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A ketal-tethered RCM strategy toward the synthesis of spiroketal related natural products

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Abstract—An unconventional approach to construct spiroketals and spiroaminals via ring-closing metathesis [RCM] of cyclic ketals and aminals, respectively, is described here. This method possesses a good generality with no loss of stereochemical integrity at the spirocenter under the standard RCM conditions. This approach has been applied to the synthesis of an insect pheromone to demonstrate its synthetic potential, and also to the synthesis of the C11-*epi*-C22-C23 fragment in spirastrellolide A. Both are proof-of-concept applications to feature a ketal-tethered RCM as an alternative strategy for construction of spiroketals.

1. Introduction

Ring-closing metathesis [RCM] represents an important strategy in natural product synthesis.[1,2] It has come to our attention that despite being well known entities, acetals or ketals have not been extensively utilized as tethers, whether 'temporary' or 'permanent', in RCMs. A survey of the literature reveals that most RCM reactions involving acetal or ketal functionalities can be divided into four types with overlaps in concept. As shown in Figure 1, type **a** [see **1**] is the most common with both olefins connected through the ketal carbon C2. However, in these cases, the ketal is used primarily as a carbonyl-protecting group and not as a tether,[1,2] and likewise, the ketal in type **b** [see **2**], another common scenario, is to primarily protect diols. Types **c** [**3**] and **d** [**4**] would best represent an acetal or ketal serving as a tether in RCM, but they are much less common. Some elegant examples of type **c** would be those reported by Burke,[3] and Grubbs and Scholl[4] in constructing bridged ketals via RCM, and by Rutjes[5] in syntheses of pyrans and piperidines via either acetal- or aminal-tethered RCMs.

It was surprising to find that there were even fewer examples of type **d** [**4**] ketal-tethered RCM besides van Boom's precedent-setting work employing more robust carbohydrate-based cyclic ketals[6] and Harrity's beautiful RO-RCM study that led to syntheses of spiroketals.[7] Type **d** ketal-tethered RCM using **4**, or in fact reactions in general, would represent a conceptually different synthesis of spiroketals or spiroaminals **5**, although spiroketals have been conventionally constructed through conventional internal ketalizations of

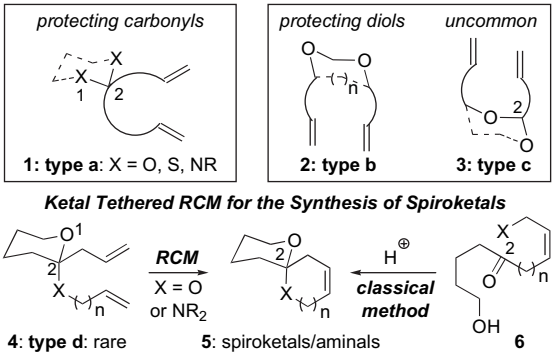

Figure 1.

ketones [**6**→**5** in Fig. 1] under acidic conditions or variations of that principle concept.[8]

Given the significance of spiroketals in natural products, we explored the type **d** RCM as part of an ongoing program in developing ketal-tethered synthetic strategies toward natural product syntheses.[9–12] Specifically, we became interested in spirastrellolide A, a novel spiroketal-rich macrolide from marine sponge *Spirastrellolide coccinea* reported by Roberge et. al.,[13a] and recently, its structure was revised as shown in Figure 2.[13b] In addition to its ability to cause untimely mitotic arrest in cells, spirastrellolide A was shown to exhibit potent inhibitory activity against protein phosphatase 2A [IC_{50}=1 nM] with an excellent selectivity for PP2A over PP1 [ratio of IC_{50} values=1:50].[13,14] The C11-C23 fragment in spirastrellolide A became an ideal proof-of-concept application to feature a ketal-tethered RCM as an alternative strategy for construction of spiroketals. We report

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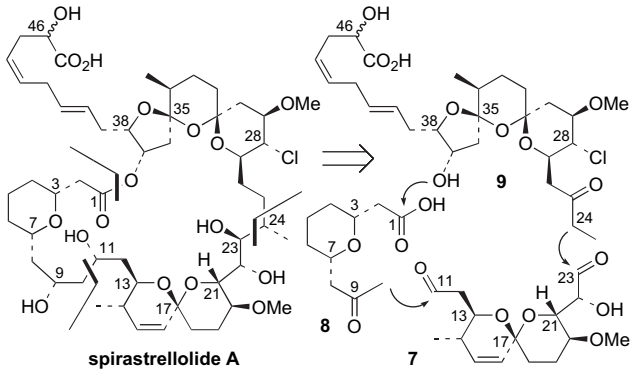


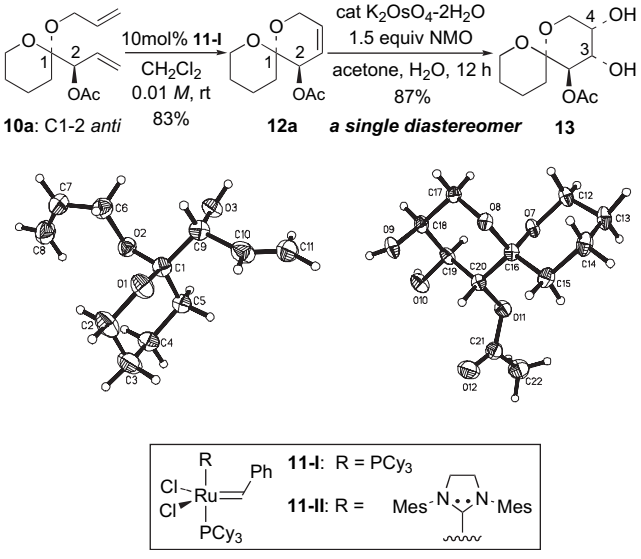
Figure 2.

here details of ketal- and aminal-tethered RCM in the synthesis of spiroketals and spiroaminals, respectively, in addition to the synthesis of the C11-*epi*-C22-C23 fragment of spirastrellolide A.

2. Results and discussions

2.1. Feasibility: RCM of 1,2-*anti*- and 1,2-*syn*-ketals

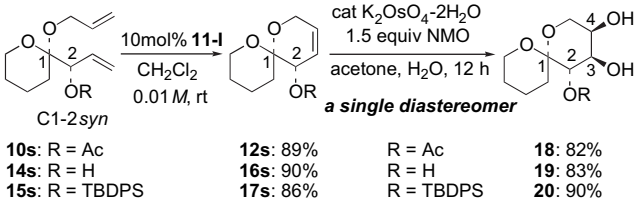
To demonstrate the feasibility of this concept, we first employed cyclic 1,2-*anti*-ketal **10a**, which was readily prepared from dihydropyran.[9] The notation '**a**' represents the *anti* [or trans] relative stereochemical relationship between the C1-*O*-allyl and C2-OAc groups. The relative stereochemistry of **10a** was unambiguously assigned using its X-ray structural analysis [Scheme 1] because we were interested in the stereointegrity of the C1 spirocenter under RCM conditions. The subsequent RCM of **10a** was carried out at rt employing the Grubbs' generation-I Ru-catalyst[1,2] [**11-I**] in CH_2Cl_2 and led to the desired C1,2-*anti* spiroketal **12a** in 83% yield, although generation-II Ru-catalyst [**11-II**][15–18] could also be employed with comparable efficiency.



Scheme 1.

We could quickly demonstrate that it was feasible to functionalize the C3-4 olefin in a highly stereoselective manner. Dihydroxylation of **12a** using K_2OsO_4 and NMO led to diol **13** in 87% yield as a single diastereomer [Scheme 1]. The relative stereochemistry of diol **13** was assigned also using X-ray structural analysis. This study suggests the possibility of building up stereochemical complexity of the spiroketal ring system using **12a** as a chiral template. It is also noteworthy that the assignment of **13** implies there was no erosion of stereochemical integrity at the C1 spirocenter during the RCM.

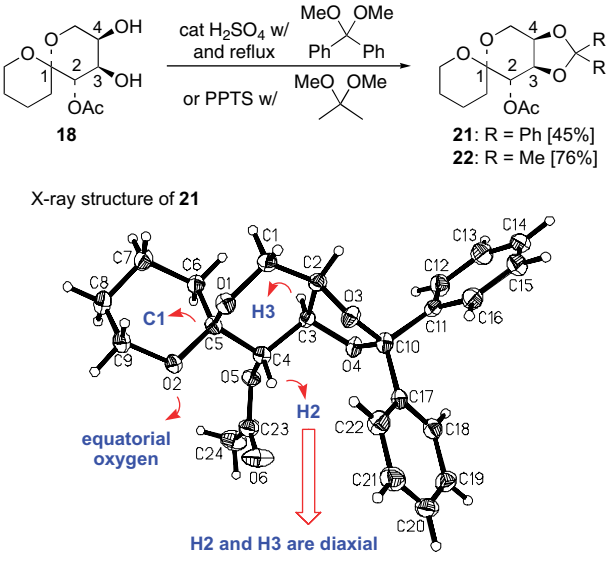
Subsequently, when we used cyclic 1,2-*syn*-ketals such as **10s**, **14s**, and **15s**, we were able to also establish the feasibility of their respective RCM without encountering any unexpected problems to afford C1,2-*syn* spiroketals **12s**, **16s**, and **17s**, respectively, in high yields [Scheme 2]. Likewise, the ensuing dihydroxylations of these *syn* spiroketals were also highly diastereoselective, leading to diols **18**–**20**, respectively, in good yields. However, this was where we observed an interesting case of equatorial or kinetic spiroketal.



Scheme 2.

2.2. A solid-state kinetic *syn* spiroketal

To confirm the relative stereochemistry of these dihydroxylated C1,2-*syn* spiroketals, and that there was no erosion of stereochemical integrity at the C1 spirocenter during the RCM, diphenyl methylidene and *iso*-propylidene acetals, **21** and **22**, respectively, were prepared from **18** using standard protection conditions [Scheme 3]. Acetal **21** was found to be quite crystalline, and an X-ray structure was obtained as shown in Scheme 3.



Scheme 3.

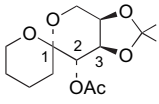
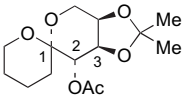
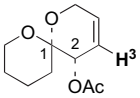
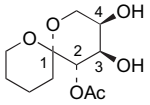
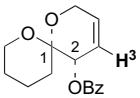
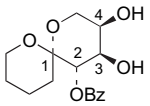
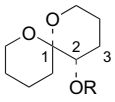
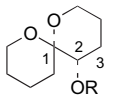
The X-ray structure of acetal **21** revealed that the oxygen atom O2 [the X-ray designation] is equatorial to the pyran ring bearing the acetal motif, whereas the oxygen atom O1 is still axial with respect to the original pyran ring. This effectively establishes acetal **21** as an equatorial spiroketal or one of those rare kinetic spiroketals.[8,19] At least, it represents one that is trapped in the solid state. We recognized that if ketal **21** is also a kinetic spiroketal in solution then coupling constants of H2 and H3 [see arrow indications in Scheme 3] should be large, as they should be for diaxial. This led us to reexamine a range of C1,2-*syn* spiroketal derivatives obtained from cyclic 1,2-*syn*-ketals.

