NPC Natural Product Communications

2013
Vol. 8
No. 0
1 - 2

Stereoselective Aminopalladation and Oxypalladation and Their Application to the Synthesis of Natural Products

Hidefumi Makabe*

Graduate School of Agriculture, Sciences of Functional Foods, Shinshu University, 8304 Minami-minowa Kami-ina, Nagano, 399-4598, Japan

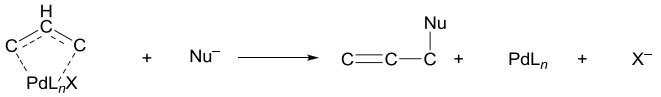
makabeh@shinshu-u.a.jp

Received: January XX, 2013; Accepted: XX, 2013

Stereoselective aminopalladation and oxypalladation are very important approaches for the synthesis of various natural products which contain *N*- and *O*-hetero-alicycles. The author reviewed recent progress of synthesis of natural products using Pd(II)-catalyzed aminopalladation and oxypalladation including our work within this decade.

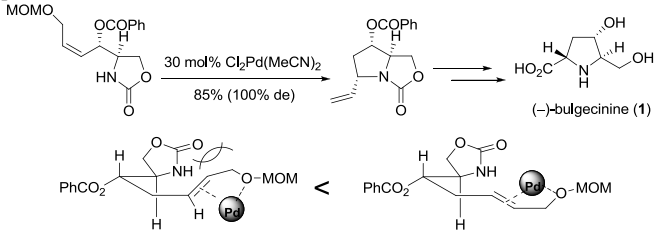
Keywords: piperidine alkaloids, polyketides, aminopalladation, stereoselective synthesis

Among the numerous numbers of the biologically active natural products, the alkaloids and polyketides, which often have complex structures, show considerable biological activities. Alkaloids and polyketides are interesting synthetic targets not only due to their potent drug candidates but also due to their structural uniqueness and complexity in many cases. Stereoselective amino-cyclization of aminoallylic alcohols and alkoxy-cyclization of hydroxyl allyllic alcohols are very important approaches for the construction of *N*- and *O*-hetero-alicycles, which are often seen in the several biologically active natural products. Many syntheses using this methodology have been reported including palladium catalyzed cyclization [1]. Nucleophilic attack on Pd-bound ligands provides a category of excellent methods for the formation of carbon-carbon bonds as represented by general transformation shown in Scheme 1.



Scheme 1

In particular, this process has extensively been applied to the synthesis of natural products. In this section, examples of the application of the amino- and oxypalladation to the synthesis of natural products are presented within this decade [2,3]. Since Hirai and co-workers reported the total synthesis of (–)-bulgecinine (**1**) using aminopalladation, many reports using this method have been published [4].



Scheme 2. Synthesis of (–)-bulgecinine (**1**) using stereoselective aminopalladation.

The author wishes to introduce the recent progress of stereoselective synthesis of piperidine alkaloids such as (–)-cassine (**2**), fagomine (**3**), and (–)-*cis*-clavicipitic acid (**4**) and polyketides such as (–)-laulimalide (**5**), (–)-diospongins A (**6**), B (**7**), pyranicin (**8**), and (–)-apicularen A (**9**) (Figure 1).

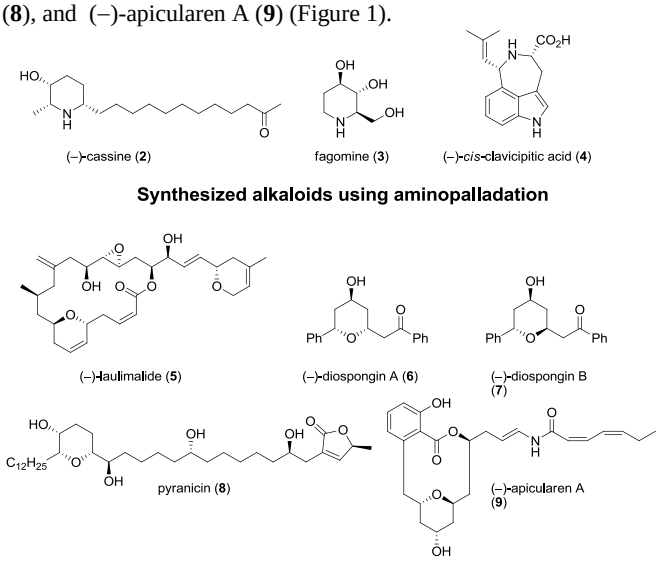
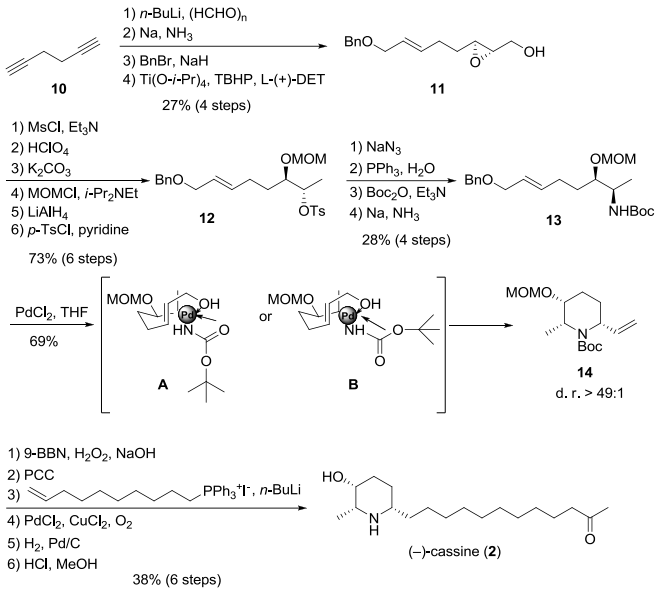


Figure 1. Synthetic targeted alkaloids and polyketides.

