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Synthetic Studies on Schisandra nortriterpenoids. Stereocontrolled Synthesis of Enantiopure C-5-*epi* ABC Ring Systems of Micrandilactone A and Lancifodilactone G Using RCM

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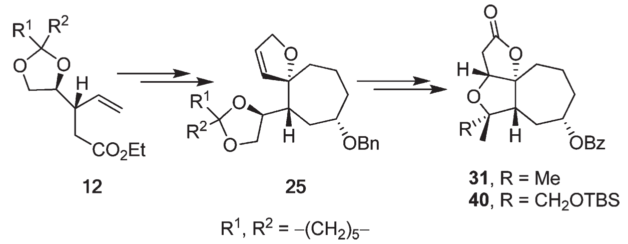

A stereocontrolled approach for the construction of ABC ring systems of micrandilactone A and lancifodilactone G has been developed. The synthesis involves construction of an enantiopure functionalized cycloheptene derivative **17** through RCM of the dienol **14** prepared from the known D-mannitol-derived unsaturated ester **12**. A remarkable regioselectivity during hydroboration of the cycloheptene derivative **17** was observed during its transformation to the cycloheptanone **20**. RCM of the diene **24** prepared stereoselectively from **20** gave the spiro-dihydrofuran **25**. The ketal unit in **25** was then converted into the carbinols **28** and **36**. A bromonium ion initiated highly stereocontrolled intramolecular etherification in **28** and **37** led to the tricyclic ethers **29** and **38**, respectively. Reductive removal of bromine from **29** and **38** followed by RuO_4 oxidation led to the furo-furanone derivatives **31** and **40**, the C-5-*epi* ABC ring systems of the schisandra nortriterpenoids **1** and **2**.

Introduction

Schisandra nortriterpenoids[1] are a group of recently discovered highly oxygenated structurally diverse polycyclic compounds isolated from various species of *Schisandracea* family. Plants of this family are widely distributed throughout Southeast Asia and North America. Many of the species of this family have been used as folk medicines in China over the years. Biosynthetically they are derived from cycloartane.[1] On the basis of the structural pattern encountered in compounds of this family, they can be classified into the following categories: schisanartane, schiartane, 18-norschiartane, 18(13→14)-*abeo*-schiartane, preschisanartane, and wuweiziartane. Representative examples include micrandilactone A **1** and lancifodilactone G **2** (schisanartane type), micrandilactone B **3** (schiartane type), rubriflordilactone B **4** (18-norschiartane type), wuweizidilactone C **5** (18(13→14)-*abeo*-schiartane type), schintrilactone A **6** and schintrilactone B **7** (wuweiziartane type),[2] etc. (Figure 1). Micrandilactones A **1** and B **3** were isolated[2] from the stems and leaves of *S. micrantha*, lancifodilactone G **2** was isolated[3] from stems and leaves of *S. lancifolia*, rubriflordilactone B **4**[4] was isolated from *S. rubriflora*, and compounds **5**−**7**[5] were isolated from *S. chinensis*. Many of the compounds isolated from these plants possess a wide range of medicinal properties. For example, compounds **1** and **3**−**7** exhibit anti-HIV activity,

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[1] Xiao, W. L.; Li, R. T.; Huang, S. X.; Pu, J. X.; Sun, H. D. *Nat. Prod. Rep.* **2008**, *25*, 871–891.

[2] (a) Li, R.; Zhao, Q.; Li, S.; Han, Q.; Sun, H.; Lu, Y.; Zhang, L.; Zheng, Q. *Org. Lett.* **2003**, *5*, 1023–1026. (b) Li, R. T.; Han, Q. B.; Zheng, Y. T.; Wang, R. R.; Yang, L. M.; Lu, Y.; Sang, S. Q.; Zheng, Q. T.; Zhao, Q. S.; Sun, H. D. *Chem. Commun.* **2005**, 2936–2938.

[3] Xiao, W. L.; Zhu, H. J.; Shen, Y. H.; Li, R. T.; Li, S. H.; Sun, H. D.; Zheng, Y. T.; Wang, R. R.; Lu, Y.; Wang, C.; Zheng, Q. T. *Org. Lett.* **2006**, *8*, 801.

[4] Xiao, W. L.; Yang, L. M.; Gong, N. B.; Wu, L.; Wang, R. R.; Pu, J. X.; Li, X. L.; Huang, S. X.; Zheng, Y. T.; Li, R. T.; Lu, Y.; Zheng, Q. T.; Sun, H. D. *Org. Lett.* **2006**, *8*, 991–994.

[5] For isolation of wuweizidilactone C, see: (a) Huang, S. X.; Yang, L. B.; Xiao, W. L.; Lei, C.; Liu, J. P.; Lu, Y.; Weng, Z. Y.; Li, L. M.; Li, R. T.; Yu, J. L.; Zheng, Q. T.; Sun, H. D. *Chem.—Eur. J.* **2007**, *13*, 4816–4822. For isolation of schintrilactones A and B, see: (b) Huang, S. X.; Yang, J.; Huang, H.; Li, L. M.; Xiao, W. L.; Li, R. T.; Sun, H. D. *Org. Lett.* **2007**, *9*, 4175–4178.

DOI: 10.1021/jo1006448

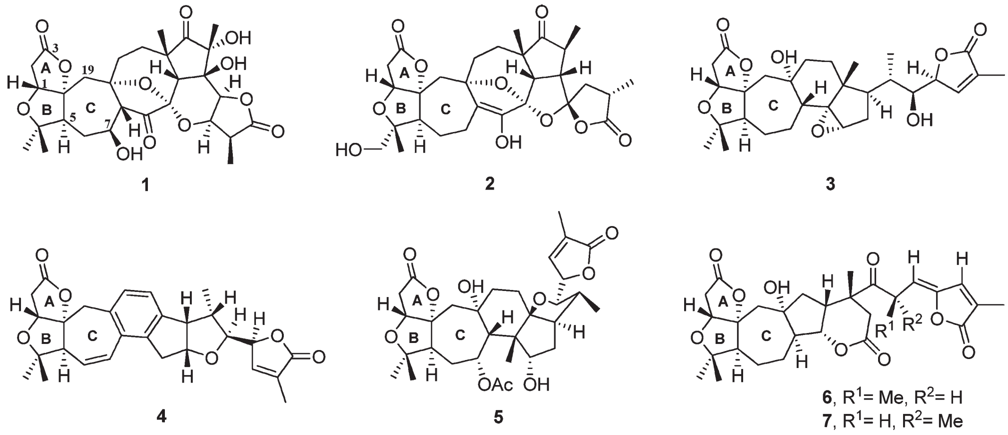
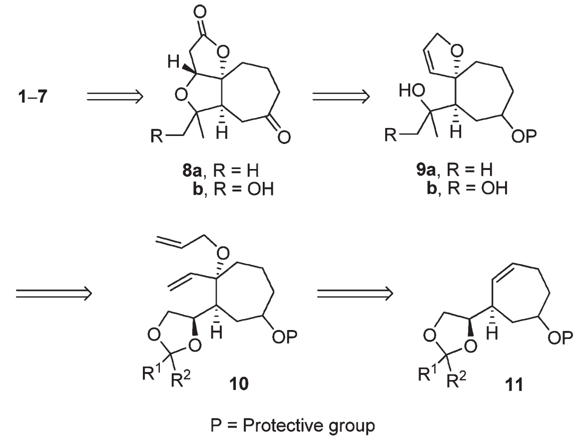


FIGURE 1. Naturally occurring nortriterpenoids.

SCHEME 1. **Retrosynthetic Plan**



and the extract of the plant from which **2** was isolated is traditionally used for the treatment of rheumatic lumbago and traumatic injury and related diseases. Compound **2** also exerts cytotoxicity against C8166 cells.

The densely functionalized novel polycyclic architecture with multiple stereogenic centers presents a considerable synthetic challenge. Interest in the synthesis of these compounds has further been increased by the broad range biological activity associated with them. We have recently initiated a program toward the development of a route for entry into nortriterpenoids of the *Schisandracea* family.

A common structural feature of the compounds in this family is the presence of the fragments **8a** and **8b**, which represent the ABC core. While the structural prototype **8a** is present in a majority of the schisandra nortriterpenoids including **1** and **3**–**7**, fragment **8b** is present in **2** (Scheme 1). We thought that construction of these fragments **8a** and **8b** having a functionalized seven-membered ring would enable their elaboration to the natural products upon annulation of the residual rings onto the seven-membered ring. Thus, we initially focused on developing a methodology that would enable construction of the fragment **8a** as well as **8b** from a common precursor. A number of approaches[6] dealing with the synthesis of various parts of some of these compounds have been reported.

However, as far as the construction of the furofuranone ring system is concerned, there are only a few reports. In these approaches, an oxy-Michael addition to either a butenolide[6h,i] or to an enoate[6b,e] with concomitant lactonization was employed as the key step. Using this concept, synthesis of the ABC ring unit present in micrandilactone A and lancifodilactone G has been achieved recently.[6b,e] To the best of our knowledge there is no report of any approach that addresses the synthesis of the ABC ring of both series represented by compounds **1** and **2**. We planned to develop a general protocol from a common precursor for access to the ABC rings of both series of natural products represented by structures **8a** and **8b** (Scheme 1). The key concept in our approach relies on bromonium ion initiated intramolecular etherification in the spiro-dihydrofuran derivative **9** followed by oxidation of the bis-tetrahydrofuran derivative to lead to **8**. The oxa-spiro[4.6]undecene derivatives **9a** and **9b** would be available from RCM[7] of the diene **10**, the ketal unit being used as the surrogate to both *gem*-dimethyl and methylhydroxymethyl units. Compound **10** would be available from the highly functionalized cycloheptene derivative **11**. Herein we report preliminary results of our investigation based on this plan culminating in the synthesis of the C-5-*epi* ABC core present in both series represented by **1** and **3**–**7** as well as **2**.