As shown in Table 1, unfortunately, among all C1,2-*syn* spiroketals, only **22** containing the *iso*-propylidene acetal motif gave a *J* value of 5.0 Hz in $CDCl_3$ for protons H2 and H3. This value indicates that protons H2 and H3 in **22** definitely do not exist as diaxial—at least not predominately—in solution. However, it does suggest that **22** could still exist as a conformational mixture in solution that would contain the kinetic spiroketal [Fig. 3]. The *J* value for H2 and H3 in acetal **21** is even lower, thereby implying that the kinetic spiroketal observed in the X-ray structure is solely a solid-state phenomenon.

With the remaining coupling constants being equally small for *syn* spiroketals **18**, **24**, **25s**, and **26s**, it indicates that they too most likely adopt an anomerically favored conformation in which H2 and H3 are also not diaxial. In the case of **12s** and **23s**, the coupling constants are also around 5–5.5 Hz, but this is likely due to H3 being a vinyl proton, and the dihedral angle of H2–H3 in these cases does not really reflect that of axial or equatorial.

Finally, we could further confirm that these C1,2-*syn* spiroketals derived from cyclic 1,2-*syn*-ketals do not likely exist as kinetic spiroketals in solution, as they do not possess less stability than those of C-1,2-*anti* spiroketals. As shown in Scheme 4, under a range of different acidic conditions, pure **27a** or **27s** could be equilibrated to a mixture of **27a** and **27s** with a ratio of 1:1.

Table 1. Proton coupling constants for H2–H3

	$J_{2\text{-}3}$		$J_{2\text{-}3}$
 **21**	d, 3.5 Hz	 **22**	d, 5.0 Hz
 **12s**	d, 5.5 Hz	 **18**	d, 3.0 Hz
 **23s**	d, 5.0 Hz	 **24**	d, 3.0 Hz
 **25s**	t, 3.0 Hz R = *p*-Br-PhCO	 **26s**	t, 3.0 Hz R = *p*-O_2N-PhCO

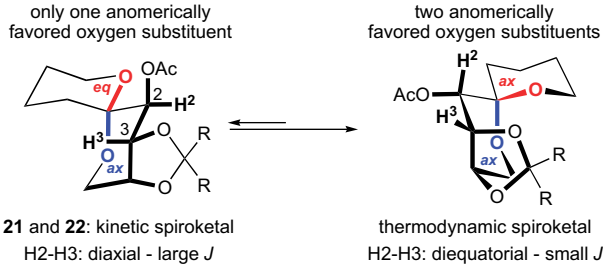
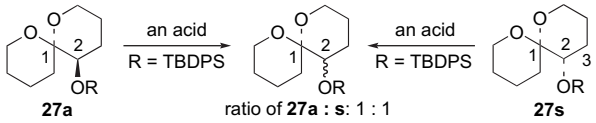


Figure 3.



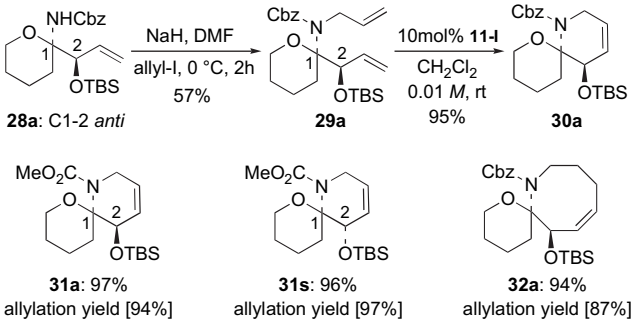
Conditions:
a) 1.1 equiv of PPTS, MeOH, rt to reflux. **b)** 1.1 equiv of *p*-TsOH, CH_2Cl_2, rt to reflux. **c)** TMSCl in MeOH, rt. **d)** TFA, benzene, rt.

Scheme 4.

2.3. Synthesis of spiroaminals

Very much unlike spiroketals, spiroaminals are far from being a prevalent structural motif among natural products.[20] Thus, it is not clear for future applications of constructing spiroaminals through a ketal-tethered RCM strategy. However, we demonstrated that it could be accomplished with comparable efficiency.

As shown in Scheme 5, the RCM precursor **29a** could be attained via allylation of the anomeric amide nitrogen atom in 1,2-*anti* cyclic aminal **28a**. RCM of **29a** employing 10 mol % **11-I** led to *anti* spiroaminal **30a** in 83% yield. Finally, both C1,2-*anti* spiroaminal **31a** and C1,2-*syn* spiroaminal **31s** could be attained through RCM of their respective cyclic *anti* and *syn* aminal precursors in a stereospecific manner. We also demonstrated here an example of eight-membered ring spiroaminal **32a**.

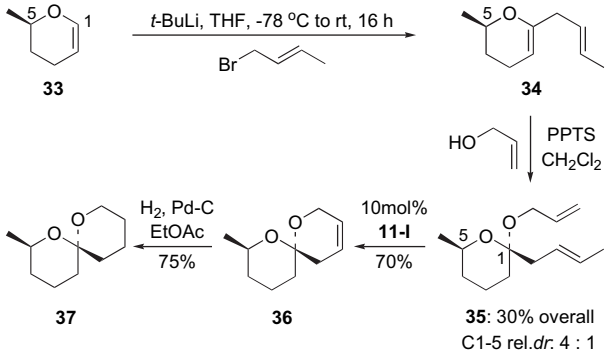


Scheme 5.

2.4. Applications in natural product synthesis

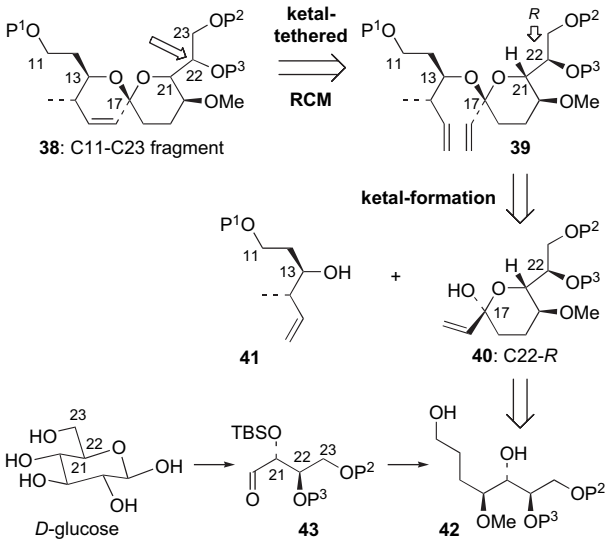
2.4.1. Synthesis of a simple insect pheromone. The ketal-tethered RCM method can be quickly applicable to a short total synthesis of an insect pheromone.[21] As shown in Scheme 6, cyclic ketal **35** could be prepared from dihydropyran **33** in 30% overall yield via addition of its 2-lithiated intermediate to crotyl bromide[22] followed by the ketal

formation using allyl alcohol and PPTS. There is a modest diastereoselective induction from the C5 methyl group with an isomeric ratio being 4:1 in favor of the addition of allyl alcohol to the oxocarbenium intermediate from the anomerically favored axial trajectory.[23–25] The ensuing RCM using the Grubbs' generation-I Ru-catalyst **11-I** led to spiroketal **36** in 70% yield, and subsequent hydrogenation provided the bee pheromone **37**.[21,26]



Scheme 6.

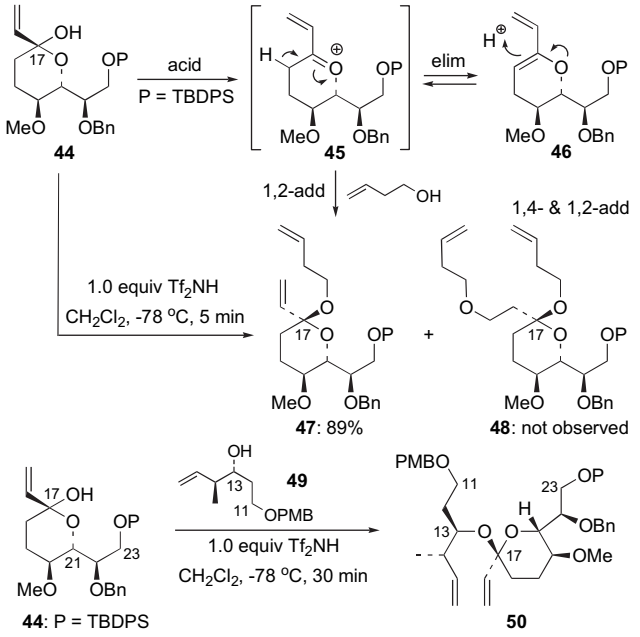
2.4.2. The C11-C23 fragment of spirastrellolide A. A more complex application would involve spirastrellolide A[27,28] and specifically the synthesis of the C11-C23 fragment. Retrosynthetically, the synthesis of the C11-C23 fragment [**38**] would feature the ketal-tethered RCM strategy employing cyclic ketal **39** [Scheme 7]. The relative stereochemistry at C22 [see the arrow] was not unassigned at the time we began our efforts,[13a] and we continued our efforts to focus on establishing the feasibility of the ketal-tethered RCM approach even after we had the knowledge that we had elected the wrong one epimerically.[13b]



Scheme 7.

Cyclic ketal **39** can be envisioned from an acid promoted ketal formation from lactol **40** and the known alcohol **41**.[29] Lactol **40** can be prepared from aldehyde **43** in which the stereocenters at C21 and C22-*R* could be borrowed from D-glucose.[30] These early stages of preparative chemistry have been communicated,[11] and thus, we will focus here on the key RCM chemistry.

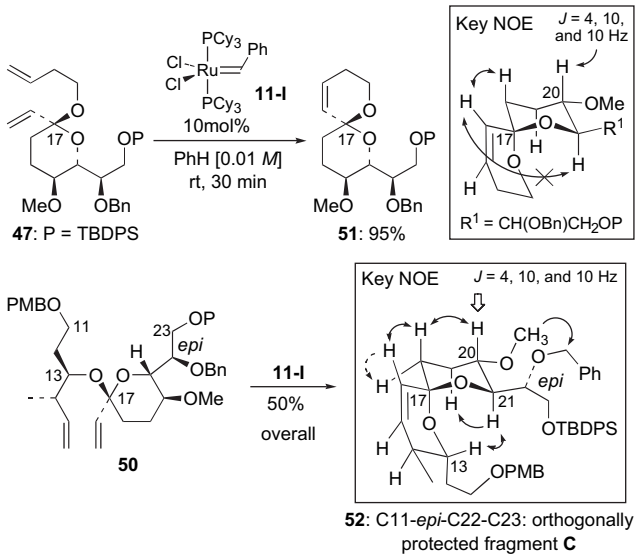
Despite having protocols that are known for the ketal formation using simple pyranyl systems[8–11,22,25] and also those reported by van Boom for more robust carbohydrate-based systems,[6a,b] the cyclic ketal formation using lactol **44** with an anomeric vinyl group at C17 proved to be difficult. The major problem involved is the competing pathways between the elimination of oxacarbenium ion **45** to give diene **46**, which surprisingly in our hand represents a dead end, and 1,2-addition of 3-buten-1-ol gave the desired ketal **47** [as shown in Scheme 8]. In addition, we faced 1,4- and 1,2-additions, which was another dead end in ketal **48**.



