Establishment of Highly Selective Radical Cyclization and Application to the Synthesis of Biologically Active Compounds

1997 Fiscal Year Final Research Report Summary

Establishment of Highly Selective Radical Cyclization and Application to the Synthesis of Biologically Active Compounds

Research Project

Project/Area Number

08672419

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

ISHIBASHI Hiroyuki Kanazawa University, Faculty of Pharmaceutical Sciences, Professor, 薬学部, 教授 (70028869)

Co-Investigator(Kenkyū-buntansha)

OHBA Masashi Kanazawa University, Faculty of Pharmaceutical Sciences, Assistant, 薬学部, 助手 (60115219)

Project Period (FY)

1996 – 1997

Keywords

alkaloid synthesis / asymmetric induction / beta-lactam / lycorane / 1beta-methylcarbapenem / 4-oxo-2-azetidineacetic acid / radical cyclization / thienamycin

Research Abstract

Bu_3SnH-mediated regio- and stereoselective radical cyclizations of alpha-holo amides have been examined. The results are summarized below.
1. The 4-exo radical cyclization of N-vinylic alpha-halo amides, bearing a chiral auxiliary on the nitrogen atom or at the alpha-position of the carbonyl group, was found to proceed with high degree of diastereoselectivy to give optically active beta-lactams. The methods were applied to the synthesis of optically active carbapenem antibiotics such as (+) -PS-5, (+) -thienamycin and 1beta-methylcarbapenem.
2. The 5-endo radical cyclization of N- (1-cyclohexenen-1-yl) -alpha-haloacetamides bearing a chiral auxiliary on the nitrogen atom was found to proceed with moderate degree of diastereoselectivy t give optically active octahydroindol-2-ones. The method was applied to the total synthesis of (-) -gamma-lycorane.
3. The radical cyclization of N- (2-phenylthio-1-cyclohexenen-1-yl) -alpha-haloacetamies has been examined, and it was found that the course of the cyclizations was atrikingly affected by the reaction temperature employed. Thus, at room temperature, 4-exo cyclization predominated, and at higher temperature (in boiling toluene), 5-endo cyclization predominated.
4. The kN-vinyl-2-bromobenzamides or N-vinyl-2- (2-bromophenyl) acetamides bearing a phenylthio group at the terminus of their N-vinylic bond were found to undergo radical cyclization in a 5-exo-trig or in a 6-exo-trig manner effectively to give isoindolone and isoquinolinones, respectively. The methods were applied to the synthesis of some alkaloids such as chilenine, lennoxamine, tetrahydropalmatine and saulatine.
5. The N- [o- (2-propenyl) phenyl] -2,2-bis (phenylthio) acetamides were found to undergo radical cyclization in an 8-endo-trig manner to give benzoazocinone derivatives.

Research Products (22 results)

All | Other

All | Publications (22 results)

[Publications] 石橋 弘行: "Asymmetric Radical CyclizationLeading to β-Lactams : StereoselectiveSynthesis of Chiral Key Intermediatesfor Carbapenem Antibiotics PS-5 and Thienamycin." Tetrahedron. 52. 489-502 (1996)

[Publications] 石橋 弘行: "Radical Cyclization of Chiral N-(1-Cycloalken-1-yl)-α-haloacetamides: Synthesis of Optically Active Bicyclic Pyrrolidionones." Tetrahedron : Asymmetry. 7. 2531-2538 (1996)

[Publications] 石橋 弘行: "Synthesis of 4-Oxo-2-azetidineacetic Acids by Means of Radical Cyclization of N-Vinylic α-Bromo Amides." Tetrahedron. 52. 13867-13880 (1996)

[Publications] 池田 正澄: "Synthesis of Tetrahydro-1-benzazocin-2(1H)-ones Using 8-Endo-Trig Radical Cyclization of 2,2-Bis(pheynlthio)-N-[o-(prop-2-enyl)phenyl] acet-amides." Heterocycles. 44. 203-212 (1997)

[Publications] 石橋 弘行: "Sulfur-Controlled 5-Exo Selective Aryl Radical Cyclisation of N-Vinylic 2-Bromobenzamides : Synthesis of Lennoxamine and Chilenine." J.Chem.Soc.,Perkin Trans.1. 817-821 (1997)

[Publications] 池田 正澄: "Triethylborane-Mediated Atom Transfer Cyclization of N-Allylic α-Iodoacet-amides : A Convenient Synthesis of β-Iodomethyl-γ-lactams." Heterocycles. 45. 863-866 (1997)

[Publications] 石橋 弘行: "Synthesis of a Chiral 1β-Methylcarbapenem Key Intermediate Using Radical Cyclization of N-Vinylic α-Bromo Amides." Tetrahedron. 53. 9611-9622 (1997)

[Publications] 石橋 弘行: "Sulfur-Controlled 6-Exo Aryl Radical Cyclisation of N-Ethenyl-2-(2-bromophynyl)acetamides : Synthesis of (±)-Tetrahydropalmatine and Saulatine." J.Chem.Soc.,Perkin Trans.1. 2291-2295 (1997)