Results and Discussion

The synthesis commenced with the construction of the functionalized cycloheptanone derivative **20** in enantiomerically pure form as delineated in Scheme 2. We initially focused our attention to demonstrate the feasibility of this

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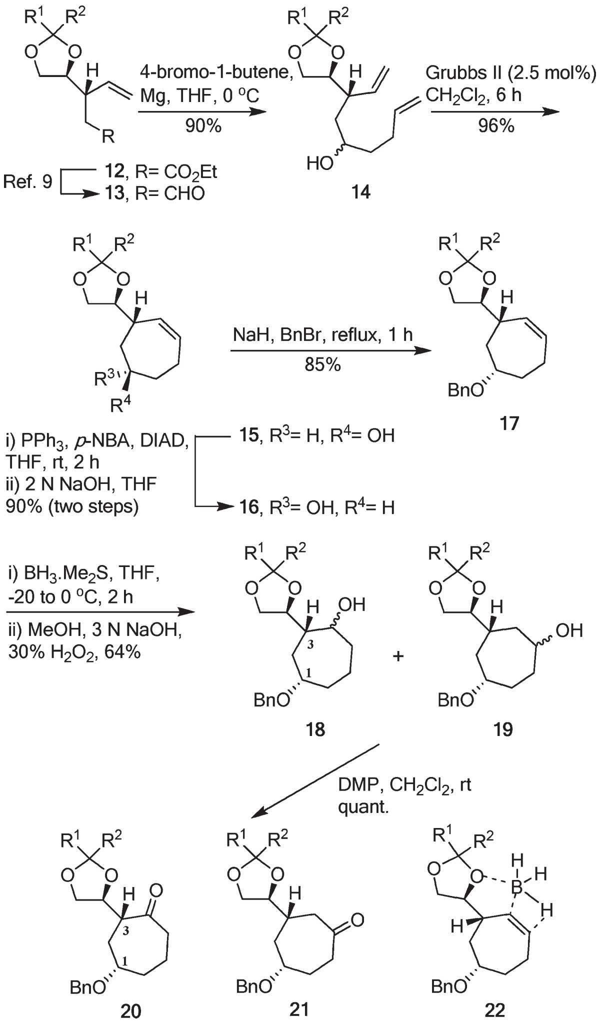
(6) (a) Tang, Y.; Zhang, Y.; Dai, M.; Luo, T.; Deng, L.; Chen, J.; Yang, Z. *Org. Lett.* **2005**, *7*, 885–888. (b) Zhang, Y. D.; Tang, Y. F.; Luo, T. P.; Shen, J.; Chen, J. H.; Yang, Z. *Org. Lett.* **2006**, *8*, 107–110. (c) Zhang, Y. D.; Ren, W. W.; Lan, Y.; Xiao, Q.; Wang, K.; Xu, J.; Chen, J. H.; Yang, Z. *Org. Lett.* **2008**, *10*, 665–668. (d) Lai, K. W.; Paquette, L. A. *Org. Lett.* **2008**, *10*, 2115–2118. (e) Paquette, L. A.; Lai, K. W. *Org. Lett.* **2008**, *10*, 2111–2113. (f) Paquette, L. A.; Lai, K. W. *Org. Lett.* **2008**, *10*, 3781–3784. (g) Cordonnier, M.-C. A.; Kan, S. B. J.; Anderson, E. A. *Chem. Commun.* **2008**, 5818–5820. (h) Mehta, G.; Bhat, B. A. *Tetrahedron Lett.* **2009**, *50*, 2474–2477. (i) Mehta, G.; Bhat, B. A.; Kumara, T. H. S. *Tetrahedron Lett.* **2009**, *50*, 6597–6600.

(7) For excellent accounts on RCM, see: (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446–452. (b) Fürstner, A. *Top. Catal.* **1997**, *4*, 285–299. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed.* **1997**, *36*, 2036–2056. (d) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450. (e) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371–388. (f) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012–3043. (g) Deiters, A.; Martin, S. F. *Chem. Rev.* **2004**, *104*, 2199–2238. (h) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4490–4527. (i) Ghosh, S.; Ghosh, S.; Sarkar, N. *J. Chem. Sci.* **2006**, *118*, 223–235. (j) Chattopadhyay, S. K.; Karmakar, S.; Biswas, T.; Majumdar, K. C.; Rahaman, H.; Roy, B. *Tetrahedron* **2007**, *63*, 3919–3952.

SCHEME 2. **Synthesis of Functionalized Cycloheptane Derivative 20**[a]



[a] For structures **12**–**22**: R^1, R^2 = $-(CH_2)_5-$.

synthetic plan. For this purpose the unsaturated ester **12** was chosen as this is readily available[8a] from D-mannitol compared to its diastereoisomer epimeric at C-3.[8b] According to the retrosynthetic plan, the ester **12** was expected to provide the enantiomer of 8a. Eventually, the ester **12** turned out to be the right choice. It led to C-5-*epi*-**8a** (vide infra) having the desired stereochemistry at all of the stereogenic centers except the one at C-5, which can be inverted in one of the subsequent steps during total synthesis. The ester **12** was transformed into the aldehyde **13**[9] using a reduction–oxidation sequence. The aldehyde **13** on reaction with 4-butenyl magnesium bromide afforded in 90% yield an inseparable mixture of alcohols **14** (ca. 3:2) as revealed by ^{13}C NMR spectra. RCM of the mixture of dienols **14** with Grubbs I did not proceed at all. However, with Grubbs II ring closure proceeded smoothly to afford a mixture of the cycloheptenols **15** and **16**. The cycloheptenols could be separated by column chromatography to give **15** and **16** in 38% and 58% yields, respectively. The minor diastereoisomer **15** was isomerized to **16** through Mitsunobu protocol. The stereochemical assignment to the hydroxyl group in **16** could not be made at this stage. The hydroxyl group in **16** was then protected to provide the benzyl ether **17** in 85% yield. The cycloheptene derivative **17** was next treated with $BH_3 \cdot Me_2S$, and the resulting alkyl borane was oxidized in situ with alkaline H_2O_2 to give a mixture of cycloheptanols (ca. 4:1). Careful chromatography of this mixture led to isolation of the compounds **18** (R_f 0.7) and **19** (R_f 0.5), each of them being obtained as diastereomeric mixtures in 64% and 16% yields, respectively. The cycloheptanols **18** and **19** were oxidized separately by DMP to afford the cycloheptanones **20** and **21** in quantitative yield. The structures of the cycloheptanones were established by comparing the ^{13}C chemical shifts of the C_3-methine carbons of **20** with that of **21**. The C_3-methine carbon next to the carbonyl group is expected to be deshielded over the one that is one carbon away from the carbonyl group. The cycloheptanone derivative obtained from oxidation of the major cycloheptanols with higher R_f value appeared at δ 51.9, while the same carbon in the cycloheptanone derivative arising from cycloheptanols with lower R_f value appeared at δ 35.8. Thus the former cycloheptanone derivative was assigned the structure **20**, and the latter was assigned the regioisomeric structure **21**. This indicated that hydroboration of the cycloheptene derivative **17** proceeded to produce predominantly the regioisomer **18**. Regioselective hydroboration[10] of the unsymmetrical cycloheptene **17** is interesting. Such regioselectivity during hydroboration has been observed only in alkenes where there is an oxygen functionality at the allylic position. Regioselectivity observed in the present case probably arises through addition of borane through the complex **22** in which borane is coordinated to the homoallylic oxygen atom of the ketal unit.

With the functionalized cycloheptanone **20** in hand, next we focused our attention on the construction of the furofuranone unit on it. Toward this end, the cycloheptanone **20** was reacted with vinylmagnesium bromide to afford the adduct **23** in 65% yield as a single diastereomer (Scheme 3). We expected that addition would take place through a metal-coordinated chelate to produce the desired adduct from the side of the substituent bearing the ketal unit. This would then lead to 4-*epi*-**28** (Scheme 3), which on bromoetherification would give rise to a tricycle with C-1, C-4, and C-5 relative stereochemistry the same as that present in the ABC ring of Schisandra natural products. Disappointingly, vinylmagnesium bromide added to the cycloheptanone **20** exclusively from the face opposite to the bulky ketal unit. This could be ascertained only after transformation of **23** to the bromo bis-tetrahydrofuran derivative **29**. The compound **23** was then converted into the allyl ether **24**. Exposure of **24** to Grubbs I precatalyst resulted in smooth formation of the dihydrofuran derivative **25** in 94% yield. Acid-induced deketalization of **25** afforded the diol **26** in excellent yield. The diol **26** was then transformed into the methyl ketone **27** through a sequence of high yielding steps involving periodate cleavage of the diol and addition of MeMgI to the resulting aldehyde followed by DMP oxidation. Addition of MeMgI to **27** afforded **28**.

