有用な生物機能多環式中分子の高効率合成

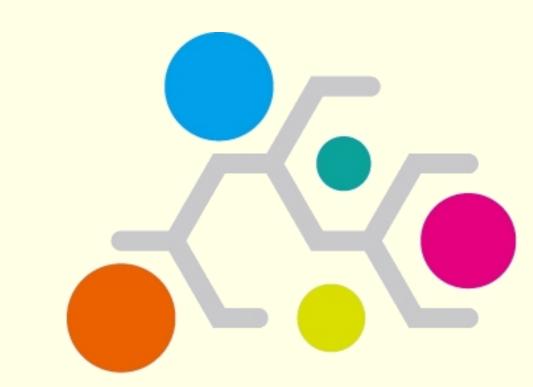
(早大院理工)中田雅久

Scheme 1. CAIMCP of 2 and Preparation of 4

1) MeSO₂Mes

2) TsN_3 , Et_3N

n-BuLi, 97%



Ligand A

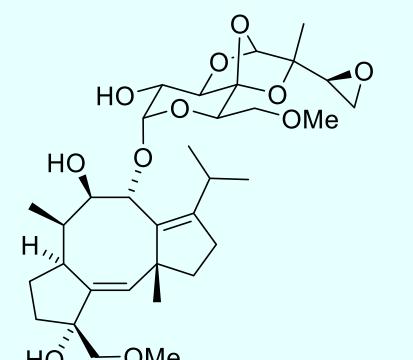
SO₂Mes

99% ee (recryst)

 $OP(O)(OEt)_2$

Enantioselective Total Synthesis of Cotylenin A

Uwamori, M.; Osada, R.; Sugiyama, R.; Nagatani, K.; Nakada, M. J. Am. Chem. Soc. 2020, 142, 5556–5561.



Isolation

•from Cladosporium sp, as a plant growth regulator. **Biological Activities**

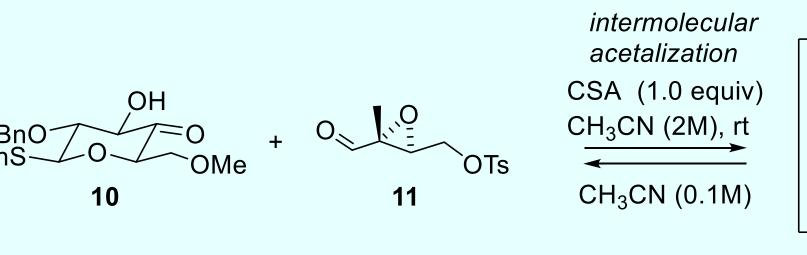
 Induces the apoptosis of human cancer cell lines by combined treatment with interferon-α. Stabilizes the interactions of 14-3-3 proteins.

- **Structural Features** •5-8-5 Tricyclic ring system (ABC ring)
- Highly oxygenated sugar part Chiral centers with quaternary stereogenic center

Figure 1. Structure and profile of cotylenin A.

cotylenin A

Scheme 4. Preparation of 15 via Acetalizations and Epoxide-Opening Cascade



intramolecular acetalization

HO'''

HO_

TMSO

TBSO

OTf

LHMDS, LiCI

1) Me₃OBF₄, 2,6-^tBu₂-4-MePy

pyridine, 0 °C, 71%

2) DIBAL, CH₂Cl₂

–78 °C, 96%

CH₂Cl₂, 0 °C; then, TMSCl,

Scheme 2. Preparation of 7 via Acyl Radical Cycliza-tion

0 °C to rt, 54% (2 steps)

2) DMP, 89%

1) 3HF•Et₃N, 88%

1) tert-C₁₂H₂₅SH, TBHP

CuCl, 2,2'-bipyridyl

TBME, 50 °C

2) PhNTf₂, LDA, THF

intramolecular epoxide opening 24 h

OTf

Ligand A

(4.5 mol %)

CuPF₆(CH₃CN)₄

(3.0 mol %)

toluene, 60 °C

86%, 86% ee

 N_2 SO₂Mes

TfO,

6 ($R^1 = CH_2OTBS$)

 \rightarrow 7 (R¹ = CHO)

