

Synthetic study on nikkomycins using addition reactions of nitrones

メタデータ	言語: jpn 出版者: 公開日: 2021-10-15 キーワード (Ja): キーワード (En): 作成者: Tamura, Osamu メールアドレス: 所属:
URL	https://doi.org/10.24517/00063858

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2001 Fiscal Year Final Research Report Summary

Synthetic study on nikkomycins using addition reactions of nitrones

Research Project

Project/Area Number

11672122

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

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Project Period (FY)

1999 - 2001

Keywords

nikkomycin Bz / α -alkoxycarbonylnitronone / (5S)-5,6-dihydro-5-phenyl-2H-1,4-oxazin-2-one N-oxide / carbocyclic polyoxin C / polyoxin C / N-terminal amino acid / b-substitued α -amino acids / clavulanine

Research Abstract

Nikkomycin Bz, a dipeptide antibiotic, possesses γ -hydroxy- α -amino acid as the N-terminal amino acid and a nucleoside amino acid as the C-terminal amino acid.

1) α -Allyloxycarbonylnitronone having a sugar auxiliary was explored. Using this method, the N-terminal amino acid moiety was synthesized.

2) (5R) [and (5S)]-5,6-Dihydro-5-phenyl-2H-1,4-oxazin-2-one N-oxides were designed and synthesized as the chiral (E)-geometry-fixed α -alkoxycarbonylnitronones. The key intermediate of carbocyclic polyoxin C, the carbocyclic analogue of the C-terminal amino acid, was synthesized by employing 1,3-dipolar cycloaddition of the cyclic nitronone.

3) Nucleophilic addition reaction of 2-trimethylsilyloxyfuran to N-Gulosyl-C-alkoxymethyl-nitronones was explored. The key intermediate of polyoxin C, the C-terminal amino acid of nikkomycin Bz, was synthesized by employing this method.


4) Methods mentioned above were applied to the synthesis of highly functionalized anti- and syn- β -substituted α -amino acids.


5) Highly stereoselective cycloaddition of (5S)-5,6-dihydro-5-phenyl-2H-1,4-oxazin-2-one N-oxide with allyl alcohol in the presence of MgBr₂ was applied to the synthesis of an antibiotic clavalanine.


Research Products (9 results)


All Other


All Publications


[Publications] O.Tamura, T.Kuroki, Y.Sakai, J.Takizawa, J.Yoshino, Y.Morita, N.Mita, K.Gotanda, M.Sakamoto: "Chelation Controlled 1,3-Dipolar Cycloaddition of 5,6-Dihydro-5-phenyl-1,4-oxazin-2-one N-Oxide with Allyl Alcohols : A Short-step Synthesis of Clavalanine Intermediate" *Tetrahedron Lett.* 40. 895-898 (1999) 


[Publications] O.Tamura, S.Yoshida, H.Sugita, N.Mita, Y.Uyama, N.Morita, M.Ishigur, T.Kawasaki, H.Ishibashi, M.Sakamoto: "Stereo-controlled Synthesis of Multi-functionalized β -Substituted α -amino acids : Nitronc cycloaddition Approach" *Synlett.* 1553-1556 (2000) 


[Publications] O.Tamura, K.Gotanda, Y.Morita, R.Terashima, M.Kikuchi, T.Miyawaki, N.Mita, M.Yamashita, H.Ishibashi, M.Sakamoto: "Design, Synthesis and 1,3-Dipolar Cycloaddition of (5R) [and (5S)]-5,6-Dihydro-5-phenyl-2H-1,4-oxazin-2-one N-Oxides as Chiral (E)-Geometry Fixed α -Alkoxy carbonylnitrones" *J. Org. Chem.* 65. 8544-8551 (2000) 


[Publications] O.Tamura, N.Mita, T.Okabe, T.Yamaguchi, C.Fukushima, M.Yamashita, N.Morita, H.Ishibashi, M.Sakamoto: "Tandem Transesterification and Intramolecular Cycloaddition of α -Methoxycarbonylnitrones with Chiral Acyclic Allyl Alcohols : Systematic Studies on the Factors Affecting Diastereofacial Selectivity of the Cycloaddition" *J. Org. Chem.* 66. 2602-2610 (2001) 

[Publications] N.Mita, O.Tamura, H.Ishibashi, M.Sakamoto: "Nucleophilic addition reaction of 2-trimethylsiloxyfuran to α -alkoxymethylnitronc bearing gulosyl group as a chiral auxiliary : synthesis of the C-terminal amino acid component of Nikkomycin Bz" *Org. Lett.* (in press). 

[Publications] O. Tamura, T. Kuroki, Y. Sakai, J. Takizawa, J. Yoshino, Y. Morita, N. Mita, K. Gotanda, M. Sakamoto: "Chelation controlled 1,3-dipolar cycloaddition of 5,6-dihydro-5-phenyl-1,4-oxazin-2-one N-oxide with allyl alcohols : A short-step synthesis of clavalanine intermediate" *Tetrahedron Lett.* 40. 895-898 (1999) 

[Publications] O. Tamura, S. Yoshida, H. Sugita, N. Mita, Y. Uyama, N. Morita, M. Ishiguro, T. Kawasaki, H. Ishibashi, M. Sakamoto: "Stereo-controlled synthesis of multi-functionalized β -Substituted α -amino acids : Nitronc cycloaddition Approach" *Synlett.* 2000. 1553-1556 

[Publications] O. Tamura, N. Mita, T. Okabe, T. Yamaguchi, C. Fukushima, M. Yamashita, Y. Morita, N. Morita, H. Ishibashi, M. Sakamoto: "Tandem transesterification and intramolecular cycloaddition of α -methoxycarbonylnitrones with chiral acyclic allyl alcohols : systematic studies on the factors affecting diastereofacial selectivity of the cycloaddition" *J. Org. Chem.* 66. 2602-2610 (2001) 

[Publications] N. Mita, O. Tamura, H. Ishibashi, M. Sakamoto: "Nucleophilic addition reaction of 2-trimethylsiloxyfuran to α -alkoxymethylnitronc bearing gulosyl group as a chiral auxiliary : synthesis of the C-terminal amino acid component of Nikkomycin Bz" *Org. Lett.* (in press). 

URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-11672122/116721222001kenkyu_seika_hokoku

Published: 2003-09-16