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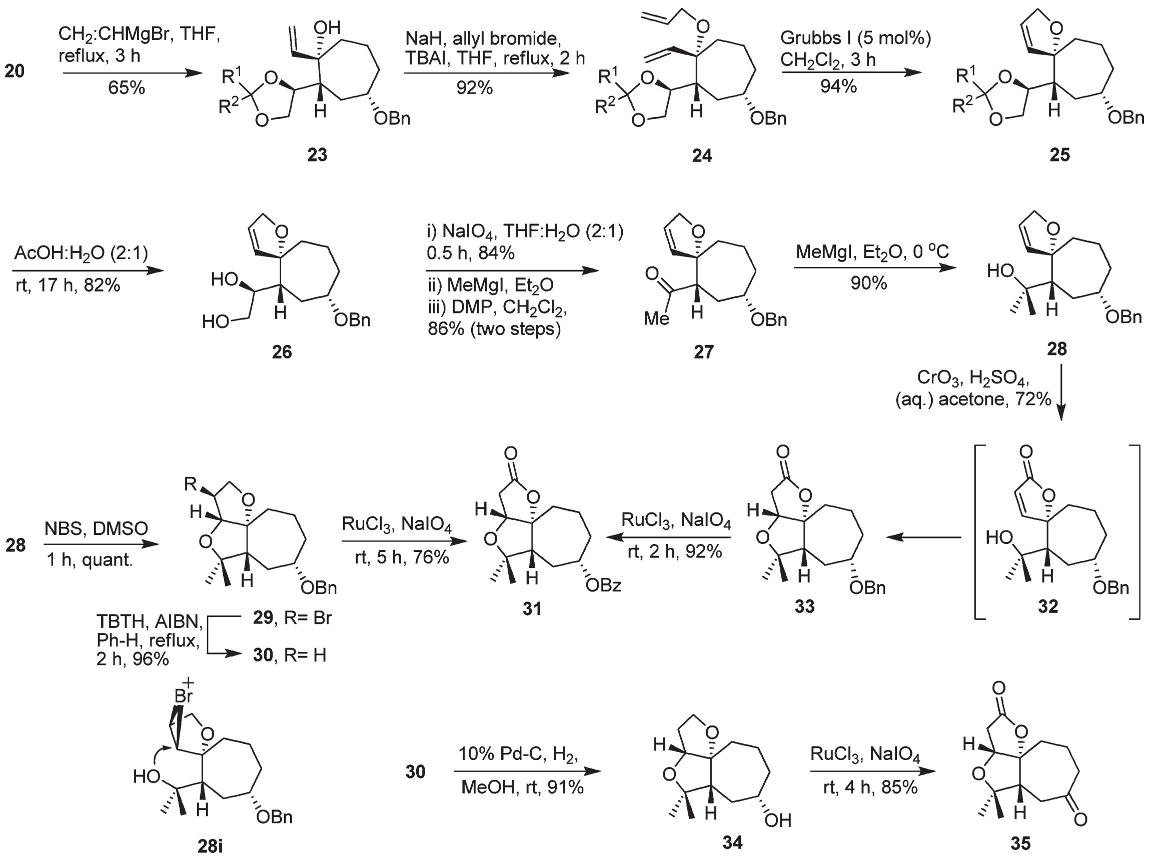
(8) (a) Matcha, K.; Ghosh, S. *Tetrahedron Lett.* **2008**, *49*, 3433–3436. (b) Banerjee, S.; Ghosh, S.; Sinha, S.; Ghosh, S. *J. Org. Chem.* **2005**, *70*, 4199–4202.

(9) Ghosh, S.; Bhaumik, T.; Sarkar, N.; Nayek, A. *J. Org. Chem.* **2006**, *71*, 9687–9694.

(10) (a) Brown, H. C.; Knights, E. F. *J. Am. Chem. Soc.* **1968**, *90*, 4439–4444. (b) Pasto, D. J.; Hickman, J. *J. Am. Chem. Soc.* **1968**, *90*, 4445–4449.

SCHEME 3. Synthesis of C-5-*epi* ABC Core of Compounds 1 and 3−7[a]



[a] For structures **23**−**25**: R^1, R^2 = $-(CH_2)_5-$.

With the availability of the precursor **28**, we proceeded for its bromonium ion initiated cyclization.[11] Compound **28** was treated with NBS in DMSO. As expected, cyclization proceeded stereoselectively through the bromonium ion intermediate **28i** formed by addition of bromine from the least hindered *re* face of the alkene. The bromo ether **29** was obtained exclusively in quantitative yield. The stereochemical assignment to **29** was established through single crystal X-ray[12] structure determination. Reductive removal of bromine from **29** could be achieved with TBTH in near quantitative yield to afford the bis-tetrahydrofuran derivative **30**. Finally, oxidation of **30** with $RuCl_3$(cat.)/$NaIO_4$ proceeded smoothly to afford the furofuranone derivative **31** in 76% isolable yield. It may be noted that oxidation of benzylic group to benzoate ester also took place during oxidation of the tetrahydrofuran ring in **30**.

At this stage we thought of exploring an alternative protocol. Thus, the dihydrofuran **28** was treated with Jones reagent with the objective of synthesizing the butenolide **32**. Amazingly, oxidation of the dihydrofuran unit took place with spontaneous intramolecular 1,4-addition of the tertiary alcohol to the resulting butenolide **32** to afford stereoselectively the tricyclic lactone **33** in 72% yield. The structure of this compound was initially determined by its transformation to the benzoate **31** on treatment with $RuCl_3$(cat.)/$NaIO_4$. This structural assignment was confirmed through single crystal X-ray analysis.[12] Finally, the projected intermediate could be prepared as follows. Debenzylation of **30** was achieved through hydrogenolysis to afford the hydroxy-compound **34** in excellent yield. Oxidation of the tetrahydrofuran unit in **34** with $RuCl_3$/$NaIO_4$ proceeded smoothly with simultaneous oxidation of the hydroxyl group to afford the cycloheptanone **35** in excellent yield. This approach thus led to the synthesis of C-5-*epi* ABC core of schisandra terpenes. The C-7 carbonyl group can be employed not only to annulate rings of appropriate size onto seven-membered ring but also to invert the configuration at the C-5 stereogenic center through reduction of the conjugated enone system derivable in principle at a late stage in the total synthesis.

With the success of the above protocol in synthesizing the diastereoisomeric ABC ring system of **1** and **3**−**7**, we next embarked upon its extension for the construction of the diastereoisomeric ABC ring system present in lancifodilactone G **2** (Scheme 4). The synthesis began with selective protection of the primary hydroxyl group of **26** as silyl ether followed by oxidation of the secondary alcohol to afford the ketone **36**. Addition of methylmagnesium iodide to **36** afforded an inseparable mixture of carbinols **37** in a 3:2 ratio in 90% yield. This mixture on treatment with NBS in DMSO gave quantitatively a mixture of two tricyclic bromides **38** and **39**. The major diastereoisomer in this mixture was separated by column chromatography to afford

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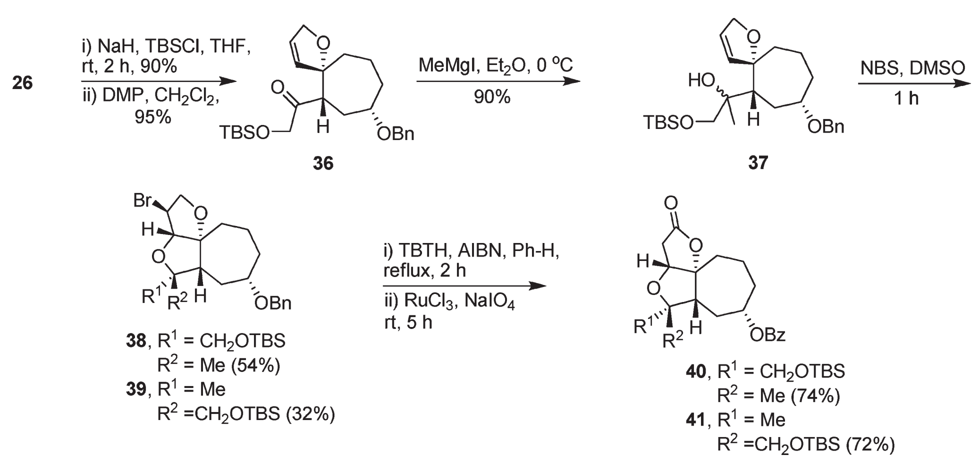
[11] Zhong, H. M.; Sohn, J. H.; Rawal, V. H. *J. Org. Chem.* **2007**, *72*, 386–397.

[12] Crystallographic data for compounds **29** and **33** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication nos. CCDC 762931and 759611, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223-336033. E-mail: deposit@ccdc.cam.ac.uk.

SCHEME 4. Synthesis of C-5-*epi* ABC Core of Lancifodilactone G 2



the bromo-ether **38** in 54% yield. The assignment of stereochemistry to **38** was based on analogy to the formation of the bromoether **29** from reaction of **28** with NBS. Reductive removal of bromine with TBTH followed by oxidation with $RuCl_3/NaIO_4$ finally afforded the tricyclic lactone **40** in 74% yield. The assignment of stereochemistry (Figure 2) to the lactone **40** is based on analysis of its NMR spectral data (HSQC, COSY, NOESY and NOE). Significant NOE enhancements observed among the marked protons corroborated the above structural assignment.

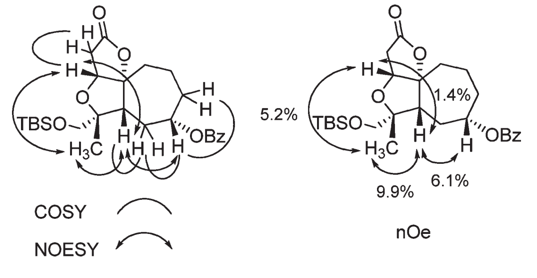


FIGURE 2. COSY, NOESY, and NOE analysis of **40**.

The minor diastereoisomer **39** was converted into the tricycle **41**, in 72% yield. The structure of the tricyclic lactone **41** was established through analysis of its NMR spectra (HSQC, COSY and NOESY) as depicted in Figure 3.

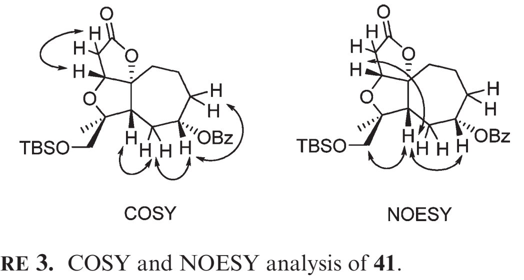


FIGURE 3. COSY and NOESY analysis of **41**.

Conclusion

In conclusion, we have developed a protocol that allows enantiopure construction of the C-5-*epi* ABC ring system present in **1** and **3**–**7**. The same protocol has been extended for the construction of the C-5-*epi* ABC core present in lancifodilactone G **2**. The key steps involve RCM to form spirodihydrofuran followed by bromonium ion initiated cyclization to form the bis-tetrahydrofuran derivative. Oxidation of the latter then furnished the furo-furanone system.

