Comprehensive Report

Nortriterpenoid, Biomimetic synthesis, Remote C—H functionalization, Ring expansion, Cascade reaction

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Development of Biomimetic Synthesis of Propindilactone G†

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Summary of main observation and conclusion The natural product propindilactone G is a complex *Schisandra* nortriterpenoid with a unique 5/5/7/6/5 pentacyclic framework. This full paper describes the development of concise biomimetic synthesis of propindilactone G from a known steroid lactone. The key C19-OH intermediate was synthesized *via* Breslow and Suárez radical remote C—H functionalizations. Wagner-Meerwein rearrangement was subsequently utilized for the expansion of the B ring. To invert the configuration of the C10 tertiary alcohol, an intramolecular peroxide cyclization catalyzed by $BF_3{\cdot}Et_2O$ was devised. The 5/5 fused lactone system was then assembled in a biomimetic transesterification/oxa-Michael addition sequence. Our work should provide experimental support for the proposed biosynthetic pathway and facilitate investigation of the biological activities of propindilactone G.

Background and Originality Content

Propindilactone G (**1**, Figure 1) and related *Schisandra* nortriterpenoids (**3**—**7**) are a large and abundant group of highly oxidized polycyclic natural products isolated from plants of the *Schisandra* genus, which can usually be divided into two genera, *Schisandra* and *Kadsura*.[1] They are widely distributed throughout East and Southeast Asia, with approximately 29 species in China. In fact, *Schisandra* genus plants are widely employed in traditional Chinese medicine to treat various diseases such as coughs, insomnia, and chronic dysentery.[2] The intriguing biological activities and complex structural diversity of schinortriterpenoids have attracted great attention from synthetic chemists[3] and led to the total syntheses of several members of this family.

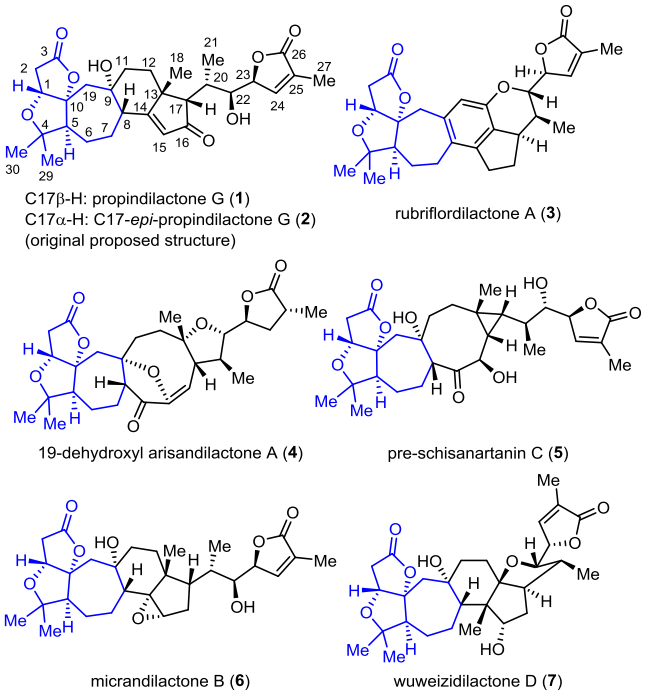

Figure 1 Representative nortriterpenoids with unique 5-5-7 tricyclic ring systems.

Following the pioneering synthesis of schinortriterpenoid schindilactone A[4a] by Yang[4] and co-workers in 2011, the elegant total syntheses of several other members were achieved in the past decade, including Yang's total syntheses of propindilactone G[4b] (2015), 19-dehydroxyl arisandilactone A[4c] (2017), lancifodilactone G acetate[4d] (2018), and pre-schisanartanin C[4e] (2019); Li's total syntheses[5] of rubriflordilactone A[5a] (2014), rubriflordilactone B[5b] (2016), and *pseudo*-rubriflordilactone B[5c] (2019); Anderson's total syntheses[6] of rubriflordilactone A[6a,6b] (2015), rubriflordilactone B[6c] (2019), and *pseudo*-rubriflordilactone B[6c] (2019); Tang's total syntheses[7] of schilancitrilactones B and C[7a] (2015), schilancitrilactone A[7b] (2017), and schilancidilactones A and B[7b] (2017); and Ding's total synthesis of atrop-schiglautone A[8] (2018).

Propindilactone G, which possesses a 29-carbon schiartane skeleton, was isolated from the stems of *Schisandra propinqua* var. *propinqua* by Sun and co-workers in 2008, alongside propindilactones E, F, and H—J.[9] Structurally, propindilactone G is characterized by a unique 5/5/7/6/5 fused ring framework and a butenolide side chain; hence, its synthesis poses an enormous challenge. In 2015, Yang and co-workers accomplished the first asymmetric total synthesis of propindilactone G in 20 steps,[4b,10] featuring several impressive transformations, including an asymmetric Diels-Alder reaction and a ring expansion reaction to construct the B ring, a Pauson-Khand reaction to build the D and E rings, and an oxidative heterocoupling reaction to install the side chain. It is worth mentioning that the stereochemistry of C17 was also revised from the initially proposed C17α-H (**2**) to C17β-H (**1**) during the synthesis.

Recently, we reported a strategy for the synthesis of propindilactone G from a known steroid lactone,[11] which was largely inspired by a biogenetic proposal. In this article, we will detail the synthesis more comprehensively.

Results and Discussion

Our retrosynthetic analysis of propindilactone G was largely inspired by the hypothetical biogenesis of schinortriterpenoids

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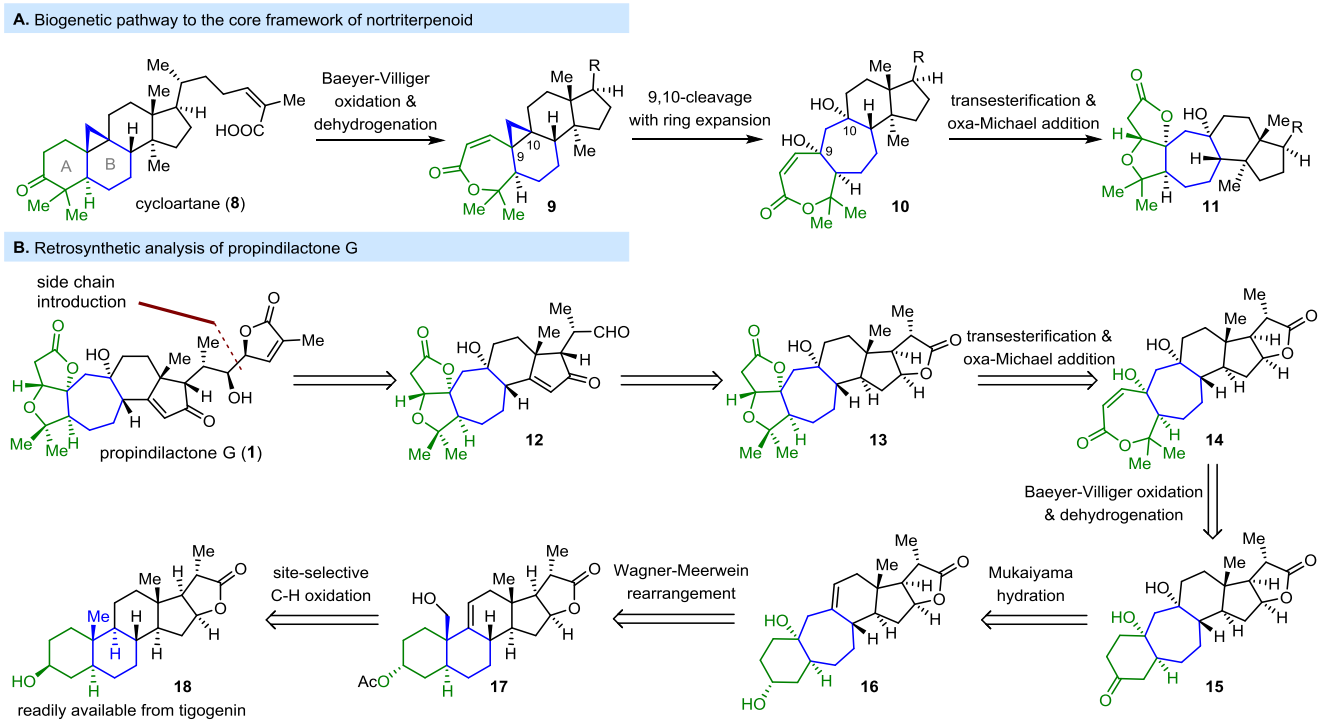
Scheme 1 Biogenetic pathway and retrosynthetic analysis



proposed by Sun and co-workers (Scheme 1A).[1b] Biosynthetically, the 5/5/7 fused ring system in **11** is thought to be produced *via* the Baeyer-Villiger oxidation and dehydrogenation of the A ring of cycloartane (**8**) to afford unsaturated lactone **9**, C9—C10 cleavage of **9** to give B-ring-expanded cycloheptanediol **10**, and finally a transesterification and oxa-Michael addition cascade (Scheme 1A).

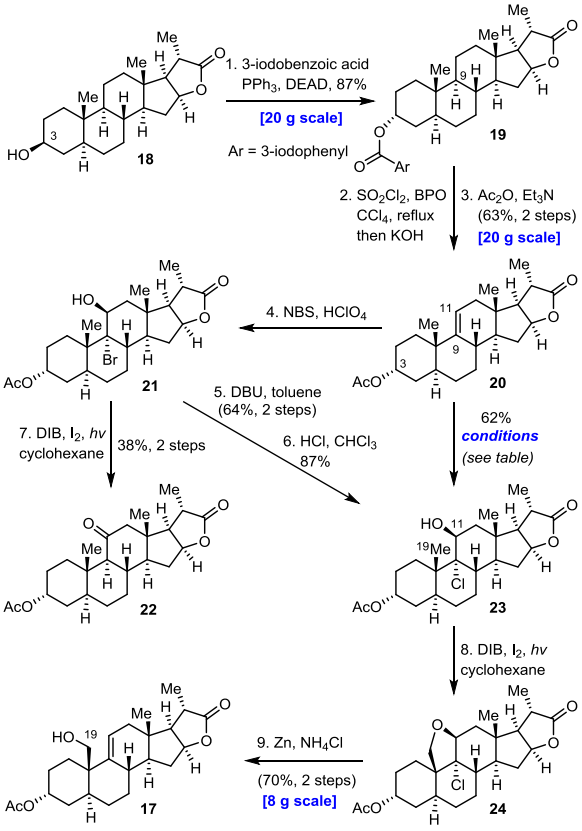
Our retrosynthetic analysis of propindilactone G was based on the above biosynthetic proposal and is outlined in Scheme 1B. We envisioned that propindilactone G could be prepared by introducing the side chain onto aldehyde **12**; its C16 ketone and C22 aldehyde groups could be accessed *via* the reduction and oxidation of the right-hand lactone of **13**. A biomimetic transesterification and oxa-Michael addition cascade was envisaged for the construction of the 5/5 fused ring system in **13** from unsaturated lactone **14**. Lactone **14** was expected to be synthesized through the Baeyer-Villiger oxidation and dehydrogenation of diol **15**, which could be prepared *via* the Wagner-Meerwein rearrangement of **17** to provide **16**, followed by Mukaiyama hydration. Finally, key intermediate **17** could be traced back to known lactone **18**,[12] a product of the degradation of commercially available tigogenin, *via* site-selective C—H oxidation at C9 and C19.

Our synthesis of propindilactone G commenced with a six-step synthesis of key C19 hydroxyl compound **17** *via* two remote C—H radical functionalizations (Scheme 2). Mitsunobu reaction[13] of **18** with 3-iodobenzoic acid afforded **19** in 87% yield on a 20 g scale. Subsequent Breslow remote C—H radical chlorination,[14] directed by the C3α iodobenzoate, afforded a C9α chlorine intermediate (not shown), which was transformed into acetate **20** on a 20 g scale *via* treatment with potassium hydroxide in boiling methanol followed by acetylation of the free C3 hydroxyl group.[15]

With a large-scale synthetic route to **20** in hand, we were poised to investigate the second C—H radical functionalization to produce **17**. Directed C—H oxidation of the C19 methyl group is generally achieved with the help of the C2β,[16] C6β,[17] or C11β[18] hydroxyl group, because a six-membered transition state essential for 1,5-hydrogen abstraction could be formed during this process. To this end, we intended to install a C11β hydroxyl group by preparing bromohydrin **21** or chlorohydrin **23** (Scheme 2). Bromohydroxylation of **20** with *N*-bromosuccinimide (NBS) and catalytic $HClO_4$ gave unstable bromohydrin **21**, which could be transformed into more stable chlorohydrin **23** *via* treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene to generate a C9,C11β epoxide compound followed by regioselective opening of the epoxide with anhydrous HCl using Ramírez's protocol.[19] However, this three-step sequence furnished **23** in only 52% overall yield from **20** and the yield decreased dramatically when the bromohydroxylation reaction was performed on a large scale. Therefore, we decided to investigate a protocol for direct olefin chlorohydroxylation[20] to furnish **23** in one step (Scheme 2). While reagents such as $Ca(ClO)_2$,[20a] *N*-chlorosuccinimide (NCS),[20b] 1,3-dichloro-5,5-dimethylhydantoin (DCDMH),[20c] and trichloroisocyanuric acid (TCCA)[20d] all resulted in low conversions or complex reaction mixtures (Scheme 2, entries 1—4), we were delighted to find that by switching the solvent from dioxane/H_2O to acetone/H_2O[21] and lowering the temperature to –50 °C, **23** could be obtained in 54% yield using TCCA as the chlorination reagent (entry 5). Further screening of solvents revealed that a mixed solvent of diglyme and H_2O was the best, furnishing **23** in 62% yield on a 5 g scale (entry 6). It is worth mentioning that a lower temperature (–62 °C) was critical in ensuring a satisfactory yield when the reaction was conducted on a 5 g scale.

