Organic LETTERS

Letter

pubs.acs.org/OrgLett

Synthetic Study of Pactamycin: Enantioselective Construction of the Pactamycin Core with Five Contiguous Stereocenters

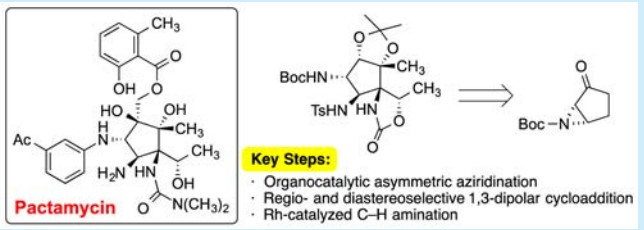
Mami Yamaguchi,[†,§] Minami Hayashi,[†,§] Yasumasa Hamada,[*,†] and Tetsuhiro Nemoto[*,†,‡]

[†]Graduate School of Pharmaceutical Sciences, Chiba University, 1-8-1, Inohana, Chuo-ku, Chiba, 260-8675, Japan

[‡]Molecular Chirality Research Center, Chiba University, 1-33, Yayoi-cho, Inage-ku, Chiba 263-8522, Japan

Supporting Information

ABSTRACT: A synthetic study of pactamycin is described. Enantioselective construction of the aminocyclopentitol core of pactamycin bearing five contiguous stereocenters was achieved based on an organocatalytic asymmetric aziridination of 2-cyclopentene-1-one, a regio- and diastereoselective 1,3-dipolar cycloaddition, and a rhodium-catalyzed C−H amination reaction.



Pactamycin (**1**) was isolated from the fermentation broth of *Streptomyces pactum var. pactum* by researchers at Upjohn in 1961 (Figure 1).[1] An X-ray crystal structure analysis of its

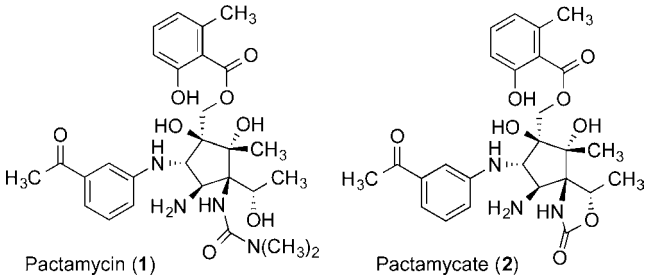
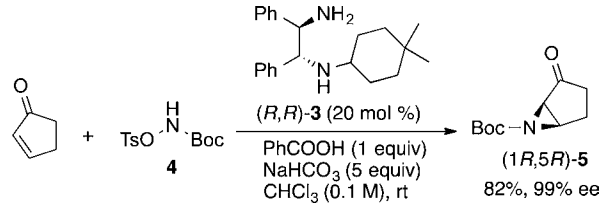


Figure 1. Structures of pactamycin (**1**) and pactamycate (**2**).

analogue, pactamycate (**2**), revealed its unique aminocyclopentitol structure,[2] which is highlighted by six contiguous stereocenters: all five carbons of the cyclopentane core are stereogenic, and three of these are tetrasubstituted carbons. Pactamycin has potent antiproliferative activity against bacteria,[3] mammalian cells,[4] viruses,[5] and protozoa.[6] This broad-spectrum bioactivity originates from its ability to inhibit translocation through binding to the highly conserved region of the 30S ribosomal subunit.[7] The densely functionalized structure and remarkable bioactivity make pactamycin an attractive target for synthetic organic chemists. Synthetic studies of pactamycin have been reported by Isobe and Nishikawa et al.,[8] Knapp et al.,[9] Looper et al.,[10] and Castle et al.[11,12] In 2011, the first total synthesis of pactamycin was achieved by Hanessian et al. in 29 steps from L-threonine.[13] More recently, Johnson and co-workers reported an elegant 15-step total synthesis of pactamycin based on a catalytic asymmetric Mannich reaction and symmetry-breaking reduction sequence.[14]

