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$CrCl_2$-Promoted Stereospecific and Stereoselective Alkyl- and Silylcyclopropanation of α,β-Unsaturated Amides

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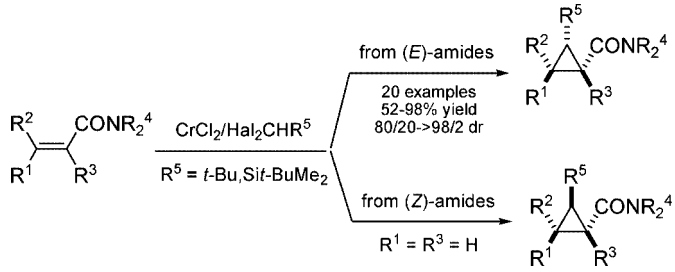

An efficient chromium-promoted alkyl- or silylcyclopropanation of α,β-unsaturated amides is described. These reactions can be carried out on (*E*)- or (*Z*)-α,β-enamides in which the C−C double bond is di-, or trisubstituted. This process takes place with total stereospecificity and the new stereogenic center is generated with high or total stereoselectivity. Some synthetic applications of the obtained silylcyclopropyl amides are also reported. Two mechanisms based on the generation of carbenoid or carbene complexes have been proposed to explain this cyclopropanation reaction.

Introduction

The cyclopropyl group is unique among carbocycles in both its properties and reactions.[1] This structural unit is found in a number of significant natural products, as well as synthetic compounds of importance in biological studies. Their utility as synthetic intermediates warrants interest in these carbocycles from a variety of fields in organic chemistry.[2]

A highly functionalized cyclopropyl moiety presents a wide number of applications in organic synthesis. Moreover, silylcyclopropane derivatives show important synthetic applications,[3] and consequently, various methods to access silylcyclopropane derivatives have been published.[4] Very recently Takai et al. reported the silylcyclopropanation of terminal alkenes, promoted by $CrCl_2$ in the presence of TMEDA.[5] However, the diastereoselectivity of this process was poor, and consequently diastereoisomeric mixtures (ranging between 63/37 and 87/13) were obtained.

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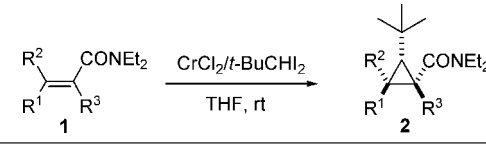
Another important class of functionalized cyclopropyl compounds are the cyclopropanecarboxylic acid derivatives. However, synthetic methods for their efficient and highly selective synthesis are still scarce. In general, these cyclopropyl derivatives can be achieved through the metal-catalyzed decomposition of diazocompounds;[2b,6] or through the cyclopropanation of different unsaturated acceptors.[2b,7] The majority of these methods present some drawbacks: (a) some methods afforded the cyclopropanecarboxylic acid derivatives with only poor stereoselectivity;[6b,c] (b) other methods gave these cyclopropanes in low yields;[6b,c] (c) in general, a scarce number of examples about the cyclopropanation of highly substituted C–C double bonds[6a,b,d,7a–c] or (Z)-alkenes, have been reported;[7a] and (d) explosive, flammable, and harmful reagents were used in the cyclopropanation of alkenes with diazocompounds. Most specifically, to the best of our knowledge, only two methods to obtain 2-silylcyclopropanecarboxylic acid derivatives have been reported.[4i,8] These methods present several drawbacks, the 2-silylcyclopropanoates were obtained in low yields, with low stereoselectivity and with poor generality and substitution patterns on the cyclopropane ring. Taking into account the synthetic applications of these derivatives,[3] an efficient and general synthesis of 2-silylcyclopropanecarboxamides, affording a single diastereoisomer in high yield, would be desirable.

Previous work in our laboratory has demonstrated the utility of $CrCl_2$ for the stereospecific cyclopropanation of α,β-unsaturated amides, in which the C−C double bond was di-, tri- or tetra-substituted.[9] Very recently we communicated our first examples on the stereospecific and stereoselective *tert*-butyl and silylcyclopropanation of α,β-unsaturated amides.[10] These preliminary results,[10] prompted us to study the generality and drawbacks of this method. Thus, we report herein full studies concerning the $CrCl_2$-promoted alkyl and silylcyclopropanation of a variety of α,β-enamides, giving special attention to the generality and main limitations of this process. Additional reactions were carried out to support the mechanistic proposal. According to these results we propose an alternative mechanism to that previously reported by us.[10] Finally some synthetic applications of the obtained silylcyclopropyl amides are also reported.

Results and Discussion

Synthesis of *tert*-Butyl Cyclopropanecarboxamides 2. The most important problem to solve in the case of the silylcyclopropanation of alkenes is the generation of a new stereogenic center with high stereoselectivity. Taking into account this fact, we have previously attempted other similar, and simpler cyclopropanation reactions. Thus, we carried out the alkylcyclopropanation of α,β-unsaturated amides using *t*-$BuCHI_2$/$CrCl_2$ as a model reaction since *t*-$BuCHI_2$ was commercially available. The best results were obtained by treatment of several α,β-enamides **1** with 4.0 equiv of $CrCl_2$ and 3.75 equiv of *t*-$BuCHI_2$ at room temperature. After hydrolysis, the corresponding *tert*-butylcyclopropylamide **2** was obtained as a single diastereoisomer (dr > 98/2) in high yields (Table 1).

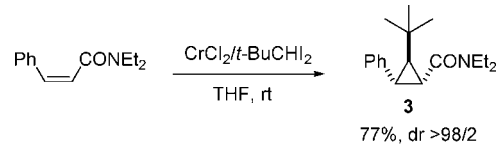
TABLE 1. Synthesis of *tert*-Butylcyclopropanecarboxamides 2 (R^2 = H)



entry	2	R^1	R^3	dr[a]	yield (%)[b]
1	**2a**	Ph	H	>98/2	82
2	**2b**	*n*-Bu	Me	>98/2	79
3	**2c**	Ph	Me	>98/2	98
4	**2d**	*p*-$MeOC_6H_4$	Me	>98/2	80

[a] Diastereoisomeric ratio (dr) was determined by GC−MS, and 300 MHz ^{1}H NMR analysis of the crude products **2**. [b] Isolated yield after column chromatography based on compound **1**.

SCHEME 1. Cyclopropanation of (*Z*)-*N,N*-Diethylcinnamamide



It is worth noting that the relative configuration of the starting alkene is conserved and that a new stereogenic center has been generated with complete stereoselectivity affording a cyclopropane ring with a 1,2,3-subsitution pattern in which the *tert*-butyl group has a *cis* disposition relative to the amide functional group.[10]

The stereospecificity of this cyclopropanation was unambiguously established starting from (*Z*)-*N,N*-diethylcinnamamide (Scheme 1). It was shown that the geometry of the C=C bond was also conserved during the cyclopropanation process, and **3** was obtained as a single diastereoisomer in 77% yield. In this case, the *tert*-butyl group adopted a *trans* position with respect to the carboxamide instead of the *cis* position observed in the cyclopropanes obtained from the (*E*)-*N,N*-diethylcinnamamide.

An explanation of the different relative disposition of the amide group in the *tert*-butyl cyclopropanation of *E*- or *Z*-unsaturated amides **1** will be discussed below.

Synthesis of Silylcyclopropanecarboxamides 4. On the basis of the results of the alkylcyclopropanation, we tested the same reaction conditions to perform the silylcyclopropanation of α,β-enamides.[10]

Thus, when a mixture of 4 equiv of $CrCl_2$ and 3.75 equiv of $Br_2CHSitBuMe_2$ was stirred at room temperature for 18 h in the presence of the corresponding α,β-enamides **1**, cyclopropylamides **4** were obtained after hydrolysis, in high yields and with total or very high stereoselectivity (Table 2).

The structure and relative configuration of *tert*-butylcyclopropylamides **2**, **3**, and silylcyclopropanes **4** (as is depicted in Table 1 and Table 2 and Scheme 1) were established by analysis of the ^{1}H NMR coupling constants between the cyclopropane protons of compounds **2a**, **2c**, **3**, **4a**, **4c**, and **4g**−**p**, by NOE experiments in the case of compounds **2a**, **3**, **4g**−**i**, and **4k**−**l**,

(6) For recent examples on the metal-catalyzed decomposition of diazocompounds, see:(a) Reddy, R. P.; Lee, G. H.; Davies, H. M. L. *Org. Lett.* **2006**, *8*, 3437–3440. (b) Bayardon, J.; Holczknecht, O.; Pozzi, G.; Sinou, D. *Tetrahedron: Asymmetry* **2006**, *17*, 1568–1572. (c) Branstetter, B.; Hossain, M. M. *Tetrahedron Lett.* **2006**, *47*, 221–223. (d) Markó, I. E.; Giard, T.; Sumida, S.; Gies, A. E. *Tetrahedron Lett.* **2002**, *43*, 2317–2320.

(7) For recent examples on the cyclopropanation of unsaturated acceptors, see:(a) Deng, X. M.; Cai, P.; Ye, S.; Sun, X. L.; Liao, W. W.; Li, K.; Tang, Y.; Wu, Y. D.; Dai, L. X . *J. Am. Chem. Soc.* **2006**, *128*, 9730–9740. (b) McCooey, S. H.; McCabe, T.; Connon, S. J. *J. Org. Chem.* **2006**, *71*, 7494–7497. (c) Papageorgiou, C. D.; Ley, S. V.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 828–831.

