Lewis Acid-Mediated Carbocyclization Reactions of Chiral (*E*)-Crotylsilanes

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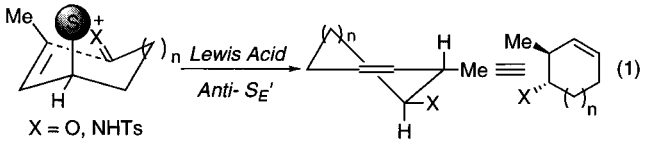
Received May 8, 1997

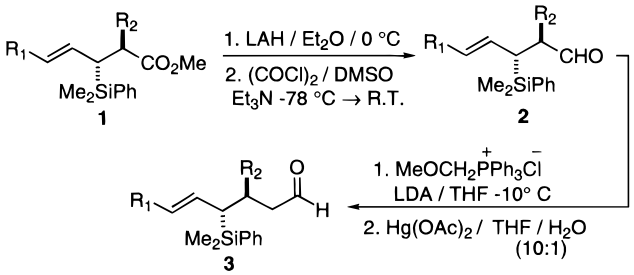
Introduction

Recent efforts in our laboratories have demonstrated that chiral (*E*)-crotylsilanes act as useful carbon nucleophiles in highly diastereo- and enantioselective intermolecular condensation reactions with aldehydes, acetals, and certain electrophilic alkenes. These studies have resulted in efficient methods for the asymmetric synthesis of functionalized homoallylic ethers, tetrahydrofurans, and tetrasubstituted cyclopentanes.[1] We have also demonstrated that chiral (*E*)-crotylsilanes participate in asymmetric C−N bond constructions for the preparation of chiral allylic amines and (*E*)-olefin dipeptide isosteres.[2] In the course of studies designed to expand the scope of electrophilic additions to the chiral allylsilane reagents, an intramolecular exo-trig cyclization[3] of chiral silyl aldehydes or *in situ* generated silyliminium ions was envisioned as a highly efficient and diastereoselective method for the formation of chiral cycloalkenols and aminocycloalkenes bearing vicinal stereogenic centers (eq 1).



Nakai and co-workers had initially demonstrated the viability of this type of carbocyclization process in the synthesis of (3*S*,4*S*)−(+)-3-methylcyclopenten-4-ol from an *E*/*Z* mixture of crotylsilanes.[4] In that report, the cyclopentenol was produced with high levels of diastereoselectivity (>98% de) from the corresponding crotylsilyl aldehyde under the action of titanium(IV) chloride; however, only a single example was illustrated. In that report, a yield of 59% for the cyclization product was achieved. The modest yield was attributed to the instability of the 4-cyclopentenol during the purification step on silica gel. Although this reaction demonstrated the feasibility of a selective method of producing functionalized cyclopentenols, to our knowledge the full scope of the reaction has not been explored. These chiral alcohols have been utilized as important intermediates in the synthesis of several natural products,[5,6] so a more efficient procedure with a broader scope would be a useful contribution to synthetic organic methodology. Additionally, the chiral cycloalkenols and aminocycloalkenes may be further elaborated upon by additions to the olefinic system to provide access to functionalized and stereochemically well-defined small molecule organics which are potentially useful building blocks for library incorporation.

Scheme 1



Preparation of the required silyl aldehyde substrates was readily accomplished by lithium aluminum hydride reduction and Swern oxidation[7] of silyl esters **1**[2c] to give the corresponding chiral silyl aldehydes **2** as demonstrated in Scheme 1 for a substrate possessing *anti* stereochemistry. The requisite aldehydes **3** needed for cyclization to the six-membered ring systems were prepared via a one-carbon homologation of silyl aldehydes **2**.

