# An Asymmetric Route to Novel Chiral Cyclohexenones with Spiro-Connected Cyclopentenes. Further Utility of Chiral Bicyclic Thiolactams and the [3,3] Thio-Claisen Products

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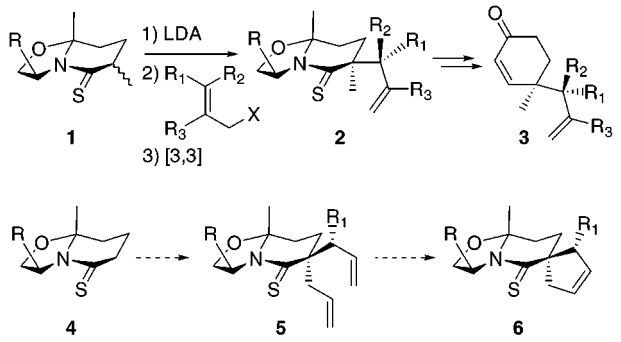
Sequential allylation of chiral, nonracemic thiolactam **8** affords clean thio-Claisen [3,3] products **11**. The stereoselectivity of the rearrangement was found to be on the order of 10−11:1, with the exo-endo products responsible for the mixture. Addition of hydride or methyllithium−cerium chloride gave clean addition to the thiolactam in the form of its iminium salts **12**. Hydrolysis gave 4,4-dialkylcyclohexenones **15**, which were cyclized to the cyclopentene derivatives **16** using Grubbs' catalyst.

We recently described the S-alkylation of α-alkanethiolactam **1** with various allylic halides and the subsequent [3,3]-sigmatropic rearrangement of the resultant intermediate *N*,*S*-ketene acetal to the thiolactam **2**.[1] This resulted in the formation of compounds bearing stereogenic vicinal quaternary centers or vicinal quaternary−tertiary centers. After removal of the chiral auxiliary, access to 4,4-disubstituted enones such as **3** was realized. As a testimony to the usefulness of this method, a more complex system was devised in which vicinal stereogenic quaternary centers were established via the thio-Claisen rearrangement and, ultimately, led to the first complete asymmetric synthesis of the sesquiterpene (−)-trichodiene.[2]




As part of an ongoing research program aimed at further developing the use of chiral nonracemic bicyclic lactams, in their thiocarbonyl form **4**, we were interested in the possibility of performing sequential thio-Claisen rearrangements to produce diastereomeric diallyl compounds such as **5**. The close proximity of the terminal alkene moieties should lend themselves to olefin metathesis[3] to generate novel, chiral spirocyclic substances **6**. We report herein the results of our efforts toward the asymmetric synthesis of diverse novel spirocyclic cyclohexenones, including those bearing additional functionality.

Bicyclic lactam **7**, whose nonracemic chirality was derived from (*R*)-phenylglycine,[4] was thionated using Belleau's reagent[5] in refluxing toluene to afford the thiolactam **8** in 87% yield (Scheme 1). Treatment of **8** with LDA at −78 °C followed by addition of allyl bromide provided a 6:1 mixture of the epimeric thiolactam **9**. The ratio was of no consequence since the next step will generate the planar thioenolate **10a**. When **9** was treated with LDA at −78 °C followed by addition of crotyl bromide **a**, the *N*,*S*-ketene acetal intermediate **10a** was formed. Subsequent heating of the reaction mixture in refluxing THF allowed smooth [3,3]-sigmatropic rearrangement of **10a** to **11a**, as a 9:1 mixture of diastereomers, in 72% isolated yield. The mixture, at this point of our studies, was assumed to be due to exo-endo variants, rather than the stereochemical position of the methyl group in **11a** (vide infra). Attempted ring-closing metathesis of **11a** to form the spirocyclopentene using Grubbs' catalyst[6] led only to recovered starting material, possibly due to the intolerance of sulfur by this catalyst.[7] It was therefore decided to cleave the chiral thiolactam to the cyclohexenone **15a** and attempt the metathesis at that stage. To reach cyclohexenone **15a**, thiolactam **11a** was treated with Meerwein's reagent in refluxing $CH_2Cl_2$. In this way, the *S*-iminium ion **12a** was generated and reduction of the latter with Red-Al furnished the *N*,*S*-ketal **13a**. Buffered hydrolysis ($Bu_4NH_2PO_4$ or $KH_2PO_4$/EtOH/$H_2O$, reflux) of **13a** liberated the ketoaldehyde **14a**, which underwent in situ spontaneous aldol condensation to the enone **15a** in 73% yield for the three-step sequence. Note that **12a**−**14a** were not purified and were used directly to reach ketone **15a.** At this point, treatment of

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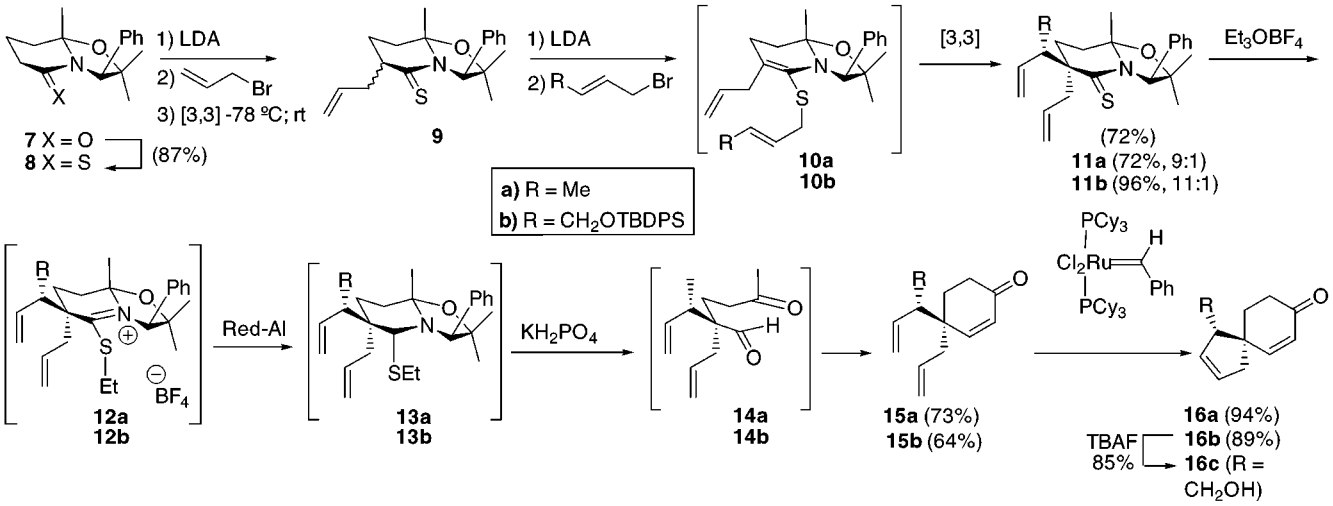
**Scheme 1**

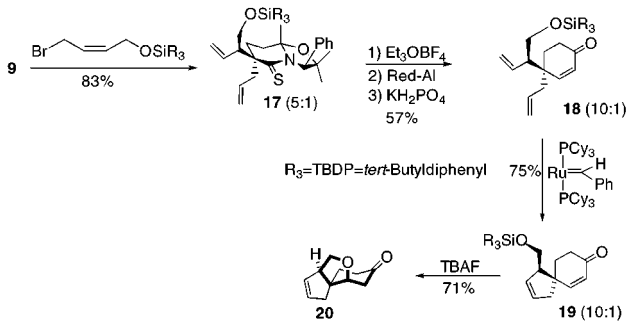



enone **15a** with Grubbs' catalyst (5%) in 1,2-dichloroethane at room temperature for 30 min smoothly effected the olefin metathesis to the desired spiro compound **16a** in 94% yield. It is noteworthy that this facile ring-closure could also be effected with as little as 0.7% catalyst in 3 h at room temperature to provide **16a** in comparable yield (89%). Furthermore, no scrambling of the stereocenter bearing the methyl group took place (NMR, GLC).

