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Asymmetric Total Synthesis of (−)-Guignardones A and B

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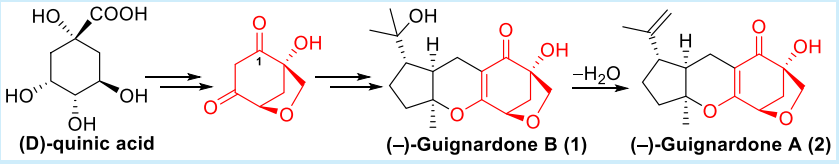

ABSTRACT: The asymmetric total synthesis of (−)-guignardones A (**2**) and B (**1**) has been accomplished. The highly oxidized 6-oxabicyclo[3.2.1]octane core was constructed from D-quinic acid via substitution/desulfurization reaction with thiophenol to forge the bridged ring scaffold, and a Pummerer rearrangement and 1,4-addition/elimination sequence was employed to install the β-carbonyl group at the congested C-1 position. A late-stage Knoevenagel condensation−6π-electrocyclization and directed hydrogenation formed (−)-guignardone B (**1**), which was subjected to dehydration to furnish (−)-guignardone A (**2**).

The 6-oxabicyclo[3.2.1] octane framework was first found in the natural products guignardones A−C, isolated by Tan and co-workers from the cultures of *Guignardia mangiferae* IFB-GLP-4, which are associated with the normal *Ilex cornuta* leaves, in 2010.[1] (Figure 1) Other members of this family of

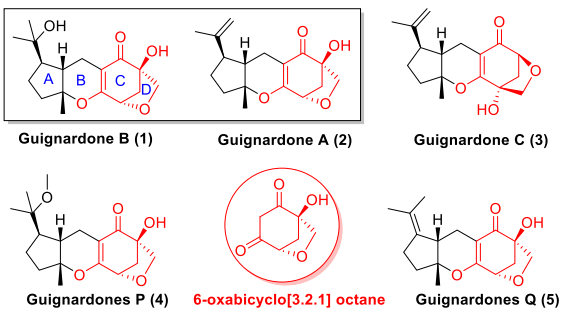

Figure 1. 6-Oxabicyclo[3.2.1] octane core fragment and structures of guignardones A (**2**) and B (**1**) and related natural products (**3**−**5**).

natural products were isolated[2] and found to possess the 6-oxabicyclo[3.2.1]octane core in common, which contains an oxygen on the bridged carbon center. More than 12 types of these tetracyclic meroterpenes have been isolated until now, and some of them exhibited interesting bioactivities, such as antibacterial[2a,d] and TLR3-regulating activities,[2b] cytotoxicity aginst MCF-7 cell lines,[2e] and inhibitory activity for *Candida albicans*. Guignardone B (**1**) exhibited the most potent inhibition of the growth of *Candida albicans* with an MIC value of 0.05 μM.[2d]

Structurally, guignardones A (**2**) and B (**1**) feature tricycloalternarenes (TCAs)[3] with an additional bridging tetrahydrofuran ring D, which possesses a highly oxidized 6-oxabicyclo[3.2.1]octane bearing a 1,3-diketone and a bridgehead hydroxyl group. The relatively uncommon structure of these tetracyclic meroterpenes attracted our interest for conducting the total synthesis of **2** and **1**. Recently, Ito and co-workers reported the first asymmetric total synthesis of tricyclic guignardones H (**6**) and I (**7**) by employing Knoevenagel condensation−6π-electrocyclization with the unsaturated aldehyde **8** and a novel 1,3-cyclohexanedione **9**, followed by a chemo- and stereoselective directed hydrogenation as the key steps and realized the construction of the A/B/C ring of guignardones (Figure 2a).[4] However, tetracyclic