Optically active aziridines are versatile building blocks for the synthesis of nitrogen-containing chiral compounds. Regioselective opening of aziridine rings with a nucleophile provides efficient access to chiral amine fragments with contiguous stereocenters. Various asymmetric synthetic methods of optically active aziridines[15] have therefore been developed based on the metal-catalyzed nitrene-transfer reaction,[16] asymmetric Brookhart−Templeton aziridination using Lewis acid catalysts[17] or organocatalysts,[18] and chiral amine catalysis.[19] We previously reported a chiral diamine-catalyzed asymmetric aziridination of cyclic enones.[20] Using 20 mol % of diphenylethylene diamine-derived organocatalyst (*R*,*R*)-**3**, asymmetric aziridination of 2-cyclopenten-1-one with *tert*-butyl *p*-toluenesulfoxy carbamate **4** proceeded smoothly to give the corresponding chiral aziridine ketone (1*R*,5*R*)-**5** in good yield with excellent enantioselectivity (Scheme 1). Compound (1*R*,5*R*)-**5** was successfully applied to

Scheme 1. Chiral Diamine-Catalyzed Asymmetric Aziridination of 2-Cyclopenten-1-one

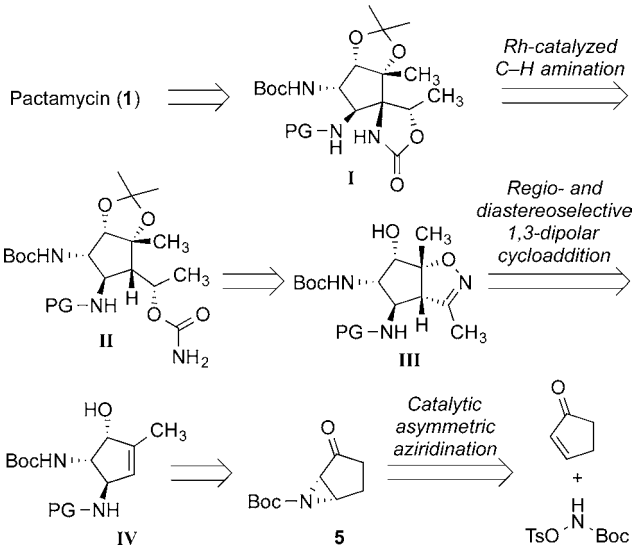


the synthesis of (−)-allosamizoline.[20b] We hypothesized that the antipode aziridine ketone (1*S*,5*S*)-**5** could be utilized as a chiral scaffold for constructing the core structure of pactamycin. Herein we report our efforts toward the synthesis of pactamycin. Enantioselective construction of the pactamycin core bearing five contiguous stereocenters is the highlight of this communication and was achieved based on the chiral diamine-catalyzed asymmetric aziridination of 2-cyclopenten-1-one, a regio- and diastereoselective 1,3-dipolar cycloaddition, and a rhodium-catalyzed C−H amination reaction.

Received: March 16, 2016
Published: May 12, 2016

DOI: 10.1021/acs.orglett.6b00761
Org. Lett. 2016, 18, 2347−2350

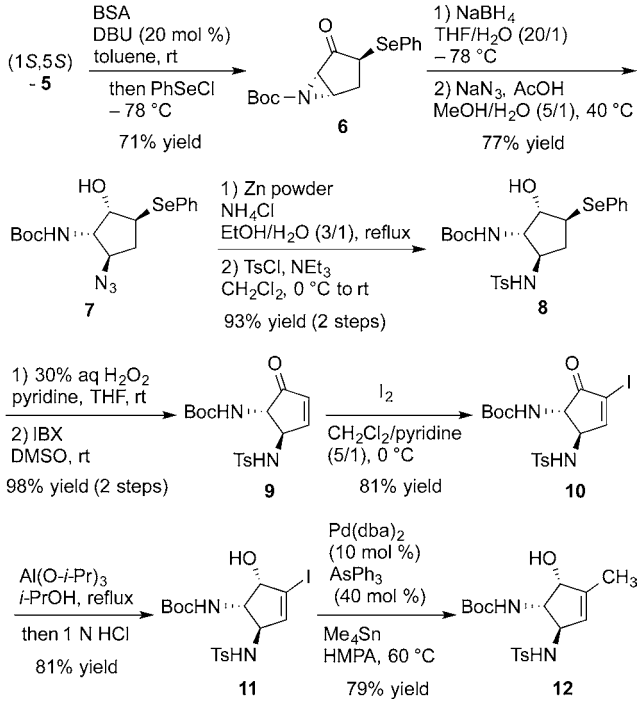
Scheme 2. Retrosynthetic Analysis of Pactamycin