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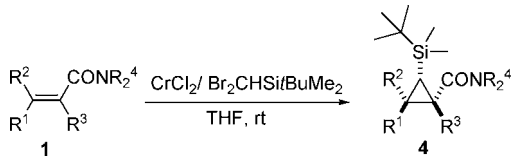
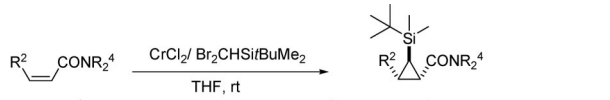
TABLE 2. Synthesis of Silylcyclopropanecarboxamides 4



entry	4[a]	R^1	R^3	R^4	dr[b]	yield (%)[c]
1	**4a**	H	Me	Et	>98/2	52
2	**4b**	Me	H	Et	>98/2	81
3	**4c**	n-C_5H_{11}	H	Et	95/5[d]	66
4	**4d**	n-C_5H_{11}	H	i-Pr	80/20	73
5	**4e**	n-C_5H_{11}	H	*e*	95/5[d]	80
6	**4f**	n-C_7H_{15}	H	Et	95/5[d]	90
7	**4g**	Cy	H	Et	>98/2	80
8	**4h**	i-Bu	H	Et	>98/2	78
9	**4i**	(*E*)-MeCH=CH	H	Et	92/8[f]	87
10	**4j**	n-Bu	Me	Et	>98/2	79
11	**4k**	i-Bu	Me	Et	>98/2	92
12	**4l**	Ph	Me	Et	>98/2	84
13	**4m**	Ph	Me	i-Pr	86/14	81
14	**4n**	Ph	Me	*e*	>98/2	79
15	**4o**	pMeOC_6H_4	Me	Et	97/3[g]	76
16	**4p**[h]	Ph	H	Et	>98/2	57

[a] Unless otherwise noted R^2 = H. [b] Diastereoisomeric ratio (dr) was determined by GC−MS, and/or 300 MHz ^{1}H NMR analysis of the crude products **4**. [c] Isolated yield after column chromatography based on compound **1**. [d] dr of the starting amide 95/5. [e] From morpholine. [f] dr of the starting amide 93/7. [g] dr of the starting amide 98/2. [h] R^2 = Et.

SCHEME 2. Synthesis of Silylcyclopropylamides Starting from (*Z*)-α,β-Enamides

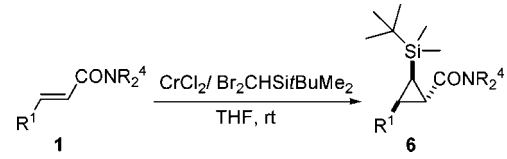


and single-crystal X-ray analysis of compounds **4g**[11] and **4l**.[10] The NOE experiments in compounds **4g** and **4l** were in accordance with the obtained X-ray structure. In most of these cases, only one diastereoisomer was obtained (determined by analysis of the crude materials by GC−MS and/or 300 MHz ^{1}H NMR spectroscopy), the new stereogenic center was therefore generated with complete or very high stereoselectivity.

In a similar manner to that for the case of *tert*-butylcyclopropanation of (*Z*)-cinnamamide (Scheme 1), when the silylcyclopropanation reaction was carried out on (*Z*)-unsaturated amides the silylcyclopropyl amides were obtained with the silyl group being *trans*-disposed relative to the amide moiety (Scheme 2). Silylcyclopropyl amides **5a** and **5b**, were also obtained with total stereoselectivity. Thus, **5b** was obtained as a single diastereoisomer and **5a** as a 77/23 mixture from pure (*Z*)-*N,N*-diethylcinnamamide and a 78/22 *Z/E* mixture of (*Z*)-*N,N*-dimethyloct-2-enamide, respectively (GC−MS and/or 300 MHz ^{1}H NMR). The relative configuration of substituents on the cyclopropane rings of compounds **5a** and **5b** was again established by NOESY experiments, and/or analysis of the ^{1}H NMR coupling constants between the cyclopropane protons. The explanation of the different relative position of the silyl group from (*E*)- or (*Z*)-α,β-unsaturated amides will be discussed in Scheme 5.

(11) CCDC 649433 contains the supplementary crystallographic data for compound **4g**. These data can be obtained free of charge via: www.ccdc.cam.ac.uk/conts/retrieving.html (or the Cambridge Data Center, 12 Union Road, Cambridge CB2 1EZ, UK; fax (+44)1223−336−033; or deposit@ccdc.cam.ac.uk).

TABLE 3. Synthesis of Silylcyclopropanecarboxamides 6 Derived from Disubstituted Cinnamamides



entry	6	R^1	R^4	dr[a]	yield (%)[b]
1	**6a**	Ph	Et	>98/2	79
2	**6b**	Ph	i-Pr	83/17	86
3	**6c**	Ph	*c*	>98/2	78
4	**6d**	pMeOC_6H_4	Et	64/36	50
5	**6e**	pMeOC_6H_4	*c*	66/34	86
6	**6f**	pFC_6H_4	Et	79/21	58
7	**6g**	pNO$_2$C$_6$H$_4$	Et	−	*d*

[a] Diastereoisomeric ratio (dr) was determined by GC−MS, and/or 300 MHz ^{1}H NMR analysis of the crude products **6**. [b] Isolated yield after column chromatography based on compound **1**. [c] From morpholine. [d] No reaction was observed, and unaltered starting material was recovered.

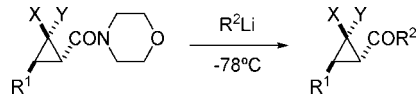
In general terms it is possible to conclude that: (1) The cyclopropanation reaction is general so, aliphatic (linear, cyclic or branched), functionalized, and aromatic α,β-unsaturated amides **1** can be employed as starting materials (Table 1 and Table 2); (2) di- and trisubstituted C−C double bonds can be efficiently cyclopropanated affording mainly only one diastereoisomer (Table 1 and Table 2); (3) this cyclopropanation process takes place in high yield; (4) the diastereoisomeric ratio was only slightly affected by the size of the groups on the nitrogen atom; so when the starting material was a diisopropylamide, the corresponding cyclopropane was obtained, although in high yields, with poorer stereocontrol (Table 2, entries 3/4, and 12/13); (5) the determination of the structure for compounds **2**−**5** has proven that the cyclopropanation process took place with complete stereospecificity since the geometry of the C=C bond of both (*E*)- or (*Z*)-α,β-enamides was conserved during the cyclopropanation process (Table 1/Scheme 1, and Table 2/Scheme 2); and finally (6) the silylcyclopropanation was carried out whitout additives using a readily available and cheaper reagent (dibromomethylsilane), in opposition to other methods in which a mixture of the most expensive diiodomethylsilane and TMEDA was used.[5]

Surprisingly, when the silylcyclopropanation process was performed on disubstituted α,β-unsaturated amides derived from (*E*)-cinnamamides, the silylcyclopropanes were obtained with the opposite spatial disposition, in which the silicon atom was *trans*-disposed with respect to the carboxamide group (Table 3).

It is noteworthy that the presence of different substituents on the aromatic ring of cinnamamides affected the stereoselectivity and yield of the silylcyclopropanation reaction (Table 3, entries 1, 4, and 6−7). A decrease in both diastereoisomeric ratio and yield (entries 4, and 6) or an absence of reaction leading to the recovery of the starting material (entry 7) was observed. The stereoselectivity of silylcyclopropanecarboxamides, **6**, was again ascertained as above (GC−MS, and 300 MHz ^{1}H NMR analysis of the crude products). The relative configuration of substituents on the cyclopropane ring was unambiguously established by analysis of the ^{1}H NMR coupling constants between the cyclopropane protons and NOESY experiments.

To confirm this unexpected structure, we initially considered carrying out X-ray analysis of compounds **6**. However, no crystals of these compounds could be obtained, and conse-

TABLE 4. Synthesis of Silylcyclopropyl Ketones 7



entry	4 or 6[a]	7	R^1	R^2	X	Y	yield (%)[b,c]
1	**4e**	**7a**	n-C_5H_{11}	n-Bu	H	Si-t-BuMe$_2$	92
2	**6c**	**7b**	Ph	Me	Si-t-BuMe$_2$	H	87
3	**6c**	**7c**	Ph	n-Bu	Si-t-BuMe$_2$	H	88
4	**6c**	**7d**	Ph	Ph	Si-t-BuMe$_2$	H	81

[a] Starting silylcyclopropanecarboxamide. [b] Isolated yield after column chromatography based on the corresponding starting material **4e** or **6c**. [c] Diastereoisomeric ratio for products **7** (determined by GC−MS and 300 MHz ^{1}H NMR analysis of the crude products) was the same as that shown for the starting materials (see Table 2).

quently, the cyclopropanamide **6a** was transformed into the corresponding cyclopropyl ketone **7d** (see below). The determination of the structure of **7d** by X-ray analysis confirmed the NOESY experiment.[12]

Synthetic Applications of Silylcyclopropanecarboxamides. To demonstrate the synthetic applications of the obtained silylcyclopropylamides, initially the cyclopropanamides **4e** and **6c** derived from morpholine[13] were readily transformed into the corresponding silylcyclopropyl ketones **7**. Thus, the reaction of **4e** or **6c** with the corresponding organolithium compound at −78 °C for 1 h afforded the corresponding ketone in very high yields (Table 4).