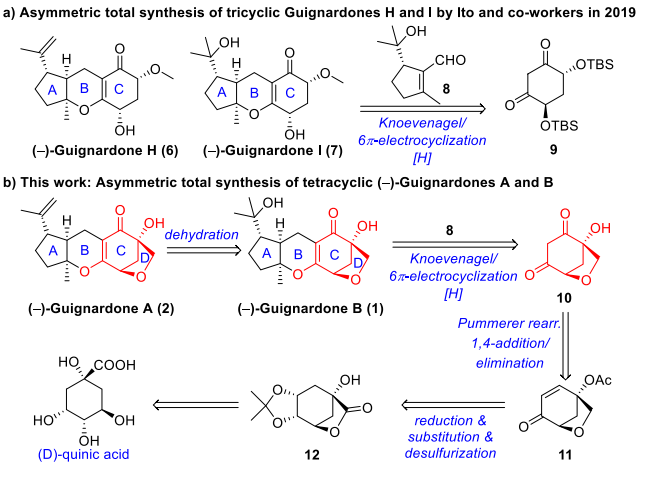

Figure 2. Total synthesis of guignardones.

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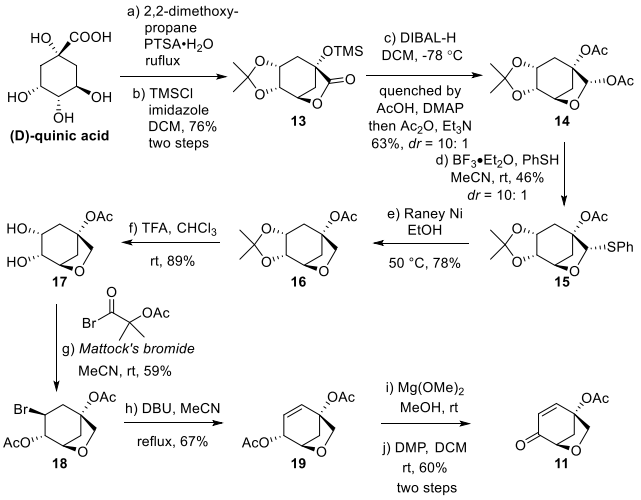
guignardones featuring the 6-oxabicyclo[3.2.1]octane core fragment remain full of synthetic challenges, and no related studies have been reported. Herein, we report the first asymmetric total synthesis of (−)-guignardones A (**2**) and B (**1**).

The retrosynthetic analysis for the total synthesis of (−)-guignardones A (**2**) and B (**1**) is delineated in Figure 2b. (−)-Guignardone A (**2**) could be obtained from (−)-guignardone B (**1**) by dehydration. We also envisioned that the B ring of (−)-guignardone B (**1**) could be formed through Knoevenagel condensation−6π-electrocyclization[5] with the known unsaturated aldehyde **8**[4] and the 1,3-cyclohexanedione **10**, followed by a chemo- and stereoselective directed hydrogenation.[4] On the other hand, 1,3-cyclohexanedione **10** could be obtained from enone **11** by α-hydrogen elimination type Pummerer rearrangement[6] and 1,4-addition/elimination for installing the β-carbonyl group at the congested C-1 position.[7] We envisioned access to enone **11** through reduction, substitution,[8] and desulfurization[9] of lactone **12**. Finally, lactone **12** could be derived from the commercially available chiral pool[10] D-quinic acid by lactonization.

Our synthetic studies began with the preparation of lactone **13** by lactonization and *cis* diol protection[11] of D-quinic acid in the presence of PTSA·H_2O, followed by the protection of the tertiary alcohol with a trimethylsilyl group, to afford **13** in 76% yield. The lactone **13** was subjected to DIBAL-H reduction in toluene at low temperature and was quenched with AcOH to remove the trimethylsilyl group. Bisacetylation delivered **14**,[12] which upon treatment with thiophenol in the presence of 1 equiv of BF_3·Et_2O[8] afforded the thiosemiacetal **15** in 46% yield as a 10:1 diastereomeric mixture. Subsequent desulfurization of **15** by treatment with Raney nickel in ethanol at 50 °C[9a] proceeded smoothly to provide the precursor 6-oxabicyclo[3.2.1]octane **16** in moderate yield. Deprotection of **16** in the presence of excess TFA provided diol **17** in 89% yield, and the use of excess Mattock's bromide[13] in dry MeCN converted the *cis* diol group to *trans* bromoacetate **18**, which upon treatment with DBU in hot MeCN led to the elimination of bromide, providing allylic diacetate **19** in good yield. With **19** in hand, in order to afford the unprotected secondary allylic alcohol, magnesium methoxide[14] was used to chemoselectively remove the acetyl group from the secondary allylic hydroxyl, rather than from the tertiary hydroxyl group. Finally, Dess−Martin oxidation[15] was employed to achieve the allylic oxidation for preparing the desired enone **11** (Scheme 1).

