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Concise Total Syntheses of (+)-Strictifolione and (6*R*)-6-[(4*R*,6*R*)-4,6-Dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one

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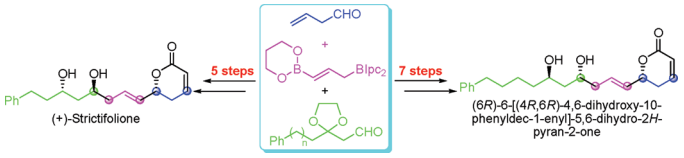

Concise and efficient asymmetric total syntheses of (+)-strictifolione **1** and (6*R*)-6-[(4*R*,6*R*)-4,6-dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one **2** have been achieved based on the strategic application of one-pot double allylboration and ring-closing metathesis reactions. The total syntheses proceeded in only five and seven steps, respectively, from readily available 3-butenal and represent the shortest syntheses of **1** and **2** reported to date.

Introduction

Natural products possessing α-pyrone (α,*β*-unsaturated-*δ*-lactone) moieties often exhibit useful pharmacological properties, which include antifungal, antitumor, antibacterial, and antigrowth effects.[1,2] The broad range of biological activities reported for this class of compounds has been ascribed to their inherent tendency to act as good Michael acceptors. (+)-Strictifolione **1** (Figure 1), an example of this class of natural products, was isolated by Aimi et al. from the stem bark of *Cryptocaria strictifolia* that grows in the Indonesian tropical rainforests and has been shown to display antifungal activity.[3] The relative and absolute stereochemistries of **1** were proposed based on spectroscopic analysis and revised by the same group after accomplishing its first total synthesis.[4] To date, four more asymmetric syntheses and a formal synthesis have been reported, with Cossy's route being the most efficient and shortest in literature (nine steps beginning with 3-phenylproprionaldehyde).[5]

(6*R*)-6-[(4*R*,6*R*)-4,6-Dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one **2** is also one such natural product,[6] isolated from *Ravensara crassifolia* by Hostetmann et al. along with a structurally similar compound (6*S*)-5,6-dihydro-6-[(2*R*)-2-hydroxy-6-phenylhexyl]-2*H*-pyran-2-one **3**,[7] which were both shown to possess antifungal activity (Figure 1).

(1) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94.
(2) (a) Yoshida, T.; Koizumi, K.; Kawamura, Y.; Matsumoto, K.; Itazaki, H. Japan Patent Kokai 5-310726, 1993. (b) Kobayashi, S.; Tsuchiya, K.; Harada, T.; Nishide, M.; Kurokawa, T.; Nakagawa, T.; Shimada, N.; Kobayashi, K. *J. Antibiot.* **1994**, *47*, 697. (c) Kobayashi, S.; Tsuchiya, K.; Kurokawa, T.; Nakagawa, T.; Shimada, N.; Iitaka, Y. *J. Antibiot.* **1994**, *47*, 703. (d) Drewes, S. E.; Schlapelo, B. M.; Horn, M. M.; Scott-Shaw, R.; Sander, O. *Phytochemistry* **1995**, *38*, 1427. (e) Yasui, K.; Tamura, Y.; Nakatani, T.; Kawada, K.; Ohtani, M. *J. Org. Chem.* **1995**, *60*, 7567. (f) Tsuchiya, K.; Kobayashi, S.; Nishikiori, T.; Nakagawa, T.; Tatsuta, K. *J. Antibiot.* **1997**, *50*, 259. (g) Kobayashi, M.; Higuchi, K.; Murakami, N.; Tajima, H.; Aoki, S. *Tetrahedron Lett.* **1997**, *38*, 2859. (h) Jodynis-Licbert, J.; Murias, M.; Bloszyik, E. *Planta Med.* **2000**, *66*, 199. (i) Pereda-Miranda, R.; Fragoso-Serrano, M.; Cerda-García-Rojas, C. M. *Tetrahedron* **2001**, *57*, 47. (j) Carda, M.; Rodríguez, S.; Segovia, B.; Marco, J. A. *J. Org. Chem.* **2002**, *67*, 6560. (k) Dumonter, V.; Van Hung, N.; Adeline, M. T.; Riche, C.; Chiaroni, A.; Sévenet, T.; Guéritte, F. *J. Nat. Prod.* **2004**, *67*, 858.
(3) Juliawaty, L. D.; Kitajima, M.; Takayama, H.; Achmad, S. A.; Aimi, N. *Phytochemistry* **2000**, *54*, 989.
(4) Juliawaty, L. D.; Watanabe, Y.; Kitajima, M.; Takayama, H.; Achmad, S. A.; Takayama, H.; Aimi, N. *Tetrahedron Lett.* **2002**, *43*, 8657.
(5) (a) Bouz, B. S.; Cossy, J. *Org. Lett.* **2003**, *5*, 1995. (b) Tosaki, S.-Y.; Nemoto, T.; Ohshima, T.; Shibaski, M. *Org. Lett.* **2003**, *5*, 495. (c) Enders, D.; Lenzen, A.; Muller, M. *Synthesis* **2004**, 1486. (d) Ramana, C. V.; Raghupathi, N.; Gurjara, M. K.; Chorghade, M. S. *Tetrahedron Lett.* **2005**, *46*, 4073. (e) Sabitha, G.; Fatima, N.; Gopal, P.; Nagendra Reddy, C.; Yadav, J. S. *Tetrahedron: Asymmetry* **2009**, *20*, 184.
(6) Raoelison, G. E.; Terreaux, C.; Queiroz, E. F.; Zsila, F.; Simonyi, M.; Antus, S.; Randriantsova, A.; Hostettmann, K. *Helv. Chim. Acta* **2001**, *84*, 3470.
(7) (a) Chandrasekhar, S.; Narsihmulu, Ch.; Sultana, S.; Srinivasa Reddy, M. *Tetrahedron Lett.* **2004**, *45*, 9299. (b) Sabitha, G.; Srinivas, C.; Sudhakar, K.; Rajkumar, M.; Maruthi, C.; Yadav, J. S. *Synthesis* **2007**, 3886. (c) Krishna, P. R.; Srinivas, R. *Tetrahedron: Asymmetry* **2007**, *18*, 2197. (d) Narasimhulu, M.; Krishna, A. S.; Rao, J. V.; Venkateswarlu, Y. *Tetrahedron* **2009**, *65*, 2989. (e) Das, B.; Laxminarayana, K.; Krishnaiah, M.; Kumar, D. N. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 6396. (f) Yadav, J. S.; Chandrakanth, D.; Rao, Y. G.; Ravindar, K.; Reddy, B. V. S. *Helv. Chim. Acta* **2010**, *93*, 1432.

