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Stereospecific Synthesis of α-Amino Allylsilane Derivatives through a [3,3]-Allyl Cyanate Rearrangement. Mild Formation of Functionalized Disiloxanes

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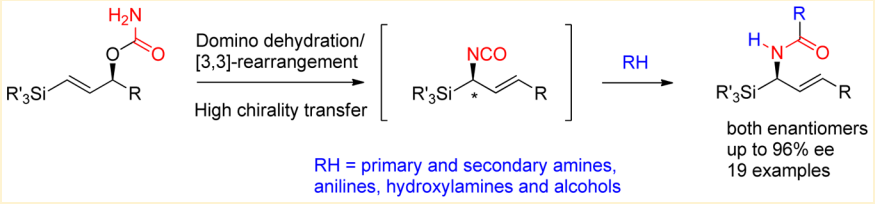
Supporting Information



ABSTRACT: An efficient asymmetric synthesis of α-amino allylsilane derivatives is reported. The strategy is based on a [3,3]-allyl cyanate sigmatropic rearrangement from enantioenriched γ-hydroxy alkenylsilyl compounds. The isocyanate intermediate can be trapped by several nucleophiles, opening the way for the preparation of unknown chiral functionalized compounds such as the α-ureido allylsilanes as well as carbamate derivatives. A computational study was conducted to rationalize the complete 1,3-chirality transfer of this kind of rearrangement. Moreover, starting from products bearing a phenyldimethyl silyl substituent, the α-amino silane derivatives or the corresponding disiloxanes can be obtained under hydrogenation conditions in an exclusive way according to the used catalyst.

INTRODUCTION

Allylmetal reagents represent very useful tools for the stereoselective construction of carbon−carbon bonds.[1] Even though the allylsilanes can be implicated in a large number of transformations,[2] their significant popularity in the community of organic chemists is partly due to their S_E2' nucleophilicity in the presence of a Lewis acid[3] coupled with their propensity to undergo annulation reactions.[4] Among this family of organosilicon compounds, the α-substituted enantioenriched allylsilanes are of particular interest as coupling partners because of the high transfer of stereochemical information.[5] For this reason, the development of new methods leading to the synthesis of optically active allylsilanes is still of high importance.

Several α-amino allylsilanes and derivatives have been reported in the literature,[6] but only few strategies are devoted to their preparation in an enantiomerically pure form. The first approach used a lithiation−substitution sequence mediated by a chiral ligand such as (−)-sparteine (Figure 1). Starting from *N*-Boc-*N*-(*p*-methoxyphenyl)cinnamylamine, the desired compound resulting from deprotonation α to nitrogen followed by a silylation reaction was obtained with excellent enantioselectivity but low yield because of the formation of γ isomer.[7] An elegant method was developed some years later based on an asymmetric reverse-aza-Brook rearrangement, albeit with some limitations concerning the amino protecting group used.[8] Another method using a tandem Mitsunobu/3,3-sigmatropic rearrangement starting from allyl alcohols was reported.[9] More recently, Meerwein−Pondorf−Verley-type reduction of *N*-tosylsilylimines with a chiral amide was described to afford α-substituted allylsilanes with high enantioselectivity.[10] In the same year, some examples of α-amino allylsilanes have been prepared through catalytic enantioselective silylation of *N*-sulfonylimines.[11,12] In order to expand the molecular diversity and considering that α-amino silane derivatives have a potential utility in medicinal chemistry,[13] we sought to develop an asymmetric strategy to access this class of compounds. During the last years, allyl cyanate-to-isocyanate rearrangement[14] appeared as an efficient approach for the preparation of allylamine derivatives in a

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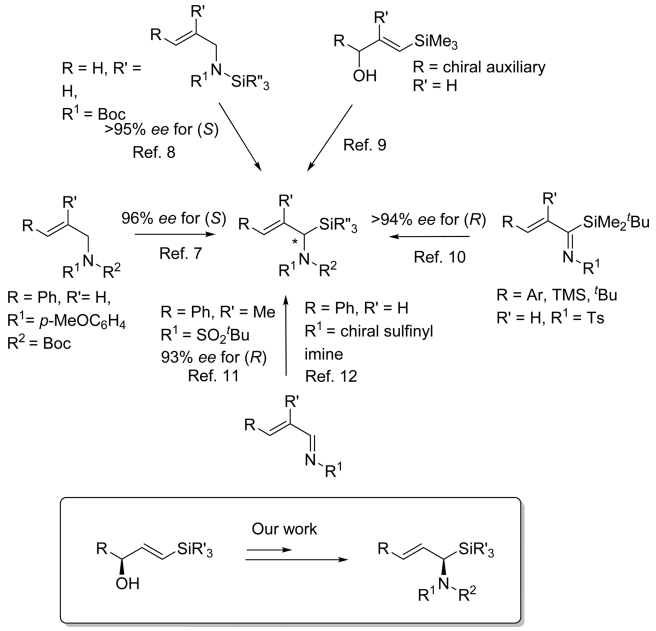


Figure 1. Different strategies for the synthesis of enantioenriched α-amino allylsilanes.

stereoselective manner as demonstrated in natural product synthesis.[15]

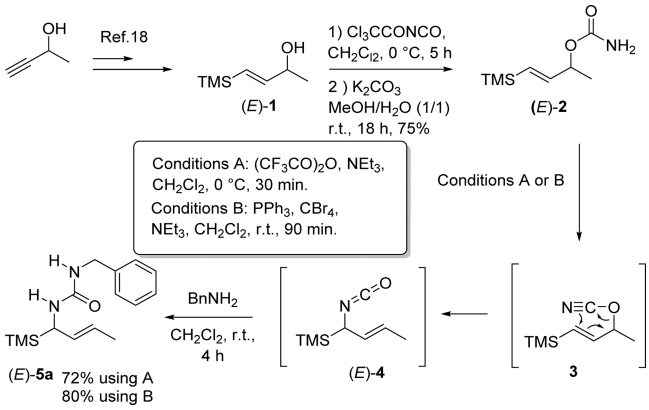
In line with our interest about this methodology,[16] we herein describe the rearrangement of enantioenriched γ-hydroxy alkenylsilicon compounds. To the best of our knowledge, only one example of this rearrangement applied on this kind of substrate was reported in the literature using a chiral auxiliary approach.[6f]

The high [1,3]-chirality transfer to the newly formed stereogenic center bearing the amino group was confirmed unambiguously. As additional information, we also realized a computational study of the mechanism of this particular rearrangement in order to bring a rational explanation for the observed stereospecificity.[17] Various nucleophiles such as amines and alcohols can react smoothly under mild conditions with the α-isocyanato allylsilane intermediates, causing the formation of enantioenriched α-ureido and α-carbamate allylsilanes in a one-pot reaction sequence. These novel compounds can be easily transformed into α-silylamine derivatives by reduction of the double bond. In some cases, we observed the unexpected formation of disiloxane derivatives by changing the catalyst of the hydrogenation reaction.

RESULTS AND DISCUSSION

Our study began with the synthesis of racemic (*E*)-4-(trimethylsilyl)but-3-en-2-ol (**1**) as a model substrate in order to validate the proposed strategy. From butyn-2-ol in two steps according to a literature procedure,[18] the formation of the carbon−silicon bond was followed by a double-bond reduction step. Treatment of **1** with trichloroacetyl isocyanate (TAI) followed by hydrolysis in a MeOH/H_2O mixture in the presence of K_2CO_3 provided the allylic carbamate **2** in 75% overall yield (Scheme 1). Among the available methods for the dehydration reaction of carbamates,[19] we first selected the use of trifluoroacetic anhydride (TFAA, 1.5 equiv) in the presence of a large excess of Et_3N at 0 °C for 30 min (conditions A). Under these conditions, the transient allyl cyanate **3** led to the complete formation of allyl isocyanate **4**, via a [3,3]-sigmatropic

Scheme 1. Optimization of the Strategy Based on an Oxygen-to-Nitrogen [3,3]-Sigmatropic Rearrangement



rearrangement, as a single isomer (*E*) whose purification was not possible due to its low stability on silica.[20] After evaporation of organic volatiles (excess of TFAA), **4** was dissolved in CH_2Cl_2 in the presence of a slight excess of benzylamine (1.2 equiv). After 4 h of stirring at room temperature, the desired compound **5a** was isolated in 72% overall yield from **2**. In view of the low boiling point of allyl isocyanate **4** under reduced pressure, we favored the dehydration reaction under Ichikawa's conditions (CBr_4, PPh_3, Et_3N, 0 °C, 90 min).[21] for the preparation of **5a**. Indeed, the addition of amine can be directly realized in the reaction mixture after completion of the rearrangement without the need to remove the excess reagents. Using this one-pot reaction sequence (conditions B), (*E*)-**5a** was easily isolated in a pure form with a slightly better yield compared to conditions A (80%).[22]

In order to bring to light the formation of the transient allyl cyanate **3** by means of NMR spectroscopy,[23,24] we studied the formation of **4** from **2** using the experimental procedure B in CD_2Cl_2. In a surprising way, we observed the transformation of **2** into **4** at very low temperature. At −70 °C, the process is relatively slow since after 8 h only 53% of isocyanate **4** was formed with the concomitant disappearance of carbamate **2** as shown in the reaction profile obtained from measuring conversion (%) versus time (min) (Figure 2). The domino dehydration/rearrangement sequence proved to be very clean,

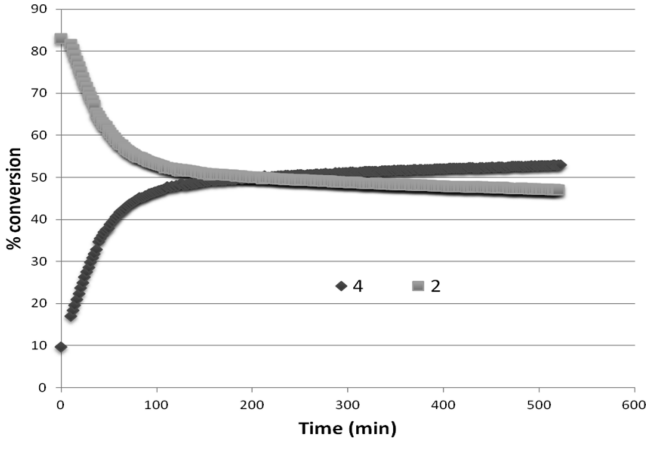


Figure 2. Reaction profile [conversion (%) versus time (min)] of the transformation of **2** into **4** at −70 °C under conditions B. Conversion determined by ^{1}H NMR spectroscopy.

