

Enantioselective Biomimetic Total Syntheses of Kuwanons I and J and Brosimones A and B**

Jianguang Han, Xia Li, Yong Guan, Wenjun Zhao, William D. Wulff,* and Xiaoguang Lei*

Abstract: The first enantioselective total syntheses of prenylflavonoid Diels–Alder natural products (–)-kuwanon I, (+)-kuwanon J, (–)-brosimone A, and (–)-brosimone B have been accomplished from a common intermediate based on a concise synthetic strategy. Key elements of the synthesis include a biosynthesis-inspired asymmetric Diels–Alder cycloaddition mediated by a chiral ligand/boron Lewis acid, as well as a process involving regioselective Schenck ene reaction, reduction, and dehydration to realize a biomimetic dehydrogenation for generation of the required diene precursor. Furthermore, a remarkable tandem inter/intramolecular asymmetric Diels–Alder cycloaddition process was applied for the synthesis of (–)-brosimone A.

The Diels–Alder reaction is likely one of the most powerful reactions for the construction of complex polycyclic structures. Even though only one well-characterized Diels–Alderase has been reported,^[1] a large number of natural products biosynthesized through Diels–Alder cycloadditions have been frequently reported in the literature.^[2] Since the initial studies by Nomura and co-workers in the 1980s, approximately 40 different kinds of structurally unique prenylflavo-

noid Diels–Alder natural products have been isolated and characterized from various *Moraceae* plants, which have been widely used in traditional Chinese medicine (TCM).^[3] Some representative examples are shown in Figure 1: kuwa-

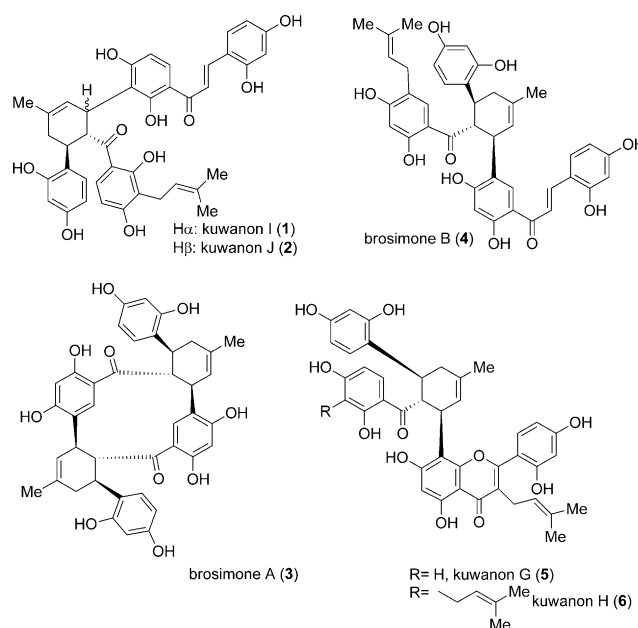


Figure 1. Representative Diels–Alder-type natural products from *Moraceae* plants.

nons I (1)^[4] and J (2),^[5] brosimones A (3)^[6] and B (4),^[7] kuwanons G (5)^[8] and H (6).^[9] The prenylflavonoid Diels–Alder natural products exhibit many promising biological activities including anticancer, anti-HIV, and anti-inflammatory activities.^[10] Structurally, these molecules all possess at least one 2'-hydroxychalcone moiety as well as polyphenol structures. Given their striking chemical structures and biological activities, prenylflavonoid Diels–Alder natural products have attracted continuing attention from the synthetic community, including the seminal total syntheses by Porco and co-workers using silver nanoparticles (AgNPs) for the key Diels–Alder cycloadditions,^[11] as well as other synthetic studies.^[12] However, because of the significant synthetic challenges, the enantioselective synthesis of this family of natural products remains elusive to date. Herein, we report our recent endeavors which culminated in the first enantioselective biomimetic total syntheses of (–)-kuwanon I, (+)-kuwanon J, (–)-brosimone A, and (–)-brosimone B.