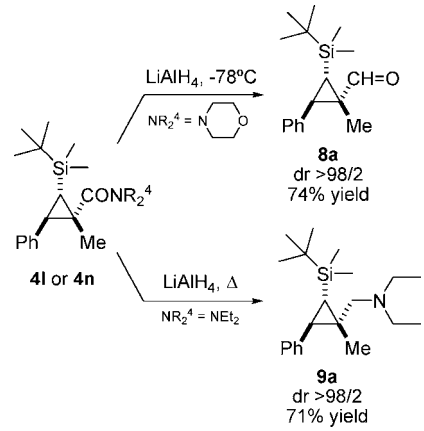
It is noteworthy that the relative configuration of the cyclopropane ring was unaffected by this transformation, with the ketone being obtained without loss of its diastereomeric purity during the transformation (GC−MS and 300 MHz ^{1}H NMR analysis of the crude products).

Remarkably, the use of morpholine amides as starting materials, to transform silylcyclopropyl amides into the ketone, is more advantageous than the employment of the corresponding Weinreb derivatives since morpholine is cheaper when compared to the amine required for the preparation of the Weinreb derivatives.[13]

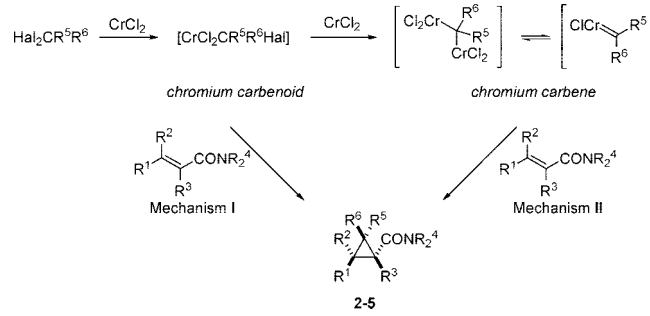
Silylcyclopropylamides could be also transformed into other functionalized cyclopropanic derivatives. Thus, on one hand, the silylcyclopropyl aldehyde **8a** was obtained in high yield (74%) as a single diastereoisomer, by reduction of **4n** (from morpholine) with lithium aluminum hydride at low temperature (−78 °C).[14] On the other hand, the treatment of the **4l** (derived from diethylamine) with $LiAlH_4$ at reflux afforded the corresponding amine **9a** (Scheme 3). In both cases the diastereoisomeric purity of the starting amides was conserved during the transformation.

Mechanism. Formation of products **2**−**5** can be rationalized by assuming that the reaction is started by the reaction of chromium dichloride with the dihalogenated reagents. Thus the monometalation of t-BuCHI$_2$ or Br$_2$CHSi-t-BuMe$_2$ could generate the corresponding chromium (III) carbenoid, Alternatively, t-BuCHI$_2$ or Br$_2$CHSi-t-BuMe$_2$ could be dimetalated affording a geminal dichromium intermediate,[15] which could be in

SCHEME 3. Synthesis of Silylcyclopropyl Aldehydes and Amines 8a and 9a



SCHEME 4. Hypothetical Mechanisms I and II



equilibrium with the corresponding chromium carbene complex.[16] Formation of products **2**−**5** can be accomplished by both organochromium intermediates and cyclopropanation of amides could be explained using two different models (**I** and **II**).

Thus, the chromium (III) carbenoids (Scheme 4, mechanism **I**) could react with the amide through a similar mechanism to that proposed by Houk for the addition of carbenoids to olefins,[17] and also utilized by us to explain the cyclopropanation[9] and the *tert*-butyl and silylcyclopropanation[10] of α,β-unsaturated amides **1**. Tentatively, we propose a transition state model depicted in Scheme 5, in which the coordination of the Cr(III) center (from the incipient:CR^{5}R ^{6}carbene) with the oxygen atom of the amide group providing the obtained cyclopropylamides **2** and **4** (R^5 = t-Bu and Si-t-BuMe$_2$ respectively), while maintaining the C=C bond geometry. In this proposed transition state the C=C bond and the C=O double bonds are not conjugated. Indirect support for this mechanistic proposal could be the fact that no cyclopropanation reaction took place on α,β-unsaturated esters under the same reaction conditions. This experimental result also suggested that the electron-donating character of the nitrogen is decisive in the cyclopropanation of the C−C double bond.

The formation of products **2** and **4** starting from (*E*)-α,β-enamides **1**, in which R^2 = H, with total or very high (**4n**) stereoselectivity could be explained by taking into account that in the most favored transition state (Scheme 5), the bulky *tert*-butyl or silyl groups prefer to occupy the R^5 position to minimize

(12) CCDC 663425 contains the supplementary crystallographic data for compound **7d**. These data can be obtained free of charge; see ref 11.

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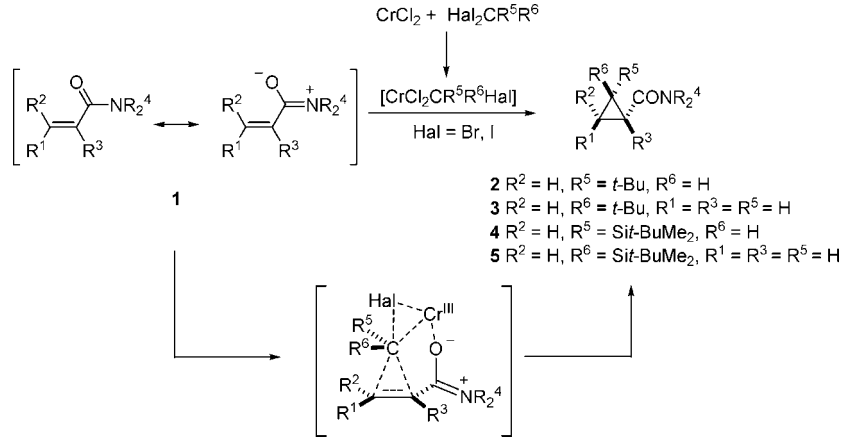
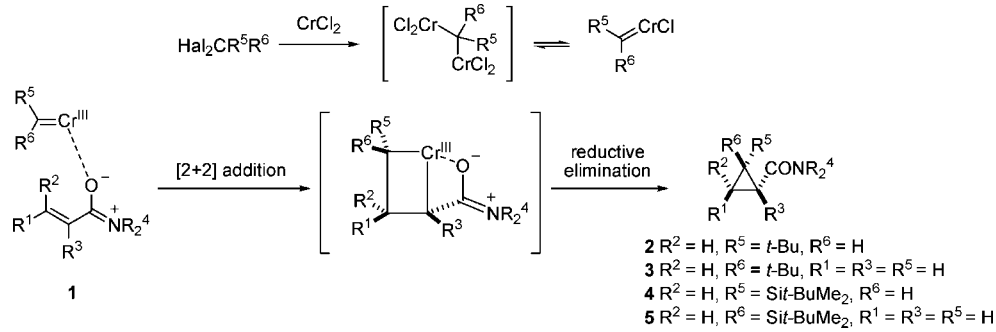
SCHEME 5. Carbenoid-Based Mechanism (I) for the Conversion of 1 into 2−5



SCHEME 6. Carbene-Based Mechanism (II) for the Conversion of 1 into 2-5



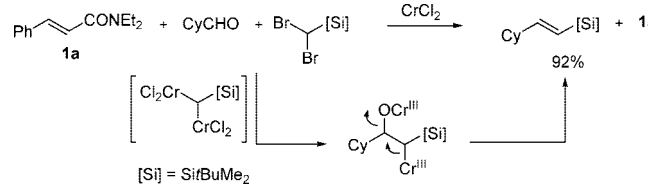
steric hindrance with R^1 (from disubstituted (*E*)-α,*β*-enamides) or with R^1 and R^3 (in the case of trisubstituted (*E*)-α,*β*-enamides). This proposed mechanism also explains the observed stereospecificity of the cyclopropanation. Thus, in cyclopropanes **3** and **5**, obtained from *Z*-amides, in which $R^1 = R^3 = H$, the bulky *tert*-butyl or silyl groups occupy the R^6 position, instead of R^5 in the transition state, since it would certainly avoid steric interactions with R^2 (Scheme 5).

Indirect support for this proposal was the fact that the cyclopropanation reaction of trisubstituted *Z*-amides ($R^1 = H$ and R^2, $R^3 \neq H$) and tetrasubstituted *Z*- or *E*-amides, failed. In both transition states the bulky *tert*-butyl or silyl group would have at least one group in a *cis*-relative position.

The other alternative mechanism **II** involving a chromium carbene complex can not be discarded. So, synthesis of **2** and **4** can be explained assuming a [2 + 2] addition reaction of the chromium alkylidene species[18] shown in Scheme 6. A reductive elimination from the generated chromacyclobutane would afford the corresponding silylcyclopropanecarboxamide. An argument similar to that shown in the addition of the chromium carbenoid to the amides can be used to explain the stereochemistry of the final products. In this context we could also assume that in the most favored transition state, to minimize the steric hindrance, the bulky *tert*-butyl or silyl groups occupy the R^5 position (from *E*-enamides), or the R^6 position (from *Z*-enamides). In a manner similar to that stated in mechanism **I**, the transition state of mechanism **II** could also explain the absence of cyclopropanation of trisubstituted *Z*-enamides or tetrasubstituted (*E*)- or (*Z*)-α,*β*-unsaturated amides.