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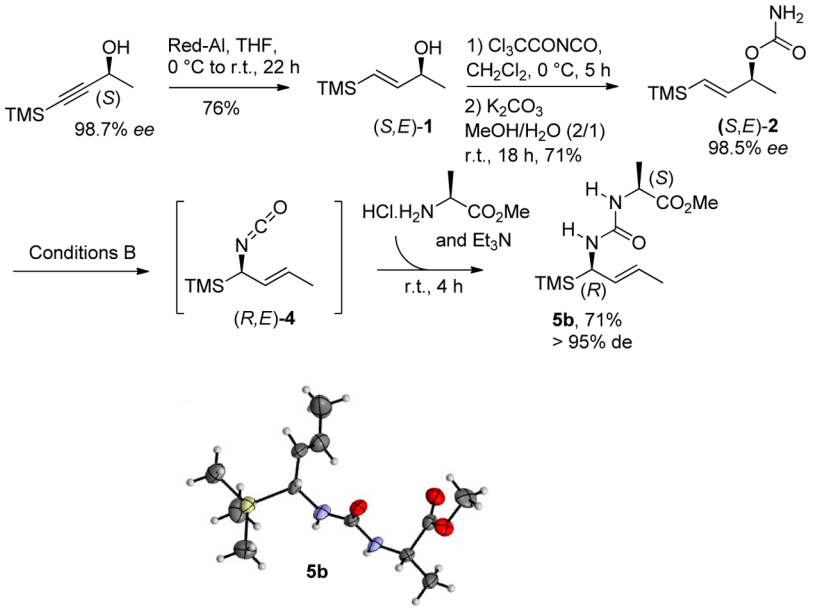
Scheme 2. Synthesis of 5b and Its X-ray Crystallographic Structure (at the 50% Probability Level)



as no side product was formed. At no moment during this study was the transient allyl cyanate **3** detected by ^{1}H NMR, confirming the short-lived nature of this species which undergoes [3,3]-sigmatropic bond reorganization, thus leading to the formation of allyl isocyanate (*E*)-**4**. The reaction was complete after return to room temperature.

The high chirality transfer during the sigmatropic rearrangement was demonstrated starting from optically active 4-(trimethylsilyl)but-3-yn-2-ol (Scheme 2). The (*S*)-(−)-enantiomer can be prepared with excellent enantioselectivity by lipase-catalyzed resolution of the corresponding racemic compound.[25] Treatment with 2.2 equiv of sodium bis(methoxyethoxy)aluminum hydride (Red-Al) provided the exclusive formation of the (*E*)-isomer of allyl alcohol (*S*,*E*)-(+)-**1**. The carbamate (*S*,*E*)-(+)-**2** was then prepared according to the previously used sequential process in 71% yield and a maintained enantiomeric excess (98.5% ee) as compared to the propargyl alcohol starting material. The formation of the allyl isocyanate intermediate (conditions B) followed by the addition of L-alanine methyl ester hydrochloride in the presence of an additional quantity of Et_3N afforded the expected *α*-ureido allyl silane **5b** in 71% yield as a single diastereoisomer.

The (*R*) absolute configuration of the stereogenic center formed in the sigmatropic rearrangement was assigned by analysis of the X-ray crystallographic structure.[26] This result thus confirms unambiguously that this type of rearrangement proceeds with complete transfer of stereochemistry.[27]

In order to determine the reasons for the high chirality transfer during this type of rearrangement, we carried out DFT calculations on the reaction profile associated with the **3** → **4** transformation. We selected (*S*,*E*)-**3** allyl cyanate as a model case. We located a local minimum energy structure (*S*,*E*)-**3′** associated with a dihedral angle $\omega = -127°$ between the $C_a{=}C_b$ and $C_c{-}O_d$ bonds (Figure 3). This conformer has an eclipsed arrangement between the $C_a{-}H$ and $C_c{-}Me$ groups (highlighted in gray in Figure 3) that results in a considerable 1,3-allylic strain. The minimum energy conformation of (*S*,*E*)-**3** corresponds to a structure in which the $C_a{-}H$ and $C_c{-}H$ bonds are coplanar and the $C_a{-}H$ and $C_c{-}Me$ groups for a dihedral angle of ca. 120°, thus avoiding the 1,3-allylic strain between both groups. The allylic strain in (*S*,*E*)-**3′** produces a

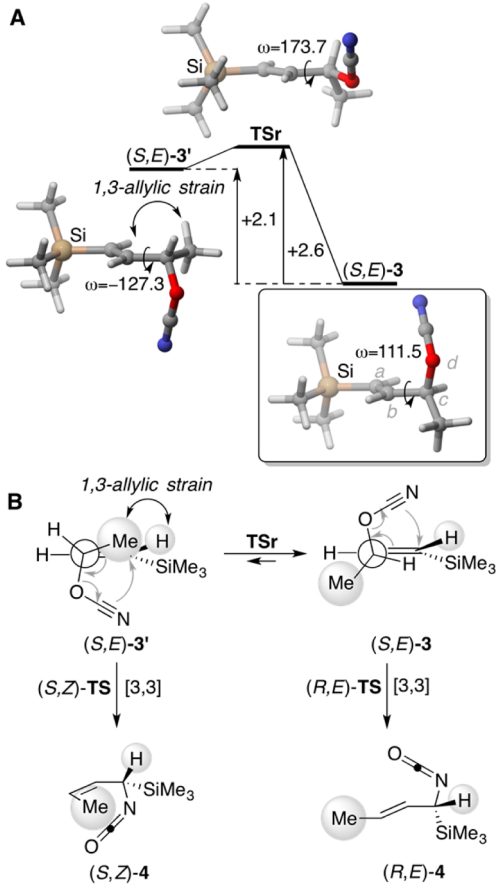


Figure 3. (A) Conformational analysis (M06-2X(PCM=CH_2Cl_2)/defTZVPP level of theory) of allyl cyanates (*S*,*E*)-**3** and (*S*,*E*)-**3′**. Dihedral angles ω = *a*−*b*−*c*−*d* are given in degrees. Relative Gibbs energies computed at 298 K are given in kcal/mol. (B) Different possible reaction paths for conformers (*S*,*E*)-**3** and (*S*,*E*)-**3′** to yield isocyanates (*R*,*E*)-**4** and (*S*,*Z*)-**4**.

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less favorable overlap between the C_a=C_b and C_c–O_d bonds that results in lower stabilization energies in (*S*,*E*)-**3′** with respect to (*S*,*E*)-**3**. Thus, the second-order stabilization energies $\Delta E(2)$ associated with the two-electron interaction $\pi_{C,C} \rightarrow \sigma^*_{C,O}$ between these localized natural bond orbitals[28] (NBOs) are −7.1 kcal/mol for (*S*,*E*)-**3′** and −9.7 kcal/mol for (*S*,*E*)-**3**. As a consequence of these combined effects, (*S*,*E*)-**3′** was calculated to be 2.1 kcal/mol less stable that (*S*,*E*)-**3** (Figure 3A).

We also located and characterized a transition structure **TSr** associated with rotation about the C_b–C_c bond, for which a ω value close to 180° was found (Figure 3A). This saddle point does not benefit from the $\pi_{C,C} \rightarrow \sigma^*_{C,O}$ two-electron donation and lies only 0.5 kcal/mol above (*S*,*E*)-**3′** at 298 K. It is important to note that the suprafacial [3,3] shift can occur from both conformers to yield different stereoisomers of isocyanates **4** (Figure 3B), Thus, conformer (*S*,*E*)-**3′** should produce compound (*S*,*Z*)-**4**, in which the *Z*-stereochemistry of the double bond stems from the orientation of the methyl group with respect to the allyl system. In contrast, the most stable conformer (*S*,*E*)-**3** should give rise to isocyanate (*R*,*E*)-**4**, with opposite configuration at the double bond and the chiral center.

After completing this conformational analysis, we studied the transformation of (*S*,*E*)-**3** into either (*S*,*Z*)-**4** or (*R*,*E*)-**4**. Within a Curtin–Hammett kinetic scheme,[29] we calculated the activation energies from the minimum energy conformer shown in Figure 3 since the above-described conformational changes take place much faster than the corresponding [3,3] sigmatropic shifts. The results obtained are gathered in Figure 4.

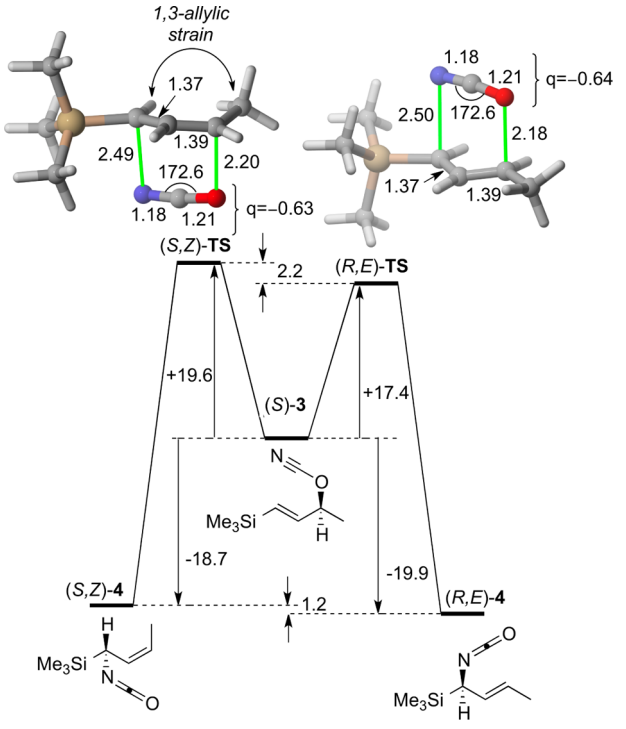


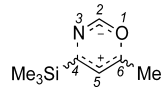
Figure 4. Reaction profiles (M06-2X(PCM=CH_2Cl_2)/defTZVPP level of theory) associated with the [3,3] sigmatropic rearrangement of allyl cyanate (*S*,*E*)-**3** to yield isocyanates (*R*,*E*)-**4** and (*S*,*Z*)-**4**. Bond distances and angles are given in angstroms and degrees, respectively. Numbers associated with the relative energies of stationary points correspond to Gibbs energies (in kcal/mol) computed at 298 K.

We located the transition structures (*S*,*Z*)-**TS** and (*R*,*E*)-**TS** postulated from conformers (*S*,*E*)-**3′** and (*S*,*E*)-**3**, leading isocyanates (*S*,*Z*)-**4** and (*R*,*E*)-**4**, respectively (Figure 3B). The shape of both transition structures closely resembles that found by Koch, Wentrup et al.[17] for the [3,3] sigmatropic shift of 3-cyanato-1-propene, with a O=C=N angle of ca. 173° and O···C and N···C bond distances of ca. 2.2 and 2.5 Å, respectively. Moreover, our calculated minimum free energy of activation for (*R*,*E*)-**TS** is ca. 17 kcal/mol, a value that corresponds to an activation energy of 16.1 kcal/mol. This latter value is in line with that computed by Koch and Wentrup[17] for the parent reaction (15 kcal/mol).