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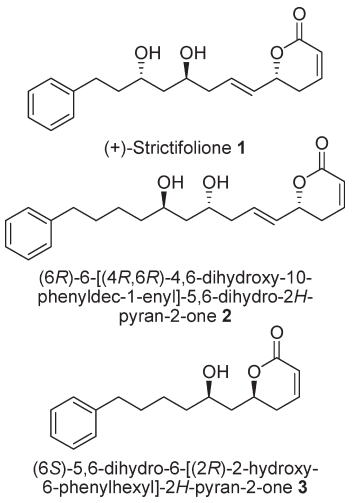


FIGURE 1. Structures of **1**, **2**, and **3**.

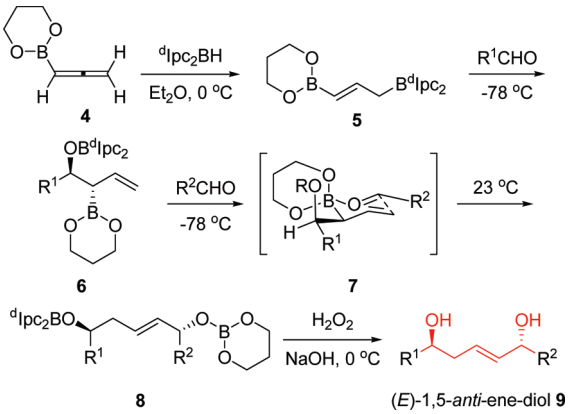
Later, the first total synthesis of **2** by iterative Jacobsen's hydrolytic kinetic resolutions was accomplished by Krishna et al. (17 steps).[8] Recently, another synthetic approach toward **2** using a combination of prins and olefin cross-metathesis reactions was displayed by Sabitha et al. (11 steps).[5e]

In context of our research in the synthesis of 6-substituted α-pyrones, several of these natural products have been reported by our group.[9] Combined with our interest aiming for ideal synthesis of natural products via a multicomponent reaction strategy,[9d,10,11] herein we describe the concise and efficient total syntheses of (+)-strictifolione **1** and (6*R*)-6-[(4*R*,6*R*)-4,6-dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one **2** with a powerful one-pot double allylboration reaction[12] and a ring-closing metathesis reaction (RCM)[13] as the key steps.

Results and Discussion

Structurally, (+)-strictifolione **1** is a 6-substituted α-pyrone embodying an (*E*)-1,5-*anti*-ene-diol subunit. The novel one-pot double allylboration reaction reported by Roush and co-workers in 2002 for the enantio- and diastereoselective synthesis of 1,5-diol seemed to be an ideal method for preparation of this fragment.[12] As shown in Scheme 1, allylboration of aldehyde with the boryl-substituted allylborane **5**, generated in situ by hydroboration of 2-allenyl-(1,3,2)-dioxaborinane **4** with diisopinocampheylborane (Ipc_2BH), gave the β-alkoxyallylboronate intermediate **6**, which subsequently reacted with a second aldehyde to produce allylboronate **8** with control over the equatorial nature of the

SCHEME 1. One-Pot Double Allylboration Reaction



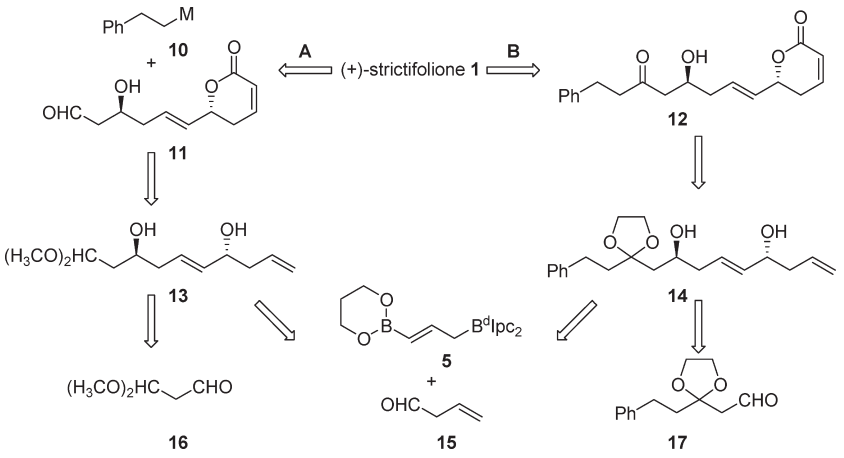
substituent α to boron in the second allylboration transition state **7**. After oxidation with H_2O_2, (*E*)-1,5-*anti*-ene-diol **9** could be obtained in high diastereo- and enantioselectivity.

First-Generation Synthesis of (+)-Strictifolione 1. The retrosynthetic analysis of (+)-strictifolione **1** is outlined in Scheme 2 (route A and route B). Our initial synthetic plan (route A) sought to complete the total synthesis of (+)-strictifolione **1** by the addition of alkyl metal species **10** to aldehyde **11**, which could be realized by several functional group transformations and the RCM reaction from intermediate (*E*)-1,5-*anti*-ene-diol **13**. The key intermediate (*E*)-1,5-*anti*-ene-diol **13** was proposed to be generated by the one-pot double allylboration reaction from boryl-substituted allylborane **5**,[12] 3-butenal **15**,[14] and the second aldehyde **16**.[15] This strategy of synthesis would be very efficient as it avoids the use of protecting groups.[16]

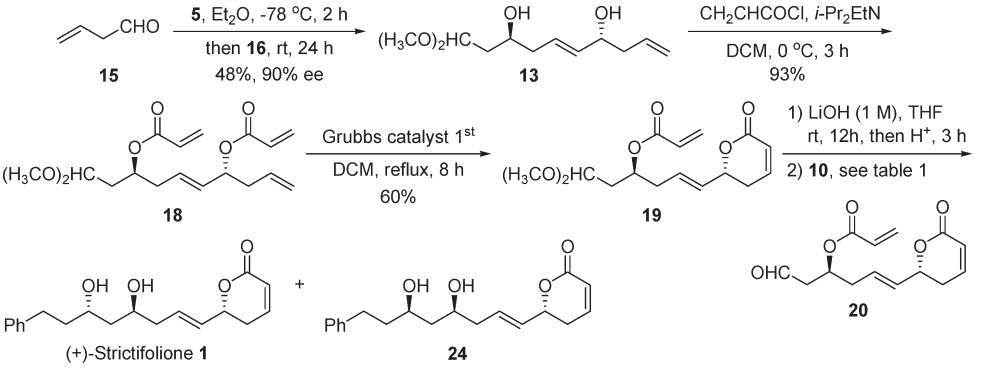
In accordance with the retrosynthetic analysis, our asymmetric synthesis of (+)-strictifolione **1** began with subjecting 3-butenal **15** to the one-pot double allylboration reaction (Scheme 3). Thus, addition of 0.6 equiv of **15** to a solution of in situ generated **5** at −78 °C for 2 h was followed by addition of an excess of aldehyde **16**. Then the reaction mixture was warmed to ambient temperature and stirred for 24 h to give (*E*)-1,5-*anti*-ene-diol **13** in 48% yield and high diastereo- and enantioselectivity (dr ≥ 20:1, 90% ee).[17] Esterification between diol **13** and acryloyl chloride proceeded smoothly to afford biacrylate **18** in 93% yield, which underwent RCM reaction utilizing first-generation Grubbs' catalyst[18] under high dilution conditions in refluxing CH_2Cl_2 to furnish α,β-unsaturated lactone **19** in 60% yield. With advanced intermediate **19** in hand, then we turned to the addition reaction to install the required 1,3-*anti*-diol by the strategy of 1,3-asymmetric induction,[19] thus completing the synthesis of (+)-strictifolione **1**. Removal of the acryloyl group and hydrolysis of the resulting acetal gave the crude aldehyde