Scheme 8.

A range of acids as well as solvents and temperatures were screened,[11] and fortuitously, while most frequently used Lewis acids and Brønsted acids in anomeric substitution[22] led to the over addition product **48**, Tf_2NH[31] [entry 5] proved to be an excellent Brønsted acid at −78 °C, leading to **47** as the sole product in 89% yield as a single diastereomer with the oxo-butenyl group at C17 being axial. Consequently, by using the known chiral alcohol **49**,[29] cyclic ketal **50** was obtained from **44** also as a single isomer under the same Tf_2NH conditions. On occasions, we still found diene **46** presumably because alcohol **49** is more sterically demanding than the model system.

The ensuing RCM of **47** gave spiroketal **51** in 95% yield using Grubbs' generation-I Ru-catalyst **11-I**[1] [Scheme 9]. Selected NOE experiments of **51** revealed that the C17 spirocenter possesses the desired relative stereochemistry. A successful RCM employing **50** was achieved to give spiroketal **52** in 50% overall yield.



Scheme 9.

It is noteworthy that comprehensive NOE experiments in $CDCl_3$ and C_6D_6 confirmed the key relative stereochemistry in spiroketal **52** [see the box in Scheme 9; the dashed arrow implies relatively a weaker NOE]. Despite being *epi* at the C22 stereocenter relative to the natural product, most proton chemical shifts in C_6D_6 [i.e., protons from C13 to C21] along with their respective couplings constants are quite similar to those reported for the methyl ester of spirastrellolide A.[13] More importantly, the key NOE enhancements observed for **52** closely matched those reported for the same region in spirastrellolide A.[13]

3. Conclusion

We have described here a ketal- and aminal-tethered RCM strategy that conceptually represents a very different or an unconventional approach toward the synthesis of spiroketals and spiroaminals. The ketal-tethered strategy was applied successfully to the synthesis of simple insect pheromone and the C11-*epi*-C22-C23 fragment of spirastrellolide A.

4. Experimental

4.1. General

All reactions were performed in flame-dried glassware under nitrogen atmosphere. Solvents were distilled prior to use. Reagents were used as purchased (Aldrich, Acros), except where noted. Chromatographic separation was performed using Bodman 60 Å SiO_2. ^1H and ^{13}C NMR spectra were obtained on Varian VI-300, VXR-300, and VI-500 spectrometers using $CDCl_3$ (except where noted) with TMS or residual solvent as standard. Melting points were determined using a Laboratory Devices MEL-TEMP and are uncorrected/calibrated. Infrared spectra were obtained using NaCl plates on a Midac M2000 FTIR. TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and vanillin or $KMnO_4$ stains. Low-resolution mass spectra were obtained using an Agilent 1100 series LS/MSD and are APCI. High-resolution mass spectral analyses were performed at University of Minnesota, Department of Chemistry, Mass Spectrometry Laboratory. X-ray analyses were performed at University of Minnesota, Department of Chemistry, X-ray facility. All spectral data obtained for new compounds are reported here.

4.2. Spiroketal syntheses

4.2.1. General procedure for the preparation of the cyclic ketal RCM precursor. To a mixture of acetic acid 1-(5,6-dihydro-4*H*-pyran-2-yl)-allyl ester [1.35 g, 7.45 mmol] and allyl alcohol [1.30 g, 22.3 mmol, 3 equiv] in anhyd CH_2Cl_2 [100 mL] at rt was added pyridinium *p*-toluene sulfonate [187.0 mg, 0.074 mmol, 10 mol %]. The reaction mixture was stirred at rt for 12 h. The solvent was removed in vacuo and the crude product was purified using silica gel flash column chromatography [gradient eluent: 5–10% EtOAc in hexanes] to afford cyclic ketals **10a** and **10s** [combined mass and yield: 1.29 g, 72%] with a 1.6:1 diastereomeric ratio. Isomers **10a** and **10s** can be cleanly separated via a second and more careful flash column chromatography.

4.2.2. Cyclic ketal 10a. R_f=0.50 [20% EtOAc in hexanes]; ^1H NMR (500 MHz, $CDCl_3$) δ 1.42–1.56 (m, 4H), 1.67–1.81 (m, 2H), 2.05 (s, 3H), 3.54–3.63 (m, 2H), 3.92 (dq, *J*=1.5, 1.5, 5.5, 13.5 Hz, 1H), 4.01 (dddd, *J*=1.5, 1.5, 5.5, 13.5 Hz, 1H), 5.07 (dq, *J*=1.5, 10 Hz, 1H), 5.15 (dt, *J*=1.5, 9.0 Hz, 1H), 5.17 (m, 1H), 5.26 (dq, *J*=1.5, 17.5 Hz, 1H), 5.41 (dt, *J*=1.5, 5.0 Hz, 1H), 5.82–5.89 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.1, 20.9, 24.9, 28.3, 61.0, 61.6, 73.4, 98.5, 115.7, 116.5, 133.2, 134.8, 169.5; IR (Neat) cm^{-1} 3091w, 2945s, 2875m, 1748s, 1371m, 1238s; mass spectrum (APCI): *m/e* (% relative intensity) 183 (24) [M−*O*-allyl]$^+$, 123 (100).

4.2.3. Cyclic ketal 10s. R_f=0.43 [20% EtOAc in hexanes]; ^1H NMR (500 MHz, $CDCl_3$) δ 1.46–1.70 (m, 5H), 1.73–1.84 (m, 1H), 2.10 (s, 3H), 3.61 (dddd, *J*=3.0, 11.0, 11.0, 11.0 Hz, 1H), 3.65–3.68 (m, 1H), 4.00 (dddd, *J*=1.5, 1.5, 5.0, 13.0 Hz, 1H), 4.17 (dddd, *J*=1.5, 1.5, 5.0, 13.0 Hz, 1H), 5.14 (dq, *J*=1.5, 10.5 Hz, 1H), 5.22 (dq, *J*=1.5, 10.5 Hz, 1H), 5.25 (dq, *J*=1.5, 17.5 Hz, 1H), 5.32 (dq, *J*=1.5, 17.5 Hz, 1H), 5.47 (dt, *J*=1.5, 5.0 Hz, 1H), 5.86 (ddd, *J*=5.5, 10.5, 17.0 Hz, 1H), 5.91 (dddd, *J*=5.5, 5.5, 15.5, 15.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.2, 21.2, 24.8, 28.0, 61.2, 62.0, 74.5, 98.7, 115.9, 117.6, 131.9, 134.8, 169.8; IR (Neat) cm^{-1} 2944s, 2873m, 1748s, 1371m, 1236s; mass spectrum (APCI): *m/e* (% relative intensity) 183 (24) [M−*O*-allyl]$^+$, 123 (100).

4.2.4. General procedure for the ring-closing metathesis of cyclic ketal 10s. To a solution of Grubbs' generation-I Ru-catalyst [16.4 mg, 0.02 mmol, 10 mol %] in anhyd benzene [30 mL] at rt was added a solution of **10s** [48.0 mg, 0.20 mmol] in benzene [10 mL] via syringe. The resulting reaction mixture was stirred at rt for 0.5 h before it was concentrated in vacuo and purified using silica gel flash column chromatography [isocratic eluent: 15% EtOAc in hexanes] to give **12s** [38.0 mg, 89%] as colorless oil.

4.2.5. Spiroketal 12a. Yield: 83%; R_f=0.31 [30% EtOAc in hexanes]; ^1H NMR (500 MHz, $CDCl_3$) δ 1.48–1.67 (m, 5H),

1.80–1.85 (m, 1H), 2.11 (s, 3H), 3.71 (ddd, J=2.0, 11.0, 11.0 Hz, 1H), 3.77–3.80 (m, 1H), 4.03 (dq, J=2.5, 16.5 Hz, 1H), 4.09–4.14 (m, 1H), 5.17–5.19 (m, 1H), 5.48 (dq, J=1.5, 10.0 Hz, 1H), 5.87 (dq, J=2.0, 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.2, 21.2, 24.7, 30.9, 60.2, 62.4, 70.4, 94.1, 121.9, 128.1, 170.8; IR (Neat) cm^{-1} 2941m, 2883w, 1735s, 1371m, 1240s; mass spectrum (APCI): *m/e* (% relative intensity) 153 (100) $[M-OAc]^+$, 135 (24), 125 (8); ESIHRMS *m/e* calcd for $C_{11}H_{16}NNaO_4$: 235.0946, found: 235.0942.

4.2.6. Spiroketal 12s. Yield: 89%; R_f=0.40 [20% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35–1.41 (m, 1H), 1.48–1.64 (m, 3H), 1.77–1.87 (m, 2H), 2.04 (s, 3H), 3.66 (ddd, J=3.0, 11.0, 11.0 Hz, 1H), 3.72–3.76 (m, 1H), 4.15 (d, J=2.0 Hz, 2H), 4.86 (d, J=5.5 Hz, 1H), 5.78–5.82 (m, 1H), 6.04 (dt, J=2.5, 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.1, 21.0, 24.8, 30.3, 60.1, 62.8, 67.7, 95.4, 120.5, 130.8, 170.2; IR (Neat) cm^{-1} 2942s, 2851m, 1743s, 1371m, 1240s; mass spectrum (APCI): *m/e* (% relative intensity) 153 (100) $[M-OAc]^+$, 135 (22), 125 (8); ESIHRMS *m/e* calcd for $C_{11}H_{16}O_4Na$: 235.0946, found: 235.0946.

4.2.7. Synthesis of diol 13. To a solution of **12a** [39.0 mg, 0.18 mmol] in acetone/water [9:1, 10 mL] was added *N*-methyl morpholine *N*-oxide [32.5 mg, 0.27 mmol, 1.5 equiv] and cat $K_2OsO_4\cdot 2H_2O$ [~5.0 mg] at rt. The reaction mixture was stirred at rt for 12 h and concentrated in vacuo. The crude product was purified by silica gel flash column chromatography [isocratic eluent: EtOAc] to afford diol **13** [35.0 mg, 87%] as a crystalline solid. R_f=0.42 [EtOAc]; mp 150–160 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51–1.60 (m, 5H), 1.60–1.85 (m, 1H), 2.19 (s, 3H), 2.92 (br s, 2H), 3.64 (ddd, J=2.5, 12.0, 12.0 Hz, 2H), 3.77 (s, 2H), 3.94–3.99 (m, 2H), 4.93 (d, J=10.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.9, 21.2, 24.5, 30.2, 61.4, 62.4, 68.9, 69.9, 74.5, 97.6, 172.2; IR (Neat) cm^{-1} 3456s, 2942s, 2874m, 1734s, 1223s; mass spectrum (APCI): *m/e* (% relative intensity) 247 (13) $(M+H)^+$, 211 (19), 187 (66), 169 (72), 157 (24), 151 (100), 139 (93), 127 (65); ESIHRMS *m/e* calcd for $C_{11}H_{18}O_6Na$: 269.1001, found: 269.0999.

