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Total Syntheses of Aflavazole and 14-Hydroxyaflavinine

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Supporting Information

ABSTRACT: The first total syntheses of aflavazole (**6**) and 14-hydroxyaflavinine (**8**), two sterically congested indole diterpenoids, were accomplished. AlI_3-promoted alkyne Prins cyclization was exploited to construct their key structural motifs. An electrocyclization−aromatization sequence assembled the pentasubstituted arene of **6**, and a Stille−Migita coupling furnished the tetrasubstituted olefin of **8**. The benzylic and allylic C−O bonds were reductively cleaved at the late stage of the syntheses, respectively.

Indole diterpenoids are intriguing targets to synthetic chemists.[1] In 1989, Gloer et al. isolated anominine (**1**, Figure 1), an unusual indole diterpenoid possessing a congested decalin scaffold, from *Aspergillus*.[2] A class of more complex congeners were also discovered (e.g., **2**−**8**), some of which exhibited promising biological properties.[3] Danishefsky et al. reported a beautiful synthesis of racemic 12-demethyl aflavinine (**7**).[4] Recently, the groups of Bonjoch and Garg accomplished elegant asymmetric syntheses of **1** and **2**, respectively,[5] and our endeavors toward indole terpenoid synthesis[6] resulted in the syntheses of **1**−**3**.[6a,b] Aflavazole[3b] (**6**) and 14-hydroxyaflavinine[3c,7] (**8**) featuring the multisubstituted arene and olefin motifs, respectively, pose considerable synthetic challenges; introduction of the C14 hydroxyl adjacent to the vicinal quaternary carbons adds extra difficulty. Herein, we describe the first and asymmetric total syntheses of **6** and **8**.

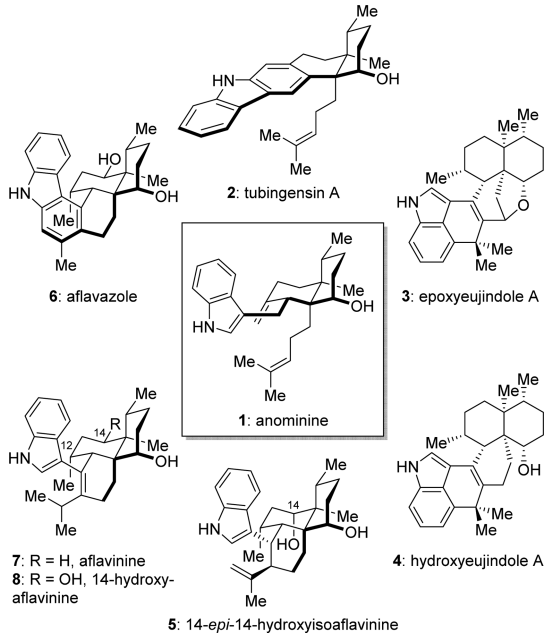

Figure 1. Selected members of the anominine family.

The structural relationship between **3** and **4** inspired us to develop a reversed bioinspired strategy for the syntheses of **6** and **8** (Figure 2). Biogenetically, **3** may arise from **4** via oxidative etherification. Conversely, we envisioned **9** as an immediate precursor of **6**; reductive cleavage of the benzyl ether[8] could afford the natural product. Our experience with electrocyclization[9] and Prins[10,11] reactions suggested an opportunity for an expedient route to the heptacyclic scaffold of **9**. Triene **10** was considered to