Our retrosynthetic analysis is outlined in Scheme 2. To establish an enantioselective synthetic route for pactamycin, we first developed an efficient method of constructing the array of the stereogenic carbons. We set compound **I** bearing five contiguous stereocenters of six in pactamycin as the key intermediate. We envisioned that a rhodium-catalyzed C–H amination reaction[21] using carbamate derivative **II** would be applicable to the construction of the tertiary amino stereocenter in **I**. Controlling the three contiguous stereocenters from the hydroxyethyl branch to the tertiary alcohol in **II** is a challenging task. We envisioned that compound **II** could be prepared from isoxazoline intermediate **III**, which in turn would be accessible via a regio- and diastereoselective 1,3-dipolar cycloaddition of functionalized cyclopenten derivative **IV** with acetonitrile oxide. Chiral aziridine ketone (1*S*,5*S*)-**5** could be utilized as a reasonable precursor for compound **IV**.

Our synthetic study started with nearly optically pure aziridine ketone (1*S*,5*S*)-**5** (99% ee), which could be prepared in multigram scale using 20 mol % of (*S*,*S*)-**3**. Introduction of a phenylselenenyl group to the α-position of the ketone proceeded diastereoselectively, affording compound **6** in 71% yield according to the reported procedure[20b] (Scheme 3). Subsequent reduction of the ketone with $NaBH_4$ in a THF–H_2O mixed solvent, followed by an aziridine opening reaction with sodium azide, provided compound **7** in a regio- and stereoselective manner (77% yield). After reduction of the azide group in **7** by using zinc powder, the resulting primary amine was protected with a tosyl group to give compound **8** in 93% yield in two steps.[22] Oxidative elimination of the phenylselenenyl group with aqueous hydrogen peroxide afforded the corresponding allylic alcohol intermediate, which was then transformed into cyclic enone derivative **9** by treating with IBX in DMSO (88% yield, two steps). To introduce a C1 unit to the α-position of the enone, a Morita–Baylis–Hillman reaction was first examined using formaldehyde as an electrophile under several reaction conditions. All trials, however, gave unsatisfactory results. On the other hand, α-iodination of the enone proceeded smoothly in the presence of iodine in a CH_2Cl_2/pyridine mixed solvent system, providing compound **10** in 81% yield. Diastereoselective reduction of the ketone using Al(O-*i*-Pr)$_3$ (81% yield),[23] followed by Stille coupling between **11** and tetramethyltin in the presence of 10 mol % of Pd(dba)$_2$ and

