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Seven-Membered Ring Formation from Cyclopropanated Oxo- and Epoxyallylsilanes

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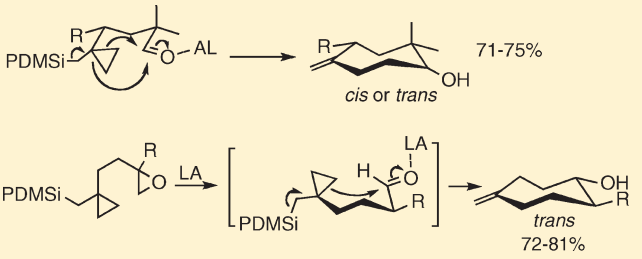
Supporting Information

ABSTRACT: A useful strategy for cycloheptane annulations from oxo- and epoxyallylsilanes, prepared by silylcupration of allenes, has been developed, and their application to the stereoselective synthesis of 4-methylenecycloheptan-1-ols is of great potential in the construction of seven-membered ring natural products presented.



During the past decade, chemists have witnessed a rapid development of organosilicon chemistry, which has proven to be very powerful in modern organic synthesis.[1] Many valuable natural product syntheses have been possible thanks to the outstanding chemical behavior of silicon compounds.[2] In particular, the chemistry of allylsilanes is probably the most useful and widely used in synthesis due to the increasing number of novel methodologies that allow relevant transformations.[3] Consequently, a great deal of effort has been directed to find new routes for the preparation of these powerful intermediates. Silylcupration of dienes and acetylenes is one of the most attractive strategies for the efficient preparation of allyl- and vinylsilanes, providing an easy entry to silicon-containing products.[4] Some of these developments have been summarized in a recent review, in which we report the scope of the silylcupration of allenes, the interest of this method for the preparation of functionalized allylsilanes, and their application to the synthesis of natural products.[5]

Functionalized allylsilanes containing electrophilic groups in their structure are readily available from allenes by silylcupration and further reaction with electrophiles.[6] They undergo *intramolecular allylsilane-terminated cyclizations* when treated with Lewis acid, affording carbocyclic structures of different size.[6,7] Oxoallylsilanes lead to cyclopentane annulation[6] or spiro-cyclopropanation[8] depending on the reaction conditions, whereas epoxyallylsilanes give methylenecyclohexanols following an unusual rearrangement–cyclization pathway.[9] In a brief review, we have reported the relevancy of the *silylcuprate strategy* in the synthesis of three- to seven-membered rings.[10] More recently, we published the first total synthesis of (−)-nomadone, the principal component of the mandibular secretion that rules the territorial behavior of the *Nomada* bees, by Pd-catalyzed cross-coupling of allylsilane–vinylcopper species and vinyl halides.[11]

In the aim of contributing to find new routes for silicon-assisted synthesis of natural products, we now report an unprecedented and stereoselective seven-membered ring formation by cyclopropanation of oxo- and epoxyallylsilanes, which might be of interest in the approach to cycloheptane-containing naturally occurring products. Although synthetic approaches to seven-membered ring systems via cyclization reactions from acyclic substrates are abundant and the number of stereoselective methods for preparing the seven-membered carbocycles has increased in the last years,[12] the metal-mediated approach to the synthesis of medium-sized rings was just recently faced.[13]

Oxoallylsilanes (**2**) and epoxyallylsilanes (**3**) are easily prepared from 1,2-propadiene and lower-order cyanosilylcuprates of type **1**, followed by reaction of the resulting vinylcopper–allylsilane intermediate with α,β-unsaturated ketones and ulterior epoxidation with sulfur ylides (Scheme 1).[6a,9a,9c]

Silylcupration of 1,2-propadiene is a reversible process whose regiochemistry depends on the reaction temperature and the nature of cuprate. Using low temperatures and lower-order cuprates, exclusive formation of the kinetic intermediate (the vinylcopper–allylsilane species) is ensured.[14]

Oxoallylsilanes **2a**–**d** (Table 1) in THF were treated with dimethylsulfonium methylide at 0 °C for 1 h. By warming up the mixture to room temperature with additional stirring of 1 h, epoxyallylsilanes **3a**–**d** were obtained in good yield (Table 1). Compounds **3a**–**d** in DCM reacted with a mixture 2 equiv of CH_2I_2 and 3 equiv of Me_3Al (a modified version of the Yamamoto reagent) at −60 °C. The mixture was left to warm to rt and kept at this temperature for 50 h with stirring. Workup of the crude (Et_3N/H_2O (1:3) at −20 °C and purification of the residue (silica gel, EtOAc/hexane) gave the cyclopropanated hydroxysilanes **4a**–**d** (eq 1, Table 1). Formation of cyclopropylhydroxysilanes **4** occurs probably by simultaneous attack of the Yamamoto reagent to both the epoxide and the alkene

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Scheme 1

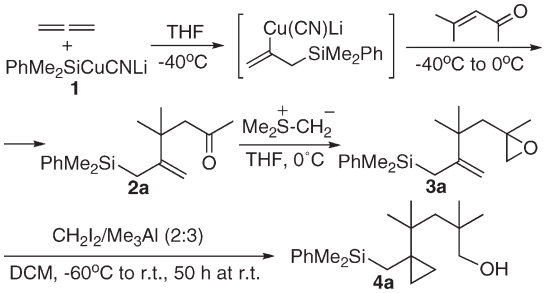
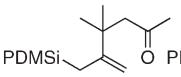
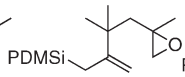
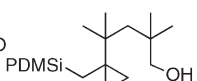
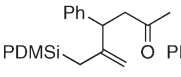
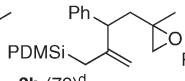
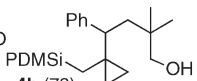
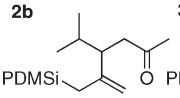
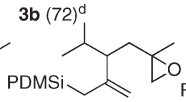
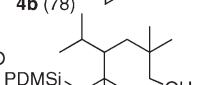
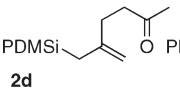
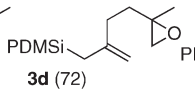
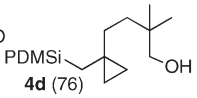