Experimental Section

(*S*)-3-((*S*)-1,4-Dioxaspiro[4.5]decan-2-yl)nona-1,8-dien-5-ol (14). 4-Bromo-1-butene (0.95 mL, 9.37 mmol) was added dropwise to a stirred suspension of magnesium turnings (450 mg, 18.74 mmol) in THF (15 mL) at 0 °C, and the mixture was stirred for 1 h to produce a clear solution. A solution of the aldehyde **13** (1.4 g, 6.24 mmol) in THF (10 mL) was added dropwise to this solution at 0 °C and allowed to stir for 1 h. The reaction mixture was quenched with saturated aqueous NH_4Cl solution (1 mL). Usual workup of the reaction mixture followed by column chromatography (15% Et_2O/petroleum ether) afforded an inseparable mixture of dienols **14** (1.57 g, 90%) as liquid: $[\alpha]^{25}{}_D$ +2.3 (*c* 5.2, $CHCl_3$); ν_{max} (film) 3445, 2935, 1640, 1448 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (for the mixture) 5.88–5.74 (m, 1H), 5.65–5.46 (m, 1H), 5.13–5.02 (m, 2H), 4.99–4.92 (m, 2H), 3.96–3.76 (m, 2H), 3.69–3.55 (m, 2H), 2.73 (br s, 1H), 2.38–2.30 (m, 1H), 2.24–2.07 (m, 2H), 1.81–1.70 (m, 1H), 1.60–1.43 (m, 11H), 1.37 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (for major isomer) 138.8, 138.2, 117.2, 114.7, 110.1, 78.4, 69.4, 68.3, 46.6, 40.6, 37.4, 36.4, 35.3, 30.2, 25.2, 24.1, 24.0; (for minor isomer) 138.7, 138.4, 117.0, 114.7, 110.1, 78.0, 69.5, 68.3, 45.8, 40.7, 36.5, 36.1, 35.2, 30.1, 25.2, 24.1, 24.0; HRMS (ESI) *m*/*z* $[M + Na]^+$, calcd for $C_{17}H_{28}O_3Na$ 303.1936; found 303.1936.

(1*R*,3*S*)-3-((*S*)-1,4-Dioxaspiro[4.5]decan-2-yl)cyclohept-4-enol (15) and (1*S*,3*S*)-3-((*S*)-1,4-Dioxaspiro[4.5]decan-2-yl)cyclohept-4-enol (16). A solution of diastereoisomeric dienols **14** (100 mg, 0.35 mmol) in dichloromethane (20 mL) was treated with Grubbs second generation catalyst (8 mg, 0.01 mmol) under Ar atmosphere and stirred at rt for 6 h. The residual mass obtained after removal of solvent was chromatographed (15% EtOAc/petroleum ether) to afford **15** (33 mg, 38%) and **16** (50 mg, 58%) as a colorless liquid. Compound **15**: $[\alpha]^{27}{}_D$ +33.4 (*c* 4.0, $CHCl_3$); ν_{max} (film) 3435, 3013, 2933, 1448 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.85–5.77 (m, 1H), 5.50 (dd, J = 11.0, 4.0 Hz, 1H), 4.21–4.15 (m, 1H), 4.03–3.96 (m, 2H), 3.63–3.56 (m, 1H), 2.80 (br s, 1H), 2.36–2.27 (m, 1H), 1.95–1.80 (m, 3H), 1.75–1.65 (m, 3H), 1.63–1.51 (m, 8H), 1.40–1.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.0, 132.0, 109.6, 78.2, 69.5, 67.4, 37.3, 36.5, 36.2, 35.1, 34.0, 25.3, 24.1, 24.0, 22.7; HRMS (ESI) *m*/*z* $[M + Na]^+$, calcd for $C_{15}H_{24}O_3Na$ 275.1628, found 275.1625. Compound **16**: $[\alpha]^{25}{}_D$ +16.5 (*c* 4.9, $CHCl_3$); ν_{max} (film) 3389, 3377, 2933, 1651, 1448 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.87–5.79 (m, 1H), 5.47 (d, J = 10.9 Hz, 1H), 4.03–3.98 (m, 2H), 3.79–3.72 (m, 1H), 3.62–3.55 (m, 1H), 2.31 (br s, 1H), 2.23−1.91 (m, 5H), 1.59 (br s, 4H), 1.55 (br s, 4H), 1.37−1.27 (m, 2H), 1.25−1.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.5, 131.6, 109.5, 78.2, 74.1, 67.1, 38.4, 38.2, 36.3, 35.3, 34.7, 25.1, 24.0, 23.7, 23.0; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{15}H_{24}O_3Na$ 275.1628, found 275.1623.

(1*S*,3*S*)-3-((*S*)-1,4-Dioxaspiro[4.5]decan-2-yl)cyclohept-4-enol (16). To a solution of cycloheptenol **15** (900 mg, 3.57 mmol) in THF were added triphenyl phosphine (1.87 g, 7.14 mmol), diisopropyl azodicarboxylate (1.4 mL, 7.14 mmol), and *p*-nitrobenzoic acid (1.2 g, 7.14 mmol), and the reaction mixture was stirred for 2 h. After being diluted with Et_2O (30 mL), the reaction mixture was washed with saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO4, and concentrated under reduced pressure. The resulting crude residue was purified by column chromatography (5% Et_2O/petroleum ether) to give *p*-nitrobenzoate derivative (1.35 g, 94%) as a colorless liquid: $[\alpha]^{24}_D$ −20.4 (*c* 4.9, $CHCl_3$); ν_{max} (film) 2936, 1720, 1608, 1529, 1448 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (d, *J* = 8.7 Hz, 2H), 8.18 (d, *J* = 8.6 Hz, 2H), 5.92−5.89 (m, 1H), 5.55 (d, *J* = 10.8 Hz, 1H), 5.24−5.17 (m, 1H), 4.10−4.02 (m, 2H), 3.68−3.62 (m, 1H), 2.46 (br s, 1H), 2.36−2.26 (m, 2H), 2.19−2.1 (m, 2H), 1.62 (br s, 5H), 1.55 (br s, 5H), 1.47−1.37 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.8, 150.5, 136.3, 132.5, 131.8, 130.8 (×2), 123.5 (×2), 109.9, 78.2, 77.9, 67.3, 38.5, 36.5, 35.0 (×2), 32.2, 25.2, 24.1, 23.9, 23.1; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{22}H_{27}NO_6Na$ 424.1737, found 424.1736.

The *p*-nitrobenzoate derivative (1.05 g, 2.61 mmol) was treated with aqueous NaOH solution (5.3 mL, 10.46 mmol, 2 N in H_2O) in THF (20 mL) at rt for overnight. After being diluted with Et_2O (50 mL), the reaction mixture was washed with brine solution, dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by column chromatography (15% EtOAc/petroleum ether) to provide cycloheptenol **16** (627 mg, 95%) as a colorless oil.

(*S*)-2-((1*S*,6*S*)-6-(Benzyloxy)cyclohept-2-enyl)-1,4-dioxaspiro[4.5]decane (17). To a magnetically stirred suspension of NaH (508 mg, 12.7 mmol, 60% in oil), freed from adhering oil by repeated washing with petroleum ether, in dry THF (20 mL) at 0 °C was added dropwise a solution of the alcohol **16** (800 mg, 3.17 mmol) in dry THF (15 mL) under N_2 atmosphere. The mixture was allowed to reflux for 1 h, and then to it was added HMPA (0.8 mL) dropwise followed by benzyl bromide (0.94 mL, 7.93 mmol). After refluxing for an additional 6 h, the reaction mixture was cooled to 0 °C and quenched by adding saturated aqueous NH_4Cl solution (1 mL). Usual workup of the reaction mixture followed by column chromatography (7% Et_2O/petroleum ether) afforded the benzyl ether **17** (923 mg, 85%) as a colorless oil: $[\alpha]^{25}_D$ +17.4 (*c* 3.7, $CHCl_3$); ν_{max} (film) 3013, 2935, 1653, 1496 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.27 (m, 5H), 5.91−5.85 (m, 1H), 5.55 (dd, *J* = 11.4, 2.5 Hz, 1H), 4.60 (s, 2H), 4.10−4.02 (m, 2H), 3.67−3.63 (m, 1H), 3.53−3.49 (m, 1H), 2.37−2.26 (m, 3H), 2.12−1.92 (m, 2H), 1.65 (br s, 5H), 1.61 (br s, 4H), 1.57−1.41 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 132.7, 131.6, 128.5 (×2), 127.6, 127.6, 127.5, 109.6, 81.0, 78.6, 70.2, 67.1, 38.3, 36.6, 35.5, 35.0, 32.3, 25.3, 24.1, 23.9, 23.4; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{22}H_{30}O_3Na$ 365.2090, found 365.2093.