With enough **21** and **23** in hand, we proceeded to investigate the C—H oxidation of the C19 Me group to prepare key intermediate **17**. Unfortunately, exposure of bromohydrin **21** to Suárez's conditions[22] ((diacetoxyiodo)benzene (DIB), I_2, *hv*) led to the formation of ketone **22** in 38% yield over two steps from **20**, possibly through the elimination of hydrogen bromide *via* hydrogen atom abstraction at C11 and subsequent bromine atom elimination.[23] However, to our delight, under the same conditions, remote functionalization of chlorohydrin **23** proceeded smoothly to produce tetrahydrofuran intermediate **24**. Treatment of **24** with activated Zn powder and aqueous NH_4Cl in boiling dimethylformamide (DMF) led to the release of the C19 hydroxyl group and the formation of the C9-C11 olefin, yielding desired compound **17** in 70% yield over two steps on an 8 g scale.

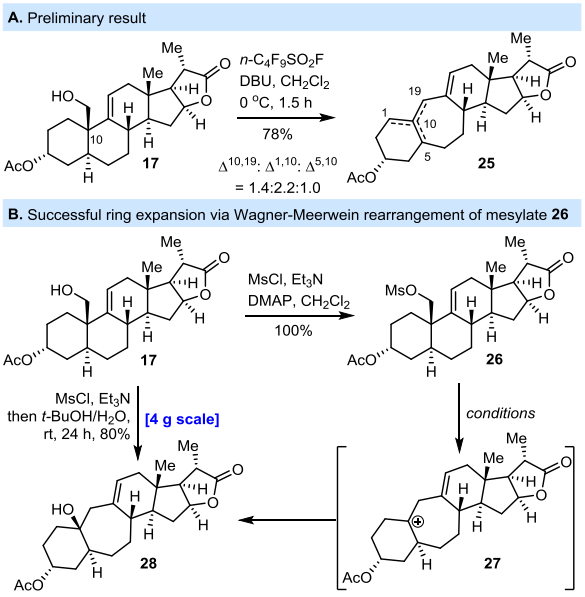
Scheme 2 Synthesis of C19 hydroxyl compound **17**



entry	conditions	**23**[a]/%
1	$Ca(ClO)_2$, $HClO_4$, dioxane/H_2O, rt	low conversion
2	NCS, $HClO_4$, dioxane/H_2O, rt	low conversion
3	DCDMH, $HClO_4$, dioxane/H_2O, rt	low conversion
4	TCCA, $HClO_4$, dioxane/H_2O, rt	complex
5	TCCA, acetone/H_2O, -50 °C	54
6	TCCA, diglyme/H_2O, -50 °C	68
7[b]	TCCA, diglyme/H_2O, -62 °C	62

[a] Isolated yield. [b] Scale: 5.0 g. Abbreviations: DEAD = diethyl azodicarboxylate; BPO = benzoyl peroxide; NBS = *N*-bromosuccinimide; DIB = (diacetoxyiodo)benzene; DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene; NCS = *N*-chlorosuccinimide; DCDMH = 1,3-dichloro-5,5-dimethylhydantoin; TCCA = trichloroisocyanuric acid; diglyme = diethylene glycol dimethyl ether.

Scheme 3 Synthesis of cycloheptanol **28**



entry	base	solvent (1:2, *V*/*V*)	temp./°C	**28**[a]/%	**25**[a]/%
1	DBU	DME/H_2O	90	50	9
2	DBU	MeCN/H_2O	90	58	13
3	DBU	THF/H_2O	90	61	13
4	Et_3N	THF/H_2O	90	64	28
5	$NaHCO_3$	THF/H_2O	90	64	15
6	—	THF/H_2O	90	69	16
7	—	*t*-BuOH/H_2O	50	78	20
8	—	*t*-BuOH/H_2O	rt	80	19

[a]Isolated yield. Abbreviations: MsCl = methanesulfonyl chloride; Et_3N = triethylamine; DMAP = 4-dimethylaminopyridine; DME = 1,2-dimethoxyethane.

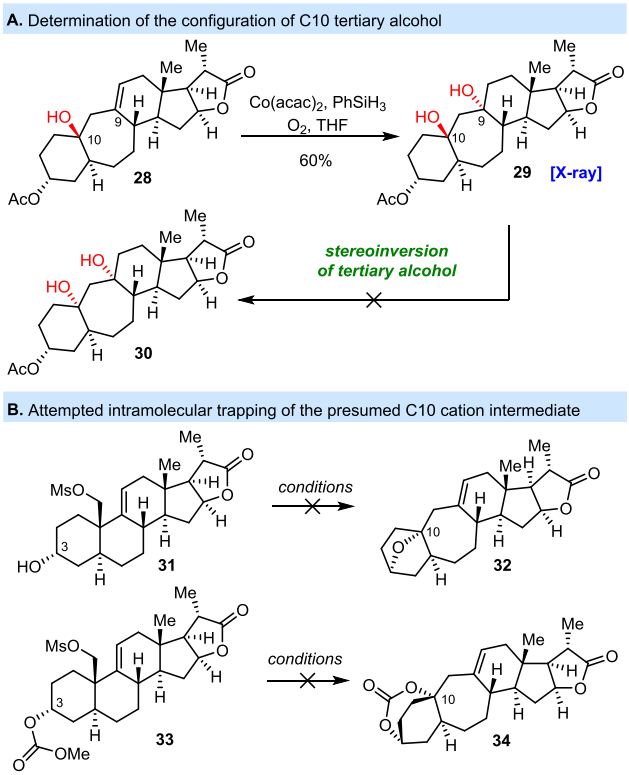
With access to alcohol **17** in only six steps, we began to investigate the key ring expansion for the seven-membered ring of propindilactone G *via* the Wagner-Meerwein rearrangement (Scheme 3). Barton and co-workers observed that the deamination of a similar C19 homoallylic amine compound resulted in the formation of the desired ring-expansion product;[24] however, the stereochemistry of the newly formed C10 stereocenter was not determined. Our preliminary work also showed that olefin regioisomers **25** possessing the 6/7/6 skeleton could be obtained in a 1.4 : 2.2 : 1.0 ratio and 78% combined yield by treating **17** with a strong activating reagent, *n*-$C_4F_9SO_2F$, and DBU in CH_2Cl_2 at 0 °C (Scheme 3A), possibly *via* the elimination of C19, C1, and C5 protons from the same C10 cation intermediate, **27**. We then attempted to capture this unstable cation intermediate, hoping to install a hydroxyl group at this position.

Alcohol **17** was mesylated to afford **26** in a quantitative yield, and it was stable enough to isolate. To our delight, heating a solution of **26** in a mixed solvent of 1,2-dimethoxyethane (DME) and H_2O in the presence of DBU as a base afforded tertiary alcohol **28** in 50% yield, along with diene isomers **25** in 9% yield (Scheme 3B, entry 1). Similar olefin side products were also observed during Gademann's biogenetic synthesis of icetexane natural products.[25] Further screening of solvents revealed that mixed solvents of tetrahydrofuran (THF) and H_2O were the best (entries 2 and 3). Similar results were obtained when a weaker organic base (Et_3N) and inorganic base ($NaHCO_3$) were used instead of DBU (entries 4 and 5). Furthermore, we found that a higher yield could be obtained when the reaction was conducted without a base (entry 6), indicating that the byproduct, methanesulfonic acid, had no impact on the rearrangement of **17**. Finally, reducing the reaction temperature and using *t*-BuOH/H_2O as the solvent resulted in higher yields (entries 7 and 8), although a longer reaction time was required. A one-pot procedure was also developed and **28** could be obtained in 80% yield on a 4 g scale.

Mukaiyama hydration[26] of **28** resulted in the formation of diol **29**, whose structure was confirmed by X-ray crystallographic analysis (Scheme 4A). Unfortunately, the stereochemistry of diol **29** at C10 was incorrect for propindilactone G. Therefore, the stereoinversion of this tetrasubstituted stereocenter was required. Initial attempts to invert the stereochemistry of the C10 tertiary alcohol *via* intermolecular substitution were met with failure and only elimination or decomposition was observed. However, we surmised that the desired stereoinversion could be realized *via* intramolecular capture of the C10 cation by a C3α hydroxyl or carbonate group. To this end, alcohol **31** and carbonate **33** were prepared (Scheme 4B); disappointingly, desired products **32** and **34** were not obtained despite attempts using various conditions and only products derived from the elimination of the C10 hydroxyl group were observed.

In light of the above failure, we turned our attention to rearrangement product **28**. We were curious as to whether a C9 peroxide group, accessible through Mukaiyama hydrosilylperoxidation,[27] could engage in an intramolecular cyclization at C10 to generate a bicyclo[4.2.1] endoperoxide compound to invert the stereochemistry at C10. Interestingly, such a bicyclo[4.2.1]

Scheme 4 Attempted installation of the correct tetrasubstituted C10 stereocenter



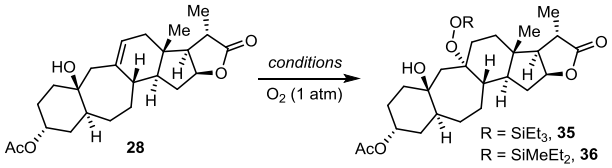
Abbreviation: acac = acetylacetonate.

endoperoxide system has been found in triterpenoid natural products schinalactone A[28] and pseudolarolide H.[29]

Our results for the optimization of the hydrosilylperoxidation reaction are shown in Table 1. When **28** was reacted with Et_3SiH and $Co(acac)_2$ in CH_2Cl_2 under an O_2 atmosphere at room temperature, only Mukaiyama-hydration-type products **29** and C9-*epi*-**29** were obtained (Table 1, entry 1). Addition of 1.0 equiv of *t*-BuOOH to the reaction system, which was expected to accelerate the formation of Co(III) active species, completely suppressed the reaction (entry 2). In stark contrast, replacing $Co(acac)_2$ with $Co(thd)_2$,[30] a superior catalyst reported by O'Neill and co-workers to be more effective in the hydrosilylperoxidation of cyclic alkenes, resulted in a 56% yield of desired product **35** (entry 3). No reaction was observed when bulkier silanes, such as Ph_3SiH and *i*-Pr_3SiH (entries 4 and 5), were used instead of Et_3SiH. However, a higher yield of **35** and a lower yield of diols **29** and C9-*epi*-**29** were obtained at 0 °C (entry 6), indicating that a low reaction temperature could suppress peroxide reduction. Finally, we were delighted to find that the yield could be further improved to 75% by using Et_2MeSiH. It is worth mentioning that the reaction yield diminished slightly on a large scale (entry 9), as **36** was obtained in 60% yield on a 5.2 g scale (entry 10).

We then investigated the intramolecular cyclization reaction[31] for the preparation of peroxide **37**. We found that **35** remained unchanged when treated with MsCl[32] in CH_2Cl_2 and desilylation was observed when a stronger activating reagent, $C_4F_9SO_2F$, was used instead (Table 2, entries 1 and 2). However, in reactions with *p*-toluenesulfonic acid (PTSA), we observed a dramatic solvent effect. Polar solvents such as THF and DMF led only to the removal of the silyl protecting group, while non-polar solvents like toluene led to desired peroxide **37** in 45% yield (entries 3 and 4). The structure of **37** was unambiguously determined through X-ray crystallographic analysis; therefore, we succeeded in inverting the C10 tetrasubstituted stereocenter. Further screening of a variety

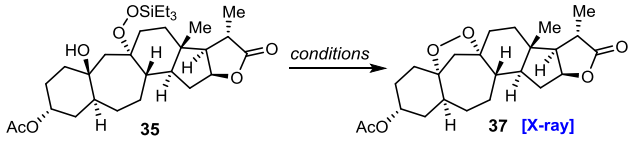
Table 1 Optimization of the hydrosilylperoxidation reaction



entry	[Si-H] (equiv)	[Co] (equiv)	solvent	temp./ °C	**35** or **36**[a]/%	C9-*epi*-**29** + **29**[a]/%
1	Et_3SiH (3.2)	$Co(acac)_2$ (0.3)	CH_2Cl_2	rt	—	33
2[b]	Et_3SiH (3.0)	$Co(acac)_2$ (0.3)	DCE	rt	NR	
3	Et_3SiH (3.0)	$Co(thd)_2$ (0.3)	DCE	rt	56	34
4	Ph_3SiH (3.0)	$Co(thd)_2$ (0.3)	DCE	rt	NR	
5	*i*-Pr_3SiH (3.0)	$Co(thd)_2$ (0.3)	DCE	rt	NR	
6	Et_3SiH (3.0)	$Co(thd)_2$ (0.3)	DCE	0	67	18
7	Et_2MeSiH (1.3)	$Co(thd)_2$ (0.3)	DCE	0	75	20
8	Et_2MeSiH (1.3)	$Co(thd)_2$ (0.2)	DCE	0	75	18
9[c]	Et_2MeSiH (1.3)	$Co(thd)_2$ (0.2)	DCE	0	62	28
10[d]	Et_2MeSiH (1.5)	$Co(thd)_2$ (0.2)	DCE	0	60	25

[a] Isolated yield. [b] *t*-BuOOH (1.0 equiv) was added. [c] Scale: 3.0 g. [d] Scale: 5.2 g.
Abbreviations: thd = 2,2,6,6-tetramethyl-3,5-heptanedionato; DCE = 1,2-dichloroethane.

Table 2 Optimization of the intramolecular cyclization of **35**



entry	conditions	isolated yields/%
1	MsCl, CH_2Cl_2, rt	NR
2	$C_4F_9SO_2F$, DBU, CH_2Cl_2, rt	desilylation
3	PTSA, THF or DMF, 50 °C	desilylation
4	PTSA, toluene, 50 °C	45
5	PPTS, or CSA, or AcOH, toluene, 50 °C	low conversion
6	BF_3•Et_2O, toluene, 50 °C	88

Abbreviations: PTSA = *p*-toluenesulfonic acid; DMF = *N*,*N*-dimethylformamide; PPTS = pyridinium *p*-toluenesulfonate; CSA = camphorsulfonic acid; NR = no reaction.