[*] J. Han, X. Li

School of Pharmaceutical Science and Technology
Tianjin University, Tianjin 300072 (China)

Y. Guan, W. Zhao, Prof. Dr. W. D. Wulff
Department of Chemistry, Michigan State University
East Lansing, MI 48824 (USA)
E-mail: wulff@chemistry.msu.edu

Prof. Dr. X. Lei

Beijing National Laboratory for Molecular Sciences, Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, Department of Chemical Biology, College of Chemistry and Molecular Engineering, Synthetic and Functional Biomolecules Center, and Peking-Tsinghua Center for Life Sciences, Peking University, Beijing 100871 (China)

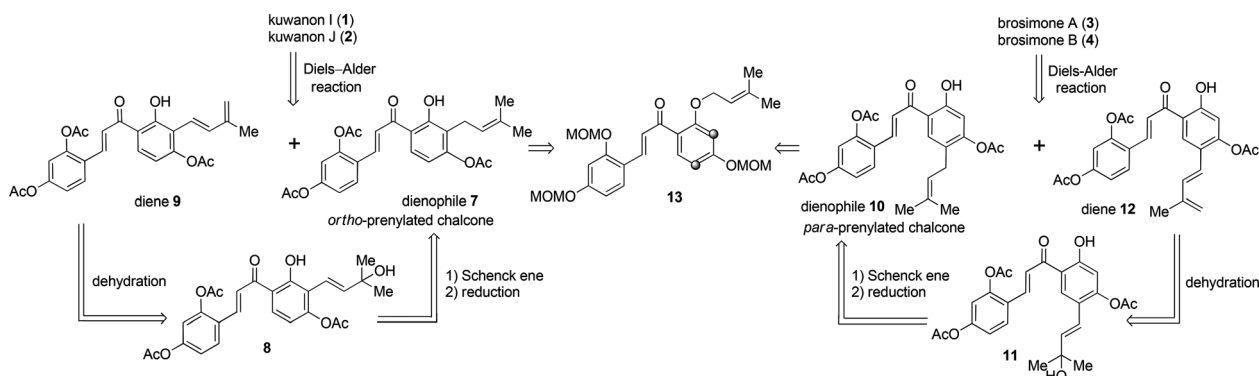
and
National Institute of Biological Sciences, Beijing (NIBS)
Changping District, Beijing 102206 (China)
E-mail: xglei@pku.edu.cn

Homepage: <http://www.chem.pku.edu.cn/leigroup/>

[**] We thank Xiaoyun Zhang and Mingjun Du for their assistance, Prof. Guangzhong Tu for NMR analysis, Dr. Jiang Zhou (Peking University) for HRMS analysis, and Ming Xiong (China University of Geosciences) for X-ray analysis. Financial support from the National High Technology Projects 973 (2012CB837400), and NNSFC (21222209, 91313303) is gratefully acknowledged. This work is also supported by the National Institute of General Medical Sciences (GM 094478 to W.W.).



Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201404499>.



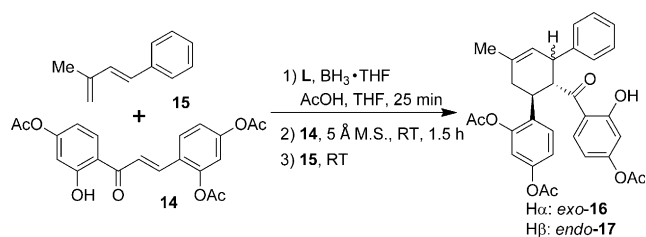
Scheme 1. Retrosynthetic analysis for kuwanons I and J, and brosimones A and B.

As shown in Scheme 1, kuwanons I and J, and brosimones A and B were chosen as our initial targets for total synthesis because we envisioned that the four natural products could be accessed from the common intermediate **13**. We expected that a rearrangement reaction of the intermediate **13** can occur to afford *ortho*-prenylated chalcone, which is the synthetic precursor for kuwanons I and J, and *para*-prenylated chalcone, which is the synthetic precursor for brosimones A and B. A key biosynthesis-inspired asymmetric Diels–Alder cycloaddition should be involved. In addition, the prenylated dienophile was considered to be a direct precursor of the diene. The group of Porco realized a biomimetic process involving an elegant direct in situ dehydrogenation with AgNPs.^[11d] In this regard, a biomimetic transformation involving a Schenck ene reaction/reduction sequence^[13] with subsequent dehydration could be used to afford the diene. The polyphenolic nature of these natural products required an appropriate protecting-group strategy which allows the effective late-stage global deprotection. Indeed, we have extensively evaluated various protecting groups including Me, MOM, MTM, and Ac, and ultimately, we chose the acyl group, which could be smoothly removed under mild basic conditions.

