

Total Synthesis of Chaetoglobin A via Catalytic, Atroposelective Oxidative Phenol Coupling

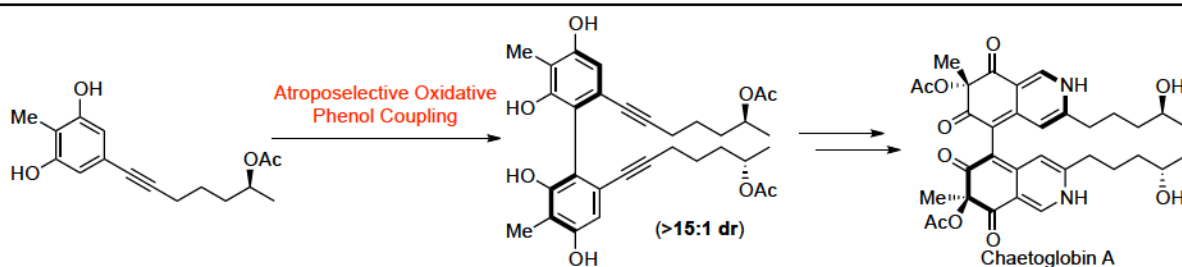
Houng Kang,[†] Carilyn Torruellas,[‡] Jinchu Liu[§] and Marisa C. Kozlowski^{*,†}

[†]Department of Chemistry, Roy and Diana Vagelos Laboratories, University of Pennsylvania, Philadelphia, Pennsylvania 19104, United States

[‡]U. S. Army Edgewood Chemical Biological Center, RDCB-DRC-P/bldg E3400, Aberdeen Proving Ground, MD, 21010-5424, United States

[§]Department of Process Research and Development, Merck Research Laboratories, Rahway, NJ, 07065, United States

Supporting Information Placeholder



ABSTRACT: The first total synthesis of chaetoglobin A (1), which features a chiral axis between two identical highly oxygenated bicyclic cores, was successfully completed in 12 steps from 2,6-dimethoxytoluene. Vanadium-catalyzed oxidative phenol coupling, as a key step, enabled generation of the axial chirality.

Chaetoglobin A is one of the azaphilone dimers, which contains two identical oxygenated bicyclic cores incorporating tertiary alcohol stereocenters that are connected through a chiral axis (Figure 1). It is isolated from the endophytic fungus *chaetomium globosum*, which lives in the stem of *Imperata cylindrical*. In 2008, Tan et al. reported its inhibitory ability on the propagation of human breast cancer and colon cancer cell lines.¹ Previous studies on the biosynthesis of azaphilone alkaloids indicate that its core backbone is of polyketide origin.² However, the nature of the dimerization and generation of attendant axial chirality has not been delineated. Specifically, it is unclear whether the stereochemistry of the chiral axis forms first and directs formation of the tertiary alcohol centers (via 3), if the tertiary alcohol centers form first and then direct formation of the chiral axis (via 4), or if these stereoelements are formed independently.

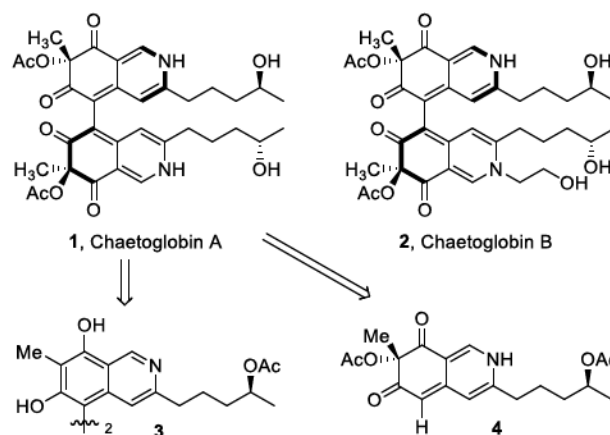


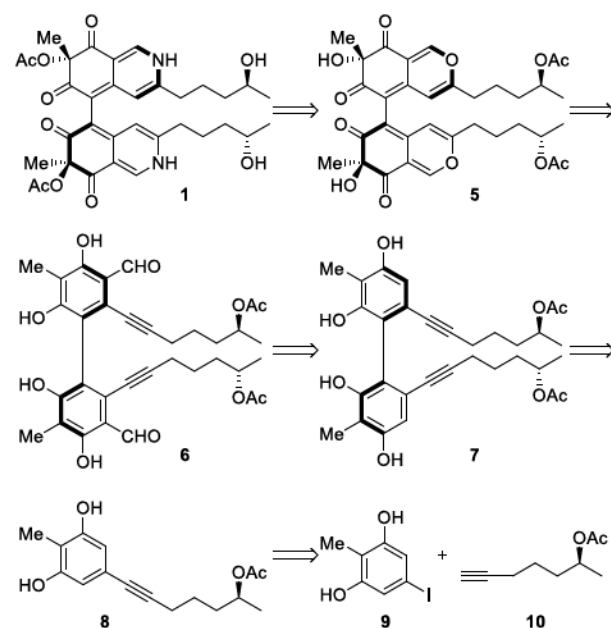
Figure 1. Structure of chaetoglobin A (1) and B (2)