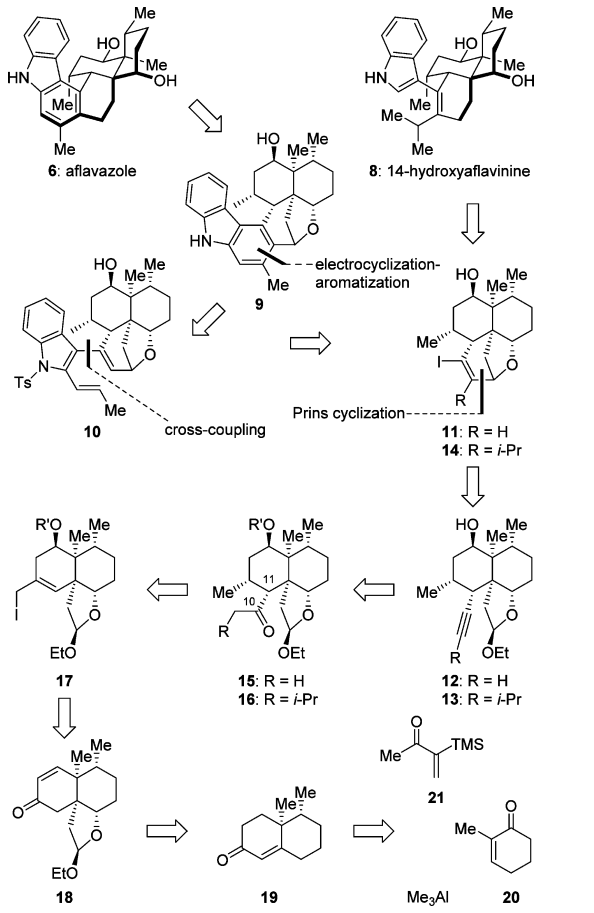

Figure 2. Retrosynthetic analysis of **6** and **8**.

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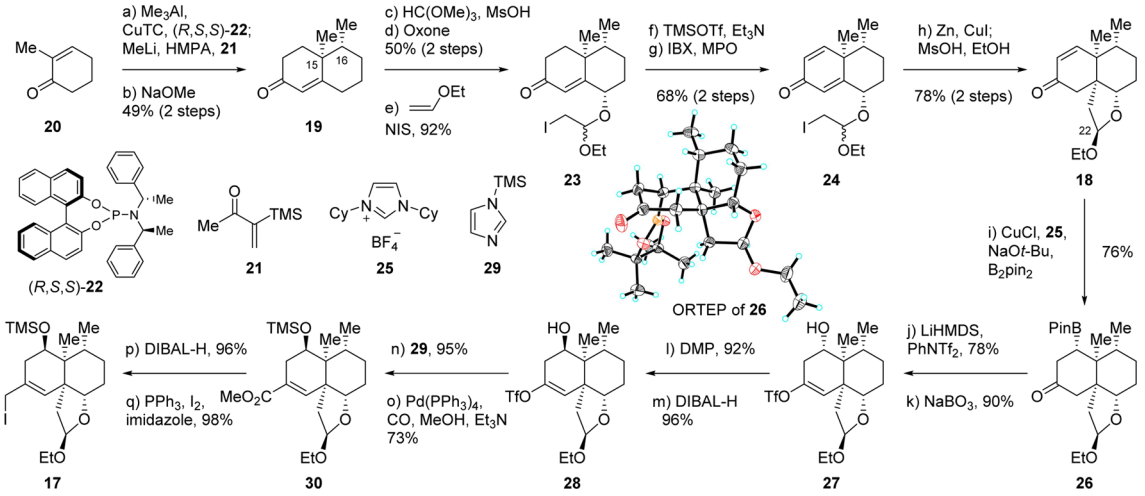
Scheme 1. Preparation of the Common Intermediate 17