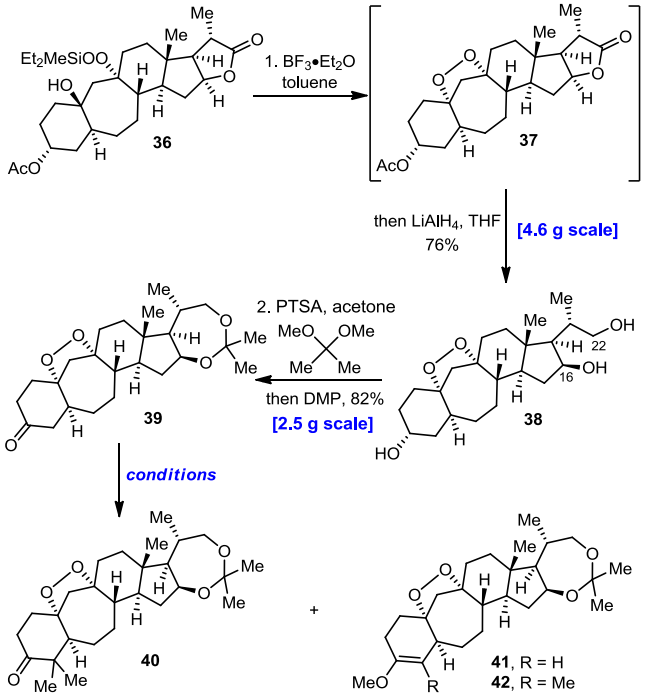
of Brønsted and Lewis acids revealed that BF_3·Et_2O was the optimal catalyst, which ultimately led to an 88% yield of **37** (entries 5 and 6).

With the optimal conditions for peroxide **37** in hand, the one-pot intramolecular cyclization of **36** and the global reduction of the acetate and lactone moieties were carried out, generating triol **38** in 76% yield on a 4.6 g scale (Scheme 5). Then, **38** was reacted with 2,2-dimethoxypropane and PTSA to selectively protect the hydroxyl groups at C16 and C22, affording an acetonide intermediate that was oxidized with Dess-Martin periodinane (DMP) to furnish ketone **39** in 82% yield on a 2.5 g scale.

Next, we turned our attention to the dimethylation of ketone **39** to obtain **40**, which proved to be difficult owing to competitive formation of methyl enol ether byproducts **41** and **42**. Among the three bases screened, potassium hexamethyldisilazide (KHMDS) afforded **40** in 24% yield (Scheme 5, entries 1—3). Addition of HMPA (hexamethylphosphoramide) as a co-solvent increased the yield dramatically (43%, entry 4). *t*-BuOK was also an effective base, leading to a similar yield of **40** in a mixed solvent of *t*-BuOH and HMPA (entry 5). Finally, we were delighted to find that the yield could be further improved by adding a third solvent, toluene (entry 6), and **40** could be obtained in 52% yield on a 1.1 g scale when cyclohexane was used as a co-solvent (entry 7).

As illustrated in the retrosynthetic analysis (Scheme 1B), we aimed to construct the 5/5 fused ring system of propindilactone G through a biomimetic transesterification/oxa-Michael addition cascade (Scheme 6). To this end, ketone **40** was treated with

Scheme 5 Elaboration of acetate **36** to ketone **40**



entry	conditions	40[a]/%	41 + 42[a]/%
1	LHMDS, MeI, THF, –78 to 0 °C	low conversion	
2	NaHMDS, MeI, THF, –78 to 0 °C	NR	
3	KHMDS, MeI, THF, –78 to –10 °C	24	19
4	KHMDS, MeI, THF/HMPA, –78 °C	43	14
5	*t*-BuOK, MeI, *t*-BuOH/HMPA, 0 °C	43	21
6	*t*-BuOK, MeI, *t*-BuOH/toluene/HMPA, 0 °C	50	16
7[b]	*t*-BuOK, MeI, *t*-BuOH/cyclohexane/HMPA, 0 °C	52	23

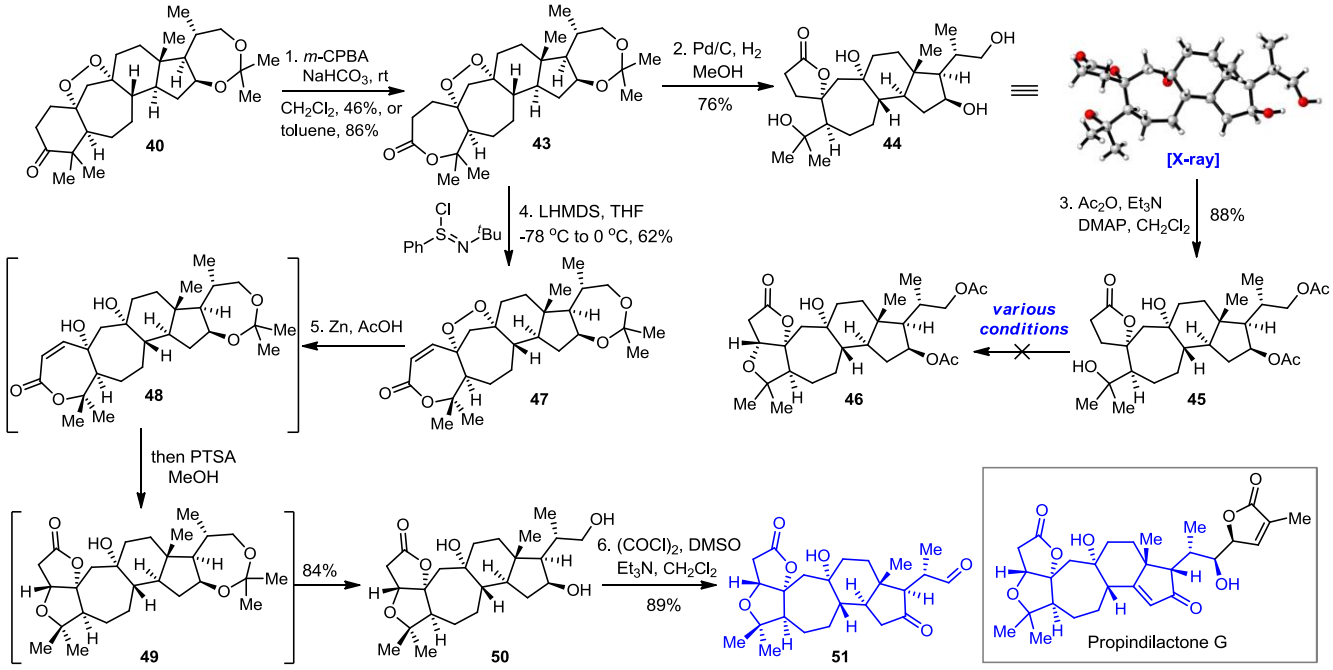
[a] Isolated yield. [b] Scale: 1.1 g. Abbreviations: $LiAlH_4$ = lithium aluminum hydride; HMPA = hexamethylphosphoramide; DMP = Dess-Martin periodinane.

3-chloroperoxybenzoic acid (*m*-CPBA) in CH_2Cl_2 to effect the desired Baeyer-Villiger rearrangement, producing lactone **43** in 46% yield; a dramatic increase in yield (86%) was observed when the reaction was performed in toluene. The peroxide in **43** was hydrogenated with 10% Pd/C in MeOH to afford a diol intermediate, which underwent intramolecular transesterification and concomitant removal of the acetonide group to afford triol **44** in 76% yield. From here, the only remaining step to access the skeleton of propindilactone G was the formation of the C—O bond in **44**. To prevent side reactions involving the free C16 and C22 hydroxyl groups, **44** was selectively acetylated to afford acetate **45**. Unfortunately, neither the dehydrogenation of the lactone nor the radical remote C—H functionalization to give desired cyclization product **46** succeeded.

However, dehydrogenation of **43** with *N*-*tert*-butylbenzenesulfinimidoyl chloride[33] (Mukaiyama reagent) generated unsaturated lactone **47** in 62% yield. Upon treatment with active zinc powder and AcOH in CH_2Cl_2,[34] **47** smoothly gave diol intermediate **48**, which underwent transesterification and oxa-Michael addition to afford 5/5 fused lactone **49**. Deprotection of the acetonide group *in situ* with the aid of PTSA and MeOH gave diol **50** in 84% yield. Subsequent Swern oxidation of **50** generated aldehyde **51** in 89% yield.

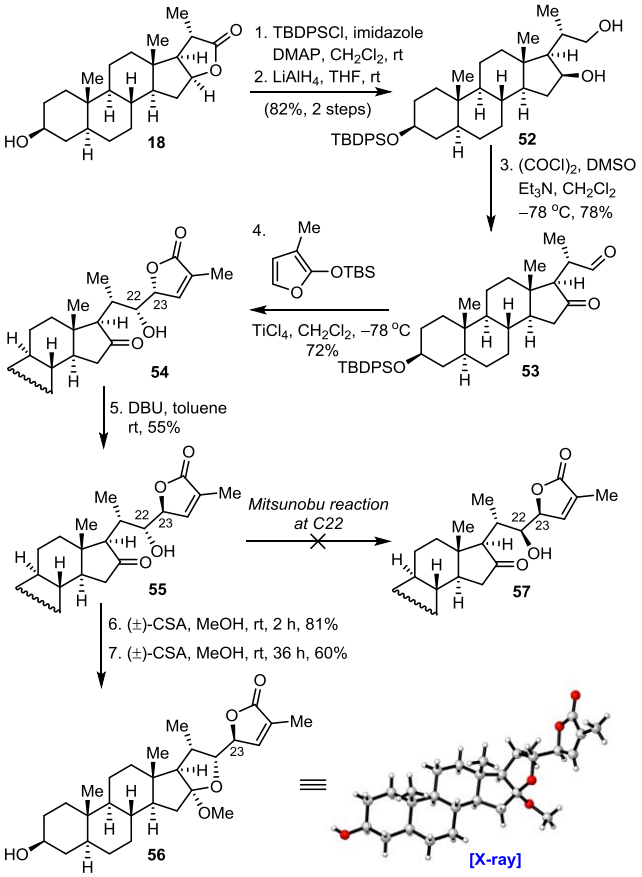
After developing a reliable route to key intermediate **51**, we turned our attention to the installation of the butenolide side chain of propindilactone G as well as the C14-C15 olefin. To this end, compound **53** bearing the same C16 ketone and C22 aldehyde groups as **51** was used as a model substrate (Scheme 7). Aldehyde **53** was easily prepared in three steps from lactone **18** *via* the silylation of the C3 hydroxyl group and reduction of the lactone to afford diol **52**, followed by the Swern oxidation of the resultant C16 and C22 hydroxyl groups. A vinylogous Mukaiyama aldol reaction between aldehyde **53** and 3-methyl-2-(*tert*-butyldimethylsilyloxy)furan[35] in the presence of $TiCl_4$ produced butenolide **54** in 72% yield.[36] However, the stereochemistry at C22 and C23 was opposite to that of propindilactone G. Fortunately, the stereochemistry at C23 could be inverted by treating **54** with

Scheme 6 Successful construction of the core skeleton



Abbreviations: *m*-CPBA = 3-chloroperoxybenzoic acid; LHMDS = lithium bis(trimethylsilyl)amide; DMSO = dimethylsulfoxide.

Scheme 7 Attempted installation of the side chain *via* Mukaiyama aldol reaction



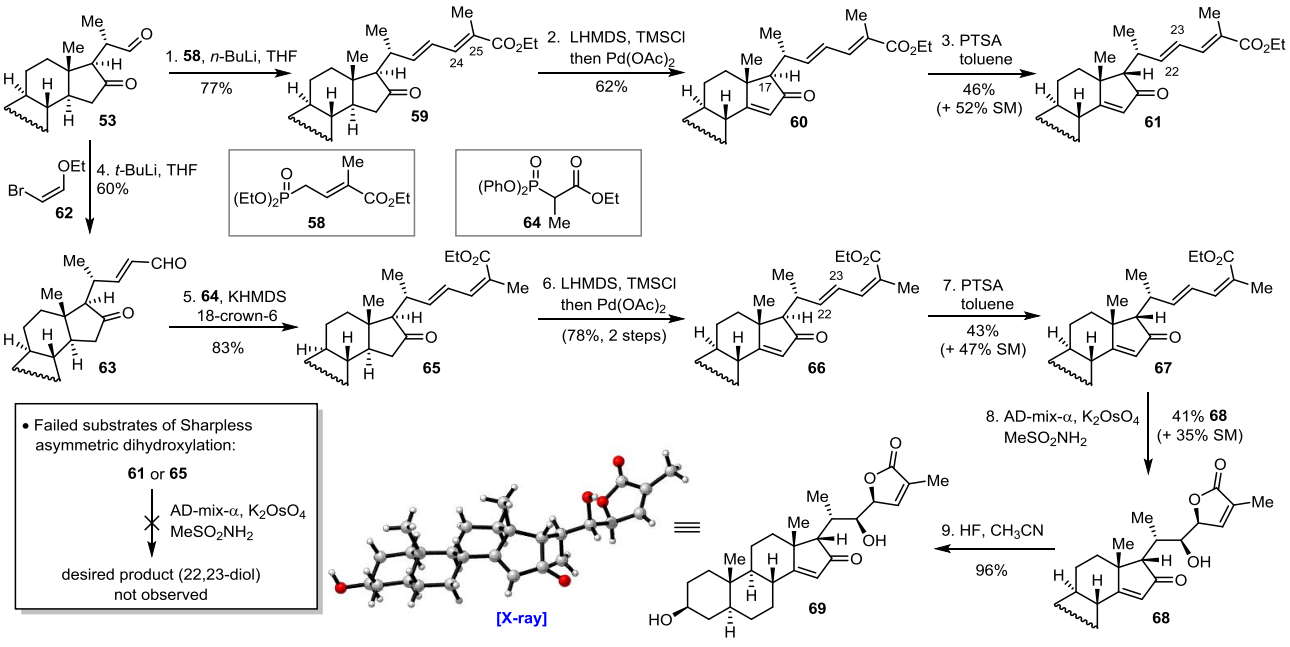
Abbreviation: TBDPSCl = *tert*-butyldiphenylsilyl chloride.