Based on the above analysis, our initial aim was to develop the required key enantioselective Diels–Alder cycloaddition on model substrates. An extensive literature search revealed that the asymmetric Diels–Alder reaction of the 2'-hydroxychalcone derivative as the dienophile is unprecedented. We examined various possible strategies including metal Lewis acid catalysis and chiral Brønsted acids. Unfortunately all these attempts failed. Ultimately, inspired by the elegant studies of enantioselective Diels–Alder reactions and chlorinations on the juglone systems, reported by Kelly et al.^[14] and Snyder et al.,^[15] respectively, we set out to examine the possibility of using a chiral boron complex to promote the enantioselective Diels–Alder reaction (Table 1). With the model substrates, the dienophile **14** and diene **15**,^[16] in hand, we initially screened (*R,R*)-TADDOL (**L1**) and (*S*)-BINOL (**L2**), and to our delight, the chiral boron complex effectively promoted the Diels–Alder reaction to afford both *exo*-**16** and *endo*-**17** in high yields. However, the enantioselectivity was unsatisfactory. We then turned to other chiral ligands such as (*S*)-VANOL (**L4**) and (*R*)-VAPOL (**L3**) which have been

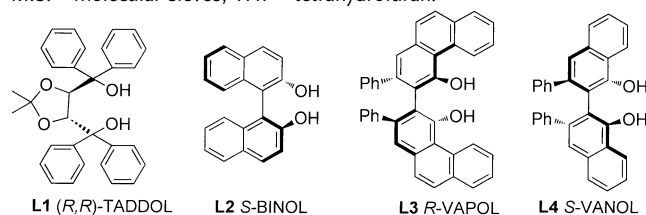
used in asymmetric Diels–Alder reactions.^[17] To our surprise, *endo*-**17** was generated in good yield (80%) and with an excellent *ee* value (entry 4) when **L4** was used, while *exo*-**16** was generated in moderate yield (41%) and *ee* value (entry 3) when **L3** was used. We also tested a panel of VANOL derivatives, but did not observe significant improvement.^[16] The chiral ligands could be largely recovered. When we used the recovered VANOL ligands, we were pleased to find that the yield and *ee* value were both retained after one or two cycles (entries 5 and 6). A control experiment showed that when the hydroxy group of the dienophile was protected by

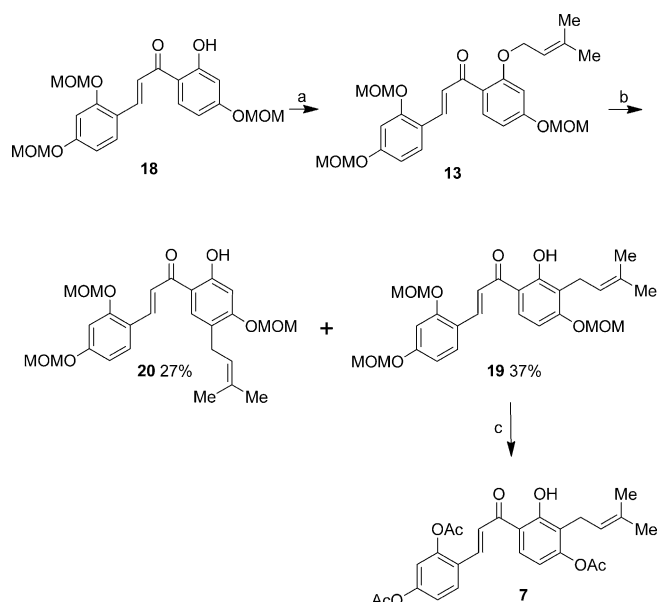
Table 1: Chiral boron complex-catalyzed asymmetric Diels–Alder cycloadditions.^[a]



Entry	Ligand ^[b]	T [h]	Yield [%] ^[c]	<i>endo</i> - 17 / <i>exo</i> - 16 ^[d]	<i>ee</i> [%] ^[e] (<i>endo</i> - 17 / <i>exo</i> - 16)
1	L1	20	92	3.2:1	1/0
2	L2	20	97	4.0:1	48/21
3	L3	23	98	1.4:1	48/72
4	L4	20	99	4.2:1	97/11
5 ^[f]	L4	20	98	4.6:1	97/10
6 ^[g]	L4	20	99	4.4:1	97/11

[a] Reaction conditions: **15** (5.0 equiv), **14** (1.0 equiv), BH₃·THF (1.2 equiv), AcOH (1.2 equiv), ligand (1.2 equiv). [b] 93–97% of ligand was recovered. [c] Yield of isolated product. [d] Based on ¹H NMR integration. [e] Determined by HPLC using a chiral stationary phase. [f] With recycled ligand, one cycle. [g] With recycled ligand, two cycles. M.S. = molecular sieves, THF = tetrahydrofuran.