According to our calculations, both reactions are quite synchronous. The Wiberg[30] NBO bond orders were first computed as indicated in Table 1, and then we calculated the variation of these bond orders during the respective reactions according to the following expression:

$$\delta B_{i,j} = \frac{B^{TS}_{i,j} - B^{R}_{i,j}}{B^{P}_{i,j} - B^{R}_{i,j}} \quad (1)$$

Table 1. Natural Bond Orders (B_{ij})[a] Associated with the [3,3]-Sigmatropic Rearrangements between Allyl Cyanate (*S*,*E*)-3 and Isocyanates (*R*,*E*)-4 and (*S*,*Z*)-4



structure	B_{12}	B_{23}	B_{34}	B_{45}	B_{56}	B_{61}
(*S*)-**3**	1.02	1.91	0.00	1.38	0.93	0.61
(*R*,*E*)-**TS**	1.26	1.80	0.11	1.22	1.14	0.16
(*S*,*Z*)-**TS**	1.14	1.62	0.12	1.22	1.15	0.15
(*R*,*E*)-**4**	1.24	1.49	0.81	0.93	1.34	0.00
(*S*,*Z*)-**4**	1.24	1.49	0.81	0.92	1.33	0.00

[a]Computed at the M06-2X(PCM=CH_2Cl_2)/def2TZVPP level of theory.

The corresponding average value was computed as

$$\delta B_{av} = \frac{1}{6} \sum_{i,j}^{6} \delta B_{i,j} \quad (2)$$

In eqs 1 and 2, descriptors *i*,*j* refer to atoms *i* and *j* (Table 1), and superscripts *TS*, *R*, and *P* stand for transition structure, reactant, and product, respectively. In both the (*S*)-**3** → (*R*,*E*)-**4** and (*S*)-**3** → (*S*,*Z*)-**4** reactions, the corresponding saddle points were found to correspond to halfway transition structures since the corresponding δB_{av} values are 0.52 and 0.51, respectively. The synchronicities[31] of these reactions were measured by means of the previously defined eq 3:[32]

$$Sy = 1 - \frac{1}{10} \sum_{i,j}^{6} \frac{|\delta B_{i,j} - \delta B_{av}|}{\delta B_{av}} \quad (3)$$

From this definition, for a perfectly synchronous reaction Sy = 1 since $\delta B_{i,j} = \delta B_{av}$ for any *i*,*j*. We obtained a value of Sy = 0.69 for the (*S*)-**3** → (*R*,*E*)-**4** reaction leading to the major product. In contrast, the sigmatropic shift leading to the minor product (*S*,*Z*)-**4** resulted to be significantly more synchronous, with a value of Sy = 0.80. Therefore, in this pericyclic reaction a higher synchronicity resulted in a more energetic saddle point.

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These DFT calculations also indicated that the formation of major product was preferred under both kinetic and thermodynamic control (Figure 4). Saddle point (*R*,*E*)-**TS** was found to be 2.2 kcal/mol less energetic than (*S*,*Z*)-**TS**, in nice agreement with the experimental results, which showed exclusive formation of the (*R*,*E*) isomer. In addition, this difference in energy corresponds almost exactly with that observed for conformers (*S*,*E*)-**3** and (*S*,*E*)-**3′**. This result indicates that the 1,3-allylic strain and related stereoelectronic effects found in the less stable conformer of the reactant are also present in transition structure (*S*,*Z*)-**TS**. We also observed a noticeable charge separation in both transition structures. Therefore, we concluded that in this kind of sigmatropic shifts the transition structures can be envisaged as loose complexes (see the low B_{34} and B_{61} bond orders for (*R*,*E*)-**TS** and (*S*,*Z*)-**TS** in Table 1) between an isocyanate anion and a silylated allylic carbocation. These resonance-stabilized moieties result in relatively low activation energies.

Our next goal was to evaluate the scope and limitations of this approach with different nucleophiles able to trap the enantioenriched (*E*)-α-isocyanato allylsilane **4** (Figure 5). High enantiomeric excesses were measured by a normal-phase chiral HPLC method for all prepared compounds **5**. When a chiral nucleophile was used, the diastereomeric excess was determined by analysis of ^{1}H NMR and ^{13}C NMR. The carbamate (*R*)-(−)-**2** (97% ee) was also synthesized from (*R*)-4-(trimethylsilyl)but-3-yn-2-ol in a similar way than its enantiomer. By mere addition of amines to the reaction mixture after completion of the dehydration step (conditions B), the urea compounds were obtained in good yields. Primary and secondary amines (**5a**, **5d**, **5e**) reacted efficiently, as well as 4-methoxyphenyl aniline (**5f**). When an amine hydrochloride was used, an additional 2 equiv of Et_3N relative to the nucleophile were also added to the reaction medium (**5b**, **5c**, **5g**). In the case of alcohols, no reaction was detected at room temperature under these conditions (4 h). The use of an amine bearing a hydroxyl group on its skeleton, such as (1*S*,2*R*)-*cis*-1-amino-2-indanol, led to the formation of **5i** with high chemoselectivity and in excellent yield (80%). With an alcohol as nucleophile, heating the reaction medium in the presence of a catalytic amount of DMAP (reflux, 18 h) was required for the obtention of the corresponding carbamate. Under these new conditions, only the use of primary alcohols gave good results. **5j** was obtained in a better yield than **5k**, **5l** and **5m** due to the use of a large excess of methanol. A slight drop of the yield was observed with isopropyl alcohol (**5n**, 40%), and no reaction occurred with *tert*-butyl alcohol. To overcome this drawback, the reaction was also performed with Ti(O-*t*-Bu)$_4$ as catalyst,[33] but without success.

In order to bring more molecular diversity to our strategy, we planned to prepare other raw materials based on the hydrosilylation of alkynes. According to a described protocol using racemic starting materials, hydrosilylation of enantiomerically enriched propargyl alcohols was carried in the presence of the $PtCl_2$/XPhos catalyst (Scheme 3).[34] In our case, we observed by analysis of ^{1}H NMR of the crude mixture, the formation of the expected (*E*)-vinyl silane **7** as well as a side product (a ratio of 80/20, respectively) which was identified as the *O*-silylated hydroxyl compound **6**.[35] The mixture was directly treated with a tetrabutylammonium fluoride solution in THF at room temperature to yield exclusively compound **7** contaminated with organosilicon residues. Afterward, novel carbamates **8a** and **8b** were prepared from the corresponding

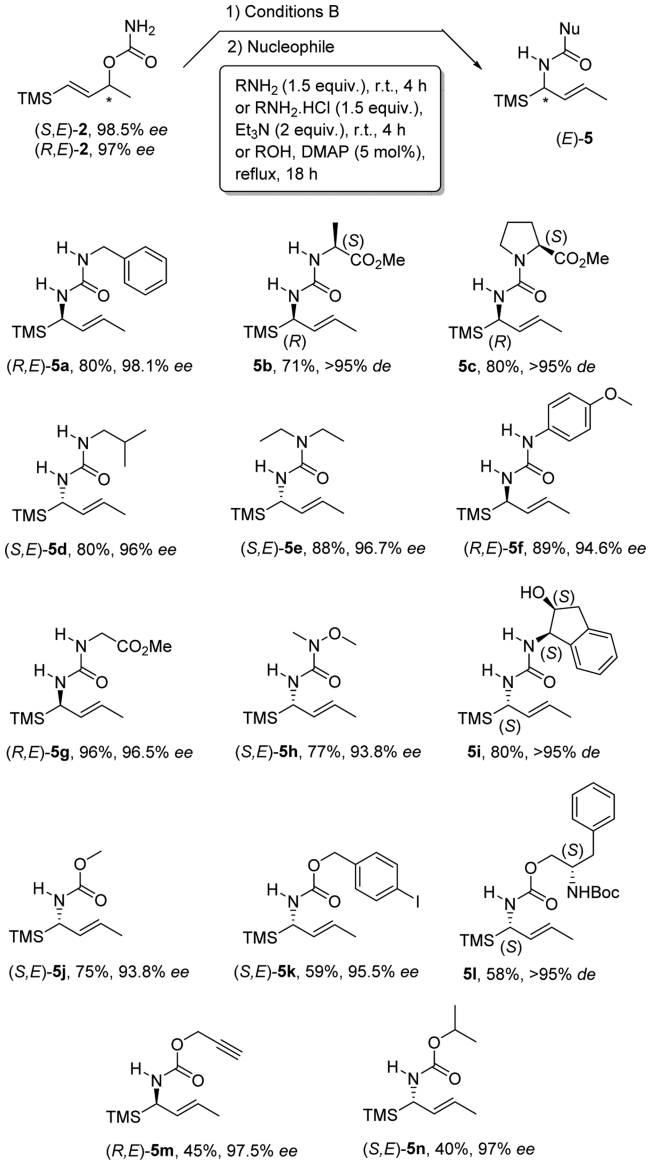

Figure 5. One-pot synthesis of various α-amino allylsilane derivatives from a common starting material.

allylic alcohols using conditions similar to those described in Scheme 1. At this stage, a few nucleophiles were selected to react with the isocyanate intermediate, thus affording the desired compounds **9** in modest to good yields from **8**. The high level of stereocontrol implemented in this new route to this class of compounds was confirmed once more by preservation of the enantioselectivity.

Having in hands an efficient asymmetric procedure prompted us to investigate whether these new compounds could be suitable precursors of optically active α-amino silane derivatives by reduction of the double bond (Scheme 4). Treatment of **5b** in the presence of catalytic amount of palladium on activated charcoal (10 mol %) under hydrogen atmosphere (balloon) afforded the reduced product **10** in a poor yield (17%), while under the same conditions, **11** was obtained in 58% yield from **9aa**. Using Adam's catalyst (PtO_2) instead of Pd/C, the compound **10** was isolated in an unoptimized yield of 80%, whereas for **11**, the yield was not significantly improved (61%). In the latter case, the formation of an undefined side product was indeed observed by ^{1}H NMR.