4.2.8. Cyclic ketal 14s. Yield: 90%; R_f=0.46 [20% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.45–1.80 (m, 6H), 2.42 (br s, OH), 3.66–3.71 (m, 2H), 4.01–4.02 (m, 1H), 4.12–4.13 (m, 1H), 4.24–4.25 (m, 1H), 5.14–5.16 (m, 2H), 5.37 (ddd, J=1.5, 17.5, 19.0 Hz, 2H), 5.82–6.00 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.2, 24.9, 26.9, 61.1, 62.2, 73.0, 99.8, 115.9, 116.6, 134.2, 134.9; IR (Neat) cm^{-1} 3487s, 2945s, 2873s; mass spectrum (APCI): *m/e* (% relative intensity) 152 (30), 141 (100).

4.2.9. Cyclic ketal 15s. Yield: 70%; R_f=0.52 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (s, 9H), 1.40–1.60 (m, 4H), 1.73–1.87 (m, 1H), 2.01 (ddd, J=4.5, 13.0, 13.0 Hz, 1H), 3.48–3.54 (m, 2H), 3.65 (dddd, J=1.5, 1.5, 3.0, 12.5 Hz, 1H), 3.90 (dddd, J=1.5, 1.5, 3.5, 13.0 Hz, 1H), 4.24 (d, J=6.5 Hz, 1H), 5.01–5.05 (m, 3H), 5.16–5.21 (m, 1H), 5.76–5.86 (m, 2H), 7.31–7.40 (m, 6H), 7.66–7.75 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.4, 19.6, 24.9, 26.8, 27.3, 60.4, 61.5, 76.0, 100.1, 115.6, 116.9, 127.0, 127.2, 129.3, 134.1, 134.4, 135.2, 135.9, 136.2, 136.4; IR (Neat) cm^{-1} 2942s, 2858s, 1428m; mass spectrum (ESI): *m/e* 459.3 $(M+Na)^+$; ESIHRMS *m/e* calcd for $C_{27}H_{36}O_3SiNa$: 459.2331, found: 459.2338.

4.2.10. Spiroketal 16s. Yield: 90%; R_f=0.22 [30% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49–1.65 (m, 3H), 1.66–1.72 (m, 1H), 1.72–1.85 (m, 1H), 2.00–2.04 (m, 1H), 2.12–2.18 (m, 1H), 3.55 (d, J=8.0 Hz, 1H), 3.69 (ddd, J=3.0, 6.5, 6.5 Hz, 1H), 3.75–3.79 (m, 1H), 4.13 (ddd, J=1.5, 17.0, 17.0 Hz, 2H), 5.90–5.95 (m, 1H), ^{13}C NMR (125 Hz, $CDCl_3$) δ 18.2, 24.8, 30.2, 60.1, 62.9, 66.8, 96.9, 124.5, 128.0; IR (Neat) cm^{-1} 3438s, 2940s, 2869m, 1083s; mass spectrum (ESI): *m/e* 431.3 $(M+Na)^+$; ESIHRMS *m/e* calcd for $C_9H_{14}O_3Na$: 193.0841, found: 193.0839.

4.2.11. Spiroketal 17s. Yield: 86%; R_f=0.46 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (s, 9H), 1.55–1.63 (m, 3H), 1.70–1.77 (m, 1H), 1.91 (dddd, J=3.5, 3.5, 8.0, 25.5 Hz, 1H), 2.24–2.30 (m, 1H), 3.73 (dd, J=2.5, 9.0 Hz, 2H), 3.85 (d, J=5.0 Hz, 1H), 4.13–4.15 (m, 2H), 5.38 (dddd, J=2.5, 2.5, 5.0, 5.0 Hz, 1H), 5.72 (dt, J=2.5, 10.0 Hz, 1H), 7.38–7.45 (m, 6H), 7.76–7.79 (m, 4H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 18.7, 19.6, 25.2, 27.0, 31.0, 60.4, 62.8, 68.7, 97.3, 124.5, 127.3, 127.8, 128.1, 129.4, 129.8, 133.8, 134.5, 135.8, 136.1; IR (Neat) cm^{-1} 2934s, 2857m, 1428m, 1094s; mass spectrum (ESI): *m/e* 431.3 $(M+Na)^+$; ESIHRMS *m/e* calcd for $C_{25}H_{32}O_3SiNa$: 431.2018, found: 431.2019.

4.2.12. Diol 18. Yield: 82%; R_f=0.57 [EtOAc]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (ddd, J=4.5, 13.0, 13.0 Hz, 1H), 1.42–1.75 (m, 5H), 2.05 (s, 3H), 2.62 (d, J=10.5 Hz, OH), 3.47 (t, J=11.5 Hz, 1H), 3.64–3.68 (m, 3H), 3.74–3.80 (m, 2H), 4.92 (d, J=3.0 Hz, 1H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 17.5, 20.7, 24.4, 30.2, 59.0, 61.2, 63.4, 69.0, 71.7, 96.9, 169.4; IR (Neat) cm^{-1} 3454s, 2945s, 2888m, 1739s; mass spectrum (ESI): *m/e* 269.2 $(M+Na)^+$; ESIHRMS *m/e* calcd for $C_{11}H_{18}O_6Na$: 269.1001, found: 269.0997.

4.2.13. Diol 19. Yield: 83%; R_f=0.37 [4% MeOH in EtOAc]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47–1.67 (m, 4H), 1.69–1.79 (m, 1H), 1.86–1.89 (m, 1H), 2.94 (br s, 3H), 3.53 (dd, J=10.0, 11.5 Hz, 1H), 3.66–3.77 (m, 3H), 3.86–3.90 (m, 1H), 3.92–4.00 (m, 2H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 17.7, 24.7, 29.5, 59.8, 61.4, 63.5, 71.5, 72.0, 98.3; IR (Neat) cm^{-1} 3423s, 2943m; mass spectrum (ESI): *m/e* 227.3 $(M+Na)^+$; ESIHRMS *m/e* calcd for $C_9H_{16}O_5Na$: 227.0895, found: 227.0886.

4.2.14. Diol 20. Yield: 90%; R_f=0.30 [50% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (ddd, J=5.0, 13.5, 13.5 Hz, 1H), 1.08 (s, 9H), 1.39–1.46 (m, 3H), 1.64–1.73 (m, 1H), 1.89 (dt, J=3.0, 13.5 Hz, 1H), 2.31 (d, J=5.0 Hz, 1H), 3.40 (t, J=11.0 Hz, 1H), 3.57–3.60 (m, 1H), 3.62–3.67 (m, 1H), 3.71–3.78 (m, 4H), 4.10 (br s, 1H), 7.37–7.45 (m, 6H), 7.60–7.70 (m, 4H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 17.8, 19.5, 24.5, 27.1, 31.2, 59.2, 61.0, 63.0, 71.2, 73.4, 98.5, 127.7, 127.8, 129.9, 130.0, 132.8, 133.1, 135.9, 136.0; IR (Neat) cm^{-1} 3459s, 2944s, 2859m, 1428m, 1114s; mass spectrum (ESI): *m/e* 465.3 $(M+Na)^+$; ESIHRMS *m/e* calcd for $C_{25}H_{34}O_5SiNa$: 465.2073, found: 465.2078.

4.2.15. Acetal 21. To a solution of the respective diol [30.0 mg, 0.12 mmol] in dichloromethane [10 mL] was added benzophenone dimethyl ketal [56.0 mg, 0.25 mmol] and catalytic amount of concd sulfuric acid. It was refluxed for 24 h, washed by water, dried, and concentrated in vacuo. The crude product was purified by silica gel flash column chromatography [isocratic eluent: 10% EtOAc in hexanes] to afford acetal **21** [25.0 mg, 45%]. R_f=0.37 [20% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48–1.54 (m, 2H), 1.58–1.64 (m, 3H), 1.71–1.78 (m, 1H), 2.08 (s, 3H), 3.62 (ddd, J=2.5, 12.0, 12.0 Hz, 1H), 3.69–3.73 (m, 2H), 3.77 (dd, J=6.5, 11.5 Hz, 1H), 4.02 (dd, J=3.5, 6.5 Hz, 1H), 4.44 (ddd, J=7.0, 9.5, 13.5 Hz, 1H), 5.31 (d, J=3.5 Hz, 1H), 7.26–7.36 (m, 6H), 7.49–7.54 (m, 4H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 18.1, 20.9, 24.5, 29.7, 59.4, 61.1, 69.6, 70.9, 74.6, 95.8, 110.1, 126.3, 126.4, 127.9, 128.1, 128.2, 142.1, 142.5, 169.3; IR (Neat) cm^{-1} 2927m, 2855w, 1753s, 1230s; mass spectrum (ESI): *m/e* 433.3 (M+Na)$^+$; ESIHRMS *m/e* calcd for $C_{24}H_{26}O_6Na$: 433.1627, found: 433.1634.

4.2.16. Acetal 22. Yield: 76%; R_f=0.25 [20% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (s, 3H), 1.52 (s, 3H), 1.41–1.76 (m, 6H), 2.12 (s, 3H), 3.70–3.74 (m, 2H), 3.77–3.81 (m, 2H), 4.07 (t, J=5.0 Hz, 1H), 4.33 (dd, J=7.0, 13.5 Hz, 1H), 5.10 (d, J=5.0 Hz, 1H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 18.0, 21.0, 24.6, 26.1, 27.9, 28.7, 59.8, 61.3, 70.0, 72.0, 74.6, 96.5, 110.1, 169.5; IR (Neat) cm^{-1} 2944s, 2884w, 1754s, 1232s; mass spectrum (ESI): *m/e* 309.4 (M+Na)$^+$; ESIHRMS *m/e* calcd for $C_{14}H_{22}O_6Na$: 309.1314, found: 309.1315.

4.2.17. Spiroketal 23s. Yield: 90%; R_f=0.32 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47–1.66 (m, 4H), 1.81–1.91 (m, 1H), 1.98–2.01 (m, 1H), 3.73 (ddd, J=2.5, 11.0, 11.0 Hz, 1H), 3.80–3.83 (m, 1H), 4.24 (t, J=1.5 Hz, 1H), 5.13 (d, J=5.0 Hz, 1H), 5.94–5.98 (m, 1H), 6.11 (dt, J=2.5, 10.5 Hz, 1H), 7.41–7.44 (m, 2H), 7.54–7.55 (m, 1H), 8.05–8.07 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.2, 24.9, 30.6, 60.2, 62.8, 68.3, 95.7, 120.5, 128.3, 129.7, 130.0, 131.1, 133.1, 165.8; IR (Neat) cm^{-1} 2943m, 2850w, 1717s, 1271s; mass spectrum (ESI): *m/e* 297.2 (M+Na)$^+$; ESIHRMS *m/e* calcd for $C_{16}H_{18}O_4Na$: 297.1103, found: 297.1101.