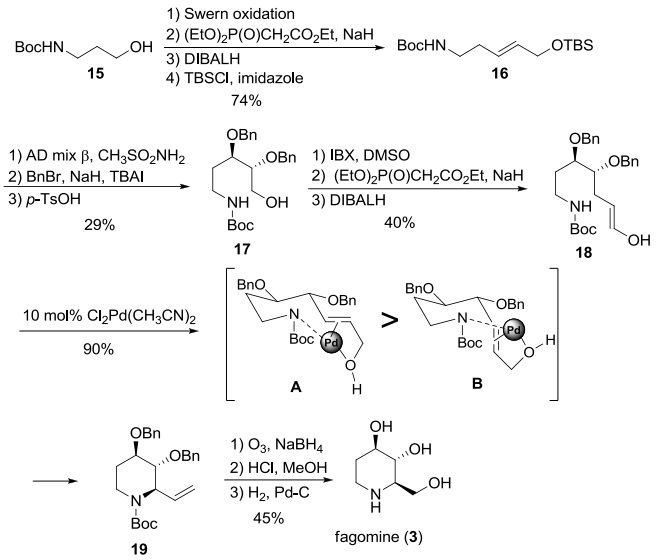
The author would like to introduce the synthesis of alkaloids using stereoselective aminopalladation. In 2003, Makabe and co-workers reported total synthesis of (–)-cassine (**2**) using Pd(II)-catalyzed aminopalladation [5]. (–)-Cassine (**2**) was isolated from the leaves and twigs of *Cassia excelsa*, and its structure was established in 1963 [6]. The absolute configuration was determined by Rice and Coke in 1966 [7]. Recently, Rejon and co-workers reported that **2** shows antimicrobial activity against *Staphylococcus aureus* [8] and Silva and co-workers reported that **2** and the related analogues are potential candidate drugs for the treatment of Alzheimer disease [9]. The precursor for aminopalladation was obtained via multi step

procedure from 1,5-hexadiyne (**10**). The dienediol was synthesized by Rosenblum's procedure in 51% yield [10]. Monobenzylation followed by Sharpless asymmetric epoxidation gave epoxide **11** with 98% ee. Then four-step reaction sequence was applied to switch the epoxide to the terminal position and resulting secondary hydroxyl group was protected as MOM ether. Regioselective ring opening with $LiAlH_4$ at 50 °C and subsequent azidation of the resulting secondary hydroxyl group via tosylate **12**. Staudinger reduction of the azide and the resulting amine was protected with Boc group. Deprotection of the benzyl ether with Na in NH_3 afforded precursor **13**, which upon treatment with 5 mol% $PdCl_2$ in THF gave piperidine ring **14** in 69% yield with more than 98% de. The stereoselective formation of **14** could be explained by assuming that the cyclization proceeded via transition state shown in Scheme 3. The chelation effect between the palladium and oxygen atoms of the allylic alcohol seems to be important. This tendency may also be explained by the chelation effect between palladium and oxygen atom of the Boc group favoring this orientation. Hydroboration subsequent oxidation with PCC afforded aldehyde. Chain elongation by Wittig reaction followed by Wacker oxidation, hydrogenation of the doublebond, and deprotection of both of the MOM and Boc groups gave (–)-cassine (**2**) (Scheme 3).



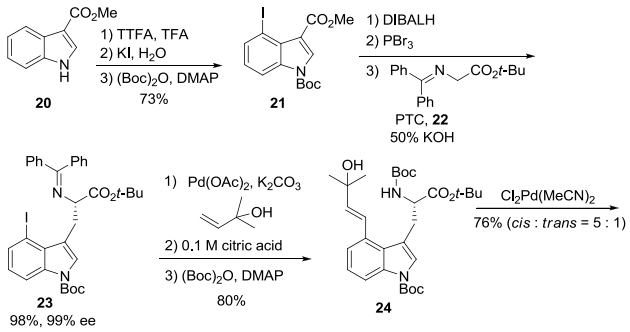
Scheme 3. Synthesis of (–)-cassine (**2**).

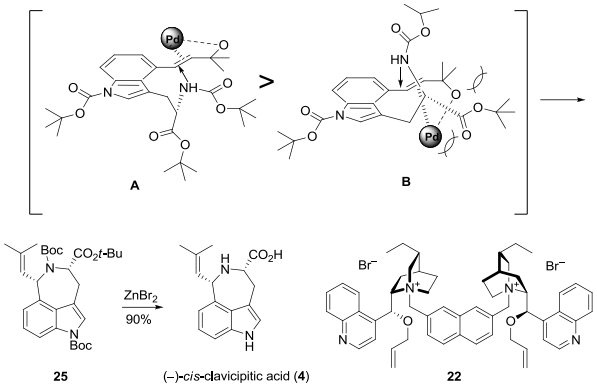
Fagomine (**3**) is a piperidine alkaloid which was isolated from buckwheat seeds (*Fagopyrum esculentum*, *Polygonaceae*) and more recently from *Xanthocericis zambesiaca*, which was found in dry forests in southern Africa [11,12]. Fagomine (**3**) exhibits inhibitory activity against mammalian α-glucosidase and β-glucosidase, respectively [13]. In 2007, Hirai and co-workers accomplished an asymmetric synthesis of **3** via Sharpless asymmetric dihydroxylation [14] and aminopalladation [15]. 3-(*t*-Butoxycarbonylamino)propanol (**15**) was used as a starting material. Swern oxidation of the primary hydroxyl group followed by HWE reaction, reduction of the ester with DIBALH and protection with TBSCl afforded silyl ether **16**. Sharpless asymmetric dihydroxylation and protection with BnBr of the resulting two hydroxyl groups and deprotection of the TBS group gave **17**. Oxidation of the primary alcohol with IBX [16] subsequent HWE reaction and reduction of the ester with DIBALH afforded cyclization precursor **18**. The allyl alcohol **18** was treated with $Cl_2Pd(MeCN)_2$ to give cyclic compound **19** as a single diastereomer in high yield. Ozonolysis of **19** followed by reductive work-up with $NaBH_4$, deprotection of the Boc group under acidic condition and removal of the benzyl groups by hydrogenolysis provided fagomine (**3**). The recation mechanism is shown in Scheme 4. The stereoselective formation of **19** could be explained by assuming the transition state **A**. The transition state **B** would be disfavored because of steric hindrance between the carbamate moiety and oxa-π-alkene-palladium complex (Scheme 4).