Continuing to explore the versatility of this asymmetric route to novel spirocyclohexenones, the process above was repeated with bifunctional allylic halides. Also, both *cis* and *trans* allylic halides were investigated. Using *trans*-4-bromo-2-butene 1-*tert*-butyldiphenylsilyl ether, the thioenol ether **10b** was obtained, which when heated in refluxing THF underwent the [3,3]-rearrangement affording **11b** in 96% yield as an 11:1 mixture of diastereomers. The latter ratio was again assumed at this time to be due to the exo-endo facial rearrangement and not the stereochemical positioning of the substituent (R = $CH_2OSiPh_2Bu^t$) in **11b**. However, it was not possible at this juncture to separate the 11:1 mixture to verify this fact. This stereochemical question will be addressed below. As described for the crotyl series **11a**, the siloxy-containing lactam **11b** was sequentially treated with Meerwein's reagent, Red-Al, and then $KH_2PO_4$. The procedure, without purification of any of the three intermediates, gave the 4,4-dialkylcyclohexenone **15b** in 64% overall yield as a single diastereomer. When the olefin metathesis was employed using Grubbs' catalyst, **16b** was obtained as a single diastereomer in 89% yield. At this point, we felt we could make some progress toward assigning the stereochemistry of the major isomer in **11b** by deprotecting the alcohol to **16c** and determining whether it would conjugatively add to the enone. The siloxy group in **16b** was therefore transformed into the free hydroxyl **16c** (R = $CH_2OH$) using TBAF, and subsequently no conjugate addition was observed. Thus, one can conclude that the hydroxy methyl group in **16c** is anti to the enone and could not cyclize to the five-membered ring ether. However, this negative evidence was deemed to be insufficient for firm stereochemical assignment and would have to await further study.

When the *cis*-allylbromide derived from 1-bromo-4-hydroxy-2-butene, as its *tert*-butyldiphenylsilyl ether, was employed to alkylate **9**, the rearrangement product **17** was obtained in 83% yield as a 5:1 ratio of diastereomers

**Scheme 2**

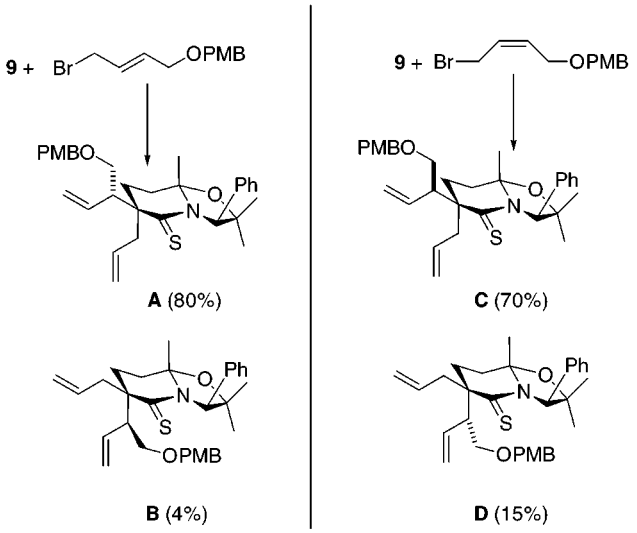



(Scheme 2). Repeating the sequence as above, **17** was transformed into the 4,4-dialkylcyclohexenone **18** (as a 10:1 diastereomeric mixture). There was present 10−15% of *tert*-butyldiphenylsilanol that could not be separated at this stage, and the mixture was carried on to the next step. The crude product **18** was subjected to the metathesis producing the spiroketone **19** in 75% yield as a diastereomeric ratio of 10:1. The silanol impurity was now absent, having been removed by column chromatography. To add further support that the spiroketones derived from the *cis*- and *trans*-allyl bromides differ only at the siloxy methyl group, the silyl group in **19** was cleaved with TBAF leading to a 71% yield of pure tricyclic ether **20**. Thus, it was now reasonably certain that the major component in the two products obtained, **17** and **11b**, was a result of exo-endo rearrangement.

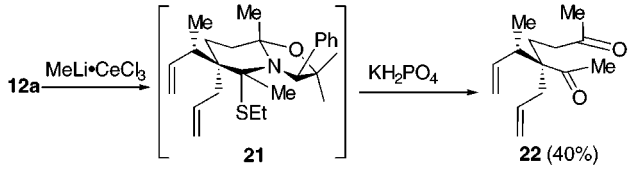
The loss of the minor isomer accompanying **15b** and **18** wherein it appeared that there was an increase in diastereomeric ratios from 5:1→10:1 for **17**→**18** and 11:1 to > 99:1 for **11b**→**15b** will now be addressed. The major reason for these apparent increases may lie in the fact that the thio-Claisen process takes place to produce a small quantity of endo-rearranged product. This minor component contains the large TBDPS substituent in the endo-face that may, due to steric effects, inhibit thione reduction such that only the major exo-substituted material is reduced and hydrolyzed.

Finally, with regard to the stereochemical assignment, another study was added to reaffirm the results. To gather further insight into the stereo assignments resulting from the thio-Claisen rearrangement, the *p*-methoxybenzyl ethers (PMB) of the *cis*- and *trans*-bro-

**Scheme 3**




**Scheme 4**

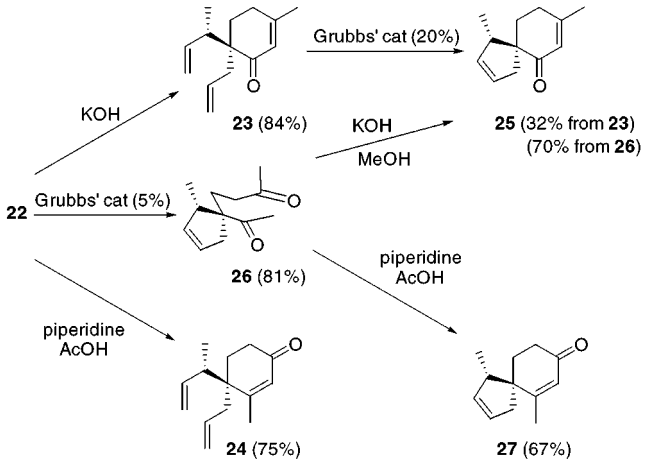



mobutenols were used to alkylate the thiolactam **9** and then subjected to the [3,3] rearrangement (Scheme 3). The reason for utilizing another derivative of the allyl bromide was based entirely on the fact that the major and minor rearranged thiolactams could be readily separated by chromatography unlike the silyl ethers, **11b** and **17**.

As shown in Scheme 3, there are four possible stereoisomers (**A**−**D**) that could be obtained from each of the Claisen rearrangements, using the *cis*- or *trans*-butenyl bromides. However, each rearrangement gave only two of the four possible products, indicating that all four may indeed be different. As stated above, **A**−**D** could be readily separated from their companion products (Scheme 3), and therefore, comparisons could be made of their $^1$H NMR spectra. None of the products were the same, supporting the conclusion made earlier that they indeed were all different, and that the diastereomers obtained with either *cis* or *trans* allylic bromides differed only at the exo-endo face (**A** + **B**) and (**C** + **D**).

To further broaden the scope of this method, it was desirable to add a carbon nucleophile, as opposed to a hydride, to the *S*-iminium ion **12a**, which would generate a diketone instead of the ketoaldehydes after hydrolysis (Scheme 4). Initial attempts to add MeLi to a solution of the *S*-iminium ion **12a** in THF at −78 °C only gave rise to a complex mixture. It was then assumed that deprotonation of the benzylic proton in **12a** could be responsible for the absence of the desired carbonyl addition product, a process observed earlier in a related system.[8] Therefore, when the MeLi·$CeCl_3$ reagent[9] was employed, addition to the *S*-iminium ion occurred smoothly to provide the alkylated intermediate **21**. Buffered hydrolysis, using potassium dihydrogen phosphate, generated

**Scheme 5**




the desired diketone **22** in 40% yield overall from thiolactam **11a**. The success of this addition to the thiocarbonyl group is undoubtedly due to the decreased basicity of the organocerate reagents compared to that of alkyllithium.