In order to support mechanism **I** or **II**, two reactions were carried out. First, the cyclopropanation process was carried out in the presence of an aldehyde affording the corresponding vinyl silane[19] as the sole product, while cyclopropanecarboxamide was not observed and the α,*β*-unsaturated amide was recovered unaltered (Scheme 7). This result is in agreement with the generation of *gem*-dichromium species, and consequently it would support mechanism **II**.

SCHEME 7. Cyclopropanation Reaction in the Presence of an Aldehyde



Second, the cyclopropanation was carried out in the presence of TMEDA. No significant differences were observed when this result was compared with the experiment performed in the absence of TMEDA. Taking into account that it has been reported that the equilibrium between dimetallic species and the carbene complex can be displaced to the alkylidene by addition of an amine (generally TMEDA),[5a] the addition of TMEDA should enhance the yield of the cyclopropanecarboxamide, in that case in which *gem*-dichromium species were involved. In this sense, the result of this latter experiment would support the generation of monometallic species and consequently would support mechanism **I**. Thus, we could conclude that it is not possible to establish a mechanism with absolute certainty due the synthesis of vinylsilanes (Scheme 7).

(19) *tert*-Butyl[(*E*)-2-cyclohexylvinyl]dimethylsilane: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.95 (dd, $J = 18.8$, 5.7 Hz, 1 H), 5.52 (d, $J = 18.8$ Hz, 1 H), 1.71−0.83 (m, 11 H), 0.99 (s, 9 H), 0.22 (s, 6 H); 13 C NMR (75 MHz, $CDCl_3$): δ 154.0 (CH), 122.9 (CH), 43.9 (CH), 33.9 (2 × CH_2), 27.1 (3 × CH_3), 26.3 (2 × CH_2), 25.8 (CH_2), 17.7 (C), −7.0 (2 × CH_3).

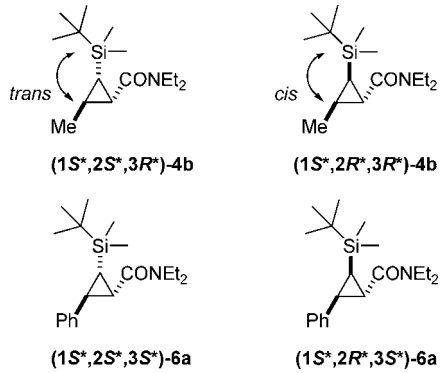


FIGURE 1. Plausible Orientation of Silyl Groups.

We have tried to establish the transition structures for the cyclopropanation reaction involving Cr(III)-intermediates, but technical problems with the Cr(III)-containing structures have prevented the location of these points of the potential energy surface until now.[20,21] However, the relative energies of the diastereoisomers of **4b** and **6a** in which silyl and methyl/phenyl groups are in a *trans*- or *cis*-relative position (Figure 1), were calculated, at the B3LYP/6-31G* level of theory, and according to what is expected on steric grounds, a *cis*-spatial disposition of the above-mentioned substituents always resulted in the less stable isomer, the difference in energy being 1.0 and 1.7 kcal mol^{-1}, for **4b** and **6a**, respectively.

All experimental results were according to these calculations except in the case of the cyclopropanation of *E*-cinnamamides (products **6**) in which the stereoselectivity could be controlled by stereoelectronic effects in the transition state rather than steric effects. Concerning these products **6**, the experimental results have also indicated the existence of stereoelectronic effects since the presence of electron donating or withdrawing groups affected the cyclopropanation process affording a mixture of diastereoisomers as the final product or yielding the starting material unaltered (Table 3).

The search for the transition states of the cyclopropanation reactions involving Cr(III)-intermediates is underway. To date, we do not have a mechanistic proposal for the different stereochemical behavior observed in the case of disubstituted cinnamamides. However, studies to fully delineate the factors involved in these transformations are currently under investigation in our laboratory.

Conclusions

In conclusion, a $CrCl_2$-promoted stereospecific alkyl- and silylcyclopropanation reaction of α,β-unsaturated amides with complete or very high stereoselectivity and in high yields was carried out. This cyclopropanation process is achieved from α,β-unsaturated amides in which the C=C bond is di- and trisubstituted. Taking into account the high yields and good stereoselectivity of this silylcyclopropanation, this method would be a valuable alternative for the stereoselective achievement of silylcyclopropanecarboxamides. We proposed two different mechanisms to explain our results. One is based on the generation of a chromium (III) carbenoid, and the other is based on a carbene complex. We have, however, concluded that it is not possible to discard one of these mechanisms with absolute certainty.

The proposed mechanisms and the theoretical studies have explained our experimental results except those of the silylcyclopropanation of disubstituted cinnamamides.

Experimental Section

Compounds **2b**−**d**, **4b**, **4c**, **4 h**, **4j**, **4l**, **4o**, and **5a** displayed analytical data in accordance with the published values.[10]

Synthesis of *tert*-Butylcyclopropanecarboxamides 2a and 3. (1*S,2*S**,3*S**)-2-(*tert*-Butyl)-*N*, *N*-diethyl-3-phenylcyclopropanecarboxamide (2a).** To a suspension of anhydrous $CrCl_2$ (1.6 mmol, 4.0 equiv) in THF (4 mL) was added dropwise (*E*)-*N*,*N*-diethylcinnamamide (*E*)-**1a** (0.4 mmol, 1.0 equiv) in THF (2 mL) and I_2CHt-Bu (1.5 mmol, 3.75 equiv) at room temperature and under an inert atmosphere. After stirring for 18 h at room temperature the reaction mixture was quenched by the addition of 1.0 M aqueous HCl (5 mL) and extracted with diethyl ether (3 × 10 mL). The combined extracts were washed with NH_4Cl sat. and water, dried over Na_2SO_4, concentrated under vacuum, and filtered through a pad of Celite. Purification by column chromatography on silica gel (hexane/EtOAc, 10:1) afforded the pure compound **2a** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29−7.15 (m, 5 H), 3.87 (m, 1 H), 3.76 (m,1 H), 3.23 (m, 1 H), 3.09 (m, 1 H), 2.93 (apparent t, *J* = 6.4 Hz, 1 H), 1.82 (dd, *J* = 9.7, 5.7 Hz, 1 H), 1.49 (dd, *J* = 9.5, 7.9 Hz, 1 H), 1.22 (t, *J* = 7.1 Hz, 3 H), 1.13 (t, *J* = 7.1 Hz, 3 H), 1.02 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6 (C), 142.1 (C), 128.1 (2 × CH), 126.5 (2 × CH), 125.7 (CH), 41.7 (2 × CH_2), 39.8 (CH), 31.4 (C), 29.8 (CH), 29.6 (3 × CH_3), 24.7 (CH), 13.9 (CH_3), 12.5 (CH_3); MS (70 eV, EI) *m*/*z* (%): 273 $[M]^+$ (41), 216 (100), 204 (69), 158 (47), 100 (95), 72 (84); IR (neat): 2963, 2871, 1641, 1462 cm^{-1}, HRMS (70 eV) calcd for $C_{18}H_{27}NO$ 273.2093. Found 273.2088; R_f = 0.42 (hexane/EtOAc, 3:1).

(1*R,2*S**,3*S**)-2-(*tert*-Butyl)-*N*,*N*-diethyl-3-phenylcyclopropanecarboxamide (3):** yellow oil.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28−7.04 (m, 5 H), 3.69−3.43 (m, 2 H), 3.15−3.03 (m, 1 H), 2.87−2.78 (m, 1 H), 2.34 (dd, *J* = 9.5, 7.0 Hz, 1 H), 2.18 (apparent t, *J* = 6.2 Hz, 1 H), 1.95 (dd, *J* = 9.5, 6.2 Hz, 1 H), 1.10 (t, *J* = 7.1 Hz, 3 H), 0.98 (s, 9 H), 0.71 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7 (C), 137.7 (C), 127.9 (2 × CH), 127.7 (2 × CH), 125.9 (CH), 41.0 (CH_2), 39.6 (CH_2), 34.6 (CH), 29.3 (C), 28.2 (3 × CH_3), 27.2 (CH), 25.9 (CH), 14.0 (CH_3), 12.3 (CH_3); MS (70 eV, EI) *m*/*z* (%): 273 $[M]^+$ (<1), 216 (100), 188 (10), 115 (20), 77 (5); IR (neat): 2960, 2364, 1639, 1462 cm^{-1}; HRMS (70 eV) calcd for $C_{18}H_{27}NO$ 273.2093. Found 273.2050; R_f = 0.30 (hexane/EtOAc, 5:1).