Due to their intriguing structures and biological activities, numerous attempts to synthesize the azaphilone alkaloids have been reported since the late 1960s.³ Approaches to introducing the bicyclic core proceed from either a keto-formyl precursor or alkynyl-formyl precursor that generate benzopyrylium salts or pyronoqui-

nones as key intermediates. Often, acid-catalyzed cycloisomerization, followed by oxidation, was used to construct the 2*H*-isoquinoline-2,6-dione backbone. However, no synthetic efforts have been reported toward azaphilone dimers to date. Recently, we reported an efficient method to construct a chiral biaryl axis by means of vanadium-catalyzed enantioselective oxidative phenol coupling.⁴ The oxidative coupling permits the formation of chiral axes effectively. Here, we describe the total synthesis of chaetoglobin A utilizing this stereoselective oxidative phenol coupling to generate an axial chiral bisphenol dimer **7** as a key intermediate.

In our retrosynthetic analysis, the final isoquinoline moiety could be prepared by amination of **5** (Scheme 1). Lewis acid-catalyzed dearomatization followed by oxidation would allow for construction of the corresponding bicyclic core from formylated dimer **6**. We hypothesize that the axial chirality of **6** could direct formation of the tertiary alcohol centers of **5**. In doing so, we could determine the feasibility one of the possible biosynthetic pathways (i.e. via **3**) (Figure 1). Vilsmeier-Haack formylation could install the necessary formyl groups on tetraphenol **7**. We envisioned the atroposelective oxidative phenol coupling of **8** to afford pure atropoisomer **7**. We anticipated that the acetoxy stereocenters of **8** would have little effect on stereochemical course of the phenol coupling with the chiral catalyst exerting control. Internal alkynyl monomer **8** would be prepared from the Sonogashira cross-coupling of bisphenol **9** and alkyne **10**.

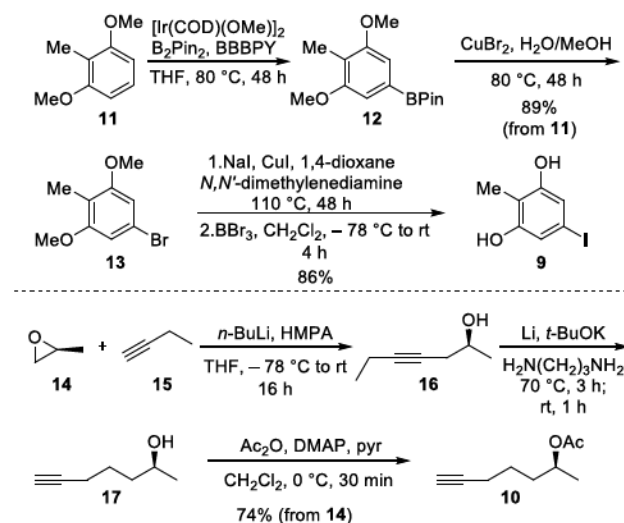
Scheme 1. Retrosynthetic Analysis of Chaetoglobin A (**1**)



Synthetic efforts commenced with preparation of phenol **9** and alkyne **10** as shown in Scheme 2. Iridium-catalyzed borylation⁵ of commercially available **11**, followed by halogenation allowed for the formation of bromide **13**. Due to the need for a more reactive electrophile for Sonogashira cross-coupling, halogen exchange was undertaken to generate iodophenol **9** after demethylation. Surprisingly, stepwise iodination via halogen exchange⁶ from bromide **13** proved to be more efficient than direct iodination⁷ from boronic ester **12**. Following a literature report⁸ to prepare enantiomerically pure hydroxyalkyne **17**, a nucleophilic ring opening with commercially available propylene oxide **14** and butyne **15** gave internal

alkyne **16**. Sequential alkyne isomerization was effected with a Li/KO*t*-Bu in 1,3-diaminopropane. Acetate protection of the free hydroxyl group provided the desired alkyne **10** in 74% yield over three steps.