Scheme 2. a) Prenyl bromide, K_2CO_3 , acetone, reflux, 24 h, 95%; b) Montmorillonite K-10, CH_2Cl_2 , $0^\circ C$, 8 h, **19** (37%), **20** (27%) and recovered **18** (33%); c) 1. conc. HCl, MeOH, RT, 20 h; 2. 4 M NaOH, RT, 2 h; 3. Ac_2O , pyridine, CH_2Cl_2 , RT, 12 h, 35% for two steps. MOM = methoxymethyl.

a methyl group, the Diels–Alder cycloaddition did not proceed.

We then set out to investigate the total syntheses of kuwanons I and J. Prenylation of the readily available chalcone **18**^[16] under standard reaction conditions^[12a] afforded the prenyl chalcone **13** (Scheme 2), which was further subjected to a montmorillonite-K-10-promoted sigmatropic rearrangement^[12c] to afford the *ortho*-prenylated chalcone **19** (37%), along with the *para*-prenylated product **20** (27%) which should be a suitable synthetic precursor for brosimones A and B. The MOM-protected compound **19** was converted into the required dienophile triacetate **7** in 35% yield over two steps.

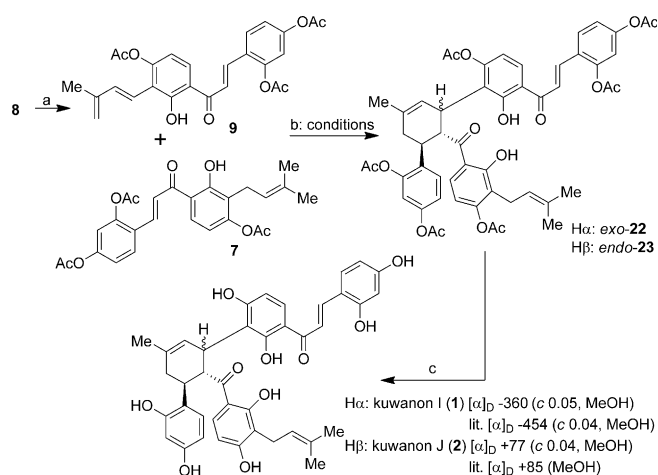
We next turned our attention to the synthesis of the diene **9**. Initial attempts using the standard Schenck ene reaction conditions^[13] with subsequent reduction using PPh_3 afforded a mixture of the tertiary allylic alcohol **8** and secondary allylic alcohol **21** in 71% combined yield with a 2:1 ratio (Table 2, entry 1). Unfortunately, several attempts for the dehydration of **21** failed because of the low reactivity. Considering that the tertiary alcohol is typically a better substrate for dehydration, we then focused our attention on improving the selectivity for the tertiary alcohol. By screening commonly used photosensitizers and solvents (entry 2–6), we found **8** was afforded in 4.3:1 ratio by using Rose bengal as the photosensitizer and MeOH as the solvent (entry 6). More interestingly, we observed that a visible-light-mediated^[18,19] regioselective Schenck ene reaction using $[Ru(bpy)_3Cl_2 \cdot 6H_2O]$ and MeOH significantly improved the ratio for the tertiary alcohol (8.0:1, entry 8). To the best of our knowledge, this step leading to **8** represents the first $[Ru(bpy)_3Cl_2 \cdot 6H_2O]$ -mediated regioselective Schenck ene reaction.

Table 2: Schenck ene reactions.^[a]

Entry	photosensitizer	Solvent	T [h]	Yield [%] ^[b]	8/21 ^[c]
1 ^[d]	TPP	CH_2Cl_2	3	71	2.0:1
2 ^[d]	TPP	MeOH	14	67	1.9:1
3 ^[d]	Methyl blue	CH_2Cl_2	5	62	2.3:1
4 ^[d]	Methyl blue	MeOH	6	70	1.9:1
5 ^[d]	Rose bengal	CH_2Cl_2	9	62	1.8:1
6 ^[d]	Rose bengal	MeOH	3	73	4.3:1
7 ^[e]	$[Ru(bpy)_3Cl_2 \cdot 6H_2O]$	CH_2Cl_2	9	63	1.8:1
8 ^[e]	$[Ru(bpy)_3Cl_2 \cdot 6H_2O]$	MeOH	26	62	8.0:1

[a] See the Supporting Information for experimental details. [b] Yield of isolated product. [c] Based on 1H NMR integration. [d] 150 W halogen lamp was used as the light source. [e] 40 W compact fluorescent light bulb was used as the light source. bpy = 2,2'-bipyridine, TPP = *meso*-tetraphenylporphyrin.