(2*S*,4*S*)-4-(Benzyloxy)-2-((*S*)-1,4-dioxaspiro[4.5]decan-2-yl)cycloheptanol (18) and (3*R*,5*S*)-5-(Benzyloxy)-3-((*S*)-1,4-dioxaspiro[4.5]decan-2-yl)cycloheptanol (19). To a solution of the cycloheptene derivative **17** (300 mg, 0.88 mmol) in dry THF (10 mL) was added borane dimethylsulfide complex solution (1.31 mL, 2.63 mmol, 2.0 M in THF) at −20 °C under argon. The mixture was then warmed to 0 °C and stirred at that temperature for an additional 2 h. The reaction mixture was then oxidized by sequential addition of MeOH (0.54 mL, 10.5 mmol), NaOH (2.64 mL, 7.92 mmol, 3 N in water), and H_2O_2 (2.8 mL, 18.6 mmol, 30%). The mixture was then stirred overnight at rt, water (5 mL) was added, and then an extraction with EtOAc (3 × 20 mL) was performed. The organic layer was dried and concentrated in vacuo. Purification of the residual mass by column chromatography (20% EtOAc/petroleum ether) afforded mixture of cycloheptanols **18** (202 mg, 64%) and **19** (50 mg, 16%) as a colorless oil. Compound **18**: $[\alpha]^{25}_D$ +11.5 (*c* 2.3, $CHCl_3$); ν_{max} (film) 3454, 2933, 2860, 1496, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (for the mixture) 7.28−7.20 (m, 5H), 4.53−4.42 (m, 2H), 4.28−4.10 (m, 1H), 4.06−3.89 (m, 2H), 3.87−3.79 (m, 1H), 3.74−3.57 (m, 1H), 3.42−3.32 (m, 1H), 2.14−1.84 (m, 2H), 1.82−1.67 (m, 2H), 1.64−1.48 (m, 10H), 1.38−1.30 (m, 3H), 1.26−1.17 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (for major isomer) 138.6, 128.3 (×2), 127.5 (×2), 127.4, 109.4, 80.4, 78.4, 70.8, 70.4, 65.7, 43.1, 35.8, 35.4, 34.7, 34.3, 31.4, 25.0, 24.0, 23.7, 17.1; (for minor isomer) 138.3, 128.2 (×2), 127.3, 127.2 (×2), 109.4, 78.8, 76.9, 70.8, 70.1, 67.3, 43.5, 36.6, 36.2, 34.6, 32.2, 28.9, 25.1, 23.9, 23.8, 16.7; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{22}H_{32}O_4Na$ 383.2198, found 383.2194. Compound **19**: $[\alpha]^{27}_D$ +6.4 (*c* 4.1, $CHCl_3$); ν_{max} (film) 3439, 3417, 2933, 2860, 1496, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (for the mixture) 7.27−7.18 (m, 5H), 4.47 (br s, 2H), 4.09−3.90 (m, 2H), 3.86−3.67 (m, 2H), 3.57−3.52 (m, 1H), 3.50−3.36 (m, 1H), 2.36−2.01 (m, 2H), 1.97−1.62 (m, 2H), 1.58−1.40 (m, 10H), 1.33 (br s, 3H), 1.28−1.10 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (for major isomer) 138.8, 128.3 (×2), 127.6 (×2), 127.4, 109.4, 79.3, 79.2, 70.3, 69.1, 67.1, 38.9, 36.8, 36.3, 34.9, 33.2, 30.8, 28.7, 25.2, 24.0, 23.8; (for minor isomer) 138.8, 128.3 (×2), 127.5 (×2), 127.4, 108.8, 79.1, 77.6, 71.7, 70.1, 66.9, 39.9, 36.9, 36.3, 35.3, 34.7, 31.6, 27.4, 25.2, 24.0, 23.8; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{22}H_{32}O_4Na$ 383.2198, found 383.2197.

(2*R*,4*S*)-4-(Benzyloxy)-2-((*S*)-1,4-dioxaspiro[4.5]decan-2-yl)cycloheptanone (20). To a solution of the cycloheptanol derivative **18** (60 mg, 0.16 mmol) in CH_2Cl_2 (5 mL) at rt was added DMP (85 mg, 0.20 mmol) portionwise, and the reaction mixture was allowed to stir for 2 h.The reaction mixture was quenched with 10% $Na_2S_2O_3$ solution (2 mL) doped with $NaHCO_3$ at ice-cold condition and stirred vigorously until the organic layer became transparent. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residual mass by column chromatography (12% Et_2O/petroleum ether) afforded cycloheptanone **20** (59 mg, 99%) as a colorless oil: $[\alpha]^{26}_D$ −35.2 (*c* 5.0, $CHCl_3$); ν_{max} (film) 2934, 2860, 1699, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.25 (m, 5H), 4.58 (dd, *J* = 17.7, 12.0 Hz, 2H), 4.30−4.22 (m, 1H), 4.15 (dd, *J* = 8.5, 6.1 Hz, 1H), 3.51−3.44 (m, 2H), 2.61−2.52 (m, 1H), 2.50−2.44 (m, 2H), 2.29−2.21 (m, 1H), 1.91−1.84 (m, 1H), 1.67−1.57 (m, 10H), 1.53−1.40 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.9, 138.6, 128.5 (×2), 127.7 (×2), 127.6, 109.2, 79.5, 75.5, 70.5, 68.8, 51.9, 43.5, 36.8, 35.3, 34.8, 32.8, 25.3, 24.2, 23.9, 19.7; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{22}H_{30}O_4Na$ 381.2042, found 381.2047.

(3*S*,5*S*)-5-(Benzyloxy)-3-((*S*)-1,4-dioxaspiro[4.5]decan-2-yl)cycloheptanone (21). Following the procedure of oxidation, the above carbinol **19** (40 mg, 0.11 mmol) was oxidized with DMP (56 mg, 0.14 mmol) to afford the title compound **21** (39 mg, 98%) as a colorless liquid: $[\alpha]^{27}_D$ +36.6 (*c* 3.6, $CHCl_3$); ν_{max} (film) 2935, 2860, 1699, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.19 (m, 5H), 4.50 (s, 2H), 3.96−3.88 (m, 2H), 3.55−3.51 (m, 1H), 3.43−3.34 (m, 1H), 2.45−2.31 (m, 4H), 2.15−2.08 (m, 1H), 1.87−1.61 (m, 2H), 1.53 (br s, 4H), 1.49 (br s, 4H), 1.38−1.29 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.2, 138.5, 128.5 (×2), 127.7, 127.6 (×2), 109.9, 79.2, 78.5, 70.6, 66.7, 45.4, 38.9, 38.0, 36.4, 35.8, 34.9, 30.0, 25.2, 24.0, 23.9; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{22}H_{30}O_4Na$ 381.2042, found 381.2043.

(1*S*,2*R*,4*S*)-4-(Benzyloxy)-2-((*S*)-1,4-dioxaspiro[4.5]decan-2-yl)-1-vinylcycloheptanol (23). To a solution of the cycloheptanone derivative **20** (350 mg, 0.97 mmol) in THF (10 mL) was added vinylmagnesium bromide (3.0 mL, 3.0 mmol, 1 M in THF), and the resulting mixture was refluxed for 3 h. Then the resulting mixture was cooled to 0 °C, quenched with saturated aqueous NH_4Cl solution, extracted with EtOAc (3 × 10 mL), washed with brine, and dried over Na_2SO_4. The crude residue was purified by column chromatography (10% EtOAc/petroleum ether), to give **23** (245 mg, 65%) as a colorless liquid: $[\alpha]^{26}_D$ −2.1 (*c* 3.0, $CHCl_3$); ν_{max} (film) 3522, 2930, 2860, 1639, 1494 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.27 (m, 5H), 5.84 (dd, *J* = 17.0, 10.6 Hz, 1H), 5.37 (dd, *J* = 17.0, 1.7 Hz, 1H), 5.08 (dd, *J* = 10.6, 1.7 Hz, 1H), 4.56 (s, 2H), 4.41 (dt, *J* = 6.9, 1.7 Hz, 1H), 3.95 (dd, *J* = 8.0, 7.1 Hz, 1H), 3.54 (dd, *J* = 8.0, 6.9 Hz, 1H), 3.46−3.38 (m, 1H), 3.32 (br s, 1H), 2.21−1.80 (m, 4H), 1.77−1.47 (m, 11H), 1.43−1.35 (m, 2H), 1.32−1.20 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.4, 139.1, 128.5 (×2), 127.6 (×2), 127.6, 112.0, 110.3, 79.6, 77.2, 75.7, 70.4, 67.4, 42.8, 42.1, 35.9, 35.2, 34.2, 26.2, 25.2, 24.2, 24.0, 18.1; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{24}H_{34}O_4Na$ 409.2355, found 409.2351.

(*S*)-2-((1*R*,2*S*,6*S*)-2-(Allyloxy)-6-(benzyloxy)-2-vinylcycloheptyl)-1,4 dioxaspiro[4.5]decane (24). To a magnetically stirred suspension of NaH (103 mg, 2.58 mmol, 60% in oil), freed from adhering oil by repeated washing with petroleum ether, in dry THF (7 mL) was added dropwise a solution of the alcohol **23** (250 mg, 0.65 mmol) in dry THF (3 mL) under Ar atmosphere. The mixture was allowed to stir at reflux for 1 h, and then to it was added TBAI (ca. 50 mg) followed by allyl bromide (0.2 mL, 2.58 mmol). After stirring for an additional 1 h at reflux, the reaction mixture was cooled to 0 °C and quenched by adding saturated aqueous NH_4Cl solution (1 mL). Usual workup of the reaction mixture followed by column chromatography (10% Et_2O/petroleum ether) afforded the allyl ether **24** (254 mg, 92%) as a colorless liquid: $[\alpha]^{28}_D$ +20.9 (*c* 1.4, $CHCl_3$); ν_{max} (film) 2933, 2860, 1645, 1495 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.28 (m, 5H), 5.96−5.83 (m, 1H), 5.80−5.71 (m, 1H), 5.37 (dd, *J* = 17.2, 1.9 Hz, 1H), 5.15−5.10 (m, 2H), 4.59 (dd, *J* = 16.2, 12.3 Hz, 2H), 4.36−4.30 (m, 1H), 3.98−3.92 (m, 3H), 3.45 (t, *J* = 8.3 Hz, 1H), 3.42−3.33 (m, 1H), 2.36 (d, *J* = 14.3 Hz, 1H), 2.18−2.08 (m, 1H), 2.01−1.87 (m, 3H), 1.84−1.70 (m, 2H), 1.67−1.48 (m, 10H), 1.41 (br s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7, 139.2, 135.8, 128.4 (×2), 127.6 (×2), 127.5, 114.7, 114.1, 108.1, 80.7, 80.6, 75.5, 70.1, 69.5, 62.8, 46.7, 36.7, 36.3, 35.8, 35.5, 29.6, 25.4, 24.2, 24.1, 18.5; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{27}H_{38}O_4Na$ 449.2668, found 449.2661.