Table 1. Cyclopropylhydroxysilanes 4 from Epoxyallylsilanes 3

Oxoallylsilane[a]	Epoxyallylsilane (%)[b]	4 (%)[c]
 **2a**	 **3a** (78)	 **4a** (74)
 **2b**	 **3b** (72)[d]	 **4b** (78)
 **2c**	 **3c** (74)[d]	 **4c** (72)
 **2d**	 **3d** (72)	 **4d** (76)

[a] Prepared according to refs 6a and 7a (see also ref 9a). [b] Yield from **2** (refs 9a,9c). Reagent used: $Me_2S{=}CH_2$ in THF at 0 °C. [c] Yield from **3**. Reagent used: CH_2I_2/Me_3Al (2:3) in DCM at −60 °C. [d] Diastereomeric mixtures.

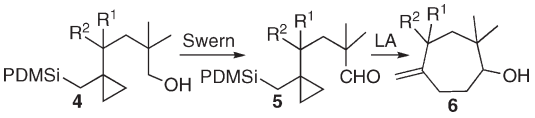
moiety. Reaction proceeds cleanly with total absence of possible side products, resulting from a single attack of the reagent to one of the functional groups.

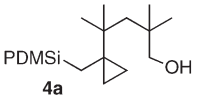
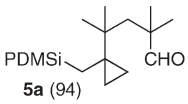
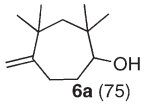
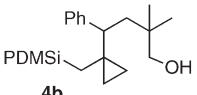
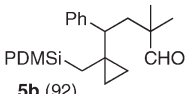
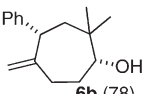
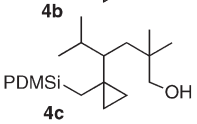
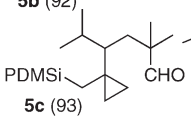
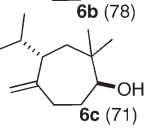
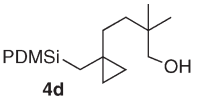
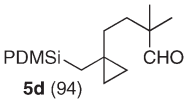
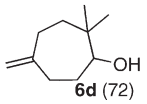
Swern oxidation of cyclopropylhydroxysilanes **4a**−**d** at −78 °C affords aldehydes **5a**−**d**, which under Lewis acid catalysis undergo silicon-mediated intramolecular cyclization leading to 5-methylenecycloheptan-1-ols **6a**−**d** selectively (Table 2). Boron trifluoride etherate in DCM at 0 °C is the most efficient catalyst, providing the best yields and a high level of stereoselectivity (Table 2).

The stereochemistry shown by cycloheptanols **6b,c** indicates that the compound attains a preferred low energy conformation (Scheme 2), where substituents OH, Ph, and ^{i}Pr arrange properly for minimal repulsions. Change of stereochemistry when 4-R substituent is Ph (**6b**) or alkyl (^{i}Pr, **6c**) is not unusual; it has been previously observed for six-membered ring formation,[9a,c] and it is probably due to the different bulkiness and stereoelectronic effect of Ph and ^{i}Pr.

An alternative method for cycloheptane ring formation from oxoallylsilanes **2** could be efficiently developed by means of a consecutive cyclopropanation−epoxidation process and further cyclization. Thus, oxoallylsilanes **2a,c**−**f** were treated with Et_2Zn/TFA/CH_2I_2 (1:1:1) in DCM at 0 °C (a recent version of the Furukawa cyclopropanation reaction[15]) to give oxocyclopropylsilanes **7a,c**−**f** in good yield (Table 3). Activation of the

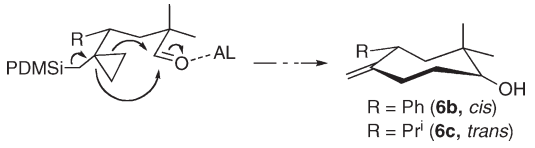
Table 2. 5-Methylenecycloheptan-1-ols 6 from Silanes 4



Hydroxycyclopropylsilane	Oxocyclopropylsilane[a]	6 (%)[b]
 **4a**	 **5a** (94)	 **6a** (75)
 **4b**	 **5b** (92)	 **6b** (78)
 **4c**	 **5c** (93)	 **6c** (71)
 **4d**	 **5d** (94)	 **6d** (72)

[a] Yield from **4**. Reagent used: oxalyl chloride/DMSO in DCM −78 to 0 °C. [b] Yield from **5**. Lewis acid used: $BF_3 \cdot OEt_2$ in DCM at 0 °C.

Scheme 2



carbenoid intermediate with TFA lowers reaction times and increases yield. The only exception to this general behavior was **2b**, which upon treatment in the former acidic conditions undergoes desilylation with concomitant cyclopropane ring cleavage leading to 5-ethyl-4-phenylhex-3-en-2-one. Compounds **7a,c**−**f** are readily epoxidated under standard conditions ($Me_2S{=}CH_2$/THF/0 °C), leading to epoxycyclopropylsilanes **8a,c**−**f** (Table 3). Silanes **8a**−**f** cannot be obtained by the opposite sequence (epoxidation−cyclopropanation) because epoxyallylsilanes are not stable enough in TFA conditions.

