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Communication

Total Syntheses of Scabrolide A and Yonarolide

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ABSTRACT: The concise total syntheses of oxidized norcembranoid terpenoids (−)-scabrolide A and (−)-yonarolide have been accomplished in 10 and 11 steps, respectively. The carbocyclic skeleton was efficiently constructed from two chiral-pool-derived fragments, including a [5,5]-bicyclic lactone accessed through a powerful Ni-catalyzed pentannulation of functionalized cyclopentenone with methylenecyclopropane and subsequent fragmentation. Additional features included a Liebeskind−Srogl coupling, induction of a cyclization/elimination cascade by a zinc-amido base, and installation of a sensitive enedione motif by late-stage γ-oxidation.

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As a rich source of cytotoxic terpenoids, soft corals of the Caribbean Sea have provided inspiration to synthetic chemists and chemical biologists in recent decades.[1] (−)-Yonarolide (**1**) and (−)-scabrolide A (**2**) (Figure 1a) are representative members of a class of norcembranoid diterpenoids first isolated in 1995 from *Sinularia*.[2] Although poor isolation yields have precluded thorough evaluation of their biological activity, preliminary studies have indicated that **2** has anticancer and anti-inflammatory properties. Additionally, several close congeners are known to demonstrate cytotoxic effects.[3] Interest in further exploration of their observed biological activity merits the development of an efficient synthetic strategy to access **1** and **2**. These compounds also possess noteworthy structural features, including a unique all-*cis* stereochemical arrangement surrounding the central cyclohexene core and a rich oxidative decoration of the carbon framework. Both **1** and **2** have resisted synthetic efforts for decades; only recently have the Stoltz and Fürstner laboratories disclosed their approaches leading to the first total syntheses of (−)-scabrolide A (**2**).[4]

Motivated by their topological complexity and demand for further biological studies, we sought to develop an efficient synthetic route to **1** and **2** featuring a [5,5]-bicyclic lactone, a conserved motif found in several members of the norcembranoid family.[5,6] Herein, we report an annulation/fragmentation strategy that enables access to this core in only five steps from readily available material and its application to the total syntheses of (−)-yonarolide (**1**) and (−)-scabrolide A (**2**).

In our retrosynthetic analysis, it was readily apparent that (−)-yonarolide (**1**) could be derived from (−)-scabrolide A (**2**) through dehydration (Figure 1b). We envisioned installing the sensitive 1,4-dicarbonyl motif at the end of the synthesis through γ-oxidation of tetracycle **3**, which could be constructed from [5,5]-bicyclic lactone **4** and cycloheptenyl fragment **5**. Installation of proelectrophilic and pronucleophilic functional handles on **4** and **5** would be necessary for their convergent coupling. Bicyclic lactone **4** could be accessed via a [3 + 2]-annulation between Maimone's enone (**6**)[7] and methylene cyclopropane (MCP). Lastly, enones **6** and **7** could both be derived from readily available chiral pool materials.[8]

Our initial synthetic efforts focused on annulation strategies to access bicyclic lactone **4** from enone **6**. A annulation method reported by Noyori et al.[9] and further developed by Binger et al. (Scheme 1a),[10] which provides complementary regioselectivity to palladium-catalyzed trimethylenemethane (TMM) cycloaddition chemistry,[11] seemed well suited to this goal. It was reported that cyclopentenone (**8**) undergoes annulation with methylenecyclopropane (**9**) under nickel catalysis to deliver annulated product **10**. Although diastereoselectivity was a concern for our system, we were pleased to note that, (1) in cases of Lewis acid-mediated conjugate additions to protected γ-hydroxycyclopentenones, additions are known to occur on the more sterically encumbered face of the olefin[12] and that (2) the annulation strategy employs triethylborane as a Lewis acid. Therefore, we hypothesized that this annulation method could be successfully translated to functionalized cyclopentenone **6**.