Scheme 4. Syntheiss of fagomine (**3**).

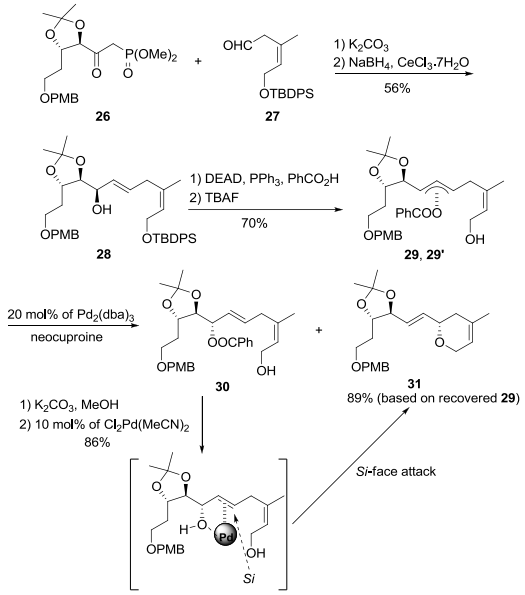
Clavicipitic acid is an ergot alkaloid isolated from SD58 and *Claviceps fusiformis* [17]. This compound was isolated as a mixture of *cis* and *trans* diastereomers. In 2007, Park and co-workers accomplished the total synthesis of (–)-*cis*-clavicipitic acid (**4**) using aminopalladation [18]. 1*H*-Indole-3-carboxylic acid methyl ester (**20**) was used for starting material. The addition of thallium (III) trifluoroacetate in a TFA solution of **20**, followed by treatment with potassium iodide and protection of the amino group with Boc_2O afforded **21**. The reduction of methyl ester of **21** with DIBALH followed by benzylic bromination and the phase-transfer catalytic alkylation from *N*-(diphenylmethylene)glycine *tert*-butyl ester using **22** as a chiral catalyst was performed to give **23** in high enantioslective manner. The Heck reaction followed by selective hydrolysis of benzophenone imine moiety and protection with Boc group afforded **24**. The intramolecular aminopalladation of **24** was performed with $Cl_2Pd(MeCN)_2$ furnished *cis*-**25** and *trans*-**25** at the ratio of 5 : 1. The plausible transition state in the aminopalladation was proposed in Scheme 5. Finally, deprotection of the Boc groups and removal of *tert*-butyl ester using $ZnBr_2$ afforded (–)-*cis*-clavicipitic acid (**4**) (Scheme 5).

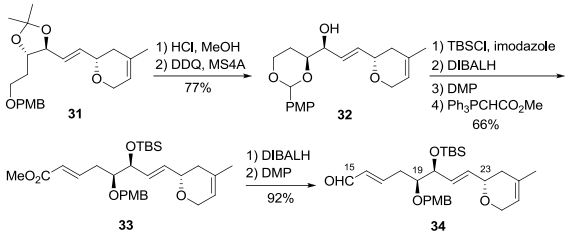




Scheme 5. Synthesis of (–)-*cis*-clavicipitic acid (**4**).

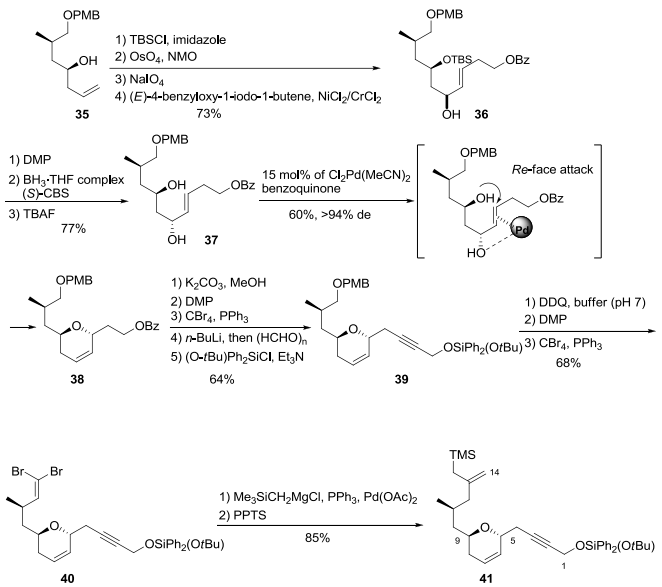
Next, the author wishes to introduce the synthesis of natural products using stereoselective oxypalladation. Laulimalide (**5**) is a cancer-therapy agent isolated from the marine sponges *Hyattella* sp. and *Cacospongia mycofijiensis* [19]. In 2005, Uenishi and co-worker reported total synthesis of (–)-laulimalide (**5**) using stereoselective oxypalladation [20]. The C17-C27 framework was prepared by HWE reaction of **26** with **27**, and successive reduction of ketone with $NaBH_4$ in the presence of $CeCl_3 \cdot 7H_2O$ gave **28**. Mitsunobu reaction [21] of **28** with benzoic acid and subsequent cleavage of the TBDPS group with TBAF gave **29** and **29'**, respectively. The mixture of diastereomers **29** and **29'** was subjected to Pd(0)-catalyzed intramelecular *O*-allylation with $Pd_2(dba)_3$ in the presence of neocuproine to afford **31** along with unreacted **30**. The conversion of **30** to **31** using oxypalladation gave desired **31** exclusively in a high yield. The 1,3-chirality transfer took place with retention by an internal *syn*-S_N2'-type attack of the oxygen nucleophile in an *exo*-trig fashion. When Pd π-complex is formed selectively on the same side of the double bond as the hydroxyl group, the oxygen nucleophile attacks the olefinic carbon center from the *Si* face by a *syn* addition and subsequent *syn* elimination of Pd(OH)Cl from the resultant Pd σ-complex to give **31**. After cleavage of the acetonide of **31**, oxidation with DDQ gave **32**. Silylation of the C20 alcohol followed by reductive opening of the benzilidene acetal, oxidation of the primary alcohol and Wittig reaction gave α,β-unsaturated ester **33**. Reduction of the ester with DIBALH and oxidation with Dess-Martin periodinane (DMP) [22] furnished desired aldehyde **34** (Scheme 6).