The strategy for constructing the corresponding cyclic 1,3-diketone derivatives starting from cyclic substrates was proven to be difficult in congested bridged or spiro ring systems.[16,17] With the requisite enone **11** in hand, we investigated an epoxidation/ring-opening sequence strategy[5d,18] and studied the typical silyl conjugate addition−Tamao oxidation approaches[7,19] and allylic oxidation strategy[16] to introduce the β-carbonyl group. However, none of those conditions were successful, probably due to the instability of enone **11** under strongly alkaline conditions and the high steric congestion at the C-1 position.[7] We considered that the C-1 position could be oxidized by an efficient rearrangement based on a previous report that carried out the conversion of a sulfoxide to a vinyl sulfide utilizing the α-hydrogen elimination type Pummerer rearrangement.[6] The thiocarbonyl compound **20** could be obtained by Michael addition between the enone **11** and thiophenol in the presence of a weak base.[20] The protection of

Scheme 1. Synthesis of 6-Oxabicyclo[3.2.1]octane 16 and Enone 11[a]



[a]Reagents and conditions: (a) 2,2-dimethylpropane (4.0 equiv), PTSA·H_2O (0.1 equiv), acetone, reflux, 7 h, 92%; (b) imidazole (2.0 equiv), TMSCl (1.5 equiv), DCM, rt, 6 h, 95%; (c) DIBAL-H (1.1 equiv), DCM, −78 °C, 1 h; then AcOH (20 equiv), −78 °C to rt, DMAP (1.0 equiv), H_2O (10 equiv), overnight; then Et_3N (30 equiv), Ac_2O (8.0 equiv), 3 h, 63%, dr = 10:1; (d) PhSH (1.1 equiv), BF_3·OEt_2 (1.2 equiv), MeCN, 0 °C to rt, 6 h, 46%, dr = 10:1; (e) Raney-Ni (50 μm in H_2O, excess), EtOH, 50 °C, 5 h, 78%; (f) TFA (20.0 equiv), $CHCl_3$, 0 °C to rt, 5 h, 89%; (g) Mattock's bromide (2.0 equiv), dry MeCN, 0 °C to rt, 3.5 h, 59%; (h) DBU (2.5 equiv), MeCN, rt to reflux, 5 h, 67%; (i) $Mg(OMe)_2$ (8.0 equiv), MeOH, rt, 4 h; (j) DMP (1.6 equiv), DCM, rt, 2 h, 60% two steps. PTSA·H_2O = *p*-toluenesulfonic acid monohydrate, DCM = dichloromethane, DIBAL-H = diisobutylaluminum hydride, TMS = trimethylsilyl, DMAP = 4-dimethylaminopyridine, TFA = trifluoroacetic acid, Mattock's bromide = 1-bromo-2-methyl-1-oxopropan-2-yl acetate, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DMP = Dess−Martin periodinane.

the carbonyl group of **20** with ethane-1,2-diol was required to prevent the occurrence of elimination in the next step, involving H_2O_2 (30% in H_2O) for the conversion of **21**[21,6d] to the sulfoxide **22** (86% yield). The sulfoxide **22** was then treated with pyridine and trifluoroacetic anhydride (TFAA), which led to the almost exclusive formation of the corresponding vinyl sulfide by α-hydrogen elimination,[6] which was followed by the HCl-mediated 1,2-diol deprotection to afford the vinyl sulfide carbonyl compound **23** in 95% yield. Next, we needed to oxidize the sulfur group to the sulfoxide to increase its ability to undergo a displacement, which was achieved by treatment with LiH in cold MeOH followed by acidification and delivered the target 1,3-cyclohexanedione 6-oxabicyclo[3.2.1]octane **10** via the Michael addition of methoxide and the elimination of sulfoxide[7] followed by the deprotection. Overall, the asymmetric construction of 6-oxabicyclo[3.2.1]octane **10** was completed with this synthetic sequence (Scheme 2).