Indeed, when compound **6** was subjected to Binger et al.'s reported conditions,[10] the annulation adduct **11** was obtained as a single diastereomer resulting from *syn*-addition relative to the sterically bulky t-butyldimethylsilyl ether (OTBS) group on the γ-carbon (Scheme 1b). Although these conditions provided irreproducible yields of adduct **11** in 40−60% yield, the desired compound could be reliably accessed in 75% yield after optimization (see the Supporting Information for full details). First, an alternative procedure for the synthesis of volatile MCP (**9**) was adopted for consistent titer and ease of operation (Scheme 1c).[13] Second, use of P(*m*-Tol)$_3$ as a ligand improved the stability and reactivity of the active nickel catalyst. Additional experiments revealed the necessity of

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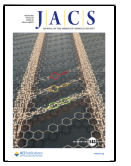

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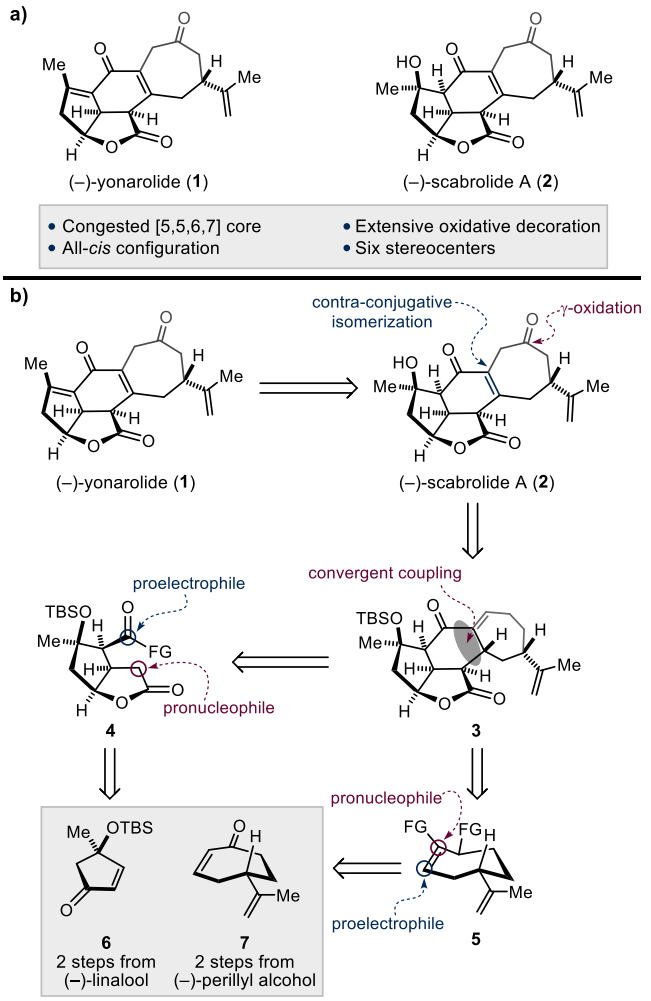


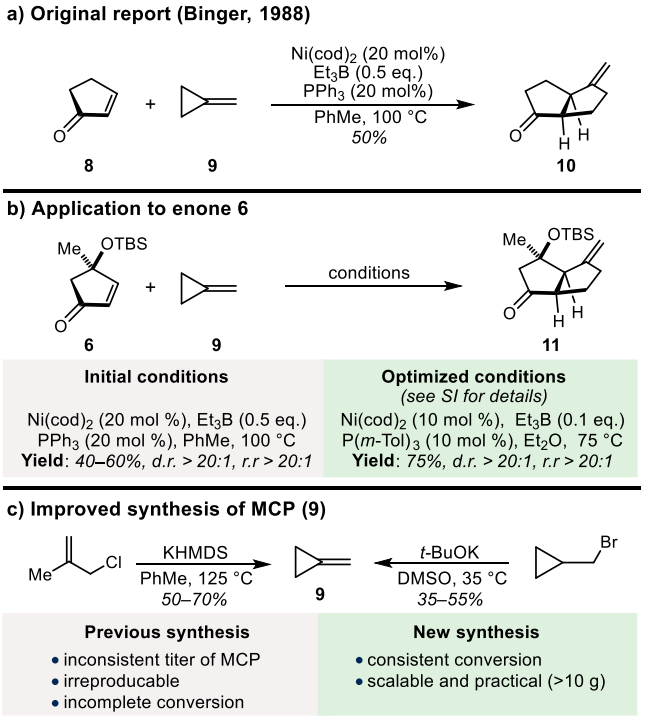
Figure 1. (a) Structures of (−)-yonarolide (**1**) and (−)-scabrolide A (**2**). (b) Retrosynthetic analysis.

triethylborane as an additive for electrophile activation. Finally, catalyst loadings of the nickel source and triethylborane were lowered to 10 mol % without erosion of yield. The optimized protocol routinely afforded multigram quantities of bicycle **11**.