be a suitable substrate for electrocyclization−aromatization.[12] Disassembly of **10** led to iodide **11**; Pd-catalyzed cross-coupling would install the indole moiety to the latter. The bridged ring system of **11** could be constructed through Prins cyclization of alkyne **12**.[13] Overman and co-workers elegantly showcased the power of alkyne Prins cyclization in their syntheses of pumiliotoxin alkaloids two decades ago.[11b−d] However, this reaction has long been underestimated in natural product synthesis since then.[11n,q] Alkyne Prins reaction is indeed of significant advantage from the following aspects: (1) the strong driving force to form congested and stained ring systems, (2) the well-defined geometry of multisubstituted olefin products, and (3) versatile transformations of the haloalkene products by transition-metal catalysis. Similarly, **8** was traced back to **13** via the intermediacy of **14**, although the bulky isopropyl posed a challenge to Prins cyclization and cross-coupling. In these syntheses, we preferred alkenyl iodides to bromides/chlorides because of their superior reactivity in Pd catalysis. Ketones **15** and **16** would serve as precursors of **12** and **13**, respectively.[14] Disconnection of the C10−C11 bonds of these ketones revealed allyl iodide **17** as a common substrate for Nozaki−Hiyama reactions. We planned to incorporate the C14 hydroxyl into a substrate such as enone **18**, which was further simplified as **19**.[6a,b] Sequential conjugate addition and Robinson annulation starting from readily available **20**, **21**, and Me_3Al were expected to deliver this known compound more efficiently.

The synthesis commenced with the construction of tricycle **18** (Scheme 1). Asymmetric 1,4-addition [CuTC, (*R*,*S*,*S*)-**22**, Me_3Al] to **20** established the C16 stereochemistry;[6b] upon in situ activation with MeLi and HMPA, the enolate attacked Stork−Ganem reagent[15] **21** to give the α-silyl ketone. Treatment with NaOMe afforded **19** in 49% overall yield with 95% ee. This two-step protocol was superior to our previous one[6b] involving Stork−Jung vinylsilane[16] for the diastereoselectivity at C15 (>30:1 vs 3.8:1). **19** underwent a known three-step sequence to reach iodide **23**,[6a] which was converted to bis-enone **24** via silyl enol ether formation and IBX oxidation.[17] Luche cyclization (Zn, CuI) followed by epimerization at C22[6b] provided **18** smoothly.

We then prepared the common intermediate **17** from **18** (Scheme 1). Functionalization at C14 was effected by boron conjugate addition (CuCl, **25**, NaO*t*-Bu, B_2pin_2).[18] However, X-ray crystallographic analysis of the resultant boronate **26** revealed an undesired configuration of C14 (Scheme 1). Triflation of this ketone followed by oxidative cleavage of the C−B bond afforded alcohol **27**, which may find direct use in the synthesis of naturally occurring **5**.[3d] Sequential DMP oxidation and DIBAL-H reduction inverted the C14 stereochemistry. The resultant alcohol **28** was silylated with **29** and subjected to Pd-catalyzed methoxycarbonylation to generate ester **30**. Reduction and iodination (Ph_3P, I_2, imidazole) furnished allyl iodide **17**.

We moved forward to the synthesis of Prins substrate **12** (Scheme 2). Nozaki−Hiyama reaction of **17** with acetaldehyde furnished alcohol **31** as a single detectable diastereomer. Hydrogenation of the exocyclic olefin ($NaBH_4$, $NiCl_2$) proceeded with excellent facial selectivity to give **32**, the structure of which was confirmed by X-ray crystallographic analysis of its desilylated derivative (Scheme 2). TPAP oxidation furnished ketone **15**, which was converted into terminal alkyne **12** through triflation and TBAF-mediated elimination[14a] and desilylation.

Investigations of the Prins cyclization of **12** are summarized in Table 1. The combination of Bu_4NI and CSA[10e,11b−d,13a] failed to activate the acetal at 22 °C (entry 1) but decomposed the substrate at elevated temperature. Treatment with TMSI[13b] resulted in a complex mixture with a small amount of the desired product **11** (entry 2). In contrast to the commonly used Prins promoters $FeCl_3$ and $FeBr_3$,[13d−f] FeI_3 is unstable due to a self-redox reaction. Thus, we made recourse to the combination of $Fe(acac)_3$ and TMSI,[13g] and **11** was obtained in 43% yield (entry 3). Although $SnCl_4$ and $SnBr_4$ worked generally well in alkyne Prins cyclization,[13i−l] SnI_4 was ineffective in this case (entry 4). Exposure to TiI_4[13m−o] and AlI_3 in CH_2Cl_2 gave **11** in 32% and 51% yields (entries 5 and 6), respectively. Replacing CH_2Cl_2 with toluene improved the yield of the AlI_3-mediated cyclization to 68% (entry 7). GaI_3 was less efficient in this transformation (entry 8). Unfortunately, we could not identify the byproducts of these reactions. The discovery of AlI_3 as a powerful promoter for the Prins reaction may enable further applications of this transformation in synthesis.