(8) Krishna, P. R.; Srinivas, R. *Tetrahedron Lett.* **2007**, *48*, 2013.
(9) (a) Zhang., J.; Li., Y.; Wang., W.; She., X.; Pan., X. *J. Org. Chem.* **2006**, *71*, 2918. (b) Xu, Y.; Huo, X.; Li, X.; Zheng, H.; She, X.; Pan, X. *Synlett* **2008**, 1665. (c) Su, Y.; Xu, Y.; Han, J.; Zheng, J.; Qi, J.; Jiang, T.; Pan, X.; She, X. *J. Org. Chem.* **2009**, *74*, 2743. (d) Wang, X.; Wang, W.; Zheng, H.; Su, Y.; Jiang, T.; He, Y.; She, X. *Org. Lett.* **2009**, *11*, 3136.
(10) (a) Liang, Q.; Sun, Y.; Yu, B.; She, X.; Pan, X. *J. Org. Chem.* **2007**, *72*, 9846. (b) For a recent review, see: Touré, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439.
(11) Gaich, T.; Baran, P. S. *J. Org. Chem.* **2010**, *75*, 4657.
(12) (a) Flamme, E. M.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 13644. (b) Flamme, E. M.; Roush, W. R. *Org. Lett.* **2005**, *7*, 1411. (c) Owen, R. M.; Roush, W. R. *Org. Lett.* **2005**, *7*, 3941.
(13) For reviews, see: (a) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199. (b) Samojłowicz, C.; Bieniek, M.; Grela, K. *Chem. Rev.* **2009**, *109*, 3708. (c) Vougioukalakis, G. C.; Grubbs, R. H. *Chem. Rev.* **2010**, *110*, 1746.
(14) 3-Butenal was freshly prepared from glyoxal over two steps and used as a solution in CH_2Cl_2: (a) Crimmins, M. T.; Wells, A. J.; Kirincich, S. J.; Choy, A. L. *Synth. Commun.* **1998**, *28*, 3675. (b) Crimmins, M. T.; Choy, A. L. *J. Am. Chem. Soc.* **1999**, *121*, 5653.
(15) (a) Hodgson, S. T.; Hollinshead, D. M.; Ley, S. V. *Tetrahedron* **1985**, *41*, 5871. (b) Bi, L.; Zhang, Y.; Zhao, M.; Wang, C.; Chan, P.; Toc, J. B.-H.; Peng, S. *Bioorg. Med. Chem.* **2005**, *13*, 5640.
(16) (a) Hoffman, R. W. *Synthesis* **2006**, 3531. (b) Baran, P. S.; Young, I. S. *Nat. Chem.* **2009**, *1*, 193.
(17) The yield was based on 3-butenal as the limiting reagent, and the enantiomeric excess was determined by analysis of the bis-Mosher ester.
(18) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413.
(19) For a review, see: Mengel, A.; Reiser, O. *Chem. Rev.* **1999**, *99*, 1191.

SCHEME 2. Retrosynthetic Analysis of (+)-Strictifolione 1



SCHEME 3. First-Generation Synthesis of (+)-Strictifolione 1



11 in good yield, which was subjected to the addition reaction directly (Table 1). However, only trace amounts of the desired product (+)-strictifolione **1** were obtained when organolithium reagent **21** was used as the nucleophile (entry 1). The same results were observed when Grignard reagent **22** and organozinc compound **23**[20] (entries 2 and 4) were employed. Fortunately, treatment of aldehyde **20** with Grignard reagent **22** followed by removal of the acryloyl group generated the desired product **1** in 9% yield along with the minor product *epi*-strictifolione **24** in 6% yield.

Second-Generation Synthesis of (+)-Strictifolione 1. Although we had succeeded in an asymmetric total synthesis of (+)-strictifolione **1**, the yield and diastereoselectivity of the final stage were unacceptable (9%, dr = 1.5:1). We felt that a second-generation synthesis of (+)-strictifolione **1** concerning the improvement of the efficiency of construction of 1,3-*anti*-diol might be possible. The most obvious variation in this respect would be the introduction of this subunit by a hydroxy-directed 1,3-*anti*-reduction of the carbonyl group with boron reagent. This idea is outlined in our second retrosynthetic analysis (Scheme 2, route B) employing the *β*-hydroxy ketone **12** as the precursor, which could be obtained by several functional group transformations and the RCM reaction from intermediate (*E*)-1,5-*anti*-ene-diol **14**. The advanced intermediate **14** was proposed to be generated from boryl-substituted allylborane **5**, 3-butenal **15**, and the known aldedhyde **17**[21] using the double allylboration methodology.[12]

TABLE 1. Optimization of the Addition of Organometallic Reagent[a]

entry	reagent **10**	conditions	**1**:**24**	yield of **1**
1	Ph–Li **21**	2.5 equiv. **21**, THF, -78 °C, 0.5 h	nd[d]	trace
2	Ph–MgBr **22**	2.5 equiv. **22**, THF, -78 °C, 1 h	nd[d]	trace
3[b]	Ph–MgBr **22**	1.5 equiv. **22**, THF, -78 °C, 1 h	1.5:1	9%
4[c]	Ph–ZnBr **23**	2.5 equiv. **23**, THF, rt, 24 h	nd[d]	trace

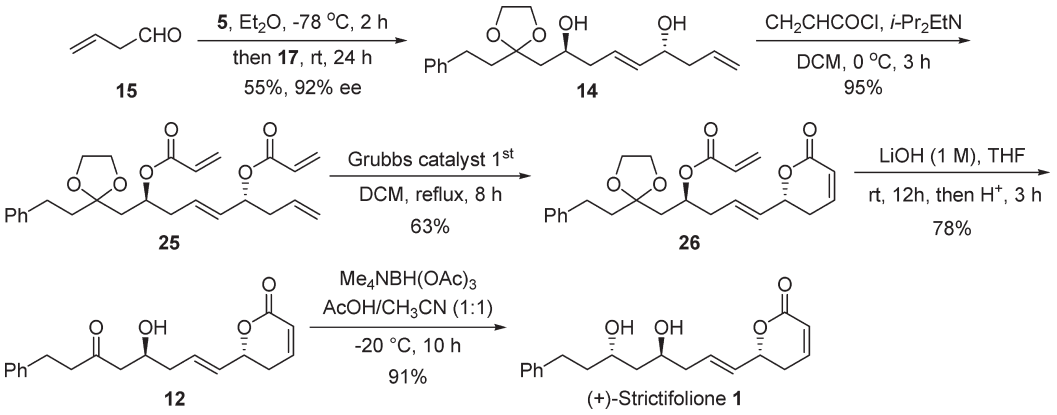
[a]All reactions were performed on 0.2 mmol scale with yields based on **19** over two steps; for details, see the Experimental Section. [b]Aldehyde **20** was used, then subsequent removal of acryloyl with LiOH. [c]See ref 20. [d]Not determined.