Cyclization of epoxycyclopropylsilanes **8a,c**−**f** in the presence of $TiCl_4$ or $BF_3 \cdot Et_2O$ affords 5-methylenecycloheptan-1-ols **9a, c**−**f** in good yield and with a high degree of stereocontrol (Table 4). Cycloheptanols **9a,d**−**f** bearing two stereocenters are selectively obtained as *trans* isomers, except for **9d** (*cis/trans* ratio 1:10) and **9a** (*cis/trans* ratio 1:10/BF_3 or 1:15/$TiCl_4$), where small amounts of the *cis* isomer are also observed (Table 4). The presence of Ti_4Cl may improve the stereoselectivity ratio; for instance, the boron-mediated cyclization of **8a** leads to the formation of a *cis*−*trans* mixture of products, in a 1:10 ratio, favoring the *trans* isomer **9a**, whereas the corresponding titanium-catalyzed reaction provides an improved *cis*−*trans* disatereomeric ratio of 1:15 (Table 4). Three stereocenter cycloheptanols as **9c** are still formed with acceptable stereocontrol (5:1 mixture of epimers at C-2, Table 4).

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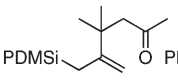
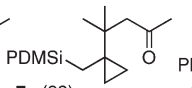
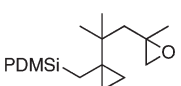
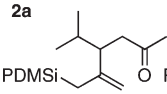
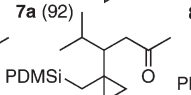
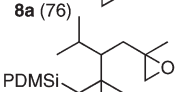
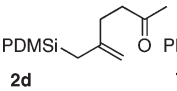
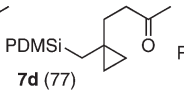
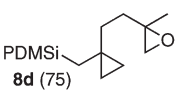
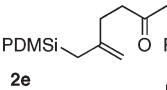
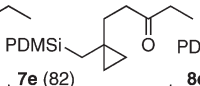
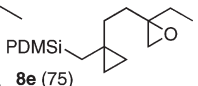
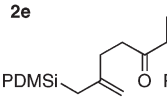
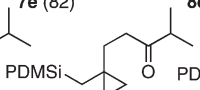
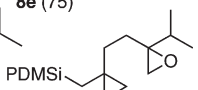
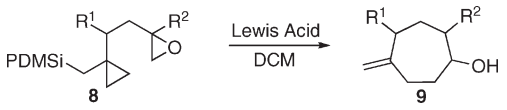
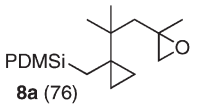
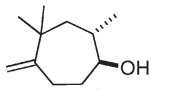
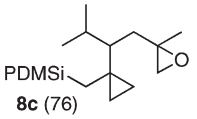
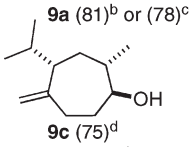
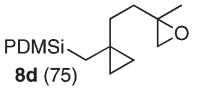
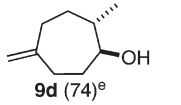
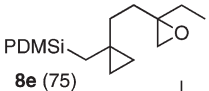
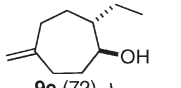
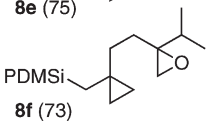
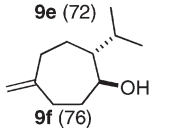
Table 3. Epoxycyclopropylsilanes 8 from Oxoallylsilanes 2

Oxoallylsilane	Oxocyclopropylsilane (%)[a]	8 (%)[b]
 **2a**	 **7a** (92)	 **8a** (76)
 **2c**	 **7c** (74)	 **8c** (76)[c]
 **2d**	 **7d** (77)	 **8d** (75)
 **2e**	 **7e** (82)	 **8e** (75)
 **2f**	 **7f** (72)	 **8f** (73)

[a] Yield from **2**. Reagent used: $Et_2Zn/TFA/CH_2I_2$ (1:1:1) in DCM at 0 °C. [b] Yield from **7**. Reagent used: $Me_2S{=}CH_2$ in THF at 0 °C. [c] Diastereomeric mixture.

Table 4. 5-Methylenecycloheptan-1-ols 9 from Epoxysilanes 8

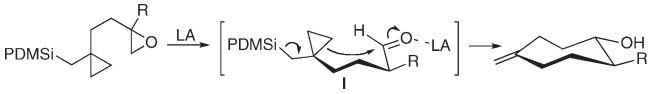


Epoxycyclopropylsilane	LA, T (°C)	Cycloheptanol **9** (%)[a]
 **8a** (76)	($BF_3{\cdot}Et_2O$, 0)[b] or ($TiCl_4$, –78)[c]	 **9a** (81)[b] or (78)[c]
 **8c** (76)	$BF_3{\cdot}Et_2O$, 0	 **9c** (75)[d]
 **8d** (75)	$BF_3{\cdot}Et_2O$, 0	 **9d** (74)[e]
 **8e** (75)	$BF_3{\cdot}Et_2O$, 0	 **9e** (72)
 **8f** (73)	$BF_3{\cdot}Et_2O$, 0	 **9f** (76)

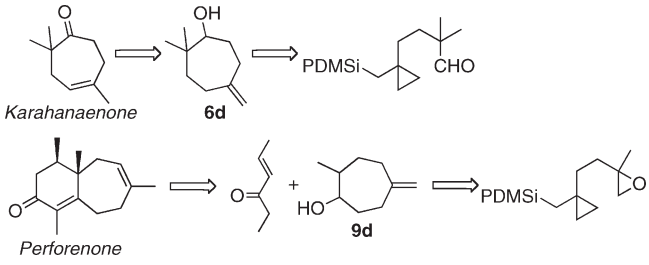
[a] Yield from **8**. Lewis acid used: $TiCl_4$ in DCM at −78 °C or $BF_3{\cdot}OEt_2$ in DCM at 0 °C. [b] Yield 81% (*cis/trans* ratio 1:10). [c] Yield 78% (*cis/trans* ratio 1:15). [d] Mixture of epimers at C-2 (ratio 5:1), the major being the one shown in the table. [e] Ratio *cis/trans* 1:10.