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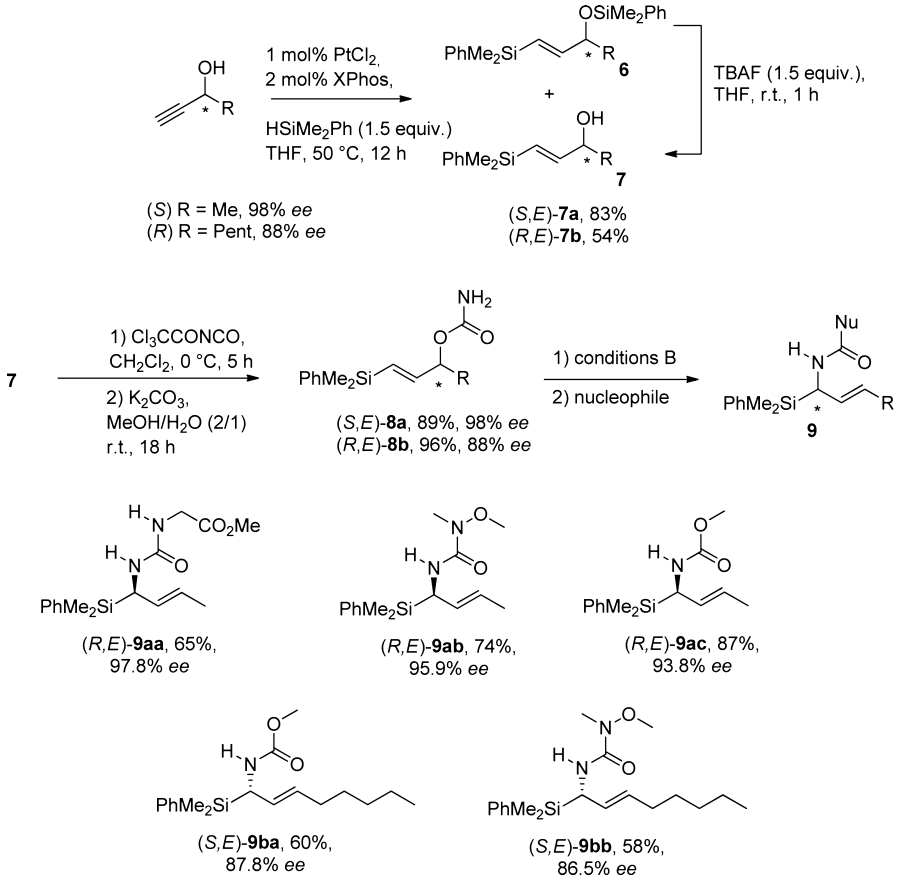
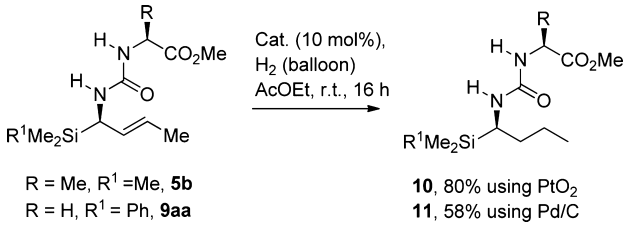
Scheme 3. Strategy Including a Platinum-Catalyzed Hydrosilylation Step



Scheme 4. Synthesis of α-Silylamine Derivatives



Keeping in mind that the presence of a (dimethyl)phenyl silyl group could be at the origin of this side reaction, we forced the hydrogenation conditions in the presence of platinum(IV) oxide using compound (*R*,*E*)-**9ab** as a prototype substrate. Results collected in Scheme 5 proved that the ratio of the side product **13a** compared to **12a** can be enhanced by changing some parameters, such as time and catalyst loading. With 40 mol % of PtO_2 during a longer time (64 h), compound **13a** was obtained exclusively. Although the starting material (*R*,*E*)-**9ab** is completely consumed, the moderate yield of disiloxane **13a** obtained after purification by column chromatography (55%) can be explained by its partial instability on silica gel. The stereoselective formation of **13a** was confirmed by analysis of the X-ray crystallographic structure showing the C_2 axis of symmetry and could be the result of an arylprotodesilylation to form a transient silanol which must dimerize. Under these conditions, compound **13b** can also be obtained in 53% yield starting from (*S*,*E*)-**9bb**.

Acidic conditions, employing a large amount of Brønsted acid,[36] are typically used in the literature for the protodesilylation of arylsilane, except in more scarce cases of photochemical conditions.[37] The addition of a small quantity of triethylamine under hydrogenation conditions indeed avoided the formation of disiloxane **13**, suggesting the presence of a trace of acid in the reaction medium and its major role in this transformation.[38] The formation of disiloxane **15** can also be performed from carbamate derivative (*R*,*E*)-**9ac** in one or two steps depending on the catalyst used (Scheme 6). The saturated compound **14** was exclusively obtained from (*R*,*E*)-**9ac** using Pd/C as catalyst, and can be subsequently transformed into **15**. It is interesting to note that the Si−C(Ph) bond cleavage of compound **14** was only observed under hydrogen atmosphere conditions together with the presence of the catalyst.[39,40] At this stage, it is difficult to propose a rational mechanism for this catalytic reaction by lack of evidence, even if we cannot exclude that the presence at the α-position of an urea or carbamate carbonyl group could assist the Si−C bond cleavage by a possible internal coordination with the silicon atom.[41,42] To the best of our knowledge, this experimental procedure for the formation of functionalized disiloxane derivatives was not reported in the literature; however, this heterogeneous catalytic method suffers from drawbacks such as reproducibility according to the batch of catalyst used as well as its supplier.

CONCLUSION

In this paper, we have described an asymmetric synthesis of a new class of α-substituted allylsilanes bearing an amino group at the stereogenic center. The strategy based on a [3,3]-sigmatropic allyl cyanate-to-isocyanate rearrangement, followed

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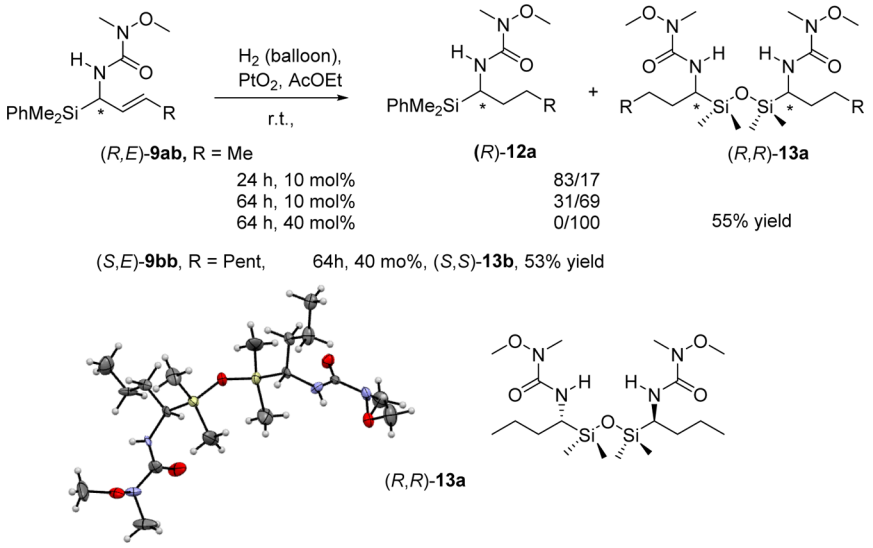
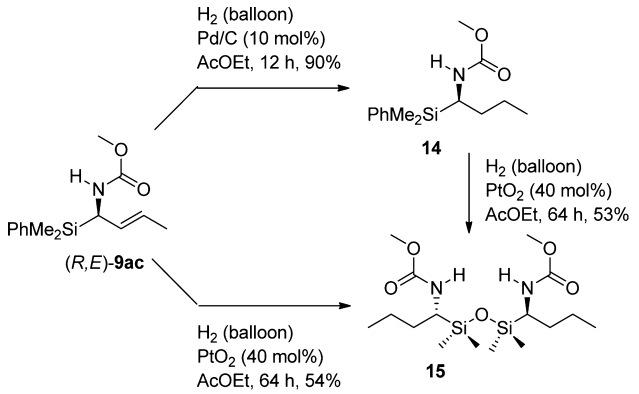
Scheme 5. Synthesis of Disiloxanes 13 under Catalytic Conditions and X-ray Structure of 13a (at the 50% Probability Level)



Scheme 6. Synthesis of Disiloxane 15 in One or Two Steps from (*R*,*E*)-9ac



by the addition of a nucleophile, allowed the preparation of a small library of novel compounds. A computational study was carried out on this rearrangement involving chiral substrates and led to conclusions in full agreement with the high level of stereocontrol observed and showed a significant zwitterionic character for this sigmatropic process. The hydrogenation of the double bond led to the α-silylamine derivatives, compounds with a potential biological interest. The unexpected formation of disiloxane derivatives was also observed under catalytic conditions which would deserve further improvement. The reactivity of these novel allylsilanes toward electrophiles is ongoing in our laboratory.

EXPERIMENTAL SECTION

General Information and Materials. Tetrahydrofuran (THF) was distilled over sodium/benzophenone, and dichloromethane (DCM) was distilled over P_2O_5 as well as trifluoroacetic anhydride (TFAA). Amines were distilled over potassium hydroxide (KOH), and alcohols were distilled over calcium hydride (CaH_2). All other commercially available chemicals were used without further purification. NMR spectra were recorded at 300, 400, or 500 MHz for ^{1}H and 75, 101, or 126 MHz for ^{13}C. Chemical shifts of ^{1}H were referenced to Me_4Si as internal reference. Data are represented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet), coupling constant J (Hz), and integration. Assignments were done with the aid of DEPT 135, COSY, and HMQC experiments. High-resolution mass spectra (HRMS) were recorded on a Micro-Tof-Q II or on a Q-Tof 2 using positive ion electrospray. Purifications on silica gel were carried out on silica gel 0.006−0.200 mm, 60 Å. Analytical thin-layer chromatography was performed on silica gel 60 F_{254} plates. Optical rotations were measured using 10 cm cell at 20 °C (sodium D line: 589 nm), and the concentration is expressed in g/dL. Melting points were measured without correction on a digital melting point apparatus. All analytical high-performance liquid chromatography (HPLC) was performed using Chiralpak IA and IC columns.

4-(Trimethylsilyl)but-3-yn-2-ol was prepared from butyn-2-ol.[43] (*R*)-4-(Trimethylsilyl)but-3-yn-2-ol (97% ee) and (*S*)-4-(trimethylsilyl)but-3-yn-2-ol (98.5% ee) were obtained by enzymatic resolution of 4-(trimethylsilyl)but-3-yn-2-ol.[25b] (*R*,*E*)-4-(Trimethylsilyl)but-3-en-2-ol ((*R*,*E*)-**1**) and (*S*,*E*)-4-(trimethylsilyl)-but-3-en-2-ol ((*S*,*E*)-**1**) were both obtained from the corresponding enantioenriched alkynes according to a literature procedure.[2c]

General Procedure for the Synthesis of Enantioenriched Vinylsilanes by Hydrosilylation. A mixture of $PtCl_2$ (0.074 mmol) and XPhos (0.148 equiv) in anhydrous THF (0.5 mL) was heated at 50 °C for 30 min. A solution of propargyl alcohol (7.14 mmol) in anhydrous THF (0.4 mL) was added, followed by the slow addition of dimethylphenylsilane (10.71 mmol). A strong emission of hydrogen gas was observed. The reaction mixture was stirred at 50 °C overnight, after which time THF was removed in vacuo. Water (3 mL) was added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. A solution of the crude product (3.52 mmol) in anhydrous THF (0.05 M) was stirred at room temperature. A solution of TBAF in THF (4.23 mmol, 1M) was added. The reaction mixture was left at room temperature for 1 h, then THF was removed in vacuo. Water was added (20 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The residue was purified by flash column chromatography on silica gel to afford the corresponding product.