4.2.18. Diol 24. Yield: 90%; R_f=0.30 [50% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.47–1.81 (m, 6H), 2.58 (br s, OH), 3.59 (t, J=11.0 Hz, 1H), 3.75–3.81 (m, 3H), 3.86–3.97 (m, 1H), 3.99–4.10 (m, 2H), 5.24 (d, J=3.0 Hz, 1H), 7.44–7.47 (m, 2H), 7.58–7.59 (m, 1H), 8.04–8.06 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.6, 24.5, 30.4, 59.1, 61.3, 63.6, 69.1, 72.0, 97.2, 128.5, 128.6, 129.1, 129.7, 129.8, 133.5, 164.9; IR (Neat) cm^{-1} 3462s, 2942s, 2879m, 1728s; mass spectrum (ESI): *m/e* 331.2 (M+Na)$^+$; ESIHRMS *m/e* calcd for $C_{16}H_{20}O_6Na$: 331.1158, found: 331.1164.

4.2.19. Benzoyl ester 25s. To a solution of the respective alcohol [28.0 mg, 0.16 mmol] in dichloromethane was added 4-bromobenzoyl chloride [63.0 mg, 0.29 mmol], triethylamine [0.10 mL, 0.72 mmol], and catalytic amount of DMAP. The reaction mixture was stirred at rt for 2 h and concentrated in vacuo. The crude product was purified by silica gel flash column chromatography [isocratic eluent: 5% EtOAc in hexanes] to give the benzoyl ester **25s** [53.0 mg, 91%]. R_f=0.40 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.31–1.42 (m, 2H), 1.51–1.61 (m, 3H), 1.69–1.85 (m, 3H), 1.92–1.96 (m, 2H), 2.13–2.19 (m, 2H), 3.66–3.83 (m, 4H), 4.92 (t, J=3.0 Hz, 1H), 7.58–7.60 (m, 1H), 7.96–7.97 (m, 1H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 18.0, 19.9, 23.7, 24.9, 31.5, 60.0, 60.5, 71.8, 94.9, 128.1, 129.2, 131.2, 131.7, 165.0; IR (Neat) cm^{-1} 2945s, 2874m, 1722s, 1590m, 1272s; mass spectrum (ESI): *m/e* 377.1 (M+Na)$^+$; ESIHRMS *m/e* calcd for $C_{16}H_{19}BrO_4Na$: 377.0364, found: 377.0360.

4.2.20. Benzoyl ester 26s. Yield: 80%; R_f=0.40 [20% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (ddd, J=2.5, 12.5, 12.5 Hz, 1H), 1.43 (dd, J=2.0, 13.5 Hz, 1H), 1.52–1.67 (m, 3H), 1.73–1.87 (m, 3H), 1.94 (dddd, J=4.5, 4.5, 9.0, 26.5 Hz, 1H) 2.16–2.23 (m, 1H), 3.67–3.84 (m, 4H), 4.95 (t, J=3.0 Hz, 1H), 8.25–8.30 (m, 4H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 17.9, 19.8, 23.7, 24.8, 31.5, 59.9, 60.5, 72.6, 94.7, 123.5, 130.8, 135.6, 140.4, 150.5, 163.8; IR (Neat) cm^{-1} 2947s, 2875m, 1726s, 1530s, 1276s; mass spectrum (ESI): *m/e* 344.1 (M+Na)$^+$; ESIHRMS *m/e* calcd for $C_{16}H_{19}NO_6Na$: 344.1110, found: 344.1116.

4.2.21. Hydrogenated spiroketal 27s. To a solution of **17s** [50.0 mg, 0.12 mmol] in EtOAc [3 mL] at rt was added 10 mg of 10% Pd/C. This heterogeneous mixture was stirred under 1 atm of H_2 for 12 h and filtered through Celite to give the hydrogenated product **27s** [43.0 mg, 90%]. R_f=0.34 [5% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.11–1.17 (m, 2H), 1.40–1.58 (m, 4H), 1.73–1.77 (m, 2H), 2.00–2.07 (m, 2H), 3.52–3.55 (m, 2H), 3.62–3.67 (m, 3H), 7.33–7.42 (m, 6H), 7.68–7.71 (m, 4H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 18.3, 19.6, 25.1, 26.1, 27.2, 31.9, 60.2, 60.4, 71.5, 96.6, 127.4, 127.5, 129.5, 129.6, 133.8, 134.4, 136.0, 136.1; IR (Neat) cm^{-1} 2957s, 2934s, 285m, 1111s; mass spectrum (ESI): *m/e* 433.3 (M+Na)$^+$; ESIHRMS *m/e* calcd for $C_{25}H_{34}O_3SiNa$: 433.2175, found: 433.2175.

4.2.22. Hydrogenated spiroketal 27a. Yield: 83%; R_f=0.35 [5% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.40–1.78 (m, 8H), 1.90 (dddd, J=5.5, 12.0, 12.0, 12.0 Hz, 1H), 2.03 (ddd, J=4.5, 13.0, 13.0 Hz, 1H), 3.37–3.45 (m, 2H), 3.54 (ddd, J=4.0, 5.0, 15.0 Hz, 1H), 3.67 (ddd, J=1.5, 10.5, 12.5 Hz, 1H), 3.76–3.83 (m, 1H), 7.33–7.42 (m, 6H), 7.69–7.75 (m, 4H); ^{13}C NMR (125 Hz, $CDCl_3$) δ 18.4, 19.4, 25.1, 25.5, 27.1, 27.5, 30.6, 59.1, 60.6, 74.6, 97.1, 127.4, 127.5, 129.5, 129.6, 133.9, 134.3, 136.0, 136.1; IR (Neat) cm^{-1} 2957s, 2934s, 2857m; mass spectrum (ESI): *m/e* 433.5 (M+Na)$^+$; ESIHRMS *m/e* calcd for $C_{25}H_{34}O_3SiNa$: 433.2175, found: 433.2173.

4.3. Spiroaminal syntheses

4.3.1. Aminal 28a. Yield: 70%; R_f=0.37 [15% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 3H), 0.02 (s, 3H), 0.89 (s, 9H), 1.46–1.70 (m, 5H), 1.85–2.0 (m, 1H), 3.69 (ddd, J=3.0, 12.0, 19.5 Hz, 1H), 3.69–3.74 (m, 1H), 4.61 (d, J=5.0 Hz, 2H), 5.04 (dd, J=15, 27 Hz, 1H), 5.12 (d, J=12 Hz, 1H), 5.18 (ddd, J=1.5, 2.0, 11.0 Hz, 1H),

5.29 (ddd, J=1.5, 2.0, 17.5 Hz, 1H), 5.96 (ddd, J=5.5, 11.0, 17.5 Hz, 1H), 7.28–7.40 (m, 5H); ^{13}C NMR (500 MHz, $CDCl_3$) δ −5.0, −4.3, 18.3, 18.9, 25.2, 26.1, 27.4, 61.6, 66.5, 75.9, 87.0, 116.6, 128.3, 128.4, 128.6, 136.7, 137.2, 154.1; IR (thin film) cm^{-1} 3441br m, 3055m, 2954s, 2858s, 1734s, 1503s, 1264s, 1099s, 739s; mass spectrum (ESI): *m/e* (% relative intensity) 444.2 (9) (M+K$^+$), 428.3 (100) (M+Na$^+$), 255.2 (3); HRMS calcd for $C_{22}H_{35}NNaO_4Si^+$ [M+Na]$^+$: 428.2233, found: 428.2240.

4.3.2. General procedure for the allylation of cyclic aminals. To a flame dried 5-mL RB-Flask under nitrogen were added NaH (9.0 mg, 0.211 mmol) and DMF (1 mL) at rt. To this stirring suspension was added a solution of cyclic aminal **28a** (57.0 mg, 0.141 mmol) in DMF (1 mL) at rt. The reaction mixture was stirred for additional 10 min. Allyl iodide (43.0 μL, 0.211 mmol) was then added to the reaction mixture at 0 °C, and the mixture was stirred for 2–3 h at this temperature until TLC analysis indicated the complete consumption of the starting material. The mixture was quenched with satd aq NH_4Cl and extracted with Et_2O (3×5 mL). The combined organic layers were washed with satd aq NaCl (2 mL), dried over Na_2SO_4, and concentrated in vacuo. The crude residue was purified using silica gel flash column chromatography [gradient eluent; 15:1–4:1 EtOAc in hexanes] to give the allylated cyclic aminal **29a** [33.0 mg, 57%] as colorless oil.

4.3.3. Aminal RCM precursor 29a. Yield: 57%; R_f=0.43 [10% EtOAc in hexanes], ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.01 (s, 3H), 0.02 (s, 3H), 0.89 (s, 9H), 1.45–1.71 (m, 5H), 3.02 (d, J=10.2 Hz, 1H), 3.52–3.70 (m, 2H), 3.89–4.04 (m, 2H), 4.24 (d, J=6.6 Hz, 1H), 5.05 (ddt, J=1.5, 1.5, 10.5 Hz, 1H), 5.09 (ddt, J=1.5, 1.5, 16.8 Hz, 1H), 5.09 (s, 2H), 5.16 (ddd, J=1.2, 1.8, 10.5 Hz, 1H), 5.19 (ddd, J=1.2, 1.8, 17.1 Hz, 1H), 5.91 (ddd, J=6.6, 10.5, 17.1 Hz, 1H), 5.95 (ddt, J=5.4, 10.8, 16.8 Hz, 1H), 7.28–7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, −4.0, 18.3, 19.4, 25.4, 26.1, 38.9, 46.6, 63.1, 67.0, 78.5, 92.5, 105.7, 115.5, 117.2, 128.0, 128.3, 128.5, 136.9, 137.6, 137.7, 155.8; IR (thin film) cm^{-1} 2955s, 2859s, 1714s, 1462s, 1272s, 1091s, 989.9s, 838s; mass spectrum (ESI): *m/e* (% relative intensity) 482.3 (8) (M+K$^+$), 468.3 (100) (M+Na$^+$), 446.3 (8) (M+H$^+$), 418.2 (1), 314.2 (1), 255.2 (5); ESIHRMS *m/e* calcd for $C_{25}H_{39}NNaO_4Si$: 468.2546, found: 468.2544.

4.3.4. General procedure for the ring-closing metathesis of cyclic aminals. Please see Section 4.2.4.

4.3.5. Spiroaminal 30a. Yield: 95%; R_f=0.33 [10% EtOAc in hexanes], ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.02 (s, 3H), 0.12 (s, 3H), 0.94 (s, 9H), 1.44–1.73 (m, 4H), 2.08 (dt, J=2.1, 7.8 Hz, 1H), 3.78 (d, J=7.8 Hz, 1H), 3.50 (ddd, J=1.2, 1.5, 6.6 Hz, 1H), 3.55 (ddd, J=1.2, 2.7, 10.8 Hz, 1H), 3.83 (ddd, J=1.2, 2.1, 6.6 Hz, 1H), 4.24 (ddd, J=1.2, 1.2, 2.4 Hz, 1H), 4.43 (ddd, J=1.2, 1.5, 10.8 Hz, 1H), 5.09 (d, J=7.5 Hz, 1H), 5.14 (d, J=7.5 Hz, 1H), 5.48 (dd, J=1.2, 6.0 Hz, 1H), 5.72 (dddd, J=1.2, 1.2, 2.4, 6.0 Hz, 1H), 7.32–7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.5, −3.9, 18.4, 19.8, 25.5, 26.2, 29.3, 43.3, 58.1, 63.0, 67.3, 71.2, 88.3, 125.9, 127.5, 128.1, 128.3, 128.7, 136.6, 154.9; IR (thin film) cm^{-1} 2953s, 2857s, 1715s, 1471s, 1399s, 1337s, 1227s, 1163s, 1026s; mass spectrum (ESI): *m/e* (% relative intensity) 456.3 (6) (M+K$^+$), 440.3 (100) (M+Na$^+$), 418.3 (11) (M+H$^+$), 268.2 (30), 195.1 (3); ESIHRMS *m/e* calcd for $C_{23}H_{35}NNaO_4Si$: 440.2233, found: 468.2239.