Scheme 6. Synthesis C17-C27 framework of (–)-laulimalide (**5**).

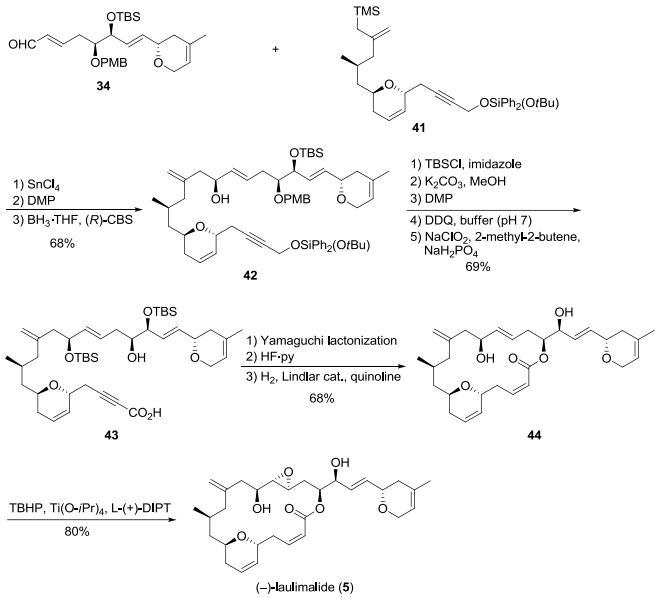
The synthesis of the C1-C14 carbon chain was started from allylic alcohol **35**. Silylation of the secondary alcohol, dihydroxylation of the double bond, and cleavage of the diol gave an aldehyde, which underwent Ni/Cr-promoted addition [23,24] with (*E*)-4-benzyloxy-1-iodo-1-butene to give a mixture of diastereomer **36**. Oxidation with Dess-Martin periodinane and selective reduction of the enone using BH_3-(*S*)-CBS ligand [25] and deprotection of the TBS group gave **37**. The diol **37** was subjected to oxypalladation in a 6-*endo*-trig fashion to give desired pyran **38** in a single diastereomer. The 6-*endo*-trig cyclization of **37** occurred through a *syn*-S_N2' process to give the desired *trans*-(*R*)-dihydropyrane ring; in this case, the hydroxyl group attacked the *Re* face of the olefinic carbon atom. Compound **38** was converted into **39** through deprotection of the benzoate, oxidation to the aldehyde, Corey-Fuchs reaction [26] and reaction of the generated lithioalkyne with paraformaldehyde, and protection of the resultant alcohol with (*t*-BuO)Ph_2SiCl. Deprotection of the PMB ether of **39** with DDQ, oxidation to the aldehyde with DMP, dibromoolefination with CBr_4 and triphenylphosphine gave **40**. The cross-coupling of the **40** with $TMSCH_2MgCl$ catalyzed by 10 mol% of $Pd(OAc)_2$ in the presence of triphenylphosphine gave the corresponding alkene which upon treatment with PPTS gave **41** (Scheme 7).



Scheme 7. Synthesis C1-C14 framework of (–)-laulimalide (**5**).

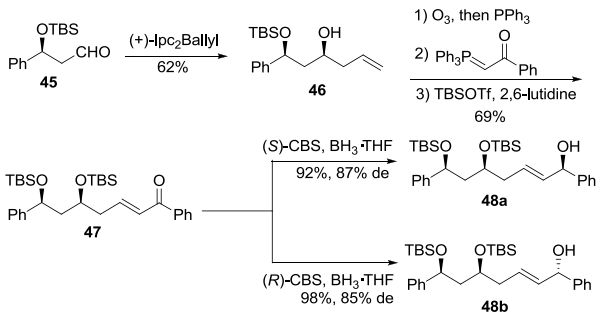
Fragment **34** and **41** were assembled by Sakurai-Hosomi reaction [27] promoted by $SnCl_4$ followed by oxidation of the alcohol with DMP and stereoselecive reduction with BH_3-(*R*)-CBS ligand gave the desired alcohol **42**. Silylation of the alcohol, chemoselective cleavage of the (*t*-BuO)Ph_2Si ether with K_2CO_3, oxidation of the propargyl alcohol, deprotection of the PMB ether, and Kraus oxidation [28] afforded **43**. Yamaguchi lactonization [29],

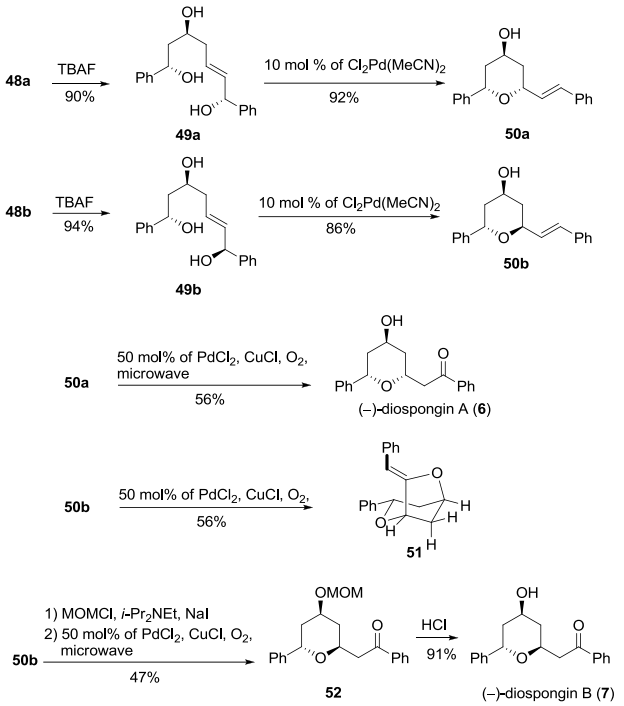
deprotection of the two silyl ethers, and partial reduction of the alkynyl group to the alkene afforded **44**. Finally, Sharpless epoxidation with L-(+)-DIPT gave (–)-laulimalide (**5**) in good yield (Scheme 8).