Results and Discussion

Intramolecular Carbocyclizations with Silyl Aldehydes. A Lewis acid-mediated carbocyclization of chiral (*E*)-crotylsilanes has been achieved to furnish chiral cyclopentenol and cyclohexenol derivatives in high yields and with high levels of diastereoselection. In an effort to determine the most effective Lewis acid to promote the cyclization, silyl aldehydes **2** and **3** were subjected to cyclization conditions in the presence of $TiCl_4$, $BF_3{\cdot}OEt_2$, and TMSOTf. Both $TiCl_4$ and TMSOTf afforded the desired cycloalkenol, whereas $BF_3{\cdot}OEt_2$ provided none of the desired product under the described reaction conditions. Although both $TiCl_4$ and TMSOTf were effective in promoting the cyclization, the $TiCl_4$-mediated cyclization proceeded in higher yields, consistent with the results of Nakai and co-workers for cyclopentenols.[4]

Initial attempts to isolate the cyclopentenols proved ineffective as a consequence of the instability of the product when subjected to purification on silica gel. A simple solution to the instability problem involved silylation of the crude cyclopentenol with *tert*-butyldiphenylchlorosilane. Literature precedent suggested that silylation of the cyclopentenol would prevent elimination and stabilize the cyclopentenyl system.[4b] Indeed, silylation of the crude cyclopentenol provided the silyl ether which could be readily chromatographed on silica gel to afford the pure cyclopentenylsilyl ether in high yield. The

† Recipient of a Graduate Fellowship from the Organic Chemistry Division of the American Chemical Society 1996−1997, sponsored by Organic Syntheses Inc.

(1))Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293−1316.

(2) (a) Beresis, R. T.; Masse, C. E.; Panek, J. S. *J. Org. Chem.* **1995**, *60*, 7714−7715. (b) Masse, C. E.; Knight, B. S.; Stavropoulos, P.; Panek, J. S. *J. Am. Chem. Soc.* **1997**, *119*, 6040−6047. (c) For the preparation of the silane reagents, see: Beresis, R. T.; Solomon, J. S.; Yang, M. J.; Jain, N. F.; Panek, J. S. *Org. Synth.*, in press.

(3) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734−736.

(4) Mikami, K.; Maeda, T.; Kishi, N.; Nakai, T. *Tetrahedron Lett.* **1984**, *25*, 5151−5154. For related examples of intramolecular allylsilylations with aldehydes, see: (a) Denmark, S. E.; Almstead, N. G. *J. Org. Chem.* **1994**, *59*, 5130−5135. (b) Ladouceur, G.; Paquette, L. A. *Synthesis* **1992**, 185−191.

(5) Partridge, J. J.; Chadha, N. K.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1973**, *95*, 532−540.

(6) Stork, G.; Paterson, I.; Lee, F. K. C. *J. Am. Chem. Soc.* **1982**, *104*, 4686−4688.

(7) Mancuso, A. J.; Huang, S.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480−2482.

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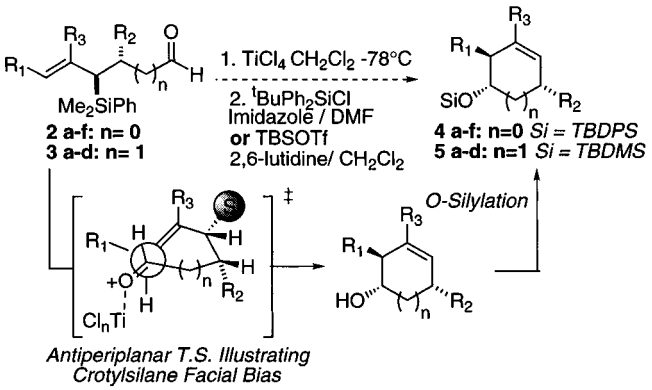
Scheme 2