With the tertiary alcohol **8** in hand, we entered the final stage of the total synthesis. Dehydration of **8** with $SOCl_2$ /DBU smoothly provided the diene **9** in 75% yield (Scheme 3). Although **9** is presumably deactivated by the electron-withdrawing acetyl groups, using the previously developed optimal reaction conditions for the [4+2] cycloaddition between the dienophile **7** and diene **9** proceeded smoothly to afford both *endo* and *exo* diastereomers in good yield (72%)^[16] in a 1.2:1 ratio, but with moderate *ee* values (58% *ee* for *endo*-**23**, 51% *ee* for *exo*-**22**; Table 3, entry 1). Gratifyingly, by increasing the amount of the chiral ligand to reduce the background reaction,^[20] we could dramatically improve the enantiomeric excess to 97% for *endo*-**23** and 60% for *exo*-**22** (entry 3). However, the chiral boron VAPOL complex did not show promising results (entry 4), and was in



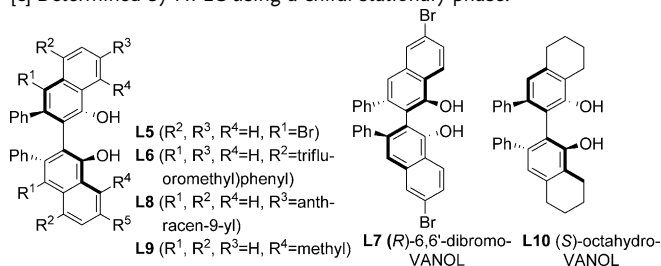
Scheme 3. a) $SOCl_2$, DBU, CH_2Cl_2 , $-78^\circ C$ to RT, 12 h, 75%; b) Ligand, $BH_3 \cdot THF$, AcOH, 5 Å M.S., THF, RT, 72 h; c) K_2CO_3 , MeOH/ H_2O (10:1), RT, 1 h, 70%. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

Table 3: Screening reaction conditions for the reaction between **9** and **7** (see structures in Scheme 3).

Entry	Ligand ^[a] (equiv)	Yield [%] ^[b]	endo- 23 /exo- 22	ee [%] ^[c] (endo- 23 /exo- 22)
1	L4 (1.2)	72	1.2:1	58/51
2	L4 (2.5)	76	1.1:1	97/57
3	(<i>R</i>)-VANOL (2.5)	80	1.1:1	97/60
4	(<i>S</i>)-VAPOL (2.5)	19	1.1:2	40/25
5	L5 (2.5)	26	1.3:1	7/22
6	L6 (2.5)	70	1.3:1	86/36
7	L7 (2.5)	51	1.1:1	85/39
8	L8 (2.5)	52	1.8:1	83/28
9	L9 (2.5)	54	1:1.2	86/84
10	L10 (2.5)	67	1.9:1	96/74

[a] 87–92% of ligand was recovered. [b] Yield of isolated product.

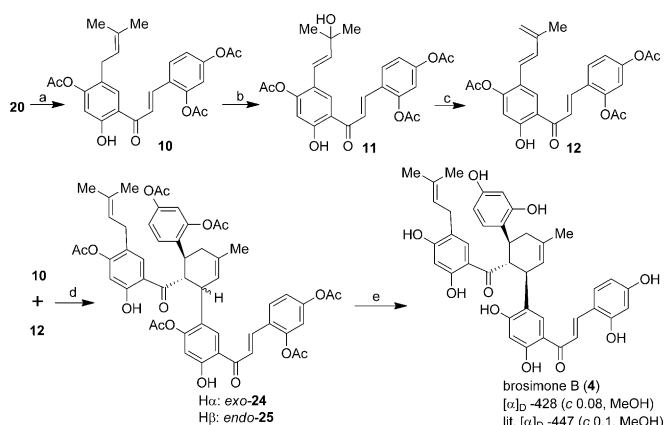
[c] Determined by HPLC using a chiral stationary phase.