Synthesis of Silylcyclopropanecarboxamides 4−6. (1*S,2*S**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diethyl-1-methylcyclopropanecarboxamide (4a).** To a suspension of anhydrous $CrCl_2$ (1.6 mmol, 4.0 equiv) in THF (4 mL) was added dropwise the amide **1a** (0.4 mmol, 1.0 equiv) in THF (2 mL) and $Br_2CHSitBuMe_2$ (1.5 mmol, 3.75 equiv) at room temperature and under an inert atmosphere. After stirring for 18 h at room temperature the reaction mixture was quenched by the addition of 1.0 M aqueous HCl (5 mL) and extracted with diethyl ether (3 × 10 mL). The combined extracts were washed with NH_4Cl sat. and water, dried over Na_2SO_4, concentrated under vacuum, and filtered through a pad of Celite. Purification by column chromatography on silica gel (hexane/EtOAc, 10:1) yielded product **4a** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.78−3.63 (m, 1 H), 3.34−3.12 (m, 3 H), 1.23 (s, 3 H), 1.10 (t, *J* = 7.1 Hz, 3 H), 1.02 (t, *J* = 7.1 Hz, 3 H), 0.83 (dd, *J* = 9.5, 4.1 Hz, 1 H), 0.79 (*s*-pentylcyclopropanecarboxamide, 9 H), 0.70 (dd, *J* = 10.1, 4.1 Hz, 1 H), 0.05 (s, 3 H), −0.26 (dd, *J* = 10.1, 8.2 Hz, 1 H), −0.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.6 (C), 41.4 (CH_2), 38.9 (CH_2), 26.7 (3 × CH_3), 25.2 (CH_3), 24.8 (C), 17.6 (CH_2), 17.5 (C), 14.0 (CH_3), 12.5 (CH_3), 10.2 (CH), −5.4 (CH_3), −8.3 (CH_3); MS (70 eV, EI) *m*/*z* (%): 269 $[M^+]$ (11), 254 (19), 212 (100), 154 (92), 73 (77); IR (neat): 2955, 2856, 1632, 1461, 1316, 1266 cm^{-1}; HRMS (70 eV) calcd for $C_{15}H_{31}NOSi$ 269.2175. Found 269.2178; R_f = 0.30 (hexane/EtOAc, 5:1).

(20) The geometries of the stationary points were fully optimized, and characterized by frequency calculations.

(21) The calculations were carried out with the Gaussian program: Frisch, M. J. et al. *Gaussian 98*, Revision A.11.3; Gaussian, Inc.: Pittsburgh, PA, 2002.

(1*S,2*S**,3*R**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diisopropyl-3-pentylcyclopropanecarboxamide (4d):** colorless oil.[1]H NMR (300 MHz, $CDCl_3$): δ 4.33−4.05 (m, 1 H), 3.79−3.22 (m, 1 H), 1.61−1.09 (m, 22 H), 0.87 (s, 9 H), 0.83 (t, J = 7.4 Hz, 3 H), 0.00 (s, 3 H), −0.04− −0.14 (m, 1 H), −0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6 (C), 47.0 (CH), 45.2 (CH), 35.3 (CH_2), 31.6 (CH_2), 28.8 (CH_2), 27.2 (CH), 26.8 (CH), 26.5 (3 × CH_3), 22.5 (CH_2), 21.5 (CH_3), 21.4 (CH_3), 20.6 (CH_3), 20.4 (CH_3), 17.2 (C), 13.9 (CH), 13.2 (CH_3), −5.9 (CH_3), −6.0 (CH_3); MS (70 eV, EI) *m*/*z* (%): 353 $[M]^+$ (<1), 297 (31), 296 (100), 254 (15), 212 (8), 73 (11); IR (neat): 2956, 2855, 1637, 1462, 823 cm^{-1}; HRMS (70 eV) calcd for $C_{21}H_{43}NOSi$ 353.3114. Found 353.3065; R_f = 0.45 (hexane/EtOAc, 10:1).

4-[(1*S,2*S**,3*R**)-2-(*tert*-Butyldimethylsilyl)-3-pentylcyclopropylcarbon-1-yl]morpholine (4e):** colorless oil.[1]H NMR (300 MHz, $CDCl_3$): δ 3.704−3.61 (m, 8 H), 1.56−1.49 (m, 2 H), 1.38−1.28 (m, 8 H), 0.92−0.89 (m, 3 H), 0.90 (s, 9 H), −0.01 (s, 3 H), −0.03− −0.15 (m, 1 H), −0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6 (C), 66.8 (CH_2), 66.6 (CH_2), 45.9 (CH_2), 42.1 (CH_2), 35.3 (CH_2), 31.6 (CH_2), 28.9 (CH_2), 26.5 (3 × CH_3), 24.2 (CH), 24.1 (CH), 22.5 (CH_2), 17.1 (C), 13.9 (CH_3), 13.4 (CH), −5.9 (CH_3), −6.0 (CH_3); MS (70 eV, EI) *m*/*z* (%): 339 $[M^+]$ (<1), 324 (8), 283 (28), 282 (100), 69 (5); IR (neat): 2955, 2855, 1642, 1463, 1231, 1117 cm^{-1}; HRMS (70 eV) calcd for $C_{19}H_{37}NO_2Si$ 339.2594. Found 339.2584; R_f = 0.35 (hexane/EtOAc, 5:1).

(1*S,2*S**,3*R**)-2-(*tert*-Butyldimethylsilyl)-*N*, *N*-diethyl-3-heptylcyclopropanecarboxamide (4f):** orange oil.[1]H NMR (300 MHz, $CDCl_3$): δ 3.64−3.48 (m, 2 H), 3.36−3.15 (m, 2 H), 1.56−1.49 (m, 2 H), 1.44−1.22 (m, 15 H), 1.17 (t, J = 7.1 Hz, 3 H), 0.94−0.87 (m, 3 H), 0.92 (s, 9 H), 0.04 (s, 3 H), −0.04 (dd, J = 9.8, 7.9 Hz, 1 H), −0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.8 (C), 41.9 (CH_2), 40.4 (CH_2), 35.4 (CH_2), 31.8 (CH_2), 29.4 (CH_2), 29.2 (2 × CH_2), 26.5 (3 × CH_3), 24.6 (CH), 24.3 (CH), 22.6 (CH_2), 17.2 (C), 14.6 (CH_3), 14.0 (CH_3), 13.3 (CH), 13.1 (CH_3), −5.9 (CH_3), −6.2 (CH_3); MS (70 eV, EI) *m*/*z* (%): 353 $[M]^+$ (<1), 296 (100), 238 (16), 73 (28); IR (neat): 2953, 2855, 1637, 1463 cm^{-1}; HRMS (70 eV) calcd for $C_{21}H_{43}NOSi$ 353.3114. Found 353.3079; R_f = 0.60 (hexane/EtOAc, 5:1).

(1*S,2*S**,3*R**)-2-(*tert*-Butyldimethylsilyl)-3-cyclohexyl-*N*,*N*-diethylcyclopropanecarboxamide (4g):** white solid.[1]H NMR (300 MHz, $CDCl_3$): δ 3.64−3.48 (m, 2 H), 3.36−3.10 (m, 2 H), 1.81−1.61 (m, 7 H), 1.53 (dd, J = 9.5, 4.4 Hz, 1 H), 1.46−1.37 (m, 1 H), 1.29−1.04 (m, 5 H), 1.23 (t, J = 7.1 Hz, 3 H), 1.09 (t, J = 7.1 Hz, 3 H), 0.89 (s, 9 H), 0.04 (s, 3 H), −0.16 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9 (C), 43.8 (CH), 41.9 (CH_2), 40.3 (CH_2), 32.9 (CH_2), 32.5 (CH_2), 31.0 (CH), 26.6 (3 × CH_3), 26.4 (CH_2), 26.1 (2 × CH_2), 22.8 (CH), 17.8 (C), 14.6 (CH_3), 13.0 (CH_3), 12.3 (CH), −5.7 (CH_3), −6.3 (CH_3); MS (70 eV, EI) *m*/*z* (%): 337 $[M]^+$ (8), 280 (53), 222 (100), 73 (45); IR (neat): 2906, 2849, 1623, 1467 cm^{-1}; HRMS (70 eV) calcd for $C_{20}H_{39}NOSi$ 337.2801. Found 337.2782; R_f = 0.51 (hexane/EtOAc, 5:1).

(1*S,2*S**,3*R**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diethyl-3-(propen-1-yl)cyclopropanecarboxamide (4i):** yellow oil.[1]H NMR (300 MHz, $CDCl_3$): δ 5.55 (dd, J = 11.4, 4.9 Hz, 1 H), 5.2 (dd, J = 11.4, 6.8 Hz, 1 H), 3.53−3.48 (m, 2 H), 3.35−3.19 (m, 2 H), 1.78−1.67 (m, 2 H), 1.63 (d, J = 4.8 Hz, 3 H), 1.17 (t, J = 5.3 Hz, 3 H), 1.08 (t, J = 5.3 Hz, 3 H), 0.90 (s, 9 H), 0.79 (apparent t, J = 7.5 Hz, 1 H),−0.09 (s, 3 H), −0.13 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.5 (C), 129.7 (CH), 125.3 (CH), 41.6 (CH_2), 40.4 (CH_2), 26.5 (3 × CH_3), 25.9 (CH), 23.5 (CH), 17.7 (CH_3), 17.1 (C), 14.4 (CH_3), 13.1 (CH), 8.9 (CH_3), −7.2 (CH_3), −7.8 (CH_3); MS (70 eV, EI) *m*/*z* (%): 295 $[M]^+$ (41), 240 (35), 180 (36), 100 (20), 73 (100); IR (neat): 2980, 2856, 1637, 1462 cm^{-1}; HRMS (70 eV) calcd for $C_{17}H_{33}NOSi$ 295.2331. Found 295.2346; R_f = 0.44 (hexane/EtOAc, 5:1).