Scheme 2. Syntheses of Sonogashira Coupling Fragments **9** and **10**



Optimization of Sonogashira coupling between iodide **9** and alkyne **10** led to the formation of oxidative phenol coupling precursor **8** in 98% yield (Scheme 3). Using our recently reported atroposelective oxidative coupling of phenols,⁴ vanadium catalyst **18** was applied to this transformation. Notably, complete catalyst control over the diastereoselectivity was observed with the opposite enantiomer of the catalyst providing the diastereomeric product with comparable dr. The additives, LiCl and HOAc, which are theorized to activate the vanadium catalyst result in significant improvements (Table 1). Treatment of **8** with LiCl as an additive gave high diastereoselectivity (Table 1, entry 2). Increased catalyst loading showed neither a significant improvement in yield, nor selectivity (Table 1, entry 3). Among alternative solvents, chlorobenzene seemed a promising candidate in terms of improving yield (Table 1, entry 2 vs 4 and entry 5 vs 6). Improved yield and comparable selectivity of dimer were realized with HOAc as the additive and chlorobenzene as solvent (Table 1, entry 6). Finally, further improved yield and diastereoselectivity was achieved under more concentrated reaction conditions (Table 1, entry 7). Use of chiral vanadyl catalyst **18** under the optimized conditions formed dimer **7** in 67% yield establishing the axial chiral element with >15:1 dr. The absolute stereochemistry of product **7** was confirmed by X-ray crystallographic analysis of the *para*-bromobenzoyl substituted derivative **19**.⁹

Scheme 3. Atroposelective Oxidative Phenol Coupling and Determination of Absolute Axial Stereochemistry

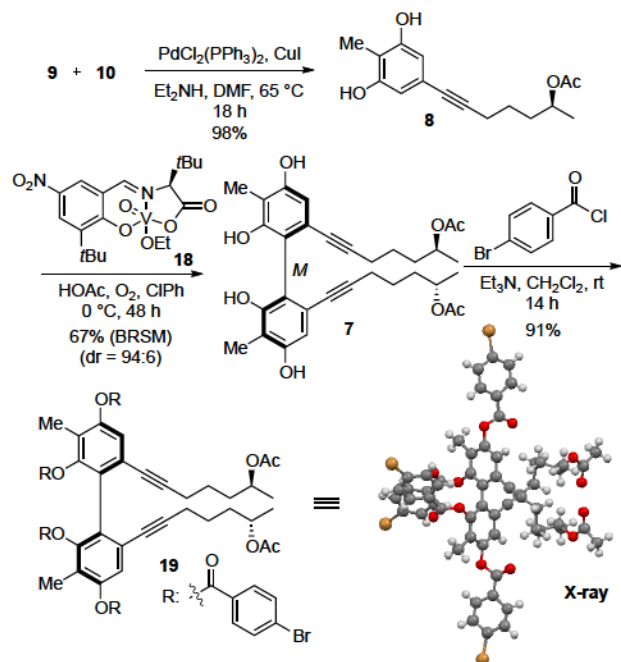


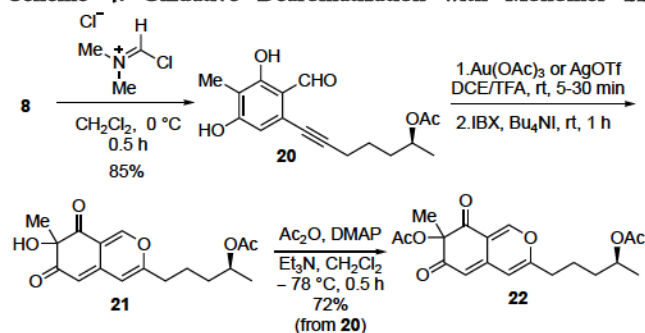
Table 1. Diastereoselective Oxidative Coupling of 8

entry	V-cat 18	additive ^a	solvent ^b	yield (%) ^c	dr
1	20 mol %	–	chlorobenzene ^d	34 (44)	79:21
2	20 mol %	LiCl	toluene	52 (59)	92:8
3	40 mol %	LiCl	toluene	49 (52)	93:7
4	20 mol %	LiCl	chlorobenzene	54 (60)	90:10
5	20 mol %	HOAc	toluene	49 (55)	87:13
6	20 mol %	HOAc	chlorobenzene	49 (64)	90:10
7	20 mol %	HOAc	chlorobenzene ^d	58 (67)	94:6

^a20 mol % ^b0.3 M ^cIsolated yield based on recovery of substrate in parentheses ^d0.5 M

With the coupled atropoisomer in hand, our attention turned to the key oxidative dearomatization reaction, developed by Porco and coworkers, to generate the bicyclic core featuring a tertiary alcohol stereocenter.¹¹ Initially, we tested this transformation using monomeric formylated phenol **20**, which was easily prepared from monomer **8** in 85% yield (Scheme 4). Based on the literature, Au(OAc)₃ was the optimal Lewis acid for this transformation. These conditions efficiently provided the desired oxygenated core **21** upon IBX oxidation as assessed by the yield of monomer **22** after acetylation (72% yield over three steps).