DBU in toluene, possibly *via* enolization and protonation, to generate **55**. To further confirm the stereochemistry of the butenolide side chain, **55** was reacted with MeOH in the presence of catalytic (±)-CSA (camphorsulfonic acid) for 2 h to afford the ketal intermediate in 81% yield, which was further desilylated using (±)-CSA in MeOH to generate **56** after 36 h in 60% yield. X-ray single-crystal analysis of **56** revealed that the C22 stereocenter had been inverted successfully. However, the subsequent inversion of the C22 stereocenter *via* the Mitsunobu reaction was met with failure, possibly because of the congestion around C22.

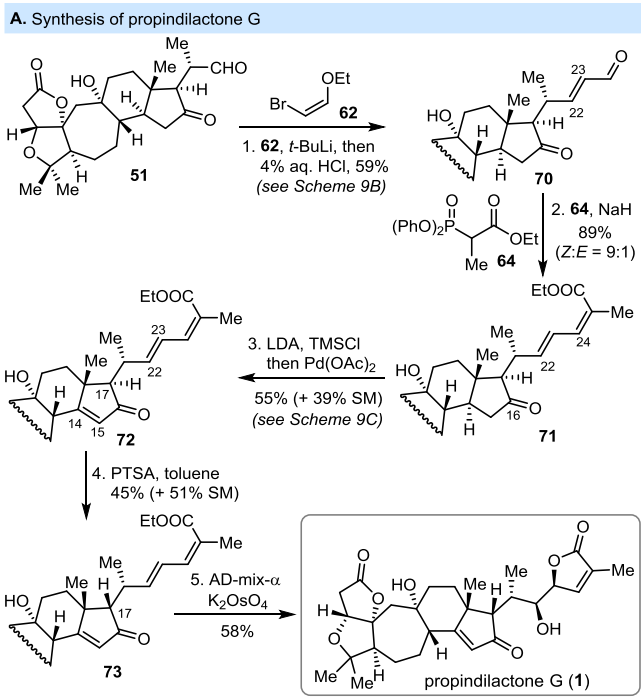
Inspired by the pioneering work of Yang and co-workers in their total synthesis of propindilactone G, we attempted to install the side chain through a sequence involving the Horner-Wadsworth-Emmons (HWE) reaction and dihydroxylation (Scheme 8). The HWE reaction of aldehyde **53** with phosphate **58**[37] afforded unsaturated ester **59** with a *trans*-C24-C25 olefin in 77% yield,[38] which was subjected to the Saegusa-Ito oxidation to produce enone **60** in 62% yield. Owing to the opposite configuration of C17 of **60** to that of propindilactone G, **60** was isomerized using catalytic PTSA in toluene to afford **61** in 46% yield, while 52% of starting material **60** was recovered. However, the subsequent dihydroxylation of **61** failed to produce the desired C22-C23 diol product, and products resulting from the dihydroxylation of the C24-C25 olefin were observed instead. Speculating that the configuration of the C24-C25 olefin might influence the dihydroxylation of the C22-C23 olefin, we decided to prepare enone **67** with a *cis*-C24-C25 olefin. To this end, two-carbon homologation[39] of **53** with vinyl bromide **62**[40] in the presence of *t*-BuLi and subsequent acid hydrolysis were carried out, generating enal **63** in 60% yield. The HWE reaction of enal **63** with phosphate **64** led to the formation of *cis*-unsaturated ester **65**,[41] which was transformed into enone **67** through Saegusa-Ito oxidation[42] and C17 epimerization. To our delight, Sharpless dihydroxylation[43] of **67** with concomitant lactonization proceeded smoothly to generate desired lactone **68** in 41% yield, along with 35% recovered **67**. The structure of **67** was confirmed by X-ray crystallographic analysis of its desilylated analog, **69**.

Having established a five-step synthetic sequence for the butenolide side chain of propindilactone G on model substrate **53**, we next focused our attention on completing the synthesis of propindilactone G (Scheme 9). The two-carbon homologation of **51** using a zinc reagent derived from vinyl bromide **62** resulted in incomplete conversion (Scheme 9B, entry 1).[44] Higher conversion of **51** was achieved at the expense of a lower yield when the reaction was conducted at a higher reaction temperature (entry 2).

Scheme 8 Installation of the side chain *via* Sharpless dihydroxylation



Scheme 9 Completion of the synthesis of propindilactone G



B. Optimization of the two-carbon homologation

entry	conditions	**70** + **51**[a]/%	**70**:**51**[b]
1	*t*-BuLi, $ZnMe_2$, THF, –78 to –40 °C	40	1:1
2	*t*-BuLi, $ZnMe_2$, THF, –78 to 0 °C	35	5:1
3	*t*-BuLi, THF, –78 °C	decomposed	
4	*t*-BuLi, $ZnMe_2$, ether/THF, –78 °C	49	3.7:1
5	*t*-BuLi, ether/THF, –78 °C	59	1:0

C. Optimization of the Saegusa oxidation

entry	conditions	**72**[a]/%	**71**[a]/%
1	$(PhSeO)_2O$, $NaHCO_3$, PhCl, 80 to 120 °C	complex	
2	LHMDS, TMSCl, THF, –78 to –10 °C; then $Pd(OAc)_2$, DMSO, 60 °C	6	60
3	LHMDS, TMSCl, THF/HMPA, –78 °C to rt	NR	
4	LDA, TMSCl, THF, -78 °C; then $Pd(OAc)_2$, DMSO, 60 °C	34	33
5	LDA, TMSCl, DME/THF, –78 °C; then $Pd(OAc)_2$, DMSO, 50 °C	55	39

[a] Isolated yield. [b] Ratio determined by ^{1}H NMR.

Exclusion of the $ZnMe_2$ additive from the reaction conditions resulted in the decomposition of starting material **51** (entry 3). After extensive solvent screening, we found that a mixed solvent of ether and THF was better, and this led to a modest yield and ratio (entry 4). Gratifyingly, **51** was fully converted when the reaction was performed without $ZnMe_2$, affording **70** in 59% yield after treatment with 4% aq. HCl (entry 5). Subsequent *Z*-selective HWE reaction of **70** with phosphate **64** gave **71** in 89% yield, which was then converted to enone **72** *via* the dehydrogenation of the C14—C15 bond (Scheme 9C). Initial direct oxidative dehydrogenation attempts with $(PhSeO)_2O$[45] led only to a complex reaction mixture (entry 1). Fortunately, we found that Saegusa oxidation of **71** could afford **72** in 6% yield, along with 60% recovered starting material. The low efficiency of the dehydrogenation was due to the low conversion in the silyl enol ether formation when **70** was treated with lithium hexamethyldisilazide (LHMDS) and trimethylsilyl chloride (TMSCl). Therefore, we focused on the optimization of the Saegusa oxidation to improve the conversion of **70** to the corresponding silyl enol ether. Disappointingly, the reaction was inhibited when HMPA was added as a co-solvent (entry 3). When LHMDS was replaced with lithium diisopropylamide (LDA), higher conversion was observed and the resulting silyl enol ether was treated with $Pd(OAc)_2$ in dimethylsulfoxide (DMSO) to afford enone **72** in 34% yield (entry 4). Further screening of solvents revealed that a mixed solvent of DME and THF was optimal, affording desired product **72** in 55% yield while 39% of starting material **71** was recovered (entry 5).

With enone **72** in hand, all that remained to complete the synthesis of propindilactone G was the epimerization of C17 and asymmetric dihydroxylation of the C22-C23 olefin (Scheme 9). To this end, **72** was isomerized with PTSA in toluene to afford **73** in 45% yield, which was subjected to the same Sharpless asymmetric dihydroxylation reaction to afford **1** in 58% yield. The nuclear magnetic resonance (NMR) spectroscopy and optical rotation data of synthetic propindilactone G were in agreement with those reported by Sun[9] and Yang.[4b]

Conclusions

In summary, the bioinspired synthesis of *Schisandra* nortriterpenoid propindilactone G (**1**) was accomplished successfully from known steroid lactone **18**, representing the first biomimetic synthesis of any member of the *Schisandra* nortriterpenoids. The route illustrates how powerful radical remote functionalization can be in oxidizing innate C—H bonds. A Wagner-Meerwein rearrangement was developed to achieve the ring expansion, transforming the classic 6/6/6 fused ring system into the 6/7/6 fused ring system. Because the stereochemistry of the newly formed C10 tertiary alcohol was opposite to that of propindilactone G, a silylperoxide was installed *via* Mukaiyama hydrosilylperoxidation, and the C10 stereocenter was successfully inverted through subsequent intramolecular peroxide cyclization. Finally, a biomimetic transesterification/oxa-Michael addition cascade was employed to assemble the 5/5 fused lactone and the synthesis of propindilactone G was completed after the introduction of the butenolide chain. Our work should enable in-depth understanding of the proposed biogenetic origin of the schinortriterpenoid and facilitate further studies on the biological activities of propindilactone G. Efforts to extend this biomimetic synthetic strategy to the syntheses of other schinortriterpenoids are currently ongoing and will be reported in due course.

Experimental

All reactions utilizing air- or moisture-sensitive reagents were carried out in flame-dried glassware under an argon atmosphere, unless otherwise stated. Dry tetrahydrofuran (THF), dichloromethane (DCM), toluene (PhMe) and diethyl ether (Et_2O) were obtained by passing the HPLC grade or pre-dried solvents through activated alumina columns. Tetrachloromethane (CCl_4), 1,2-dichloroethane (DCE), cyclohexane, *t*-BuOH, triethylamine (Et_3N) and hexamethylphosphoramide (HMPA) were distilled from CaH_2. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were magnetically stirred and monitored by thin layer chromatography (TLC) with 0.15—0.2 mm pre-coated silica gel (10—40 μm) plates, using UV light as the visualizing agent or ethanolic phosphomolybdic acid and heating as developing agents. Flash chromatography was performed with silica gel (200—300 mesh) under pressure. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous material, unless otherwise stated. NMR spectra were recorded on Bruker-400 and Bruker-600 spectrometers. ^{1}H NMR spectra were calibrated using residual undeuterated solvent as an internal reference ($CDCl_3$: δ 7.26; MeOH-d_4: δ 3.31; C_5D_5N: δ 8.74) and ^{13}C NMR spectra were calibrated against the deuterated solvent peak ($CDCl_3$: δ 77.2; MeOH-d_4: δ 49.0; C_5D_5N: δ 150.3). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t =

triplet, q = quartet, m = multiplet, br = broad. IR spectra were collected on Avatar 330 FT-IR spectrometer. Melting points were determined on SGW X-4 microscopic melting point apparatus and were uncorrected. Optical rotations were determined on JASCO P-1030 Polarimeter in the solvent indicated. High-resolution mass spectra were recorded on IonSpec 4.7 Tesla FTMS or Bruker Daltonics, Inc. APEXIII 7.0 TESLA FTMS.

Synthesis of compound 22. To a solution of **20** (300 mg, 0.777 mmol, 1.0 equiv) in 1,4-dioxane and H_2O (37 mL, 3.6 : 1) was added a solution of 70% $HClO_4$ (0.1 mL, 1.17 mmol, 1.5 equiv) in 2.9 mL H_2O at room temperature. NBS (194 mg, 1.09 mmol, 1.4 equiv) was added slowly in 5 min at 0 °C and the resulting reaction mixture was stirred at room temperature for another 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ (10 mL), and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 3 : 1 petroleum ether : EtOAc) to provide compound **21**.

To a solution of the bromohydrin **21** obtained above in 25 mL dry cyclohexane was added DIB (490 mg, 1.52 mmol, 2.0 equiv) and I_2 (389 mg, 1.53 mmol, 2.0 equiv) at room temperature under argon. The reaction mixture was heated to reflux by irradiation with an infrared lamp (275 W) for 0.5 h. After cooled to room temperature, the reaction was quenched with sat. aq. $Na_2S_2O_3$ (15 mL) and extracted with EtOAc (3×15 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 6 : 1→4 : 1 petroleum ether : EtOAc) to provide **22** (117 mg, 38% over 2 steps) as a white solid.

22: mp: 258.3—260.8 °C; TLC (petroleum ether : EtOAc, 3 : 1 *V*/*V*): R_f = 0.28; $[\alpha]_D^{27}$ –1.0 (*c* 1.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 5.01 (td, *J* = 7.7, 4.4 Hz, 1H), 4.96 (t, *J* = 2.9 Hz, 1H), 2.53 (q, *J* = 7.5 Hz, 1H), 2.38 (dt, *J* = 13.8, 7.3 Hz, 1H), 2.28 (d, *J* = 12.0 Hz, 1H), 2.23 (dt, *J* = 13.2, 3.4 Hz, 1H), 2.18 (d, *J* = 12.1 Hz, 1H), 2.06 (d, *J* = 7.5 Hz, 1H), 2.00 (s, 3H), 1.88—1.78 (m, 2H), 1.76 (d, *J* = 11.4 Hz, 1H), 1.73—1.60 (m, 3H), 1.56 (dd, *J* = 13.4, 4.4 Hz, 1H), 1.52—1.36 (m, 3H), 1.29 (d, *J* = 7.6 Hz, 3H), 1.24—1.09 (m, 4H), 0.99 (s, 3H), 0.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 208.7, 180.3, 170.5, 82.3, 69.7, 64.2, 57.6, 55.9, 54.1, 45.3, 39.8, 36.4, 35.9, 35.5, 32.6, 32.4, 32.3, 31.5, 27.4, 25.8, 21.5, 17.7, 14.7, 11.0; IR (KBr) *v*: 2974, 2925, 1770, 1727, 1698, 1373, 1262, 1188 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{24}H_{35}O_5$, 403.2479; found, 403.2477.

Synthesis of compound 23. To a solution of **20** (330 mg, 0.855 mmol, 1.0 equiv) in 1,4-dioxane and H_2O (40 mL, 4 : 1) was added a solution of 70% $HClO_4$ (0.11 mL, 1.3 mmol, 1.5 equiv) in 3.2 mL H_2O at room temperature. NBS (213 mg, 1.20 mmol, 1.4 equiv) was added slowly in 5 min at 0 °C and the resulting reaction mixture was stirred at room temperature for another 0.5 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ (15 mL), and extracted with EtOAc (3×20 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude bromohydrin **21**, which was used in the next step without further purification.