(1*S,2*S**,3*R**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diethyl-3-isobutyl-1-methylcyclopropanecarboxamide (4k):** orange oil.[1]H NMR (300 MHz, $CDCl_3$): δ 3.71−3.58 (m, 1 H), 3.35−3.16 (m, 3 H), 1.66−1.62 (m, 1 H), 1.22 (t, J = 6.6 Hz, 1 H), 1.17 (s, 3 H), 1.15−0.97 (m, 8 H), 0.88 (d, J = 6.6 Hz, 3 H), 0.86 (d, J = 6.5 Hz, 3 H), 0.75 (s, 9 H), −0.02 (s, 3 H), −0.37 (s, 3 H), −0.62 (d, J = 8.2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.6 (C), 41.3 (CH_2), 39.5 (CH_2), 38.8 (CH_2), 29.4 (C), 27.8 (CH), 26.9 (3 × CH_3), 24.1 (CH), 23.1 (CH_3), 22.5 (CH_3), 19.0 (CH_3), 17.8 (CH), 17.3 (C), 13.9 (CH_3), 12.5 (CH_3), −5.3 (CH_3), −7.3 (CH_3); MS (70 eV, EI) *m*/*z* (%): 323 $[M^+]$ (<1), 310 (28), 268 (100), 73 (56); IR (neat): 2954, 2897, 1640, 1470 cm^{-1}; HRMS (70 eV) calcd for $[C_{19}H_{39}NOSi\text{-}CH_3]$ 310.2566. Found 310.2570; R_f = 0.32 (hexane/EtOAc, 10:1).

(1*S,2*S**,3*R**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diisopropyl-1-methyl-3-phenylcyclopropanecarboxamide (4m):** white solid.[1]H NMR (300 MHz, $CDCl_3$): δ 7.31−7.03 (m, 5 H), 4.38−4.22 (m, 1 H), 3.28−3.16 (m, 1 H), 2.15 (d, J = 8.5 Hz, 1 H), 1.33 (d, J = 6.7 Hz, 3 H), 1.31 (d, J = 6.7 Hz, 3 H), 1.24 (d, J = 6.7 Hz, 3 H), 1.04 (d, J = 6.7 Hz, 3 H), 1.00 (s, 3 H), 0.77 (s, 9 H), 0.33 (d, J = 8.5 Hz, 1 H), 0.24 (s, 3 H), −0.26 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.6 (C), 137.8 (C), 128.1 (2 × CH), 127.9 (2 × CH), 126.0 (CH), 48.2 (CH), 45.5 (CH), 34.4 (C), 31.8 (CH), 26.8 (3 × CH_3), 21.2 (CH_3), 20.8 (CH_3), 20.7 (CH_3), 20.1 (CH_3), 18.2 (CH_3), 17.6 (C), 14.2 (CH), −5.1 (CH_3), −7.8 (CH_3); MS (70 eV, EI) *m*/*z* (%): 373 $[M]^+$ (11), 358 (13), 316 (100), 274 (38), 73 (63); IR (neat): 2967, 2361, 1627, 1440 cm^{-1}; HRMS (70 eV) calcd for $C_{23}H_{39}NOSi$ 373.2801. Found 373.2799; R_f = 0.31 (hexane/EtOAc, 5:1).

4-{(1*S,2*S**,3*R**)-[2-(*tert*-Butyldimethylsilyl)-1-methyl-3-phenylcyclopropyl]carbon-1-yl}morpholine (4n):** white solid.[1]H NMR (300 MHz, $CDCl_3$): δ 7.32−7.13 (m, 5 H), 3.71−3.54 (m, 8 H), 2.31 (d, J = 8.7 Hz, 1 H), 1.09 (s, 3 H), 0.85 (s, 9 H), 0.48 (d, J = 8.7 Hz, 1 H), 0.26 (s, 3 H), −0.20 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.5 (C), 137.2.8 (C), 128.1 (2 × CH), 128.2 (2 × CH), 126.3 (CH), 66.8 (2 × CH_2), 46.6 (CH_2), 42.3 (CH_2), 32.0 (CH), 31.9 (C), 26.7 (3 × CH_3), 18.2 (CH_3), 17.5 (C), 14.4 (CH), −5.3 (CH_3), −7.9 (CH_3); MS (70 eV, EI) *m*/*z* (%): 359 $[M^+]$ (15), 303 (25), 302 (100), 268 (15), 244 (8), 73 (26); IR (neat): 3053, 2856, 1638, 1430, 1259, 1115 cm^{-1}; HRMS (70 eV) calcd for $C_{21}H_{33}NO_2Si$ 359.2281. Found 359.2321; R_f = 0.28 (hexane/EtOAc, 5:1).

(1*S,2*S**,3*S**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diethyl-3-ethyl-3-phenylcyclopropanecarboxamide (4p):** yellow oil.[1]H NMR (300 MHz, $CDCl_3$): δ 7.34−7.19 (m, 5 H), 4.01−3.70 (m, 2 H), 3.47−3.16 (m, 2 H), 2.17 (d, J = 7.3 Hz, 1 H), 2.07−1.99 (m, 1 H), 1.82−1.72 (m, 1 H), 1.36 (t, J = 7.1 Hz, 3 H), 1.15 (t, J = 7.1 Hz, 3 H), 1.08 (d, J = 7.3 Hz, 1 H), 0.86 (s, 9 H), 0.64 (t, J = 7.3 Hz, 3 H), −0.11 (s, 3 H), −0.87 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.6 (C), 143.3 (C), 129.3 (2 × CH), 128.0 (2 × CH), 126.3 (CH), 42.1 (CH_2), 40.7 (CH_2), 40.3 (C), 29.4 (CH_2), 27.1 (CH), 26.4 (3 × CH_3), 17.2 (C), 17.0 (CH), 14.6 (CH_3), 12.8 (CH_3), 11.4 (CH_3), −5.9 (CH_3), −7.8 (CH_3); MS (70 eV, EI) *m*/*z* (%): 359 $[M]^+$ (37), 344 (92), 302 (70), 244 (56), 73 (100); IR (neat): 2930, 2855, 1632, 1462 cm^{-1}; HRMS (70 eV) calcd for $C_{22}H_{37}NOSi$ 359.2644. Found 359.2648; R_f = 0.43 (hexane/EtOAc, 5:1).

(1*R,2*S**,3*S**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diethyl-3-phenylcyclopropanecarboxamide (5b):** white solid.[1]H NMR (400 MHz, $CDCl_3$): δ 7.37−7.04 (m, 5 H), 3.62−3.44 (m, 2 H), 3.17−2.71 (m, 2 H), 2.31 (apparent t, J = 8.6 Hz, 1 H), 1.95 (dd, J = 8.6, 7.4 Hz, 1 H), 1.36 (dd, J = 8.3, 7.4 Hz, 1 H), 1.10 (t, J = 7.1 Hz, 3 H), 0.98 (s, 9 H), 0.64 (t, J = 7.1 Hz, 3 H), 0.00 (s, 3 H), −0.04 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7 (C), 137.8 (C), 127.9 (2 × CH), 127.7 (2 × CH), 126.0 (CH), 41.0 (CH_2), 39.7 (CH_2), 27.3 (CH), 26.5 (3 × CH_3), 26.4 (CH), 17.0 (C), 14.1 (CH_3), 12.3 (CH_3), 6.7 (CH), −7.4 (CH_3), −7.7 (CH_3); MS (70 eV, EI) *m*/*z* (%): 331 $[M]^+$ (4), 316 (25), 274 (100), 115 (42), 59 (35); IR (neat): 3055, 2986, 1632, 1462 cm^{-1}; HRMS (70 eV) calcd for $C_{20}H_{33}NOSi$ 331.2331. Found 331.2339; R_f = 0.38 (hexane/EtOAc, 5:1).

(1*S,2*R**,3*S**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diethyl-3-phenylcyclopropanecarboxamide (6a):** yellow oil. [1]H NMR (300

MHz, $CDCl_3$): δ 7.24−7.02 (m, 5 H), 3.52−3.07 (m, 4 H), 2.54 (dd, J = 8.2, 4.5 Hz, 1 H), 1.94 (dd, J = 10.2, 4.5 Hz, 1 H), 1.09 (t, J = 7.1 Hz, 3 H), 1.01 (t, J = 7.1 Hz, 3 H), 0.78 (s, 9 H), 0.51 (dd, J = 10.2, 8.2 Hz, 1 H), 0.04 (s, 3 H), −0.12 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.8 (C), 139.3 (C), 128.8 (2 × CH), 127.9 (2 × CH), 126.2 (CH), 41.8 (CH_2), 41.1 (CH_2), 29.9 (CH), 26.5 (3 × CH_3), 20.4 (CH), 16.9 (C), 14.4 (CH), 14.0 (CH_3), 13.9 (CH_3), −5.9 (CH_3), −6.1 (CH_3); MS (70 eV, EI) m/z (%): 331 $[M]^+$ (3), 316 (27), 274 (100), 171 (33), 115 (44), 59 (34); IR (KBr): 3061, 2954, 1638, 1462 cm^{-1}; HRMS (70 eV) calcd for $C_{20}H_{33}NOSi$ 331.2331. Found 331.2331; R_f = 0.29 (hexane/EtOAc, 5:1).