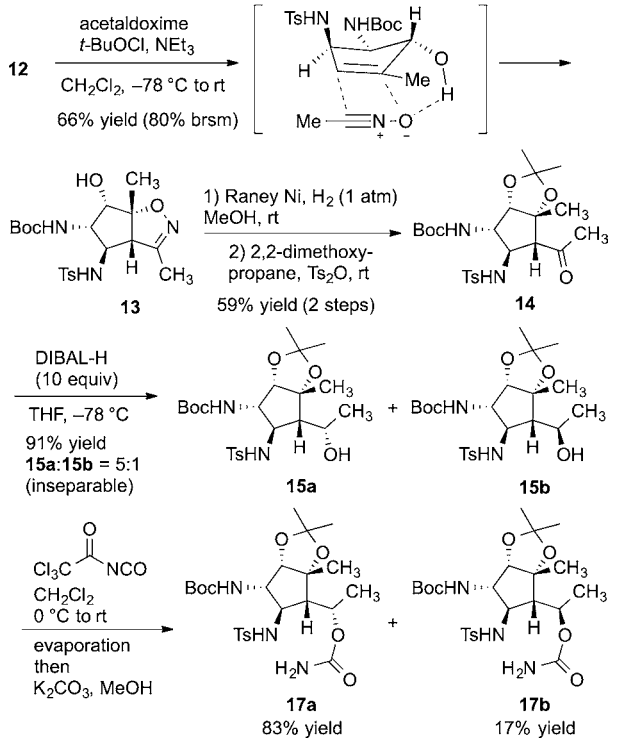
Scheme 3. Synthesis of Compound 12



40 mol % of Ph_3As in HMPA, afforded the methylated product **12** in 79% yield.

With the key intermediate **12** in hand, we next examined the regio- and stereoselective 1,3-dipolar cycloaddition using acetonitrile oxide as a 1,3-dipole (Scheme 4). Metal ion mediated cycloaddition of nitrile oxides to allylic alcohols is a useful strategy for the regio- and stereoselective synthesis of isoxazoline derivatives.[24] We first examined the reaction using a magnesium

Scheme 4. Synthesis of the Key Intermediate 15a



DOI: 10.1021/acs.orglett.6b00761
Org. Lett. 2016, 18, 2347–2350

ion as a mediator,[25] but no desired product was obtained and deprotection of the Boc group partially occurred. In contrast, acetonitrile oxide generated from acetaldoxime and *tert*-butyl hypochlorite in the presence of triethylamine reacted with **12** in a regio- and diastereoselective manner, producing isoxazoline derivative **13** in 66% yield (80% yield based on the recovery of **12**).[26] We expected that the regioselectivity and facial selectivity of the olefin would be controlled by the hydrogen-bonding interaction between the anionic oxygen of the nitrile oxide and the alcohol, as well as the steric repulsion between the tosyl amide moiety and acetonitrile oxide. Reductive cleavage of the N−O bond under a hydrogen atmosphere in the presence of Raney-Ni, followed by acetonide formation with the resulting diol, gave compound **14** in 59% yield in two steps. Diastereoselective reduction of the methyl ketone was then examined under several reaction conditions. Combination of the reducing agent and solvent dramatically affected the diastereoselectivity.[26] When **14** was treated with 10 equiv of DIBAL-H in THF at −78 °C, the corresponding products **15a** and **15b** were obtained in 91% yield as an inseparable 5:1 mixture of diastereomers. The relative configuration of the major diastereomer **15a** was determined by X-ray crystal structure analysis after esterification of the mixture with *p*-nitrobenzoyl chloride and chromatographic separation of the diastereomers.[27] The X-ray structure of the major isomer **16a** (Figure 2) revealed

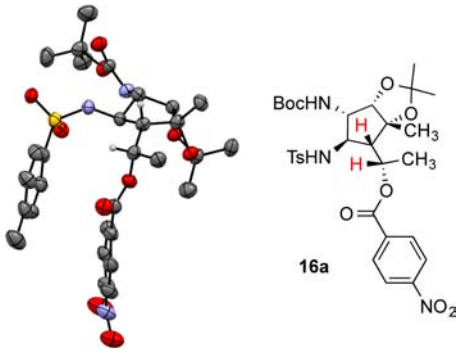
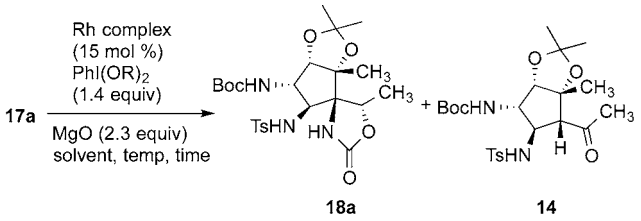


Figure 2. X-ray structure of **16a**. Hydrogen atoms except for the protons indicated in red have been omitted for clarity.

that **15a** was the desired isomer for this study. Because of the difficult separation of **15a** and **15b**, the obtained mixture was used for the next reaction without further purification. A carbamoyl unit was introduced into the secondary alcohol using a 5:1 mixture of **15a** and **15b** as the substrate, affording compound **17a** and **17b** in excellent yield. These compounds were separable by silica gel column chromatography.