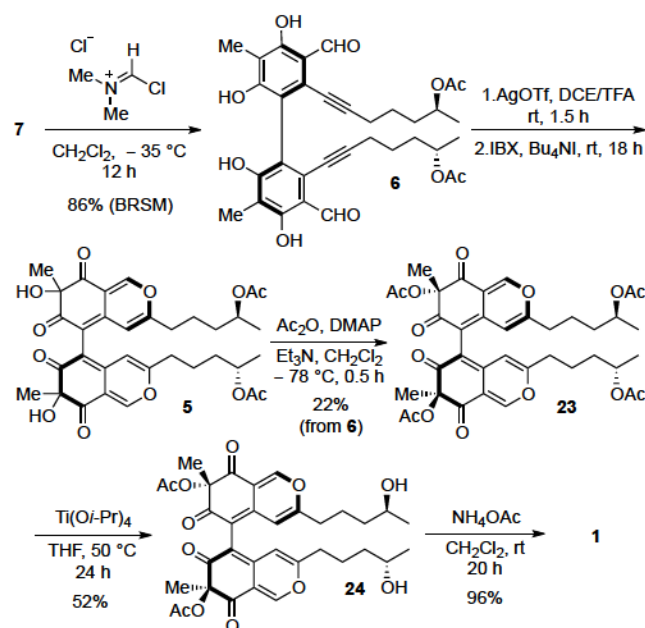
Scheme 4. Oxidative Dearomatization with Monomer 22



With dimer **7**, several methods to formylate adjacent to the alkyne chain were surveyed.¹⁰ Ultimately, the Vilsmeier-Haack formylation with preformed (chloromethylene)dimethyliminium chloride at –35 °C provided bisformylated product **6** in 86% yield (Scheme 5) without acyl deprotection, which occurred in many of the other conditions screened due to acid byproducts formed during generation of the active acylating species.

With dimer **6**, however, Au(OAc)₃-catalyzed dearomatization did not generate desired product **5**, but caused decomposition. After screening several Lewis acids, we found that AgOTf¹² gave a similar result in the model system from Scheme 4 (63% overall yield from **20**). To our delight, cycloisomerization of **6** performed similarly with AgOTf, and subsequent oxidation with a hypervalent iodine reagent, IBX, allowed access to bicyclic dimer **5** (Scheme 5). We had theorized that the chiral axis would influence the stereochemistry during formation of this tertiary alcohol center with the bulk of the 2*H*-isoquinoline-2,6-dione backbone blocking one stereoface. However, the reaction gave a 1:1:1 mixture of the three possible isomers (7*S*,7'*S*; 7*S*,7'*R*; 7*R*,7'*R*), indicating that the axial stereochemistry does not create a strong facial bias. Fortunately, sufficient amounts of each isomer could be obtained to proceed with the synthesis. The following section describes the results obtained with the faster eluting symmetric diastereomer, which could not be definitively assigned as 7*S*,7'*S* or 7*R*,7'*R* at this stage.

Scheme 5. Completion of Synthesis of Chaetoglobins A (1)



At this juncture, selective acylation of the tertiary alcohol centers was needed, which could be achieved either by deacylation of the secondary alcohols followed by selective acylation of the tertiary alcohols or by global acetylation followed by selective deacylation of the less hindered secondary alcohols. The former possibility takes advantage of the greater reactivity of the alcohols adjacent to the ketone.¹³ Upon removal of the acetyl groups from **5**, the resultant product was found to be prone to decomposition. As such, the latter alternative became a focus. Acetylation of **5** afforded product **23** in 22% over three steps from **6**, which represent six sets of chemical transformations due to the dimeric nature of the material (Scheme 4). Unexpectedly, selective deprotection of the secondary acetoxy group in the presence of the sterically congested tertiary acetoxy group was challenging. Attempted hydrolysis of **23** with acidic or basic conditions led decomposition that was faster than deprotection. We explored a wide range of hydrolysis conditions,¹⁴ including enzymatic methods,¹⁵ and finally established that 10 equiv of $\text{Ti}(\text{O}i\text{-Pr})_4$ in CH_2Cl_2 at elevated temperature afforded free hydroxylated **24** in 52% yield (Scheme 4). Exposure of oxygenated bicycle **24** to excess NH_4OAc furnished synthetic chaetoglobins A (**1**) in nearly quantitative yield.