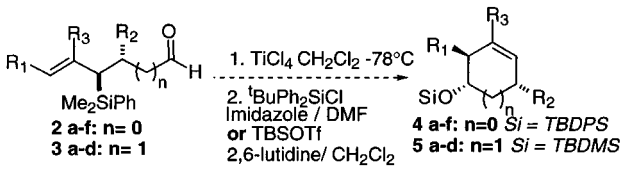


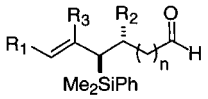
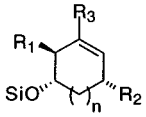
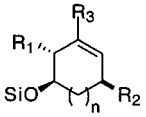
corresponding cyclohexenols required a more active silylating agent (TBSOTf) for complete silylation as the typical procedure with a chlorosilane and imidazole led to complex mixtures. Therefore, treatment of the crude cyclohexenols with TBSOTf/2,6-lutidine provided the cyclohexenols as their TBS protected ethers. Thus, the ultimate methodology necessitated a two-step process: (i) $TiCl_4$-mediated intramolecular carbocyclization and (ii) silylation of the resulting cycloalkenol (Scheme 2). The chirality of the emerging stereocenters solely originates from and is controlled by the nature of the silicon-bearing stereocenter and is consistent with an anti-S_E' addition process.[8] The silylated chiral cyclopentenols (**4a**−**f**) and cyclohexenols (**5a**−**d**) were produced in high overall yields with high levels of stereoselectivity and excellent levels of 1,4-remote asymmetric induction.[9]

To expand the scope of this methodology, a variety of aldehydes were synthesized as substrates for the cyclization reaction. Variations of the alkyl group at the R_1 or R_3 position of the aldehyde did not affect the yield or diastereoselection of the reaction. However, changing the substituent at the R_2 position to an alkoxy substituent had a pronounced effect on the outcome of the cyclization. None of the desired cyclization product was observed when an alkoxy group was introduced at R_2. The failure of this reaction may be attributed to chelation of the $TiCl_4$ (or TMSOTf) to the oxygen of the alkoxy substituent, which resulted in decomposition of the substrate. The results of the intramolecular carbocyclization reactions are summarized in Table 1.

Intramolecular Aminocarbocyclizations with Silyliminium Ions. In an effort to extend this methodology to aminocycloalkenes, we investigated the possibility of *in situ* iminium ion formation to generate the aminocycloalkene in a one-pot procedure. We had previously established the viability of such an approach in *intermolecular* additions to achiral aryl and alkyl *N*-acyliminium ions.[10] Thus, aldehydes **2** were subjected to a $BF_3{\cdot}OEt_2$-promoted cyclization in the presence of *p*-$TsNH_2$ to generate the *N*-tosyliminium ions according to the previously established procedure (Scheme 3).[11] These experiments have shown that silyl aldehydes **2a**/**2g**−**j** exhibit high levels of diastereo- and enantioselectivity in intramolecular additions to *in situ* generated *N*-tosylimin-

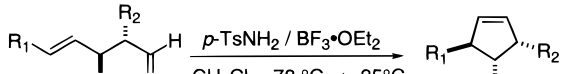
Table 1. Asymmetric Carbocyclization of (*E*)-Crotylsilanes



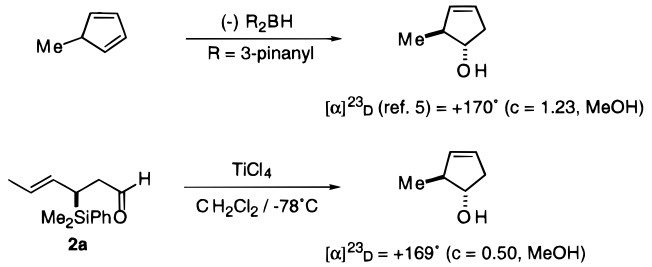
(*E*)-Crotylsilane Entry(n) (abs. stereochem) (R_1, R_2, R_3)	Major Product (% Yield **4**[a]; de[b])
	
1. **2a** (n=0); (3*R*); (Me, H, H)	(3*S*, 4*S*)-**4a** (90; > 30:1)
2.**3a** (n=1); (4*R*); (Me, H, H)	(3*S*, 4*S*)-**5a** (90; >30:1)
3. **2b** (n=0); (2*R*, 3*S*); (Me, Me, H)	(3*S*, 4*S*, 5*S*)-**4b** (80; > 30:1)
4.**3b** (n=1); (3*R*, 4*R*); (Me, Me, H)	(3*S*, 4*S*, 6*R*)-**5b** (92; >30:1)
5. **2c** (n=0); (3*R*); (Me, H, Me)	(3*S*, 4*R*)-**4c** (95; > 30:1)
	