Having the key diketone **22** in hand, access to other methyl-substituted spiro compounds (e.g., **25** and **27**) appeared to be within reach. Thus, treatment of **22** with KOH in refluxing MeOH furnished the aldol condensation product **23** in 84% yield (Scheme 5). Similarly, when diketone **22** was heated in refluxing benzene in the presence of piperidine and acetic acid,[10] the regioisomeric enone **24** was obtained as a single compound in good yield (75%). The ring-closure metathesis to these novel products was initially attempted with enone **23**, since it was anticipated that the methyl group in the $\beta$-position of the enone would be less sterically demanding for the metallocycle than the corresponding $\beta$-methyl group in enone **24**. Treatment of **23** with Grubbs' catalyst (5% every 12 h; total of 20%) in refluxing 1,2-dichloroethane for 48 h provided the spiroketone **25**, albeit in low yield (32%). As expected, the olefin metathesis proved very slow and sluggish in these cyclohexenone systems. It was therefore decided to reverse the order of the last two steps leading to the spiro compound and perform the ring-closure metathesis on the *acyclic* precursor to the enones, namely diketone **22**. Thus, when **22** was stirred at room temperature in the presence of Grubbs' catalyst (5%), conversion of the starting material to the cyclopentene **26** was complete in 2 h. It is interesting to note that a small structural change in the substrate, i.e., **22** vs **23**, allowed the same transformation to be effected in a very facile manner. It now remained only to cyclize diketone **26** to the corresponding enones. When **26** was subjected to piperidine and acetic acid in refluxing benzene for 15 h, the spiro compound **27** was obtained in 67% yield. Alternatively, treatment of **26** with KOH in refluxing MeOH[10] for 2 h generated a mixture of **25** (70%) and the regioisomer **27** (20%).

In conclusion, we have shown that the sequential thio-Claisen rearrangement can be utilized to introduce two different allylic moieties in a diastereoselective fashion. Furthermore, the presence of functionality (e.g., OH) on the allylic bromide allows the rearrangement to proceed

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with a high degree of stereoselectivity. The *S*-iminium ions, **12a** and **12b**, derived from the [3,3]-sigmatropic rearrangement product, can undergo nucleophilic addition with a hydride or a carbon nucleophile to generate the corresponding ketoaldehyde **14** or diketone **22**. Finally, the combination of the aldol condensation−olefin metathesis reaction sequence allows entry into a series of chiral spiro[4.5]decane systems.

## Experimental Section

Thin-layer chromatography (TLC) and flash chromatography were performed with E. Merck silica gel (230−400 mesh). TLC grade flash chromatography was performed using Sigma Type H silica gel (10−40 $\mu$m, no binder). All reagents were purchased from Aldrich. All reactions were conducted under an argon atmosphere in oven- or flame-dried apparatus. All solvents and reagents were purified using established procedures. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, GA.

**Bicyclic Thiolactam 8.** To a stirred solution of lactam **7**[4] (2.50 g, 9.64 mmol) in toluene (50 mL) was added Belleau's reagent[5] (3.06 g, 5.78 mmol), and the reaction mixture was heated to reflux for 20 h. The solution was cooled to room temperature, the solvent was removed under reduced pressure, and the acquired residue was subjected to flash chromatography (9:1 Hex/EtOAc) to afford 2.30 g (87%) of the title compound as a colorless solid: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.06 (s, 3H), 1.56 (s, 3H), 1.71 (s, 3H), 1.75−2.16 (m, 3H), 2.19−2.28 (m, 1H), 2.93−3.06 (m, 1H), 3.24 (ddd, $J$ = 18.0, 9.1, 5.7 Hz, 1H), 5.63 (s, 1H), 7.02−7.19 (m, 2H), 7.24−7.38 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 16.5, 26.0, 27.2, 32.0, 36.5, 39.0, 74.8, 81.7, 95.1, 126.5, 127.2, 128.3, 136.7, 198.3; IR (thin film) 1438 cm$^{-1}$; HRMS (EI) for $C_{16}H_{21}NOS$ ($M^+$) calcd 275.1344, found 275.1344; $[\alpha]^{25}_D$ −147 (*c* 1.66, $CHCl_3$).

**Bicyclic Thiolactam 9.** To a cold (−78 °C) stirred solution of LDA (11.1 mmol) in dry THF (100 mL) was added a solution of the thiolactam **8** (2.90 g, 10.5 mmol) in THF (10 mL) via a cannula. The reaction mixture was stirred at −78 °C for 20 min, and then allyl bromide (1.34 g, 0.96 mL, 11.1 mmol) was added via a syringe. The mixture was stirred for 15 min, warmed to room temperature, and then stirred for an additional 20 min. The solution was diluted with EtOAc, and the organic layer was washed with water and brine, dried over $MgSO_4$, and then filtered; the solvent was removed under reduced pressure. $^1$H NMR analysis of the crude product indicated a 6:1 mixture of epimers. The residue acquired was subjected to flash chromatography (gradient elution from 19:1 to 6:1 Hex/EtOAc) to afford two fractions. The first epimer to be eluted afforded 455 mg (14%) of a light yellow oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.02 (s, 3H), 1.51 (s, 3H), 1.53−1.66 (m, 1H), 1.72 (s, 3H), 1.78−1.90 (m, 1H), 1.98−2.13 (m, 1H), 2.21 (ddd, $J$ = 12.5, 7.8, 2.8 Hz, 1H), 2.28−2.38 (m, 1H), 2.58−2.71 (m, 1H), 3.01−3.11 (m, 1H), 5.00−5.14 (m, 2H), 5.64 (s, 1H), 5.76−5.92 (m, 1H), 7.11−7.38 (m, 5H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 22.7, 26.6, 27.1, 31.7, 35.8, 40.1, 44.2, 75.1, 82.0, 95.3, 116.8, 126.7, 127.2, 128.3, 136.6, 136.8, 202.3; IR (thin film) 1639, 1417 cm$^{-1}$. The second epimer to be eluted afforded 2.80 g (84%) of a yellow oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.06 (s, 3H), 1.55 (s, 3H), 1.65 (s, 3H), 1.67−1.83 (m, 2H), 1.93−2.03 (m, 1H), 2.17−2.25 (m, 1H), 2.62−2.73 (m, 1H), 2.74−2.84 (m, 1H), 3.12 (ddd, $J$ = 17.1, 8.6, 3.9 Hz, 1H), 5.10−5.13 (m, 1H), 5.14−5.19 (m, 1H), 5.70−5.85 (m, 2H; therein 5.80 (s, 1H)), 7.02−7.10 (m, 2H), 7.22−7.36 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 22.6, 26.7, 27.7, 32.8, 36.2, 43.2, 48.1, 75.5, 81.8, 94.5, 118.0, 126.0, 127.1, 128.4, 134.9, 137.0, 201.9; IR (thin film) 1640, 1422 cm$^{-1}$.