[Publications] 池田 正澄: "5-Endo-Trig Radical Cyclization of 2-Chloro-and 2,2-Bis(phenyilthio)-N-methyl-N-(6-phenyl-cyclohex-1-en-1-yl)acetamidews" Heterocycles. 47. 181-186 (1998)

[Publications] 石橋 弘行: "Effect of Temperature on 5-Endo-and 4-Exo-Trig Radical Cyclizations of N-Vinylic α-Halo Amides." Tetrahedron Lett.39. 75-78 (1998)

[Publications] 池田 正澄: "Triethylborane-Mediated Atom Transfer Cyclization of 2-Iodo-N-(prop-2-enyl)acetamides and Related Compounds" J.Chem.Soc.,Perkin Trans.1. (印刷中).

[Publications] Ishibashi, H. ; Kameoka, C. ; Kodama, K. ; Ikeda, M.: "Asymmetric Radical Cyclization leading to beta-Lactams : Stereoselective Synthesis of Chiral Key Intermediates for Carbapenem Antibiotics PS-5 and Thienamycin" Tetrahedron. 52. 489-502 (1996)

[Publications] Ishibashi, H. ; Fuke, Y. ; Yamashita, T. ; Ikeda, M.: "Radical Cyclization of Chiral N- (1-Cycloalken-1-yl) -alpha-haloacetamides : Synthesis of Optically Active Bicyclic Pyrrolidinones" Tetrahedron : Asymmetry. 7. 2531-2538 (1996)

[Publications] Ishibashi, H. ; Kodama, K. ; Kameoka, C. ; Kawanami, H. ; Ikeda, M.: "Synthesis of 4-Oxo-2-azetidineacetic Acids by Means of Radical Cyclization of N-Vinylic alpha-Bromo Amides" Tetrahedron. 52. 13867-13880 (1996)

[Publications] Ikeda, M. ; Obata, K. ; Oka, J. ; Ishibashi, H. ; Sato, T.: "Synthesis of Tetrahydro-1-benzazocin-2 (1H) -ones Using 8-Endo-Trig Radical Cyclization of 2,2-Bis- (Phenylthio) -N- [o- (prop-2-enyl) phenyl] acetamides" Heterocycles. 44. 203-212 (1997)

[Publications] Ishibashi, H. ; Kawanami, H. ; Ikeda, M.: "Sulfur-Controlled 5-Exo Selective Aryl Radical Cyclisation of N-Vinylic 2-Bromobenzamides : Synthesis of Lennoxamine and Chilenine" J.Chem.Soc., Perkin Trans. 1. 817-821 (1997)

[Publications] Ikeda, M. ; Teranishi, H. ; Iwamura, N. ; Ishibashi, H.: "Triethylborane-Mediated Atom Transfer Cyclization of N-Allylic alpha-Iodoacetamieds : A Convenient Synthesis of beta-Iodomethyl-gamma-lactams" Heterocycles. 45. 863-866 (1997)

[Publications] Ishibashi, H. ; Kameoka, C. ; Kodama, K. ; Kawanami, H. ; Hamada, M. ; Ikeda, M.: "Synthesis of a Chiral 1beta-Methylcarbapenem Key Intermediate Using Radical Cyclization of N-Vinylic alpha-Bromo Amides" Tetrahedron. 53. 9611-9622 (1997)

[Publications] Ishibashi, H. ; Kawanami, H. ; Nakagawa, H. ; Ikeda, M.: "Sulfur-Controlled 6-Exo Aryl Radical Cyclisation of N-Ethenyl-2- (2-bromophenyl) acetamides : Synthesis of ((]SY.+-。[)) -Tetrahydropalmatine and Saulatine" J.Chem.Soc., Perkin Trans.1. 2291-2295 (1997)

[Publications] Ikeda, M. ; Ohtani, S. ; Okada, M. ; Minakuchi, E. ; Sato, T. ; Ishibashi, H.: "5-Endo-Trig Radical Cyclization of 2-Chloro- and 2,2-Bis (phenylthio) -N-methyl-N- (6-phenylcyclohex) -1-en-1-yl) acetamides" Heterocycles. 47. 181-186 (1998)

[Publications] Ishibashi, H. ; Higuchi, M. ; Ohba, M. ; Ikeda, M.: "Effect of Temperature on 5-Endo- and 4-Exo-Trig Radical Cyclizations of N-Vinylic alpha-Halo Amides" Tetrahedron Lett.39. 75-78 (1998)

[Publications] Ikeda, M. ; Teranishi, H. ; Nozaki, K. ; Ishibashi, H.: "Triethylborane-Mediated Atom Transfer Cyclisation of 2-Iodo-N- (prop-2-enyl) acetamides and Related Compounds." J.Chem.Soc., Perkin Trans. 1 (in press).

URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-08672419/086724191997kenkyu_seika_hokoku_

Published: 1999-03-15