The final stage of the synthesis of **6** is depicted in Scheme 2. Stille−Migita coupling of **11** with **33** gave compound **34**, which underwent Julia−Kocienski olefination to reach triene **10**. 6π electrocyclization of the triene occurred at 90 °C, and subsequent DDQ oxidation[9e] furnished arene **36** in 82% overall yield. Reductive cleavage of the benzyl ether ($TiCl_4$, Et_3SiH), followed by desulfonation with Mg, afforded **6**. Its structure was verified by X-ray crystallographic analysis (Scheme 2).

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Scheme 2. Completion of the Synthesis of 6

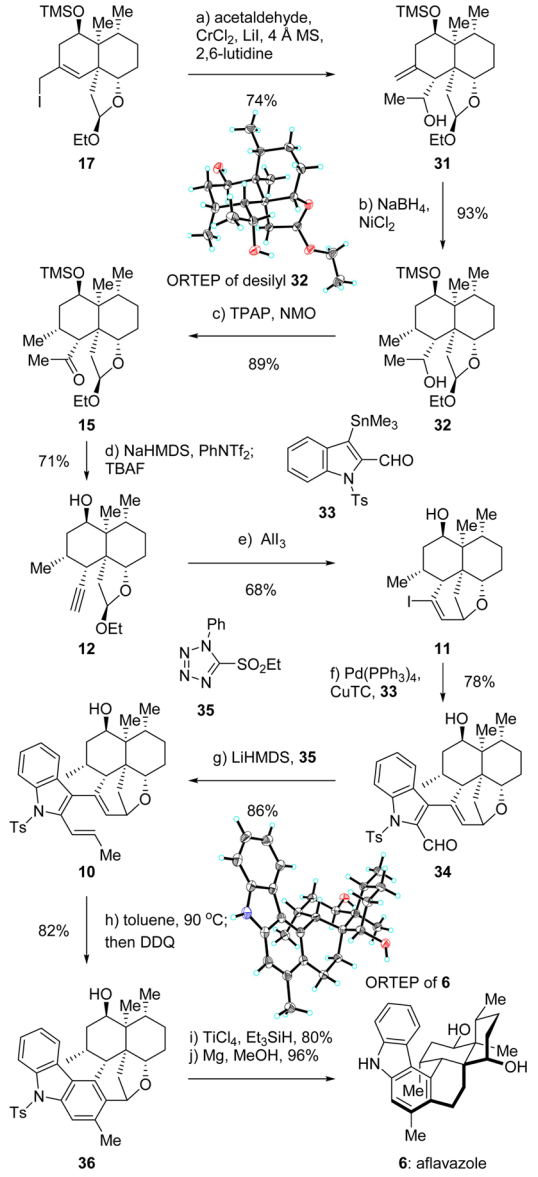
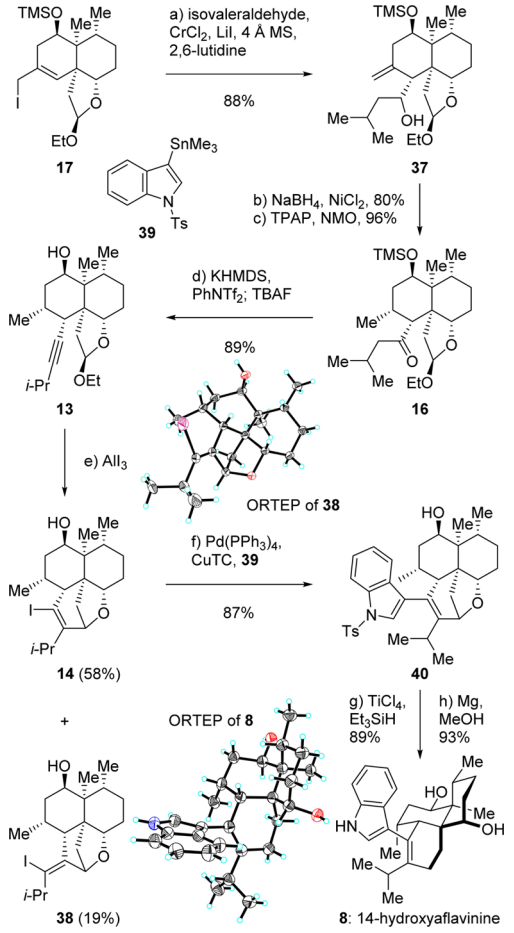