6. **2d** (n=0); (3*S*); (Me, H, H)	(3*R*, 4*R*)-**4d** (90; > 30:1)
7.**3c** (n=1); (4*S*); (Me, H, H)	(3*R*, 4*R*)-**5c** (89; >30:1)
8. **2e**[c] (n=0); (3*S*); (^{i}Pr, H, H)	(3*R*, 4*R*)-**4e** (85; > 30:1)
9.**3d** (n=1); (4*S*); (^{i}Pr, H, H)	(3*R*, 4*R*)-**5d** (88; >30:1)
10.**2f**[c] (n=0); (3*S*); (Ph, H, H)	(3*S*, 4*R*)-**4f** (80; >30:1)

[a] Overall yield for the two-step sequence. [b] Ratios of products were determined by ^{1}H NMR (400 MHz) operating at S/N of >200:1. [c] Silanes **2e**,**f** were prepared by an analogous Claisen strategy; see Experimental Section for details.

Scheme 3



(8) (a) Matassa, V. G.; Jenkins, P. R.; Kumin, A.; Damm, L.; Schreiber, J.; Felix, D.; Zass, E.; Eschenmoser, A. *Israel J. Chem.* **1989**, *29*, 321−343. (b) Denmark, S. E.; Weber, E. J.; Wilson, T. M. *Tetrahedron* **1989**, *45*, 1053−1065. The absolute stereochemistry of the cyclopentenols was obtained by correlation to the identical cyclopentenol obtained via asymmetric hydroboration of 5-methylcyclopentadiene (see ref 5). The absolute stereochemistry of the corresponding cyclohexenols and aminocyclopentenes was assigned by analogy to the cyclopentenols.

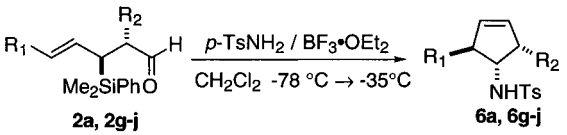


(9) All new compounds were isolated as chromatographically pure materials and exhibited acceptable ^{1}H NMR, ^{13}C NMR, IR, MS, and HRMS spectral data.

(10) Panek, J. S.; Jain, N. *J. Org. Chem.* **1994**, *59*, 2674−2675.

(11) In the case of substrate **2h**, the $TiCl_4$- or TMSOTf-catalyzed reactions resulted in decomposition of the substrate.

Table 2. Asymmetric Aminocarbocyclization of (*E*)-Crotylsilanes



2a, 2g-j 6a, 6g-j

Entry	(*E*)-Crotylsilane (abs. stereochem) (R_1, R_2)	Major Product (% Yield **6**[a]; de[b])
1.	**2a** (3*R*); (Me, H)	(3*S*, 4*S*)-**6a** (80; > 30:1)
2.	**2g** (3*R*); (^{i}Pr, H)	(3*S*, 4*S*)-**6g** (82; > 30:1)
3.	**2h**[c] (2*R*, 3*S*); (Me, NHTs)	(3*S*, 4*R*, 5*S*)-**6h** (80; > 30:1)
4.	**2i** (2*S*, 3*R*); (Me, Me)	(3*R*, 5*R*)-**6i** (85; > 30:1)
5.	**2j** (2*S*, 3*R*); (Me, ^{i}Pr)	(3*R*, 4*S*, 5*R*)-**6j** (82; > 30:1)

[a] Overall yield for the two-step sequence. [b] Ratios of products were determined by ^{1}H NMR (400 MHz) operating at S/N of >200:1. [c] Silane **2h** was prepared from the corresponding azido ester silane; see Experimental Section for details.

ium ions. The results of the intramolecular aminocarbocyclization reactions are summarized in Table 2.