In the latter stage of the synthetic route, we first investigated various hetero-Diels−Alder conditions for the reaction of 1,3-cyclohexanedione **10**, formaldehyde, and the simple unactivated olefins (1-methylcyclopent-1-ene derivatives), such as the use of L-proline catalysis,[22a] hydroquinone catalysis,[22b] and $Cu(OAc)_2$ catalysis,[22c] to construct the B ring of guignardone B (**1**). Unfortunately, 1,3-cyclohexanedione **10** decomposed

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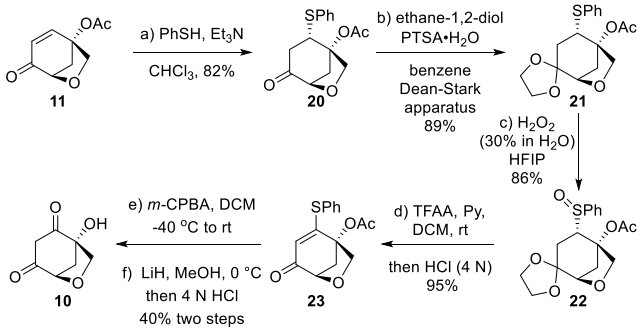
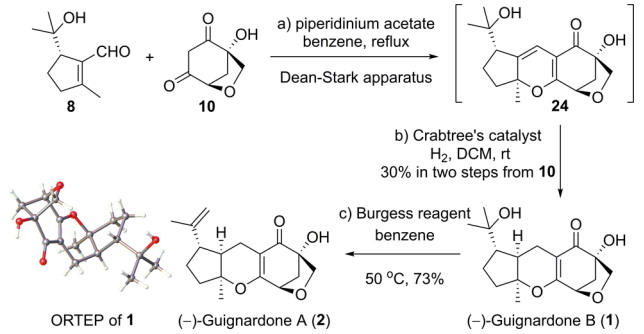
Scheme 2. Synthesis of 1,3-Cyclohexanedione 6-Oxabicyclo[3.2.1]octane 10[a]



[a]Reagents and conditions: (a) PhSH (1.1 equiv), Et_3N (1.2 equiv), $CHCl_3$, rt, 3 h, 82%; (b) ethane-1,2-diol (10 equiv), PTSA·H_2O (0.1 equiv), benzene, reflux, 5 h, 89%; (c) H_2O_2 (2.0 equiv, 30 ω% in H_2O), HFIP, rt, 2 h, 86%; (d) pyridine (10.0 equiv), TFAA (5.0 equiv), DCM, rt, 2 h; then 4 N HCl, 95%; (e) *m*-CPBA (1.1 equiv, ω = 85%), DCM, −40 °C to rt, 4 h; (f) LiH (5.0 equiv), dry MeOH, 0 °C, 3 h; then 4 N HCl, 0 °C to rt, 40% two steps. HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol, Py = pyridine, TFAA = trifluoroacetic anhydride, *m*-CPBA = 3-chloroperoxybenzoic acid.

under these heating conditions. Next, we synthesized the known unsaturated aldehyde **8** from (−)-limonene in five steps[4] and employed intermolecular Knoevenagel condensation to combine the aldehyde **8** and 1,3-cyclohexanedione **10**, which set the stage for the key 6π-electrocyclization (Scheme 3). The resulting crude tetracyclic compound **24** was refluxed

Scheme 3. Asymmetric Total Synthesis of (−)-Guignardones A (2) and B (1)[a]



[a]Reagents and conditions: (a) **10** (1.0 equiv), **8** (1.2 equiv), piperidinium acetate (1.0 equiv), benzene, reflux with Dean−Stark apparatus under argon atmosphere, 4 h; (b) Crabtree's catalyst (0.5 equiv), H_2, DCM, rt, 5 h, 30% in two steps from **10**; (c) Burgess reagent (2 equiv), benzene, 50 °C, 3 h, 73%. Crabtree's catalyst = (1,5-cyclooctadiene)(pyridine)(tricyclohexylphosphine)iridium(I) hexafluorophosphate, Burgess reagent = (methoxycarbonylsulfamoyl)-triethylammonium hydroxide inner salt.