Table 1. Iodo-Prins Cyclization of 12

entry	conditions	**11** (%)
1	Bu_4NI (5 equiv), CSA (2 equiv), MeCN, 22 °C	0
2	TMSI (5 equiv), toluene, −10 °C	12
3	$Fe(acac)_3$ (20 mol %), TMSI (3 equiv), MeI, 22 °C	43
4	SnI_4 (6 equiv), CH_2Cl_2, 22 °C	0
5	TiI_4 (6 equiv), CH_2Cl_2, −40 °C	32
6	AlI_3 (6 equiv), CH_2Cl_2, −78 °C	51
7	AlI_3 (6 equiv), toluene, −78 °C	68
8	GaI_3 (6 equiv), toluene, −40 °C	42

We further studied the more challenging Prins reaction for the synthesis of **8** (Scheme 3). The common intermediate **17** was subjected to a similar sequence (vide supra) to give internal alkyne **13** via the intermediacy of **37** and **16**. The cyclization (AlI_3, toluene, −78 °C) proceeded smoothly to give a pair of regioisomers; the desired product **14** was isolated in 58% yield, along with its five-membered ring counterpart **38** (19% yield). Treatment of **13** with InI_3 altered the ratio of **14** and **38** (34% and 30% yields, respectively). **14** underwent sequential cross-coupling (with stannane **39**), C−O bond cleavage, and desulfonation to reach **8**. The structures of **38** and **8** were confirmed by X-ray crystallographic analysis (Scheme 3), respectively. The spectra and physical properties of synthetic **6** and **8** were identical to those reported for the natural products. Notably, the alkenyl triflates derived from ketones **15** and **16** performed poorly in Pd-catalyzed cross-coupling due to the rapid elimination to form the corresponding alkynes, respectively, which hampered the potential application of the alkene Prins cyclization strategy developed in our epoxyeujindole A synthesis to the syntheses of **6** and **8**.

Scheme 3. Completion of the Synthesis of 8



In summary, we accomplished the first total syntheses of aflavazole (**6**) and 14-hydroxyaflavinine (**8**), featuring a reversed bioinspired strategy and AlI_3-mediated alkyne Prins reactions. The chemistry developed may find further use in the construction of sterically congested ring systems and facilitate the biological and biosynthetic studies of the indole diterpenoids.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b10880.

Experimental procedures; compound characterization (PDF)

Crystallographic data (CIF, CIF, CIF, CIF, CIF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Selected recent syntheses of indole diterpenoids: (a) Zou, Y.; Melvin, J. E.; Gonzales, S. S.; Spafford, M. J.; Smith, A. B. *J. Am. Chem. Soc.* **2015**, *137*, 7095. (b) Sharpe, R. J.; Johnson, J. S. *J. Am. Chem. Soc.* **2015**, *137*, 4968. (c) George, D. T.; Kuenstner, E. J.; Pronin, S. V. *J. Am. Chem. Soc.* **2015**, *137*, 15410. (d) Enomoto, M.; Morita, A.; Kuwahara, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 12833.

