a Sulfur-containing Benzyltetrahydroisoquinoline Alkaloid from the Starfish Dermasterias imbricata.

Research Project

Project/Area Number

06672097

Research Category

Grant-in-Aid for General Scientific Research (C)

Allocation Type

Single-year Grants

Research Field

Chemical pharmacy

Research Institution

Kanazawa University

Principal Investigator

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Project Period (FY)

1994 – 1995

Keywords

Imbricatine / Benzyltetrahydroisoquinoline alkaloid / D-Phenylalanine derivative / L-Histidine derivative / Sulfur-containing amino acid / Bischler-Napieralski cyclization / Bis-lactim ether / Demethylation

Research Abstract

With a view to confirming the structure and absolute configuration of imbricatine (1), a benzyltetrahydroisoquinoline alkaloid, isolated from the starfish Dermasterias imbricata, we have undertaken the chiral synthesis of the candidate structure 1.
1. Lithiation of N,N-diethyl-3,5-dimethoxybenzamide followed by successive treatment with elemental sulfur and 4-methoxybenzyl chloride provided the sulfide, which was then converted to the chloride 2 via reduction with LiAlH_4 and chlorination with ClCO_2Et. On application of asymmetric synthesis of alpha-amino acid developed by Schollkopf, 2 afforded the sulfur-containing D-phenylalanine derivative 3 in good yield.

2. Schotten-Baumann reaction of 3 with 4-methoxyphenylacetyl chloride furnished the amide, which was subjected to Bischler-Napieralski cyclization with trimethylsily polyphosphate followed by reduction with NaBH_4 at-78°C,giving the 1,3-cis-benzyltetrahydroisoquinoline derivative 4.
3. In order to avoid epimerization of 4 at the 3-position, the ester group of 4 was reduced with LiAlH_4 to give the amino alcohol 5. After conversion of 5 into the oxazolone 6, deprotection of 4-methoxybenzyl group of 6 was performed with (CF_3CO_2)_2Hg followed by NaBH_4 treatment, providing the southern hemisphere of 1 as the thiol 7.
4. Application of our general synthetic route for 5-arylthio-3-methyl-L-histidines to 7 led to the construction of 3-methyl-L-histidine portion (the northern hemisphere of 1). The histidine derivative 8 was then transformed to the ester 9 via hydrolysis of the oxazole ring of 8, protection of two amino groups, Swern oxidation, and alkaline iodine oxidation in MeOH.Thus, we have achieved the synthesis of the penultimate ester 9 possessing the parent framework of 1.
Deprotection of 9 leading to 1 is currently under way.

Research Products (4 results)

All Other

All Publications (4 results)

[Publications] M.Ohba: "Preparatory Study for the Synthesis of the Starfish Alkaloid Imbricatine.Syntheses of 5-Arylthio-3-methyl-L-histidines." Chem.Pharm.Bull.42. 1784-1790 (1994)

[Publications] M.Ohba: "Syntheses of L-Phenylalanine Derivatives Containing a Sulfur Substituent at the 2-Position." Heterocycles. 42. 219-228 (1996)

[Publications] Masashi Ohba, Takafumi Mukaihira, and Tozo Fujii: ""Preparatory Study for the Synthesis of the Starfish Alkaloid Imbricatine. Syntheses of 5-Aryl-thio-3-methyl-L-histidines, "" Chem. Pharm. Bull.42. 1784-1790 (1994)

[Publications] Masashi Ohba, Masaaki Imasho, and Tozo Fujii: ""Syntheses of L-Phenyl-alanine Derivatives Containing a Sulfur Substituent at the 2-Position, "" Heterocycles. 42. 219-228 (1996)

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