contrast to the previous model study. In terms of both reactivity and enantioselectivity, (*S*)-VANOL displayed better results than (*S*)-VAPOL. To further improve the enantioselectivity of the *exo*-product, we decided to evaluate a number of new VANOL derivatives containing various substituents at different positions of the naphthalene core of VANOL (entry 5–10).^[21] To our delight, the *ee* value of the *exo* product was significantly improved from 60% to 84% when (*S*)-8,8'-dimethyl-VANOL (**L9**) was used (entry 9). Finally, global deprotection of *exo*-**22** and *endo*-**23** under a mild basic conditions efficiently furnished the desired natural products kuwanons I (**1**) and J (**2**), both in 70% yield (Scheme 3). The spectroscopic data for synthetic **1** and **2** were in agreement with those reported for the natural product.^[16]

We next turned our attention to the syntheses of brosimones A and B. Initially, MOM groups were converted into acyl groups to afford **10** in 33% yield over two steps (Scheme 4). Unfortunately, when applying the previously developed optimal reaction conditions ($Ru(bpy)_3Cl_2 \cdot 6H_2O$, MeOH) to the *ortho*-prenylated chalcone, we did not observe good regioselectivity for the Schenck ene reduction. In this case, after screening different photosensitizers and solvents again, we found that the tertiary allylic alcohol **11** and secondary allylic alcohol were afforded in 3.2:1 ratio with 63% combined yield (48% yield for **11**) by using TPP as photosensitizer and MeOH as solvent. The diene **12** then prepared, by dehydration of **11**, in 68% yield.

With the *para*-prenylated dienophile **10** and diene **12** in hand, we set out to investigate the key asymmetric Diels–Alder reaction for the synthesis of (–)-brosimone B (Scheme 4). As a result, (*S*)-VANOL proved to be the best

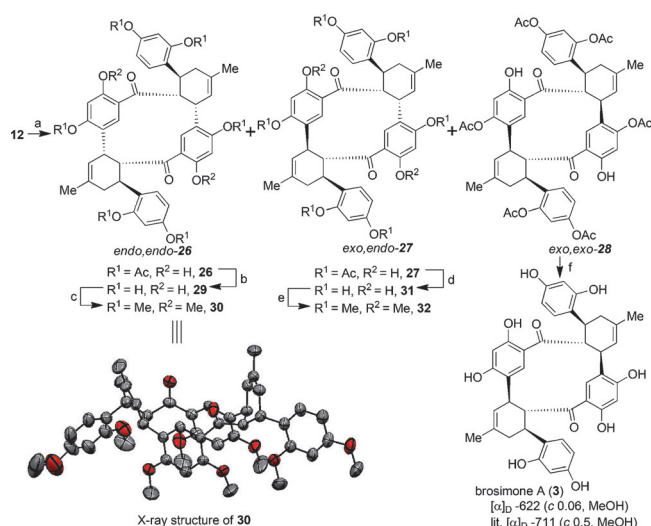


Scheme 4. a) 1. 3 M HCl, MeOH, resorcinol, 80°C, 23 min; 2. 4 M NaOH, RT, 2 h; 3. Ac_2O , pyridine, CH_2Cl_2 , RT, 12 h, 33% for two steps; b) 1. hv, O_2 , TPP, MeOH, RT, 10 h; 2. PPh_3 , CH_2Cl_2 , RT, 16 h, 48%; c) $SOCl_2$, DBU, THF, –78°C to RT, 9 h, 68%; d) (*S*)-VANOL, $BH_3 \cdot THF$, AcOH, 5 Å M.S., THF, RT, 72 h, 71% (**25**:**24** = 1.2:1), 93% *ee* for *exo*-**24**, 98% *ee* for *endo*-**25**, recovered (*S*)-VANOL (90%); e) K_2CO_3 , MeOH/ H_2O (10:1), RT, 1 h, 70%.

ligand to afford both *endo*-**25** and *exo*-**24** in 71% yield with a 1.2:1 ratio, and remarkably, with excellent *ee* values for both (98% *ee* for *endo*-**25**, 93% *ee* for *exo*-**24**). The structure of *endo*-**25** was confirmed by extensive two-dimensional NMR analysis.^[16] Final deprotection of the acetyl groups of *exo*-**24** afforded (–)-brosimone B in 70% yield. The spectroscopic data for synthetic **4** were in agreement with those reported for the natural product.^[7]

Encouraged by the aforementioned results, we ultimately sought to explore the synthesis of (–)-brosimone A, which is a homodimer of **12**.