Cyclization of epoxycyclopropylsilanes **8** to methylenecycloheptanols **9** takes place by a tandem rearrangement−cyclization process,[9a] with isomerization of the epoxy group to carbonyl prior to cyclization. Reaction leads to the 1,7-*trans* isomer preferentially, suggesting the intervention of an intermediate oxocyclopropylsilane **I** (Scheme 3) with both the C-7 substituent and the carbonyl-LA groups equatorial for minimal steric repulsions.

Scheme 3



Scheme 4



The substituted 5-methylenecycloheptan-1-ols **6** and **9** synthesized by this route might be excellent building blocks for the total synthesis of cycloheptane-containing naturally occurring terpenes. For example, **6d** is very close in structure to the natural product Karahanaenone (Scheme 4), a monoterpene present in hop essential oil, which is widely used in food industry as a flavoring and stability agent in beer.[16] Compound **6d** might be envisaged as a useful precursor for a short and convenient synthesis of Karahanaenone. Similarly, compound **9d** seems to be a near precursor of Perforenone (Scheme 4), a sesquiterpene isolated from the extract of red alga *Laurentia perforata* having multifunctional ecological roles. Many secondary metabolites obtained from the genus *Laurentia* have been proposed to behave as antifeedant, antimicrobial, and cytotoxic principles.[17] A plausible route for the design and synthesis of this natural sesquiterpene might involve a Robinson annelation as the key step, followed by a short number of standard chemical transformations.

In conclusion, a new and useful strategy for cycloheptane annulations from cyclopropanated allylsilanes has been devised, and their application to the stereoselective synthesis of methylenecycloheptanols of much potential in the construction of seven-membered ring natural products was presented.

EXPERIMENTAL SECTION

General Experimental Methods. Spectroscopic data were recorded as follows: ^1H NMR and ^{13}C NMR spectra were run at 300 and 75 MHz, respectively. Peak asignments were performed with the aid of the DEPT technique and 2D-COSY spectra. Tetrahydrofuran was distilled from sodium benzophenone. All compounds were obtained as colorless oils except where melting points are mentioned. The stereochemistry of the compounds has been assigned on the basis of NOESY experiments.

Synthesis of Hydroxycyclopropylsilanes ***4***: To a solution of epoxyallylsilanes **3** (1.1 mmol) in DCM (2 mL), under nitrogen atmosphere and at 0 °C, was added 2.2 mmol of CH_2I_2 (0.12 mL). At −60 °C, 3.3 mmol of Me_3Al (2 M in hexane, 1.65 mL) was added dropwise, and the

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reaction mixture was allowed to warm to rt and stirred for 50 h. Then, 0.5 mL of a Et_3N/H_2O (1/3) mixture was carefully added, and after 20 min stirring, the mixture was extracted with ether, dried, and evaporated to dryness. The residue was purified by chromatography to give hydroxycyclopropylsilanes **4a**−**d**.

*2,2,4-Trimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]pentan-1-ol (**4a**):* Colorless oil (74%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.27 (m, 5H), 3.33 (s, 2H), 1.46 (s, 2H), 1.31 (s, 2H), 1.27 (s, 1H), 1.00 (s, 6H), 0.86 (s, 6H), 0.50 (t, J = 5.4 Hz, 2H), 0.28 (s, 6H), 0.21 (t, J = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 133.4, 128.7, 127.7, 73.9, 46.5, 37.5, 36.7, 25.9, 25.8, 25.7, 20.5, 10.4, 10.3, −1.2. Anal. Calcd for $C_{20}H_{34}SiO$: C, 75.40; H, 10.76. Found: C, 75.77; H, 11.05.

*2,2-Dimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]-4-phenylbutan-1-ol (**4b**):* Colorless oil (78%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.23 (m, 10H), 3.10 (s, 2H), 2.26 (d, J = 11 Hz, 1H), 2.06 (dd, J = 14, 11 Hz, 1H), 1.65 (d, J = 14 Hz, 1H), 1.40 (s, 1H), 1.28 (d, J = 15 Hz, 1H), 1.10 (d, J = 15 Hz, 1H), 0.86 (s, 3H), 0.73 (s, 3H), 0.33 (s, 6H), 0.46−0.29 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 140.0, 133.6, 128.8, 128.5, 128.1, 127.8, 126.2, 71.4, 49.1, 40.1, 35.7, 25.5, 24.3, 24.1, 20.3, 13.1, 12.4, −1.2; IR (film, cm^{-1}) 3401, 2954, 1426, 1111. Anal. Calcd for $C_{24}H_{34}SiO$: C, 78.63; H, 9.35. Found: C, 78. 93; H, 9.59.

*2,2,5-Trimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]hexan-1-ol (**4c**):* Colorless oil (72%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61−7.38 (m, 5H), 3.26 (s, 2H), 2.08−1.85 (m, 2H), 1.41 (d, J = 15 Hz, 1H), 1.30 (d, J = 15 Hz, 1H), 1.15−1.12 (m, 2H), 1.01−0.85 (m, 1H), 0.93 (s, 3H), 0.91 (s, 3H), 0.87 (d, J = 6.7 Hz, 6H), 0.50−0.25 (m, 4H), 0.38 (s, 3H), 0.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0, 133.5, 128.8, 127.7, 72.8, 45.8, 35.5, 35.3, 32.0, 24.9, 24.7, 22.3, 22.0, 20.4, 19.9, 13.4, 12.4, −1.3, −1.4; IR (film, cm^{-1}) 3367, 1426, 1112. Anal. Calcd for $C_{21}H_{36}SiO$: C, 75.84; H, 10.91. Found: C, 76.17; H, 11.26.