To a solution of the bromohydrin **21** obtained above in 30 mL toluene was added DBU (0.5 mL, 3.42 mmol, 4.0 equiv) at room temperature. The reaction mixture was stirred at room temperature for 0.5 h and concentrated *in vacuo* to provide the crude residue. Purification by flash chromatography (SiO_2, 12 : 1 → 10 : 1 petroleum ether : acetone) afforded the epoxide intermediate **74** (220 mg, 64% over 2 steps) as a white solid.

To a solution of the epoxide **74** (330 mg, 0.828 mmol, 1.0 equiv) obtained above in 50 mL $CHCl_3$ was added HCl (0.7 mL, 4.0 M in 1,4-dioxane, 2.73 mmol, 3.3 equiv) at 0 °C. The reaction mixture was stirred at 0 °C for 40 min and quenched with H_2O. The organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 8 : 1 petroleum ether : acetone) to provide **23** (313 mg, 87%) as a white solid.

74: mp: 191.9—193.5 °C; TLC (petroleum ether : acetone, 4 : 1 *V*/*V*): R_f = 0.43; $[\alpha]_D^{27}$ –8.6 (*c* 1.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.95 (t, *J* = 2.8 Hz, 1H), 4.86 (td, *J* = 7.8, 4.7 Hz, 1H), 3.40 (s, 1H), 2.58 (q, *J* = 7.6 Hz, 1H), 2.32 (dt, *J* = 13.9, 7.3 Hz, 1H), 2.17 (dd, *J* = 14.5, 2.6 Hz, 1H), 2.13—2.04 (m, 2H), 2.02 (s, 3H), 1.78 (d, *J* = 7.8 Hz, 1H), 1.71—1.55 (m, 3H), 1.55—1.47 (m, 3H), 1.43 (dd, *J* = 13.5, 4.8 Hz, 1H), 1.36—1.23 (m, 2H), 1.27 (d, *J* = 7.7 Hz, 3H), 1.23—1.15 (m, 2H), 1.15—1.07 (m, 2H), 0.93 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 181.0, 170.5, 82.0, 69.4, 66.6, 60.3, 60.1, 55.5, 39.9, 39.5, 37.6, 37.0, 36.3, 33.9, 33.7, 33.2, 33.1, 28.5, 26.4, 25.5, 21.6, 18.0, 16.8, 14.5; IR (KBr) *v*: 2929, 2867, 1768, 1732, 1375, 1246, 1189, 975 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{34}O_5Na$, 425.2298; found, 425.2299.

Synthesis of compound 31. A solution of **26** (300 mg, 0.625 mmol, 1.0 equiv) and K_2CO_3 (518 mg, 3.75 mmol, 6.0 equiv) in 15 mL MeOH was stirred at room temperature for 14 h. Concentration under reduced pressure afforded the crude reaction mixture, which was neutralized with 2.4 M aq. HCl to pH<7 and stirred at room temperature for another 20 min. The aqueous layer was extracted with EtOAc (3×10 mL) and the combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 2 : 1 → 1 : 1 petroleum ether : EtOAc) to provide **31** (180 mg, 66%) as a white foam.

31: TLC (petroleum ether : EtOAc, 1 : 1 *V*/*V*): R_f = 0.21; $[\alpha]_D^{25}$ –29.4 (*c* 2.30, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 5.42 (d, *J* = 6.3 Hz, 1H), 4.97 (td, *J* = 7.7, 4.3 Hz, 1H), 4.36 (d, *J* = 9.6 Hz, 1H), 4.29 (d, *J* = 9.6 Hz, 1H), 4.10 (br s, 1H), 2.91 (s, 3H), 2.61 (q, *J* = 7.5 Hz, 1H), 2.40 (dt, *J* = 14.2, 7.4 Hz, 1H), 2.32 (s, 1H), 2.13—2.03 (m, 2H), 2.02—1.92 (m, 3H), 1.91—1.71 (m, 4H), 1.71—1.46 (m, 4H), 1.41—1.28 (m, 3H), 1.30 (d, *J* = 7.6 Hz, 3H), 1.15—1.01 (m, 1H), 0.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 181.1, 140.5, 120.5, 83.0, 66.1, 65.6, 58.6, 52.6, 41.8, 40.3, 40.1, 37.8, 37.3, 36.6, 35.9, 35.9, 34.1, 32.9, 28.5, 27.8, 24.3, 17.9, 13.3; IR (KBr) *v*: 3446, 2925, 1757, 1635, 1351, 1174, 947, 734 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{23}H_{35}O_6S$, 439.2149; found, 439.2149.

Synthesis of compound 33. To a solution of **31** (120 mg, 0.274 mmol, 1.0 equiv) and DMAP (4-dimeththylaminopyridine, 6.68 mg, 0.0548 mmol, 0.2 equiv) in 5 mL CH_2Cl_2 was added pyridine (66 μL, 0.822 mmol, 3.0 equiv) and $ClCO_2Me$ (43 μL, 0.548 mmol, 2.0 equiv). The reaction mixture was stirred at room temperature for 10 h, quenched with dilute aq. HCl, and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 2 : 1→1 : 1 petroleum ether : EtOAc) to provide **33** (21 mg, 15%) as a colorless oil and recovered **31** (80 mg, 67%).

33: TLC (petroleum ether : EtOAc, 2 : 1 *V*/*V*): R_f = 0.39; $[\alpha]_D^{25}$ –11.3 (*c* 0.12, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 5.43 (d, *J* = 5.8 Hz, 1H), 5.03—4.93 (m, 2H), 4.37 (d, *J* = 10.0 Hz, 1H), 4.32 (d, *J* = 9.4 Hz, 1H), 3.78 (s, 3H), 2.94 (s, 3H), 2.63 (q, *J* = 7.5 Hz, 1H), 2.42 (dt, *J* = 14.1, 7.3 Hz, 1H), 2.17—2.05 (m, 2H), 2.06—1.93 (m, 4H), 1.93—1.70 (m, 4H), 1.69—1.60 (m, 1H), 1.55—1.48 (m, 1H), 1.43—1.36 (m, 2H), 1.35—1.30 (m, 1H), 1.33 (d, *J* = 7.7 Hz, 3H), 1.25—1.19 (m, 1H), 1.18—1.04 (m, 1H), 0.73 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 181.0, 155.2, 140.1, 120.8, 83.0, 73.3, 65.8, 58.7, 54.8, 52.7, 41.5, 40.4, 40.1, 38.4, 37.4, 36.6, 35.8, 34.1, 33.1, 32.8, 27.6, 25.7, 24.9, 18.0, 13.3; IR (KBr) *v*: 2917, 2854, 1738, 1732, 1274, 1261, 764, 749 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{25}H_{37}O_8S$, 497.2204; found, 497.2204.

Synthesis of compound 35, 29, C9-*epi*-29. To a solution of **28** (100 mg, 0.249 mmol, 1.0 equiv) and $Co(thd)_2$ (31.8 mg, 0.0746 mmol, 0.3 equiv) in 10 mL dry DCE was added Et_3SiH (120 μL, 0.747 mmol, 3.0 equiv) under O_2 atmosphere (1 atm). The reaction mixture was stirred at room temperature for 0.5 h and then at 0 °C for 2 h under O_2 (balloon). The reaction mixture was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 7 : 1 → 4 : 1 → 1 : 2 petroleum ether : EtOAc) to provide compound **35** (91.0 mg, 67%) as a white solid, **29** and C9-*epi*-**29** (19.0 mg, 18%, 1.2 : 1) as a white foam.

35: mp: 152.1—155.4 °C; TLC (petroleum ether : EtOAc, 2 : 1 *V*/*V*): R_f = 0.63; $[\alpha]_D^{25}$ −12.4 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 5.01 (t, *J* = 2.9 Hz, 1H), 4.95 (td, *J* = 7.7, 4.5 Hz, 1H), 2.57 (q, *J* = 7.6 Hz, 1H), 2.29 (d, *J* = 15.7 Hz, 1H), 2.23 (dt, *J* = 13.8, 7.1 Hz, 1H), 2.19—2.13 (m, 1H), 2.09—2.02 (m, 1H), 2.05 (s, 3H), 1.98 (dd, *J* = 14.0, 4.6 Hz, 1H), 1.89—1.81 (m, 1H), 1.85 (d, *J* = 7.4 Hz, 1H), 1.77 (d, *J* = 15.8 Hz, 1H), 1.80—1.63 (m, 3H), 1.59—1.51 (m, 2H), 1.47 (dd, *J* = 13.7, 4.8 Hz, 2H), 1.43—1.34 (m, 6H), 1.31 (d, *J* = 7.6 Hz, 3H), 1.11 (s, 1H), 1.00 (t, *J* = 7.9 Hz, 9H), 0.78 (s, 3H), 0.75—0.67 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 181.4, 170.8, 84.8, 82.7, 73.0, 69.8, 59.1, 53.2, 47.8, 45.2, 42.0, 40.3, 37.0, 36.3, 34.3, 34.2, 33.6, 33.4, 32.2, 27.4, 25.4, 21.6, 18.1, 13.4, 7.0, 4.1; IR (KBr) *v*: 3460, 2940, 2874, 1761, 1733, 1258, 1017, 745 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{30}H_{51}O_7Si$, 551.3399; found, 551.3395.

C9-*epi*-**29**: mp: 147.5—150.3 °C; TLC (petroleum ether : EtOAc, 2 : 1 *V*/*V*): R_f = 0.18; $[\alpha]_D^{25}$ −45.3 (*c* 1.40, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 5.07—4.94 (m, 2H), 2.58 (q, *J* = 7.7 Hz, 1H), 2.37—2.27 (m, 1H), 2.27—2.15 (m, 1H), 2.05 (s, 3H), 1.99 (d, *J* = 14.9 Hz, 1H), 1.91 (d, *J* = 7.7 Hz, 1H), 1.91—1.87 (m, 1H), 1.87—1.80 (m, 1H), 1.79—1.66 (m, 5H), 1.65—1.42 (m, 8H), 1.39—1.33 (m, 1H), 1.33—1.18 (m, 3H), 1.31 (d, *J* = 7.6 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 181.3, 170.8, 82.8, 78.6, 73.5, 70.0, 58.4, 52.0, 47.9, 44.3, 43.1, 42.1, 41.4, 36.7, 36.2, 35.1, 34.6, 33.0, 30.0, 28.4, 24.7, 21.7, 18.1, 14.1; IR (KBr) *v*: 3391, 2933, 2873, 1769, 1731, 1242, 1020, 735 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{36}O_6Na$, 551.3399; found, 551.3395.

Synthesis of compound 40, 41, 42. To a solution of **39** (1.10 g, 2.63 mmol, 1.0 equiv) in *t*-BuOH/cyclohexane/HMPA (61.0 mL, 2.8 : 2.2 : 1) was added *t*-BuOK (1.0 M in THF, 7.9 mL, 7.89 mmol, 3.0 equiv) and MeI (0.49 mL, 7.89 mmol, 3.0 equiv) at 0 °C. After stirred at 0 °C for 25 min, *t*-BuOK (5.3 mL×2, 5.26 mmol×2, 2.0 equiv×2) and MeI (0.33 mL×2, 5.26 mmol×2, 2.0 equiv×2) were added in two portions every 25 min. *t*-BuOK (2.6 mL, 2.63 mmol, 1.0 equiv) and MeI (0.16 mL, 2.63 mmol, 1.0 equiv) were added and stirring was continued for another 25 min under the same condition. Finally, another portion of *t*-BuOK (1.3 mL, 1.31 mmol, 0.5 equiv) and MeI (0.08 mL, 1.31 mmol, 0.5 equiv) were added and stirring was continued for 25 min at 0 °C. The reaction mixture was quenched with water (20 mL) and extracted with EtOAc (3×40 mL). The combined organic layers were washed with aq. NaCl (water/brine = 1 : 1, *V*/*V*, 30 mL) for 8 times and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 31 : 6 : 1 → 25 : 6 : 1 petroleum ether : CH_2Cl_2 : EtOAc) to provide compound **40** (610 mg, 52%) as a white solid, **41** and **42** (263 mg, 23%) as white foams.

41: TLC (petroleum ether : EtOAc, 9 : 1 *V*/*V*): R_f = 0.61; $[\alpha]_D^{25}$ +5.3 (*c* 0.17, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.52 (q, *J* = 8.0 Hz, 1H), 4.21 (s, 1H), 3.80 (dd, *J* = 11.9, 5.7 Hz, 1H), 3.47 (s, 3H), 3.19 (t, *J* = 10.8 Hz, 1H), 2.55 (d, *J* = 12.0 Hz, 1H), 2.41—2.27 (m, 2H), 2.19—2.10 (m, 2H), 2.08—1.88 (m, 5H), 1.87—1.75 (m, 2H), 1.70—1.60 (m, 2H), 1.56—1.52 (m, 1H), 1.47 (td, *J* = 11.7, 4.2 Hz, 1H), 1.39 (s, 3H), 1.35—1.16 (m, 5H), 1.27 (s, 3H), 0.86 (s, 3H), 0.81 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 154.0, 100.6, 97.7, 86.8, 86.1, 71.9, 70.1, 58.8, 54.5, 50.4, 46.9, 45.2, 42.3, 40.6, 37.1, 34.8, 34.0, 33.3, 32.5, 31.4, 27.4, 27.2, 25.9, 23.8, 16.9, 12.7; IR (KBr) *v*: 2947, 2858, 1666, 1454, 1379, 1260, 1096, 808 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+Na]^+$ calcd for $C_{26}H_{40}O_5Na$, 455.2768; found, 455.2765.