*(S,E)-4-(Dimethyl(phenyl)silyl)but-3-en-2-ol ((S,E)-**7a**).*[44] Prepared from (*S*)-butyn-2-ol and purified as an inseparable mixture of α/β isomer (14/86 respectively) using a cyclohexane/ethyl acetate mixture (90/10, R_f 0.24) as eluent. The mixture was isolated as a yellow oil (1.22 g) in 83% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57−7.47 (m, 2H), 7.39−7.33 (m, 3H), 6.17 (dd, J = 18.7, 4.8 Hz, 1H), 5.97 (dd, J = 18.7, 1.3 Hz, 1H), 4.36−4.28 (m, 1H), 1.28 (d, J = 6.5 Hz, 3H), 0.36 (s, 6H). $[\alpha]_D$ = +6.1 (*c* 2.45, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{12}H_{19}OSi$ $[M + H]^+$ 207.1205, found 207.1204.

*(R,E)-1-(Dimethyl(phenyl)silyl)oct-1-en-3-ol ((R,E)-**7b**).*[45] Prepared from (*R*)-octyn-2-ol and purified as an inseparable mixture of α/β isomer (11/89 respectively) using a cyclohexane/ethyl acetate mixture

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(90/10, R_f 0.37) as eluent. The mixture was isolated as a yellow oil (1.01 g) in 54% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53−7.50 (m, 2H), 7.38−7.34 (m, 3H), 6.13 (dd, J = 18.8, 5.1 Hz, 1H), 5.97 (dd, J = 18.8, 1.2 Hz, 1H), 4.16−4.09 (m, 1H), 3.53−3.45 (m, 1H), 1.66−1.21 (m, 8H), 0.94−0.83 (m, 3H), 0.35 (s, 6H), 0.35 (s, 6H). $[\alpha]_D$ = −1.6 (c 2.57, CH_2Cl_2). HRMS (ESI): m/z calcd for $C_{16}H_{27}OSi$ $[M + H]^+$ 263.1831, found 263.1830.

General Procedure for the Synthesis of Allylic Carbamates. A solution of vinylsilane (4.6 mmol) in anhydrous CH_2Cl_2 (0.12 M) under argon atmosphere was cooled to 0 °C, and trichloroacetyl isocyanate (6.9 mmol) was added slowly. The reaction mixture was stirred at 0 °C for 5 h. CH_2Cl_2 was removed in vacuo and K_2CO_3 (13.8 mmol) in a mixture of MeOH (92 mL) and water (24 mL) was added. The solution was stirred at room temperature overnight, and then MeOH was removed in vacuo. The aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to afford the corresponding product.

*(S,E)-4-(Trimethylsilyl)but-3-en-2-yl Carbamate ((S,E)-**2**).* Prepared from (*S*,*E*)-**1** and purified using a cyclohexane/ethyl acetate mixture (80/20, R_f 0.21) as eluent. The mixture was isolated as a white solid (654 mg) in 76% yield. Mp: 54−56 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.01 (dd, J = 18.8, 4.6 Hz, 1H), 5.85 (dd, J = 18.8, 1.3 Hz, 1H), 5.28−5.17 (m, 1H), 4.61 (s, 2H), 1.31 (d, J = 6.5 Hz, 3H), 0.07 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 145.1, 130.3, 73.1, 20.1−1.3. Chiralpak IA, heptane/*i*-PrOH = 99/1, flow rate = 1 mL/min, 220 nm, the (*S*,*E*) enantiomer t_R = 24.9 min (major), the (*R*,*E*) enantiomer t_R = 27.9 min (minor), ee = 98.5%. The 1/1 mixture of (*S*,*E*)-**2** and (*R*,*E*)-**2** was obtained from the racemic (*E*)-**1**. $[\alpha]_D$ = −24.2 (c 1.10, CH_2Cl_2). HRMS (ESI): m/z calcd for $C_8H_{17}NO_2SiNa$ $[M + Na]^+$ 210.0921, found 210.0919.

*(R,E)-4-(Trimethylsilyl)but-3-en-2-yl Carbamate ((R,E)-**2**).* Prepared from (*R*,*E*)-**1** and purified using a cyclohexane/ethyl acetate mixture (80/20, R_f 0.21) as eluent. The mixture was isolated as a white solid (793 mg) in 92% yield. Mp: 54−56 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.01 (dd, J = 18.8, 4.6 Hz, 1H), 5.85 (dd, J = 18.8, 1.3 Hz, 1H), 5.28−5.17 (m, 1H), 4.61 (s, 2H), 1.31 (d, J = 6.5 Hz, 3H), 0.07 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 145.1, 130.3, 73.1, 20.1−1.3. Chiralpak IA, heptane/*i*-PrOH = 99/1, flow rate =1 mL/min, 220 nm, the (*S*,*E*) enantiomer t_R = 25.4 min (minor), the (*R*,*E*) enantiomer t_R = 27.2 min (major), ee = 97%. The 1/1 mixture of (*S*,*E*)-**2** and (*R*,*E*)-**2** was obtained from the racemic (*E*)-**1**. $[\alpha]_D$ = +21.2 (c 2.32, CH_2Cl_2). HRMS (ESI): m/z calcd for $C_8H_{17}NO_2SiNa$ $[M + Na]^+$ 210.0921, found 210.0920.

*(S,E)-4-(Dimethyl(phenyl)silyl)but-3-en-2-yl Carbamate ((S,E)-**8a**).* Prepared from ((*S*,*E*)-**7a**) and purified as an inseparable mixture of α/β isomer (14/86 respectively) using a cyclohexane/ethyl acetate mixture (80/20, R_f 0.26) as eluent. The mixture was isolated as a colorless oil (1.02 g) in 89% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.59−7.48 (m, 2H), 7.42−7.33 (m, 3H), 6.12 (dd, J = 18.8, 4.3 Hz, 1H), 6.00 (dd, J = 18.8, 1.1 Hz, 1H), 5.33−5.25 (m, 1H), 4.65 (s, 2H), 1.34 (d, J = 6.5 Hz, 3H), 0.37 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.1, 138.5, 134.0, 133.7, 129.2, 128.0, 127.9, 73.0, 20.1, −2.5. Chiralpak IC, heptane/*i*-PrOH = 90/10, flow rate = 1 mL/min, 272 nm, the (*S*,*E*) enantiomer t_R = 8.5 min (major), the (*R*,*E*) enantiomer t_R = 10.3 min (minor), ee = 98%. The 1/1 mixture of (*S*,*E*)-**8a** and (*R*,*E*)-**8a** was obtained from the racemic (*E*)-**7a**. $[\alpha]_D$ = −16.2 (c 2.62, CH_2Cl_2). HRMS (ESI): m/z calcd for $C_{13}H_{19}NO_2SiNa$ $[M + Na]^+$ 272.1083, found 272.1083.

*(R,E)-1-(Dimethyl(phenyl)silyl)oct-1-en-3-yl Carbamate ((R,E)-**8b**).* Prepared from ((*R*,*E*)-**7b**) and purified as an inseparable mixture of α/β isomer (11/89 respectively) using a cyclohexane/ethyl acetate mixture (90/10, R_f 0.19) as eluent. The mixture was isolated as a colorless oil (1.35 g) in 96% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 54−7.46 (m, 2H), 7.37−7.33 (m, 3H), 6.05−5.98 (m, 2H), 5.16 (td, J = 6.5, 3.8 Hz, 1H), 1.59−1.22 (m, 8H), 0.93−0.83 (m, 3H), 0.34 (d, J = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.0, 146.2, 138.4, 133.9, 129.0, 128.4, 127.8, 76.6, 34.3, 31.6, 24.8, 22.6, 14.0, −2.4, −2.6. Chiralpak IC, heptane/*i*-PrOH = 95/5, flow rate = 1 mL/min, 272 nm, the (*S*,*E*) enantiomer t_R = 11.9 min (minor), the (*R*,*E*) enantiomer t_R = 14.3 min (major), ee = 88%. The 1/1 mixture of (*S*,*E*)-**8b** and (*R*,*E*)-**8b** was obtained from the racemic (*E*)-**7b**. $[\alpha]_D$ = +8.8 (c 1.65, CH_2Cl_2). HRMS (ESI): m/z calcd for $C_{17}H_{27}NO_2SiNa$ $[M + Na]^+$ 328.1709, found 328.1709.

General Procedure for the Synthesis of α-Ureido Allylsilanes. In an oven-dried, 10 mL, round-bottom flask, under argon atmosphere, were stirred carbamate (0.32 mmol) and triphenylphosphine (0.80 mmol) in anhydrous CH_2Cl_2 (3 mL, 0.16 M). Triethylamine (0.64 mmol) was added, and the reaction mixture was cooled at 0 °C. A solution of tetrabromomethane (0.90 mmol) in CH_2Cl_2 (0.90 M) was added at 0 °C. The reaction mixture was stirred at 0 °C for 2 h, and the amine (0.48 mmol) was added. In the case of an amine hydrochloride salt, an additional quantity of triethylamine (0.64 mmol) was added. The reaction mixture was stirred at room temperature for 4 h. Water was added, and the aqueous layer was extracted three times with CH_2Cl_2. The collected organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to afford the corresponding product.

*(R,E)-1-Benzyl-3-(1-(trimethylsilyl)but-2-en-1-yl)urea ((R,E)-**5a**).* Prepared from (*S*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (75/25, R_f 0.25) as eluent. The product was isolated as a white solid (83 mg) in 94% yield. Mp: 144−146 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41−7.21 (m, 5H), 5.51−5.31 (m, 2H), 5.05−4.97 (br s, 1H), 4.54−4.30 (m, 3H), 3.45−3.39 (br s, 1H), 1.74−1.59 (m, 3H), −0.06 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.5, 139.5, 130.3, 128.6, 127.4, 127.2, 123.2, 45.3, 44.5, 17.8, −3.7. Chiralpak IA, heptane/*i*-PrOH = 90/10, flow rate = 1 mL/min, 254 nm, the (*R*,*E*) enantiomer t_R = 8.5 min (major), the (*S*,*E*) enantiomer t_R = 10.1 min (minor), ee = 98.1%. The 1/1 mixture of (*R*,*E*)-**5a** and (*S*,*E*)-**5a** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = +8.1 (c 0.61, CH_2Cl_2). HRMS (ESI): m/z calcd for $C_{15}H_{24}N_2OSiNa$ $[M + Na]^+$ 299.1550, found 299.1549.

*Methyl [((R,E)-1-(Trimethylsilyl)but-2-en-1-yl)carbamoyl]-L-alaninate (**5b**).* Prepared from (*S*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (70/30, R_f 0.26) as eluent. The product was isolated as a yellow solid (71 mg) in 81% yield. Mp: 138−140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.57−5.32 (m, 3H), 4.88 (d, J = 6.3 Hz, 1H), 4.48 (qd, J = 6.3, 6.3 Hz, 1H), 3.70 (s, 3H), 3.56−3.42 (br s, 1H), 1.67 (ddd, J = 6.3, 1.4, 1.4 Hz, 3H), 1.34 (d, J = 7.2 Hz, 3H), 0.03 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 174.8, 158.6, 130.2, 123.1, 52.3, 48.9, 45.3, 19.3, 17.9, −3.7. The diastereomeric excess was determined by ^{13}C NMR, de > 95%. $[\alpha]_D$ = +40.9 (c 0.64, CH_2Cl_2). HRMS (ESI): m/z calcd for $C_{12}H_{24}N_2O_3SiNa$ $[M + Na]^+$ 295.1448, found 295.1450.