The realization of the second-generation synthesis of (+)-strictifolione **1** is shown in Scheme 4. The similar procedure that was employed for the preparation of **13** was applied to generate (*E*)-1,5-*anti*-ene-diol **14** in 55% yield and high diastereo- and enantioselectivity (dr ≥ 20:1, 92% ee). The esterification reaction between **14** and acryloyl chloride afforded the RCM precursor biacrylate **25** in 95% yield. Treatment of **25** with the first-generation Grubbs' catalyst under high dilution conditions in refluxing CH_2Cl_2 furnished

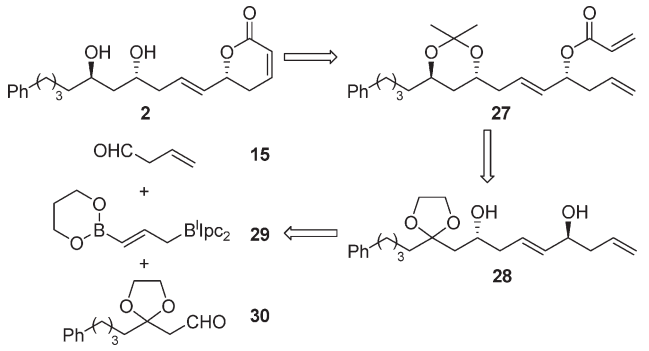
(20) Metzger, A.; Bernhardt, S.; Manolikakes, G.; Knochel, P. *Angew. Chem., Int. Ed.* **2010**, *49*, 4665 and references therein.

(21) (a) Bowman, R. K.; Johnson, J. S. *Org. Lett.* **2006**, *8*, 573. (b) Allen, C. P.; Benkovics, T.; Turek, A. K.; Yoon, T. P. *J. Am. Chem. Soc.* **2009**, *131*, 12560.

SCHEME 4. Second-Generation Synthesis of (+)-Strictifolione 1



SCHEME 5. Retrosynthetic Analysis of 2



the desired α,β-unsaturated lactone **26** in 63% yield. Removal of acryloyl group by aqueous LiOH solution (1 M) in THF and acid-promoted hydrolysis of the resulting acetal gave the ketone **12** in moderate yield (78%). Reduction of the carbonyl group with $Me_4NBH(OAc)_3$ in AcOH and CH_3CN (1:1) at −20 °C for 10 h completed the synthesis of (+)-strictifolione **1** (91%, dr = 96:4).[22] The analytical and spectral data of synthetic **1** were in good agreement with the previously reported data of (+)-strictifolione **1**.[3−5]

Synthesis of 2. Having achieved concise synthesis of target **1**, then we turned to use of similar strategy to synthesis of **2**. The retrosynthetic analysis is depicted in Scheme 5.

As shown in Scheme 6, the intermediate 1,5-diol **28** was smoothly obtained in 52% yield with excellent enantiomeric excess (92%) by the above protocol from 3-butenal **15**, boryl-substituted allylborane **29** (generated form $^{l}Ipc_2BH$), and aldehyde **30**.[23] Treatment of **28** with PPTS in refluxing wet acetone deprotected the acetal group to furnish ketone **31** in 91% yield.[24] Reduction of the carbonyl group with $Me_4NBH(OAc)_3$ and protection of the resulting 1,3-*anti*-diol with DMP gave the acetonide **32** in 89% yield in a 94:6 diastereoselectivity.[22] The *anti* relative configuration of the hydroxy groups was conformed by the analysis of the ^{13}C NMR spectra (δ = 24.73 and 24.84 ppm for the methyl groups and 100.16 ppm for the quaternary center).[25] The construction of the δ-lactone of **2** required the inversion of the chiral center at C-6, which was achieved by a Mitsunobu reaction.[26] Treatment of **32** with acrylic acid, TPP, and DIAD in anhydrous benzene gave the desired acrylate **27** in 71% yield. The obtained acrylate was subjected to RCM reaction (first-generation Grubbs' catalyst, DCM, reflux)[18] and deprotection (PPTS, acetone−H_2O)[5c] completing the synthesis of (6*R*)-6-[(4*R*,6*R*)-4,6-dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one **2**, the spectral data of which were in good agreement with those of the natural product.[6,5e]

Conclusion

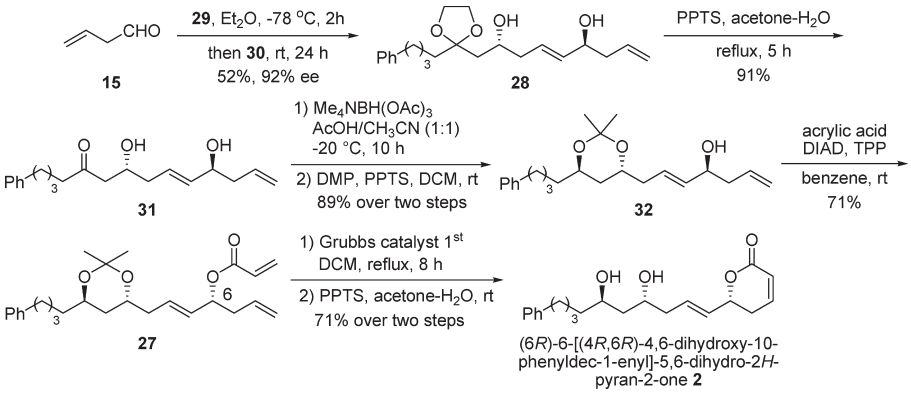
In conclusion, the total asymmetric syntheses of (+)-strictifolione **1** and (6*R*)-6-[(4*R*,6*R*)-4,6-dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one **2** have been accomplished, which proceeded in only five and seven steps with overall yields of 23 and 21%, respectively, from readily available 3-butenal. The syntheses reported here represent the shortest asymmetric syntheses of **1** and **2** reported to date. Highlights of the synthetic venture included the successful utilization of organoboron reagents to introduce all the stereogenic centers in **1** and **2** and the RCM reaction to build up the δ-lactone. Further investigations on the utility of the organoboron methodology for other bioactive natural products are currently underway in our laboratory and will be reported in due course.