4.3.6. Spiroaminal 31a. *RCM precursor.* Yield: 94%; R_f=0.37 [10% EtOAc in hexanes]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.01 (s, 3H), 0.03 (s, 3H), 0.89 (s, 9H), 1.45–1.70 (m, 5H), 2.90–3.10 (m, 1H), 3.50–3.70 (m, 2H), 3.64 (s, 3H), 3.79 (dddd, J=1.2, 1.5, 5.1, 16.2 Hz, 1H), 3.95 (dddd, J=1.2, 1.8, 6.3, 16.2 Hz, 1H), 4.22 (d, J=6.3 Hz, 1H), 5.06 (ddt, J=1.5, 1.5, 10.2 Hz, 1H), 5.11 (ddt, J=1.5, 1.5, 17.4 Hz, 1H), 5.19 (ddd, J=1.2, 1.8, 10.2 Hz, 1H), 5.22 (ddd, J=1.2, 1.8, 17.4 Hz, 1H), 5.90 (ddd, J=6.3, 10.5, 17.4 Hz, 1H), 5.97 (ddt, J=5.4, 10.2, 17.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.8, −4.1, 18.2, 19.3, 25.3, 25.9, 28.7, 46.3, 52.0, 62.8, 78.3, 92.3, 115.3, 117.0, 137.5, 137.7; IR (thin film) cm^{-1} 2987s, 2857s, 1757s, 1671s, 1415s, 1333w, 1265s, 1032m, 950m, 837s; mass spectrum (EI): *m/e* (% relative intensity) 369 (1) (M$^+$), 312 (10), 255 (3), 198 (100), 115 (10).

Compound **31a**. Yield: 97%; R_f=0.29 [10% EtOAc in hexanes]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 3H), 0.13 (s, 3H), 0.94 (s, 9H), 1.45–1.76 (m, 4H), 2.08 (dt, J=3.9, 13.0 Hz, 1H), 2.47 (d, J=13.0 Hz, 1H), 3.43–3.54 (m, 1H), 3.51 (dddd, J=1.8, 1.8, 3.6, 18.0 Hz, 1H), 3.69 (s, 3H), 3.78–3.88 (m, 1H), 4.22 (ddd, J=1.8, 3.3, 3.9 Hz, 1H), 4.36 (dddd, J=1.8, 1.8, 3.6, 18.0 Hz, 1H), 5.46 (dddd, J=1.8, 1.8, 2.7, 10.5 Hz, 1H), 5.71 (dddd, J=2.1, 2.1, 4.2, 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.6, −4.1, 18.3, 19.6, 25.4, 26.0, 29.2, 42.1, 52.5, 62.9, 71.1, 86.1, 125.8, 127.9; IR (thin film) cm^{-1} 2987s, 2857s, 1757s, 1415s, 1333w, 1265s, 1100s, 1032m, 837s; mass spectrum (GC–MS): *m/e* (% relative intensity) 341 (1) (M$^+$), 284 (30), 210 (7), 184 (60), 127 (100), 59 (10); ESIHRMS *m/e* calcd for $C_{17}H_{31}NNaO_4Si$: 364.1915, found: 364.1911.

4.3.7. Spiroaminal 31s. *RCM precursor.* Yield: 97%; R_f=0.40 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.07 (s, 3H), 0.90 (s, 9H), 1.43–1.69 (m, 4H), 1.85 (dt, J=4.0, 13.0 Hz, 1H), 2.81 (d, J=13.0 Hz, 1H), 3.50 (dt, J=2.5, 12.5 Hz, 1H), 3.63–3.70 (m, 1H), 3.65 (s, 3H), 3.92 (dd, J=6.0, 16.0 Hz, 1H), 4.02 (dd, J=6.0, 16.0 Hz, 1H), 4.20 (d, J=6.0 Hz, 1H), 5.08 (ddd, J=1.5, 2.0, 10.5 Hz, 1H), 5.14 (ddt, J=1.5, 1.5, 17.0 Hz, 1H), 5.15 (ddt, J=1.5, 1.5, 11.0 Hz, 1H), 5.26 (ddd, J=1.5, 2.0, 17.0 Hz, 1H), 5.82 (ddd, J=6.0, 10.5, 17.0 Hz, 1H), 5.94 (ddd, J=5.0, 11.0, 17.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.5, −4.3, 18.5, 19.4, 25.3, 26.1, 26.2, 46.0, 52.2, 62.8, 77.0, 92.7, 115.9, 116.9, 136.8, 137.3; IR (thin film) cm^{-1} 2987s, 2857s, 1757s, 1671s, 1415s, 1333w, 1265s, 1032m, 950m, 837s; mass spectrum (EI): *m/e* (% relative intensity) 369 (1) (M$^+$), 312 (10), 255 (3), 198 (100), 115 (10).

Compound **31s**. Yield: 96%; R_f=0.31 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.41 (dt, J=5.5, 10.3 Hz, 1H), 1.48–1.55 (m, 1H), 1.60–1.78 (m, 3H), 3.28 (d, J=13.0 Hz, 1H), 3.50 (dddd, J=2.0, 2.0, 4.0, 18.5 Hz, 1H), 3.51 (dd, J=2.0, 11.0 Hz, 1H), 3.66 (s, 3H), 3.72 (dd, J=1.5, 5.0 Hz, 1H),

3.78 (dd, J=2.0, 11.0 Hz, 1H), 4.55 (dd, J=3.0, 18.5 Hz, 1H), 5.67 (dddd, J=2.5, 2.5, 5.0, 10.0 Hz, 1H), 5.82 (dddd, J=2.0, 2.0, 4.0, 10.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.6, −3.6, 18.10, 20.0, 25.4, 25.8, 32.8, 43.1, 52.5, 63.5, 71.7, 88.4, 125.2, 127.9; IR (thin film) cm^{-1} 2987s, 2857s, 1757s, 1415s, 1333w, 1265s, 1100s, 1032m, 837s; mass spectrum (EI): *m/e* (% relative intensity) 341 (1) (M^+), 284 (30), 210 (7), 184 (60), 127 (100), 59 (10); ESIHRMS *m/e* calcd for $C_{17}H_{31}NNaO_4Si$: 364.1915, found: 364.1911.

4.3.8. Spiroaminal 32a. *RCM precursor.* Yield: 87%; R_f=0.45 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.00 (s, 3H), 0.03 (s, 3H), 0.88 (s, 9H), 1.44–1.95 (m, 7H), 1.98 (q, J=6.6 Hz, 2H), 2.93 (d, J=6.0 Hz, 1H), 3.17–3.35 (m, 2H), 3.54 (dt, J=3.6, 11.1 Hz, 1H), 3.72 (dt, J=1.2, 2.4 Hz, 1H), 4.26 (d, J=6.6 Hz, 1H), 4.92 (ddt, J=1.4, 1.9, 10.5 Hz, 1H), 4.97 (ddt, J=1.4, 1.9, 17.1 Hz, 1H), 5.09 (s, 2H), 5.15 (ddd, J=1.2, 1.8, 10.5 Hz, 1H), 5.20 (ddd, J=1.2, 1.8, 17.1 Hz, 1H), 5.74 (ddt, J=6.6, 10.5, 17.1 Hz, 1H), 5.90 (ddd, J=6.6, 10.5, 17.1 Hz, 1H), 7.28–7.37 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.6, −4.0, 18.4, 19.4, 25.3, 26.1, 29.0, 29.4, 32.1, 43.8, 62.7, 66.9, 78.6, 92.3, 114.8, 117.1, 128.1, 128.3, 128.6, 136.5, 137.0, 137.8, 138.4, 155.9; IR (thin film) cm^{-1} 2952s, 2858s, 1715s, 1446s, 1394s, 1247s, 1090s, 995s, 839s; mass spectrum (ESI): *m/e* (% relative intensity) 512.3 (8) ($M+K^+$), 496.3 (100) ($M+Na^+$), 474.3 (5) (M), 365.1 (5), 255.2 (7); ESIHRMS *m/e* calcd for $C_{27}H_{43}NNaO_4Si^+$: 496.2854, found: 496.2855.

Compound **32a**: Yield: 94%; R_f=0.44 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.04 (s, 3H), 0.08 (s, 3H), 0.91 (s, 9H), 1.25–1.40 (m, 2H), 1.44 (d, J=7.5 Hz, 1H), 1.55–1.75 (m, 2H), 1.81–1.85 (m, 1H), 1.92–1.93 (m, 1H), 2.06 (dt, J=2.1, 8.1 Hz, 1H), 2.14–2.25 (m, 1H), 2.90–3.10 (m, 1H), 3.20–3.40 (m, 2H), 3.40 (dd, J=3.6, 5.4 Hz, 1H), 3.75 (dd, J=3.0, 6.9 Hz, 1H), 4.47 (s, 1H), 5.14 (d, J=7.5 Hz, 1H), 5.17 (d, J=7.5 Hz, 1H), 5.49–5.56 (m, 2H), 7.31–7.41 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.9, −4.7, 18.2, 18.7, 23.7, 25.0, 25.6, 25.8, 28.1, 38.8, 52.5, 63.0, 66.7, 73.0, 94.2, 126.8, 128.0, 128.1, 128.4, 135.3, 136.4, 155.8; IR (thin film) cm^{-1} 2956s, 2859s, 1707s, 1471s, 1408s, 1338s, 1301s, 1279s, 1179s, 1026s; mass spectrum (ESI): *m/e* (% relative intensity) 484.4 (7) ($M+K^+$), 468.4 (100) ($M+Na^+$), 446.4 (24) ($M+H^+$), 314.6 (14); ESIHRMS *m/e* calcd for $C_{25}H_{39}NNaO_4Si$: 468.2541, found: 468.2539.

4.4. Insect hormone synthesis

4.4.1. Synthesis of cyclic ketal 35. To a solution of dihydropyran [460.0 mg, 4.68 mmol] in anhyd THF [10 mL] at −78 °C was added 3.0 mL of *t*-BuLi [1.7 M in pentane, 5.15 mmol]. It was stirred at 0 °C for 45 min before being cooled back down to −78 °C. A solution of HMPA [0.95 mL, 5.5 mmol] in THF [4 mL] was added to the mixture followed by the dropwise addition of a solution of crotyl bromide [371.0 mg, 2.75 mmol] in THF [3 mL]. The mixture was allowed to warm to rt and stirred for an additional 16 h. After the standard quenching, solvent was reduced in vacuo and the residue was filtered through a small bed of silica gel column chromatography [isocratic eluent: 2% EtOAc in hexanes] to give the desired crotylated product [416.0 mg, 58% yield] as light yellow oil.