However, conceivably, several synthetic challenges remained to be addressed. First, on the basis of molecular modeling studies, the core of (–)-brosimone A is [3.3]metacyclophane which exists with significant ring strain imparted by the 12-membered ring system. Second, it might be difficult to achieve the intramolecular Diels–Alder reaction catalyzed by the boron VANOL complex because of the steric hindrance. Third, when the boron VANOL complex is added in one portion, it might be problematic because while it might activate the dienophile, the diene could be deactivated simultaneously. Not surprisingly, very few reports regarding this type of one-pot inter-/intramolecular Diels–Alder cycloaddition cascade have been reported to date.^[22] To our delight, when slightly excess chiral boron complex was used, a one-pot inter-/intramolecular Diels–Alder cycloaddition cascade was smoothly achieved to afford the three expected products including *endo*,*endo*-**26** in 28% yield with 98% *ee*, *exo*,*endo*-**27** in 20% yield, and *exo*,*exo*-**28** in 13% yield with 95% *ee* (Scheme 5). After removing the Ac groups of **26** followed by methylation, *endo*,*endo*-**30** was obtained in 56% yield over two steps. The structure of *endo*,*endo*-**30** was unambiguously confirmed by X-ray crystallographic analysis. However, it was challenging for us to measure the *ee* value of *exo*,*endo*-**27** because of the equilibrium mixture of conformational isomers. Removal of the acetyl groups of *exo*,*endo*-**27**



Scheme 5. a) (S)-VANOL, BH₃·THF, AcOH, 5 Å M.S., THF, RT, 96 h, 61 % (26/27/28 = 28%:20%:13 %), 98 % ee for endo,endo-26, 95 % ee for exo,exo-28, recovered (S)-VANOL (91 %); b) K₂CO₃, MeOH/H₂O (10:1), RT, 1.5 h, 75 %; c) Me₂SO₄, K₂CO₃, acetone, reflux, 16 h, 74 %, d) K₂CO₃, MeOH/H₂O (10:1), RT, 1 h, 75 %; e) MeI, K₂CO₃, acetone, reflux, 24 h, 63 %; f) K₂CO₃, MeOH/H₂O (10:1), RT, 1 h, 70 %. Thermal ellipsoids shown at 50 % probability.^[23]

and subsequent methylation afforded **32** in 47 % yield over two steps. The NMR data for synthetic **32** were fully matched with the compound obtained by permethylation of the exo,endo hexamethyl ether which had been previously reported by the group of Porco.^[11d] Finally, global deprotection of exo,exo-28 under mild basic conditions efficiently afforded the desired natural product (–)-brosimone A in 70 % yield. The spectroscopic data for synthetic **3** were in agreement with those reported for the natural product.^[6]

In summary, we have accomplished the first enantioselective total syntheses of (–)-kuwanon I, (+)-kuwanon J, (–)-brosimone A, and (–)-brosimone B in seven steps from the common precursor **13** based on a biosynthesis-inspired approach. The synthesis features a novel asymmetric Diels–Alder cycloaddition of a 2'-hydroxychalcone derivative promoted by a chiral boron VANOL complex, and an unprecedented [Ru(bpy)₃Cl₂·6H₂O]-mediated regioselective Schenck ene reaction, as well as a novel tandem inter-/intramolecular asymmetric Diels–Alder cycloaddition process to construct six stereogenic centers in a single operation. The chiral VANOL ligand as well as its derivative have proven to be remarkably efficient in controlling the enantioselectivities for both endo- and exo-selective Diels–Alder cycloadducts. The chemistry developed should pave the way for the enantioselective synthesis of other related complex Diels–Alder natural products, which will be disclosed in due course.

Received: April 20, 2014

Revised: June 8, 2014

Published online: July 7, 2014

Keywords: boron · cyclization · natural products · synthetic methods · total synthesis