A rhodium-catalyzed C−H amination to construct the tertiary amino stereocenter was then examined using **17a** (Scheme 5).[28] First, we performed the reaction in CH_3CN using 15 mol % of the $Rh_2(esp)_2$ complex, the benchmark catalyst for this chemistry.[21c,d] The desired spirocyclic adduct **18a** was obtained in only 7% yield, accompanied by the formation of compound **14** in 37% yield. Screening of other rhodium complexes revealed that $Rh_2(OAc)_4$ was the most suitable catalyst for this purpose. When the reaction was performed using 15 mol % of $Rh_2(OAc)_4$, 1.4 equiv of $PhI(OAc)_2$, and 2.3 equiv of MgO in CH_3CN at 80 °C, **18a** was produced in 47% yield and recyclable product **14** was also formed in 32% yield.[29] The yield of **18a** was slightly improved (51% yield) when benzene was used as the solvent. Finally, the desired product **18a** was obtained in 70% yield by

Scheme 5. Rhodium-Catalyzed C−H Amination Reaction



Conditions	Yield
$Rh_2(esp)_2$, $PhI(OAc)_2$/ CH_3CN, 80 °C, 6 h	**18a** (7%), **14** (37%)
$Rh_2(NHCOCF_3)_4$ $PhI(OAc)_2$ / CH_3CN, 80 °C, 9 h	**18a** (48%), **14** (22%)
$Rh_2(OAc)_4$, $PhI(OAc)_2$ / CH_3CN, 80 °C, 6 h	**18a** (47%), **14** (32%)
$Rh_2(OAc)_4$, $PhI(OAc)_2$ / benzene, 60 °C, 6 h	**18a** (51%), **14** (22%)
$Rh_2(OAc)_4$, $PhI(OCOt\text{-}Bu)_2$ / benzene, 40 °C, 6 h	**18a** (70%), **14** (30%)

using $PhI(OCOt\text{-}Bu)_2$ as the oxidant and **14** was recovered in 30% yield.[30]

In conclusion, we successfully synthesized **18a**, the advanced intermediate in a projected synthesis of pactamycin. Introduction of the chirality was accomplished using organocatalytic asymmetric aziridination of 2-cyclopenten-1-one. Regioselective opening of the aziridine with an azide nucleophile furnished the *trans*-diamine motif. Construction of the three contiguous stereocenters including two tetrasubstituted carbons was realized via a regio- and diastereoselective 1,3-dipolar cycloaddition and a rhodium-catalyzed C−H amination reaction. The 17-step reaction sequence from 2-cyclopenten-1-one provided access to the key intermediate bearing five of the six contiguous stereocenters in pactamycin. Further studies toward the enantioselective synthesis of pactamycin are ongoing.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00761.

Experimental procedures, additional experimental data, ^1H and ^{13}C NMR spectra of new compounds (PDF)

Crystallograhic data (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: yk4710h@yahoo.co.jp (Y.H.).

*E-mail: tnemoto@faculty.chiba-u.jp (T.N.).

Author Contributions

§M.Y. and M.H. contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by a Grant-in-Aid for Scientific Research on Innovative Areas "Advanced Molecular Transformations by Organocatalysts" (Grant Number. 26105707) from The Ministry of Education, Culture, Sports, Science and Technology, Japan, and Chiba University.