under Dean−Stark conditions in benzene, in the presence of piperidinium acetate, to remove the generated water. Next, the chemo- and stereoselective directed hydrogenation of compound **24**, directed using the tertiary alcohol of the left wing, was carried out using Crabtree's catalyst[4,23] in DCM at room temperature and successfully afforded (−)-guignardone B (**1**) in 30% yield in two steps from 1,3-cyclohexanedione **10**. The structure of the prepared **1** was verified by X-ray crystallography, and optical rotation ($[\alpha]_D^{25}$= −65, *c* = 0.76 in acetone; isolated (+)-guignardone B (**1**), $[\alpha]_D^{20}$= +67, c = 0.76 in acetone).[1] Finally, Burgess reagent-mediated[4,24] dehydration of (−)-guignardone B (**1**) delivered (−)-guignardone A (**2**) in 73% yield ($[\alpha]_D^{25}$= −35, *c* = 0.30 in acetone; isolated (+)-guignardone A (**1**), $[\alpha]_D^{20}$= +42, *c* = 0.30 in acetone).[1]

In conclusion, we completed the asymmetric total synthesis of (−)-guignardones A (**2**) and B (**1**). The key features of convergent synthetic approach included (i) construction of the highly oxidized 6-oxabicyclo[3.2.1]octane core fragment by a substitution/desulfurization reaction with thiophenol; (ii) installation of the β-carbonyl group at the congested C-1 position utilizing α-hydrogen elimination type Pummerer rearrangement and 1,4-addition/elimination in the 6-oxabicyclo[3.2.1]octane; and (iii) Knoevenagel condensation−6π-electrocyclization and chemo-/stereoselective directed hydrogenation to afford (−)-guignardone B (**1**), followed by dehydration to prepare (−)-guignardone A (**2**). On the basis of this synthetic approach, total syntheses of other guignardones and related challenging molecules are currently underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c00241.

Experimental procedures and characterization data for all new compounds (PDF)

Accession Codes

CCDC 1969699 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Yuan, W. H.; Liu, M.; Jiang, N.; Guo, Z. K.; Ma, J.; Zhang, J.; Song, Y. C.; Tan, R. X. *Eur. J. Org. Chem.* **2010**, *2010*, 6348.

(2) (a) Mei, W.-L.; Zheng, B.; Zhao, Y.-X.; Zhong, H.-M.; Chen, X.-L. W.; Zeng, Y.-B.; Dong, W.-H.; Huang, J.-L.; Proksch, P.; Dai, H.-F. *Mar. Drugs* **2012**, *10*, 1993. (b) Han, W. B.; Dou, H.; Yuan, W. H.; Gong, W.; Hou, Y. Y.; Ng, S. W.; Tan, R. X. *Planta Med.* **2015**, *81*, 145. (c) Bai, Z.-Q.; Lin, X.; Wang, J.; Zhou, X.; Liu, J.; Yang, B.; Yang, X.; Liao, S.; Wang, L.; Liu, Y. *Mar. Drugs* **2015**, *13*, 237. (d) Li, T.-X.; Yang, M.-H.; Wang, X.-B.; Wang, Y.; Kong, L.-Y. *J. Nat. Prod.* **2015**, *78*, 2511. (e) Sun, Z.-H.; Liang, F.-L.; Wu, W.; Chen, Y.-C.; Pan, Q.-L.; Li, H.-H.; Ye, W.; Liu, H.-X.; Li, S.-N.; Tan, G.-H.; Zhang, W.-M. *Molecules* **2015**, *20*, 22900.

(3) (a) Kono, Y.; Gardner, J. M.; Suzuki, Y.; Kondo, H.; Takeuchi, S. *J. Pestic. Sci.* **1989**, *14*, 223. (b) Liebermann, B.; Ellinger, R.; Günther, W.; Ihn, W.; Gallander, H. *Phytochemistry* **1997**, *46*, 297. (c) Nussbaum, R.-P.; Günther, W.; Heinze, S.; Liebermann, B. *Phytochemistry* **1999**, *52*, 593. (d) Liebermann, B.; Nussbaum, R.-P.; Günther, W. *Phytochemistry* **2000**, *55*, 987. (e) Liebermann, B.; Nussbaum, R.-P.; Günther, W.; Teuscher, J.-M. *Phytochemistry* **2001**, *56*, 551.