(1*S,2*R**,3*S**)-2-(*tert*-Butyldimethylsilyl)-3-phenyl-*N*,*N*-diisopropylcyclopropanecarboxamide (6b):** white solid.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23−7.04 (m, 5 H), 4.21−4.15 (m, 1 H), 3.70−3.57 (m, 1 H), 2.57 (dd, J = 8.1, 4.5 Hz, 1 H), 1.93 (dd, J = 10.3, 4.5 Hz, 1 H), 1.27−1.11 (m, 12 H), 0.79 (s, 9 H), 0.51 (dd, J = 10.3, 8.1 Hz, 1 H), 0.00 (s, 3 H), −0.06 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.0 (C), 142.5 (C), 128.3 (2 × CH), 125.8 (CH), 125.7 (2 × CH), 47.4 (CH), 45.5 (CH), 30.5 (CH), 27.4 (CH), 26.5 (3 × CH_3), 21.5 (CH_3), 21.4 (CH_3), 20.6 (CH_3), 20.4 (CH_3), 17.2 (C), 15.9 (CH), −5.7 (CH_3), −6.3 (CH_3); MS (70 eV, EI) m/z (%): 359 $[M]^+$ (17), 316 (25), 268 (69), 244 (50), 73 (100); IR (neat): 2927, 2366, 2243, 1633, 1470 cm^{-1}; HRMS (70 eV) calcd for [$C_{22}H_{37}NOSi$-H] 358.2566. Found 358.2584; R_f = 0.50 (hexane/EtOAc, 5:1).

4-{(1*S,2*R**,3*S**)-[2-(*tert*-Butyldimethylsilyl)-3-phenylcyclopropyl]carbon-1-yl}morpholine (6c).** White solid.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31−7.13 (m, 5 H), 3.82−3.27 (m, 8 H), 2.93 (dd, J = 10.1, 4.4 Hz, 1 H), 2.25 (dd, J = 6.4, 4.4 Hz, 1 H), 0.97 (apparent t, J = 10.1, 6.4 Hz, 1 H), 0.89 (s, 9 H), −0.26 (s, 3 H), −0.52 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6 (C), 138.8 (C), 128.8 (2 × CH), 127.9 (2 × CH), 126.3 (CH), 66.7 (2 × CH_2), 45.9 (CH_2), 42.6 (CH_2), 29.8 (CH), 26.3 (3 × CH_3), 19.9 (CH), 16.9 (C), 14.5 (CH), −6.2 (2 × CH_3); MS (70 eV, EI) m/z (%): 345 $[M]^+$ (39), 330 (9), 288 (100), 254 (25), 73 (66); IR (neat): 2954, 2360, 1632, 1462 cm^{-1}; HRMS (70 eV) calcd for $C_{20}H_{31}NO_2Si$ 345.2124. Found 345.2147; R_f = 0.23 (hexane/EtOAc, 3:1).

(1*S,2*R**,3*S**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diethyl-3-(4-methoxyphenyl)cyclopropanecarboxamide (6d):** yellow oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.12 (d, J = 8.6 Hz, 2 H), 6.79 (d, J = 8.6 Hz, 2 H), 3.78 (s, 3 H), 3.58 (q, J = 7.1 Hz, 2 H), 3.43 (m, 2 H), 2.79 (dd, J = 10.8, 4.5 Hz, 1 H), 2.18 (dd, J = 6.5, 4.5 Hz, 1 H), 1.34 (t, J = 7.0 Hz, 3 H), 1.13 (t, J = 7.0 Hz, 3 H), 0.92 (dd, J = 10.8, 6.5 Hz, 1 H), 0.85 (s, 9 H), −0.28 (s, 3 H) −0.46 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.9 (C), 158.0 (C), 131.3 (C), 129.8 (2 × CH), 113.3 (2 × CH), 55.1 (CH_3), 41.9 (CH_2), 41.0 (CH_2), 29.2 CH), 26.4 (3 × CH_3), 20.5 (CH), 16.9 (C), 15.1 (CH_3), 14.2 (CH), 13.1 (CH_3), −5.9 (CH_3), −6.0 (CH_3); MS (70 eV, EI) m/z (%): 361 [M^+] (44), 346 (17), 304 (48), 246 (21), 240 (46), 73 (100); IR (neat): 2955, 2856, 1626, 1515, 1463, 1265 cm^{-1}; HRMS (70 eV) calcd for $C_{21}H_{35}NO_2Si$ 361.2437. Found 361.2448; R_f = 0.28 (hexane/EtOAc, 5:1).

4-{(1*S,2*R**,3*S**)-[2-(*tert*-Butyldimethylsilyl)-3-(4-methoxyphenyl)cyclopropyl]carbon-1-yl}morpholine (6e):** yellow oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.06 (d, J = 8.7 Hz, 2 H), 6.67 (d, J = 8.7 Hz, 2 H), 3.78 (s, 3 H), 3.67−3.60 (m, 8 H), 2.61 (dd, J = 8.2, 4.5 Hz, 1 H), 1.95 (dd, J = 10.2, 4.5 Hz, 1 H), 0.90 (s, 9 H), 0.61 (dd, J = 10.2, 8.2 Hz, 1 H), 0.07 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3 (C), 158.0 (C), 133.7 (C), 127.0 (2 × CH), 113.8 (2 × CH), 66.8 (CH_2), 66.6 (CH_2), 55.2 (CH_3), 45.9 (CH_2), 42.2 (CH_2), 27.7 (CH), 27.1 (CH), 26.5 (3 × CH_3), 17.1 (C), 14.9 (CH), −5.8 (CH_3), −6.2 (CH_3); MS (70 eV, EI) m/z (%): 375 [M^+] (16), 360 (8), 319 (24), 318 (100), 254 (7), 69 (12); IR (neat): 3053, 2856, 1638, 1515, 1266, 1116 cm^{-1}; HRMS (70 eV) calcd for $C_{21}H_{33}NO_3Si$ 375.223. Found 375.2270; R_f = 0.23 (hexane/EtOAc, 3:1).

(1*S,2*R**,3*S**)-2-(*tert*-Butyldimethylsilyl)-*N*,*N*-diethyl-3-(4-fluorophenyl)cyclopropanecarboxamide (6f):** yellow oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16 (dd, J = 8.6, 5.5 Hz, 2 H), 6.94 (t, J = 8.6 Hz, 2 H), 3.62−3.52 (m, 2 H), 3.50−3.35 (m, 2 H), 2.81 (dd, J = 10.9, 4.4 Hz, 1 H), 2.19 (dd, J = 6.8, 4.4 Hz, 1 H), 1.33 (t, J = 7.1 Hz, 3 H), 1.13 (t, J = 7.1 Hz, 3 H), 0.93 (dd, J = 10.9, 6.8 Hz, 1 H), 0.84 (s, 9 H), −0.30 (s, 3 H), −0.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6 (C), 161.4 (d, $^1J_{CF}$ = 243.3 Hz, C), 135.0 (C), 130.3 (CH), 130.2 (CH), 114.7 (d, $^3J_{CF}$ = 21.3 Hz, 2 × CH), 42.0 (CH_2), 41.0 (CH_2), 29.1 (CH), 26.3 (3 × CH_3), 20.6 (CH), 16.9 (C), 15.1 (CH_3), 14.5 (CH), 13.1 (CH_3), −5.9 (CH_3), −6.0 (CH_3); MS (70 eV, EI) m/z (%): 349 [M^+] (43), 292 (100), 234 (26), 180 (23), 118 (34); IR (neat): 2955, 2856, 1636, 1513, 1463, 825 cm^{-1}; HRMS (70 eV) calcd for $C_{20}H_{32}FNOSi$ 349.2237. Found 349.2236; R_f = 0.30 (hexane/EtOAc, 5:1).

Synthesis of Silylcyclopropyl ketones 7. Butyl[(1*R,2*R**,3*S**)-2-(*tert*-butyldimethylsilyl)-3-pentylcycloprop-1-yl]ketone (7a).** A 2.0 M solution of *n*-BuLi in di-*n*-butyl ether (1.2 mmol, 3.0 equiv) was added dropwise to a solution of the amide **4e** (0.4 mmol, 1.0 equiv) in anhydrous THF (2 mL) at −78 °C under nitrogen atmosphere. The mixture was stirred at −78 °C for 1 h. Then, the reaction was quenched with an aqueous saturated solution of ammonium chloride (5 mL) and extracted with dichloromethane (3 × 10 mL). The organic layers were washed with water, dried over Na_2SO_4, and concentrated under vacuum. Purification by column chromatography on silica gel (hexane/EtOAc, 5:1) yielded the butyl ketone **7a** as colorless oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 2.54 (t, J = 7.4 Hz, 1 H), 2.52 (t, J = 7.4 Hz, 1 H), 1.79 (dd, J = 9.2, 3.7 Hz, 1 H), 1.62−1.52 (m, 3 H), 1.39−1.25 (m, 13 H), 0.91 (t, J = 7.3 Hz, 3 H), 0.88 (s, 9 H), 0.15 (apparent t, J = 9.2 Hz, 1 H), 0.08 (s, 3 H), −0.15 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 211.6 (C), 44.1 (CH_2), 35.5 (CH_2), 33.3 (CH), 31.5 (CH_2), 29.6 (CH), 28.9 (CH_2), 26.5 (3 × CH_3), 26.1 (CH_2), 22.5 (CH_2), 22.3 (CH_2), 18.4 (CH), 17.2 (C), 14.0 (CH_3), 13.8 (CH_3), −5.9 (2 × CH_3); MS (70 eV, EI) m/z (%): 310 [M^+] (<1), 253 (100), 169 (44), 141 (20), 75 (64); IR (neat): 2956, 2856, 1700, 1465, 1246, 1132 cm^{-1}; HRMS (70 eV) calcd for $C_{19}H_{38}OSi$ 310.2692. Found 310.2688; R_f = 0.64 (hexane/EtOAc, 10:1).