■ REFERENCES

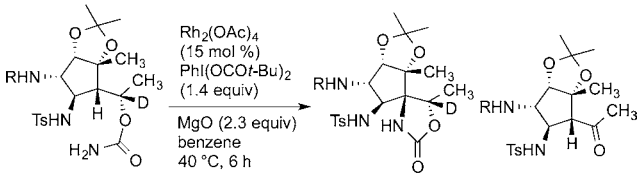
(1) Argoudelis, A. D.; Jahnke, H. K.; Fox, J. A. *Antimicrob. Agents Chemother.* **1962**, 191.

(2) Duchamp, D. J. American Crystallographic Association Winter Meeting, Albuquerque, NM, 1972, 23.

(3) Bhuyan, B. K. *Appl. Microbiol.* **1962**, *10*, 302.

DOI: 10.1021/acs.orglett.6b00761
Org. Lett. 2016, 18, 2347−2350

(4) White, F. R. *Cancer Chemother. Rep.* **1962**, *24*, 75.
(5) Taber, R.; Rekosh, D.; Baltimore, D. *J. Virol.* **1971**, *8*, 395.
(6) Otoguro, K.; Iwatsuki, M.; Ishiyama, A.; Namatame, M.; Nishihara-Tsukashima, A.; Shibahara, S.; Kondo, S.; Yamada, H.; Omura, S. *J. Antibiot.* **2010**, *63*, 381.
(7) Brodersen, D. E.; Clemons, W. M., Jr.; Carter, A. P.; Morgan-Warren, R. J.; Wimberly, B. T.; Ramakrishnan, V. *Cell* **2000**, *103*, 1143.
(8) (a) Tsujimoto, T.; Nishikawa, T.; Urabe, D.; Isobe, M. *Synlett* **2005**, *3*, 433. (b) Matsumoto, N.; Tsujimoto, T.; Nakazaki, A.; Isobe, M.; Nishikawa, T. *RSC Adv.* **2012**, *2*, 9448.
(9) Knapp, S.; Yu, Y. *Org. Lett.* **2007**, *9*, 1359.
(10) Haussener, T. J.; Looper, R. E. *Org. Lett.* **2012**, *14*, 3632.
(11) Loertscher, B. M.; Young, P. R.; Evans, P. R.; Castle, S. L. *Org. Lett.* **2013**, *15*, 1930.
(12) For a synthetic study of jogyamycin, a natural product with a similar structure to pactamycin, see: Gerstner, N. C.; Adams, C. S.; Grigg, R. D.; Tretbar, M.; Rigoli, J. W.; Schomaker, J. M. *Org. Lett.* **2016**, *18*, 284.
(13) (a) Hanessian, S.; Vakiti, R. R.; Dorich, S.; Banerjee, S.; Lecomte, F.; DelValle, J. R.; Zhang, J.; Deschênes-Simard, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 3497. (b) Hanessian, S.; Vakiti, R. R.; Dorich, S.; Banerjee, S.; Deschênes-Simard, B. *J. Org. Chem.* **2012**, *77*, 9458.
(14) (a) Malinowski, J. T.; Sharpe, R. J.; Johnson, J. S. *Science* **2013**, *340*, 180. (b) Malinowski, J. T.; McCarver, S. J.; Johnson, J. S. *Org. Lett.* **2012**, *14*, 2878. (c) Sharpe, R. J.; Malinowski, J. T.; Johnson, J. S. *J. Am. Chem. Soc.* **2013**, *135*, 17990.
(15) For reviews on the synthesis of aziridines, see: (a) Sweeney, J. B. *Chem. Soc. Rev.* **2002**, *31*, 247. (b) Pellacani, L.; Fioravanti, S.; Tardella, P. A. *Curr. Org. Chem.* **2011**, *15*, 1465. For a review of synthetic applications of aziridines, see: (c) McCoull, W.; Davis, F. A. *Synthesis* **2000**, *2000*, 1347.
(16) For representative examples, see: (a) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726. (b) Li, Z.; Quan, R. W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1995**, *117*, 5889. (c) Sanders, C. J.; Gillespie, K. M.; Bell, D.; Scott, P. *J. Am. Chem. Soc.* **2000**, *122*, 7132. (d) Dauban, P.; Saniere, L.; Tarrade, A.; Dodd, R. H. *J. Am. Chem. Soc.* **2001**, *123*, 7707. (e) Aggarwal, V. K.; Alonso, E.; Fang, G.; Ferrara, M.; Hynd, G.; Porcelloni, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1433. (f) Kim, C.; Uchida, T.; Katsuki, T. *Chem. Commun.* **2012**, *48*, 7188 and references cited therein.