Experimental Section

(*E*)-1,5-*anti*-Ene-diol 13. In a glovebox, $^{d}IpcBH$[27] (2.87 g, 10 mmol) was weighed into a 250 mL round-bottom flask containing a stir bar. The flask was capped with a rubber septum and removed from the glovebox and cooled in an ice bath. Ether (30 mL) was added to the flask followed by the allenylboronic ester[12] (1.23 g, 10 mmol) added neat via syringe. The reaction was stirred 2 h at 0 °C during which time the solid borane dissolved to

(22) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560.
(23) The aldehyde **30** was prepared using the similar procedure of preparation of the aldehyde **17**; for details, see the Supporting Information.
(24) Sterzycki, R. *Synthesis* **1979**, 724.
(25) Rychnovsky, S. D.; Rogers, B. N.; Richardson, R. I. *Acc. Chem. Res.* **1998**, *31*, 9.
(26) (a) Mitsunobu, O.; Yamada, M.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 935. (b) Mitsunobu, O.; Yamada, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380. (c) Mitsunobu, O.; Wada, M.; Sano, T. *J. Am. Chem. Soc.* **1972**, *94*, 679. (d) Mitsunobu, O. *Synthesis* **1981**, 1. (e) But, T. Y. S.; Toy, P. H. *Chem. Asian J.* **2007**, *2*, 1340. (f) Kumara Swamy, K. C.; Bhuvan Kumar, N. N.; Balaraman, E.; Pavan Kumar, K. V. P. *Chem. Rev.* **2009**, *109*, 2551.
(27) Brown, H. C.; Singaram, B. *J. Org. Chem.* **1984**, *49*, 945.

SCHEME 6. Synthesis of 2



leave a colorless solution. The ice bath was removed, and the reaction was cooled to −78 °C. To the solution of the above generated **5** at −78 °C was added dropwise aldehyde **15** (420 mg, 6 mmol), and the mixture was stirred at −78 °C for 2 h. Subsequently, aldehyde **16** (2.36 g, 20 mmol) was added dropwise, and the reaction was stirred an additional hour at −78 °C. The reaction was allowed to warm to rt over 3 h and then stirred for an additional 24 h at rt. The reaction was cooled by an ice bath, and 10 mL of 3.0 M aqueous NaOH solution was added dropwise followed by 4 mL of a 50% aqueous H_2O_2 solution. (*Caution: Rapid addition of the peroxide can cause a vigorous exotherm.*) The reaction was allowed to stir at rt for 4 h at which time it was diluted with 400 mL of CH_2Cl_2 and 200 mL of saturated aqueous $NaHCO_3$ and 50 mL of brine. The biphasic mixture was vigorously stirred for 20 min. Then the organic layer was separated and the aqueous layer washed with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure to give a residual which was purified by flash column chromatography on silica gel (hexane/EtOAc, 1:1) to afford diol **13** (662 mg, 48% yield) as a colorless oil: 90% ee; $[\alpha]^{20}_D$ −1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.66−5.85 (m, 2H), 5.58 (dd, *J* = 15.6, 6.4 Hz, 1H), 5.10−5.17 (m, 2H), 4.58 (t, *J* = 5.6 Hz, 1H), 4.15 (dt, *J* = 4.4, 2.4 Hz, 1H), 3.82−3.84 (m, 1H), 3.37 (s, 3H), 3.35 (s, 3H), 2.99 (s, 1H), 2.20−2.37 (m, 4H), 2.07 (s, 1H), 1.69−1.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 134.3, 127.3, 118.1, 103.7, 71.5, 67.7, 53.8, 53.0, 41.9, 40.1, 38.7; IR ν (cm^{-1}) 3393, 2955, 2922, 1738, 1643, 1460, 1378, 1127, 1054, 972, 914, 736, 639; HRMS (ESI) calcd for $C_{12}H_{22}NaO_4$ $[M + Na]^+$ 253.1410, found 253.1405.

Biacrylate 18. Acryloyl chloride (724 mg, 0.65 mL, 8.0 mmol) was added dropwise to a solution of **13** (460 mg, 2.0 mmol) and anhydrous diisopropylethylamine (2.064 g, 2.9 mL, 16 mmol) in anhydrous dichloromethane (20 mL) at 0 °C under an argon atmosphere. The mixture was stirred for 3 h at 0 °C. Then the mixture was concentrated under reduced pressure to give a residual which was purified by flash column chromatography on silica gel (hexane/EtOAc, 8:1) to afford the title compound **18** (627 mg, 93% yield) as a colorless oil: $[\alpha]^{20}_D$ +41 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.33−6.38 (m, 2H), 6.03−6.10 (m, 2H), 5.76−5.80 (m, 2H), 5.63−5.71 (m, 2H), 5.49 (dd, *J* = 15.2, 7.2 Hz, 1H), 5.29 (dd, *J* = 13.2, 6.4 Hz, 1H), 5.01−5.10 (m, 3H), 4.40 (dd, *J* = 6.4, 4.8 Hz, 1H), 3.27 (s, 3H), 3.26 (s, 3H), 2.28−2.41 (m, 4H), 1.81−1.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 165.2, 133.0, 131.3, 130.6, 130.5, 128.6, 128.5, 128.4, 117.9, 101.6, 73.5, 69.9, 53.2, 52.4, 38.8, 37.2, 36.6; IR ν (cm^{-1}) 3430, 2926, 1724, 1406, 1270, 1193, 1052, 973, 809, 676; HRMS (ESI) calcd for $C_{18}H_{26}NaO_6$ $[M + Na]^+$ 361.1622, found 361.1613.

α,β-Unsaturated Lactone 19. To a solution of first-generation Grubbs' catalyst (124 mg, 0.15 mmol) in 80 mL of CH_2Cl_2 was added a solution of the ring-closing metathesis precursor **18** (338 mg, 1.0 mmol) in 2 mL of CH_2Cl_2 under argon atmosphere. The mixture was heated to reflux for 8 h. Then the mixture was concentrated under reduced pressure to give a residual which was purified by flash column chromatography on silica gel (hexane/EtOAc, 3:1) to afford the title compound **19** (186 mg, 60% yield) as a colorless oil: $[\alpha]^{20}_D$ +71 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81−6.86 (m, 1H), 6.37 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.98−6.11 (m, 2H), 5.71−5.83 (m, 2H), 5.63 (dd, *J* = 15.6, 6.4 Hz, 1H), 5.07−5.11 (m, 1H), 4.85 (dd, *J* = 6.4, 2.8 Hz, 1H), 4.40 (dd, *J* = 6.8, 4.8 Hz, 1H), 3.29 (s, 3H), 3.27 (s, 3H), 2.31−2.43 (m, 4H), 1.83−1.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 163.7, 144.5, 130.8, 130.4, 129.4, 128.4, 121.5, 101.7, 77.6, 69.8, 53.5, 52.6, 37.3, 36.9, 29.5; IR ν (cm^{-1}) 3425, 2925, 1721, 1636, 1385, 1247, 1195, 1056, 972, 815, 666, 484; HRMS (ESI) calcd for $C_{16}H_{22}NaO_6$ $[M + Na]^+$ 333.1309, found 333.1303.