(2) Gloer, J. B.; Rinderknecht, B. L.; Wicklow, D. T.; Dowd, P. F. *J. Org. Chem.* **1989**, *54*, 2530.

(3) (a) Gloer, J. B. *Acc. Chem. Res.* **1995**, *28*, 343. (b) TePaske, M. R.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *J. Org. Chem.* **1990**, *55*, 5299. (c) Gloer, J. B.; TePaske, M. R.; Sima, J. S.; Wicklow, D. T.; Dowd, P. F. *J. Org. Chem.* **1988**, *53*, 5457. (d) TePaske, M. R.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *Tetrahedron* **1989**, *45*, 4961. (e) Gallagher, R. T.; McCabe, T.; Hirotsu, K.; Clardy, J.; Nicholson, J.; Wilson, B. J. *Tetrahedron Lett.* **1980**, *21*, 243. (f) Nakadate, S.; Nozawa, K.; Yaguchi, T. *Heterocycles* **2011**, *83*, 1867.

(4) Danishefsky, S.; Chackalamannil, S.; Harrison, P.; Silvestri, M. *J. Am. Chem. Soc.* **1985**, *107*, 2474.

(5) (a) Bradshaw, B.; Etxebarria-Jardí, G.; Bonjoch, J. *J. Am. Chem. Soc.* **2010**, *132*, 5966. (b) Goetz, A. E.; Silberstein, A. L.; Corsello, M. A.; Garg, N. K. *J. Am. Chem. Soc.* **2014**, *136*, 3036.

(6) (a) Bian, M.; Wang, Z.; Xiong, X.; Sun, Y.; Matera, C.; Nicolaou, K. C.; Li, A. *J. Am. Chem. Soc.* **2012**, *134*, 8078. (b) Lu, Z.; Li, H.; Bian, M.; Li, A. *J. Am. Chem. Soc.* **2015**, *137*, 13764. (c) Sun, Y.; Li, R.; Zhang, W.; Li, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 9201. (d) Sun, Y.; Chen, P.; Zhang, D.; Baunach, M.; Hertweck, C.; Li, A. *Angew. Chem., Int. Ed.* **2014**, *53*, 9012. (e) Lu, Z.; Yang, M.; Chen, P.; Xiong, X.; Li, A. *Angew. Chem., Int. Ed.* **2014**, *53*, 13840. (f) Sun, Y.; Meng, Z.; Chen, P.; Zhang, D.; Baunach, M.; Hertweck, C.; Li, A. *Org. Chem. Front.* **2016**, *3*, 368. (g) Zhou, S.; Chen, H.; Luo, Y.; Zhang, W.; Li, A. *Angew. Chem., Int. Ed.* **2015**, *54*, 6878. (h) Meng, Z.; Yu, H.; Li, L.; Tao, W.; Chen, H.; Wan, M.; Yang, P.; Edmonds, D. J.; Zhong, J.; Li, A. *Nat. Commun.* **2015**, *6*, 6096. (i) Li, Y.; Zhu, S.; Li, J.; Li, A. *J. Am. Chem. Soc.* **2016**, *138*, 3982.

(7) 20-Hydroxyaflavinine (**8**) is renamed 14-hydroxyaflavinine by us for consistency with the unified numbering system of the anominine family.

(8) (a) Qin, H.-L.; Lowe, J. T.; Panek, J. S. *J. Am. Chem. Soc.* **2007**, *129*, 38. For allylic C−O bond cleavage, see: (b) Mack, D. J.; Guo, B.; Njardarson, J. T. *Chem. Commun.* **2012**, *48*, 7844.