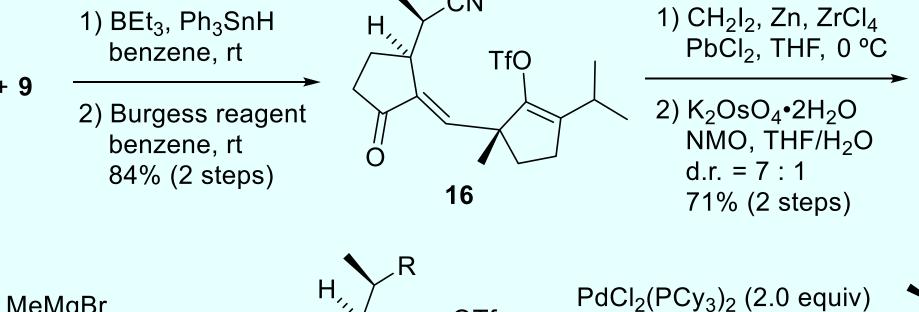
`SO₂Mes

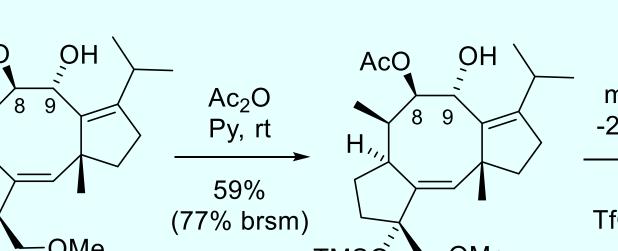
SO₂Mes

Scheme 3. Preparation of 9

0 °C, 82%

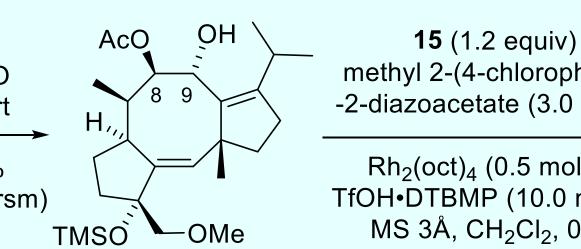






TMSO

23



methyl 2-(4-chlorophenyl) -2-diazoacetate (3.0 equiv) $Rh_2(oct)_4$ (0.5 mol %) TfOH•DTBMP (10.0 mol %) MS 3Å, CH_2Cl_2 , 0 °C -OMe **TMSO** 24

MoOPH $Me_4NBH(O_2CiPr)_3$ THF, -50 °C CH₃CN, rt 80% 52% (**22**) single diastereomer 19% (C9 epimer) TMSO -OMe 21 **22** HO AcQ 1) MeLi, Et₂O, –78 °C 2) TBAF, THF, rt 3) H₂, Pd black, 45 °C 6% (7% brsm) (4 steps)

cotylenin A

TMSO'''

MeO[′]

19

NaH, THF, rt (2 steps)

NaCN, DMSO

80 °C, 77%

THF, 0 °C;

CIP(O)(OEt)₂

quant

第3776号 規チガー 発見期待の成功の成功の

・日本化学会第99春季年会のハイライト講演に選出 ・科学新聞ほか、インターネットで朝日新聞、毎日新聞、 日経新聞など26社により報道

An Enantio- and Stereoselective Construction of Atisane Scaffold via Organocatalytic Intramolecular Michael Reaction and Diels-Alder Reaction

Sekita, H.; Adachi, K.; Kobayashi, I.; Sato, Y.; Nakada, M. Org. Lett. 2017, 19, 2390-2392.

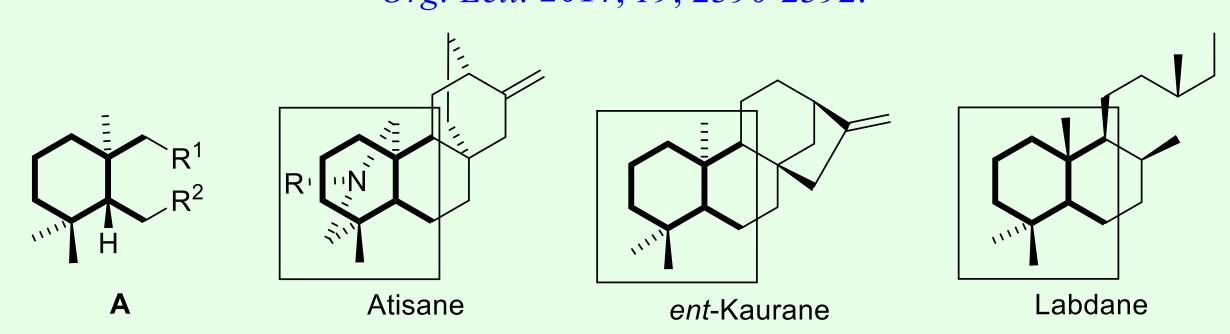


Figure 2. Structures of A and terpenoids involving A.