The spectroscopic data from synthetic **1** was in accord with those reported in the literature for chaetoglobins A.¹ In particular, the ^{13}C NMR gave 17 differentiable carbons supporting the symmetric structure. The chemical shifts of those signals closely matched those from the natural product securing evidence that the correct diastereomeric relationship between the tertiary alcohols and the stereoaxis had been generated. Importantly, circular dichroism data obtained from the synthetic material proved identical to that from the natural product (Figure 2), which indicates that both the same absolute and relative stereochemistries are established.

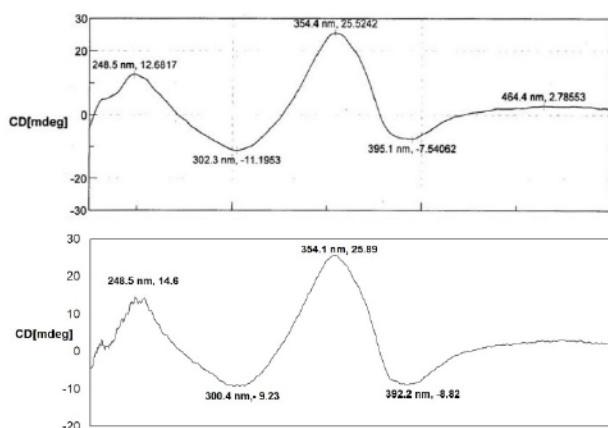


Figure 2. Comparing circular dichroism of chaetoglobins A (**1**) (a) CD spectrum of natural product isolate. Adapted from reference 1 with permission of The Royal Society of Chemistry; (b) synthetic **1** CD spectrum.

In conclusion, we have accomplished the first total synthesis of chaetoglobins A in 4.3% overall yield, with 12 steps in the longest linear sequence. A vanadium-catalyzed atroposelective oxidative phenol coupling serves as a key step in the formation of stereoaxis of chiral azaphilone dimer **1**. The stereochemical results from oxi-

dative cyclization after formation of the stereoaxis raise interesting questions about the operating biosynthetic pathways.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, compound characterization, crystallographic data, NMR spectra. The Supporting Information is available free of charge on the ACS Publications website.

AUTHOR INFORMATION

Corresponding Author

* E-mail: marisa@sas.upenn.edu

Author Contributions

The manuscript was written through contributions of all authors. / All authors have given approval to the final version of the manuscript.

ACKNOWLEDGMENT

We are grateful to the NIH (GM-112684) and the NSF (CHE1464778, CHE1764298) for financial support of this research. Partial instrumentation support was provided by the NIH and NSF (1S10RR023444, 1S10RR022442, CHE 0840438, CHE-0848460, 1S10OD011980). Drs. Rakesh Kohli and Charles W. Ross III (UPenn) are acknowledged for obtaining HRMS data. We thank Prof. Virgil Percec and Benjamin Partridge (UPenn) for assistance with CD measurements. We are grateful to Dr. Patrick Carroll for assistance with crystallographic structures.

REFERENCES

- (1) Ming Ge, H.; Yun Zhang, W.; Ding, G.; Saparpakorn, P.; Chun Song, Y.; Hannongbua, S.; Xiang Tan, R. Chaetoglobins A and B, Two Unusual Alkaloids from Endophytic Chaetomium Globosum Culture. *Chem. Commun.* **2008**, 5978–5980.
- (2) (a) Colombo, L.; Gennari, C.; Ricca, G. S.; Scolastico, C.; Aragozzini, F. Detection of One Symmetrical Precursor during the Biosynthesis of the Fungal Metabolite Austdiol Using $[1,2-^{13}\text{C}_2]$ Acetate and $[\text{Me}-^{13}\text{C}]$ Methionine. *J. Chem. Soc. Chem. Commun.* **1981**, 575–576. (b) Takahashi, M.; Koyama, K.; Natori, S. Four New Azaphilones from Chaetomium Globosum Var. Flavo-Viridae. *Chem. Pharm. Bull. (Tokyo)* **1990**, 38, 625–628. (c) Seto, H.; Tanabe, M. Utilization of ^{13}C - ^{13}C Coupling in Structural and Biosynthetic Studies. III. Ochreophilone - a New Fungal Metabolite. *Tetrahedron Lett.* **1974**, 15, 651–654. (d) Duncan, S. J.; Williams, D. H.; Ainsworth, M.; Martin, S.; Ford, R.; Wrigley, S. K. On the Biosynthesis of an Inhibitor of the P53/MDM2 Interaction. *Tetrahedron Lett.* **2002**, 43, 1075–1078. (e) Nakazawa, T.; Ishiuchi, K.; Sato, M.; Tsunematsu, Y.; Sugimoto, S.; Gotanda, Y.; Noguchi, H.; Hotta, K.; Watanabe, K. Targeted Disruption of Transcriptional Regulators in Chaetomium Globosum Activates Biosynthetic Pathways and Reveals Transcriptional Regulator-Like Behavior of Aureonitol. *J. Am. Chem. Soc.* **2013**, 135, 13446–13455.
- (3) (a) Chong, R.; King, R. R.; Whalley, W. B. The Synthesis of Sclerotiorin and of an Analogue of Rotiorin. *J. Chem. Soc. Chem. Commun.* **1969**, 1512–1513. (b) Chong, R.; Gray, R. W.; King, R. R.; Whalley, W. B. The Synthesis of (\pm) Mitorubrin. *J. Chem. Soc. Chem. Commun.* **1970**, 0, 101a–101a. (c) Galbraith, M. N.; Whalley, W. B. The Chemistry of Fungi. Part LIX. The Synthesis of (\pm) -Ascochitine. *J. Chem. Soc. C* **1971**, 3557–3559. (d) Chong, R.; Gray, R. W.; King, R. R.; Whalley, W. B. The Chemistry of Fungi. Part LXII. The Synthesis of $(+/-)$ -Mitorubrin, a Metabolite of Penicillium Rubrum. *J. Chem. Soc. C* **1971**, 3571–3575. (e) Zhu, J.; Grigoriadis, N. P.; Lee, J. P.; Porco, J. A. Synthesis of the Azaphilones Using Copper-Mediated Enantioselective Oxidative Dearomatization. *J.*