Sharpless allylic oxidation[14] of **11** followed by treatment with ruthenium tetroxide[15] afforded diacid **12** (Scheme 2a). Reduction and careful acidification led to *in situ* lactonization. Finally, Steglich thioesterification[16] afforded thioester **13** in multigram quantities. With scalable access to the western fragment achieved, we turned our attention to constructing the cycloheptenyl coupling partner from **7**, which is available in 2 steps from commercial (*S*)-perillyl alcohol.[17] Our intended coupling strategy required installation of both an allylic electrophile and a vinyl nucleophile in fragment **15**. To this end, α-iodination[18] followed by Luche reduction[19] afforded alcohol **14**, and subsequent etherification secured the appropriate allylic nucleofuge. Finally, sequential lithium−halogen exchange and trapping with tributyltin chloride provided vinyl stannane **15**.

The stage was then set for the convergent assembly of the carbon skeleton. We hypothesized that formation of the C-6/C-7 linkage followed by base-mediated cyclization would provide the central ring with the requisite all-*cis* stereochemical configuration. Liebeskind−Srogl coupling[20] afforded tricycle **16** in 89% yield on gram scale. We then investigated C-12/C-13 cyclization through an addition/elimination sequence (see the Supporting Information for details). Initial screening of standard amide bases yielded trace conversion to **3** (Scheme 2b). We speculated that a metal additive could promote the desired coupling by chelating the central ketone at C-6 and the proximal PMB-ether, thereby enforcing a reactive conformation for cyclization. The addition of zinc and magnesium salts improved reactivity but provided inconsistent yields. Control experiments indicated that premixing zinc iodide with two equivalents of LDA was necessary, which suggests that a bis-amidozinc base may be operative under the reaction conditions.[21] The developed protocol was reliable on gram scale and allowed access to tetracycle **3** in 53% yield as a single diastereomer. The stereochemistry at C-12 and C-13 was confirmed with X-ray crystallography.

Scheme 1. Optimization of Ni-Catalyzed Annulation



With the carbon framework fully assembled, we next pursued oxidative decoration of the core. Initial attempts to install the 1,4-dicarbonyl with chromium oxidants[22] and traditional allylic oxidation conditions[23] resulted in decomposition or trace conversion (see Scheme 2c and the Supporting Information for details). Therefore, we adopted a two-step oxidative sequence to access the desired enedione. While Rubottom oxidation produced intractable mixtures,[24] aerobic oxidation under mild basic conditions provided the α-hydroxy ketone **17** in 59% yield as a single diastereomer.[25] The accompanying olefin migration was likely driven by release of ring strain in the eastern hemisphere of the tetracyclic core. Though the stereochemistry of the hydroxyl group could not be assigned with NMR spectroscopy, it was rendered inconsequential by subsequent oxidative transposition. Standard chromium-mediated conditions and oxoammonium salts[26] provided the desired 1,4-dicarbonyl in variable yield (Scheme 2d). The observed variability was likely a consequence of product instability. Additional screening revealed that PCC absorbed on SiO_2[27] reliably provided the desired enedione in 70% yield.