**Thiolactam 11a.** To a cold (−78 °C) stirred solution of LDA (3.51 mmol) in anhydrous THF (30 mL) was added thiolactam **9** (1.01 g, 3.19 mmol) in THF (5 mL) via a cannula. The reaction mixture was stirred for 20 min, and then crotyl bromide (85% isomeric purity, 0.46 mL, 0.60 g, 4.5 mmol) was added via a syringe. The resulting mixture was warmed to room temperature and then was heated to reflux for 24 h. The solution was cooled to room temperature and was diluted with EtOAc (150 mL). The organic layer was washed with water and brine, dried over $MgSO_4$, and then filtered; the solvent was removed under reduced pressure. $^1$H NMR analysis of the crude product indicated a 9:1 mixture of diastereomers. The oil thus acquired was subjected to flash chromatography (19:1 Hex/EtOAc) to afford 847 mg (72%) of an inseparable mixture of two diastereomers (9:1) as a colorless solid: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.97 (d, $J$ = 6.7 Hz, 3H), 1.03 (s, 3H), 1.49 (s, 3H), 1.60−1.66 (m, 4H; therein 1.63 (s, 3H)), 1.78−2.14 (m, 3H), 2.28 (dd, $J$ = 13.2, 9.6 Hz, 1H), 2.89 (dq, $J$ = 8.9, 6.7 Hz, 1H), 3.12 (dd, $J$ = 13.2, 4.7 Hz, 1H), 4.89−4.96 (m, 1H), 5.01−5.18 (m, 3H), 5.64−5.81 (m, 2H), 5.86 (s, 1H), 7.02−7.35 (m, 5H); $^{13}$C NMR (75 MHz, $CDCl_3$); $\delta$ 16.4, 24.1, 27.66, 27.74, 33.2, 35.2, 51.0, 51.3, 53.1, 76.4, 81.6, 94.0, 117.0, 117.1, 126.2, 127.0, 128.2, 135.8, 137.4, 139.1, 205.2; IR (thin film) 1636, 1404 cm$^{-1}$; HRMS ($FAB^+$) for $C_{23}H_{32}NOS$ ($M + H)^+$ calcd 370.2205, found 370.2202; $[\alpha]^{25}_D$ −68.7 (*c* 1.57, $CHCl_3$).

**(4*R*)-4-Allyl-4-((3*S*)-but-1-en-3-yl)cyclohex-2-enone (15a).** To a stirred solution of thiolactam **11a** (846 mg, 2.29 mmol), as a 9:1 mixture of diastereomers, in anhydrous $CH_2Cl_2$ (25 mL) was added a solution of $Et_3OBF_4$ (2 M in $CH_2Cl_2$, 2.86 mL, 5.72 mmol). The reaction mixture was heated to reflux for 2 h and then was cooled to −78 °C. A solution of Red-Al (3.2 M in toluene, 0.86 mL, 2.8 mmol) was added via a syringe, and the mixture was stirred for 25 min. The reaction mixture was treated with MeOH (0.5 mL), was stirred for an additional 10 min at −78 °C, and then was warmed to room temperature. The solution was diluted with EtOAc (100 mL), the organic layer was washed with water (2 × 10 mL), and the solvent was removed under reduced pressure. The residue acquired was taken in EtOH−$H_2O$ (1:1, 46 mL total), and $Bu_4NH_2PO_4$ buffer (1 M in $H_2O$, 46 mL) was added. The reaction was heated to reflux overnight and then was cooled to room temperature, and the EtOH was removed under reduced pressure. The residue was diluted with water and then was extracted with $Et_2O$. The combined organic layers were washed successively with 1 M HCl, saturated aqueous $NaHCO_3$, $H_2O$, and brine, dried over $MgSO_4$, and then filtered; the solvent was removed under reduced pressure. The residue acquired was subjected to flash chromatography (7:1 Hex/EtOAc) to afford 318 mg (73%) of the title compound as a light yellow oil exhibiting a single diastereomer: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.96 (d, $J$ = 7.0 Hz, 3H), 1.73 (dtd, $J$ = 13.8, 5.9, 1.3 Hz, 1H), 1.97 (ddd, $J$ = 13.8, 10.4, 5.9 Hz, 1H), 2.16−2.51 (m, 5H), 4.96−5.12 (m, 4H), 5.58−5.80 (m, 2H), 5.94 (d, $J$ = 10.0 Hz, 1H), 6.64 (dd, $J$ = 10.0, 2.0 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 15.4, 27.8, 33.9, 40.2, 41.0, 44.1, 116.3, 118.5, 128.8, 133.5, 139.2, 157.0, 199.3; IR (thin film) 1681, 1638 cm$^{-1}$; HRMS ($FAB^+$) for $C_{13}H_{19}O$ ($M + H)^+$ calcd 191.1436, found 191.1441; $[\alpha]^{25}_D$ +42.6 (*c* 1.72, $CHCl_3$).

**(1*S*,5*R*)-1-Methyl-8-oxaspiro[4.5]deca-2,6-diene (16a).** To a degassed (three freeze−pump−thaw cycles) solution of enone **15a** (82.8 mg, 0.435 mmol) in 1,2-dichloroethane (60 mL) was added Grubbs' catalyst (17.9 mg, 0.022 mmol). The reaction mixture was degassed (one cycle) and then was stirred at room temperature for 30 min, at which time the starting material had been completely consumed. The solvent was removed under reduced pressure, the residue acquired was filtered through Florisil ($Et_2O$ as eluant) and the solvent was removed under reduced pressure. The derived oil was distilled (bulb-to-bulb, 150−160 °C/0.5 mmHg) to afford 66.6 mg (94%) of the title compound as a clear colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.97 (d, $J$ = 7.2 Hz, 3H), 1.84−1.94 (m, 1H), 1.98−2.09 (m, 1H), 2.24−2.33 (m, 1H), 2.42 (t, $J$ = 6.6 Hz, 2H), 2.48 (dq, $J$ = 16.1, 2.0 Hz, 1H), 2.54−2.65 (m, 1H), 5.61−5.72 (m, 2H), 5.82 (d, $J$ = 10.0 Hz, 1H), 6.82 (d, $J$ = 10.0 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 15.3, 29.1, 35.5, 42.5, 45.6, 47.9, 126.5, 127.4, 136.0, 160.0, 199.8; IR (thin film) 1682, 1610 cm$^{-1}$; HRMS ($FAB^+$) for $C_{11}H_{15}O$ ($M + H)^+$ calcd 163.1123, found 163.1118; $[\alpha]^{25}_D$ +103 (*c* 1.65, $CHCl_3$).

**(5*S*,6*S*)-5-Acetyl-5-allyl-6-methyloct-7-en-2-one (22).** Cerium trichloride heptahydrate (1.64 g, 4.40 mmol) was dried overnight at 140 °C at 0.1 mmHg. The solids were cooled to

room temperature, and dry THF (20 mL) was added. The resulting suspension was stirred at room temperature for 3 h and was cooled to −78 °C, and then a solution of MeLi (1.40 M in $Et_2O$, 2.83 mL, 3.96 mmol) was added and the slurry was stirred for an additional 1 h at this temperature. In the meantime, to a stirred solution of thiolactam **11a** (615 mg, 1.66 mmol) in dry $CH_2Cl_2$ (20 mL) was added a solution of $Et_3OBF_4$ (2 M in $CH_2Cl_2$, 1.33 mL, 2.66 mmol), and the reaction mixture was heated to reflux for 2 h. The solution was cooled to room temperature and the solvent was removed in vacuo. The residue was rapidly dissolved in dry THF (15 mL) and was cooled immediately to −78 °C. The solution of *S*-iminium ion was added, via a cannula, to the cerium slurry. The resulting mixture was stirred at −78 °C for 10 min and warmed to 0 °C and then was allowed to stir for an additional 1 h. The mixture was diluted with $Et_2O$ and washed with water; the solvent was removed under reduced pressure. The residue thus acquired was dissolved in EtOH/$H_2O$ (1:1, 33 mL total), and a solution of $Bu_4NH_2PO_4$ (1 M in $H_2O$, 33 mL, 33 mmol) was added. The mixture was heated to reflux overnight and cooled to room temperature, and the EtOH was removed under reduced pressure. The aqueous layer was diluted with $H_2O$ and was extracted with $Et_2O$. The combined organic layers were washed successively with 1 M HCl, saturated aqueous $NaHCO_3$, $H_2O$, and brine, dried over $MgSO_4$, and then filtered. The solvent was removed under reduced pressure, and the resulting oil was subjected to flash chromatography (6:1 Hex/EtOAc) to afford 148 mg (40%) of the title compound as a clear colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.97 (d, $J$ = 6.9 Hz, 3H), 1.80 (ddd, $J$ = 14.6, 11.0, 5.5 Hz, 1H), 1.93 (ddd, $J$ = 14.6, 11.0, 4.8 Hz, 1H), 2.08 (s, 3H), 2.10 (s, 3H), 2.19−2.52 (m, 5H), 4.99−5.12 (m, 4H), 5.62−5.82 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 14.4, 25.3, 26.6, 29.1, 36.3, 38.0, 42.7, 55.4, 115.2, 117.1, 133.5, 138.5, 207.1, 210.9; IR (thin film) 1714, 1700, 1637 cm$^{-1}$; HRMS (FAB$^+$) for $C_{14}H_{23}O_2$ (M + H)$^+$ calcd 223.1698, found 223.1692; $[\alpha]^{25}_D$ −33.0 (*c* 1.48, $CHCl_3$).