Scheme 8. Completion of the synthesis of (–)-laulimalide (**5**).

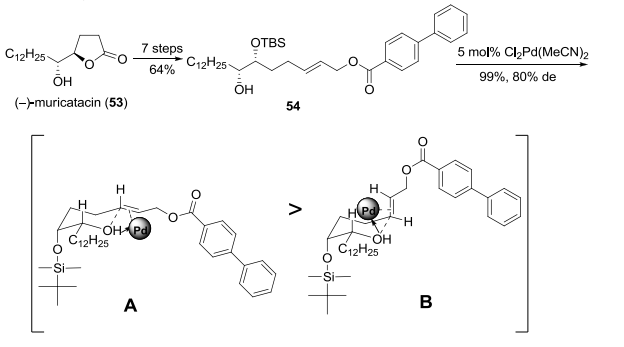
Diospongins A (**6**) and B (**7**) are cyclic 1,7-diarylheptanoids that were isolated from rhizomes of *Dioscorea spongicosa* [30]. In 2007, Uenishi and co-workers reported the stereoselective synthesis of (–)-diospongins A (**6**) and B (**7**) along with their stereoisomers [31]. The aldehyde **45** derived from (*R*)-(–)-mandelate was used as a starting material. Treatment of **45** with Brown's chiral allyborane, (+)-Ipc$_2$Ballyl [32] gave **46**. Oxidative cleavage of the alkenyl bond with O_3 followed by Wittig reaction, and silylation of the hydroxyl group afforded α,β-unsaturated ketone **47**. Diastereoselective reductions of **47** was performed using BH$_3$-(*S*)-CBS and BH$_3$-(*R*)-CBS **48a** and **48b**, respectively. Deprotection of the TBS groups of **48a** and **48b** gave **49a** and **49b**. Triol **49a** and **49b** were subjected to oxypalladation using 10 mol% of $Cl_2Pd(MeCN)_2$ to give cyclized products **50a** and **50b**. Regioselective introduction of the carbonyl group was accomplished by Wacker oxidation. Treatment of alkene **50a** with 50 mol% of $PdCl_2$ and CuCl irradiated by microwave gave (–)-diospongins A (**6**) in 56% yield. In contrast, the reaction of **50b** under above conditions gave unexpected bicyclic compound **51**. Therefore, the hydroxyl group of **50b** was protected as a MOM ether subsequent Wacker oxidation irradiated by microwave gave desired compound **52**. Finally, deprotection of the MOM ether under acidic condition afforded (–)-diospongins B (**7**) (Scheme 9).

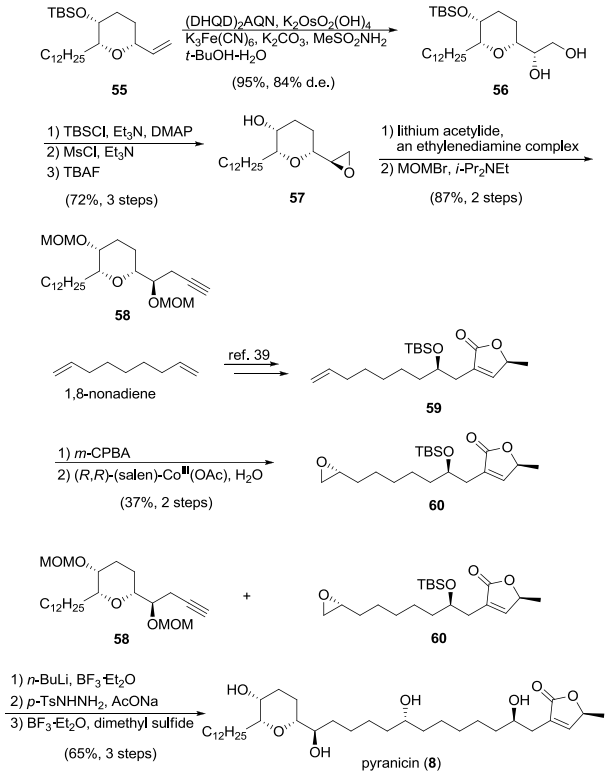




Scheme 9. Synthesis of (–)-diospongins A (**6**) and B (**7**).