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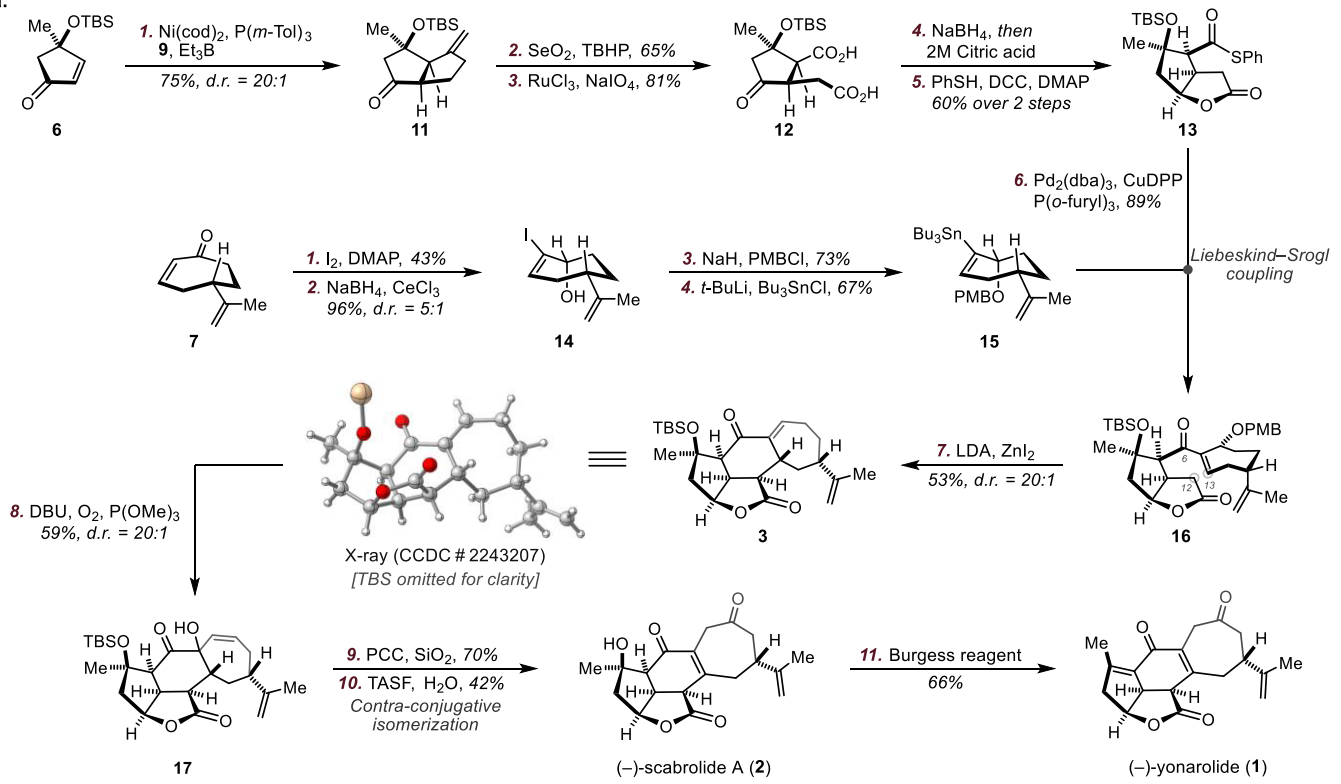
Scheme 2. Syntheses of Yonarolide (1) and (−)-Scabrolide A (2)

a.



b. 7. Cyclization		c. 8. Oxidation		d. 9. Oxidative transposition		e. 10. Deprotection	
(1) MHDS (M = Na, K)	decomp.	(1) CrO_3, 3,5-DMP	10%	(1) PCC	26–55%	(1) TBAF, THF	elimination
(2) LDA or LHMDS	5–10%	(2) $Mn(OAc)_3$, TBHP	decomp.	(2) PCC, NaOAc	40%	(2) TBAF, AcOH	no reaction
(3) LDA, $ZnCl_2$	30–40%	(3) $Pd(OH)_2$, TBHP	decomp.	**(3) PCC, SiO_2**	**70%**	(3) TASF, DMF	elimination
(4) LDA, ZnI_2	**53%**	(4) $Rh_2(cap)_4$, TBHP	decomp.	(4) PDC	32%	(4) TASF, H_2O (1:2)	17%
(5) LDA, $MgBr_2$	decomp.	**(5) DBU, O_2, $P(OMe)_3$**	**59%**	(5) Bobbitt's salt	no reaction	**(5) TASF, H_2O (1:10)**	**42%**

The final deprotection proved to be challenging because the β-siloxy ether was prone to undergo elimination in both acidic and basic conditions (Scheme 2e). Ultimately, TASF/H_2O[28] afforded (−)-scabrolide A (**2**) in 42% yield through concurrent deprotection/isomerization. Spectroscopic analysis of our synthetic sample matched spectral data from the natural isolate, as well as data provided by Fürstner and Stoltz.[4] Our synthetic strategy enabled preparation of (−)-scabrolide A (**2**) in batches >20 mg at a time. Furthermore, (−)-yonarolide (**1**) was obtained in 66% yield by treating (−)-scabrolide A (**2**) with Burgess reagent.[29]

Efficient total syntheses of (−)-scabrolide A (**2**) and (−)-yonarolide (**1**) were achieved in 10 and 11 steps (longest linear sequence), respectively, from enone **6**. Our synthetic strategy featured a powerful pentannulation with MCP to establish two key stereocenters in a single operation. This method, which has not seen prior use in total synthesis, is analogous to classical TMM-cycloaddition, but synergy between a Lewis acid and nickel catalyst achieved orthogonal regio- and diastereoselectivity. The carbon skeleton was constructed as a single diastereomer from a tandem cyclization/elimination cascade, and the desired natural products were accessed through subsequent chemoselective oxidations. We believe our reported strategy will contribute to future synthetic efforts toward the remaining members in the norcembranoids class of natural products.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.3c02317.