42: TLC (petroleum ether : EtOAc, 9 : 1 *V*/*V*): R_f = 0.57; $[\alpha]_D^{25}$ +5.2 (*c* 0.14, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.52 (q, *J* = 7.9 Hz, 1H), 3.80 (dd, *J* = 11.9, 5.7 Hz, 1H), 3.47 (s, 3H), 3.19 (t, *J* = 11.4 Hz, 1H), 2.56 (d, *J* = 12.0 Hz, 1H), 2.39—2.29 (m, 1H), 2.29—2.20 (m, 2H), 2.20—2.10 (m, 2H), 2.09—1.95 (m, 2H), 1.97 (d, *J* = 11.9 Hz, 1H), 1.94—1.77 (m, 3H), 1.70—1.59 (m, 3H), 1.57 (s, 3H), 1.46 (td, *J* = 11.7, 4.3 Hz, 1H), 1.39 (s, 3H), 1.32—1.17 (m, 5H), 1.27 (s, 3H), 0.85 (s, 3H), 0.81 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 147.6, 116.5, 100.6, 87.0, 86.2, 71.9, 70.1, 58.8, 56.4, 50.8, 46.8, 45.0, 44.8, 42.4, 37.1, 35.0, 33.9, 32.2, 31.4, 29.7, 27.7, 25.9, 23.7, 23.7, 16.9, 12.7, 12.6; IR (KBr) *v*: 2934, 2855, 1454, 1377, 1260, 1221, 1096, 802 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+Na]^+$ calcd for $C_{27}H_{42}O_5Na$, 469.2924; found, 469.2919.

Synthesis of compound 44. A solution of **43** (117 mg, 0.253 mmol, 1.0 equiv) and 10% Pd/C (11.7 mg, 10% *w*/*w*) in 5 mL MeOH was stirred at room temperature under 1 atm H_2 for 80 min. The reaction mixture was filtered through celite and concentrated under reduced pressure to afford the crude product. Purification by flash chromatography (SiO_2, 3 : 1 → 2 : 1 petroleum ether : acetone) provided compound **44** (82.0 mg, 76%) as a white solid.

44: mp: 228.1—230.2 °C; TLC (petroleum ether : acetone, 2 : 1 *V*/*V*): R_f = 0.18; $[\alpha]_D^{25}$ −24.0 (*c* 0.42, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.40 (td, *J* = 7.6, 4.2 Hz, 1H), 3.69—3.53 (m, 2H), 3.06 (ddd, *J* = 13.3, 10.6, 8.4 Hz, 1H), 2.76—2.64 (m, 2H), 2.63—2.52 (m, 1H), 2.27—2.15 (m, 2H), 2.11 (d, *J* = 15.6 Hz, 1H), 1.94 (d, *J* = 15.8 Hz, 1H), 1.85—1.71 (m, 4H), 1.70—1.63 (m, 3H), 1.55—1.47 (m, 2H), 1.45—1.34 (m, 3H), 1.33—1.23 (m, 3H), 1.29 (s, 3H), 1.27 (s, 3H), 1.19—1.07 (m, 2H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 177.8, 93.3, 74.2, 72.8, 72.6, 70.9, 62.0, 55.8, 54.0, 47.3, 46.4, 43.2, 39.8, 35.7, 35.4, 32.6, 32.5, 32.5, 29.7, 29.5, 27.5, 26.3, 16.9, 12.5; IR (KBr) *v*: 3401, 2932, 2877, 1748, 1274, 1260, 764, 749 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+Na]^+$ calcd for $C_{24}H_{42}O_6Na$, 447.2717; found, 447.2714.

Synthesis of compound 45. To a solution of **44** (50.0 mg, 0.118 mmol, 1.0 equiv) and DMAP (4.32 mg, 0.0354 mmol, 0.3 equiv) in 3 mL dry CH_2Cl_2 was added Et_3N (82 μL, 0.589 mmol, 5.0 equiv) and Ac_2O (39 μL, 0.413 mmol, 3.5 equiv) at room temperature. After stirring at the same temperature for 4.5 h, Ac_2O (11 μL, 0.118 mmol, 1.0 equiv) was added and stirring was continued for another 1 h at room temperature. Et_3N (82 μL, 0.589 mmol, 5.0 equiv) and Ac_2O (39 μL, 0.413 mmol, 3.5 equiv) were added and stirring was continued for another 1 h at room temperature. Finally, another portion of Et_3N (82 μL, 0.589 mmol, 5.0 equiv) and Ac_2O (39 μL, 0.413 mmol, 3.5 equiv) were added and stirring was continued for 1 h at room temperature. Solvent was removed under reduced pressure and the resulting crude product was purified by flash chromatography (SiO_2, 3 : 1 petroleum ether : acetone) to provide compound **45** (53.0 mg, 88%) as a white solid.

45: mp: 200.3—202.4 °C; TLC (petroleum ether : acetone, 3 : 1 *V*/*V*): R_f = 0.32; $[\alpha]_D^{25}$ +23.6 (*c* 1.32, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 5.09 (td, *J* = 7.7, 4.2 Hz, 1H), 4.07 (dd, *J* = 10.7, 3.4 Hz, 1H), 3.65 (dd, *J* = 10.7, 6.8 Hz, 1H), 3.03 (ddd, *J* = 13.3, 10.7, 8.1 Hz, 1H), 2.77—2.63 (m, 1H), 2.66 (d, *J* = 8.5 Hz, 1H), 2.55 (ddd, *J* = 18.3, 10.7, 8.1 Hz, 1H), 2.35 (dt, *J* = 13.5, 7.7 Hz, 1H), 2.25—2.15 (m, 1H), 2.09 (d, *J* = 15.8 Hz, 1H), 2.031 (s, 3H), 2.025 (s, 3H), 1.97 (s, 1H), 1.95 (d, *J* = 14.7 Hz, 1H), 1.79—1.67 (m, 4H), 1.66—1.51 (m, 4H), 1.45—1.30 (m, 4H), 1.28 (s, 3H), 1.25 (s, 3H), 1.23—1.14 (m, 1H), 1.09—0.99 (m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 177.5, 171.2, 170.8, 93.0, 74.9, 74.2, 72.7, 68.8, 55.7, 55.7, 54.0, 47.4, 46.4, 43.1, 39.8, 35.10, 35.08, 32.7, 32.3, 30.3, 29.6, 29.5, 27.4, 26.2, 21.4, 21.1, 16.6, 12.0; IR

(KBr) *v*: 3524, 3457, 2967, 2938, 1761, 1736, 1374, 1248 cm^{-1}; HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{28}H_{44}O_8Na$, 531.2928; found, 531.2932.

Synthesis of compound 52. To a solution of **18** (5.00 g, 14.5 mmol, 1.0 equiv), imidazole (2.95 g, 43.4 mmol, 3.0 equiv) and DMAP (177 mg, 1.45 mmol, 0.1 equiv) in 40 mL CH_2Cl_2 was added TBDPSCl (*tert*-butyldiphenylsilyl chloride, 7.7 mL, 28.9 mmol, 2.0 equiv) at room temperature. After stirred at the same temperature for 2.5 h, the reaction mixture was quenched with H_2O and extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 20 : 1 petroleum ether : EtOAc) to furnish the silylated product which was used in the next step without further purification.

To a solution of the silylated product obtained above in 80 mL dry THF was added $LiAlH_4$ (1.38 g, 36.3 mmol, 2.5 equiv) at room temperature over 10 min. After stirred at room temperature for 70 min, the reaction mixture was quenched slowly with 1.4 mL H_2O, 1.4 mL 15% aq. NaOH and 4.2 mL H_2O at 0 °C. The reaction mixture was filtered through celite and concentrated under reduced pressure to afford the crude product which was purified by flash chromatography (SiO_2, 5 : 1 → 3 : 1 petroleum ether : EtOAc) to provide compound **52** (6.90 g, 82% over 2 steps) as a white foam.

52: TLC (petroleum ether : EtOAc, 2 : 1 *V/V*): R_f = 0.25; $[\alpha]_D^{30}$ –7.9 (*c* 1.07, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.71—7.63 (m, 4H), 7.44—7.31 (m, 6H), 4.35 (td, *J* = 7.7, 4.8 Hz, 1H), 3.64—3.50 (m, 3H), 3.31 (s, 1H), 2.49 (s, 1H), 2.23—2.12 (m, 2H), 1.89 (dt, *J* = 12.6, 3.4 Hz, 1H), 1.69—1.60 (m, 2H), 1.59—1.50 (m, 2H), 1.47—1.33 (m, 5H), 1.29—1.09 (m, 4H), 1.04 (s, 9H), 1.02—0.96 (m, 2H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.89—0.84 (m, 1H), 0.87 (s, 3H), 0.82—0.77 (m, 1H), 0.79 (s, 3H), 0.73 (dd, *J* = 13.1, 4.2 Hz, 1H), 0.55—0.44 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 135.9, 135.0, 134.9, 129.49, 129.48, 127.53, 127.51, 72.9, 72.6, 70.6, 62.4, 54.3, 44.8, 43.0, 40.4, 38.4, 37.0, 35.6, 35.5, 35.1, 32.7, 32.1, 31.8, 28.7, 27.1, 21.0, 19.3, 17.1, 13.4, 12.5; IR (KBr) *v*: 3300, 2930, 2855, 1111, 1067, 739, 701, 612 cm^{-1}; HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{38}H_{56}O_3SiNa$, 611.3891; found, 611.3867.

Synthesis of compound 53. To a solution of $(COCl)_2$ (1.9 mL, 23.1 mmol, 4.0 equiv) in 67 mL dry CH_2Cl_2 was added DMSO (2.4 mL, 34.7 mmol, 6 equiv) at –78 °C. After stirring at the same temperature for 0.5 h, a solution of **23** (3.40 g, 5.78 mmol, 1.0 equiv) in 44 mL CH_2Cl_2 was added and stirring was continued for 0.5 h at –78 °C. Et_3N (7.9 mL, 57.8 mmol, 10.0 equiv) was added and stirring was continued for 1 h at –78 °C and 2 h at 0 °C. The reaction mixture was quenched with sat. aq. NH_4Cl and extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 25 : 1 → 15 : 1 petroleum ether : EtOAc) to furnish compound **53** (2.60 g, 78%) as a white foam.

53: TLC (petroleum ether : EtOAc, 2 : 1 *V/V*): R_f = 0.89; $[\alpha]_D^{30}$ –74.3 (*c* 1.18, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.81 (d, *J* = 2.7 Hz, 1H), 7.75—7.63 (m, 4H), 7.45—7.31 (m, 6H), 3.66—3.51 (m, 1H), 2.59—2.46 (m, 1H), 2.37 (d, *J* = 9.7 Hz, 1H), 2.21 (dd, *J* = 18.6, 6.6 Hz, 1H), 1.99—1.89 (m, 1H), 1.81—1.69 (m, 1H), 1.69—1.61 (m, 1H), 1.61—1.42 (m, 8H), 1.42—1.32 (m, 2H), 1.26—1.17 (m, 2H), 1.07 (d, *J* = 7.1 Hz, 3H), 1.05 (s, 9H), 0.98—0.85 (m, 2H), 0.82 (s, 3H), 0.78—0.65 (m, 2H), 0.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 217.6, 203.6, 135.8, 134.8, 134.7, 129.45, 129.43, 127.5, 127.4, 72.6, 65.1, 53.9, 51.2, 44.6, 43.5, 42.2, 38.7, 38.2, 37.5, 36.7, 35.5, 34.4, 32.0, 31.6, 28.4, 27.0, 20.7, 19.2, 13.6, 13.1, 12.3; IR (KBr) *v*: 2931, 2855, 1738, 1110, 1066, 823, 739, 702 cm^{-1}; HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{38}H_{52}O_3SiNa$, 607.3578; found, 607.3558.

Synthesis of compound 54 (**54** was in an equilibrium of C16-ketone and hemiketal). To a solution of **53** (400 mg, 0.685 mmol, 1.0 equiv) in 24 mL CH_2Cl_2 was added $TiCl_4$ (2.7 mL, 1.0 M in CH_2Cl_2, 4.0 equiv) at –78 °C. After stirring at the same temperature for 10 min, 3-methyl-2-(*tert*-butyldimethylsilyloxy)furan (436 mg, 2.05 mmol, 3.0 equiv) was added. The reaction mixture was stirred at –78 °C for 4 h and quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (3×10 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 4 : 1 petroleum ether : EtOAc) to furnish compound **54** (337 mg, 72%) as a white foam.

54: TLC (petroleum ether : EtOAc, 3 : 1 *V/V*): R_f = 0.39; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.70—7.65 (m, 4.37H), 7.44—7.34 (m, 6.31H), 7.07 (t, *J* = 1.6 Hz, 0.85H), 7.01 (t, *J* = 1.6 Hz, 0.15H), 5.00—4.97 (m, 0.17H), 4.96—4.91 (m, 0.88H), 4.29 (dd, *J* = 8.5, 3.8 Hz, 0.15H), 4.05 (dt, *J* = 5.3, 2.6 Hz, 0.85H), 3.63—3.54 (m, 1.10H), 3.49 (d, *J* = 5.4 Hz, 0.84H), 2.91 (s, 0.14H), 2.48 (td, *J* = 7.8, 3.1 Hz, 0.16H), 2.28—2.16 (m, 1.79H), 2.01—1.91 (m, 5.07H), 1.82—1.69 (m, 1.29H), 1.68—1.49 (m, 6.05H), 1.48—1.31 (m, 6.40H), 1.31—1.23 (m, 1.40H), 1.22—1.08 (m, 2.84H), 1.06—1.03 (m, 11.11H), 0.96—0.84 (m, 2.18H), 0.81 (s, 2.73H), 0.80—0.75 (m, 4.16H), 0.75—0.65 (m, 1.85H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 221.1, 174.2, 146.7, 146.6, 135.9, 135.02, 134.96, 134.9, 131.4, 130.9, 129.53, 129.50, 127.6, 127.54, 127.52, 116.6, 85.2, 82.9, 80.9, 77.5, 77.4, 77.2, 76.8, 73.7, 72.8, 72.7, 71.9, 66.1, 55.1, 54.2, 54.0, 50.7, 44.8, 44.7, 43.4, 42.9, 40.8, 39.0, 38.74, 38.71, 38.4, 38.3, 37.0, 36.8, 35.63, 35.61, 34.8, 34.5, 34.2, 33.7, 32.0, 31.8, 31.7, 28.6, 28.5, 27.1, 20.8, 19.3, 17.9, 14.3, 14.1, 13.3, 12.5, 12.4, 11.0, 10.9; IR (KBr) *v*: 3500, 2930, 2856, 1760, 1731, 1110, 1068, 740 cm^{-1}; HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{43}H_{58}O_5SiNa$, 705.3946; found, 705.3947.