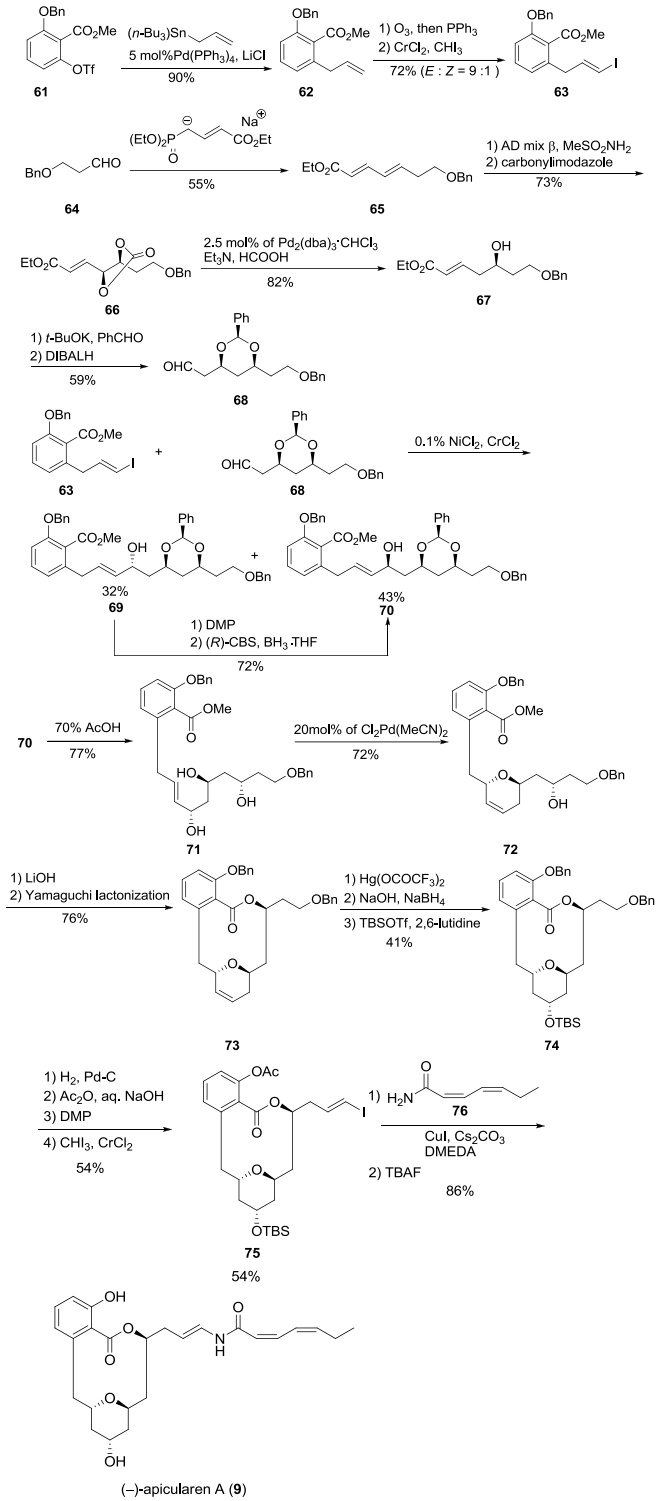
Pyranicin (**8**) is a mono-tetrahydropyran annonaceous acetogenin isolated from the stem bark of *Goniothalamus giganteus* in 1998 [33]. In 2008, Makabe and co-workers reported total synthesis of pyranicin (**8**) using $Cl_2Pd(MeCN)_2$-catalyzed diatereoselective cyclization [34,35]. The strating material was (–)-muricatacin (**53**) which is a degradation product of mono-THF annonaceous acetogenin [36,37]. The cyclization precursor **54** was obtained routine seven-step reaction sequence. The Pd(II)-catalyzed diastereoselective cyclization was attained with 80% de when biphenyl ester **54** was used as a substrate. Diastereoselective dihydroxylation of **55** by the Sharpless procedure using (DHQD)$_2$AQN [38] as a ligand gave **56** in 84% de. The undesired diastereomer was removed by silica gel column chromatography. Silylation of the primary hydroxyl group of **56** and the mesylation of the secondary hydroxyl group, subsequent treatment with TBAF furnished terminal epoxide **57**. Alkynylation of **57** with lithium acetylide, an ethylenediamine complex, followed by protection of the corresponding hydroxyl group with MOMBr and *i*-Pr$_2$NEt afforded **58**. The γ-lactone moiety **60** was prepared by Keinan's method [39] with Jacobsen's hydrolytic kinetic resolution [40]. Both lithiumacetylide of **58** and **60** were coupled in the presence of BF$_3$· Et$_2$O, followed by diimide reduction. Finally, deprotectioj of the TBS and MOM ether with BF$_3$· Et$_2$O afforded pyranicin (**8**) (Scheme 10).





Scheme 10. Synthesis of pyranicin (**8**).

(–)-Apicularen A (**9**) is 12-membered macrolide isolated by Kunze and co-workers [41]. This compound shows potent cytotoxic activity against wide range of human cancer cell lines such as ovarian, prostate, lung, kidney, cervix, leukemia, and histiocytic cells with IC_{50} values in the range of 0.23-6.79 nM [41]. Recently, Uenishi and co-workers reported a convergent total synthesis of **9** using oxypalladation and 1,3-chirality transfer reaction [42,43]. The starting material **61** was coupled with allyltributyltin in the presence of $Pd(PPh_3)_4$ gave terminal alkene **62**. Ozonolysis of **62** provided aldehyde which was subjected to Takai iodoolefination [44] to afford **63**. Synthesis of another fragment was started from aldehyde **64**. The HWE reaction of **64** with triethy phosphonate aster gave **65**. Sharpless asymmetric dihydroxylation of **65** afforded diol, which was converted to cyclic carbonate **66**. Hydrogen transfer hydropalladation of **66** provided **67** in good yield. The δ-hydroxy enoate **67** was converted to the benzylidene acetal subsequent reduction of the ester by DIBALH afforded **68**. The fragment **63** and **68** were coupled using NHK reaction [23,24] to provide a mixture of diastereomers **69** and **70**. The undesired isomer **69** was transformed into **70** via Dess-Martin oxidation followed by stereoselective reduction using (*R*)-CBS reagent. Deprotection of the benzilidene group of **70** with 70%-AcOH gave triol **71**. Compound **71** was subjected to oxypalladation using 20 mol% of $Cl_2Pd(MeCN)_2$ gave 2,6-*trans*-dihydropyrane **72** in a single diastereomer. Hydrolysis of the methyl ester using LiOH subsequent Yamaguchi macrolactonization afforded core macrolactone **73** in good yield. Treatment of **73** with $Hg(OCOCF_3)_2$ followed by reductive removal of mercury with $NaBH_4$, and silylation gave **74** along with its diastereomer. Hydrogenolysis of both of benzyl groups, chemoselective protection of the phenolic hydroxyl group with acetic anhydride followed by Dess-Martin oxidation of the primary alcohol, and Takai iodoolefination gave**75**. Coupling reaction between **75** and **76** using Buchwald's conditions [45] with an excess of CuI, subsequent desilylation with TBAF provided (–)-apicularen A (**9**) in excellent yield (Scheme 11).



Scheme 11. Synthesis of (–)-apicularen A (**9**).

Conclusion

Nucleophilic attack on Pd-bound ligands provides a category of excellent methods for the formation of C-N and C-O bonds. In

particular, this process has extensively been applied to the synthesis of natural products. This attention has resulted in various novel approaches to synthesize various alkaloids and polyketides. In this review, the author described the most recent (2003-2012) examples of the total synthesis of them.