(5*S*,6*R*,8*S*)-8-(Benzyloxy)-6-((*S*)-1,4-dioxaspiro[4.5]decan-2-yl)-1-oxaspiro[4.6]undec-3-ene (25). A solution of the diene **24** (240 mg, 0.56 mmol) in anhydrous deoxygenated CH_2Cl_2 q(50 mL) was treated with Grubbs first generation catalyst (23 mg, 5 mol %) under argon atmosphere and stirred at rt for 3 h. The residual mass obtained after removal of the solvent was chromatographed (10% Et_2O/petroleum ether) to afford the spiro compound **25** (210 mg, 94%) as a colorless liquid: $[\alpha]^{27}_D$ +30.7 (*c* 1.0, $CHCl_3$); ν_{max} (film) 2932, 2858, 1604, 1494 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.25 (m, 5H), 5.81−5.78 (m, 1H), 5.69−5.65 (m, 1H), 4.65−4.51 (m, 4H), 4.10−4.04 (m, 1H), 3.87 (dd, *J* = 8.0, 2.1 Hz, 1H), 3.40−3.34 (m, 2H), 2.37−2.31 (m, 1H), 2.09−2.02 (m, 1H), 1.96−1.81 (m, 3H), 1.80−1.69 (m, 2H), 1.65−1.53 (m, 10H), 1.39 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 134.3, 128.4 (×2), 127.6 (×2), 127.4, 125.7, 108.1, 93.2, 80.2, 75.8, 74.7, 70.1, 69.2, 45.9, 40.8, 36.5, 35.8, 35.3, 29.5, 25.3, 24.1, 24.0, 18.8; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{25}H_{34}O_4Na$ 421.2355, found 421.2354.

(*S*)-1-((5*S*,6*R*,8*S*)-8-(Benzyloxy)-1-oxaspiro[4.6]undec-3-en-6-yl)ethane-1,2-diol (26). A mixture of the spiro-cyclic compound **25** (450 mg, 1.13 mmol) and acetic acid (8 mL, 80% in water) was stirred at rt for 17 h. The resulting solution was concentrated in reduced pressure. Purification of the residual mass by column chromatography (40% EtOAc/petroleum ether) afforded diol **26** (295 mg, 82%) as a colorless oil: $[\alpha]^{27}_D$ +12.7 (*c* 5.9, $CHCl_3$); ν_{max} (film) 3435, 2933, 2860, 1641, 1496, 1454 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.25 (m, 5H), 5.90 (d, *J* = 6.1 Hz, 1H), 5.71−5.68 (m, 1H), 4.64 (s, 2H), 4.55 (dd, *J* = 21.3, 12.0 Hz, 2H), 3.90 (dd, *J* = 7.9, 4.9 Hz, 1H), 3.65 (dd, *J* = 10.7, 8.0 Hz, 1H), 3.39 (dd, *J* = 10.9, 4.8 Hz, 1H), 3.36−3.30 (m, 1H), 3.01 (br s, 1H), 2.16−2.12 (m, 1H), 2.05−2.00 (m, 2H), 1.96−1.68 (m, 4H), 1.52−1.48 (m, 2H), 1.25−1.12 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 133.6, 128.5 (×2), 127.6 (×2), 127.5, 126.2, 96.9, 80.9, 74.9, 72.7, 70.4, 65.0, 42.4, 39.7, 36.3, 28.1, 18.8; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{19}H_{26}O_4Na$ 341.1729, found 341.1729.

1-((5*S*,6*S*,8*S*)-8-(Benzyloxy)-1-oxaspiro[4.6]undec-3-en-6-yl)-ethanone (27). To a magnetically stirred ice-cold solution of the diol **26** (90 mg, 0.28 mmol) in THF/water (2:1, 3 mL) was added $NaIO_4$ (121 mg, 0.56 mmol) in multiple portions. The reaction mixture was allowed to stir at 0 °C for 30 min. The precipitated white solid was filtered off after washing it thoroughly with diethyl ether. Usual workup of the filtrate afforded the aldehyde (68 mg, 84%) as a colorless oil: $[\alpha]^{27}_D$ +11.5 (*c* 0.8, $CHCl_3$); ν_{max} (film) 2932, 2860, 1722, 1639, 1452 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.48 (d, *J* = 2.2 Hz, 1H), 7.27−7.18 (m, 5H), 5.86−5.80 (m, 2H), 4.57−4.39 (m, 4H), 3.38−3.21 (m, 1H), 2.25−2.20 (m, 2H), 1.99−1.82 (m, 2H), 1.79−1.58 (m, 4H), 1.32−1.17 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.4, 138.9, 132.9, 128.5 (×2), 127.7 (×2), 127.6, 126.8, 92.8, 79.5, 75.2, 70.4, 55.0, 40.8, 35.7, 27.7, 18.8; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{18}H_{22}O_3Na$ 309.1467, found 309.1466.

To a solution of the aldehyde (80 mg, 0.28 mmol) in dry diethyl ether (1 mL) was added methylmagnesiumbromide [prepared from magnesium turnings (47 mg, 1.95 mmol) in dry diethyl ether (3 mL) and methyl iodide (0.10 mL, 1.40 mmol)] at 0 °C. The mixture was stirred at that temperature for 1 h and quenched with saturated aqueous NH_4Cl solution. After stirring for 15 min at rt, the mixture was extracted with diethyl ether (2 × 5 mL). The combined organic layer was dried and concentrated in vacuo. The resulting crude product was chromatographed (15% Et_2O/petroleum ether) affording the mixture of corresponding methyl addition products (74 mg, 87%) as a colorless liquid. Major diastereoisomer: $[\alpha]^{29}_D$ +2.5 (*c* 3.0, $CHCl_3$); ν_{max} (film) 3402, 2930, 1653, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.25 (m, 5H), 5.85−5.78 (m, 2H), 4.63−4.48 (m, 4H), 3.98−3.91 (m, 1H), 3.49−3.42 (m, 1H), 2.19 (br s, 1H), 2.05−1.99 (m, 2H), 1.95−1.78 (m, 3H), 1.73−1.60 (m, 3H), 1.32−1.23 (m, 1H), 1.17 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 134.7, 128.3 (×2), 127.5 (×2), 127.3, 125.0, 94.0, 80.3, 73.9, 70.2, 69.5, 48.1, 40.7, 34.9, 29.0, 20.2, 18.7; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{19}H_{26}O_3Na$ 325.1780, found 325.1781. Minor diastereoisomer: $[\alpha]^{26}_D$ +20.6 (*c* 2.4, $CHCl_3$); ν_{max} (film) 3387, 2858, 1653, 1496 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.24 (m, 5H), 5.89 (d, *J* = 6.1 Hz, 1H), 5.71−5.67 (m, 1H), 4.65 (s, 2H), 4.64 (d, *J* = 11.8 Hz, 1H), 4.53 (d, *J* = 12.1 Hz, 1H), 4.01(q, *J* = 6.4 Hz, 1H), 3.35−3.26 (m, 1H), 2.19−2.12 (m, 2H), 1.92 (m, 5H), 1.62−1.50 (m, 1H), 1.33 (d, *J* = 9.5 Hz, 1H), 1.12 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 133.9, 128.5 (×2), 127.6 (×2), 127.5, 125.9, 96.9, 81.3, 74.9, 70.3, 67.3, 46.1, 40.0, 36.5, 26.8, 20.7, 19.0; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{19}H_{26}O_3Na$ 325.1780, found 325.1782.

Following the procedure of oxidation, the above carbinol (50 mg, 0.16 mmol) was oxidized with DMP (84 mg, 0.20 mmol) to afford the title compound **27** (48 mg, 98%) as a colorless liquid: $[\alpha]^{26}_D$ +38.3 (*c* 5.5, $CHCl_3$); ν_{max} (film) 2932, 2860, 1701, 1651, 1454 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.16 (m, 5H), 5.74−5.66 (m, 2H), 4.50−4.39 (m, 4H), 3.44−3.38 (m, 1H), 2.44−2.24 (m, 2H), 2.00 (s, 3H), 1.95−1.73 (m, 5H), 1.59−1.48 (m, 1H), 1.30−1.21 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.6, 138.8, 133.7, 128.4 (×2), 127.5 (×3), 125.5, 92.4, 78.8, 74.5, 70.4, 57.1, 41.0, 34.2, 30.5, 28.0, 18.5; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{19}H_{24}O_3Na$ 323.1623, found 323.1624.

2-((5*S*,6*R*,8*S*)-8-(Benzyloxy)-1-oxaspiro[4.6]undec-3-en-6-yl)-propan-2-ol (28). Following the procedure of Grignard reaction, the methyl ketone **27** (100 mg, 0.33 mmol) was reacted with MeMgI to afford the carbinol **28** (95 mg, 90%) as a colorless liquid: $[\alpha]^{27}_{D}$ −6.7 (*c* 1.2, $CHCl_3$); ν_{max} (film) 3466, 2930, 2860, 1496, 1454 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.27 (m, 5H), 6.04 (td, *J* = 6.2, 2.4 Hz, 1H), 5.74 (td, *J* = 6.2, 1.5 Hz, 1H), 4.65 (t, *J* = 2.0 Hz, 2H), 4.58 (dd, *J* = 20.0, 12.1 Hz, 2H), 3.46−3.36 (m, 1H), 2.12−1.90 (m, 5H), 1.76−1.56 (m, 5H), 1.27 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 138.0, 128.5 (×2), 127.6 (×2), 127.5, 123.3, 95.2, 80.3, 74.8, 73.3, 70.3, 50.3, 41.8, 35.6, 31.9, 30.5, 27.8, 19.2; HRMS (ESI) *m/z* [M + Na]$^+$, calcd for $C_{20}H_{28}O_3Na$ 339.1936, found 339.1939.