Synthesis of compound 55 (**55** was in an equilibrium of C16-ketone and hemiketal). A solution of **54** (30.0 mg, 0.0439 mmol, 1.0 equiv) and DBU (99 μL, 0.660 mmol, 15 equiv) in 2.5 mL toluene was stirred at room temperature for 9 h. The reaction mixture was quenched with sat. aq. NH_4Cl and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 5 : 1 petroleum ether : EtOAc) to furnish compound **55** (17.0 mg, 55%) as a white foam.

55: TLC (petroleum ether : EtOAc, 3 : 1 *V/V*): R_f = 0.46; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.70—7.63 (m, 4H), 7.44—7.33 (m, 6.78H), 7.31—7.28 (m, 0.21H), 5.08 (dt, *J* = 9.5, 1.9 Hz, 0.20H), 4.73 (dt, *J* = 9.3, 1.8 Hz, 0.78H), 4.41 (d, *J* = 4.2 Hz, 0.76H), 3.58 (dd, *J* = 9.4, 5.0 Hz, 0.20H), 3.64—3.53 (m, 0.99H), 3.50 (dd, *J* = 9.4, 3.9 Hz, 0.78H), 2.66 (s, 0.19H), 2.52—2.40 (m, 0.20H), 2.30—2.16 (m, 1.51H), 1.97—1.86 (m, 4.71H), 1.86—1.76 (m, 1.02H), 1.71—1.62 (m, 1.72H), 1.61—1.50 (m, 3.74H), 1.49—1.41 (tt, *J* = 9.2, 4.8 Hz, 2.97H), 1.40—1.30 (m, 1.73H), 1.30—1.23 (m, 2.00H), 1.22—1.13 (m, 2.01H), 1.09 (d, *J* = 7.2 Hz, 2.39H), 1.05 (s, 8.91H), 0.97—0.83 (m, 2.07H), 0.82 (s, 2.36H), 0.79 (s, 0.90H), 0.75 (s, 2.37H), 0.73 (s, 0.84H), 0.71—0.65 (m, 0.85H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 222.8, 174.2, 150.2, 149.8, 135.9, 135.0, 134.93, 134.89, 130.0, 129.6, 129.5, 127.53, 127.51, 117.0, 87.7, 80.6, 79.8, 77.5, 77.2, 76.8, 74.9, 72.7, 71.5, 69.2, 55.4, 54.3, 54.2, 50.7, 44.8, 43.7, 42.8, 41.8, 39.4, 38.9, 38.3, 37.9, 37.0, 36.8, 35.7, 35.6, 34.7, 34.50, 34.47, 32.9, 32.1, 31.7, 28.6, 28.4, 27.1, 20.7, 20.5, 19.2, 17.1, 15.7, 14.1, 13.9, 12.5, 12.4, 10.9, 10.8; IR (KBr) *v*: 3456, 2930, 2856, 1764, 1449, 1111, 1064, 823 cm^{-1}; HRMS (ESI, *m/z*): $[M+Na]^+$ calcd for $C_{43}H_{58}O_5SiNa$, 705.3946; found, 705.3939.

Synthesis of compound 56. To a solution of **55** (64.0 mg, 0.0938 mmol, 1.0 equiv) in 6 mL MeOH was added (±)-CSA (2.18 mg, 0.00938 mmol, 0.1 equiv) at room temperature. After stirred at the same temperature for 2 h, the reaction mixture was quenched with sat. aq. $NaHCO_3$. MeOH was removed under reduced pressure, and the resulting residue was dissolved in H_2O and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2,

20 : 1 petroleum ether : EtOAc) to furnish the ketal intermediate **75** (53.0 mg, 81%) as a white foam.

To a solution of the ketal **75** (53.0 mg, 0.0761 mmol, 1.0 equiv) in 5 mL MeOH was added (±)-CSA (1.77 mg, 0.00761 mmol, 0.1 equiv) at room temperature. After stirred at room temperature for 36 h, the reaction mixture was quenched with sat. aq. $NaHCO_3$. MeOH was removed under reduced pressure and the resulting residue was dissolved in H_2O and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 3 : 1 petroleum ether : EtOAc) to furnish compound **56** (21.0 mg, 60%) as a white solid.

56: mp: 248.9—251.2 °C; TLC (petroleum ether : EtOAc, 3 : 1 *V*/*V*): R_f = 0.25; $[\alpha]_D^{25}$ –103.5 (*c* 1.43, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.29 (t, *J* = 1.6 Hz, 1H), 4.97 (dt, *J* = 9.6, 1.8 Hz, 1H), 3.85 (dd, *J* = 9.6, 8.0 Hz, 1H), 3.58 (tt, *J* = 10.6, 4.8 Hz, 1H), 3.27 (s, 3H), 2.52—2.38 (m, 1H), 2.11—1.98 (m, 1H), 1.93 (t, *J* = 1.7 Hz, 3H), 1.83 (d, *J* = 2.1 Hz, 1H), 1.87—1.75 (m, 1H), 1.71—1.36 (m, 8H), 1.29 (d, *J* = 7.3 Hz, 3H), 1.36—1.22 (m, 6H), 1.19—1.05 (m, 2H), 1.03—0.84 (m, 2H), 0.81 (s, 3H), 0.74 (s, 3H), 0.73—0.62 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 174.4, 150.2, 130.3, 120.4, 87.7, 79.5, 72.3, 71.3, 55.4, 54.4, 50.5, 44.9, 41.6, 38.5, 38.2, 37.0, 35.7, 35.0, 34.2, 33.9, 32.1, 31.6, 28.6, 20.7, 17.4, 13.6, 12.5, 10.9; IR (KBr) *v*: 3515, 3093, 2920, 1727, 1461, 1299, 891, 517 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+Na]^+$ calcd for $C_{28}H_{42}O_5Na$, 481.2924; found, 481.2916.

Synthesis of compound 59. To a solution of **58** (678 mg, 2.57 mmol, 1.5 equiv) in 20 mL dry THF was added *n*-BuLi (1.3 mL, 1.9 M in hexane, 2.40 mmol, 1.4 equiv) at –78 °C. After stirring at –78 °C for 0.5 h, a solution of **53** (1.00 g, 1.71 mmol, 1.0 equiv) in 20 mL dry THF was added and stirring was continued for 1 h at –78 °C and 1 h at room temperature. The reaction mixture was quenched with sat. aq. NH_4Cl and extracted with EtOAc (3×40 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 20 : 1 → 15 : 1 petroleum ether : EtOAc) to furnish compound **59** (910 mg, 77%) as a white foam.

59: TLC (petroleum ether : EtOAc, 5 : 1 *V*/*V*): R_f = 0.75; $[\alpha]_D^{30}$ –36.0 (*c* 1.15, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, *J* = 7.1 Hz, 4H), 7.45—7.33 (m, 6H), 7.17 (d, *J* = 9.6 Hz, 1H), 6.40—6.24 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.65—3.52 (m, 1H), 2.66—2.55 (m, 1H), 2.16 (dd, *J* = 18.3, 7.4 Hz, 1H), 1.98—1.89 (m, 1H), 1.92 (s, 3H), 1.87 (d, *J* = 5.6 Hz, 1H), 1.81—1.58 (m, 3H), 1.58—1.51 (m, 3H), 1.51—1.39 (m, 4H), 1.36—1.24 (m, 7H), 1.22—1.16 (m, 1H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.05 (s, 9H), 0.96—0.85 (m, 2H), 0.82 (s, 3H), 0.74 (s, 3H), 0.71—0.64 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 217.7, 168.7, 147.4, 138.9, 135.9, 134.9, 134.8, 129.5, 127.5, 127.5, 125.2, 124.6, 72.8, 68.6, 60.5, 54.2, 50.8, 44.8, 43.3, 39.0, 38.8, 38.3, 36.8, 35.6, 35.0, 34.3, 32.2, 31.7, 28.5, 27.1, 20.9, 20.7, 19.2, 14.7, 14.5, 12.7, 12.4; IR (KBr) *v*: 2930, 2855, 1737, 1703, 1635, 1107, 753, 702 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+Na]^+$ calcd for $C_{45}H_{62}O_4SiNa$, 717.4310; found, 717.4281.

Synthesis of compound 60. To a solution of **59** (159 mg, 0.229 mmol, 1.0 equiv) in 1.6 mL dry THF was added LHMDS (0.35 mL, 1.3 M in THF, 0.458 mmol, 2.0 equiv) dropwise at –78 °C. After stirring at the same temperature for 1 h, TMSCl (87 μL, 0.687 mmol, 3.0 equiv) was added and stirring was continued for another 0.5 h at –78 °C and 1 h at room temperature. The reaction mixture was quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The resulting silyl enol ether was used directly in the next step without further purification.

To a solution of the silyl enol ether obtained above in 11 mL DMSO and 1 mL CH_2Cl_2 was added $Pd(OAc)_2$ (61.5 mg, 0.275 mmol, 1.2 equiv) at room temperature. After stirred at 60 °C for 1 h, the reaction mixture was cooled to room temperature, diluted with 30 mL EtOAc and washed twice with 10 mL H_2O. The organic layer was washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 25 : 1 → 20 : 1 petroleum ether : EtOAc) to provide compound **60** (98.0 mg, 62%) as a white foam and recovered **59** (22.0 mg, 14%).

60: TLC (petroleum ether : EtOAc, 10 : 1 *V*/*V*): R_f = 0.28; $[\alpha]_D^{25}$ +117.0 (*c* 1.04, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.72—7.58 (m, 4H), 7.46—7.31 (m, 6H), 7.16 (d, *J* = 9.3 Hz, 1H), 6.46—6.14 (m, 2H), 5.69 (s, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.65—3.46 (m, 1H), 2.92—2.73 (m, 1H), 2.43—2.24 (m, 1H), 2.12 (d, *J* = 4.3 Hz, 1H), 2.05—1.97 (m, 1H), 1.91 (s, 3H), 1.86—1.76 (m, 1H), 1.70—1.53 (m, 4H), 1.52—1.38 (m, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.34—1.21 (m, 7H), 1.13 (s, 3H), 1.05 (s, 9H), 0.95—0.84 (m, 1H), 0.87 (s, 3H), 0.83—0.70 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 208.1, 190.6, 168.7, 146.6, 138.7, 135.9, 134.9, 134.8, 129.59, 129.57, 127.59, 127.56, 125.4, 125.2, 124.3, 72.6, 64.6, 60.6, 54.7, 47.6, 44.1, 41.3, 38.2, 37.0, 36.5, 36.3, 36.1, 31.7, 29.7, 28.0, 27.1, 21.5, 21.2, 20.8, 19.3, 14.5, 12.7, 12.3; IR (KBr) *v*: 3070, 2931, 2857, 1699, 1635, 1612, 1233, 1110 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{45}H_{61}O_4Si$, 693.4334; found, 693.4321.

Synthesis of compound 61. A solution of **60** (56.0 mg, 0.0809 mmol, 1.0 equiv) and PTSA (3.3 mg, 0.0162 mmol, 0.2 equiv) in 2.7 mL toluene was stirred at 110 °C for 0.5 h. The reaction mixture was cooled to room temperature, quenched with sat. aq. $NaHCO_3$, and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 25 : 1 petroleum ether : EtOAc) to provide compound **61** (26.0 mg, 46%) as a white foam and recovered **60** (29.0 mg, 52%).

61: TLC (petroleum ether : EtOAc, 6 : 1 *V*/*V*): R_f = 0.61; $[\alpha]_D^{25}$ +125.1 (*c* 0.21, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.71—7.62 (m, 4H), 7.46—7.31 (m, 6H), 7.14 (d, *J* = 10.8 Hz, 1H), 6.28 (dd, *J* = 15.3, 10.7 Hz, 1H), 6.16 (dd, *J* = 15.2, 7.6 Hz, 1H), 5.70 (d, *J* = 1.5 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.66—3.46 (m, 1H), 2.90—2.77 (m, 1H), 2.44—2.30 (m, 1H), 2.19 (d, *J* = 5.5 Hz, 1H), 1.91 (d, *J* = 1.4 Hz, 3H), 1.86—1.77 (m, 1H), 1.63—1.41 (m, 10H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.32—1.25 (m, 4H), 1.22 (s, 3H), 1.20 (d, *J* = 6.8 Hz, 3H), 1.04 (s, 9H), 0.88 (s, 3H), 0.83—0.71 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 208.6, 191.6, 168.7, 147.1, 138.6, 135.9, 134.9, 134.8, 129.61, 129.59, 127.61, 127.59, 125.8, 124.5, 124.0, 72.6, 62.8, 60.6, 55.6, 47.2, 44.2, 38.2, 37.0, 36.7, 36.4, 36.0, 35.6, 31.7, 29.7, 28.0, 27.1, 26.3, 21.0, 19.3, 18.4, 14.5, 12.8, 12.3; IR (KBr) *v*: 3447, 2929, 2856, 1701, 1636, 1611, 797, 703 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{45}H_{61}O_4Si$, 693.4334; found, 693.4340.

Synthesis of compound 63. To a solution of vinyl bromide **62** (15.4 mg, 0.103 mmol, 2.0 equiv) in 0.4 mL dry THF was added *t*-BuLi (1.3 M in pentane, 0.16 mL, 0.206 mmol, 4.0 equiv) dropwise. After the reaction mixture was stirred at –78 °C for 0.5 h, $ZnMe_2$ (1.0 M in toluene, 0.11 mL, 0.108 mmol, 2.1 equiv) was added and stirring was continued for another 0.5 h at –78 °C. A solution of aldehyde **53** (30.0 mg, 0.0514 mmol, 1.0 equiv) in 0.4 mL THF was added and the reaction mixture was stirred at –78 °C for another 1 h before being quenched with 1 mL 2% aq. HCl. The resulting mixture was stirred at room temperature for 0.5 h and quenched with sat. aq. $NaHCO_3$. The aqueous layer was extracted with EtOAc (3×10 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 10 : 1 petroleum ether : EtOAc) to furnish compound **63** (18.9 mg, 61%) as a white foam.