*2,2-Dimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]butan-1-ol (**4d**):* Colorless oil (76%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.27 (m, 5H), 3.14 (s, 2H), 1.22−1.17 (m, 2H), 1.08−1.02 (m, 2H), 0.88 (s, 2H), 0.69 (s, 6H), 0.34 (s, 6H), 0.22−0.21 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3, 133.5, 128.7, 127.7, 72.0, 35.3, 34.5, 32.7, 23.8, 23.5, 23.4, 17.5, 14.2, 14.1, −1.7. Anal. Calcd for $C_{18}H_{30}SiO$: C, 74.42; H, 10.41. Found: C, 74.78; H, 10.76.

*Swern Oxidation of Hydroxycyclopropylsilanes **4**:* To a solution of oxallyl chloride (1.5 mmol, 0.14 mL) in DCM (5 mL) at −78 °C was added a solution of dry DMSO (1.6 mmol, 0.1 mL) in DCM (0.5 mL), and the mixture was stirred for 10 min. Then, a solution of hydroxycyclopropylsilanes **4** in DCM (1 mmol) was added and the mixture stirred for an additional 20 min. Triethylamine (5 mmol, 2.2 mL) was then added, the reaction allowed to warm to rt, and the mixture extracted with ether, dried, and evaporated to dryness. The residue was purified by chromatography to give oxocyclopropylsilanes **5a**−**d**.

*2,2,4-Trimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]pentanal (**5a**):* Colorless liquid (94%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.54−7.27 (m, 5H), 1.80 (s, 2H), 1.29 (s, 2H), 1.11 (s, 6H), 0.76 (s, 6H), 0.47 (t, J = 5.4 Hz, 2H), 0.30 (s, 6H), 0.24 (t, J = 5.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 139.9, 133.4, 128.8, 127.7, 47.9, 46.7, 37.1, 25.8, 25.2, 25.1, 24.1, 24.0, 20.5, 10.3, 10.2, −1.2. Anal. Calcd for $C_{20}H_{32}SiO$: C, 75.88; H, 10.19. Found: C, 75.51; H, 10.48.

*2,2-Dimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]-4-phenylbutanal (**5b**):* Colorless liquid (92%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.05 (s, 1H), 7.49−7.06 (m, 10H), 2.20 (d, J = 11 Hz, 1H), 2.20 (dd, J = 13, 11 Hz, 1H), 1.80 (d, J = 13 Hz, 1H), 1.18 (d, J = 15 Hz, 1H), 1.03 (d, J = 15 Hz, 1H), 0.91 (s, 3H), 0.89 (s, 3H), 0.61−0.53 (m, 1H), 0.43−0.33 (m, 1H), 0.31−0.24 (m, 2H), 0.30 (s, 3H), 0.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.0, 142.7, 139.8, 133.6, 128.7, 128.1, 127.8, 126.6, 48.7, 45.8, 39.9, 23.3, 23.2, 21.1, 21.0, 12.9, 11.7, −1.2, −1.3. Anal. Calcd for $C_{24}H_{32}SiO$: C, 79.06; H, 8.85. Found: C, 79.41; H, 9.17.

*2,2,5-Trimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]hexanal (**5c**):* Colorless liquid (93%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.42 (s, 1H), 7.60−7.27 (m, 5H), 1.79−1.67 (m, 2H), 1.40 (dd, J = 15, 3 Hz, 1H), 1.24 (d, J = 15 Hz, 1H), 1.15−1.07 (m, 1H), 1.07 (d, J = 15 Hz, 1H), 1.02 (s, 3H), 1.01 (s, 3H), 0.89 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H), 0.58−0.25 (m, 3H), 0.32 (s, 3H), 0.31 (s, 3H), 0.11−0.00 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.9, 139.6, 133.5, 128.8, 127.7, 48.8, 45.9, 37.8, 31.9, 24.0, 22.2, 21.1, 20.7, 19.7, 14.1, 12.9, −1.4. Anal. Calcd for $C_{21}H_{34}SiO$: C, 76.30; H, 10.37. Found: C, 76.67; H, 10.61.

*2,2-Dimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]butanal (**5d**):* Colorless liquid (94%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.55−7.27 (m, 5H), 1.43−1.37 (m, 2H), 1.02−0.94 (m, 2H), 0.87 (s, 2H), 0.84 (s, 6H), 0.21 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.4, 140.1, 133.5, 128.8, 127.7, 45.2, 34.2, 33.1, 23.7, 21.1, 21.0, 17.3, 14.1, 14.0, −1.8. Anal. Calcd for $C_{18}H_{28}SiO$: C, 74.94; H, 9.78. Found: C, 75.29; H, 10.04.

*Intramolecular Acid-Catalyzed Cyclization of Compounds **5a**−**d**:* To a solution of compounds **5** (1 mmol) in DCM (5 mL), at 0 °C and under nitrogen atmosphere, was added dropwise $BF_3 \cdot Et_2O$ (0.18 mL, 1.4 mmol), and the mixture was stirred for 30 min. Then, brine was added (5 mL) and the mixture extracted with ether, dried, and evaporated to dryness. The residue was purified by chromatography to give methylenecycloheptanols **6a**−**d**.

*2,2,4,4-Tetramethyl-5-methylenecycloheptanol (**6a**):* Colorless liquid (75%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.77 (s, 1H), 4.73 (s, 1H), 3.32 (dd, J = 8, 4 Hz, 1H), 2.34−2.28 (m, 1H), 2.12−2.04 (m, 2H), 1.98−1.84 (m, 1H), 1.71 (d, J = 15.3 Hz, 1H), 1.71−1.56 (m, 2H), 1.13 (s, 3H), 1.10 (s, 3H), 0.95 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.3, 107.9, 79.4, 48.5, 38.6, 36.8, 32.0, 31.5, 29.1, 28.8, 28.0, 22.6. Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.39; H, 12.35.