General Procedure for the Addition of Organometallic Reagent 10 (Table 1, entry 3). To a solution of compound **19** (62 mg, 0.2 mmol) in 4.0 mL of THF was added 4.0 mL of aqueous HCl solution (1.0 M), and the mixture was stirred for 3 h at rt. Then the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with water (5 mL), saturated aqueous $NaHCO_3$ solution (2 × 5 mL), and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude **20** as a colorless oil, which was used directly in the next step.

To a solution of the above-prepared aldehyde **20** in anhydrous THF (2 mL) was added dropwise Grignard reagent **22** (1.0 M, 0.3 mL) at −78 °C under an argon atmosphere, and the mixture was stirred for an additional hour at −78 °C. Then the mixture was quenched with saturated aqueous NH_4Cl solution, and the resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a residue which was dissolved in 4.0 mL of THF, and 1.0 mL of aqueous LiOH solution (1.0 M, 1 mmol) was added. The mixture was then stirred at rt for 12 h. After that, it was quenched with saturated aqueous NH_4Cl solution, and the resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a residual oil which was purified by flash column chromatography on silica gel (hexane/EtOAc, 1:2) to afford (+)-strictifolione **1** (6 mg, 9% yield) and the product **24** (4 mg, 6% yield). The analytical and spectral data of our synthetic **1** were in good agreement with the previously reported data of (+)-strictifolione **1** (for details see the section (+)-Strictifolione **1** (Second-Generation Synthesis)). Compoud **24**: colorless oil; $[\alpha]^{20}_D$ +6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18−7.31 (m, 5H), 6.86−6.91 (m, 1H), 6.05 (d, *J* = 8.4 Hz, 1H), 5.86 (dt, *J* = 15.6, 7.2 Hz, 1H), 5.69 (dd, *J* = 15.6, 6.4 Hz, 1H), 4.91 (dt, *J* = 9.2, 6.0 Hz,

1H), 3.88−3.94 (m, 1H), 3.23 (s, 1H), 3.02 (s, 1H), 2.68−2.78 (m, 2H), 2.42−2.46 (m, 2H), 2.25−2.28 (m, 2H), 1.77−1.84 (m, 2H), 1.53−1.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 144.6, 141.8, 130.8, 130.0, 128.4, 128.3, 125.9, 121.6, 77.7, 72.2, 71.8, 42.5, 40.9, 39.7, 31.7, 29.8; IR ν (cm^{-1}) 3399, 2921, 2855, 1710, 1494, 1385, 1250, 1054, 1020, 970, 818, 701, 575, 486.

(*E*)-1,5-*anti*-Ene-diol 14. Diol **14** was prepared by a similar protocol that was employed for the preparation of (*E*)-1,5-*anti*-ene-diol **13** from 3-butenal **15**, boryl-substituted allylborane **5**, and aldehyde **17** in 55% yield as a colorless oil: 92% ee; $[\alpha]^{20}_D$ +1 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17−7.30 (m, 5H), 5.66−5.84 (m, 2H), 5.57 (dd, J = 15.2, 6.4 Hz, 1H), 5.09−5.14 (m, 2H), 4.14 (q, J = 6.4 Hz, 1H), 3.94−4.04 (m, 5H), 3.60 (s, 1H), 2.67 (t, J = 8.4 Hz, 2H), 2.17−2.32 (m, 4H), 2.07 (s, 1H), 1.94−2.04 (m, 2H), 1.75−1.88 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 135.1, 134.4, 128.4, 128.2, 127.4, 125.8, 117.9, 111.5, 71.5, 67.4, 65.0, 64.7, 42.3, 41.8, 40.1, 39.1, 30.0; IR ν (cm^{-1}) 3420, 2925, 1642, 1496, 1428, 1311, 1133, 1034, 975, 916, 750, 702, 505; HRMS (ESI) calcd for $C_{20}H_{32}NO_4$ [M + NH_4]$^+$ 350.2326, found 350.2320.

Biacrylate 25. Biacrylate **25** was prepared by a similar protocol that was employed for the preparation of biacrylate **18** from (*E*)-1,5-*anti*-ene-diol **14** in 95% yield as a colorless oil: $[\alpha]^{20}_D$ +31 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16−7.28 (m, 5H), 6.37 (dt, J = 17.2, 1.6 Hz, 2H), 6.05−6.12 (m, 2H), 5.79 (dt, J = 10.4, 1.6 Hz, 2H), 5.68−5.72 (m, 2H), 5.52 (dd, J = 15.6, 7.2 Hz, 1H), 5.33 (q, J = 6.4 Hz, 1H), 5.22−5.28 (m, 1H), 5.04−5.10 (m, 2H), 3.92−3.97 (m, 4H), 2.67 (dq, J = 8.0, 2.4 Hz, 2H), 2.34−2.41 (m, 4H), 2.04 (q, J = 7.6 Hz, 1H), 1.86−1.95 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 165.3, 141.9, 133.1, 131.3, 130.5, 130.4, 128.9, 128.8, 128.7, 128.3, 128.2, 125.7, 117.9, 109.9, 69.4, 64.9, 64.8, 40.1, 39.5, 38.9, 38.0, 29.9; IR ν (cm^{-1}) 3074, 2955, 2929, 1722, 1638, 1406, 1271, 1193, 1045, 973, 809, 702, 503; HRMS (ESI) calcd for $C_{26}H_{36}NO_6$ [M + NH_4]$^+$ 458.2537, found 458.2532.

α,β-Unsaturated Lactone 26. α,β-Unsaturated lactone **26** was prepared by a similar protocol that was employed for the preparation of α,β-unsaturated lactone **19** from biacrylate **25** in 63% yield as a colorless oil: $[\alpha]^{20}_D$ +52 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17−7.28 (m, 5H), 6.82−6.87 (m, 1H), 6.38 (dd, J = 17.2, 1.2 Hz, 1H), 6.01−6.13 (m, 2H), 5.76−5.82 (m, 2H), 5.65 (dd, J = 15.6, 6.4 Hz, 1H), 5.23−5.29 (m, 1H), 4.87 (dt, J = 15.2, 6.4 Hz, 1H), 3.93−4.00 (m, 4H), 2.65−2.71 (m, 2H), 2.31−2.49 (m, 4H), 2.08 (dd, J = 14.8, 7.6 Hz, 1H), 1.87−1.95 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 163.8, 144.5, 141.8, 130.6, 130.3, 129.8, 128.7, 128.3, 128.2, 125.8, 121.6, 109.9, 77.7, 69.2, 64.9, 64.8, 40.4, 39.4, 38.1, 29.9, 29.6; IR ν (cm^{-1}): 3060, 2926, 1720, 1406, 1383, 1246, 1197, 1047, 972, 815, 702, 666; HRMS (ESI) calcd for $C_{24}H_{32}NO_6$ [M + NH_4]$^+$ 430.2224, found 430.2218.