Acknowledgments - The author thanks a-Grant-in-Aid from the Japan Society for the Promotion of Science for financial support (24580160).

References

[1] Muzart J. (**2005**) Palladium-catalyzed reactions of alcohols, Part C: Formation of ether linkages. *Tetrahedron*, ***61***, 5955-6008.
[2] Xu C, Negishi, E –i. (**2002**) Organopalladium Chemistry for Organic Synthesis. (Ed.: E.-i. Negishi), Wiley-Interscience, New York, Vol. II , 2289-2305.
[3] Yokoyama H, Hirai Y. (**2008**) Palladium(II)-catalyzed cyclization via N-alkylation of an allyl alcohol with an urethane and its application to the synthesis of natural products. *Heterocycles*, ***75***, 2133-2153.
[4] Hirai Y, Tetrada T, Amemiya Y, Momose T. (**1992**) An Efficient Synthesis of (–)-Bulgecinine. *Tetrahedron Letters*, ***33***, 7893-7894.
[5] Makabe H, Looi, KK, Hirota M. (**2003**) Total Synthesis of (–)-Cassine. *Organic Letters*, ***5***, 27-29.
[6] Highet RJ. (**1964**) Alkaloids of Cassia Species. I. Cassine. *The Journal of Organic Chemistry*, ***29***, 471-474.
[7] Rice WY, Coke JL. (**1966**) Structure and Configuration of Alkaloids. II. Cassine. *The Journal of Organic Chemistry*, ***31***, 1010-1012.
[8] Peraza PS, Vallado MR, Loeza WB, Mena-Rejón GJ, Quijano, L. (**2000**) Cassine, an antimicrobial alkaloid from *Senna racemosa*. *Fitoterapia*, ***71***, 690-692.
[9] Silva DHS, Viegas Jr.C, Santos LA, Castro-Gamboa I, Cavalheiro A.J, Bolzani Vda S, Pivatto M, Young M CM, Castro NG, Rocha MS, Fraga CAM, Barreiro EJ. (**2010**) Espectalina, cassina e análogos semissintéticos como potenciais candidatos a fármacos para o tratamento da doença de Alzheimer. *Revista Virtual de Quimica*, ***2***, 38-46.
[10] Lennon P, Rosenblum M. (**1983**) Carbon-carbon bond formation by condensation at metal-activated olefins. Regio- and stereoselectivity of cycloaddition reactions. *Journal of the American Chemical Society*, ***105***, 1233-1241.
[11] Koyama M, Sakamura S. (**1974**) The Structure of a New Piperidine Derivative from Buckwheat Seeds. *Agricultural and Biological Chemistry*, ***38***, 1111-1112.
[12] Kato A, Asano N, Kizu H, Matsui A, Watson AA, Nash RJ. (**1997**) Fagomine Isomers and Glycosides from *Xanthocercis zambesiaca*. *Journal of Natural Products*, ***60***, 312-314.
[13] Nojima H, Kimura, I, Chen F –J, Sugiura Y, Haruno M, Kato A, Asano N. (**1998**) Antihyperglycemic Effects of N-Containing Sugars from *Xanthocercis zambesiaca*, *Morus bombycis*, *Aglaonema treubii*, and *Castanospermum australe* in Streptozotocin-Diabetic Mice. *Journal of Natural Products*, ***61***, 397-400.
[14] Kolb HC, VanNieuwenhze MS, Sharpless KB. (**1994**) Catalytic Asymmetric Dihydroxylation. *Chemical Reviews*, ***94***, 2483-2547.
[15] Yokoyama H, Ejiri H, Miyazawa M, Yamaguchi S, Hirai Y. (**2007**) Asymmetric synthesis of fagomine. *Tetrahedron: Asymmetry*, ***18***, 852-856.
[16] Munari SD, Frigerio M, Santagostino M. (**1996**) Hypervalent Iodine Oxidants: Structure and Kinetics of the Reactive Intermediates in the Oxidation of Alcohols and 1,2-Diols by *o*-Iodoxybenzoic Acid (IBX) and Dess−Martin Periodinane. A Comparative ^{1}H-NMR Study. *The Journal of Organic Chemistry*, ***61***, 9272-9279.
[17] Robbers JE, Otsuka H, Floss HG, Arnold EV, Clardy J. (**1980**) Clavicipitic acid: its structure, biosynthesis, and role in ergot alkaloid formation. *The Journal of Organic Chemistry*, ***45***, 1117-1121.
[18] Ku J –M, Jeong B –S, Jew S –S, Park H –G. (**2007**) Enantioselective Synthesis of (–)-*cis*-Clavicipitic Acid. *The Journal of Organic Chemistry*, ***72***, 8115-8118.
[19] Corley DG, Herb R, Moore RE, Scheuer PJ, Paul VJ. (1988) Laulimalides. New potent cytotoxic macrolides from a marine sponge and a nudibranch predator. *The Journal of Organic Chemistry*, ***53***, 3644-3646.
[20] Uenishi J, Ohmi M. (**2005**) Total Synthesis of (–)-Laulimalide: Pd-Catalyzed Stereospecific Ring Construction of the Substituted 3,6-Dihydro[2*H*]pyran Units. *Angewante Chemie International Edition*, **44**, 2756-2760.
[21] Mitsunobu O. (**1981**) The Use of Diethyl Azodicarboxylate and Triphenylphosphine in Synthesis and Transformation of Natural Products. *Synthesis*, 1-28.
[22] Dess DB, Martin JC. (**1991**) A useful 12-I-5 triacetoxyperiodinane (the Dess-Martin periodinane) for the selective oxidation of primary or secondary alcohols and a variety of related 12-I-5 species. *Journal of the American Chemical Society*, ***113***, 7277-7287.
[23] Jin H, Uenishi J–i, Christ WJ, Kishi Y. (1986) Catalytic effect of nickel(II) chloride and palladium(II) acetate on chromium(II)-mediated coupling reaction of iodo olefins with aldehydes. *Journal of the American Chemical Society*, ***108***, 5644-5646.
[24] Takai K, Tagashira M, Kuroda T, Oshima K, Utimoto K, Nozaki H. (**1986**) Reactions of alkenylchromium reagents prepared from alkenyl trifluoromethanesulfonates (triflates) with chromium(II) chloride under nickel catalysis. *Journal of the American Chemical Society*, ***108***, 6048-6050.
[25] Corey EJ, Bakshi RK, Shinata, S. (**1987**) Highly enantioselective borane reduction of ketones catalyzed by chiral oxazaborolidines. Mechanism and synthetic implications. *Journal of the American Chemical Society*, ***109***, 5551-5553.
[26] Corey EJ, Fuchs PL. (**1972**) A synthetic method for formyl⟶ethynyl conversion (RCHO⟶RC≡CH or RC≡CR'. *Tetrahedron Letters*, ***13***, 3769-3772.
[27] Hosomi A, Sakurai H. (**1976**) Syntheses of γ,δ-unsaturated alcohols from allylsilanes and carbonyl compounds in the presence of titanium tetrachloride. *Tetrahedron Letters*, ***17***, 1295-1298.
[28] Kraus GA, Roth B. (**1980**) Synthetic studies toward verrucarol. 2. Synthesis of the AB ring system. *The Journal of Organic Chemistry*, ***45***, 4825-4830.
[29] Inanaga J, Hirata, K, Saeki, H, Katsuki, T, Yamaguchi M. (**1979**) A Rapid Esterification by Means of Mixed Anhydrideand Its Application to Large-ring Lactonization. *Bulltein of the Chemical Society Japan*, ***52***, 1989-1993.
[30] Yin J, Kouda K, Tezuka Y, Trans QL, Miyahara T, Chen Y, Kadota S. (**2004**) New Diarylheptanoids from the Rhizomes of *Dioscorea spongiosa* and Their Antiosteoporotic Activity. *Planta Medica*, ***70***, 54-58.
[31] Kawai N, Hande SM, Uenishi J. (**2007**) Stereoselective synthesis of (–)-diospongins A and B and their stereoisomers at C-5. *Tetrahedron*, ***63***, 9049-9056.