*(1RS,4RS)-2,2-Dimethyl-5-methylene-4-phenylcycloheptanol (**6b**):* Colorless liquid (75%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63−7.14 (m, 5H), 4.92 (s, 1H), 4.69 (s, 1H), 3.64 (dd, J = 12.5, 4.5 Hz, 1H), 3.60 (m, 1H), 2.68 (td, J = 12.5, 2.6 Hz, 1H), 2.30 (dd, J = 14.5, 12.5 Hz, 1H), 2.27 (dq, J = 12.5, 3.0 Hz, 1H), 2.05−1.97 (m, 1H), 1.83 (tq, J = 12, 2.8 Hz, 1H), 1.38−1.27 (m, 2H), 1.05 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.3, 148.2, 128.3, 126.9, 125.8, 113.3, 77.1, 47.5, 39.9, 38.3, 34.5, 30.0, 29.0, 23.8. Anal. Calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.11; H, 9.94.

*(1RS,4SR)-4-Isopropyl-2,2-dimethyl-5-methylenecycloheptanol (**6c**):* White solid, mp 53.3−54.2 °C (71%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89 (s, 1H), 4.66 (s, 1H), 3.24 (dd, J = 4.8, 11.3 Hz, 1H), 2.22−2.13 (m, 2H), 2.03 (dt, J = 13, 6.4 Hz, 1H), 1.91 (t, J = 13 Hz, 1H), 1.62 (m, 1H), 1.54 (sept, J = 6.8 Hz, 1H), 1.42 (d, J = 13 Hz, 1H), 1.37 (dd, J = 13 Hz, 1H), 1.45−1.29 (m, 1H), 1.01 (s, 3H), 0.87 (d, J = 6.8 Hz, 3H), 0.85 (s, 3H), 0.81 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 112.4, 80.9, 47.6, 39.3, 37.6, 37.3, 34.0, 31.1, 31.0, 19.9, 19.7, 16.5. Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.88; H, 12.61.

*2,2-Dimethyl-5-methylenecycloheptanol (**6d**):* Colorless liquid (72%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.72 (s, 1H), 4.68 (s, 1H), 3.40−3.14 (m, 1H), 2.45−1.40 (m, 9H), 0.98 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.6, 109.8, 79.5, 36.0, 32.5, 30.8, 29.2, 27.6, 22.6. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 78.08; H, 12.05.

*Synthesis of Oxocyclopropylsilanes **7a**−**f**:* To a solution of Et_2Zn (1 M in hexane, 2 mmol, 2 mL) in dry DCM (2 mL), under nitrogen and at 0 °C, was added a solution of trifluoroacetic acid (2 mmol, 0.15 mL) in DCM (1 mL), and the mixture was stirred for 40 min. Then, CH_2I_2 (2 mmol, 0.16 mL) was added dropwise and stirred for an additional 35 min before a solution of the oxoallylsilane **2** (1 mmol) in DCM (1 mL) was added. The reaction mixture was stirred at 0 °C for 30 min and then at rt for 4 h. The mixture was quenched with saturated NH_4Cl, extracted with ether, dried, and evaporated to dryness. The residue was purified by chromatography to give oxocyclopropylsilanes **7a**−**f**.

4-Methyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]pentan-2-one (***7a***): Colorless liquid (92%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.35 (m, 5H), 2.47 (s, 2H), 2.14 (s, 3H), 1.29 (s, 2H), 0.90 (s, 6H), 0.50 (t, J = 5.3 Hz, 2H), 0.30 (s, 6H), 0.24 (t, J = 5.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.6, 139.8, 133.4, 128.8, 127.8, 52.2, 37.0, 32.7, 24.5, 24.0, 20.3, 9.6, 9.5, −1.3. Anal. Calcd for $C_{18}H_{28}SiO$: C, 74.94; H, 9.78. Found: C, 75.31; H, 10.06.

5-Methyl-4-[1-(dimethylphenylsilyl)methyl)cyclopropyl]hexan-2-one (***7c***): Colorless liquid (74%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.27 (m, 5H), 2.41−2.37 (m, 2H), 2.12 (s, 3H), 1.79−1.64 (m, 1H), 1.17 (d, J = 15 Hz, 1H), 1.13−1.07 (m, 1H), 1.00 (d, J = 15 Hz, 1H), 0.91 (d, J = 6.7 Hz, 3H), 0.75 (d, J = 6.7 Hz, 3H), 0.47−0.38 (m, 2H), 0.30 (s, 3H), 0.29 (s, 3H), 0.29−016 (m, 1H), 0.09−0.03 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.6, 139.7, 133.4, 128.8, 127.7, 49.3, 46.4, 31.4, 30.3, 21.7, 20.8, 20.6, 18.7, 15.5, 10.7, −1.42; IR (film, cm^{-1}) 3100, 2956, 1720, 1430, 1110. Anal. Calcd for $C_{19}H_{30}SiO$: C, 75.43; H, 10.00. Found: C, 75.78; H, 10.31.

4-[1-(Dimethylphenylsilylmethyl)cyclopropyl]butan-2-one (***7d***): Colorless liquid (77%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 −7.33 (m, 5H), 2.30 (t, J = 7.9 Hz, 2H), 1.92 (s, 3H), 1.40 (t, J = 7.9 Hz, 2H), 0.87 (s, 2H), 0.36 (s, 6H), 0.35−0.24 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.7, 140, 133.4, 128.8, 127.8, 41.0, 33.0, 29.6, 23.8, 16.7, 14.1, 14.0, −1.9; IR (film, cm^{-1}) 3070, 2955, 1718, 1426, 1111. Anal. Calcd for $C_{16}H_{24}SiO$: C, 73.79; H, 9.29. Found: C, 74.06; H, 9.53.