To a solution of the above crotylated product [235.0 mg, 1.5 mmol] and allyl alcohol [200.0 mg, 3.5 mmol] in anhyd CH_2Cl_2 [15 mL] was added pyridinium *p*-toluene sulfonate [40.0 mg, 0.010 mmol] at −78 °C. The reaction mixture was stirred for 2 h at −78 °C before it was concentrated in vacuo and purified by silica gel flash column chromatography [isocratic eluent: 5% EtOAc in hexanes] to give **35** [150.0 mg, 46%, *dr*=4:1] as colorless oil. *Major isomer*: R_f=0.31 [5% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (d, J=6.0 Hz, 3H), 1.16–1.38 (m, 2H), 1.52–1.62 (m, 2H), 1.66 (dd, J=1.0, 6.0 Hz, 3H), 1.72–1.86 (m, 2H), 2.14–2.18 (m, 1H), 2.43–2.47 (m, 1H), 3.67–3.74 (m, 1H), 3.89–3.98 (m, 1H), 3.99–4.04 (m, 1H) 5.13 (dq, J=1.5, 10.0 Hz, 1H), 5.32 (dq, J=1.5, 17.0 Hz, 1H), 5.35–5.45 (m, 1H), 5.47–5.53 (m, 1H), 5.85–6.00 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.0, 18.9, 21.8, 32.5, 32.6, 41.0, 60.6, 66.5, 99.4, 115.6, 125.5, 128.2, 135.4; mass spectrum (LC–MS) for $C_{13}H_{22}O_2$: *m/e* (% relative intensity) 153 (100) [M−*O*-allyl]$^+$.

4.4.2. Spiroketal 36. To a solution of Grubbs' generation-I Ru-catalyst [35.0 mg, 0.042 mmol, 10 mol %] in anhyd benzene [30 mL] at rt was added a solution of the major isomer of **35** [90.0 mg, 0.42 mmol] in anhyd benzene [10 mL] via syringe. The reaction mixture was stirred for 1 h before it was concentrated and purified by silica gel flash column chromatography [isocratic eluent: 5% EtOAc in hexanes] to give **36** [46.0 mg, 70%] as colorless oil. R_f=0.38 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (d, J=5.5 Hz, 3H), 1.17–1.25 (m, 1H), 1.46 (ddd, J=4.5, 14.0, 14.0 Hz, 1H), 1.57–1.62 (m, 2H), 1.67–1.71 (m, 1H), 1.85–1.95 (m, 1H), 2.03–2.08 (m, 1H), 2.17–2.23 (m, 1H), 3.80–3.86 (m, 1H), 4.00–4.04 (m, 1H), 4.09–4.15 (m, 1H), 5.67–5.71 (m, 1H), 5.73–5.77 (m, 1H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.0, 21.9, 32.5, 34.3, 35.9, 59.7, 66.5, 95.0, 121.6, 124.8; mass spectrum (LC–MS) for $C_{10}H_{16}O_2$: *m/e* (% relative intensity) 169 (20) ($M+H)^+$, 151 (100).

4.4.3. Synthesis of 37. To a solution of spiroketal **36** [30.0 mg, 0.17 mmol] in EtOAc [5 mL] at rt was added 10.0 mg of 10% Pd/C. This heterogeneous mixture was stirred under 1 atm of H_2 for 3 h and filtered through Celite to give the hydrogenated product **37** [24.0 mg, 75%] as colorless liquid. R_f=0.44 [10% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (d, J=6.0 Hz, 3H), 1.24–1.66 (m, 10H), 1.78–1.93 (m, 2H), 3.55–3.58 (m, 1H), 3.62–3.67 (m, 1H), 3.70–3.76 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.5, 18.9, 21.8, 25.4, 32.6, 35.0, 35.8, 60.2, 65.1, 95.6; mass spectrum (LC–MS) for $C_{10}H_{18}O_2$: *m/e* (% relative intensity) 171 (100) ($M+H)^+$, 153 (30), 135 (17). The synthetic compound spectroscopically [^{1}H and ^{13}C NMR] matched with those reported from the isolation work.[21,26]

4.5. The C11-C23 of spirastrellolide A

4.5.1. Diol 42. Yield: 78%; R_f=0.3 [50% EtOAc in hexanes]; $[\alpha]_D^{23}$ −22.5 [*c* 3.97, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.093 (s, 6H), 0.092 (s, 9H), 1.51–1.69 (m, 4H), 2.64 (br,

2H), 3.36 (s, 3H), 3.38 (m, 1H), 3.53 (m, 1H), 3.57 (t, J=6.0 Hz, 1H), 3.86 (dd J=5.0, 6.0 Hz, 1H), 3.93 (dd, J=4.5, 6.5 Hz, 1H), 3.98 (dd, J=3.5, 11.0 Hz, 1H), 4.56 (d, J=11.5 Hz, 1H), 4.75 (d, J=11.5 Hz, 1H), 7.29 (m, 1H), 7.34 (m, 4H); ^{13}C NMR (500 MHz, $CDCl_3$) δ −5.4, −5.4, 18.3, 25.0, 25.9, 28.6, 57.2, 62.8, 63.8, 70.9, 72.3, 79.0, 81.4, 127.7, 128.0, 128.4, 138.4; IR (film) cm^{-1} 3420br s, 3071w, 2930s, 2858s, 1671m, 1255m, 1085s; mass spectrum (APCI): *m/e* 399.2 $(M+H)^+$; ESIHRMS *m/e* calcd for $C_{21}H_{38}O_5SiNa$: 421.2381, found: 421.2384.

4.5.2. Lactol 44. To a solution of the respective lactone precursor [223.0 mg, 0.43 mmol] in Et_2O [3 mL] was added vinyl magnesium bromide [0.45 mL, 1 M] dropwise at −78 °C. The solution was stirred at −78 °C for 1 h and quenched with satd aq NH_4Cl [5 mL] at −78 °C. The organic phase was separated and the aqueous fraction was extracted with Et_2O [3×5 mL]. The combined organic phases were washed with satd aq NaCl, dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by flash column chromatography on silica gel [gradient eluent: 22–35% EtOAc in hexanes] to lactol **44** in 73% yield [92.7 mg] as pale yellow oil based on the starting material recovered [99.1 mg]. *Lactone*: R_f=0.32 [50% EtOAc in hexanes]; $[\alpha]_D^{23}$ 5.00 [*c* 5.115, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 9H), 1.92 (m, 2H), 2.38 (ddd, J=5.0, 5.0, 17.0 Hz, 1H), 2.61 (ddd, J=7.0, 10.5, 17.5 Hz, 1H), 3.29 (s, 3H), 3.74 (dd, J=4.0, 8.0 Hz, 1H), 3.80 (m, 2H), 4.51 (d, J=11.0 Hz, 1H), 4.61 (d, J=11.0 Hz, 1H), 4.64 (dd, J=3.5, 2.5 Hz, 1H), 7.25 (m, 2H), 7.31 (m, 3H), 7.39 (m, 4H), 7.41 (m, 2H), 7.68 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.0, 22.2, 25.9, 26.6, 55.8, 50.2, 62.4, 71.3, 73.4, 60.0, 81.2, 127.7, 127.8, 128.3, 129.8, 132.8, 132.9, 135.5, 137.7, 171.1; IR (film) cm^{-1} 3070w, 2931s, 2858s, 1742s, 1428m, 1113s; mass spectrum (APCI): *m/e* 519.2 $(M+H)^+$; ESIHRMS *m/e* calcd for $C_{31}H_{38}NaO_5Si$: 541.2381, found: 541.2382. Compound **44**: R_f=0.32 [50% EtOAc in hexanes]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.85 (m, 1H), 1.91 (m, 1H), 2.60 (ddd, J=6.5, 9.0, 17.0 Hz, 1H), 2.71 (br, 1H), 2.73 (dddd, J=6.0, 9.0, 17.0, 17.0 Hz, 1H), 3.28 (s, 3H), 3.38 (ddd, J=4.5, 4.5, 8.5 Hz, 1H), 3.94 (ddd, J=0.5, 5.0, 11.0 Hz, 1H), 3.61 (ddd, J=3.5, 3.5, 7.5 Hz, 1H), 4.01 (ddd, J=1.0, 3.5, 11.5 Hz, 1H), 4.53 (d, J=11.5 Hz, 1H), 4.72 (d, J=11.5 Hz, 1H), 5.80 (dd, J=1.0, 10.5 Hz, 1H), 6.22 (d, J=17.5 Hz, 1H), 6.35 (dd, J=10.5, 17.5 Hz, 1H), 7.27–7.45 (m, 11H), 7.72 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2, 22.7, 26.9, 57.1, 64.2, 70.9, 72.3, 76.9, 79.0, 80.2, 96.5, 127.6, 127.7, 127.8, 127.9, 128.4, 129.8, 129.8, 133.0, 133.2, 135.6, 135.7, 135.7, 136.6, 138.4; IR (film) cm^{-1} 3459br s, 3069m, 2932s, 2859s, 1681m, 1428m, 1113s; mass spectrum (APCI): *m/e* 529.3 $(M-H_2O+H)^+$; ESIHRMS *m/e* calcd for $C_{33}H_{42}O_5SiNa$: 569.2694, found: 569.2697.

4.5.3. Cyclic ketal 47. To a solution of **44** [5.00 mg, 0.0094 mmol] in CH_2Cl_2 [0.1 mL] were added MS 4 Å [10 mg] and 3-butene-1-ol [6.77 mg, 0.094 mmol] followed by Tf_2NH [2.64 mg, 0.0094 mmol] at −78 °C. The solution was stirred at −78 °C for 5 min before quenching with Et_3N [0.10 mL] at −78 °C. The mixture was warmed to rt and filtered through Celite. After evaporation of the solvent under reduced pressure, the resulting crude residue was purified by flash column chromatography on silica gel [gradient eluent: 2–10% EtOAc in hexanes] to provide cyclic ketal **47** in 89% yield [5.00 mg]. R_f=0.80 [25% EtOAc in hexanes]; $[\alpha]_D^{23}$ 28.9 [*c* 0.36, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.45 (ddd, J=4.0, 14.0, 14.0 Hz, 1H), 1.74 (ddd, J=4.0, 14.0, 24.0 Hz, 1H), 1.88 (ddd, J=4.0, 4.0, 14.0 Hz, 1H), 1.95 (dddd, J=4.0, 4.0, 8.0, 8.0 Hz, 1H), 3.23 (s, 3H), 3.25 (ddd, J=5.0, 10.5, 10.5 Hz, 1H), 3.37 (ddd, J=7.0, 7.0, 9.5 Hz, 1H), 3.40 (ddd, J=7.0, 7.0, 9.5 Hz, 1H), 3.76 (d, J=9.5 Hz, 1H), 3.92 (m, 3H), 4.73 (d, J=11.5 Hz, 1H), 4.79 (d, J=11.5 Hz, 1H), 5.00 (dd, J=1.0, 10.5 Hz, 1H), 5.17 (dd, J=1.5, 11.0 Hz, 1H), 5.31 (dd, J=2.0, 17.5 Hz, 1H), 5.70 (dd, J=11.0, 17.5 Hz, 1H), 5.78 (ddt, J=10.5, 17.5, 7.0 Hz, 1H), 7.27–7.41 (m, 11H), 7.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.2, 24.1, 26.9, 34.0, 34.3, 56.0, 60.5, 64.5, 73.1, 73.6, 74.7, 80.9, 97.3, 116.2, 116.3, 127.2, 127.6, 127.6, 127.6, 127.9, 128.2, 129.5, 133.6, 133.8, 135.6, 135.7, 135.7, 138.8, 139.3; IR (film) cm^{-1} 3071w, 2929s, 2857s, 1456m, 1104s; mass spectrum (ESI): *m/e* 623.3 $(M+Na)^+$.