This methodology was more tolerant of functionality at the R_2 position than the corresponding $TiCl_4$-promoted carbocyclizations of silyl aldehydes. This is apparent by the successful use of an *N*-tosyl substituent (Table 2, entry 3) in the cyclization. The Lewis acid $BF_3{\cdot}OEt_2$ proved most effective in the *in situ* generation of the *N*-tosyliminium ion and subsequent carbocyclization process, although the use of higher reaction temperatures (−35 °C) was required to obtain satisfactory yields. Attempts to utilize alternative Lewis acids ($TiCl_4$ or TMSOTf) resulted in a predominance of the carbocyclization product (cyclopentenol) with little or none of the desired aminocyclopentene being isolated.[11] It appears that $BF_3{\cdot}OEt_2$ is capable of inducing iminium ion formation without competing intramolecular carbocyclization of the starting aldehyde.

Conclusion

In summary, the intramolecular carbocyclization of chiral silyl aldehydes and silyliminium ions provides an efficient method of producing stereochemically well-defined and functionalized cycloalkenols and aminocycloalkenes. In the context of stereochemical diversity, this approach can be applied to the preparation of all possible diastereomers of the chiral cycloalkenols or aminocycloalkenes in a stereocontrolled fashion by the proper selection of the silane reagent.

Experimental Section

^{1}H NMR spectra were recorded on a 400-MHz spectrometer at ambient temperature. ^{13}C NMR were recorded on a 75.5-MHz spectrometer at ambient temperature. Chemical shifts are reported in parts per million relative to chloroform (^{1}H, δ 7.24; ^{13}C, δ 77.0). All ^{13}C NMR were recorded with complete proton decoupling. Infrared spectra were recorded on a FT-spectrophotometer. Optical rotations were recorded on a digital polarimeter at 589 nm. High-resolution mass spectra were obtained in the Boston University Mass Spectrometry Laboratory. Analytical thin-layer chromatography was performed on 0.25-mm silica gel 60-F plates. Flash chromatography was performed as previously described.[12] When specified as "anhydrous", solvents were distilled and/or stored over 4-Å sieves prior to use. All reactions were carried out in oven-dried glassware under a dry argon atmosphere. Dichloromethane (CH_2Cl_2), triethylamine, and diisopropylamine were distilled from calcium hydride. Dimethyl sulfoxide was vacuum-distilled from calcium hydride prior to use. Oxalyl chloride was distilled immediately prior to use. Titanium(IV) chloride was distilled from copper powder under vacuum immediately prior to use. The *p*-toluenesulfonamide (*p*-$TsNH_2$) was recrystallized from ethanol. The $BF_3{\cdot}OEt_2$ was distilled immediately prior to use. Anhydrous *N*,*N*-dimethylformamide, mercuric acetate, (*tert*-butyldimethylsilyl)trifluoromethanesulfonate (TBSOTf), 2,6-lutidine, and (methoxymethyl)triphenylphosphonium chloride were purchased from Aldrich and used as received. The *tert*-butyldiphenylchlorosilane was purchased from United Chemical Technologies and used as received.

Representative Experimental Procedure for the Preparation of the Chiral (*E*)-Crotylsilyl Alcohols. (3*R*)-(*E*)-3-(Dimethylphenylsilyl)-4-hexenal (2a). A solution of **1a**[2c] (2.0 g, 8.06 mmol) in 30 mL of anhydrous Et_2O (0.25 M) was cooled to 0 °C. To this solution was added lithium aluminum hydride (LAH) (0.31 g, 8.06 mmol, 1.0 equiv), and the reaction mixture vigorously stirred at 0 °C for 30 min. The reaction was subsequently quenched with a quantitative amount of H_2O (0.31 mL), 15% NaOH (0.31 mL), and additional H_2O (0.93 mL). The resulting suspension was filtered through Celite and concentrated *in vacuo*. Purification on SiO_2 (5% EtOAc/PE → 20% EtOAc/PE gradient elution) afforded the silyl alcohol[2b] as a pale yellow oil, 1.85 g (98%, 1.89 g theoretical).