(4) Kobayashi, T.; Takizawa, I.; Shinobe, A.; Kawamoto, Y.; Abe, H.; Ito, H. *Org. Lett.* **2019**, *21*, 3008.

(5) (a) Hsung, R. P.; Kurdyumov, A. V.; Sydorenko, N. *Eur. J. Org. Chem.* **2005**, *2005*, 23. (b) Malerich, J. P.; Maimone, T. J.; Elliott, G. I.; Trauner, D. *J. Am. Chem. Soc.* **2005**, *127*, 6276. (c) Riveira, M. J.; Quiroga, G. N.; Mata, E. G.; Gandon, V.; Mischne, M. P. *J. Org. Chem.* **2015**, *80*, 6515. (d) Schuppe, A. W.; Zhao, Y.; Liu, Y.; Newhouse, T. R. *J. Am. Chem. Soc.* **2019**, *141*, 9191.

(6) (a) Mukherjee, A.; Jayaraman, N. *Tetrahedron* **2012**, *68*, 8746. (b) Saint-Dizier, F.; Simpkins, N. S. *Chem. Sci.* **2017**, *8*, 3384. (c) Kumamoto, H.; Imoto, S.; Amano, M.; Kuwata-Higashi, N.; Baba, M.; Mitsuya, H.; Odanaka, Y.; Matsubayashi, S. S.; Tanaka, H.; Haraguchi, K. *ACS Med. Chem. Lett.* **2018**, *9*, 1211. (d) Tao, Z.; Robb, K. A.; Zhao, K.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 3569.

(7) Shimizu, Y.; Shi, S.-L.; Usuda, H.; Kanai, M.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 1103.

(8) (a) Dunkel, R.; Hoffmann, H. M. R. *Tetrahedron* **1999**, *55*, 8385. (b) Parent, J.-F.; Deslongchamps, P. *Org. Biomol. Chem.* **2016**, *14*, 11183. (c) Blaukopf, M.; Atamanyuk, D.; Xavier, N.; Gerusz, V.; Kosma, P. *Synthesis* **2017**, *49*, 5320. (d) Dey, S.; Lo, H.-J.; Wong, C.-H. *J. Am. Chem. Soc.* **2019**, *141*, 10309.

(9) (a) Herrera, A.; Martínez-Alvarez, R.; Ramiro, P.; Molero, D.; Almy, J. *J. Org. Chem.* **2006**, *71*, 3026. (b) Rentner, J.; Kljajic, M.; Offner, L.; Breinbauer, R. *Tetrahedron* **2014**, *70*, 8983.

(10) (a) Brill, Z. G.; Condakes, M. L.; Ting, C. P.; Maimone, T. J. *Chem. Rev.* **2017**, *117*, 11753. (b) Li, F.; Tu, Q.; Chen, S.; Zhu, L.; Lan, Y.; Gong, J.; Yang, Z. *Angew. Chem., Int. Ed.* **2017**, *56*, 5844. (c) Zhang, P.-P.; Yan, Z.-M.; Li, Y.-H.; Gong, J.-X.; Yang, Z. *J. Am. Chem. Soc.* **2017**, *139*, 13989. (d) Han, Y.-X.; Jiang, Y.- L.; Li, Y.; Yu, H.-X.; Tong, B.-Q.; Niu, Z.; Zhou, S.-J.; Liu, S.; Lan, Y.; Chen, J.-H.; Yang, Z. *Nat. Commun.* **2017**, *8*, 14233.

(11) (a) Trost, B. M.; Romero, A. G. *J. Org. Chem.* **1986**, *51*, 2332. (b) Federspiel, M.; Fischer, R.; Hennig, M.; Mair, H. J.; Oberhauser, T.; Rimmler, G.; Albiez, T.; Bruhin, J.; Estermann, H.; Gandert, C.; Gockel, V.; Gotzo, S.; Hoffmann, U.; Huber, G.; Janatsch, G.; Lauper, S.; Rockel-Stabler, O.; Trussardi, R.; Zwahlen, A. G. *Org. Process Res. Dev.* **1999**, *3*, 266. (c) Li, M.; Li, Y.; Ludwik, K. A.; Sandusky, Z. M.; Lannigan, D. A.; O'Doherty, G. A. *Org. Lett.* **2017**, *19*, 2410.