(17) For representative examples, see: (a) Antilla, J. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1999**, *121*, 5099. (b) Patwardhan, A. P.; Pulgam, V. R.; Zhang, Y.; Wulff, W. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 6169. (c) Desai, A.; Wulff, W. D. *J. Am. Chem. Soc.* **2010**, *132*, 13100. (d) Larson, S. E.; Li, G.; Rowland, G. B.; Junge, D.; Huang, R.; Woodcock, H. L.; Antilla, J. C. *Org. Lett.* **2011**, *13*, 2188. (e) Gupta, A. K.; Mukherjee, M.; Wulff, W. D. *Org. Lett.* **2011**, *13*, 5866.
(18) (a) Hashimoto, T.; Uchiyama, N.; Maruoka, K. *J. Am. Chem. Soc.* **2008**, *130*, 14380. (b) Akiyama, T.; Suzuki, T.; Mori, K. *Org. Lett.* **2009**, *11*, 2445. (c) Zeng, X.; Zeng, X.; Xu, Z.; Lu, M.; Zhong, G. *Org. Lett.* **2009**, *11*, 3036. (d) Hashimoto, T.; Nakatsu, H.; Yamamoto, K.; Maruoka, K. *J. Am. Chem. Soc.* **2011**, *133*, 9730.
(19) (a) Shen, Y.-M.; Zhao, M.-X.; Xu, J.; Shi, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 8005. (b) Armstrong, A.; Baxter, C. A.; Lamont, S. G.; Pape, A. R.; Wincewicz, R. *Org. Lett.* **2007**, *9*, 351. (c) Pesciaioli, F.; De Vincentiis, F.; Galzerano, P.; Bencivenni, G.; Bartoli, G.; Mazzanti, A.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2008**, *47*, 8703. (d) Minakata, S.; Murakami, Y.; Tsuruoka, R.; Kitanaka, S.; Komatsu, M. *Chem. Commun.* **2008**, 6363. (e) Arai, H.; Sugaya, N.; Sasaki, N.; Makino, K.; Lectard, S.; Hamada, Y. *Tetrahedron Lett.* **2009**, *50*, 3329. (f) Deiana, L.; Zhao, G.-L.; Lin, S.; Dziedzic, P.; Zhang, Q.; Leijonmarck, H.; Córdova, A. *Adv. Synth. Catal.* **2010**, *352*, 3201. (g) Deiana, L.; Dziedzic, P.; Zhao, G.-L.; Vesely, J.; Ibrahem, I.; Rios, R.; Sun, J.; Córdova, A. *Chem. - Eur. J.* **2011**, *17*, 7904. (h) Armstrong, A.; Pullin, R. D. C.; Jenner, C. R.; Foo, K.; White, A. J. P.; Scutt, J. N. *Tetrahedron: Asymmetry* **2014**, *25*, 74. (i) Nemoto, T.; Hayashi, M.; Xu, D.; Hamajima, A.; Hamada, Y. *Tetrahedron: Asymmetry* **2014**, *25*, 1133.
(20) (a) Menjo, Y.; Hamajima, A.; Sasaki, N.; Hamada, Y. *Org. Lett.* **2011**, *13*, 5744. (b) Nemoto, T.; Muramoto, R.; Ruengsatra, T.; Hamada, Y. *Tetrahedron* **2016**, *72*, 1991.
(21) (a) Espino, C. G.; Du Bois, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 598. (b) Espino, C. G.; Wehn, P. M.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935. (c) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378. (d) Zalatan, D. N.; Du Bois, J. *J. Am. Chem. Soc.* **2009**, *131*, 7558. For reviews on Rh-catalyzed C−H insertion, see: (e) Du Bois, J. *Org. Process Res. Dev.* **2011**, *15*, 758. (f) Roizen, J. L.; Harvey, M. E.; Du Bois, J. *Acc. Chem. Res.* **2012**, *45*, 911.