Experimental section including supporting crystallographic information, characterization data, and NMR spectra of new compounds (PDF)

Accession Codes

CCDC 2243207 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) (a) Li, Y.; Pattenden, G. Novel macrocyclic and polycyclic norcembranoid diterpenes from *Sinularia* species of soft coral: Structural relationships and biosynthetic speculations. *Nat. Prod. Rep.* **2011**, *28*, 429−440. (b) Li, Y.; Pattenden, G. Biomimetic syntheses of ineleganolide and sinulochmodin C from 5-episinuleptolide via sequences of transannular Michael reactions. *Tetrahedron* **2011**, *67* (51), 10045−10052.

(2) For isolations, see: (a) Iguchi, K.; Kajiyama, K.; Yamada, K. Yonarolide: a new marine norditerpenoid possessing a novel tricyclic skeleton, from the Okinawan soft coral of the genus, *Sinularia*. *Tetrahedron Lett.* **1995**, *36* (48), 8807−8808. (b) Sheu, J.; Ahmed, F.; Shiue, R.; Dai, C.; Kuo, Y. Scabrolides A-D, Four New Norditerpenoids Isolated from the Soft Coral *Sinularia scabra*. *J. Nat. Prod.* **2002**, *65* (12), 1904−1908. (c) Cui, W.-X.; Yang, M.; Li, H.; Li, S.-W.; Yao, L.-G.; Li, G.; Tang, W.; Wang, C.-H.; Liang, L.-F.; Guo, Y.-W. Polycyclic furanobutenolide-derived norditerpenoids from the South China Sea soft corals *Sinularia scabra* and *Sinularia polydactyla* with immunosuppressive activity. *Bioorganic Chemistry* **2020**, *94*, 103350. (d) Du, Y.; Yao, L.; Li, X.; Guo, Y. Yonarolide A, an unprecedented furanobutenolide-containing norcembranoid derivative formed by photoinduced intramolecular [2 + 2] cycloaddition. *Chin. Chem. Lett.* **2023**, *34* (2), 107512.

(3) Marrero, J.; Rodriguez, A. D.; Baran, P.; Raptis, R. G.; Sanchez, J.; Ortega-Barria, E.; Capson, T. Bielschowskysin, a Gorgonian-Derived Biologically Active Diterpene with an Unprecedented Carbon Skeleton. *Org. Lett.* **2004**, *6* (10), 1661−1664.

(4) For previous syntheses, see: (a) Hafeman, N.; Loskot, S.; Reimann, C.; Pritchett, B.; Virgil, S.; Stoltz, B. M. The Total Synthesis of (−)-Scabrolide A. *J. Am. Chem. Soc.* **2020**, *142* (19), 8585−8590. (b) Meng, Z.; Fürstner, A. Total Syntheses of Scabrolide A and Nominal Scabrolide B. *J. Am. Chem. Soc.* **2022**, *144* (4), 1528−1533.

(5) Craig, R. A., II; Stoltz, B. M. Polycyclic Furanobutenolide-Derived Cembranoid and Norcembranoid Natural Products: Biosynthetic Connections and Synthetic Efforts. *Chem. Rev.* **2017**, *117* (12), 7878−7909.

(6) For recent syntheses of closely related cembranoids and norcembranoids, see: (a) Tuccinardi, J. P.; Wood, J. L. Total Syntheses of (+)-Ineleganolide and (−)-Sinulochmodin C. *J. Am. Chem. Soc.* **2022**, *144* (44), 20539−20547. (b) Truax, N. J.; Ayinde, S.; Liu, J. O.; Romo, D. Total Synthesis of Rameswaralide Utilizing a Pharmacophore-Directed Retrosynthetic Strategy. *J. Am. Chem. Soc.* **2022**, *144* (40), 18575−18585. (c) Scesa, P.; Wangpaichitr, M.; Savaraj, N.; West, L.; Roche, S. P. A Kinetic Dearomatization Strategy for an Expedient Biomimetic Route to the Bielschowskysin Skeleton. *Angew. Chem., Int. Ed.* **2018**, *57* (5), 1316−1321.