**(6*S*)-6-Allyl-6-((3*S*)-but-1-en-3-yl)-3-methylcyclohex-2-enone (23).** To a stirred solution of diketone **22** (34.3 mg, 0.154 mmol) in MeOH (5 mL) was added a solution of KOH in MeOH (10%, three drops), and the reaction mixture was heated to reflux for 1 h. The solution was cooled to room temperature, and the solvent was removed under reduced pressure. The residue acquired was subjected to flash chromatography (19:1 Hex/EtOAc) to afford 26.4 mg (84%) of the title compound as a clear colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.94 (d, $J$ = 7.0 Hz, 3H), 1.78 (app dt, $J$ = 13.9, 5.8 Hz, 1H), 1.87 (s, 3H), 1.95 (ddd, $J$ = 13.9, 7.7, 5.9 Hz, 1H), 2.11 (dd, $J$ = 14.0, 7.7 Hz, 1H), 2.23−2.31 (m, 2H), 2.35 (dd, $J$ = 14.0, 6.6 Hz, 1H), 2.70 (app quint, $J$ = 7.0 Hz, 1H), 4.92−5.04 (m, 4H), 5.60−5.79 (m, 3H; therein 5.77 (s, 1H)); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 15.2, 24.0, 27.4, 28.0, 37.5, 40.0, 49.2, 115.7, 117.5, 126.5, 134.3, 139.4, 160.0, 201.8; IR (thin film) 1667 cm$^{-1}$; HRMS (EI) for $C_{14}H_{20}O$ (M$^+$) calcd 204.1514, found 204.1515; $[\alpha]^{25}_D$ −4.5 (*c* 1.39, $CHCl_3$).

**(4*S*)-4-Allyl-4-((3*S*)-but-1-en-3-yl)-3-methylcyclohex-2-enone (24).** To a stirred solution of diketone **22** (23.7 mg, 0.107 mmol) in benzene (5 mL) were added successively piperidine (two drops) and glacial acetic acid (two drops), and the reaction mixture was heated to reflux overnight. The solution was cooled to room temperature and then was diluted with $Et_2O$, and the organic layer was washed with $H_2O$ and brine, dried over $MgSO_4$, and then filtered; the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (12:1 Hex/EtOAc) to afford 16.4 mg (75%) of the title compound as a clear colorless oil. $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.93 (d, $J$ = 6.9 Hz, 3H), 1.70 (dt, $J$ = 14.1, 6.2 Hz, 1H), 1.91 (s, 3H), 1.99 (ddd, $J$ = 13.9, 10.6, 5.8 Hz, 1H), 2.26−2.55 (m, 5H), 4.97−5.14 (m, 4H), 5.64−5.84 (m, 2H), 5.96 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 16.3, 20.5, 27.3, 34.6, 42.8, 44.7, 44.8, 116.7, 117.9, 130.3, 134.7, 139.1, 165.2, 199.2; IR (thin film) 1668 cm$^{-1}$; HRMS (EI) for $C_{14}H_{20}O$ (M$^+$) calcd 204.1514, found 204.1512; $[\alpha]^{25}_D$ +53.2 (*c* 1.02, $CHCl_3$).

**(1*S*,5*S*)-1,8-Dimethyl-6-oxaspiro[4.5]deca-2,7-diene (25).** To a stirred solution of the diketone **23** (30.3 mg, 0.156 mmol) in MeOH (5 mL) was added a solution of KOH in MeOH (10%, three drops), and the mixture was heated to reflux for 2 h. The solution was cooled to room temperature, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (19:1 then 9:1 Hex/EtOAc) to afford 19.3 mg (70%) of the title compound as a clear colorless oil and 5.5 mg (20%) of the regioisomeric enone **27** (vide infra): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.91 (d, $J$ = 7.3 Hz, 3H), 1.80−1.96 (m, 5H; therein 1.91 (s, 3H)), 2.17−2.46 (m, 4H), 3.28−3.40 (m, 1H), 5.42−5.49 (m, 1H), 5.55−5.62 (m, 1H), 5.81 (s, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 15.1, 23.9, 28.2, 28.9, 40.4, 43.2, 52.7, 125.0, 125.5, 136.4, 160.0, 202.4; IR (thin film) 1666 cm$^{-1}$; HRMS (EI) for $C_{12}H_{16}O$ (M$^+$) calcd 176.1201, found 176.1201; $[\alpha]^{25}_D$ +167 (*c* 0.93, $CHCl_3$).

**(3*S*)-3-((2*S*)-2-Methylcyclopent-3-ene-1,1-diyl)hepta-2,7-dione (26).** To a degassed (three freeze−pump−thaw cycles) solution of diketone **22** (90.1 mg, 0.405 mmol) in 1,2-dichloroethane (60 mL) was added Grubbs' catalyst (17 mg, 0.020 mmol). The solution was degassed (one cycle) and stirred at room temperature for 2 h, and then the solvent was removed under reduced pressure. The residue was filtered through Florisil ($Et_2O$ as eluent), and the solvent was removed under reduced pressure. The derived oil was subjected to flash chromatography (6:1 Hex/EtOAc) to afford 63.3 mg (81%) of the title compound as a clear colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.99 (d, $J$ = 7.3 Hz, 3H), 1.69−1.81 (m, 1H), 1.91−2.14 (m, 8H; therein 2.07 (s, 3H), 2.09 (s, 3H)), 2.23 (t, $J$ = 7.9 Hz, 2H), 2.79−2.87 (m, 2H), 5.45−5.59 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 15.1, 25.6, 25.9, 29.9, 38.6, 39.8, 44.8, 60.3, 127.7, 135.0, 207.9, 211.5; IR (thin film) 1715, 1704 cm$^{-1}$; HRMS (FAB$^+$) for $C_{12}H_{19}O_2$ (M + H)$^+$ calcd 195.1385, found 195.1390; $[\alpha]^{25}_D$ +15.3 (*c* 1.43, $CHCl_3$).

**(1*S*,5*S*)-1,6-Dimethyl-8-oxaspiro[4.5]deca-2,6-diene (27).** To a stirred solution of the diketone **26** (25.2 mg, 0.130 mmol) in benzene (5 mL) were added successively piperidine (two drops) and glacial acetic acid (two drops), and the reaction mixture was heated to reflux overnight. The solution was cooled to room temperature and was diluted with $Et_2O$. The organic layer was washed with $H_2O$ and brine and dried over $MgSO_4$, and after filtration, the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (9:1 Hex/EtOAc) to afford 15.3 mg (67%) of the title compound as a clear colorless oil: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 0.99 (d, $J$ = 7.4 Hz, 3H), 1.81−1.92 (m, 4H; therein 1.89 (d, $J$ = 1.5 Hz, 3H)), 1.96−2.08 (m, 1H), 2.32−2.50 (m, 4H), 2.89−3.01 (m, 1H), 5.58−5.66 (m, 2H), 5.78 (d, $J$ = 1.5 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 15.5, 21.1, 29.4, 35.0, 42.5, 45.8, 48.4, 127.0, 127.5, 136.2, 168.2, 199.5; IR (thin film) 1672, 1610 cm$^{-1}$; HRMS (EI) for $C_{12}H_{16}O$ (M$^+$) calcd 176.1201, found 176.1202; $[\alpha]^{25}_D$ +90.1 (*c* 1.01, $CHCl_3$).