(9) Syntheses of natural products by us using electrocyclization: (a) Lu, Z.; Li, Y.; Deng, J.; Li, A. *Nat. Chem.* **2013**, *5*, 679. (b) Li, J.; Yang, P.; Yao, M.; Deng, J.; Li, A. *J. Am. Chem. Soc.* **2014**, *136*, 16477. (c) Yang, M.; Li, J.; Li, A. *Nat. Commun.* **2015**, *6*, 6445. (d) Yang, M.; Yang, X.; Sun, H.; Li, A. *Angew. Chem., Int. Ed.* **2016**, *55*, 2851. (e) Yang, P.; Yao, M.; Li, J.; Li, Y.; Li, A. *Angew. Chem., Int. Ed.* **2016**, *55*, 6964. For more examples from other groups, see the references in ref 9e.

(10) Selected reviews of Prins reaction: (a) Pastor, I. M.; Yus, M. *Curr. Org. Chem.* **2007**, *11*, 925. (b) Pastor, I. M.; Yus, M. *Curr. Org. Chem.* **2012**, *16*, 1277. (c) Olier, C.; Kaafarani, M.; Gastaldi, S.; Bertrand, M. P. *Tetrahedron* **2010**, *66*, 413. (d) Snider, B. B. Prins Reactions and Carbonyl, Imine, and Thiocarbonyl Ene Reactions. In *Comprehensive Organic Synthesis II*; Knochel, P., Molander, G. A., Eds.; Elsevier: Amsterdam, 2014; Vol. 2, pp 148−191. (e) Franklin, A. S.; Overman, L. E. *Chem. Rev.* **1996**, *96*, 505. (f) Overman, L. E.; Pennington, L. D. *J. Org. Chem.* **2003**, *68*, 7143. (g) Crane, E. A.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2010**, *49*, 8316. (h) Han, X.; Peh, G.; Floreancig, P. E. *Eur. J. Org. Chem.* **2013**, *2013*, 1193.

(11) Selected syntheses of natural products using Prins reaction: (a) MacMillan, D. W. C.; Overman, L. E. *J. Am. Chem. Soc.* **1995**, *117*, 10391. (b) Overman, L. E.; Robinson, L. A.; Zablocki, J. *J. Am. Chem. Soc.* **1992**, *114*, 368. (c) Caderas, C.; Lett, R.; Overman, L. E.; Rabinowitz, M. H.; Robinson, L. A.; Sharp, M. J.; Zablocki, J. *J. Am. Chem. Soc.* **1996**, *118*, 9073. (d) Lin, N.-H.; Overman, L. E.; Rabinowitz, M. H.; Robinson, L. A.; Sharp, M. J.; Zablocki, J. *J. Am. Chem. Soc.* **1996**, *118*, 9062. (e) Kopecky, D. J.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2001**, *123*, 8420. (f) Bahnck, K. B.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2008**, *130*, 13177. (g) Ruggeri, R. B.; Hansen, M. M.; Heathcock, C. H. *J. Am. Chem. Soc.* **1988**, *110*, 8734. (h) LaCour, T. G.; Guo, C.; Bhandaru, S.; Boyd, M. R.; Fuchs, P. L. *J. Am. Chem. Soc.* **1998**, *120*, 692. (i) Hanessian, S.; Tremblay, M.; Petersen, J. F. W. *J. Am. Chem. Soc.* **2004**, *126*, 6064. (j) Lee, H. M.; Nieto-Oberhuber, C.; Shair, M. D. *J. Am. Chem. Soc.* **2008**, *130*, 16864. (k) Fortner, K. C.; Kato, D.; Tanaka, Y.; Shair, M. D. *J. Am. Chem. Soc.* **2010**, *132*, 275. (l) Nishimura, T.; Unni, A. K.; Yokoshima, S.; Fukuyama, T. *J. Am. Chem. Soc.* **2011**, *133*, 418. (m) Chen, Z.-H.; Tu, Y.-Q.; Zhang, S.-Y.; Zhang, F.-M. *Org. Lett.* **2011**, *13*, 724. (n) Lin, H.-Y.; Snider, B. B. *Org. Lett.* **2011**, *13*, 1234. (o) Ruider, S. A.; Sandmeier, T.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2015**, *54*, 2378. (p) Millán, A.; Smith, J. R.; Chen, J. L. Y.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2016**, *55*, 2498. (q) Ma, D.; Zhong, Z.; Liu, Z.; Zhang, M.; Xu, S.; Xu, D.; Song, D.; Xie, X.; She, X. *Org. Lett.* **2016**, *18*, 4328. Also see refs 6b−f for our contribution.