- [1] H. J. Kim, M. W. Ruszczycky, S. H. Choi, Y. N. Liu, H. W. Liu, *Nature* **2011**, 473, 109.
- [2] H. Oikawa, T. Tokiwano, *Nat. Prod. Rep.* **2004**, 21, 321.
- [3] a) T. Nomura, Y. Hano, *Nat. Prod. Rep.* **1994**, 11, 205; b) T. Nomura, *Pure Appl. Chem.* **1999**, 71, 1115.
- [4] T. Nomura, T. Fukai, J. Matsumoto, A. Imashimizu, S. Terda, M. Hama, *Planta Med.* **1982**, 46, 167.
- [5] S. Ueda, T. Nomura, T. Fukai, J. Matsumoto, *Chem. Pharm. Bull.* **1982**, 30, 3042.
- [6] I. Messana, F. Ferrari, *Tetrahedron* **1988**, 44, 6693.
- [7] I. Messana, F. Ferrari, J. F. de Mello, M. Do Carmo Mesquita de Araujo, *Heterocycles* **1989**, 29, 683.
- [8] T. Nomura, T. Fukai, *Chem. Pharm. Bull.* **1980**, 28, 2548.
- [9] T. Nomura, T. Fukai, T. Narita, *Heterocycles* **1980**, 14, 1943.
- [10] For selected references on biological activities, see: a) S. J. Dai, Y. Wu, Y. H. Wang, W. Y. He, R. Y. Chen, D. Q. Yu, *Chem. Pharm. Bull.* **2004**, 52, 1190; b) Z. P. Zheng, K. W. Cheng, Q. Zhu, X. C. Wang, Z. X. Lin, M. Wang, *J. Agric. Food Chem.* **2010**, 58, 5368.
- [11] a) H. Cong, C. F. Becker, S. J. Elliott, M. W. Grinstaff, J. A. Porco, Jr., *J. Am. Chem. Soc.* **2010**, 132, 7514; b) H. Cong, J. A. Porco, Jr., *Org. Lett.* **2012**, 14, 2516; c) H. Cong, J. A. Porco, Jr., *ACS Catal.* **2012**, 2, 65; d) C. Qi, H. Cong, K. J. Cahill, P. Müller, R. P. Johnson, J. A. Porco, Jr., *Angew. Chem.* **2013**, 125, 8503; *Angew. Chem. Int. Ed.* **2013**, 52, 8345.
- [12] a) C. Gunawan, M. A. Rizzacasa, *Org. Lett.* **2010**, 12, 1388; b) S. Boonsri, C. Gunawan, E. H. Krenske, M. A. Rizzacasa, *Org. Biomol. Chem.* **2012**, 10, 6010; c) C. F. Chee, Y. k. Lee, M. J. C. Buckle, N. A. Rahman, *Tetrahedron Lett.* **2011**, 52, 1797.
- [13] J. J. Helesbeux, O. Duval, D. Guilet, D. Seraphin, D. Rondeau, P. Richomme, *Tetrahedron* **2003**, 59, 5091.
- [14] T. R. Kelly, A. Whiting, N. S. Chandrakumar, *J. Am. Chem. Soc.* **1986**, 108, 3510.
- [15] S. A. Snyder, Z. Y. Tang, R. Gupta, *J. Am. Chem. Soc.* **2009**, 131, 5744.
- [16] For details see the Supporting Information.
- [17] For selected recent examples of using VANOL and VAPOL for the asymmetric Diels–Alder reaction, see: a) J. M. Bao, W. D. Wulff, *J. Am. Chem. Soc.* **1993**, 115, 3814–3815; b) D. P. Heller, D. R. Goldberg, H. Q. Wu, W. D. Wulff, *Can. J. Chem.* **2006**, 84, 1487.
- [18] For selected excellent reviews on visible light photoredox catalysis, see: a) T. P. Yoon, M. A. Ischay, J. Du, *Nat. Chem.* **2010**, 2, 527; b) J. M. R. Narayanam, C. R. Stephenson, *Chem. Soc. Rev.* **2011**, 40, 102; c) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, 113, 5322.
- [19] For selected references on visible-light-mediated formation the peroxide bond, see: a) Z. Lu, J. D. Parrish, T. P. Yoon, *Tetrahedron* **2014**, 70, 4270; b) J. D. Parrish, M. A. Ischay, Z. Lu, S. Gao, N. R. Peters, T. P. Yoon, *Org. Lett.* **2012**, 14, 1640; c) J. Yin, L. L. Kong, C. Wang, Y. B. Shi, S. J. Cai, S. H. G. G, *Chem. Eur. J.* **2013**, 19, 13040.
- [20] We obtained the Diels–Alder cycloadducts exo-22 and endo-23 in 12 % yield when only BH₃·THF and AcOH were used without the addition of chiral ligand.
- [21] Y. Guan, Z. Ding, W. D. Wulff, *Chem. Eur. J.* **2013**, 19, 15565.
- [22] For selected references on one-pot inter-/intramolecular Diels–Alder reactions, see: a) W. R. Roush, R. J. Sciotti, *J. Am. Chem. Soc.* **1998**, 120, 7411; b) C. C. Yuan, B. Du, L. Yang, B. Liu, *J. Am. Chem. Soc.* **2013**, 135, 9291.
- [23] CCDC 991774 (**30**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.