*Methyl (((R,E)-1-(Trimethylsilyl)but-2-en-1-yl)carbamoyl)-L-prolinate (**5c**).* Prepared from (*S*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (70/30, R_f 0.18) as eluent. The product was isolated as an orange solid (76 mg) in 80% yield. Mp: 83−85 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.52−5.26 (m, 2H), 4.39 (m, 2H), 3.95−3.89 (br s, 1H), 3.72 (s, 3H), 3.58−3.34 (m, 2H), 2.25−1.93 (m, 4H), 1.74−1.62 (m, 3H), 0.03 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.8, 156.8, 130.1, 121.7, 59.2, 52.3, 46.2, 44.2, 30.0, 24.5, 18.0, −3.5. The diastereomeric excess was determined by ^{1}H NMR, de > 95%. $[\alpha]_D$ = −35.0 (c 3.83, CH_2Cl_2). HRMS (ESI): m/z calcd for $C_{14}H_{26}N_2O_3SiNa$ $[M + Na]^+$ 321.1605, found 321.1604.

*(S,E)-1-Isobutyl-3-(1-(trimethylsilyl)but-2-en-1-yl)urea ((S,E)-**5d**).* Prepared from (*R*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (75/25, R_f 0.12) as eluent. The product was isolated as an orange oil (62 mg) in 80% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.59−5.35 (m, 2H), 4.85−4.82 (br s, 1H), 4.41 (d, J = 5.8 Hz, 1H), 3.39−3.29 (m, 1H), 3.16−3.05 (m, 1H), 2.97−2.87 (m, 1H), 1.72 (ddd, J = 6.0, 1.2, 1.2 Hz, 3H), 0.90 (d, J = 6.7 Hz, 6H), 0.07 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.8, 130.8, 123.5, 48.0, 45.8, 28.9, 20.2, 20.1, 17.8, −3.7. Chiralpak IA, heptane/*i*-PrOH = 90/10, flow rate = 1 mL/min, 230 nm, the (*R*,*E*) enantiomer t_R = 6.1 min (minor), the (*S*,*E*) enantiomer t_R = 7.1 min (major), ee = 96%. The 1/1 mixture of (*R*,*E*)-**5d** and (*S*,*E*)-**5d** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ =

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−20.0 (*c* 2.37, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{12}H_{26}N_2OSiNa$ $[M + Na]^+$ 265.1707, found 265.1706.

*(S,E)-1,1-Diethyl-3-(1-(trimethylsilyl)but-2-en-1-yl)urea ((S,E)-**5e**).* Prepared from (*R*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (85/15 up to 80/20, R_f 0.24) as eluent. The product was isolated as a yellow oil (68 mg) in 88% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.51−5.24 (m, 2H), 4.22 (d, *J* = 8.1 Hz, 1H), 3.97−3.85 (m, 1H), 3.27 (q, *J* = 7.2 Hz, 4H), 1.65 (ddd, *J* = 6.0, 1.4, 1.4 Hz 3H), 1.14 (t, *J* = 7.2 Hz, 6H), 0.03 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.3, 130.6, 121.4, 44.2, 41.5, 17.9, 14.0, −3.4. Chiralpak IA, heptane/*i*-PrOH = 97/3, flow rate = 1 mL/min, 230 nm, the (*R*,*E*) enantiomer t_R = 8.6 min (minor), the (*S*,*E*) enantiomer t_R = 9.2 min (major), ee = 96.7%. The 1/1 mixture of (*R*,*E*)-**5e** and (*S*,*E*)-**5e** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = +2.0 (*c* 1.02, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{12}H_{26}N_2OSiNa$ $[M + Na]^+$ 265.1707, found 265.1707.

*(R,E)-1-(4-Methoxyphenyl)-3-(1-(trimethylsilyl)but-2-en-1-yl)urea ((R,E)-**5f**).* Prepared from (*S*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (70/30, R_f 0.23) as eluent. The product was isolated as a brown solid (83 mg) in 89% yield. Mp: 110−112 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23−7.19 (m, 2H), 6.83 (m, 2H), 6.72−6.65 (br s, 1H), 5.50−5.39 (m, 2H), 4.78−4.72 (br s, 1H), 3.78 (s, 3H), 3.71−3.67 (br s, 1H), 1.71−1.69 (m, 3H), 0.03 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.3, 156.1, 132.1, 130.2, 122.8, 122.6, 114.4, 55.6, 27.0, 18.0, −3.6. Chiralpak IA, heptane/*i*-PrOH = 90/10, flow rate =1 mL/min, 230 nm, the (*R*,*E*) enantiomer t_R = 11.4 min (major), the (*S*,*E*) enantiomer t_R = 15.9 min (minor), ee = 94.6%. The 1/1 mixture of (*R*,*E*)-**5f** and (*S*,*E*)-**5f** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = +17.7 (*c* 0.82, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{15}H_{24}N_2O_2SiNa$ $[M + Na]^+$ 315.1499, found 315.1501.

*Methyl (R,E)-[(1-(Trimethylsilyl)but-2-en-1-yl)carbamoyl]-glycinate ((R,E)-**5g**).* Prepared from (*S*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (60/40, R_f 0.23) as eluent. The product was isolated as an orange oil (79 mg) in 96% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.62−5.57 (br s, 1H), 5.57−5.33 (m, 2H), 5.01 (d, *J* = 6.4 Hz, 1H), 4.11−3.91 (m, 2H), 3.73 (s, 3H), 3.53−3.49 (br s, 1H), 1.69 (ddd, *J* = 6.1, 1.2, 1.2 Hz, 3H), 0.05 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.7, 159.3, 130.1, 123.5, 52.2, 45.4, 42.4, 17.9, −3.7. Chiralpak IA, heptane/*i*-PrOH = 93/7, flow rate = 0.8 mL/min, 220 nm, the (*R*,*E*) enantiomer t_R = 14.9 min (major), the (*S*,*E*) enantiomer t_R = 17.0 min (minor), ee = 96.5%. The 1/1 mixture of (*R*,*E*)-**5g** and (*S*,*E*)-**5g** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = +12.9 (*c* 2.86, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{11}H_{22}N_2O_3SiNa$ $[M + H]^+$ 281.1292, found 281.1293.

*(S,E)-1-Methoxy-1-methyl-3-(1-(trimethylsilyl)but-2-en-1-yl)urea ((S,E)-**5h**).* Prepared from (*R*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (80/20, R_f 0.41) as eluent. The product was isolated as a yellow oil (57 mg) in 77% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.74 (d, *J* = 8.6 Hz, 1H), 5.47−5.26 (m, 2H), 3.91−3.81 (m, 1H), 3.65 (s, 3H), 3.06 (s, 3H), 1.70−1.61 (m, 3H), 0.02 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.4, 129.5, 122.0, 61.4, 43.7, 36.1, 17.9, −3.6. Chiralpak IA, heptane/*i*-PrOH = 97/3, flow rate = 1 mL/min, 230 nm, the (*R*,*E*) enantiomer t_R = 7.6 min (minor), the (*S*,*E*) enantiomer t_R = 8.3 min (major), ee = 93.8%. The 1/1 mixture of (*R*,*E*)-**5h** and (*S*,*E*)-**5h** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = −2.5 (*c* 2.60, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{10}H_{22}N_2O_2SiNa$ $[M + Na]^+$ 253.1348, found 253.1348.

*1-((1R,2S)-2-Hydroxy-2,3-dihydro-1H-inden-1-yl)-3-((S,E)-1-(trimethylsilyl)but-2-en-1-yl)urea (**5i**).* Prepared from (*R*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (70/30, R_f 0.13) as eluent. The product was isolated as a yellow solid (81 mg) in 80% yield. Mp: 62−64 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.23−7.10 (m, 4H), 5.75 (d, *J* = 8.0 Hz, 1H), 5.45−5.29 (m, 2H), 5.19−5.05 (m, 2H), 4.36−4.28 (m, 1H), 3.58−3.55 (br s, 1H), 2.98 (dd, *J* = 16.4, 5.2 Hz, 2H), 2.81 (dd, *J* = 16.4, 2.0 Hz, 1H), 1.67−1.61 (m, 3H), 0.03 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.9, 141.7, 140.2, 130.1, 127.9, 126.9, 125.2, 124.5, 122.9, 73.8, 58.7, 45.2, 39.2, 17.8, −3.6. The diastereomeric excess was determined by ^{13}C NMR, de > 95%. $[\alpha]_D$ = −47.1 (*c* 3.48, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{17}H_{26}N_2O_2SiNa$ $[M + Na]^+$ 341.1661, found 341.1661.

*Methyl (R,E)-((1-(Dimethyl(phenyl)silyl)but-2-en-1-yl)carbamoyl)-glycinate ((R,E)-**9aa**).* Prepared from (*S*,*E*)-**8a** and purified using a cyclohexane/ethyl acetate mixture (60/40, R_f 0.42) as eluent. The product was isolated as a yellow solid (67 mg) in 65% yield. Mp: 88−90 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55−7.44 (m, 2H), 7.41−7.30 (m, 3H), 5.44−5.36 (m, 2H), 4.79 (d, *J* = 7.3 Hz, 1H), 4.04−3.84 (m, 2H), 3.75−3.71 (br s, 1H), 3.69 (s, 3H), 1.67 (dd, *J* = 4.9, 1.3 Hz, 3H), 0.33 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6, 158.9, 135.3, 134.2, 129.8, 129.7, 128.0, 123.8, 52.2, 44.7, 42.3, 17.9, −5.0, −5.1. Chiralpak IA, heptane/*i*-PrOH = 90/10, flow rate = 1 mL/min, 230 nm, the (*R*,*E*) enantiomer t_R = 10.5 min (major), the (*S*,*E*) enantiomer t_R = 13.0 min (minor), ee = 97.8%. The 1/1 mixture of (*R*,*E*)-**9aa** and (*S*,*E*)-**9aa** was obtained from racemic (*E*)-**8a**. $[\alpha]_D$ = +7.3 (*c* 2.25, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{16}H_{24}N_2O_3SiNa$ $[M + Na]^+$ 343.1454, found 343.1452.