Ketone 12. To a solution of compound **26** (83 mg, 0.2 mmol) in 4.0 mL of THF was added 1.0 mL of aqueous LiOH solution (1.0 M, 1 mmol), and the mixture was stirred for 12 h at rt. Then 3.0 mL of aqueous HCl solution (2.0 M, 6 mmol) was added, and the mixture was stirred for 3 h at rt. After that, it was quenched with saturated aqueous NH_4Cl solution, and the resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a residual oil which was purified by flash column chromatography on silica gel (hexane/EtOAc, 2:1) to afford the title compound **12** (49 mg, 78% yield) as a colorless oil: $[\alpha]^{20}_D$ +58 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16−7.29 (m, 5H), 6.85−6.90 (m, 1H), 6.38 (dt, J = 9.6, 1.6 Hz, 1H), 5.79−5.87 (m, 1H), 5.66 (dd, J = 15.6, 6.4 Hz, 1H), 4.87 (dt, J = 15.2, 6.4 Hz, 1H), 4.08−4.13 (m, 1H), 3.17 (d, J = 3.6 Hz, 1H), 2.90 (t, J = 7.6 Hz, 2H), 2.77 (t, J = 7.6 Hz, 2H), 2.40−2.61 (m, 4H), 2.19−2.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.6, 163.9, 144.7, 140.5, 130.6, 129.8, 128.4, 128.2, 126.1, 121.4, 77.7, 66.8, 48.5, 44.9, 39.1, 29.6, 29.3; IR ν (cm^{-1}) 3424, 2922, 1710, 1383, 1248, 1046, 970, 817, 749, 701, 480; HRMS (ESI) calcd for $C_{19}H_{26}NO_4$ [M + NH_4]$^+$ 332.1856, found 332.1850.

(+)-Strictifolione 1 (Second-Generation Synthesis). To a stirred suspension of tetramethylammonium triacetoxyborohydride (145 mg, 0.55 mmol) in acetonitrile (0.5 mL) was added glacial acetic acid (0.5 mL). The mixture was stirred at rt for 30 min. After cooling to −20 °C, the β-hydroxy ketone **12** (35 mg, 0.11 mmol) in a mixture of acetic acid and acetonitrile (v/v = 1:1, 0.6 mL) was added dropwise. The mixture was stirred at −20 °C for over 10 h. A saturated solution of sodium potassium tartrate (2 mL) and EtOAc (2 mL) was added followed by vigorous stirring at rt for 30 min. The mixture was extracted with EtOAc (3 × 15 mL). The combined organic layers were washed with water (5 mL), saturated aqueous $NaHCO_3$ solution (2 × 5 mL), and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (hexane/EtOAc, 1:2) to afford (+)-strictifolione **1** (32 mg, 91% yield, dr = 96:4) as a white solid: mp 112−114 °C; $[\alpha]^{20}_D$ = +43 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15−7.29 (m, 5H), 6.85−6.89 (m, 1H), 6.02 (dd, J = 9.6, 1.6 Hz, 1H), 5.85 (dt, J = 15.6, 7.2 Hz, 1H), 5.65 (dd, J = 15.6, 6.4 Hz, 1H), 4.86 (q, J = 3.2 Hz, 1H), 3.94−4.03 (m, 2H), 2.90−3.20 (br, 2H), 2.75−2.79 (m, 1H), 2.65−2.69 (m, 1H), 2.40−2.43 (m, 2H), 2.25−2.29 (m, 2H), 1.75−1.87 (m, 2H), 1.63 (t, J = 6.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 144.9, 141.9, 131.4, 129.6, 128.4, 128.3, 125.8, 121.3, 77.8, 68.5, 68.2, 42.2, 40.2, 38.9, 32.1, 29.6; IR ν (cm^{-1}) 3343, 2932, 1719, 1494, 1393, 1242, 1050, 967, 818, 751, 701, 484; HRMS (ESI) calcd for $C_{19}H_{28}NO_4$ [M + NH_4]$^+$ 334.2013, found 334.2023.

(*E*)-1,5-*anti*-Ene-diol 28. Diol **28** was prepared by a similar protocol that was employed for the preparation of (*E*)-1,5-*anti*-ene-diol **13** from 3-butenal **15**, boryl-substituted allylborane **29** (generated from ^{l}Ipc$_2$BH), and aldehyde **30** in 52% yield as a colorless oil: 92% ee; $[\alpha]^{20}_D$ −2 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15−7.29 (m, 5H), 5.66−5.82 (m, 2H), 5.57 (dd, J = 15.6, 6.4 Hz, 1H), 5.10−5.15 (m, 2H), 4.14 (d, J = 6.0 Hz, 1H), 3.90−3.99 (m, 5H), 3.58 (s, 1H), 2.61 (t, J = 7.6 Hz, 2H), 2.16−2.32 (m, 4H), 1.86 (s, 1H), 1.81 (dd, J = 14.4, 1.6 Hz, 1H), 1.59−1.73 (m, 5H), 1.37−1.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.4, 135.0, 134.4, 128.3, 128.2, 127.6, 125.7, 117.9, 112.0, 71.6, 67.5, 64.9, 64.6, 42.1, 41.9, 40.1, 37.1, 35.8, 31.5, 23.5; IR ν (cm^{-1}) 3428, 3025, 2931, 1641, 1496, 1427, 1314, 1137, 1040, 974, 827, 742, 701, 498; HRMS (ESI) calcd for $C_{22}H_{32}NaO_4$ [M + Na]$^+$ 383.2193, found 383.2186.

Ketone 31. A solution of diol **28** (180 mg, 0.5 mmol) in wet acetone (10 mL) containing PPTS (63 mg, 0.25 mmol) was refluxed for 5 h. Excess solvent was then removed under reduced pressure. The residual mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated by rotary evaporation. Purification by flash chromatography on silica gel (hexane/EtOAc, 2:1) afforded 144 mg (0.456 mmol, 91% yield) of ketone **31** as a colorless oil: $[\alpha]^{20}_D$ −26 (c = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15−7.29 (m, 5H), 5.74−5.85 (m, 1H), 5.64−5.71 (m, 1H), 5.57 (dd, J = 15.6, 6.4 Hz, 1H), 5.10−5.15 (m, 2H), 4.14 (q, J = 6.4 Hz, 1H), 4.08 (s, 1H), 3.12 (s, 1H), 2.42−2.61 (m, 6H), 2.19−2.32 (m, 4H), 2.07 (s, 1H), 1.60−1.63 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.6, 142.0, 135.6, 134.2, 128.3, 128.2, 126.9, 125.7, 118.1, 71.4, 67.1, 48.3, 43.4, 41.9, 39.2, 35.6, 30.8, 23.1; IR ν (cm^{-1}) 3398, 2930, 1706, 1496, 1408, 1028, 975, 916, 746, 700, 638, 497; HRMS (ESI) calcd for $C_{20}H_{28}NaO_3$ [M + Na]$^+$ 339.1931, found 339.1941.