**4-Bromo-2(*E*)-butene 1-*tert*-Butyldiphenylsilyl Ether.** A solution of known 4-*tert*-butyldiphenylsiloxy-2(*E*)-buten-1-ol[11] (1.01 g, 3.10 mmol) in $CH_2Cl_2$ (20 mL) was added dropwise via cannula to a suspension of NBS (1.16 g, 6.51 mmol) and dimethyl sulfide (0.58 mL, 7.90 mmol) with stirring in cold (0 °C) $CH_2Cl_2$ (15 mL). The mixture was allowed to warm to room temperature and stirred for an additional 1 h. The resulting suspension was diluted with ether and washed with brine, and the combined organic extracts were concentrated in vacuo. Purification by column chromatography (6:1 Hex/EtOAc) afforded the desired *trans* bromide (0.927 mg, 77%), which was immediately carried on into the next reaction: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.06 (s, 9H), 3.98 (dd, $J$ = 7.5, 1.1 Hz, 2H), 4.20−4.24 (m, 2H), 5.84 (dt, $J$ = 15.0, 4.4 Hz, 1H), 6.02 (dtt, $J$ = 15.0, 7.5, 1.9 Hz, 1H), 7.33−7.46 (m, 6H), 7.67 (dd, $J$ = 7.7, 1.8 Hz, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.2, 26.8 (3C), 32.5, 63.2, 125.8, 127.7 (4C), 129.7 (2C), 133.4 (2C), 134.2, 135.5 (4C).

**Thiolactam 11b.** To a solution of LDA (2.42 mmol) in anhydrous THF (15 mL) at −78 °C was added thiolactam **9** (548 mg, 1.74 mmol) in THF (10 mL) via cannula. After being stirred for 40 min, the mixture was treated with 4-bromo-2(*E*)-

(11) Roush, W. R.; Straub, J. A.; Van Nieuwenhze, M. S. *J. Org. Chem.* **1991**, *56*, 1636−1648.

butene 1-*tert*-butyldiphenylsilyl ether (898 mg, 2.31 mmol) as described above. The resulting solution was warmed to room temperature and allowed to stir until complete conversion to *N*,*S*-ketene acetal **10b** was observed by TLC analysis (1 h, 9:1 Hex/EtOAc). The reaction mixture was then heated to reflux for 20 h. The resulting solution was cooled to room temperature, washed with $H_2O$, and extracted with ether. Concentration of the organic extracts in vacuo provided a crude oil, which indicated an 11:1 mixture of diastereomers by $^1$H NMR analysis. Further purification by column chromatography (9:1 Hex/EtOAc) afforded 1.04 g (96%) of an inseparable mixture of two diastereomers (11:1 thiolactam **11b**/diastereomer) as a white foam: $^1$H NMR of the 11:1 mixture with only the major signals being reported (300 MHz, $CDCl_3$) $\delta$ 1.00 (s, 3H), 1.04 (s, 9H), 1.42 (s, 3H), 1.49 (s, 3H), 1.77, (dt, $J$ = 13.8, 3.4 Hz, 1H), 1.88−2.14 (m, 3H), 2.36 (dd, $J$ = 13.2, 9.3 Hz, 1H), 3.01−3.12 (m, 2H), 3.67 (dd, $J$ = 9.3, 8.4 Hz, 1H), 3.85 (dd, $J$ = 9.6, 4.1 Hz, 1H), 4.96 (br d, $J$ = 10.1 Hz, 1H), 5.08 (br d, $J$ = 17.0 Hz, 1H), 5.27 (dd, $J$ = 11.8, 2.0 Hz, 1H), 5.32 (dd, $J$ = 5.5, 2.0 Hz, 1H), 5.64−5.86 (m, 2H), 5.78 (s, 1H), 6.88 (d, $J$ = 7.5 Hz, 2H), 6.98−7.16 (m, 3H), 7.24−7.43 (m, 6H), 7.58−7.70 (m, 4H); $^{13}$C NMR selected (75 MHz, $CDCl_3$) $\delta$ 19.3, 25.4, 26.9 (3C), 27.3, 27.7, 33.1, 35.2, 51.3, 51.9, 58.9, 64.0, 76.4, 81.6, 94.0, 117.3, 120.4, 125.9 (2C), 126.7, 127.6 (2C), 127.6 (2C), 128.2 (2C), 129.5, 129.6, 133.3, 134.0, 135.5, 135.7 (2C), 135.7 (2C), 135.9, 137.2, 204.4; IR (thin film) 1402 cm$^{-1}$; HRMS (FAB$^+$) for $C_{39}H_{49}NO_2SiS$ (M + H)$^+$ calcd 624.3332, found 624.3310.

**Cyclohexenone 15b.** To a stirred solution of thiolactam **11b** (957 mg, 1.54 mmol), as an 11:1 mixture of diastereomers in anhydrous $CH_2Cl_2$ (20 mL), was added a solution of $Et_3OBF_4$ (2 M in $CH_2Cl_2$, 1.92 mL, 3.84 mmol). The reaction mixture was heated to reflux for 2 h and then was cooled to −78 °C. A solution of Red-Al (3.12 M in toluene, 0.65 mL, 2.03 mmol) was added via syringe, and the mixture was stirred for 40 min. The latter was quenched with MeOH (0.5 mL), stirred for an additional 10 min at −78 °C, and then warmed to room temperature. The solution was diluted with EtOAc, and the organic layer was washed with $H_2O$. Concentration of the organic extracts in vacuo provided a crude oil that was dissolved in EtOH−$H_2O$ (1:1, 38 mL total) followed by the addition of $KH_2PO_4$ buffer (1 M in $H_2O$, 38 mL). The resulting suspension was heated to reflux for 20 h and cooled to room temperature, and the EtOH was removed under reduced pressure. The residue was diluted with $H_2O$ and extracted with ether. The combined organic layers were concentrated in vacuo, and the resulting crude oil was shown by $^1$H NMR analysis to be composed of a 2.8:1.0 mixture of aldehyde **14b**/enone **15b**. This mixture was immediately dissolved in MeOH (5 mL) and treated with 0.1 M KOH in MeOH (5 mL). The mixture was heated to reflux for 2 h, cooled to room temperature, and quenched with saturated $NH_4Cl$. Extraction with ether, concentration in vacuo, and purification by column chromatography (6:1 Hex/EtOAc) afforded cyclohexenone **15b** (439 mg, 64%), which was a 4:1 mixture with *tert*-butyldiphenylsilyl alcohol. These compounds were not readily separated by column chromatography: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.03 (s, 9H), 1.78 (dddd, $J$ = 13.8, 5.7, 5.7, 1.2 Hz, 1H), 2.02 (ddd, $J$ = 13.8, 10.8, 5.5 Hz, 1H), 2.25−2.32 (m, 2H), 2.33−2.45 (m, 3H), 3.71 (d, $J$ = 5.7 Hz, 2H), 4.98−5.10 (m, 2H), 5.15 (dd, $J$ = 17.0, 2.0 Hz, 1H), 5.24 (dd, $J$ = 10.3, 2.0 Hz, 1H), 5.60−5.82 (m, 2H), 5.89 (d, $J$ = 10.2 Hz, 1H), 6.61 (dd, $J$ = 10.4, 1.2 Hz, 1H), 7.35−7.45 (m, 6H), 7.61−7.66 (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.2, 26.8 (3C), 28.6, 33.9, 40.4, 40.8, 52.8, 64.2, 118.8, 119.3, 127.7 (4C), 128.4, 129.7, 129.7, 129.7, 133.2, 133.3, 133.3, 135.6 (2C), 135.7 (2C), 157.5, 199.3; IR (thin film) 1682 cm$^{-1}$; HRMS (FAB$^+$) for $C_{29}H_{37}O_2Si$ (M + H)$^+$ calcd 445.2563, found 445.2566.