(12) Belanger, F.; Chase, C. E.; Endo, A.; Fang, F. G.; Li, J.; Mathieu, S. R.; Wilcoxen, A. Z.; Zhang, H. *Angew. Chem., Int. Ed.* **2015**, *54*, 5108.

(13) (a) Greenberg, S.; Moffatt, J. G. *J. Am. Chem. Soc.* **1973**, *95*, 4016. (b) Wood, H. B.; Ganem, B. *J. Am. Chem. Soc.* **1990**, *112*, 8907. (c) Guidot, J. P.; Gall, T. L. *J. Org. Chem.* **1993**, *58*, 5271. (d) Shie, J.-J.; Fang, J.-M.; Wong, C.-H. *Angew. Chem., Int. Ed.* **2008**, *47*, 5788.

(14) Xu, Y.-C.; Bizuneh, A.; Walker, C. *J. Org. Chem.* **1996**, *61*, 9086.

(15) (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. (b) Nagata, H.; Kawamura, M.; Ogasawara, K. *Synthesis* **2000**, *2000*, 1825.

(16) (a) Elkin, M.; Szewczyk, S. M.; Scruse, A. C.; Newhouse, T. R. *J. Am. Chem. Soc.* **2017**, *139*, 1790. (b) Yang, M.; Yin, F.; Fujino, H.; Snyder, S. A. *J. Am. Chem. Soc.* **2019**, *141*, 4515. (c) Sparling, B. A.; Moebius, D. C.; Shair, M. D. *J. Am. Chem. Soc.* **2013**, *135*, 644.

(17) King, S. M.; Calandra, N. A.; Herzon, S. B. *Angew. Chem., Int. Ed.* **2013**, *52*, 3642.

(18) (a) Inouye, Y.; Kojima, T.; Owada, J.; Kakisawa, H. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 4369. (b) Desmaéle, D.; d'Angelo, J. *J. Org. Chem.* **1994**, *59*, 2292. (c) Sharp, M. J.; Fang, F. G. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3291. (d) Cole, K. P.; Hsung, R. P. *Org. Lett.* **2003**, *5*, 4843. (e) Muchalski, H.; Xu, L.; Porter, N. A. *Org. Biomol. Chem.* **2015**, *13*, 1249.

(19) (a) Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, *29*, 29. (b) Yu, G.; Clive, D. L. J. *Org. Biomol. Chem.* **2016**, *14*, 1653.

(20) (a) Groot, A. D.; Peperzak, R. M.; Vader, J. *Synth. Commun.* **1987**, *17*, 1607. (b) Biechy, A.; Hachisu, S.; Quiclet-Sire, B.; Ricard, L.; Zard, S. Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 1436.

(21) (a) Ravikumar, K. S.; Bégué, J.-P.; Bonnet-Delpon, D. *Tetrahedron Lett.* **1998**, *39*, 3141. (b) Li, X.; Carter, R. G. *Org. Lett.* **2018**, *20*, 5546. (c) Rautschek, J.; Jager, A.; Metz, P. *Org. Lett.* **2018**, *20*, 832.

(22) (a) Wei, L.; Xiao, M.; Xie, Z. *Org. Lett.* **2014**, *16*, 2784. (b) Hoffmann, H. M. R.; Koser, S. *Heterocycles* **1994**, *37*, 661. (c) Krause, M.; Hoffmann, H. M. R. *Tetrahedron Lett.* **1990**, *31*, 6629.

(23) (a) Crabtree, R. H. *Acc. Chem. Res.* **1979**, *12*, 331. (b) Crabtree, R. H.; Davis, M. W. *J. Org. Chem.* **1986**, *51*, 2655.

(24) (a) Atkins, G. M.; Burgess, E. M. *J. Am. Chem. Soc.* **1968**, *90*, 4744. (b) Burgess, E. M.; Penton, H. R.; Taylor, E. A. *J. Am. Chem. Soc.* **1970**, *92*, 5224.