1-[1-(Dimethylphenylsilylmethyl)cyclopropyl]pentan-3-one (***7e***): Colorless liquid (82%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57−7.34 (m, 5H), 2.34 (t, J = 8 Hz, 2H), 2.21 (q, J = 7.3 Hz, 2H), 1.43 (t, J = 8 Hz, 2H), 0.98 (t, J = 7.3 Hz, 3H), 0.87 (s, 2H), 0.37 (s, 6H), 0.30−0.27 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.7, 140.0, 133.5, 129.0, 127.8, 39.7, 35.6, 33.1, 23.8, 16.7, 14.1, 14.0, 7.7, −1.8. Anal. Calcd for $C_{17}H_{26}SiO$: C, 74.39; H, 9.55. Found: C,74.71; H, 9.88.

4-Methyl-1-[1-(dimethylphenylsilylmethyl)cyclopropyl]pentan-3-one (***7f***): Colorless liquid (72%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55−7.33 (m, 5H), 2.43−2.35 (m, 1H), 2.35 (t, J = 7.9 Hz, 2H), 1.42 (t, J = 7.9 Hz, 2H), 1.00 (d, J = 6.9 Hz, 6H), 0.87 (s, 2H), 0.36 (s, 6H), 0.34−0.23 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.7, 140.0, 133.4, 128.7, 127.7, 40.6, 37.7, 33.0, 23.9, 18.3, 18.2, 16.7, 14.1, 14.0, −1.9. Anal. Calcd for $C_{18}H_{28}SiO$: C, 74.94; H, 9.78. Found: C, 75.32; H, 10.06.

Synthesis of Epoxycyclopropylsilanes ***8a***−***f***: To a solution of trimethylsulfonium iodide (1 mmol, 208 mg) in dry THF (5 mL) was added dropwise BuLi (1 mmol, 1.6 M *n*-BuLi in hexanes), and the mixture was stirred for 5 min at 0 °C. Then, a solution of the oxocyclopropylsilane (0.8 mmol) in THF (1 mL) was added. After stirring for an additional 30 min at 0 °C and 1 h at rt, brine (10 mL) was added and the mixture extracted with ether, dried, and evaporated to dryness. The residue was purified by chromatography to give epoxycyclopropylsilanes **8a**−**f**.

2,2,4-Trimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]-1,2-epoxypentane (***8a***): Colorless liquid (76%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52−7.27 (m, 5H), 2.64 (d, J = 4.8 Hz, 1H), 2.58 (d, J = 4.8 Hz, 1H), 1.96 (d, J = 14.2 Hz, 1H), 1.44 (d, J = 14.2 Hz, 1H), 1.40 (s, 3H), 1.27 (s, 2H), 0.90 (s, 3H), 0.84 (s, 3H), 0.53−0.44 (m, 2H), 0.29 (s, 6H), 0.27−0.20 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.9, 133.4, 128.7, 127.7, 56.0, 55.0, 46.8, 36.4, 25.1, 25.0, 24.6, 23.6, 20.2, 10.0, 9.7, −1.2. Anal. Calcd for $C_{19}H_{30}SiO$: C, 75.43; H, 10.00. Found: C, 75.76; H, 10.32.

2,5-Dimethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]-1,2-epoxyhexane (***8c***): Colorless liquid obtained as a 1:1 mixture of diastereoisomers **A** + **B** (76%). **A**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59−7.36 (m, 5H), 2.62−2.56 (m, 2H), 1.91−1.72 (m, 2H), 1.29 (s, 3H), 1.21−1.05 (m, 2H), 0.98−0.92 (m, 8H), 0.38 (s, 6H), 0.34−0.31 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7, 133.4, 129.2, 127.8, 56.5, 54.8, 51.2, 37.2, 31.3, 22.1, 21.6, 21.1, 19.9, 18.1, 14.2, 11.4, 0.86, −1.3. **B**: ^{1}H NMR (300 MHz, $CDCl_3$) δ (recognizable signals) 1.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.8, 133.0, 128.9, 127.6, 56.7, 54.4, 49.7, 37.0, 31.3, 22.2, 20.7, 20.2, 20.1, 19.4, 14.4, 11.5, 0.86, −1.4.

2-Methyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]-1,2-epoxybutane (***8d***): Colorless liquid (75%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58−7.36 (m, 5H), 2.45 (d, J = 5 Hz, 1H), 2.37 (d, J = 5 Hz, 1H), 1.58−1.41 (m, 2H), 1.22 (t, J = 8.7 Hz, 2H), 1.12 (s, 3H), 0.92 (d, J = 15 Hz, 1H), 0.85 (d, J = 15 Hz, 1H), 0.40 (s, 6H), 0.28−0.25 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1, 133.5, 128.8, 127.7, 56.8, 53.7, 34.2, 33.9, 23.8, 20.8, 17.0, 14.2, 14.1, −1.7; IR (film, cm^{-1}) 3068, 2956, 1427, 1248, 1111. Anal. Calcd for $C_{17}H_{26}SiO$: C, 74.39; H, 9.55. Found: C, 74.71; H, 9.84.

2-Ethyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]-1,2-epoxybutane (***8e***): Colorless liquid (75%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57−7.27 (m, 5H), 2.46 (d, J = 4.7 Hz, 1H), 2.31 (d, J = 4.7 Hz, 1H), 1.58 (t, J = 8.5 Hz, 2H), 1.44 (q, J = 7.5 Hz, 2H), 1.18 (t, J = 8.5 Hz, 2H), 0.87 (s, 2H), 0.83 (t, J = 7.5 Hz, 3H), 0.37 (s, 3H), 0.36 (s, 3H), 0.28−0.24 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1, 133.4, 128.7, 127.7, 59.9, 51.8, 33.8, 31.2, 26.9, 23.7, 17.1, 14.1, 8.7, −1.8. Anal. Calcd for $C_{18}H_{28}SiO$: C, 74.94; H, 9.78. Found: C, 75.29; H, 9.49.