4.5.4. Diene 46. R_f=0.80 [25% EtOAc in hexanes]; $[\alpha]_D^{23}$ −5.87 [*c* 0.92, $CHCl_3$]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9H), 2.17 (t, J=3.9 Hz, 2H), 3.40 (s, 3H), 3.74 (ddd, J=3.0, 5.1, 10.2 Hz, 1H), 3.79 (ddd, J=7.5, 7.5, 7.5 Hz, 1H), 3.93 (dd, J=5.4, 11.4 Hz, 1H), 4.01 (dd, J=3.3, 11.4 Hz, 1H), 4.35 (dd, J=14.5, 6.9 Hz, 1H), 4.56 (d, J=11.8 Hz, 1H), 4.71 (dd, J=3.9, 3.9 Hz, 1H), 4.84 (d, J=11.8 Hz, 1H), 4.97 (d, J=10.8 Hz, 1H), 5.40 (d, J=17.1 Hz, 1H), 6.01 (dd, J=10.8, 17.1 Hz, 1H), 7.43 (m, 11H), 7.75 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 24.0, 26.7, 56.4, 63.4, 71.6, 72.5, 73.9, 78.0, 99.4, 112.5, 127.5, 127.6, 127.8, 128.2, 129.5, 131.6, 133.3, 135.6, 138.3, 148.9; IR (film) cm^{-1} 3070m, 2931s, 2858s, 1428m, 1112s; mass spectrum (APCI): *m/e* (% relative intensity) 529.2 $(M+H)^+$; ESIHRMS *m/e* calcd for $C_{33}H_{41}O_4Si$: 529.2769, found: 529.2780.

4.5.5. Cyclic ketal 48. R_f=0.80 [25% EtOAc in hexanes]; $[\alpha]_D^{23}$ 46.1 [*c* 0.33, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.48 (ddd, J=4.0, 13.0, 13.0 Hz, 1H), 1.65 (dddd, J=4.0, 13.0, 13.0, 13.0 Hz, 1H), 1.81 (m, 2H), 1.95 (m, 2H), 2.29 (ddd, J=6.0, 6.0, 6.0 Hz, 1H), 3.15 (ddd, J=4.5, 10.5, 10.5 Hz, 1H), 3.21 (s, 3H), 3.39 (m, 5H), 3.49 (dd, J=7.0, 14.0 Hz, 1H), 3.68 (d, J=9.5 Hz, 1H), 3.92 (m, 3H), 4.74 (s, 2H), 5.00 (d, J=10.5 Hz, 1H), 5.02 (dd, J=1.0, 11.0 Hz, 1H), 5.06 (d, J=18.0 Hz, 1H), 5.07 (dd, J=1.5, 17.5 Hz, 1H), 5.79 (ddt, J=10.0, 17.0, 7.0 Hz, 1H), 7.27–7.41 (m, 11H), 7.69 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2, 23.9, 26.9, 32.3, 34.2, 34.4, 36.1, 56.0, 59.2, 64.4, 66.7, 70.2, 73.1, 73.7, 74.8, 80.7, 98.0, 116.3, 116.4, 127.2, 127.6, 127.6, 127.6, 129.2, 129.5, 133.6, 133.8, 135.3, 135.5, 135.6, 135.6, 135.7, 139.2; IR (film) cm^{-1} 3071m, 2931s, 2858s, 1428m, 1105s; mass spectrum (ESI): *m/e* 695.6 $(M+Na)^+$; ESIHRMS *m/e* calcd for $C_{41}H_{56}O_6SiNa$: 695.3738, found: 695.3760.

4.5.6. Cyclic ketal 50. To a solution of **44** [40.0 mg, 0.075 mmol] in CH_2Cl_2 [0.8 mL] were added MS 4 Å [40 mg], alcohol **49** [187.0 mg, 0.75 mmol], and Tf_2NH [10.5 mg, 0.038 mmol] at −78 °C. The solution was stirred at −78 °C for 15 min before quenching with Et_3N [1 mL] at −78 °C. The mixture was warmed to rt and filtered through

Celite™. After evaporating the solvent under reduced pressure, the resulting crude residue was purified by flash column chromatography on silica gel [gradient eluent: 2–10% EtOAc in hexanes] to provide cyclic ketal **50** and diene **46** as an inseparable mixture in 2:1 ratio. R_f=0.80 [25% EtOAc in hexanes]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.99 (d, J=6.9 Hz, 3H), 1.06 (s, 9H), 1.54 (ddd, J=9.0, 12.0, 12.0 Hz, 1H), 1.71 (m, 2H), 1.85 (m, 1H), 1.94 (m, 1H), 2.01 (m, 1H), 2.36 (ddd, J=3.0, 7.2, 7.2 Hz, 1H), 3.21 (s, 3H), 3.31 (ddd, J=3.6, 12.0, 12.0 Hz, 1H), 3.39 (m, 1H), 3.73 (m, 1H), 3.78 (s, 3H), 3.78 (m, 1H), 3.85 (m, 1H), 3.88–3.97 (m, 3H), 4.22 (d, J=11.4 Hz, 1H), 4.34 (d, J=11.4 Hz, 1H), 4.71 (d, J=11.7 Hz, 1H), 4.79 (d, J=11.7 Hz, 1H), 4.94–4.99 (m, 2H), 5.16 (dd, J=2.1, 10.8 Hz, 1H), 5.36 (dd, J=1.8, 17.1 Hz, 1H), 5.75 (dd, J=9.6, 17.4 Hz, 1H) 5.80 (m, 1H), 6.82 (d, J=8.7 Hz, 1H), 7.19 (d, J=8.7 Hz, 1H), 7.34 (m, 11H), 7.70 (m, 4H).

4.5.7. Spiroketal 51. To the solution of Grubbs' generation-I Ru-catalyst [0.60 mg, 0.00072 mmol] in benzene [1.5 mL] was added slowly the solution of cyclic ketal **47** (4.30 mg, 0.0072 mmol] in benzene [0.5 mL] at rt. The solution was stirred at rt for 30 min and benzene was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel [gradient eluent: 5–10% EtOAc in hexanes] to provide the spiroketal **51** in 95% yield [3.90 mg] as colorless oil. R_f=0.75 [25% EtOAc in hexanes]; $[\alpha]_D^{23}$ 0.44 [c 0.45, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.56 (ddd, J=4.0, 13.0, 13.0 Hz, 1H), 1.75 (m, 2H), 1.86 (ddd, J=4.0, 4.0, 18.0 Hz, 1H), 1.99 (ddd, J=4.0, 4.0, 8.5 Hz, 1H), 2.29 (dddd, J=3.0, 6.0, 12.0, 21.5 Hz, 1H), 3.21 (s, 3H), 3.28 (ddd, J=5.0, 10.0, 10.0 Hz, 1H), 3.72 (dd, J=6.5, 12.0 Hz, 1H), 3.92 (m, 5H), 4.73 (d, J=12.0 Hz, 1H), 4.77 (d, J=12.0 Hz, 1H), 5.55 (dd, J=1.0, 10.5 Hz, 1H), 5.92 (dd, J=5.0, 10.5 Hz, 1H), 7.27–7.41 (m, 11H), 7.71 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.2, 24.0, 24.7, 29.7, 33.6, 56.0, 57.8, 64.6, 73.0, 73.1, 74.7, 81.4, 93.0, 127.1, 127.5, 127.6, 127.6, 127.9, 128.1, 129.5, 129.5, 129.9, 133.8, 133.9, 135.7, 137.5, 139.5; IR (film) cm^{-1} 3070m, 2961s, 2857s, 1428m, 1261m, 1102s; mass spectrum (ESI): *m/e* 595.3 $(M+Na)^+$; ESIHRMS *m/e* calcd for $C_{35}H_{44}NaO_5Si$: 595.2850, found: 595.2852.

4.5.8. Spiroketal 52. To the solution of Grubbs' generation-I Ru-catalyst [1.60 mg, 0.0020 mmol] in benzene [3 mL] was added the solution of the mixture of cyclic ketal **50** and diene **46** obtained above in benzene [1.0 mL] at rt. The solution was stirred at rt for 30 min and benzene was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel [gradient eluent: 5–15% EtOAc in hexanes] to provide the desired spiroketal **52** in 50% overall yield [20.8 mg] from **44** as colorless oil in addition to recovered diene **46** [10.0 mg]. R_f=0.65 [25% EtOAc in hexanes]; $[\alpha]_D^{23}$ 11.4 [c 0.63, $CHCl_3$]; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (d, J=7.0 Hz, 3H), 1.04 (s, 9H), 1.56 (ddd, J=4.0, 13.0, 13.0 Hz, 1H), 1.72 (m, 3H), 1.97 (m, 2H), 2.06 (ddd, J=2.0, 7.0, 7.0 Hz, 1H), 3.20 (s, 3H), 3.25 (ddd, J=4.0, 9.5, 9.5 Hz, 1H), 3.47 (ddd, J=6.5, 8.5, 8.5 Hz, 1H), 3.53 (ddd, J=2.5, 9.5, 9.5 Hz, 1H), 3.70 (m, 1H), 3.78 (s, 3H), 3.85 (m, 1H), 3.92 (m, 2H), 4.29 (d, J=12.0 Hz, 1H), 4.32 (d, J=12.0 Hz, 1H), 4.75 (s, 2H), 5.49 (dd, J=2.5, 10.5 Hz, 1H), 5.64 (dd, J=1.5, 10.0 Hz, 1H), 6.84 (d, J=9.0 Hz, 2H), 7.21 (ddd, J=9.0 Hz, 2H), 7.26–7.38 (m, 11H), 7.70 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.7, 19.2, 23.9, 26.9, 33.1, 33.7, 34.4, 55.3, 56.0, 65.0, 67.5, 71.1, 72.7, 73.1, 73.8, 74.7, 81.3, 93.4, 113.7, 127.1, 127.5, 127.6, 127.6, 128.1, 128.6, 129.3, 129.5, 129.5, 130.7, 133.7, 133.9, 134.4, 135.7, 135.8, 139.6, 159.1; IR (film) cm^{-1} 3070m, 2958s, 2930s, 2858s, 1513m, 1249m, 1103s; mass spectrum (APCI): *m/e* (% relative intensity) 751.2 $(M+H)^+$; ESIHRMS *m/e* calcd for $C_{46}H_{58}NaO_7Si$: 773.3844, found: 773.3840.

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