Scheme 6. Developed Asymmetric Organocatalysis

BnBr, TBAI

powder KOH

34 (R = OAc)

3.5 h, 66%

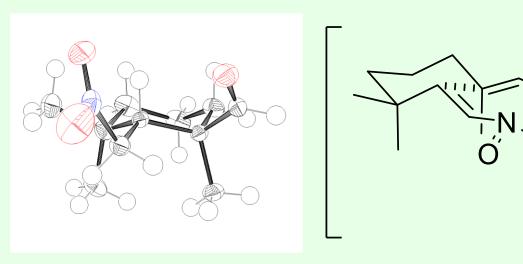


Figure 3. X-Ray crystal structure of the product and a proposed transition state model

35

1) SOCI₂, Et₃N, THF, 0 °C

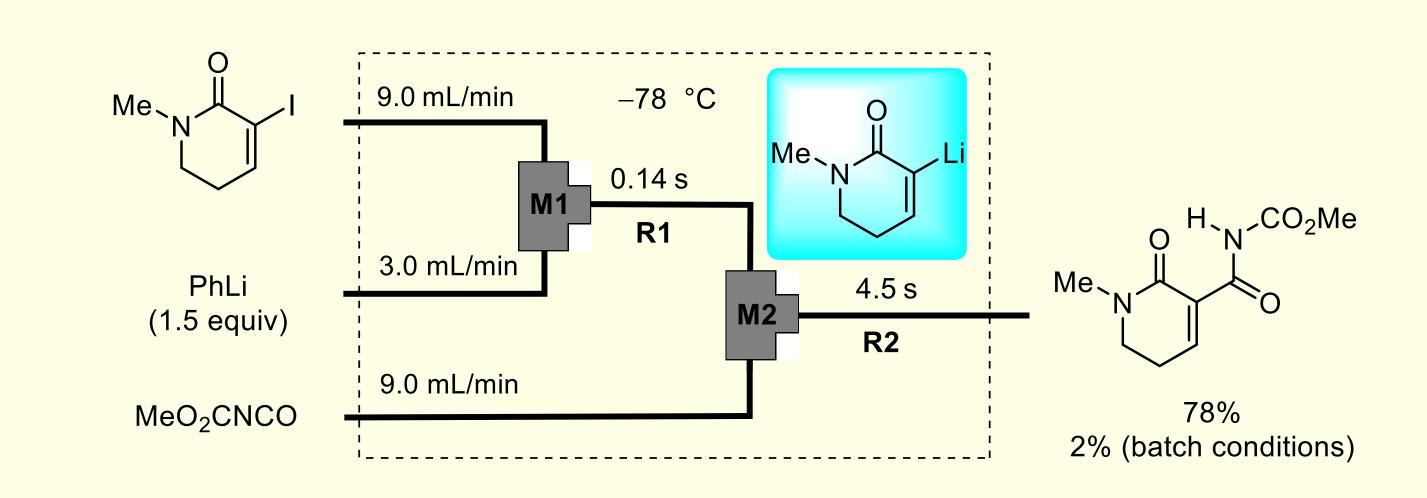
15 min, 93%

Scheme 1-2. Synthesis and Stereoselective Diels-Alder Reaction of 34 Affording Atisane Scaffold

2) DMP, CH₂Cl₂, 0 °C, 25 min, 95%

Efficient Preparation of Cyclic α-Alkylidene β-Oxo Imides Using a Flow Microreactor System

Komuro, K.; Nagaki, A.; Shimoda, H.; Uwamori, M.; Yoshida, J.-i.; Nakada, M. Synlett 2018, 29, 1989-1994.



Palladium-Catalyzed Carbothiolation via Trapping of the σ-Alkyl Palladium Intermediate with RSTIPS

Hosoya, Y.; Kobayashi, I.; Mizoguchi, K.; Nakada, M. Org. Lett. 2019, 21, 8280-8284.

Synthesis and Reaction of ortho-Benzoquinone Monohemiaminals

Saito, E.; Matsumoto, Y.; Nakamura, A.; Namera, Y.; Nakada, M. Org. Lett. 2018, 20, 692-695.

OH OH NHTS PIDA (1.1 equiv)

HFIP/CH₂Cl₂

$$0 \, ^{\circ}$$
C, 30 min 66%, dr = 12/1

Ph N-phenylmaleimide (3.0 equiv)

90 $^{\circ}$ C, 14 h, 96% single isomer