2-Isopropyl-4-[1-(dimethylphenylsilylmethyl)cyclopropyl]-1,2-epoxybutane (***8f***): Colorless liquid (76%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.27 (m, 5H), 2.44 (d, J = 4.6 Hz, 1H), 2.27 (d, J = 4.6 Hz, 1H), 1.74−1.52 (m, 1H), 1.58 (t, J = 7 Hz, 2H), 1.20−0.79 (m, 4H), 0.89 (d, J = 6.7 Hz, 3H), 0.84 (d, J = 6.7 Hz, 3H), 0.37 (s, 3H), 0.35 (s, 3H), 0.30−0.23 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.1, 133.4, 128.7, 127.7, 62.2, 50.1, 33.1, 32.2, 28.0, 23.8, 18.2, 17.8, 17.1, 14.1, 14.0, −1.6. Anal. Calcd for $C_{19}H_{30}SiO$: C, 75.43; H, 10.00. Found: C, 75.76; H, 10.29.

Cyclization of Epoxycyclopropylsilanes ***8a***−***f***: $BF_3\cdot OEt_2$ (1.2 mmol) or $TiCl_4$ (0.7 mmol) was slowly added to a solution of the epoxycyclopropylsilane **8** (1 mmol) in DCM (10 mL) under nitrogen. After stirring for 30 min at the corresponding temperature (0 or −78 °C), 2 mL of MeOH was added and the mixture was allowed to warm to room temperature. The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue purified by chromatography to give methylenecycloheptanols **9a**−**f**. The relative stereochemistry of cyclic products was determined by extensive NMR experiments and in particular with COSY and NOESY data.

(1SR,2SR)-2,4,4-Trimethyl-5-methylenecycloheptanol (***9a***): Colorless liquid (81%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.80 (s, 2H), 3.20 (td, J = 9.7, 5.0 Hz, 1H), 2.27−2.08 (m, 3H), 1.56 (t, J = 14.1 Hz, 1H), 1.55 (d, J = 14.1 Hz, 1H), 1.46 (dd, J = 9.3, 6.6 Hz, 1H), 1.43−1.25 (m, 2H), 1.14 (s, 3H), 1.00 (d, J = 6.7 Hz, 3H), 0.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 109.3, 78.5, 46.6, 40.8, 38.4, 36.5, 32.1, 29.9, 27.4, 20.8; IR (film, cm^{-1}) 3426, 2962, 1721, 1456. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.83; H, 12.31.

(1SR,2SR,4SR)-4-Isopropyl-2-methyl-5-methylenecycloheptanol (***9c***): Colorless liquid (75%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.88 (s, 1H), 4.68 (s, 1H), 3.16 (td, J = 9.7, 5 Hz, 1H), 2.26−1.83 (m, 5H), 1.68−1.28 (m, 5H), 1.04 (d, J = 6.9 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H), 0.82 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6, 112.9, 78.8, 51.6, 40.9, 38.7, 35.3, 33.0, 29.1, 20.7, 20.6, 19.8. Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.40; H, 12.37.

(1SR,2SR)-2-Methyl-5-methylenecycloheptanol (***9d***): Colorless liquid (74%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.70 (s, 1H), 4.67 (s, 1H), 3.31 (td, J = 8.8, 3.3 Hz, 1H), 2.45−2.38 (m, 2H), 2.32 (d, J = 13.5 Hz, 1H), 2.26 (d, J = 13.5 Hz, 1H), 1.92 (tt, J = 10.8, 3 Hz, 1H), 1.74−1.50 (m, 4H), 1.36−1.23 (m, 1H), 1.04 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 109.6, 78.3, 42.2, 35.6, 34.1, 31.4, 30.6, 19.8. Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.43; H, 11.79.

(1SR,2SR)-2-Ethyl-5-methylenecycloheptanol (***9e***): Colorless liquid (72%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.69 (s, 1H), 4.67 (s, 1H), 3.51 (td, J = 8.1, 3.4 Hz, 1H), 2.47−2.38 (m, 2H), 2.30−2.18 (m, 2H), 1.93−1.83 (m, 1H), 1.79−1.55 (m, 3H), 1.53−1.50 (m, 2H), 1.45−1.24 (m, 2H),

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0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.0, 110.0, 75.5, 48.1, 35.5, 33.9, 30.3, 26.8, 25.3, 11.0. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 78.54; H, 12.07.

*(1SR,2RS)-2-Isopropyl-5-methylenecycloheptanol (**9f**):* Colorless liquid (76%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (s, 1H), 4.66 (s, 1H), 3.61 (td, J = 8.2, 3.7 Hz, 1H), 2.47 (ddd, J = 15, 6.6, 3 Hz, 1H), 2.38 (ddd, J = 14.5, 8.9, 1.4 Hz, 1H), 2.23−2.14 (m, 2H), 2.08 (td, J = 6.9, 3.6 Hz, 1H), 1.96−1.87 (m, 1H), 1.74−1.61 (m, 3H), 1.33−1.22 (m, 1H), 1.19−1.13 (m, 1H), 0.93 (d, J = 6.8 Hz, 3H), 0.81 (d, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.0, 109.6, 73.7, 52.2, 36.7, 35.2, 30.3, 27.7, 22.3, 21.0, 16.6. Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.85; H, 12.26.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra for the new compounds **4a**−**d**, **5a**−**d**, **6a**−**d**, **7a**,**c**−**f**, **8a**,**c**−**f**, and **9a**, **c**−**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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