(7) Brill, Z.; Grover, H.; Maimone, T. Enantioselective synthesis of an ophiobolin sesterterpene via a programmed radical cascade. *Science* **2016**, *352*, 1078−1082.

(8) Brill, Z. G.; Condakes, M. L.; Ting, C. P.; Maimone, T. J. Navigating the Chiral Pool in the Total Synthesis of Complex Terpene Natural Products. *Chem. Rev.* **2017**, *117* (18), 11753−11795.

(9) Noyori, R.; Odagi, T.; Takaya, H. Nickel(0)-catalyzed reaction of methylenecyclopropanes with olefins. A novel [σ2+π2] cycloaddition. *J. Am. Chem. Soc.* **1970**, *92* (19), 5780−5781.

(10) Binger, P.; Schafer, B. 6-methylen-bicyclo[3.3.0]octan-2-one durch nickel(0)-katalysierte [3 + 2]cycloaddition von methylencyclopropanen mit 2-cyclopentenon. *Tetrahedron Lett.* **1988**, *29* (36), 4539−4542.

(11) Yamago, S.; Nakamura, E. [3 + 2] Cycloaddition of Trimethylenemethane and its Synthetic Equivalents. *Org. React.* **2002**, *61*, 1.

(12) For Diels−Alder, see: (a) Jeroncic, L. O.; Cabal, M.; Danishefsky, S. J.; Shulte, G. M. On the diastereofacial selectivity of Lewis acid-catalyzed carbon-carbon bond forming reactions of conjugated cyclic enones bearing electron-withdrawing substituents at the.gamzma.-position. *J. Org. Chem.* **1991**, *56* (1), 387−395. (b) see also ref 4b. For Mukaiyama−Michael, see: (c) Danishefsky, S. J.; Paz Cabal, M.; Chow, K. Novel stereospecific silyl group transfer reactions: practical routes to the prostaglandins. *J. Am. Chem. Soc.* **1989**, *111* (9), 3456−3457. For Sakurai allylation, see: (d) Michalak, K.; Wicha, J. A convenient preparation of (S)-(−)-4-hydroxy-2-methylcyclopent-2-en-1-one and its application as a chiral synthetic equivalent of 2-methylcyclopent-2-en-1-one in the terpenoid synthesis. *Tetrahedron* **2014**, *70* (34), 5073−5081.

(13) (a) Salaun, J. R.; Champion, J.; Conia, J. M. Cyclobutanone from Methylenecyclopropane via Oxaspiropentane. *Org. Synth.* **1977**, *57*, 36. (b) Binger, P.; Brinkmann, A.; Wedemann, P. Highly Efficient Synthesis of Methylenecyclopropane. *Synthesis* **2002**, *2002* (10), 1344−1346. (c) LeFevre, G.; Crawford, R. J. Kinetics of some methylenecyclopropane rearrangements. *J. Org. Chem.* **1986**, *51* (5), 747−749.

(14) Umbreit, M.; Sharpless, K. B. Allylic oxidation of olefins by catalytic and stoichiometric selenium dioxide with tert-butyl hydroperoxide. *J. Am. Chem. Soc.* **1977**, *99* (16), 5526−5528.

(15) Carlsen, P. H.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. A greatly improved procedure for ruthenium tetroxide catalyzed oxidations of organic compounds. *J. Org. Chem.* **1981**, *46* (19), 3936−3938.

(16) Neises, B.; Steglich, W. Simple Method for the Esterification of Carboxylic Acids. *Angew. Chem., Int. Ed. Engl.* **1978**, *17* (7), 522−524.

(17) (a) Barney, R.; Richardson, M.; Wiemer, D. F. Direct Conversion of Benzylic and Allylic Alcohols to Phosphonates. *J. Org. Chem.* **2011**, *76* (8), 2875−2879. (b) Yang, P.; Yao, M.; Li, J.; Li, Y.; Li, A. Total Synthesis of Rubriflordilactone B. *Angew. Chem., Int. Ed.* **2016**, *55*, 6964−6968.