63: TLC (petroleum ether : EtOAc, 3 : 1 *V*/*V*): R_f = 0.55; $[\alpha]_D^{25}$ –63.5 (*c* 0.89, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 9.50 (d, *J* = 7.9 Hz, 1H), 7.72—7.61 (m, 4H), 7.47—7.30 (m, 6H), 7.19 (dd, *J* = 15.7, 7.9 Hz, 1H), 6.06 (dd, *J* = 15.7, 7.9 Hz, 1H), 3.67—3.51 (m, 1H), 2.79—2.61 (m, 1H), 2.20 (dd, *J* = 18.5, 7.4 Hz, 1H), 2.01—1.87 (m,

2H), 1.77 (dd, *J* = 18.5, 13.0 Hz, 1H), 1.69—1.52 (m, 5H), 1.48—1.28 (m, 6H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.24—1.13 (m, 2H), 1.05 (s, 9H), 0.98—0.85 (m, 3H), 0.82 (s, 3H), 0.75 (s, 3H), 0.73—0.65 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 217.4, 194.6, 163.7, 135.9, 135.0, 134.9, 131.4, 129.5, 127.58, 127.56, 72.8, 68.4, 54.2, 50.9, 44.8, 43.3, 38.8, 38.7, 38.3, 36.8, 35.7, 34.6, 34.4, 32.2, 31.7, 28.5, 27.1, 20.7, 19.9, 19.3, 14.3, 12.5; IR (KBr) *v*: 3070, 2931, 2855, 1738, 1670, 1110, 823, 703 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{40}H_{55}O_3Si$, 611.3915; found, 611.3914.

Synthesis of compound 65. To a solution of 18-crown-6 (2.16 g, 8.20 mmol, 5.0 equiv) in 38 mL dry THF was added KHMDS (2.3 mL, 1.0 M in THF, 2.29 mmol, 1.4 equiv) at –78 °C. After stirring at –78 °C for 10 min, a solution of phosphate **64** (822 mg, 2.46 mmol, 1.5 equiv) in 16 mL THF was added and stirring was continued for another 0.5 h at –78 °C. A solution of **63** (1.0 g, 1.64 mmol, 1.0 equiv) in 60 mL THF was added and stirring was continued for another 1 h at –78 °C and 1 h at 0 °C. The reaction mixture was quenched with sat. aq. NH_4Cl and extracted with EtOAc (3×50 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 35 : 1 petroleum ether : EtOAc) to provide compound **65** (970 mg, 83%) as a white foam and isomer **59** (103 mg, 9%).

65: TLC (petroleum ether : EtOAc, 5 : 1 *V*/*V*): R_f = 0.50; $[\alpha]_D^{25}$ –54.5 (*c* 1.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.73—7.63 (m, 4H), 7.46—7.30 (m, 6H), 7.09 (dd, *J* = 15.4, 11.1 Hz, 1H), 6.40 (d, *J* = 11.1 Hz, 1H), 6.22 (dd, *J* = 15.4, 8.1 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.66—3.50 (m, 1H), 2.65—2.51 (m, 1H), 2.15 (dd, *J* = 18.3, 7.4 Hz, 1H), 1.93 (s, 3H), 1.86 (d, *J* = 5.4 Hz, 1H), 1.73 (dd, *J* = 18.2, 13.3 Hz, 1H), 1.67—1.38 (m, 8H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.37—1.22 (m, 4H), 1.17 (d, *J* = 7.1 Hz, 3H), 1.21—1.11 (m, 2H), 1.05 (s, 9H), 0.96—0.83 (m, 2H), 0.81 (s, 3H), 0.74 (s, 3H), 0.77—0.62 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 217.9, 167.9, 146.3, 141.4, 135.9, 135.0, 134.9, 129.5, 127.57, 127.55, 126.4, 124.1, 72.8, 68.9, 60.2, 54.3, 50.9, 44.8, 43.3, 39.1, 38.8, 38.4, 36.8, 35.7, 34.6, 34.3, 32.2, 31.7, 28.5, 27.1, 21.0, 20.8, 20.7, 19.3, 14.7, 14.5, 12.4; IR (KBr) *v*: 3070, 2931, 2856, 1738, 1705, 1110, 822, 756 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{45}H_{63}O_4Si$, 695.4490; found, 695.4489.

Synthesis of compound 66. To a solution of **65** (300 mg, 0.432 mmol, 1.0 equiv) in 3 mL dry THF was added LHMDS (0.66 mL, 1.3 M in THF, 0.864 mmol, 2.0 equiv) dropwise at –78 °C. After stirring at the same temperature for 1 h, TMSCl (0.17 mL, 1.29 mmol, 3.0 equiv) was added and stirring was continued for another 0.5 h at –78 °C and 1 h at room temperature. The reaction mixture was quenched with sat. aq. $NaHCO_3$ and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The resulting silyl enol ether was used directly in the next step without further purification.

To a solution of the silyl enol ether obtained above in 20 mL DMSO and 5 mL CH_2Cl_2 was added $Pd(OAc)_2$ (96.8 mg, 0.432 mmol, 1.0 equiv) at room temperature. After stirred at 60 °C for 1 h, the reaction mixture was cooled to room temperature, diluted with 50 mL EtOAc and washed twice with 20 mL H_2O. The organic layer was washed with brine and dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 26 : 1 petroleum ether : EtOAc) to provide compound **66** (229 mg, 76%) as a white foam.

66: TLC (petroleum ether : EtOAc, 10 : 1 *V*/*V*): R_f = 0.35; $[\alpha]_D^{25}$ +92.2 (*c* 0.71, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.71—7.64 (m, 4H), 7.45—7.32 (m, 6H), 7.10 (dd, *J* = 15.2, 11.2 Hz, 1H), 6.39 (d, *J* = 11.2 Hz, 1H), 6.10 (dd, *J* = 15.3, 8.1 Hz, 1H), 5.67 (d, *J* = 1.6 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.69—3.47 (m, 1H), 2.92—2.71 (m, 1H), 2.35 (t, *J* = 10.4 Hz, 1H), 2.10 (d, *J* = 4.1 Hz, 1H), 2.00 (d, *J* = 12.9 Hz, 1H), 1.92 (s, 3H), 1.86—1.76 (m, 1H), 1.69—1.35 (m, 8H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.33—1.28 (m, 1H), 1.27 (d, *J* = 6.9 Hz, 3H), 1.28—1.24 (m, 2H), 1.12 (s, 3H), 1.04 (s, 9H), 0.95—0.89 (m, 1H), 0.87 (s, 3H), 0.82—0.70 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 208.4, 190.7, 167.9, 145.4, 141.1, 135.9, 134.9, 134.8, 129.61, 129.59, 127.61, 127.59, 127.1, 124.34, 124.28, 72.6, 64.7, 60.2, 54.8, 47.7, 44.1, 41.3, 38.2, 37.0, 36.5, 36.3, 35.8, 31.7, 29.7, 28.0, 27.1, 21.5, 21.4, 20.85, 20.80, 19.3, 14.5, 12.3; IR (KBr) *v*: 3070, 2931, 2857, 1670, 1612, 1111, 824, 703 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{45}H_{61}O_4Si$, 693.4334; found, 693.4331.

Synthesis of compound 67. A solution of **66** (110 mg, 0.159 mmol, 1.0 equiv) and PTSA (30.2 mg, 0.159 mmol, 1.0 equiv) in 5 mL toluene was stirred at 80 °C for 0.5 h. The reaction mixture was cooled to room temperature, quenched with sat. aq. $NaHCO_3$, and extracted with EtOAc (3×10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 22 : 1 petroleum ether : EtOAc) to provide compound **67** (47.0 mg, 43%) as a white foam and recovered **66** (52.0 mg, 47%).

67: TLC (petroleum ether : EtOAc, 6 : 1 *V*/*V*): R_f = 0.55; $[\alpha]_D^{25}$ +109.4 (*c* 1.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.73—7.59 (m, 4H), 7.48—7.32 (m, 6H), 7.07 (dd, *J* = 15.2, 11.3 Hz, 1H), 6.39 (d, *J* = 11.1 Hz, 1H), 6.03 (dd, *J* = 15.3, 7.8 Hz, 1H), 5.69 (s, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.64—3.47 (m, 1H), 2.84—2.72 (m, 1H), 2.37 (t, *J* = 9.3 Hz, 1H), 2.17 (d, *J* = 5.2 Hz, 1H), 1.93 (s, 3H), 1.87—1.74 (m, 2H), 1.67—1.56 (m, 3H), 1.55—1.49 (m, 1H), 1.49—1.40 (m, 4H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.33—1.25 (m, 3H), 1.20 (s, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.05 (s, 9H), 0.93—0.85 (m, 1H), 0.87 (s, 3H), 0.82—0.70 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 209.0, 191.7, 167.9, 146.3, 141.0, 135.9, 134.85, 134.77, 129.59, 129.57, 127.58, 127.56, 126.0, 124.7, 124.0, 72.6, 62.6, 60.3, 55.5, 47.1, 44.2, 38.2, 37.0, 36.7, 36.4, 35.7, 35.1, 31.7, 29.7, 28.0, 27.1, 26.4, 20.9, 20.8, 19.3, 18.1, 14.4, 12.2; IR (KBr) *v*: 3070, 2931, 2857, 1698, 1616, 1111, 823, 703 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{45}H_{61}O_4Si$, 693.4334; found, 693.4330.

Synthesis of compound 68. A solution of AD-mix-α (60.0 mg, 0.0434 mmol, 1.0 equiv), $MeSO_2NH_2$ (4.1 mg, 0.0434 mmol, 1.0 equiv) and $K_2OsO_4{\cdot}2H_2O$ (1.6 mg, 0.00434 mmol, 0.1 equiv) in *t*-BuOH and H_2O (1 mL, 1 : 1, *V*/*V*) was stirred at room temperature for 10 min. **67** (30.0 mg, 0.0434 mmol, 1.0 equiv) was added at 0 °C and stirring was continued for 12 h at the same temperature. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$. The aqueous layer was extracted with EtOAc (3×10 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO_2, 5 : 2 petroleum ether : EtOAc) to furnish compound **68** (12.0 mg, 41%) as a white foam and recovered **67** (10.5 mg, 35%).

68: TLC (petroleum ether : EtOAc, 3 : 2 *V*/*V*): R_f = 0.48; $[\alpha]_D^{25}$ +72.6 (*c* 0.93, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.75—7.60 (m, 4H), 7.47—7.29 (m, 6H), 7.16—7.04 (m, 1H), 5.74 (d, *J* = 1.6 Hz, 1H), 5.00—4.94 (m, 1H), 4.54 (d, *J* = 5.2 Hz, 1H), 4.01—3.91 (m, 1H), 3.62—3.50 (m, 1H), 2.76 (s, 1H), 2.47—2.34 (m, 1H), 2.18—2.05 (m, 1H), 1.93 (s, 3H), 1.87—1.79 (m, 1H), 1.70—1.59 (m, 4H), 1.52—1.41 (m, 5H), 1.32—1.25 (m, 4H), 1.21 (s, 3H), 1.04 (s, 9H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 3H), 0.82—0.73 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 211.6, 195.5, 174.4, 147.2, 135.9, 134.84, 134.76, 130.8, 129.6, 127.60, 127.58, 123.8, 83.0, 74.5, 72.5, 57.7, 55.4, 46.6, 44.1, 38.1, 37.2, 37.0, 36.4, 34.1, 33.2, 31.7, 29.7, 27.9, 27.1, 26.4, 20.9, 19.2, 16.2, 12.3, 11.0; IR (KBr) *v*: 3400, 2930, 2857, 1761, 1684, 1607, 740, 703 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{43}H_{57}O_5Si$, 681.3970; found, 681.3967.

Synthesis of compound 69. To a solution of **68** (24.0 mg, 0.0347 mmol, 1.0 equiv) in 2.5 mL CH_3CN was added 40% aq. HF (36 μL, 0.694 mmol, 20.0 equiv) at room temperature. After stirred at room temperature for 2 h, the reaction mixture was quenched with sat. aq. $NaHCO_3$ and extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were washed with brine and

dried over Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by flash chromatography (SiO_2, 2 : 1 petroleum ether : EtOAc) to provide compound **69** (15.0 mg, 97%) as a white solid.

69: mp: 241.3—242.5 °C; TLC (EtOAc, *V*/*V*): R_f = 0.46; $[\alpha]_D^{25}$ +100.2 (*c* 0.77, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.12 (s, 1H), 5.79 (s, 1H), 4.99 (brs, 1H), 4.53 (d, *J* = 5.3 Hz, 1H), 3.98 (q, *J* = 3.8 Hz, 1H), 3.67—3.54 (m, 1H), 2.80 (s, 1H), 2.47 (t, *J* = 10.8 Hz, 1H), 2.22—2.11 (m, 1H), 1.98—1.89 (m, 1H), 1.94 (s, 3H), 1.88—1.70 (m, 4H), 1.69—1.53 (m, 4H), 1.47—1.31 (m, 5H), 1.24 (s, 3H), 1.19—1.09 (m, 1H), 1.03 (dd, *J* = 13.2, 3.6 Hz, 1H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.95—0.87 (m, 1H), 0.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 211.5, 195.2, 174.4, 147.2, 130.8, 123.9, 83.0, 74.5, 71.0, 57.7, 55.5, 46.6, 44.2, 37.9, 37.2, 37.0, 36.5, 34.2, 33.3, 31.4, 29.7, 27.9, 26.4, 21.0, 16.3, 12.3, 11.0; IR (KBr) *v*: 3407, 2926, 2857, 1750, 1669, 1604, 1077, 736 cm^{-1}; HRMS (ESI, *m*/*z*): $[M+H]^+$ calcd for $C_{27}H_{39}O_5$, 443.2792; found, 443.2789.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.202000293.

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