(22) A tosyl group is a tentative protecting group for this synthetic study. Other protecting groups will be also examined in a future study.
(23) Reduction of the ketone **10** under general reaction conditions, such as $NaBH_4$/MeOH, DIBAL-H/CH_2Cl_2, etc., gave the corresponding alcohol as a nearly 1:1 mixture of diastereomers. Only the reduction using $Al(O\text{-}i\text{-}Pr)_3$ gave the product with significant diastereoselectivity. This is probably due to the reversible property of this reduction via Oppenauer oxidation. For the detailed data, see the Supporting Information.
(24) For a review, see: Kanemasa, S. *Synlett* **2002**, *2002*, 1371.
(25) (a) Kanemasa, S.; Nishiuchi, M.; Kamimura, A.; Hori, K. *J. Am. Chem. Soc.* **1994**, *116*, 2324. (b) Bode, J. W.; Fraefel, N.; Muri, D.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 2082. (c) Becker, N.; Carreira, E. M. *Org. Lett.* **2007**, *9*, 3857.
(26) See Supporting Information for details.
(27) X-ray structure of **16a**: CCDC 1457178.
(28) For representative examples of total synthesis of natural products using a rhodium-catalyzed C−H amination reaction, see: (a) Wehn, P. M.; Du Bois, J. *J. Am. Chem. Soc.* **2002**, *124*, 12950. (b) Hinman, A.; Du Bois, J. *J. Am. Chem. Soc.* **2003**, *125*, 11510. (c) Conrad, R. M.; Du Bois, J. *Org. Lett.* **2007**, *9*, 5465. (d) Yakura, T.; Yoshimoto, Y.; Ishida, C.; Mabuchi, S. *Tetrahedron* **2007**, *63*, 4429. (e) Tanino, T.; Ichikawa, S.; Shiro, M.; Matsuda, A. *J. Org. Chem.* **2010**, *75*, 1366. (f) Tanino, T.; Ichikawa, S.; Matsuda, A. *Org. Lett.* **2011**, *13*, 4028. (g) Takahashi, K.; Yamaguchi, D.; Ishihara, J.; Hatakeyama, S. *Org. Lett.* **2012**, *14*, 1644.
(29) Formation of **14** decreased when the deuterated compound **17a(D)** was used as a substrate. The observed deuterium kinetic isotope effect suggested that compound **14** should be formed via a rhodium-catalyzed nitrene insertion into the geminal C−H bond. For the deuterium kinetic isotope effect in the nitrene insertion reaction, see: (a) Fiori, K. W.; Espino, C. G.; Brodsky, B. H.; Du Bois, J. *Tetrahedron* **2009**, *65*, 3042. (b) Quasdorf, K. W.; Huters, A. D.; Lodewyk, M. W.; Tantillo, D. J.; Garg, N. K. *J. Am. Chem. Soc.* **2012**, *134*, 1396.



(30) He and co-workers reported a silver-catalyzed C−H amination: (a) Cui, Y.; He, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 4210. (b) Li, Z.; Rahaman, R.; He, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 5184. We also examined the C−H amination of **17a** using the silver catalysis [AgOTf (15 mol %), 4,7-diphenyl-1,10-phenanthroline (18 mol %), $PhI(OAc)_2$ (1.4 equiv), MS 4Å, CH_2Cl_2, 50 °C, 6 h]. However, compound **18a** was not produced under those conditions.

DOI: 10.1021/acs.orglett.6b00761
Org. Lett. 2016, 18, 2347−2350