Synthesis of 29. N-Bromosuccinimide (78 mg, 0.44 mmol) was added to a solution of **28** (70 mg, 0.22 mmol) in DMSO (2 mL). After stirring for 1 h, the reaction was quenched by addition of 10% aqueous $Na_2S_2O_3$ solution (0.3 mL) and then concentrated in vacuo. The residue was partitioned between diethyl ether (10 mL) and water (2 mL), the phases were separated, and the aqueous layer was further extracted with diethyl ether (2 × 5 mL). The combined organic extracts were dried and concentrated in vacuo. Purification of the residual mass by column chromatography (7% Et_2O/petroleum ether) afforded **29** (86 mg, 98%) as crystalline solid: mp 133−135 °C; $[\alpha]^{26}_{D}$ −32.6 (*c* 1.20, $CHCl_3$); ν_{max} (KBr plate) 2937, 2868, 1452, 1363 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.25 (m, 5H), 4.60−4.48 (m, 3H), 4.44 (d, *J* = 0.9 Hz, 1H), 4.22 (dt, *J* = 6.4, 1.4 Hz, 1H), 4.13 (dd, *J* = 10.5, 5.2 Hz, 1H), 3.57−3.48 (m, 1H), 2.32−2.23 (m, 1H), 2.06−1.74 (m, 6H), 1.60−1.43 (m, 2H), 1.21 (s, 3H), 1.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 128.5 (×2), 127.6 (×2), 127.5, 95.8, 94.4, 85.8, 79.0, 75.4, 70.3, 52.4, 50.6, 35.8, 32.0, 30.0, 29.7, 24.0, 19.6; HRMS (ESI) *m/z* [M + Na]$^+$, calcd for $C_{20}H_{27}BrO_3Na$ 417.1041, found 417.1042.

Synthesis of 30. Tributyltin hydride (41 μL, 0.15 mmol) was added to a degassed solution of **29** (50 mg, 0.13 mmol) and catalytic AIBN in benzene (5 mL), and the resultant solution was refluxed for 2 h. On cooling, the reaction was quenched via the addition of carbon tetrachloride (0.5 mL), and the flask contents were concentrated in vacuo. The residue was taken up in ethyl acetate (10 mL), and saturated aqueous KF solution (5 mL) was added and stirred vigorously for 30 min. The flask contents were filtered through Celite, the aqueous layer was separated and further extracted with ethyl acetate (2 × 5 mL) and the combined organic extracts were dried and concentrated in vacuo. Column chromatography (10% Et_2O/petroleum ether) afforded **30** (39 mg, 96%) as a colorless liquid: $[\alpha]^{26}_{D}$ +0.4 (*c* 4.3, $CHCl_3$); ν_{max} (liquid film) 2932, 2876, 1452 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36−7.27 (m, 5H), 4.55 (dd, *J* = 17.9, 12.0 Hz, 2H), 4.22 (dd, *J* = 4.2, 1.8 Hz, 1H), 4.06 (dd, *J* = 16.0, 8.1 Hz, 1H), 4.00−3.92 (m, 1H), 3.59−3.50 (m, 1H), 2.08−1.93 (m, 4H), 1.90−1.69 (m, 5H), 1.53−1.37 (m, 2H), 1.23 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3, 128.4 (×2), 127.6 (×2), 127.5, 94.6, 87.1, 84.6, 79.0, 70.2, 67.1, 52.2, 35.7, 33.6, 32.5, 30.2, 30.1, 24.0, 19.4; HRMS (ESI) *m/z* [M + Na]$^+$, calcd for $C_{20}H_{28}O_3Na$ 339.1936, found 339.1935.

Synthesis of 31. A mixture of **30** (6 mg, 0.02 mmol), ruthenium trichloride (5 mg, 0.02 mmol), and sodium metaperiodate (40 mg, 0.19 mmol) in 2:2:1 $CH_3CN/CCl_4/H_2O$ (1 mL) was stirred for 5 h, diluted with CH_2Cl_2 (5 mL), dried, and filtered. After solvent evaporation, the residue was subjected to flash chromatography (30% Et_2O/petroleum ether) to afford **31** (5 mg, 76%) as a colorless oil: $[\alpha]^{26}_{D}$ −18.8 (*c* 0.4, $CHCl_3$); ν_{max} (liquid film) 2930, 2856, 1776, 1712, 1452 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.1, 1.0 Hz, 2H), 7.59−7.53 (m, 1H), 7.47−7.42 (m, 2H), 5.26−5.20 (m, 1H), 4.40 (d, *J* = 5.2 Hz, 1H), 2.78 (dd, *J* = 18.4, 5.3 Hz, 1H), 2.65 (d, *J* = 18.4 Hz, 1H), 2.24−1.90 (m, 7H), 1.80−1.66 (m, 2H), 1.31 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ175.5, 166.1, 133.1, 130.6, 129.8 (×2), 128.5 (×2), 97.4, 85.3, 82.1, 74.0, 51.5, 38.3, 36.6, 32.7, 29.8, 29.0, 24.7, 19.1; HRMS (ESI) *m/z* [M + Na]$^+$, calcd for $C_{20}H_{24}O_5Na$ 367.1521, found 367.1522.

Synthesis of 33. To a solution of substrate **28** (30 mg, 0.09 mmol) in acetone (1 mL) was added 0.2 mL of a premix solution [chromium trioxide (540 mg, 5.40 mmol) in water (1.3 mL) and 2 drops of conc H_2SO_4]. The reaction was stirred at 50 °C for 1 h before being quenched by addition of brine (0.1 mL). The solution was then extracted with CH_2Cl_2 (3 × 5 mL). The combined organics were dried over Na_2SO_4, filtered, and evaporated in vacuo to give the crude product. Flash chromatography (30% Et_2O/petroleum ether) afforded the lactone **33** (23 mg, 72%) as a crystalline solid: mp 135−137 °C; $[\alpha]^{28}_{D}$ −21.7 (*c* 0.6, $CHCl_3$); ν_{max} (KBr plate) 2976, 2933, 1768, 1494, 1456 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.24 (m, 5H), 4.54 (dd, *J* = 19.0, 12.0 Hz, 2H), 4.34 (d, *J* = 5.1 Hz, 1H), 3.62−3.56 (m, 1H), 2.74 (dd, *J* = 18.4, 5.2 Hz, 1H), 2.62 (d, *J* = 18.4 Hz, 1H), 1.99−1.84 (m, 6H), 1.68−1.57 (m, 3H), 1.26 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 139.0, 128.5 (×2), 127.6, 127.5 (×2), 97.4, 85.3, 82.0, 78.3, 70.3, 51.7, 38.3, 36.7, 32.2, 29.8, 29.6, 24.7, 19.0; HRMS (ESI) *m/z* [M + Na]$^+$, calcd for $C_{20}H_{26}O_4Na$ 353.1729, found 353.1726.

Synthesis of 34. A solution of compound **30** (20 mg, 0.06 mmol) in dry methanol (2 mL) containing Pd−C (10%) was stirred under hydrogen atmosphere at room temperature for 15 h. The catalyst was filtered off, and removal of solvent in vacuo afforded the alcohol **34** (13 mg, 91%) as a colorless liquid: $[\alpha]^{27}_{D}$ −14.1 (*c* 5.0, $CHCl_3$); ν_{max} (liquid film) 3420, 2930, 2880, 1454 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.24 (dd, *J* = 5, 1.5 Hz, 1H), 4.09 (dd, *J* = 16.0, 8.0 Hz, 1H), 4.01−3.97 (m, 1H), 3.94 (dt, *J* = 8.5, 5.0 Hz, 1H), 2.51 (br s, 1H), 2.09−1.96 (m, 4H), 1.90−1.79 (m, 3H), 1.75 (td, *J* = 14.0, 4.5 Hz, 1H), 1.67−1.62 (m, 1H), 1.55−1.50 (m, 1H), 1.44−1.38 (m, 1H), 1.21 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 95.4, 86.8, 84.9, 69.7, 67.6, 53.9, 36.3, 34.2, 33.6, 33.4, 30.3, 24.7, 18.0; HRMS (ESI) *m/z* [M + Na]$^+$, calcd for $C_{13}H_{22}O_3Na$ 249.1467, found 249.1467.

Synthesis of 35. Following the above methods of RuO_4 mediated oxidation, the compound **34** (10 mg, 0.04 mmol) was transformed into lactone **35** (9 mg, 85%) as a crystalline solid: mp 174−175 °C; $[\alpha]^{28}_{D}$ −134.0 (*c* 2.6, $CHCl_3$); ν_{max} (KBr plate) 2974, 2930, 1769, 1695 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.47 (d, *J* = 5.5 Hz, 1H), 2.85−2.78 (m, 2H), 2.71−2.65 (m, 2H), 2.62−2.56 (m, 1H), 2.37−2.31 (m, 2H), 2.07−2.03 (m, 1H), 2.00−1.94 (m, 1H), 1.93−1.87 (m, 1H), 1.76 (dt, *J* = 13.5, 3.5 Hz, 1H), 1.31 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.2, 174.9, 96.1, 85.1, 81.2, 51.1, 44.1, 38.7, 38.0, 37.9, 29.7, 24.7, 19.3; HRMS (ESI) *m/z* [M + Na]$^+$, calcd for $C_{13}H_{18}O_4Na$ 261.1103, found 261.1105.

1-((5*S*,6*S*,8*S*)-8-(Benzyloxy)-1-oxaspiro[4.6]undec-3-en-6-yl)-2-(tert-butyldimethylsilyloxy)ethanone (36). To a magnetically stirred suspension of NaH (50 mg, 1.25 mmol, 60% in oil), freed from adhering oil by repeated washing with petroleum ether, in dry THF (3 mL) was added dropwise a solution of the alcohol **26** (100 mg, 0.32 mmol) in dry THF (1 mL) under Ar atmosphere. The mixture was allowed to stir at rt for 1 h, and then to it was added TBSCl (71 mg, 0.47 mmol). After stirring overnight, the reaction mixture was cooled to 0 °C and quenched by adding saturated aqueous NH_4Cl solution (0.5 mL). Usual workup of the reaction mixture followed by column chromatography (10% Et_2O/petroleum ether) afforded the silyl ether (122 mg, 90%) as a colorless liquid: $[\alpha]^{26}_{D}$ +3.7 (*c* 1.2, $CHCl_3$); ν_{max} (film) 3481, 2954, 1643, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.27 (m, 5H), 5.89 (d, *J* = 6.2 Hz, 1H), 5.70−5.68 (m, 1H), 4.65 (br s, 2H), 4.60 (d, *J* = 11.9 Hz, 1H), 4.50 (d, *J* = 11.9 Hz, 1H), 3.84 (dd, *J* = 8.9, 5.4 Hz, 1H), 3.61 (dd, *J* = 9.9, 5.4 Hz, 1H), 3.47 (t, *J* = 9.4 Hz, 1H), 3.41−3.32 (m, 1H), 2.18−2.04 (m, 2H), 1.96−1.71 (m, 6H), 1.59−1.46 (m, 1H), 1.27−1.15 (m, 1H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1, 134.0, 128.5 (×2), 127.7 (×2), 127.5, 125.8, 97.2, 81.4, 74.8, 72.3, 70.5, 63.4, 40.6, 40.2, 36.5, 26.8, 26.0 (×3), 19.0, 18.3, −5.1, −5.2; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{25}H_{40}O_4SiNa$ 455.2594, found 455.2592.