The above silyl alcohol (1.2 g, 5.13 mmol) was dissolved in 20 mL of anhydrous CH_2Cl_2 (0.25 M). Oxalyl chloride (0.49 mL, 5.64 mmol, 1.1 equiv) was added to a precooled solution of dimethyl sulfoxide (0.96 mL, 12.3 mmol, 2.4 equiv) in CH_2Cl_2 (22 mL, 0.25 M) at −78 °C. The solution was stirred at −78 °C for 15 min at which time the solution of the alcohol was cannulated into the reaction mixture. The white suspension was vigorously stirred at −78 °C for 30 min. After 30 min, Et_3N (1.8 mL, 12.8 mmol, 2.5 equiv) was added and the reaction allowed to stir vigorously at room temperature for an additional 1 h. After 1 h, the reaction mixture was diluted with H_2O (20 mL) and the mixture extracted with CH_2Cl_2 (2 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification on SiO_2 (2.5% EtOAc/PE) afforded **2a** as a colorless oil, 1.1 g (93%, 1.18 g theoretical): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (q, 1H), 7.45 (m, 2H), (7.35, m, 3H), 5.27 (m, 2H), 2.30−2.32 (m, 2H), 1.62 (d, 3H, J = 5.2 Hz), 0.28 (s, 3H), 0.27 (s, 3H); ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 203.6, 136.6, 133.9, 129.5, 129.3, 127.8, 124.4, 42.6, 26.5, 18.1, −4.56, −5.53; IR (neat) ν_{max} 2959, 2855, 1724, 1653, 1428, 1378, 1411, 1378, 1113; CIMS (NH_3 gas) 233.1, 217.1, 154.1, 137.0, 136.1, 135.1, 81.0, 75.0; CIHRMS M + H^+ calcd for $C_{14}H_{21}SiO$ 233.1316, found 233.1315; $[\alpha]^{23}_D = +25.3$ (c = 1.73, $CHCl_3$).

Representative Experimental Procedure for the $TiCl_4$-Mediated Carbocyclization of the Chiral (*E*)-Crotylsilyl Aldehydes. (3*S*,4*S*)-3-Methyl-4-(*tert*-butyldiphenylsilyl)cyclopenten-4-ol (4a). Silyl aldehyde **2a** (0.50 g, 2.15 mmol) was dissolved in 20 mL of CH_2Cl_2 (0.1 M) and the solution cooled to −78 °C under argon. To this solution was added freshly distilled $TiCl_4$ (0.26 mL, 2.37 mmol, 1.1 equiv), and the deep red homogeneous solution was stirred for 1 h at −78 °C. After 1 h, the reaction mixture was diluted with H_2O (40 mL) and the mixture extracted with CH_2Cl_2 (2 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The crude cyclopentenol was redissolved in 4.3 mL of DMF (0.5 M) and the solution cooled to 0 °C. To this solution were added imidazole (0.39 g, 6.45 mmol, 3.0 equiv)

(12) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.

and *tert*-butyldiphenylchlorosilane (0.59 g, 2.15 mmol, 1.0 equiv), and the reaction mixture was allowed to warm to room temperature over a 12-h period. The reaction mixture was diluted with H_2O (15 mL) and the mixture extracted with Et_2O (2 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification on SiO_2 (Petroleum Ether) afforded **4a** as a colorless oil, 0.65 g (90%, 0.72 g theoretical): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68−7.30 (m, 10H), 5.52 (s, 2H), 3.98 (m, 1H), 2.65 (m, 1H), 2.43 (dd, 1H, J_1 = 6.4 Hz, J_2 = 1.6 Hz), 2.37 (dd, 1H, J_1 = 1.2 Hz, J_2 = 2.8 Hz), (1.04, s, 9H), 0.72 (d, 3H, J = 6.8 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 135.9, 135.1, 134.8, 133.0, 129.5, 129.3, 127.7, 127.5, 80.8, 49.1, 41.7, 27.0, 19.2, 17.9, 0.87; IR (neat) ν_{max} 3136, 3090, 3070, 3000, 2958, 2931, 2898, 1657, 1487, 1364, 1119; CIMS (NH_3 gas) 337.3, 296.2, 279.2, 199.1, 81.0; CIHRMS M + H^+ calcd for $C_{22}H_{29}SiO$ 337.1987, found 337.1952; $[\alpha]^{23}_D$ = +23.8 (c = 0.63, $CHCl_3$).