[32] Brown HC, Bhat KS, Randad RS. (**1989**) Chiral synthesis via organoboranes. 21. Allyl- and crotylboration of alpha.-chiral aldehydes with diisopinocampheylboron as the chiral auxiliary. *The Journal of Organic Chemistry*, ***54***, 1570-1576.

[33] Alali FQ, Rogers LL, Zhang Y, McLaughlin JL. (**1998**) Unusual bioactive annonaceous acetogenins from *Goniothalamus giganteus*. *Tetrahedron*, ***54***, 5833-5844.

[34] Hattori Y, Furuhata S. –i, Okajima M, Konno H, Abe M, Miyoshi H, Goto T, Makabe H. (**2008**) Synthesis of Pyranicin and Its Inhibitory Action with Bovine Heart Mitochondrial Complex I. *Organic Letters*, ***10***, 717-720.

[35] Furuhata S. –i, Hattori Y, Okajima M, Konno H, Abe M, Miyoshi H, Goto T, Makabe H. (**2008**) Synthesis of pyranicin and its deoxygenated analogues and their inhibitory action with bovine heart mitochondrial complex I. *Tetrahedron*, ***64***, 7695-7703.

[36] Rieser MJ, Kozlowski JF, Wood KV, McLaughlin JL. (**1991**) Muricatacin: A simple biologically active acetogenin derivative from the seeds of annona muricata (annonaceae). *Tetrahedron Letters*, ***32***, 1137-1140.

[37] Makabe H, Tanaka A, Oritani T. (**1993**) Synthesis of (–)-Muricatacin. *Bioscience Biotechnology and Biochemistry*, ***57***, 1028-1029.

[38] Becker H, Sharpless KB. (**1996**) A New Ligand Class for the Asymmetric Dihydroxylation of Olefins. *Angewante Chemie International Edition*, **35**, 448-451.

[39] Han H, Shinha MK, D'Souza LJ, Keinan E, Shinha SC. (**2004**) Total Synthesis of 34-Hydroxyasimicin and Its Photoactive Derivative for Affinity Labeling of the Mitochondrial Complex I. *Chemistry-A European Journal*, ***10***, 2149-2158.

[40] Schaus SE, Brandes BD, Larrow JF, Tokunaga M, Hansen KB, Alexandra EG, Furrow ME, Jacobsen EN. (**2002**) Highly Selective Hydrolytic Kinetic Resolution of Terminal Epoxides Catalyzed by Chiral (salen)Co^{III} Complexes. Practical Synthesis of Enantioenriched Terminal Epoxides and 1,2-Diols. *Journal of the American Chemical Society*, ***124***, 1307-1315.

[41] Kunze B, Jansen R, Sasse F, Höfle G, Reichenbach H. (**1998**) Apicularens A and B, New Cytostatic Macrolides from Chondromyces Species (Myxobacteria). *The Journal of Antibiotics*, ***51***, 1075-1080.

[42] Palimkar SS, Uenishi J –i. (**2010**) Total Synthesis of (–)-Apicularen A. *Organic Letters*, ***12***, 4160-4163.

[43] Palimkar SS, Uenishi J –i, Ii H. (**2012**) Total Synthesis and Biological Evaluation of (–)-Apicularen A and Its Analogues. *The Journal of Organic Chemistry*, ***77***, 388-399.

[44] Takai K, Nitta K, Utimoto K. (**1986**) Simple and selective method for aldehydes (RCHO)⟶(*E*)-haloalkenes (RCH=CHX) conversion by means of a haloform-chromous chloride system. *Journal of the American Chemical Society*, ***108***, 7408-7410.

[45] Jiang L, Job GE, Klapars A, Buchwald SL. (**2003**) Copper-Catalyzed Coupling of Amides and Carbamates with Vinyl Halides. *Organic Letters*, ***5***, 3667-3669.