Acetonide 32. To a stirred suspension of tetramethylammonium triacetoxyborohydride (316 mg, 1.2 mmol) in acetonitrile (1.0 mL) was added glacial acetic acid (1.0 mL). The mixture was stirred at rt for 30 min. After cooling to −20 °C, the β-hydroxy ketone **31** (63 mg, 0.20 mmol) in a mixture of acetic acid and acetonitrile (v/v = 1:1, 1.0 mL) was added dropwise. The mixture

was stirred at −20 °C for over 10 h. A saturated solution of sodium potassium tartrate (4 mL) and EtOAc (4 mL) was added followed by vigorous stirring at rt for 30 min. The mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with water (10 mL), saturated aqueous $NaHCO_3$ solution (2 × 5 mL), and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give a residue which was filtered by a short silica gel column (hexane/EtOAc, 1:2) to afford pure triol (60 mg, 0.19 mmol) which was used directly in the next step.

To a solution of the above-prepared triol (60 mg, 0.19 mmol) in CH_2Cl_2 (3 mL) were added 2,2-dimethoxypropane (52 mg, 0.5 mmol) and PPTS (5 mg, 0.02 mmol) in ambient atmosphere. After stirring for 10 h at rt, saturated $NaHCO_3$ (aq) was added and the mixture was stirred for additional 10 min. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (hexane/EtOAc, 30:1) to afford acetonide **32** (64 mg, 89% yield over two steps, dr = 95:5) as a colorless liquid: $[\alpha]^{20}_D$ −28 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15−7.28 (m, 5H), 5.76−5.85 (m, 1H), 5.62−5.67 (m, 1H), 5.56 (dd, *J* = 15.6, 6.4 Hz, 1H), 5.10−5.15 (m, 2H), 4.13 (d, *J* = 5.2 Hz, 1H), 3.71−3.86 (m, 2H), 2.60 (t, *J* = 8.0 Hz, 2H), 2.17−2.32 (m, 4H), 1.76 (s, 1H), 1.38−1.65 (m, 8H), 1.34 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 134.6, 134.2, 128.3, 128.2, 127.3, 125.6, 118.0, 100.2, 71.6, 66.5, 66.2, 41.9, 38.5, 38.1, 35.8, 35.7, 31.4, 25.0, 24.8, 24.7; IR ν (cm^{-1}) 3417, 2986, 2934, 2858, 1641, 1454, 1378, 1224, 1119, 1031, 973, 746, 699, 495; HRMS (ESI) calcd for $C_{23}H_{38}NO_3$ $[M + NH_4]^+$ 376.2846, found 376.2833.

Acrylate 27. To a mixture of acetonide **32** (54 mg, 0.15 mmol), TPP (60 mg, 0.23 mmol), and DIAD (61 mg, 0.3 mmol) in 2.0 mL of dry benzene was dissolved acrylic acid (22 mg, 0.3 mmol) in 1.0 mL of dry benzene and slowly added dropwise at 0 °C. The resulting reaction mixture was warmed to rt and stirred for an additional 6 h. After that, the reaction was quenched by adding water and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (hexane/EtOAc, 30:1) to afford the acrylate **27** (44 mg, 71% yield) as a colorless oil: $[\alpha]^{20}_D$ −6 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15−7.28 (m, 5H), 6.38 (dd, *J* = 17.2, 1.6 Hz, 1H), 6.10 (dd, *J* = 17.2, 10.4 Hz, 1H), 5.70−5.81 (m, 3H), 5.53 (dd, *J* = 15.6, 7.2 Hz, 1H), 5.35 (q, *J* = 6.4 Hz, 1H), 5.05−5.11 (m, 2H), 3.78−3.82 (m, 2H), 2.60 (t, *J* = 8.0 Hz, 2H), 2.39−2.44 (m, 2H), 2.24−2.31 (m, 1H), 2.11−2.18 (m, 1H), 1.37−1.64 (m, 8H), 1.32 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 142.6, 133.2, 130.4, 130.1, 130.0, 128.8, 128.3, 128.2, 125.6, 117.8, 100.2, 73.8, 66.5, 66.2, 39.0, 38.5, 38.1, 35.9, 35.7, 31.4, 25.1, 24.8, 24.7; IR ν (cm^{-1}) 3442, 2986, 2933, 1724, 1405, 1294, 1191, 973, 810, 699, 482; HRMS (ESI) calcd for $C_{26}H_{36}NaO_4$ $[M + Na]^+$ 435.2506, found 435.2514.

(6*R*)-6-[(4*R*,6*R*)-4,6-Dihydroxy-10-phenyldec-1-enyl]-5,6-dihydro-2*H*-pyran-2-one 2. To a solution of first-generation Grubbs' catalyst (7 mg, 0.008 mmol) in 3 mL of dry CH_2Cl_2 was added a solution of the ring-closing metathesis precursor **27** (17 mg, 0.041 mmol) in 2 mL of CH_2Cl_2 under argon atmosphere. The mixture was heated to reflux for 8 h. Then the mixture was concentrated in vacuo, and the residual oil was filtered by a short silica gel column. The crude product was dissolved in a mixture of acetone (2.4 mL) and water (0.4 m). PPTS (5 mg, 0.02 mmol) was added, and the reaction mixture was stirred for 5 h and monitored by TLC. When the reaction was completed, it was quenched by saturated aqueous $NaHCO_3$ solution and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (hexane/EtOAc, 1:2) to afford the title compound **2** (10 mg, 71% yield) as a white solid: mp 61−64 °C; $[\alpha]^{20}_D$ = +36 (*c* = 1.0, $CHCl_3$); ^{1}H **NMR** (400 MHz, $CDCl_3$) δ 7.16−7.29 (m, 5H), 6.85−6.90 (m, 1H), 6.04 (dt, *J* = 9.6, 1.6 Hz, 1H), 5.83−5.91 (m, 1H), 5.69 (dd, *J* = 15.2, 6.8 Hz, 1H), 4.89 (q, *J* = 8.0 Hz, 1H), 4.00 (s, 1H), 3.92 (s, 1H), 2.71 (s, 1H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.41−2.45 (m, 2H), 2.26−2.29 (m, 2H), 1.33−1.70 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 144.7, 142.5, 131.3, 129.9, 128.4, 128.3, 125.7, 121.5, 77.8, 69.1, 68.2, 42.1, 40.3, 37.3, 35.8, 31.4, 29.7, 25.4; IR ν (cm^{-1}) 3405, 2932, 1710, 1494, 1384, 1250, 1149, 1019, 970, 818, 700, 575; HRMS (ESI) calcd for $C_{21}H_{32}NO_4$ $[M + NH_4]^+$ 362.2326, found 362.2339.

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Supporting Information Available: Experimental procedures, spectral data, and copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.