Career of Masayuki Inoue (井上 将行)

Total synthesis and functional analysis of biologically active natural products

I. New synthetic methodologies for total synthesis
II. Highly oxygenated polycyclic natural products
III. Ion channel-forming molecules
IV. Antimicrobial molecules

Ximing Li

Masayuki Inoue (50)

Professor, Department of Medicinal Chemistry, The University of Tokyo

1989-1993 The University of Tokyo, B.S. in Chemistry,
1993-1998 The University of Tokyo, Ph.D. in Organic Chemistry,
Research advisor: Professor Kazuo Tachibana (橘 和夫)

![Image of Ciguatoxin]

Ciguatoxin

1998-2000 Sloan-Kettering Institute for Cancer Research, Postdoctoral Fellow,
Research advisor: Professor Samuel J. Danishefsky

![Image of Frondosin A and B]

Frondosin A and B

Associate Editor, The Journal of Organic Chemistry
Consulting Board of Editor, Tetrahedron/Tetrahedron Letters
Board of Editors, Organic Syntheses
1. Development of new synthetic methodologies for total synthesis

Direct assembly of multiply oxygenated carbon chains by decarbonylative radical–radical coupling reactions

Kengo Masuda, Masanori Nagatomo and Masayuki Inoue*
1. Development of new synthetic methodologies for total synthesis

Radical-radical coupling strategies for the synthesis of contiguously substituted polyol structures.
1. Development of new synthetic methodologies for total synthesis

Radical-radical cross-coupling reaction for the synthesis of the hikizimycin carbon chain $SS$

Et$_3$B (15 eq.), air Benzene/DCM, rt

+ $SS$ (17%)
+ $RS$ (7.8%)
+ $SR$ (5.2%)
+ $RS$ (1.7%)
Et$_3$B-Mediated Radical-Polar Crossover Reaction for Single-Step Coupling of O, Te-Acetal, $\alpha,\beta$-Unsaturated Ketones, and Aldehydes/Ketones

Daigo Kamimura, Daisuke Urabe, Masanori Nagatomo, and Masayuki Inoue*

1. Development of new synthetic methodologies for total synthesis

Et$_3$B-mediated three-component coupling reaction between O,Te-acetal, $\alpha,\beta$-unsaturated ketones, and aldehydes/ketones.
1. Development of new synthetic methodologies for total synthesis

Proposed mechanism.
2. Total synthesis of highly oxygenated polycyclic natural products

**Total Synthesis of 1-Hydroxytaxinine**

Yusuke Imamura†, Shun Yoshioka†, Masanori Nagatomo, and Masayuki Inoue*

[Chemical structures and reactions diagram]

Retrosynthesis
Total Synthesis of Resiniferatoxin Enabled by Radical-Mediated Three-Component Coupling and 7-endo Cyclization

Satoshi Hashimoto, Shun-ichiro Katoh, Takehiro Kato, Daisuke Urabe, † and Masayuki Inoue* 

Retrosynthesis
Total Synthesis of Zaragozic Acid C: Implementation of Photochemical C(sp³)-H Acylation

Takahiro Kawamata, Masanori Nagatomo, and Masayuki Inoue

Site- and stereoselective C(sp³)-H acylation

Key step of retrosynthesis
2. Total synthesis of highly oxygenated polycyclic natural products

**A convergent total synthesis of ouabagenin†**

Ken Mukai, Satoshi Kasuya, Yuki Nakagawa, Daisuke Urabe and Masayuki Inoue*

[Chem. Sci., 2015, 6, 3383]

**Chemical Science**

**EDGE ARTICLE**

Cite this: Chem. Sci., 2015, 6, 3383

![Diagram of the synthesis process]

**Retrosynthesis**

- **aldol reaction**
- **radical cyclization (Et$_3$B method)**

$X$-$Y$ = (MeO)CH-CH or CH=C

1 → 2 → 3 → 4 → 5 + 6
2. Total synthesis of highly oxygenated polycyclic natural products

A concise route to the $C_2$-symmetric tricyclic skeleton of ryanodine
Koji Hagiwara$^{a,b}$, Masafumi Himuro$^b$, Masahiro Hirama$^b$, Masayuki Inoue$^{a,*}$

Chemical Science

Symmetry-driven synthesis of 9-demethyl-10, 15-dideoxyryanodol$^+$
Daisuke Urabe, Masanori Nagatomo, Koji Hagiwara, Kengo Masuda and Masayuki Inoue$^{*}$

Total Synthesis of Ryanodol
Masanori Nagatomo, Masaki Koshimizu, Kengo Masuda, Toshiki Tabuchi, Daisuke Urabe, and Masayuki Inoue$^{*}$
2. Total synthesis of highly oxygenated polycyclic natural products

![Chemical Reaction Diagram]

Ryanodine
2. Total synthesis of highly oxygenated polycyclic natural products

- **a.** TMSOTf, Et₃N
- **b.** DMDO
- **c.** TfOH, MeOH
- **d.** Sm²⁺
- **e.** TfOH

**C11-deoxygenation**

**transannular pinacol coupling**

**NOE**

**5 steps**

**8 steps**

**22 steps**

**Ryanodine**
Design, Synthesis and Functional Analysis of Dansylated Polytheonamide Mimic: An Artificial Peptide Ion Channel

Hiroaki Itoh,† Shigeru Matsuoka,† Mohamed Kreir,‡ and Masayuki Inoue*†

Structures of polytheonamide B and dansylated polytheonamide mimic. Residue # indicated in red are the amino acid residues artificially modified from natural polytheonamide B.
Total synthesis of the large non-ribosomal peptide polytheonamide B

Masayuki Inoue*, Naoki Shinohara, Shintaro Tanabe, Tomoaki Takahashi, Ken Okura, Hiroaki Itoh, Yuki Mizoguchi, Maiko Iida, Nayoung Lee and Shigeru Matsuoka

Four peptide segments for the total synthesis of polytheonamide
Total Synthesis and Biological Mode of Action of WAP-8294A2: A Menaquinone-Targeting Antibiotic

Hiroaki Itoh,†‡ Kotaro Tokumoto,† Takuya Kaji,† Atmika Paudel,‡ Suresh Panthee,‡ Hiroshi Hamamoto,‡ Kazuhisa Sekimizu,‡ and Masayuki Inoue*†‡

Structures of WAP-8294A2(botilibcin, 1), deoxy analogue (2), and lysocin E (3).
Unified Total Synthesis of Polyoxins J, L, and Fluorinated Analogues on the Basis of Decarbonylative Radical Coupling Reactions

Haruka Fujino, Masanori Nagatomo, Atmika Paudel, Suresh Panthee, Hiroshi Hamamoto, Kazuhisa Sekimizu, and Masayuki Inoue*

polyoxin J: X = CH₃
polyoxin L: X = H
trifluoropolyoxin J: X = CF₃
fluoropolyoxin L: X = F
Questions?