***tert*-Butyldiphenylsilyl alcohol:** $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.06 (s, 9H), 2.26 (br s, 1H), 7.32−7.41 (m, 6H), 7.68−7.72 (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.0, 26.5 (3C), 127.7 (2C), 129.6, 134.8 (2C), 135.2; IR (thin film) 3422 (br) cm$^{-1}$.

**Cyclopentene 16b.** To a solution of enone **15b** (335 mg, 0.755 mmol) in degassed 1,2-dichloroethane (10.8 mL, degassed by bubbling through Ar(g) for 30 min) was added Grubbs' catalyst (62.7 mg, 0.076 mmol). The reaction mixture was stirred at room temperature for 4 h, and the solvent was subsequently removed under reduced pressure. Purification by column chromatography (6:1 Hex/EtOAc) afforded the desired spiro compound **16b** as an oil (280 mg, 89%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.03 (s, 9H), 1.96 (ddd, $J$ = 13.3, 6.5, 6.5 Hz, 1H), 2.21 (dd, $J$ = 13.3, 6.6, 6.6 Hz, 1H), 2.31 (br d, $J$ = 16.5 Hz, 1H), 2.41−2.48 (m, 2H), 2.57 (ddd, $J$ = 16.3, 4.3, 2.1 Hz, 1H), 2.70−2.77 (m, 1H), 3.65 (dd, $J$ = 10.4, 6.4 Hz, 1H), 3.70 (dd, $J$ = 10.6, 5.8 Hz, 1H), 5.63−5.68 (m, 1H), 5.76−5.81 (m, 1H), 5.85 (d, $J$ = 10.1 Hz, 1H), 6.84 (d, $J$ = 10.1 Hz, 1H), 7.34−7.46 (m, 6H), 7.62−7.67 (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.1, 26.7 (3C), 28.6, 35.5, 43.3, 45.3, 56.0, 63.3, 126.4, 127.6 (4C), 129.7, 129.7, 129.9, 131.4, 133.2, 133.3, 135.5 (2C), 135.6 (2C), 159.7, 199.8; IR (thin film) 1674 cm$^{-1}$; HRMS (FAB$^+$) for $C_{27}H_{33}O_2Si$ (M + H)$^+$ calcd 417.2250, found 417.2260; $[\alpha]^{25}_D$ +17.6 (*c* 1.06, $CHCl_3$).

**Alcohol 16c.** Enone **16b** (254 mg, 0.610 mmol) was dissolved in THF (8 mL) and treated with TBAF (1.6 mL of a 1 M solution in THF, 1.6 mmol). The reaction mixture was allowed to stir for 2 h at room temperature, quenched by additon of saturated $NH_4Cl$, and extracted with ether. After concentration in vacuo, purification of the resulting oil by column chromatography (1.3:1.0 Hex/EtOAc) afforded the desired alcohol **16c** as a clear oil (92.5 mg, 85%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 2.00−2.11 (m, 2H), 2.25 (ddd, $J$ = 13.5, 8.7, 5.5 Hz, 1H), 2.34 (br d, $J$ = 16.4 Hz, 1H), 2.44−2.53 (m, 2H), 2.58 (ddd, $J$ = 16.5, 4.4, 2.2 Hz, 1H), 2.66−2.73 (m, 1H), 3.71 (d, $J$ = 5.1 Hz, 2H), 5.70−5.76 (m, 1H), 5.85 (d, $J$ = 10.0 Hz, 1H), 5.88−5.94 (m, 1H), 6.86 (d, $J$ = 10.2 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 28.9, 35.6, 43.8, 45.0, 55.5, 62.0, 126.3, 130.6, 131.2, 159.6, 199.9; IR (thin film) 3418 (br), 1668 cm$^{-1}$; HRMS (FAB$^+$) for $C_{11}H_{15}O_2$ (M + H)$^+$ calcd 179.1072, found 179.1075; $[\alpha]^{25}_D$ +46.3 (*c* 2.21, $CHCl_3$).

**4-Bromo-2(*Z*)-buten-1-*tert*-butyldiphenylsilyl Ether.** A solution of known 4-*tert*-butyldiphenylsiloxy-2(*Z*)-buten-1-ol[11] (3.18 g, 9.74 mmol) in $CH_2Cl_2$ (20 mL) was added dropwise via cannula to a suspension of NBS (3.64 g, 20.5 mmol) and dimethyl sulfide (1.86 mL, 25.3 mmol) with stirring in cold $CH_2Cl_2$ (0 °C, 40 mL). The mixture was allowed to warm to room temperature and stirred for an additional 1 h. The resulting suspension was diluted with ether and washed with brine, and the combined organic extracts were concentrated in vacuo. Purification by column chromatography (6:1 Hex/EtOAc) afforded the desired *cis* bromide (3.26 g, 86%), which was immediately carried on into the next reaction: $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.05 (s, 9H), 3.85 (dd, $J$ = 5.5, 2.0 Hz, 2H), 4.32 (d, $J$ = 4.2 Hz, 2H), 5.70−5.76 (m, 2H), 7.36−7.45 (m, 6H), 7.68 (dd, $J$ = 7.7, 1.8 Hz, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.1, 26.8 (3C), 26.8, 59.7, 126.2, 127.7 (4C), 129.7 (2C), 133.3, 133.7 (2C), 135.5 (4C).

**Thiolactam 17.** To a solution of LDA (1.90 mmol) in anhydrous THF (10 mL) at −78 °C was added thiolactam **9** (407 mg, 1.29 mmol) in THF (5 mL) via cannula. After being stirred for 40 min, the reaction mixture was treated with 4-bromo-2(*Z*)-butene 1-*tert*-butyldiphenylsilyl ether (739 mg, 1.90 mmol) as described above. The resulting solution was warmed to room temperature and allowed to stir until complete conversion to the thioether intermediate was observed by TLC analysis (9:1 Hex/EtOAc). The solution was subsequently diluted with ether, washed with saturated $NH_4Cl$, and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residual yellow oil was dissolved in dry DMF (10 mL), anhydrous $K_2CO_3$ (270 mg, 1.95 mmol) was added, and the resulting suspension was heated to 100 °C for 20 h. The reaction mixture was then cooled to room temperature, diluted with ether, and washed with $H_2O$. The organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. $^1$H NMR analysis of the resulting crude oil indicated a 5:1 mixture of diastereomers. Further purification by column chromatography (9:1 Hex/EtOAc) afforded 669 mg (83%) of an inseparable mixture of two diastereomers (5:1 thiolactam **17**/diastereomer) as a white foam: $^1$H NMR of the 5:1 mixture with only the major signals reported (300 MHz, $CDCl_3$) $\delta$ 1.05 (s, 9H), 1.06 (s, 3H), 1.52 (s, 3H), 1.57 (s, 3H), 1.78−2.20 (m, 4H), 2.39 (dd, $J$ = 13.1, 9.4 Hz, 1H), 3.05−3.18 (m, 2H), 3.84

(dd, $J$ = 10.5, 6.7 Hz, 1H), 3.92 (dd, $J$ = 10.5, 4.6 Hz, 1H), 4.93−5.37 (m, 4H), 5.66−5.84 (m, 1H), 5.88 (s, 1H), 5.86−6.04 (m, 1H), 7.06−7.12 (m, 2H), 7.23−7.46 (m, 9H), 7.65−7.74 (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.2, 25.9, 26.8(3C), 27.4, 27.7, 33.2, 35.1, 49.6, 53.1, 57.1, 63.1, 76.0, 81.4, 93.9, 117.2, 119.6, 126.5, 127.0, 127.7(2C), 128.0, 129.7, 133.4, 133.5, 135.7, 135.7, 135.8, 135.9, 136.2, 137.2, 204.0; IR (thin film) 1407 cm$^{-1}$; HRMS (FAB$^+$) for $C_{39}H_{49}NO_2SiS$ (M + H)$^+$ calcd 624.3332, found 624.3319.