- Am. Chem. Soc.* **2005**, *127*, 9342–9343. (f) Marsini, M. A.; Gowin, K. M.; Pettus, T. R. R. Total Synthesis of (±)-Mitorubrinic Acid. *Org. Lett.* **2006**, *8*, 3481–3483. (g) Zhu, J.; Porco, J. A. Asymmetric Syntheses of (–)-Mitorubrin and Related Azaphilone Natural Products. *Org. Lett.* **2006**, *8*, 5169–5171. (h) Lee, S. Y.; Clark, R. C.; Boger, D. L. Total Synthesis, Stereochemical Reassignment, and Absolute Configuration of Chlorofusin. *J. Am. Chem. Soc.* **2007**, *129*, 9860–9861. (i) Qian, W.-J.; Wei, W.-G.; Zhang, Y.-X.; Yao, Z.-J. Total Synthesis, Assignment of Absolute Stereochemistry, and Structural Revision of Chlorofusin. *J. Am. Chem. Soc.* **2007**, *129*, 6400–6401. (j) Clark, R. C.; Yeul Lee, S.; Boger, D. L. Total Synthesis of Chlorofusin, Its Seven Chromophore Diastereomers, and Key Partial Structures. *J. Am. Chem. Soc.* **2008**, *130*, 12355–12369. (k) Clark, R. C.; Lee, S. Y.; Searcey, M.; Boger, D. L. The Isolation, Total Synthesis and Structure Elucidation of Chlorofusin, a Natural Product Inhibitor of the P53–MDM2 Protein–Protein Interaction. *Nat. Prod. Rep.* **2009**, *26*, 465–477. (l) Boulangé, A.; Peixoto, P. A.; Franck, X. Diastereoselective IBX Oxidative Dearomatization of Phenols by Remote Induction: Towards the Epicoconone Core Framework. *Chem. – Eur. J.* **2011**, *17*, 10241–10245. (m) Germain, A. R.; Bruggemeyer, D. M.; Zhu, J.; Genet, C.; O'Brien, P.; Porco, J. A. Synthesis of the Azaphilones (+)-Sclerotiorin and (+)-8-O-Methylsclerotiorinamine Utilizing (+)-Sparteine Surrogates in Copper-Mediated Oxidative Dearomatization. *J. Org. Chem.* **2011**, *76*, 2577–2584. (n) Somoza, A. D.; Lee, K.-H.; Chiang, Y.-M.; Oakley, B. R.; Wang, C. C. Reengineering an Azaphilone Biosynthesis Pathway in *Aspergillus nidulans* To Create Lipoxigenase Inhibitors. *Org. Lett.* **2012**, *14*, 972–975. (o) Lin, L.; Mulholland, N.; Wu, Q.-Y.; Beattie, D.; Huang, S.-W.; Irwin, D.; Clough, J.; Gu, Y.-C.; Yang, G.-F. Synthesis and Antifungal Activity of Novel Sclerotiorin Analogues. *J. Agric. Food Chem.* **2012**, *60*, 4480–4491. (p) Achard, M.; Beeler, A. B.; Porco, J. A. Synthesis of Azaphilone-Based Chemical Libraries. *ACS Comb. Sci.* **2012**, *14*, 236–244. (q) Gao, J.-M.; Yang, S.-X.; Qin, J.-C. Azaphilones: Chemistry and Biology. *Chem. Rev.* **2013**, *113*, 4755–4811. (r) Peixoto, P. A.; Boulangé, A.; Ball, M.; Naudin, B.; Alle, T.; Cosette, P.; Karuso, P.; Franck, X. Design and Synthesis of Epicoconone Analogues with Improved Fluorescence Properties. *J. Am. Chem. Soc.* **2014**, *136*, 15248–15256. (s) Qiu, H.-B.; Qian, W.-J.; Yu, S.-M.; Yao, Z.-J. Stereodivergent Total Synthesis of Chlorofusin and Its All Seven Chromophore Diastereomers. *Tetrahedron* **2015**, *71*, 370–380.
- (4) Kang, H.; Lee, Y. E.; Reddy, P. V. G.; Dey, S.; Allen, S. E.; Niederer, K. A.; Sung, P.; Hewitt, K.; Torruellas, C.; Herling, M. R.; Kozlowski, M. C. Asymmetric Oxidative Coupling of Phenols and Hydroxycarbazoles. *Org. Lett.* **2017**, *19*, 5505–5508.