*(R,E)-3-(1-(Dimethyl(phenyl)silyl)but-2-en-1-yl)-1-methoxy-1-methylurea ((R,E)-**9ab**).* Prepared from (*S*,*E*)-**8a** and purified using a cyclohexane/ethyl acetate mixture (80/20, R_f 0.28) as eluent. The product was isolated as a yellow oil (69 mg) in 74% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55−7.46 (m, 2H), 7.44−7.30 (m, 3H), 5.65 (d, *J* = 9.2 Hz, 1H), 5.49−5.20 (m, 2H), 4.16−4.02 (m, 1H), 3.50 (s, 3H), 3.03 (s, 3H), 1.66 (ddd, *J* = 6.2, 1.4, 1.4 Hz, 3H), 0.36 (s, 3H), 0.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.4, 135.6, 134.2, 129.7, 129.3, 128.0, 122.4, 61.4, 43.0, 35.9, 17.9, −4.8, −5.0. Chiralpak IA, heptane/*i*-PrOH = 90/10, flow rate = 1 mL/min, 230 nm, the (*R*,*E*) enantiomer t_R = 5.8 min (major), the (*S*,*E*) enantiomer t_R = 7.1 min (minor), ee = 95.9%. The 1/1 mixture of (*R*,*E*)-**9ab** and (*S*,*E*)-**9ab** was obtained from racemic (*E*)-**8a**. $[\alpha]_D$ = +9.7 (*c* 2.62, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{15}H_{24}N_2O_2SiNa$ $[M + Na]^+$ 315.1505, found 315.1506.

*(S,E)-3-(1-(Dimethyl(phenyl)silyl)oct-2-en-1-yl)-1-methoxy-1-methylurea ((S,E)-**9bb**).* Prepared from (*R*,*E*)-**8b** and purified using a cyclohexane/ethyl acetate mixture (80/20, R_f 0.28) as eluent. The product was isolated as a yellow oil (65 mg) in 58% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55−7.47 (m, 2H), 7.42−7.32 (m, 3H), 5.66 (d, *J* = 9.3 Hz, 1H), 5.39 (dd, *J* = 15.3, 6.1 Hz, 1H), 5.26 (dtd, *J* = 15.3, 6.1, 1.4 Hz, 1H), 4.16−4.04 (m, 1H), 3.51 (s, 3H), 3.04 (s, 3H), 2.03−1.93 (m, 2H), 1.37−1.20 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 3H), 0.36 (s, 3H), 0.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.3, 135.6, 134.3, 129.7, 128.1, 128.1, 128.0, 61.4, 43.0, 36.0, 32.5, 31.5, 29.4, 22.6, 14.2, −4.7, −5.0. Chiralpak IA, heptane/*i*-PrOH = 95/5, flow rate = 1 mL/min, 220 nm, the (*R*,*E*) enantiomer t_R = 8.0 min (minor), the (*S*,*E*) enantiomer t_R = 8.7 min (major), ee = 86.5%. The 1/1 mixture of (*R*,*E*)-**9bb** and (*S*,*E*)-**9bb** was obtained from racemic (*E*)-**8b**. $[\alpha]_D$ = −17.5 (*c* 1.69, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{19}H_{32}N_2O_2SiNa$ $[M + Na]^+$ 371.2131, found 371.2130.

General Procedure for the Synthesis of α-Carbamoyl Allylsilanes. In an oven-dried, 10 mL, round-bottom flask, under argon atmosphere, carbamate (3 mL, 0.32 mmol) and triphenylphosphine (0.80 mmol) were stirred in anhydrous CH_2Cl_2 (0.16 M). Triethylamine (0.64 mmol) was added, and the reaction mixture was cooled at 0 °C. A solution of tetrabromomethane (0.90 mmol) in CH_2Cl_2 (0.90 M) was added at 0 °C. The reaction mixture was stirred at 0 °C for 2 h, and then a slight excess of alcohol (0.48 mmol), except in the case of methanol and 2-propanol (1.3 mL), with a catalytic amount of DMAP (5 mol %) were added. The reaction mixture was stirred at reflux for 18 h. Water was added, and the aqueous layer was extracted three times with CH_2Cl_2. The collected organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel to afford the corresponding product.

*Methyl (S,E)-(1-(trimethylsilyl)but-2-en-1-yl)carbamate ((S,E)-**5j**).* Prepared from (*R*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (90/10, R_f 0.32) as eluent. The product was isolated as a white solid (48 mg) in 75% yield. Mp: 60−62 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.47−5.26 (m, 2H), 4.62−4.58 (br s, 1H), 3.74−3.70 (br s, 1H), 3.65 (s, 3H), 1.67 (ddd, *J* = 3.8, 1.4, 1.4 Hz,, 3H), 0.02 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.4, 129.4, 122.4, 52.2, 45.3, 17.9, −3.6. Chiralpak IA, heptane/*i*-PrOH = 98/2, flow rate = 1 mL/min, 272 nm, the (*R*,*E*) enantiomer t_R = 6.2 min (minor), the (*S*,*E*)

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enantiomer t_R = 6.8 min (major), ee = 93.8%. The 1/1 mixture of (*R*,*E*)-**5j** and (*S*,*E*)-**5j** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = −28.4 (*c* 1.74, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_9H_{19}NO_2SiNa$ $[M + Na]^+$ 224.1083, found 224.1082.

*4-Iodobenzyl (S,E)-(1-(Trimethylsilyl)but-2-en-1-yl)carbamate ((S,E)-**5k**).* Prepared from (*R*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (95/5, R_f 0.24) as eluent. The product was isolated as a yellow oil (76 mg) in 59% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 2H), 5.42−5.35 (m, 2H), 5.03 (s, 2H), 4.68−4.64 (br s, 1H), 3.75−3.71 (br s, 1H), 1.71−1.64 (m, 3H), 0.03 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.5, 137.7, 136.6, 130.1, 129.2, 122.6, 93.8, 66.2, 45.4, 17.9, −3.6. Chiralpak IA, heptane/*i*-PrOH = 90/10, flow rate = 1 mL/min, 230 nm, the (*R*,*E*) enantiomer t_R = 6.1 min (minor), the (*S*,*E*) enantiomer t_R = 6.9 min (major), ee = 95.5%. The 1/1 mixture of (*R*,*E*)-**5k** and (*S*,*E*)-**5k** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = −6.8 (*c* 2.72, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{15}H_{22}INO_2SiNa$ $[M + Na]^+$ 426.0362, found 426.0363.

*(S)-2-((tert-Butoxycarbonyl)amino)-3-phenylpropyl ((S,E)-1-(Trimethylsilyl)but-2-en-1yl)carbamate (**5l**).* Prepared from (*R*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (95/5, R_f 0.24) as eluent. The product was isolated as a white solid (78 mg) in 58% yield. Mp: 124−126 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34−7.15 (m, 5H), 5.46−5.37 (m, 2H), 4.82−4.78 (br s, 1H), 4.68 (d, *J* = 8.5 Hz, 1H), 4.16−3.94 (m, 3H), 3.75−3.70 (m, 1H), 2.95−2.73 (m, 2H), 1.71−1.68 (m, 3H), 1.43 (s, 9H), 0.08 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 156.5, 155.3, 137.4, 129.4, 129.0, 128.5, 126.5, 122.5, 79.4, 65.4, 51.4, 45.2, 38.0, 28.4, 17.8, −3.7. The diastereomeric excess was determined by ^{13}C NMR, de > 95%. $[\alpha]_D$ = −17.3 (*c* 1.30, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{22}H_{36}N_2O_4SiNa$ $[M + Na]^+$ 443.2342, found 443.2341.

*Prop-2-yn-1-yl (R,E)-(1-(Trimethylsilyl)but-2-en-1-yl)carbamate ((R,E)-**5m**).* Prepared from (*S*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (90/10, R_f 0.25) as eluent. The product was isolated as an orange oil (43 mg) in 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.44−5.33 (m, 2H), 4.75−4.70 (br s, 1H), 4.68 (dd, *J* = 2.5, 1.0 Hz, 2H), 3.72 (d, *J* = 9.3 Hz, 1H), 2.48 (t, *J* = 2.5 Hz, 1H), 1.68 (ddd, *J* = 3.4, 1.4, 1.4 Hz, 3H), 0.04 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 129.0, 122.8, 78.5, 77.4, 74.7, 52.7, 45.4, 18.0, −3.6. Chiralpak IA, heptane/*i*-PrOH = 97/3, flow rate = 0.8 mL/min, 220 nm, the (*R*,*E*) enantiomer t_R = 14.9 min (major), the (*S*,*E*) enantiomer t_R = 17.0 min (minor), ee = 96.5%. The 1/1 mixture of (*R*,*E*)-**5m** and (*S*,*E*)-**5m** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = −15.8 (*c* 1.46, CH_2Cl_2). HRMS (ESI) *m*/*z* calcd for $C_{11}H_{19}NO_2SiNa$ $[M + Na]^+$ 248.1077, found 248.1076.

*Isopropyl (S,E)-(1-(Trimethylsilyl)but-2-en-1-yl)carbamate ((S,E)-**5n**).* Prepared from (*R*,*E*)-**2** and purified using a cyclohexane/ethyl acetate mixture (90/10, R_f 0.38) as eluent. The product was isolated as a colorless oil (29 mg) in 40% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.43−5.33 (m, 2H), 4.90 (hept, *J* = 6.3 Hz, 1H), 4.49 (br s, 1H), 3.70 (br, 1H), 1.71−1.64 (m, 3H), 1.22 (dd, *J* = 6.3, 2.2 Hz, 6H), 0.03 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.6, 129.5, 122.1, 68.1, 45.0, 22.3, 22.2, 17.9, −3.7. Chiralpak IC, heptane/*i*-PrOH = 99/1, flow rate = 0.5 mL/min, 200 nm, the (*R*,*E*) enantiomer t_R = 15.9 min (minor), the (*S*,*E*) enantiomer t_R = 14.6 min (major), ee = 97.2%. The 1/1 mixture of (*R*,*E*)-**5n** and (*S*,*E*)-**5n** was obtained from racemic (*E*)-**2**. $[\alpha]_D$ = −19.8 (*c* 2.25, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{11}H_{23}NO_2SiNa$ $[M + Na]^+$ 252.1396, found 252.1396.

*Methyl (S,E)-(1-(Dimethyl(phenyl)silyl)oct-2-en-1-yl)carbamate ((S,E)-**9ba**).* Prepared from (*R*,*E*)-**8b** and purified using a cyclohexane/ethyl acetate mixture (85/15, R_f 0.52) as eluent. The product was isolated as a yellow oil (61 mg) in 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56−7.47 (m, 2H), 7.44−7.34 (m, 3H), 5.45−5.24 (m, 2H), 4.55−4.51(m, 1H), 4.01−3.96 (br s, 1H), 3.65 (s, 3H), 2.03−1.94 (m, 2H), 1.40−1.19 (m, 6H), 0.90 (t, *J* = 6.9 Hz, 3H), 0.37 (s, 3H), 0.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.2, 135.4, 134.3, 129.8, 128.5, 128.1, 128.1, 128.0, 52.3, 44.6, 32.5, 31.5, 29.4, 22.6, 14.2, −4.7, −5.1. Chiralpak IC, heptane/*i*-PrOH = 90/10, flow rate = 1 mL/min, 272 nm, the (*R*,*E*) enantiomer t_R = 4.2 min (minor), the (*S*,*E*) enantiomer t_R = 5.1 min (major), ee = 87.8%. The 1/1 mixture of (*R*,*E*)-**9ba** and (*S*,*E*)-**9ba** was obtained from racemic (*E*)-**8b**. $[\alpha]_D$ = −19.0 (*c* 1.00, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{18}H_{29}NO_2SiNa$ $[M + Na]^+$ 342.1865, found 342.1865.