**Cyclohexenone 18.** To a stirred solution of the thiolactam 5:1 mixture **17** (1.48 g, 2.37 mmol), in anhydrous $CH_2Cl_2$ (20 mL), was added a solution of $Et_3OBF_4$ (2 M in $CH_2Cl_2$, 3.00 mL, 6.00 mmol). The reaction mixture was heated to reflux for 2 h and then cooled to −78 °C. A solution of Red-Al (3.12 M in toluene, 0.96 mL, 3.00 mmol) was subsequently added via syringe, and the reaction mixture was allowed to stir for 40 min. The resulting solution was quenched with MeOH (0.5 mL), stirred for an additional 10 min at −78 °C, and then warmed to room temperature. The solution was then diluted with EtOAc, and the organic layer was washed with $H_2O$. Concentration of the organic extracts in vacuo provided a crude oil that was redissolved in EtOH−$H_2O$ (1:1, 60 mL total) followed by the addition of $KH_2PO_4$ buffer (1 M in $H_2O$, 60 mL). The resulting suspension was heated to reflux for 20 h and cooled to room temperature with the EtOH being removed under reduced pressure. The residue was diluted with $H_2O$ and extracted with ether. The combined organic extracts were concentrated in vacuo, and the crude oil obtained was shown by $^1$H NMR analysis to be composed of a 1.4:1.0 mixture of intermediate ketoaldehyde/enone **18**. The crude oil was dissolved in MeOH (5 mL) and treated with 0.1 M KOH in MeOH (5 mL). The resulting suspension was heated to reflux for 2 h, cooled to room temperature, and quenched with saturated $NH_4$Cl. Extraction with ether, concentration in vacuo, and purification by column chromatography (6:1 Hex/EtOAc) afforded cyclohexenone **18** (599 mg, 57%) as a 10:1 mixture of diastereomers as observed by $^1$H NMR analysis. Enone **18** was also not readily separated from *tert*-butyldiphenylsilyl alcohol (7:1 enone **18**/silyl alcohol), which is a minor byproduct of the hydrolysis reaction: $^1$H NMR of the 10:1 mixture with only the major signals being reported (300 MHz, $CDCl_3$) $\delta$ 1.04 (s, 9H), 1.84 (ddd, $J$ = 13.8, 6.8, 6.8 Hz, 1H), 1.96 (ddd, $J$ = 13.8, 6.8, 6.8 Hz, 1H), 2.18−2.51 (m, 5H), 3.70 (dd, $J$ = 10.5, 6.6 Hz, 1H), 3.80 (dd, $J$ = 10.5, 5.2 Hz, 1H), 5.02 (dd, $J$ = 16.8, 1.6 Hz, 1H), 5.07 (dd, $J$ = 10.2, 2.0 Hz, 1H), 5.12 (dd, $J$ = 17.0, 1.5 Hz, 1H), 5.20 (dd, $J$ = 10.4, 1.9 Hz, 1H), 5.86 (d, $J$ = 10.4 Hz, 1H), 5.60−5.91 (m, 2H), 6.79 (d, $J$ = 10.4 Hz, 1H), 7.34−7.44 (m, 6H), 7.64 (dd, $J$ = 7.8, 1.8 Hz, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.2, 26.8 (3C), 29.5, 33.6, 40.1, 40.3, 52.5, 63.6, 118.7, 118.7, 127.7 (4C), 127.9, 129.7, 129.8, 133.2, 133.6 (2C), 135.6 (2C), 135.6 (2C), 136.0, 157.4, 199.2; IR (thin film) 1679 cm$^{-1}$; HRMS (FAB$^+$) for $C_{29}H_{37}O_2Si$ (M + H)$^+$ calcd 445.2563, found 445.2565.

**Spirocyclopentene 19.** To a solution of enone **18** (331 mg, 0.745 mmol) in degassed 1,2-dichloroethane (10.6 mL) was added Grubbs' catalyst (61.6 mg, 0.075 mmol). The reaction mixture was stirred at room temperature for 3 h, and the solvent was subsequently removed under reduced pressure. Purification by column chromatography (6:1 Hex/EtOAc) afforded the desired spiro compound **19** (232 mg, 75%) as a 10:1 mixture of diastereomers by $^1$H NMR analysis. This accounts for an 81% yield of the diastereomeric mixture due to contamination of the starting enone with *tert*-butyldiphenylsilyl alcohol (7:1 enone **18**/silyl alcohol): $^1$H NMR of the 10:1 mixture with only the major signals being reported (300 MHz, $CDCl_3$) $\delta$ 1.03 (s, 9H), 1.95 (ddd, $J$ = 13.2, 6.8, 6.8 Hz, 1H), 2.09 (ddd, $J$ = 13.2, 6.8, 6.8 Hz, 1H), 2.35−2.45 (m, 3H), 2.58 (ddd, $J$ = 16.5, 4.8, 2.4 Hz, 1H), 2.75−2.83 (m, 1H), 3.65 (d, $J$ = 5.7 Hz, 2H), 5.63−5.68 (m, 1H), 5.76−5.81 (m, 1H), 5.92 (d, $J$ = 10.2 Hz, 1H), 7.03 (d, $J$ = 10.2 Hz, 1H), 7.33−7.44 (m, 6H), 7.60−7.67 (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 19.1, 26.7(3C), 34.9, 35.8, 45.1, 46.0, 57.3, 63.9, 127.6(2C), 127.6, 128.2, 129.7, 129.7, 129.8, 131.0, 133.1, 133.3, 135.5(2C), 135.6-(2C), 156.4, 199.7; IR (thin film) 1681 cm$^{-1}$; HRMS (FAB$^+$) for $C_{27}H_{33}O_2Si$ (M + H)$^+$ calcd 417.2250, found 417.2252.

**Cyclohexanone 20.** The spirocyclopentene *tert*-butyldiphenylsilyl ether **19** (205 mg, 0.492 mmol) was dissolved in THF (10 mL) and treated with TBAF (1.25 mL of a 1 M solution in THF, 1.25 mmol). The mixture was allowed to stir for 4 h at room temperature, quenched by addition of saturated $NH_4$Cl, and extracted with ether. After concentration of the organic extracts in vacuo, purification of the resulting oil by column chromatography (3:1 Hex/EtOAc) afforded the cyclized product **20** as a single diastereomer by $^1$H NMR analysis (62.2 mg, 71%): $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 1.87−2.07 (m, 2H), 2.24−2.52 (m, 4H), 2.61 (dd, $J$ = 16.5, 3.8 Hz, 1H), 2.70 (dd, $J$ = 16.6, 3.5 Hz, 1H), 3.12−3.21 (m, 1H), 3.42 (dd, $J$ = 8.8, 6.4 Hz, 1H), 3.85 (dd, $J$ = 3.6, 3.6 Hz, 1H), 4.19 (dd, $J$ = 8.4, 8.4 Hz, 1H), 5.62−5.70 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ 32.1, 36.5, 41.8, 43.6, 51.7, 59.1, 72.5, 83.7, 129.1, 131.8, 210.4; IR (thin film) 1715 cm$^{-1}$; HRMS (FAB$^+$) for $C_{11}H_{14}O_2$ (M + H)$^+$ calcd 179.1072, found 179.1073; $[\alpha]^{25}_D$ +57.9 (*c* 1.39, $CHCl_3$).

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**Supporting Information Available:** Spectral data ($^1$H and $^{13}$C) of all key intermediates. This material is available free of charge via the Internet at http://pubs.acs.org.

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