Synthetic Studies on Adenine-Diterpene Alkaloids Asmarines A-F, Cytotoxic Metabolites from the Marine Sponge Raspailia Species

2002 Fiscal Year Final Research Report Summary

Synthetic Studies on Adenine-Diterpene Alkaloids Asmarines A-F, Cytotoxic Metabolites from the Marine Sponge Raspailia Species

Research Project

Project/Area Number

12672051

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Chemical pharmacy

Research Institution

Kanazawa University

Principal Investigator

OHBA Masashi Kanazawa University, Center for Instrumental Analysis, Associate Professor, 機器分析センター, 助教授 (60115219)

Project Period (FY)

2000 – 2002

Keywords

Marine sponge metabolite / Asmarine / Adenine / Clerodane diterpenoid / Hydroxylamine / Pyrimidine / Purine / Anti-cancer activity

Research Abstract

With a view to confirming the structures and absolute configurations of asmarines A-F, novel adenine-diterpene alkaloids, isolated from the marine sponge Raspailia sp., we have undertaken their chiral syntheses and obtained the following results.
1. Alkylation of 6-chloropurine with N-(3-bromopropyl)-N-(methoxymethoxy) carbamic acid allyl ester in the presence of Co-complex provided preferentially the 7-isomer, which was then converted to the hydroxylamine possessing a [1,4]diazepino[1,2,3-gh]purine skeleton corresponding to the heterocyclic portion of asmarines A,B via the intramolecular amination at the 6-position.
2. Separate alkylation of 6-chloro-7,9-dihydro-9-methyl-8H-purin-8-one at the 7-position with N-(3-bromopropyl)carbamic acid tert-butyl ester and with N-(3-bromopropyl)-N-methoxycarbamic acid tert-butyl ester and the subsequent cyclization at the 6-position afforded the amine and the methoxyamine corresponding to the heterocyclic moieties of asmarines C,D and asmarines E,F, respectively.
3. (4aR)-1,4a-Dimethyl-4,4a,7,8-tetrahydronaphthalene-2,5(3H, 6H)-dione , obtained by asymmetric Robinson annulation, was converted to (4'aR,5'S,6'R,8'aR)-octahydro-5',6',8'a-trimethylspiro[1,-dioxolane-2,1'(2'H)-naphthalene]-5'-carboxaldehyde having all stereogenic centers consistent with the trans-decalin skeleton of

asrnarines A,D,E via highly stereoselective reactions (Li/NH_3 reduction, hydroxymethylation of the silyl enol ether, and catalytic hydrogenation using Ir catalyst). Completion of two diterpene portions by side chain modification and subsequent introduction of the heterocyclic moieties are currently under way.

Research Products (4 results)

All | Other

All | Publications

[Publications] Masashi Ohba: "Adenine Diterpenoids"Res.Adv.in Organic Chem.. 1. 1-11 (2000)

[Publications] Masashi Ohba: "Preparatory Study for the Synthesis of the Marine Sponge Alkaloids Asmarines A-F : Synthesis of their Heterocyclic Portions"Heterocycles. 57. 1235-1238 (2002)

[Publications] Masashi Ohba: "Adenine Diterpenoids"Res. Adv. In Organic Chem.. 1. 1-11 (2000)

[Publications] Masashi Ohba and Takahiro Tashiro: "Preparatory Study for the Synthesis of the Marine Sponge Alkaloids Asmarines A-F : Synthesis of Their Heterocyclic Portions"Heterocycles. 57. 1235-1238 (2002)

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