Representative Experimental Procedure for the Preparation of the Homologated Chiral (*E*)-Crotylsilyl Adehydes 3. (4*R*)-(*E*)-4-(Dimethylphenylsilyl)-5-heptenal (3a). To a stirred solution of (methoxymethyl)triphenylphosphonium chloride (1.66 g, 4.84 mmol, 1.1 equiv) in THF (6.1 mL, 0.78 M) at −10 °C was added dropwise lithium diisopropylamide (5.28 mmol, 1.2 equiv). The deep red solution was stirred at −10 °C for 30 min, after which time a solution of **2a** (1.02 g, 4.40 mmol) in THF (11 mL, 0.40 M) was added. The reaction mixture was stirred at −10 °C for 1 h, subsequently diluted with $NaHCO_3$ solution, and stirred to room temperature. The reaction mixture was extracted with Et_2O (3 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo* leaving the crude enol ether which was immediately dissolved in 18 mL of THF/H_2O (10:1, 0.25 M). To the stirred solution of enol ether was added mercuric acetate (2.80 g, 8.80 mmol, 2.0 equiv) and the suspension was stirred at room temperature for 1 h; the reaction mixture was subsequently diluted with 50 mL of a 7% aqueous KI solution. The gray suspension was stirred at room temperature for 2 h, extracted with Et_2O (3 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo* to afford the crude aldehyde. Purification on SiO_2 (2.5% EtOAc/PE) afforded **3a** as a colorless oil (70%, two steps, 0.76 g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (t, 1H, J = 1.6 Hz), 7.47−7.45 (m, 2H), 7.35−7.33 (m, 3H), 5.26−5.21 (m, 1H), 5.14−5.08 (m, 1H), 2.49−2.42 (m, 1H), 2.33−2.25 (m, 1H), 1.78−1.76 (m, 1H), 1.63 (dd, 3H, J = 1.2 Hz), 1.56−1.54 (m, 2H), 0.26 (s, 3H), 0.24 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 203.2, 134.0, 133.0, 130.6, 129.0, 127.7, 124.8, 43.7, 32.3, 21.6, 18.1, −4.34, −5.38; IR (neat) ν_{max} 3428, 3070, 3013, 2959, 1724, 1653, 1249; CIMS (NH_3 gas) 247.1, 231.1, 220.1, 211.1, 209.0, 205.1; CIHRMS M^+ calc for $C_{15}H_{22}SiO$ 246.1440, found 246.1409; $[\alpha]^{23}_D$ = +9.14 (c = 0.35, $CHCl_3$).