Following the procedure of oxidation, the above carbinol (140 mg, 0.32 mmol) was oxidized with DMP (178 mg, 0.42 mmol) to afford the title compound **36** (132 mg, 95%) as a colorless liquid: $[\alpha]^{26}_D$ +14.0 (*c* 2.2, $CHCl_3$); ν_{max} (film) 2930, 2856, 1717, 1497 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25−7.17 (m, 5H), 5.78−5.72 (m, 2H), 4.54−4.39 (m, 4H), 4.15 (d, *J* = 17.7 Hz, 1H), 4.01 (d, *J* = 17.7 Hz, 1H), 3.45−3.37 (m, 1H), 2.93 (d, *J* = 9.9 Hz, 1H), 2.34−2.24 (m, 1H), 1.98−1.74 (m, 5H), 1.60−1.54 (m, 1H), 1.34−1.27 (m, 1H), 0.85 (s, 9H), 0.01 (d, *J* = 4.5 Hz, 6H); ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.8, 139.0, 133.5, 128.5 (×2), 127.6 (×2), 127.5, 126.1, 92.1, 78.5, 74.8, 70.2, 68.8, 51.1, 41.2, 34.4, 30.0, 26.0 (×3), 18.7, 18.5, −5.3 (×2); HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{25}H_{38}O_4SiNa$ 453.2437, found 453.2435.

2-((5*S*,6*R*,8*S*)-8-(Benzyloxy)-1-oxaspiro[4.6]undec-3-en-6-yl)-1-(tert-butyldimethylsilyloxy)propan-2-ol (37). Following the procedure of Grignard reaction, the ketone **36** (85 mg, 0.20 mmol) was reacted with MeMgI to afford the mixture of carbinols **37** (95 mg, 90%) in a ca. 3:2 ratio. $[\alpha]^{26}_D$ +3.2 (*c* 3.0, $CHCl_3$); ν_{max} (film) 3558, 3485, 2928, 2856, 1496 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28−7.15 (m, 5H), 5.97−5.86 (m, 1H), 5.58−5.54 (m, 1H), 4.55−4.42 (m, 4H), 3.41 (br s, 2H), 3.39−3.33 (m, 1H), 2.78 (br s, 1H), 2.23 (dd, *J* = 6.4, 2.8 Hz, 1H), 1.96−1.88 (m, 2H), 1.87−1.75 (m, 2H), 1.74−1.48 (m, 3H), 1.22−1.17 (m, 1H), 1.08 and 1.06 (both s, total 3H), 0.82 (s, 9H), −0.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (for major isomer) 139.3, 137.8, 128.4 (×2),127.6 (×2), 127.4, 122.7, 94.1, 81.2, 76.2, 73.5, 70.3, 69.5, 46.4, 42.7, 35.5, 29.5, 26.0 (×3), 22.7, 19.0, 18.4, −5.2, −5.3, (for minor isomer) 139.2, 138.1, 128.4 (×2), 127.5 (×2), 127.4, 121.8, 94.7, 80.5, 76.2, 73.3, 70.3, 69.3, 45.2, 42.8, 35.1, 30.1, 26.0 (×3), 23.3, 19.0, 18.4, −5.2, −5.3; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{26}H_{42}O_4SiNa$ 469.2750, found 469.2754.

Synthesis of 38 and 39. Following the method of bromonium-ion mediated cyclization, the above mixture of carbinols **37** (55 mg, 0.12 mmol) was cyclized with NBS (28 mg, 0.16 mmol) to afford after column chromatography, the bromo bis-tetrahydrofuran derivative **38** (35 mg, 54%) and **39** (20 mg, 32%) as a colorless liquid. Compound **38**: $[\alpha]^{27}_D$ −13.0 (*c* 3.5, $CHCl_3$); ν_{max} (film) 2930, 2858, 1454, 1362 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.20 (m, 5H), 4.52−4.48 (m, 3H), 4.41 (s, 1H), 4.14 (t, *J* = 5.5 Hz, 1H), 4.09 (dd, *J* = 10.5, 5.0 Hz, 1H), 3.58 (d, *J* = 10.0 Hz, 1H), 3.44−3.42 (m, 1H), 3.41 (d, *J* = 9.5 Hz, 1H), 2.25−2.21 (m, 1H), 2.14−2.11 (m, 1H), 1.97−1.93 (m, 1H), 1.91−1.80 (m, 3H), 1.79−1.72 (m, 1H), 1.51−1.42 (m, 2H), 1.24 (s, 3H), 0.85 (s, 9H), 0.03 (d, *J* = 4.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 128.4 (×2), 127.5 (×2), 127.5, 95.6, 94.5, 87.1, 78.9, 75.5, 70.2, 66.2, 52.6, 50.1, 35.4, 32.3, 28.0, 26.1 (×3), 24.8, 19.5, 18.4, −5.3, −5.4; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{26}H_{41}BrO_4SiNa$ 549.1839, found 549.1836. Compound **39**: $[\alpha]^{27}_D$ −32.1 (*c* 1.6, $CHCl_3$); ν_{max} (film) 2951, 2862, 1456, 1363 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28−7.21 (m, 5H), 4.56−4.52 (m, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.32 (s, 1H), 4.21−4.14 (m, 2H), 3.47−3.45 (m, 1H), 3.35 (d, *J* = 10.5 Hz, 1H), 3.26 (d, *J* = 10.5 Hz, 1H), 2.30−2.25 (m, 1H), 2.23 (d, *J* = 12.5 Hz, 1H), 2.00−1.82 (m, 3H), 1.83−1.75 (m, 2H), 1.58−1.53 (m, 1H), 1.46−1.42 (m, 1H), 1.01 (s, 3H), 0.85 (s, 9H), 0.00 (d, *J* = 4.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.2, 128.4 (×2), 127.6 (×2), 127.5, 96.2, 94.0, 87.4, 79.1, 76.0, 70.3, 69.5, 50.5, 46.0, 36.4, 32.3, 30.0, 26.0 (×3), 19.8, 19.7, 18.3, −5.2, −5.4; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{26}H_{41}BrO_4SiNa$ 547.1855, found 547.1851.

Synthesis of 40 and 41. Following the above methods of reductive removal of bromide followed by RuO_4 mediated oxidation, the compound **38** (12 mg, 0.02 mmol) was transformed into lactone **40** (8 mg, 74%) and **39** (10 mg, 0.02 mmol) to **41** (6.5 mg, 72%). Compound **40**: $[\alpha]^{28}_D$ −22.0 (*c* 0.3, $CHCl_3$); ν_{max} (liquid film) 2928, 2855, 1778, 1712, 1454 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 7.0, 1.0 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 5.17−5.15 (m, 1H), 4.40 (d, *J* = 5.0 Hz, 1H), 3.55 (d, *J* = 10.0 Hz, 1H), 3.34 (d, *J* = 10.0 Hz, 1H), 2.75 (dd, *J* = 18.5, 5.0 Hz, 1H), 2.64 (d, *J* = 18.5 Hz, 1H), 2.39−2.36 (m, 1H), 2.18−1.90 (m, 6H), 1.77−1.73 (m, 2H), 1.33 (s, 3H), 0.82 (s, 9H), 0.00 (d, *J* = 2.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ175.2, 166.0, 133.0, 130.7, 129.8 (×2), 128.5 (×2), 97.1, 86.8, 82.5, 74.5, 66.8, 51.8, 38.0, 36.0, 32.3, 28.2, 26.0 (×3), 25.1, 19.3, 18.3, −5.5 (×2); HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{26}H_{38}O_6SiNa$ 497.2336, found 497.2337. Compound **41**: $[\alpha]^{23}_D$ −26.9 (*c* 0.3, $CHCl_3$); ν_{max} (film) 2951, 2857, 1782, 1715, 1452 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 5.26−5.21 (m, 1H), 4.34 (d, *J* = 3.5 Hz, 1H), 3.49 (d, J = 11.0 Hz, 1H), 3.38 (d, *J* = 11.0 Hz, 1H), 2.71 (d, *J* = 4.0 Hz, 1H), 2.70 (s, 1H), 2.59 (dd, *J* = 12.5, 2.0 Hz, 1H), 2.19−2.10 (m, 2H), 2.03−1.88 (m, 4H), 1.74−1.68 (m, 2H), 1.03 (s, 3H), 0.91 (s, 9H), 0.06 (d, *J* = 3.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.4, 166.0, 133.1, 130.7, 129.8 (×2), 128.5 (×2), 97.7, 87.3, 82.7, 74.0, 68.7, 44.2, 38.2, 36.0, 32.8, 29.0, 26.0 (×3), 20.4, 19.1, 18.3, −5.2, −5.3; HRMS (ESI) *m*/*z* [M + Na]$^+$, calcd for $C_{26}H_{38}O_6SiNa$ 497.2336, found 497.2333.

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Supporting Information Available: General experimental methods along with copies of NMR spectra and X-ray crystal data with ORTEP plot. This material is available free of charge via the Internet at http://pubs.acs.org.