- (5) Murphy, J. M.; Liao, X.; Hartwig, J. F. Meta Halogenation of 1,3-Disubstituted Arenes via Iridium-Catalyzed Arene Borylation. *J. Am. Chem. Soc.* **2007**, *129*, 15434–15435.
- (6) Klapars, A.; Buchwald, S. L. Copper-Catalyzed Halogen Exchange in Aryl Halides: An Aromatic Finkelstein Reaction. *J. Am. Chem. Soc.* **2002**, *124*, 14844–14845.
- (7) Partridge, B. M.; Hartwig, J. F. Sterically Controlled Iodination of Arenes via Iridium-Catalyzed C–H Borylation. *Org. Lett.* **2013**, *15*, 140–143.
- (8) Wu, Y.; Gao, J. Total Synthesis of (+)-Brefeldin A. *Org. Lett.* **2008**, *10*, 1533–1536.
- (9) Opposite chiral axis compound (*P*)-**19** crystallographic data included in Supporting Information.
- (10) (a) Ramadas, S.; Krupadanam, G. L. D. Enantioselective Acylation of 2-Hydroxymethyl-2,3-Dihydrobenzofurans Catalysed by Lipase from *Pseudomonas cepacia* (Amano PS) and Total Stereoselective Synthesis of (–)-(R)-MEM-Protected Arthrographol. *Tetrahedron Asymmetry* **2000**, *11*, 3375–3393. (b) Phan, D. H. T.; Kim, B.; Dong, V. M. Phthalides by Rhodium-Catalyzed Ketone Hydroacylation. *J. Am. Chem. Soc.* **2009**, *131*, 15608–15609. (c) Ohsawa, K.; Yoshida, M.; Doi, T. A Direct and Mild Formylation Method for Substituted Benzenes Utilizing Dichloromethyl Methyl Ether–Silver Trifluoromethanesulfonate. *J. Org. Chem.* **2013**, *78*, 3438–3444.
- (11) Zhu, J.; Germain, A. R.; Porco, J. A. Synthesis of Azaphilones and Related Molecules by Employing Cycloisomerization of O-Alkynylbenzaldehydes. *Angew. Chem. Int. Ed.* **2004**, *43*, 1239–1243.
- (12) Feng, X.; Wang, H.; Yang, B.; Fan, R. One-Pot Synthesis of Highly Substituted 4-Acetylindoles via Sequential Dearomatization and Silver-Catalyzed Domino Reaction. *Org. Lett.* **2014**, *16*, 3600–3603.
- (13) Holton, R. A.; Zhang, Z.; Clarke, P. A.; Nadizadeh, H.; Procter, D. J. Selective Protection of the C(7) and C(10) Hydroxyl Groups in 10-Deacetyl Baccatin III. *Tetrahedron Lett.* **1998**, *39*, 2883–2886.
- (14) (a) Plattner, J. J.; Gless, R. D.; Rapoport, H. Synthesis of Some DE and CDE Ring Analogs of Camptothecin. *J. Am. Chem. Soc.* **1972**, *94*, 8613–8615. (b) Mori, K.; Tominaga, M.; Takigawa, T.; Matsui, M. A Mild Transesterification Method. *Synthesis* **1973**, 790–791. (c) Askin, D.; Angst, C.; Danishefsky, S. An Approach to the Synthesis of Bactobolin and the Total Synthesis of N-Acetylactinobolamine: Some Remarkably Stable Hemiacetals. *J. Org. Chem.* **1987**, *52*, 622–635. (d) Nudelman, A.; Herzig, J.; Gottlieb, H. E.; Keinan, E.; Sterling, J. Selective Deacetylation of Anomeric Sugar Acetates with Tin Alkoxides. *Carbohydr. Res.* **1987**, *162*, 145–152. (e) Baptistella, L. H. B.; Santos, J. F. D.; Ballabio, K. C.; Marsailio, A. J. 1,8-Diazabicyclo[5.4.0]Undec-7-Ene as a Mild Deprotective Agent for Acetyl Groups. *Synthesis* **1989**, *21*, 436–439. (f) Roush, W. R.; Lin, X.