Representative Experimental Procedure for the $TiCl_4$-Mediated Carbocyclization of the Chiral (*E*)-Crotylsilyl Aldehydes 3. (3*S*,4*S*)-3-Methyl-4-(*tert*-butyldimethylsilyl)-cyclohexen-4-ol (5a). Silyl aldehyde **3a** (0.090 g, 0.37 mmol) was dissolved in 3.7 mL of CH_2Cl_2 (0.1 M) and the solution cooled to −78 °C under argon. To this solution was added freshly distilled $TiCl_4$ (0.045 mL, 0.41 mmol, 1.1 equiv), and the deep red homogeneous solution was stirred for 1 h at −78 °C. After 1 h, the reaction mixture was diluted with H_2O (10 mL) and the mixture extracted with CH_2Cl_2 (2 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The crude cyclohexenol was redissolved in 3.7 mL of CH_2Cl_2 (0.1 M) and the solution cooled to 0 °C. To this solution were added 2,6-lutidine (0.13 mL, 1.11 mmol, 3.0 equiv) and TBSOTf (0.13 mL, 0.56 mmol, 1.5 equiv), and the reaction mixture was stirrred at 0 °C for 2 h. The reaction mixture was diluted with H_2O (10 mL) and the mixture extracted with CH_2Cl_2 (2 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification on SiO_2 (petroleum ether) afforded **5a** as a colorless oil, 0.075 g (90%, two steps): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56−5.53 (m, 1H), 5.52−5.48 (m, 1H), 3.94−3.90 (m, 1H), 2.23−2.22 (m, 1H), 2.10−1.95 (m, 2H), 1.72−1.65 (m, 1H), 1.57−1.42 (m, 1H), 0.97 (d, 3H, J = 7.2 Hz), 0.37 (s, 3H), 0.32 (s, 9H), 0.059 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 127.7, 125.6, 70.4, 35.5, 27.5, 23.7, 15.5, 1.02, 0.85, −1.05, −1.16; IR (neat) ν_{max} 3420, 3070, 3022, 2959, 1653, 1428, 1254, 1119; CIMS (NH_3 gas) 209.0, 135.0, 105.0, 95.0, 67.0; CIHRMS M + H^+ calcd for $C_{13}H_{27}SiO$ 227.1832, found 227.1848; $[\alpha]^{23}_D$ = +25.0 (c = 0.38, $CHCl_3$).

Representative Experimental Procedure for the BF_3·OEt_2-Mediated Aminocarbocyclization of the Chiral (*E*)-Crotylsilyl Aldehydes 2. (3*S*,4*S*)-3-Methyl-4-[*N*-(*p*-toluenesulfonyl)amino]cyclopentene (6a). To a cooled solution of **2a** (0.100 g, 0.45 mmol) and *p*-$TsNH_2$ (0.078 g, 0.45 mmol) in CH_2Cl_2 (2 mL, 0.3 M) at −78 °C was added BF_3·OEt_2 (0.11 mL, 0.90 mmol, 2.0 equiv). The reaction mixture was warmed to room temperature, stirred for 10 min (the reaction mixture becomes light yellow and homogeneous), and then recooled to −35 °C. The reaction mixture was stirred for 24 h at −35 °C, subsequently diluted with $NaHCO_3$ solution, and stirred to room temperature. The reaction mixture was extracted with CH_2Cl_2 (3 × 25 mL), dried ($MgSO_4$), and concentrated *in vacuo* to afford the crude aminocyclopentene. Purification on SiO_2 (20% → 30% EtOAc/PE) afforded **6a** as a colorless oil, 0.090 g (80%, 0.11 g theoretical): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 2H, J = 8.0 Hz), 7.28 (d, 2H, J = 8.4 Hz), 5.51 (s, 2H), 4.55 (d, 1H, J = 8.8 Hz), 3.44−3.39 (m, 1H), 2.55−2.39 (m, 3H), 2.41 (s, 3H), 0.92 (d, 3H, J = 17 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 134.7, 129.7, 127.4, 127.1, 60.7, 47.4, 39.7, 22.4, 21.6, 18.1, 14.1; IR (neat) ν_{max} 3277, 3063, 2958, 1653, 1599, 1428, 1326, 1305, 1159; CIMS (NH_3 gas) 252.0, 96.0, 80.0; CIHRMS M + H^+ calcd for $C_{13}H_{18}NO_2S$ 252.1058, found 252.1056; $[\alpha]^{23}_D$ = +40.8 (c = 0.36, $CHCl_3$).

Acknowledgment. This work has been financially supported by the National Institutes of Health (RO1CA56304).

Supporting Information Available: ^{1}H and ^{13}C NMR data for all reaction products as well as full characterization data for compounds **2b**−**j**, **4b**−**f**, **3b**−**d**, **5b**−**d**, and **6g**−**j** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO970832O