(18) Ohshima, T.; Xu, Y.; Takita, R.; Shimizu, S.; Zhong, D.; Shibasaki, M. Enantioselective Total Synthesis of (−)-Strychnine Using the Catalytic Asymmetric Michael Reaction and Tandem Cyclization. *J. Am. Chem. Soc.* **2002**, *124* (49), 14546−14547.
(19) Gemal, A. L.; Luche, J. L. Lanthanoids in organic synthesis. 6. Reduction of α−enones by sodium borohydride in the presence of lanthanoid chlorides: synthetic and mechanistic aspects. *J. Am. Chem. Soc.* **1981**, *103* (18), 5454−5459.
(20) (a) Li, H.; Yang, H.; Liebeskind, L. Synthesis of High Enantiopurity N-Protected α-Amino Ketones by Thiol Ester−Organostannane Cross-Coupling Using pH-Neutral Conditions. *Org. Lett.* **2008**, *10* (19), 4375−4378. (b) Ferrié, L.; Fenneteau, J.; Figadère, B. Total Synthesis of the Marine Macrolide Amphidinolide F. *Org. Lett.* **2018**, *20* (11), 3192−3196.
(21) (a) Hlavinka, M.; Hagadorn, J. $Zn(tmp)_2$: A Versatile Base for the Selective Functionalization of C−H Bonds. *Organometallics* **2007**, *26* (17), 4105−4108. (b) Rohbogner, C. J.; Wunderlich, S.; Clososki, G.; Knochel, P. New Mixed Li/Mg and Li/Mg/Zn Amides for the Chemoselective Metallation of Arenes and Heteroarenes. *Eur. J. Org. Chem.* **2009**, *2009* (11), 1781−1795.
(22) Salmond, W.; Barta, M. A.; Havens, J. Allylic oxidation with 3,5-dimethylpyrazole. Chromium trioxide complex steroidal.DELTA.5−7-ketones. *J. Org. Chem.* **1978**, *43* (10), 2057−2059.
(23) (a) Catino, A. J.; Forslund, R. E.; Doyle, M. P. Dirhodium(II) Caprolactamate: An Exceptional Catalyst for Allylic Oxidation. *J. Am. Chem. Soc.* **2004**, *126* (42), 13622−13623. (b) Yu, J.-Q.; Corey, E. J. A Mild, Catalytic, and Highly Selective Method for the Oxidation of α,β-Enones to 1,4-Enediones. *J. Am. Chem. Soc.* **2003**, *125* (11), 3232−3233. (c) Shing, T. K. M.; Yeung, Y.-Y.; Su, P. L. Mild Manganese(III) Acetate Catalyzed Allylic Oxidation: Application to Simple and Complex Alkenes. *Org. Lett.* **2006**, *8* (14), 3149−3151.
(24) (a) Brooke, A. G.; Macrae, D. M. 1,4-Silyl rearrangements of siloxyalkenes to siloxyketones during peroxidation. *J. Organomet. Chem.* **1974**, *77* (2), 19−21. (b) Rubottom, G. M.; Gruber, J. M.; Boeckman, R. K., Jr; Ramaiah, M.; Medwid, J. B. Clarification of the mechanism of rearrangement of enol silyl ether epoxides. *Tetrahedron Lett.* **1978**, *19* (47), 4603−4606.
(25) Schuppe, A.; Newhouse, T. Assembly of the Limonoid Architecture by a Divergent Approach: Total Synthesis of (±)-Andirolide N via (±)-8α-Hydroxycarapin. *J. Am. Chem. Soc.* **2017**, *139* (2), 631−634.
(26) (a) Dauben, W.; Michno, D. Direct oxidation of tertiary allylic alcohols. A simple and effective method for alkylative carbonyl transposition. *J. Org. Chem.* **1977**, *42* (4), 682−685. (b) Shibuya, M.; Tomizawa, M.; Iwabuchi, Y. Oxidative Rearrangement of Tertiary Allylic Alcohols Employing Oxoammonium Salts. *J. Org. Chem.* **2008**, *73* (12), 4750−4752.
(27) Luzzio, F.; Fitch, R.; Moore, W.; Mudd, K. A Facile Oxidation of Alcohols Using Pyridinium Chlorochromate/Silica Gel. *J. Chem. Educ.* **1999**, *76* (7), 974.
(28) Scheidt, K.; Bannister, T.; Tasaka, A.; Wendt, M.; Savall, B.; Fegley, G.; Roush, W. R. Total Synthesis of (−)-Bafilomycin A_1. *J. Am. Chem. Soc.* **2002**, *124* (24), 6981−6990.
(29) Atkins, G. M., Jr.; Burgess, E. M. The reactions of an N-sulfonylamine inner salt. *J. Am. Chem. Soc.* **1968**, *90* (17), 4744−4745.

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