-F. Studies on the Synthesis of Aureolic Acid Antibiotics: Highly Stereoselective Synthesis of Aryl 2-Deoxy-β-Glycosides via the Mitsunobu Reaction and Synthesis of the Olivomycin A-B Disaccharide. *J. Am. Chem. Soc.* **1995**, *117*, 2236–2250. (g) Yamamoto, N.; Nishikawa, T.; Isobe, M. Synthesis of Bicyclic Hydroxy Lactone Intermediates toward (–)-Tetrodotoxin. *Synlett* **1995**, 505–506. (h) Yanada, R.; Negoro, N.; Bessho, K.; Yanada, K. Metallic Samarium and Iodine in Alcohol. Deacylation and Dealkyloxycarbonylation of Protected Alcohols and Lactams. *Synlett* **1995**, 1261–1263. (i) Xu, Y.-C.; Bizuneh, A.; Walker, C. A Reagent for Selective Deprotection of Alkyl Acetates. *J. Org. Chem.* **1996**, *61*, 9086–9089. (j) Kajiro, H.; Mitamura, S.; Mori, A.; Hiyama, T. Scandium Trifluoromethanesulfonate-Catalyzed Mild, Efficient, and Selective Cleavage of Acetates Bearing a Coordinative Group. *Tetrahedron Lett.* **1999**, *40*, 1689–1692. (k) Sharma, G. V. M.; Ilangoan, A. Ytterbium Triflate Mediated Selective Deprotection of Acetates. *Synlett* **1999**, 1963–1965. (l) Yoshimoto, K.; Kawabata, H.; Nakamichi, N.; Hayashi, M. Tris(2,4,6-Trimethoxyphenyl)Phosphine (TMPP): A Novel Catalyst for Selective Deacetylation. *Chem. Lett.* **2001**, *30*, 934–935. (m) Ravindranathan Kartha, K. P.; Mukhopadhyay, B.; Field, R. A. Practical De-O-Acylation Reactions Promoted by Molecular Sieves. *Carbohydr. Res.* **2004**, *339*, 729–732. (n) Wang, S.-M.; Ge, W.-Z.; Liu, H.-M.; Zou, D.-P.; Yan, X.-B. Syntheses of Acetylated Steroid Glycosides and Selective Cleavage of O-Acetyl Groups in Sugar Moiety. *Steroids* **2004**, *69*, 599–604. (o) Ren, B.; Cai, L.; Zhang, L.-R.; Yang, Z.-J.; Zhang, L.-H. Selective Deacetylation Using Iodine–methanol Reagent in Fully Acetylated Nucleosides. *Tetrahedron Lett.* **2005**, *46*, 8083–8086. (p) Yeom, C.-E.; Lee, S. Y.; Kim, Y. J.; Kim, B. M. Mild and Chemoselective Deacetylation Method Using a Catalytic Amount of Acetyl Chloride in Methanol. *Synlett* **2005**, 1527–1530. (q) B. C. Ranu, S. K. Guchhait, M. Saha, *J. Indian Chem. Soc.* **1999**, *76*, 547.
- (15) (a) Sakaki, J.; Sakoda, H.; Sugita, Y.; Sato, M.; Kaneko, C. Lipase-Catalyzed Asymmetric Synthesis of 6-(3-Chloro-2-Hydroxypropyl)-1,3-Dioxin-4-Ones and Their Conversion to Chiral 5,6-Epoxyhexanoates. *Tetrahedron Asymmetry* **1991**, *2*, 343–346. (b) Lopez, R.; Montero, E.; Sanchez, F.; Canada, J.; Fernandez-Mayoralas, A. Regioselective Acetylations of Alkyl β-D-Xylopyranosides by Use of Lipase PS in Organic Solvents and Application to the Chemoenzymic Synthesis of Oligosaccharides. *J. Org. Chem.* **1994**, *59*, 7027–7032. (c) Houille, O.; Schmittberger, T.; Uguen, D. A Remarkably Simple Process for Monoprotecting Diols. *Tetrahedron Lett.* **1996**, *37*, 625–628.
- (16) CCDC 1822188 ((*P*)-**19**), and 1822189 (**19**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.