Methyl[(1*R,2*S**,3*R**)-2-(*tert*-butyldimethylsilyl)-3-phenylcycloprop-1-yl]ketone (7b):** yellow oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16−7.10 (m, 5 H), 2.84 (dd, J = 11.1, 4.4 Hz, 1 H), 2.34 (dd, J = 6.8, 4.4 Hz, 1 H), 2.25 (s, 3 H), 0.85 (dd, J = 11.1, 6.8 Hz, 1 H), 0.74 (s, 9 H), −0.35 (s, 3 H), −0.68 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 207.9 (C), 138.4 (C), 129.0 (2 × CH), 128.0 (2 × CH), 126.6 (CH), 32.7 (CH), 30.7 (CH), 30.3 (CH_3), 26.4 (3 × CH_3), 18.0 (CH), 17.0 (C), −6.1 (CH_3), −6.5 (CH_3); MS (70 eV, EI) m/z (%): 274 [M^+] (23), 218 (11), 217 (61), 143 (17), 128 (11), 75 (100), 73 (41); IR (neat): 3057, 2955, 1697, 1408, 1254, 1182 cm^{-1}; HRMS (70 eV) calcd for $C_{17}H_{26}OSi$ 274.1753. Found 274.1764; R_f = 0.65 (hexane/EtOAc, 5:1).

Butyl[(1*R,2*S**,3*R**)-2-(*tert*-butyldimethylsilyl)-3-phenylcycloprop-1-yl]ketone (7c):** colorless oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29−7.21 (m, 5 H), 2.93 (dd, J = 11.1, 4.4 Hz, 1 H), 2.73 (dd, J = 16.2, 7.3 Hz, 1 H), 2.63 (dd, J = 16.2, 7.3 Hz, 1 H), 2.47 (dd, J = 6.8, 4.4 Hz, 1 H), 1.75−1.65 (m, 2 H), 1.46−1.33 (m, 2 H), 1.00 (dd, J = 11.1, 6.8 Hz, 1 H), 0.96 (t, J = 7.3 Hz, 3 H), 0.87 (s, 9 H), −0.24 (s, 3 H), −0.53 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 210.2 (C), 138.6 (C), 129.0 (2 × CH), 128.0 (2 × CH), 126.5 (CH), 43.4 (CH_2), 32.8 (CH), 29.8 (CH), 26.4 (3 × CH_3), 26.2 (CH_2), 22.3 (CH_2), 17.6 (CH), 17.0 (C), 13.8 (CH_3), −6.1 (CH_3), −6.4 (CH_3); MS (70 eV, EI) m/z (%): 316 [M^+] (24), 259 (75), 159 (14), 129 (16), 75 (100), 73 (69); IR (neat): 3054, 2956, 2360, 1691, 1420, 1254, 1265 cm^{-1}; HRMS (70 eV) calcd for $C_{20}H_{32}OSi$ 316.2222. Found 316.2227; R_f = 0.80 (hexane/EtOAc, 3:1).

Phenyl[(1*R,2*S**,3*R**)-2-(*tert*-butyldimethylsilyl)-3-phenylcycloprop-1-yl]ketone (7d):** white solid.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02−7.99 (m, 2 H), 7.52−7.39 (m, 3 H), 7.23−7.09 (m, 5 H), 3.11 (dd, J = 6.9, 4.4 Hz, 1 H), 3.03 (dd, J = 11.0, 4.4 Hz, 1 H),

1.17 (dd, J = 11.0, 6.9 Hz, 1 H), 0.73 (s, 9 H), −0.31 (s, 3 H), −0.54 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.7 (C), 138.8 (C), 138.0 (C), 132.8 (CH), 128.9 (2 × CH), 128.6 (2 × CH), 128.1 (2 × CH), 127.9 (2 × CH), 126.6 (CH), 34.2 (CH), 26.6 (CH), 26.4 (3 × CH_3), 18.9 (CH), 17.0 (C), −6.0 (CH_3), −6.1 (CH_3); MS (70 eV, EI) m/z (%): 336 [M^+] (47), 280 (20), 279 (100), 205 (12), 119 (11), 69 (13); IR (neat): 3055, 2955, 1665, 1406, 1265, 1012 cm^{-1}; HRMS (70 eV) calcd for $C_{22}H_{28}OSi$ 336.1909. Found 336.1904; R_f = 0.70 (hexane/EtOAc, 5:1).

Synthesis of (1*S,2*S**,3*R**)-2-(*tert*-Butyldimethylsilyl)-1-methyl-3-phenylcyclopropanecarboxaldehyde (8a).** To the amide **4n** (0.4 mmol, 1 equiv) in anhydrous THF (4 mL) was added $LiAlH_4$ (2 mmol, 5 equiv) at 0 °C. The reaction was followed by TLC. Once the reaction was complete, it was hydrolyzed by addition of saturated $NaHCO_3$ solution (5 mL) and extracted with diethyl ether (3 × 10 mL). The organic layers were washed with water, dried over Na_2SO_4, and concentrated under vacuum. Purification by flash column chromatography on silica gel (hexane/EtOAc, 5:1) afforded the pure compound **8a** as a pale-yellow oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 8.93 (s, 1 H), 7.24−7.06 (m, 5 H), 2.73 (d, J = 9.6 Hz, 1 H), 0.87 (s, 9 H), 0.85 (s, 3 H), 0.70 (d, J = 9.6 Hz, 1 H), 0.03 (s, 3 H), −0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.7 (CH), 136.5 (C), 128.9 (2 × CH), 128.3 (2 × CH), 127.0 (CH), 40.1 (C), 34.3 (CH), 26.5 (3 × CH_3), 18.1 (CH_3), 17.0 (C), 13.7 (CH), −4.7 (CH_3), −5.0 (CH_3); MS (70 eV, EI) m/z (%): 274 [M^+] (100), 217 (45), 143 (38), 129 (21), 128 (27), 75 (55), 73 (41); IR (neat): 2955, 2931, 1702, 1265, 840 cm^{-1}; HRMS (70 eV) calcd for $C_{17}H_{26}OSi$ 274.1753. Found 274.1739; R_f = 0.73 (hexane/EtOAc, 5:1).

Synthesis of (1*R,2*R**,3*S**)-2-(*tert*-Butyldimethylsilyl)-1-(*N*,*N*-diethylaminomethyl)-1-methyl-3-phenylcyclopropane (9a).** To a suspension of $LiAlH_4$ (2 mmol, 5 equiv) in THF (2 mL) was added dropwise a solution of **4l** (0.4 mmol, 1 equiv) in anhydrous THF (4 mL) at 0 °C. The mixture was stirred for 15 h at reflux, then cooled at 0 °C and quenched by the addition of a mixture of ice/water. It was then filtered through a pad of Celite and extracted with diethyl ether (3 × 10 mL). The organic layers were washed with water, dried over Na_2SO_4, and concentrated under vacuum. Purification by chromatography on silica gel (hexane/EtOAc, 5:1) afforded the pure compound **9a** as a pale-yellow oil.^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31−7.16 (m, 5 H), 2.93 (d, J = 12.4 Hz, 1 H), 2.85−2.74 (m, 2 H), 2.57−2.45 (m, 2 H), 2.02−1.97 (m, 2 H), 1.04 (t, J = 7.1 Hz, 6 H), 0.94 (s, 9 H), 0.91 (s, 3 H), 0.12 (d, J = 8.0 Hz, 1 H), 0.05 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.2 (C), 128.5 (2 × CH), 127.9 (2 × CH), 125.6 (CH), 61.1 (CH_2), 46.1 (2 × CH_2), 34.9 (CH), 27.6 (C), 26.7 (3 × CH_3), 19.2 (CH_3), 16.9 (C), 11.8 (CH), 11.0 (2 × CH_3), −4.4 (CH_3), −4.5 (CH_3); MS (70 eV, EI) m/z (%): 331 [M^+] (2), 201 (30), 142 (23), 130 (8), 129 (12), 86 (100), 73 (26); IR (neat): 2954, 2928, 1248, 1066, 825 cm^{-1}; HRMS (70 eV) calcd for $C_{21}H_{37}NSi$ 331.2695. Found 331.2697; R_f = 0.48 (hexane/EtOAc, 5:1).

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Supporting Information Available: Complete ref 21; CIFs for **3e** and **7a**; copies of ^{1}H and ^{13}C NMR spectra for unpublished compounds **2**−**9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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