(12) Hussain, M.; Tùng, T. Đ.; Langer, P. *Synlett* **2009**, *2009*, 1822.

(13) Selected examples of alkyne Prins reaction: (a) Overman, L. E.; Sharp, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 612. (b) Takami, K.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Synlett* **2001**, 293. (c) Chavre, S. N.; Choo, H.; Lee, J. K.; Pae, A. N.; Kim, Y.; Cho, Y. S. *J. Org. Chem.* **2008**, *73*, 7467. (d) Miranda, P. O.; Díaz, D. D.; Padrón, J. I.; Bermejo, J.; Martín, V. S. *Org. Lett.* **2003**, *5*, 1979. (e) Miranda, P. O.; Ramírez, M. A.; Martín, V. S.; Padrón, J. I. *Org. Lett.* **2006**, *8*, 1633. (f) Carballo, R. M.; Ramírez, M. A.; Rodríguez, M. L.; Martín, V. S.; Padrón, J. I. *Org. Lett.* **2006**, *8*, 3837. (g) Miranda, P. O.; Carballo, R. M.; Martín, V. S.; Padrón, J. I. *Org. Lett.* **2009**, *11*, 357. (h) Balog, A.; Geib, S. V.; Curran, D. P. *J. Org. Chem.* **1995**, *60*, 345. (i) Lolkema, L. D. M.; Hiemstra, H.; Semeyn, C.; Speckamp, W. N. *Tetrahedron* **1994**, *50*, 7115. (j) Metais, E.; Overman, L. E.; Rodriguez, M. I.; Stearns, B. A. *J. Org. Chem.* **1997**, *62*, 9210. (k) Jaber, J. J.; Mitsui, K.; Rychnovsky, S. D. *J. Org. Chem.* **2001**, *66*, 4679. (l) Hanessian, S.; Tremblay, M.; Marzi, M.; Del Valle, J. R. *J. Org. Chem.* **2005**, *70*, 5070. (m) Melany, M. L.; Lock, G. A.; Thompson, D. W. *J. Org. Chem.* **1985**, *50*, 3925. (n) Kim, Y.-H.; Lee, K.-Y.; Oh, C.-Y.; Yang, J.-G.; Ham, W.-H. *Tetrahedron Lett.* **2002**, *43*, 837. (o) Shimizu, M.; Baba, T.; Toudou, S.; Hachiya, I. *Chem. Lett.* **2007**, *36*, 12. (p) Yadav, J. S.; Thrimurtulu, N.; Lakshmi, K. A.; Prasad, A. R.; Reddy, B. V. S. *Tetrahedron Lett.* **2010**, *51*, 661.

(14) (a) Okutani, M.; Mori, Y. *Chem. Pharm. Bull.* **2015**, *63*, 393. (b) Yang, X.; Wu, D.; Lu, Z.; Sun, H.; Li, A. *Org. Biomol. Chem.* **2016**, *14*, 5591.

(15) (a) Stork, G.; Ganem, B. *J. Am. Chem. Soc.* **1973**, *95*, 6152. (b) Boeckman, R. K. *J. Am. Chem. Soc.* **1973**, *95*, 6867.

(16) Stork, G.; Jung, M. E. *J. Am. Chem. Soc.* **1974**, *96*, 3682.

(17) Nicolaou, K. C.; Gray, D. L. F.; Montagnon, T.; Harrison, S. T. *Angew. Chem., Int. Ed.* **2002**, *41*, 996.

(18) (a) Lee, K.-S.; Zhugralin, A. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2009**, *131*, 7253. (b) Marcus, A. P.; Sarpong, R. *Org. Lett.* **2010**, *12*, 4560.

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