*Methyl (R,E)-(1-(Dimethyl(phenyl)silyl)but-2-en-1-yl)carbamate ((R,E)-**9ac**).* Prepared from (*S*,*E*)-**8a** and purified using a cyclohexane/ethyl acetate mixture (90/10, R_f 0.23) as eluent. The product was isolated as a colorless oil (73 mg) in 87% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52−7.47 (m, 2H), 7.41−7.34 (m, 3H), 5.45−5.25 (m, 2H), 4.52−4.48 (br s, 1H), 3.97−3.93 (br s, 1H), 3.63 (s, 3H), 1.71−1.62 (m, 3H), 0.35 (s, 3H), 0.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 157.3, 135.3, 134.3, 129.8, 129.1, 128.1, 122.8, 52.2, 44.6, 18.0, −4.8, −5.0. Chiralpak IA, heptane/*i*-PrOH = 98/2, flow rate = 1 mL/min, 234 nm, the (*R*,*E*) enantiomer t_R = 8.3 min (major), the (*S*,*E*) enantiomer t_R = 9.4 min (minor), ee = 96.2%. The 1/1 mixture of (*R*,*E*)-**9ac** and (*S*,*E*)-**9ac** was obtained from racemic (*E*)-**8a**. $[\alpha]_D$ = +10.2 (*c* 1.53, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{14}H_{21}NO_2SiNa$ $[M + Na]^+$ 286.1239, found 286.1241.

General Procedure for Hydrogenation Reaction. In a round-bottom flask, **5** or **9** (0.15 mmol) was dissolved in AcOEt (0.25 M) followed by the addition of catalyst. After replacement of air by hydrogen via vacuum (procedure repeated twice), the mixture was stirred at room temperature. The mixture was filtered through a pad of Celite, rinsed with AcOEt, and concentrated in vacuo. The crude product was purified by silica gel chromatography.

*Methyl (((R)-1-(Trimethylsilyl)butyl)carbamoyl)-L-alaninate (**10**).* Prepared from **5b** using PtO_2 (10 mol %) as catalyst for 16 h and purified using a cyclohexane/ethyl acetate mixture (60/40, R_f 0.37) as eluent. The product was isolated as a white solid (33 mg) in 80% yield. Mp: 136−138 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.16−4.93 (m, 1H), 4.54−4.27 (m, 2H), 3.72 (s, 3H), 3.16−3.12 (br s, 1H), 1.50−1.40 (m, 2H), 1.37 (dd, *J* = 7.1, 1.5 Hz, 3H), 1.33−1.25 (m, 2H), 0.88 (t, *J* = 6.3 Hz, 3H), 0.02 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.0, 158.0, 53.6, 52.4, 49.1, 34.2, 31.1, 20.6, 19.2, −3.3. $[\alpha]_D$ = +6.0 (*c* 0.91, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{12}H_{26}N_2O_3SiNa$ $[M + Na]^+$ 297.1610, found 297.1608.

*Methyl (R)-((1-(Dimethyl(phenyl)silyl)butyl)carbamoyl)glycinate (**11**).* Prepared from (*R*,*E*)-**9aa** using Pd/C (10 mol %) as catalyst for 16 h and purified using a cyclohexane/ethyl acetate mixture (60/40, R_f 0.24) as eluent. The product was isolated as a white solid (28 mg) in 58% yield. Mp: 61−63 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58−7.48 (m, 2H), 7.40−7.30 (m, 3H), 5.00 (t, *J* = 5.2 Hz, 1H), 4.41 (d, *J* = 10.0 Hz, 1H), 4.03−3.86 (m, 2H), 3.69 (s, 3H), 3.45−3.41 (br s, 1H), 1.51−1.17 (m, 4H), 0.83 (t, *J* = 6.9 Hz, 3H), 0.34 (s, 3H), 0.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.9, 158.3, 136.7, 134.2, 129.5, 128.0, 52.2, 42.4, 34.3, 27.0, 20.5, 14.1, −4.4, −5.1. $[\alpha]_D$ = −15.7 (*c* 1.02, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{16}H_{26}N_2O_3SiNa$ $[M + Na]^+$ 345.1610, found 345.1612.

*1,1′-((1R,1′R)-(1,1,3,3-Tetramethyldisiloxane-1,3-diyl)bis(butane-1,1-diyl))bis(3-methoxy-3-methylurea) ((R,R)-**13a**).* Prepared from (*R*,*E*)-**9ab** using PtO_2 (40 mol %) as catalyst for 64 h and purified using a cyclohexane/ethyl acetate mixture (70/30, R_f 0.21) as eluent. The product was isolated as a white solid (37 mg) in 55% yield. Mp: 71−73 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.63 (d, *J* = 9.6 Hz, 2H), 3.65 (s, 6H), 3.31−3.15 (m, 2H), 3.07 (s, 6H), 1.61−1.18 (m, 8H), 0.91 (td, *J* = 6.9, 1.6 Hz, 6H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.8, 61.4, 40.8, 36.1, 33.2, 20.3, 14.0, −1.0, −1.4. $[\alpha]_D$ = −4.0 (*c* 3.63, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{18}H_{42}N_4O_5Si_2Na$ $[M + Na]^+$ 473.2586, found 473.2587.

*1,1′-((1S,1′S)-(1,1,3,3-Tetramethyldisiloxane-1,3-diyl)bis(octane-1,1-diyl))bis(3-methoxy-3-methylurea) ((S,S)-**13b**).* Prepared from (*S*,*E*)-**9bb** using PtO_2 (40 mol %) as catalyst for 64 h and purified using a cyclohexane/ethyl acetate mixture (70/30, R_f 0.34) as eluent. The product was isolated as a colorless oil (44 mg) in 53% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.62 (d, *J* = 9.6 Hz, 2H), 3.65 (s, 6H), 3.27−3.14 (m, 2H), 3.07 (s, 6H), 1.46−1.19 (m, 24H), 0.87 (t, *J* = 6.6 Hz, 6H), 0.15 (s, 6H), 0.13 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.9, 61.5, 41.3, 36.3, 32.0, 31.1, 29.8, 29.4, 27.3, 22.8, 14.2, −0.8, −1.2. $[\alpha]_D$ = +15 (*c* 0.26, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{26}H_{58}N_4O_5Si_2Na$ $[M + Na]^+$ 585.3838, found 585.3839.

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*Methyl (R)-(1-(Dimethyl(phenyl)silyl)butyl)carbamate (**14**).* Prepared from (*R*,*E*)-**9ac** using Pd/C (10 mol %) as catalyst for 16 h and purified using a cyclohexane/ethyl acetate mixture (90/10, R_f 0.22) as eluent. The product was isolated as a colorless oil (36 mg) in 90% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56−7.46 (m, 2H), 7.43−7.33 (m, 3H), 4.23 (d, J = 10.3 Hz, 1H), 3.63 (s, 3H), 3.44−3.31 (m, 1H), 1.50−1.20 (m, 4H), 0.90−0.78 (m, 3H), 0.33 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.5, 136.2, 134.1, 129.5, 128.1, 52.2, 41.1, 33.9, 20.4, 14.0, −4.5, −5.1. $[\alpha]_D$ = −2.3 (*c* 1.90, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{14}H_{23}NO_2SiNa$ $[M + Na]^+$ 288.1390, found 288.1389.

*Dimethyl ((1R,1′R)-(1,1,3,3-Tetramethyldisiloxane-1,3-diyl)bis-(butane-1,1-diyl))dicarbamate (**15**).* Prepared from (*R*,*E*)-**9ac** using PtO_2 (40 mol %) as catalyst for 64 h and purified using a cyclohexane/ethyl acetate mixture (70/30, R_f 0.41) as eluent. The product was isolated as a white solid (32 mg) in 54% yield. Mp: 59−61 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.64 (d, J = 9.9 Hz, 2H), 3.66 (s, 6H), 3.05 (td, J = 9.4, 3.3 Hz, 2H), 1.52−1.19 (m, 8H), 0.90 (t, J = 6.6 Hz, 6H), 0.11 (s, 6H), 0.10 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 157.7, 52.2, 42.4, 33.2, 20.3, 14.1, −1.1, −1.2. $[\alpha]_D$ = −11.8 (*c* 0.55, CH_2Cl_2). HRMS (ESI): *m*/*z* calcd for $C_{16}H_{36}N_2O_5Si_2Na$ $[M + Na]^+$ 415.2055, found 415.2053.

Computational Methods. All of the calculations reported in this work were carried out with the GAUSSIAN 09 suite of programs[46] and using the hybrid DFT functional M06-2X[47] and the def2TZVPP basis set.[48] All the stationary points were characterized by harmonic analysis. Reactants and products showed positive definite Hessians. Transition structures (TSs) showed one and only one imaginary frequency associated with nuclear motion along the chemical transformation under study. Free energies at 298.15 K were calculated by including the corresponding thermal corrections to Gibbs free energies (TCGE). Solvent effects were considered by means of the PCM method.[49] The solvent introduced in the calculations was dichloromethane. Natural bonding analysis calculations were performed using the NBO program[50] as implemented in Gaussian 09.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00505.

Selected NMR spectra of the rearrangement (**2** → **4**) and copies of ^{1}H, ^{13}C NMR spectra and chiral HPLC chromatography of all new compounds. Cartesian coordinates, number of imaginary frequencies (NIMAG), and energy data of stationary points gathered in Figure 3. (PDF)

Crystal data for **5b** and **13a** (ZIP)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Fleming, I. *Science of Synthesis: Houben−Weyl Methods of Molecular Transformations*; Thieme: Stuttgart, 2001; Vol.4. (b) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763. (c) Yus, M.; González-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774.

(2) For examples, see: (a) Binanzer, M.; Fang, G. Y.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2010**, *49*, 4264. (b) Rouquet, G.; Robert, F.; Méreau, R.; Castet, F.; Landais, Y. *Chem. - Eur. J.* **2011**, *17*, 13904. (c) Mizuta, S.; Engle, K. M.; Verhoog, S.; Galicia-Lopez, O.; O'Duill, M.; Médebielle, M.; Wheelhouse, K.; Rassias, G.; Thompson, A. L.; Gouverneur, V. *Org. Lett.* **2013**, *15*, 1250.

(3) (a) Sakurai, H. *Pure Appl. Chem.* **1982**, *54*, 1. (b) Langkopf, E.; Schinzer, D. *Chem. Rev.* **1995**, *95*, 1375. (c) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (d) Chabaud, L.; James, P.; Landais, Y. *Eur. J. Org. Chem.* **2004**, *2004*, 3173.

(4) For recent examples, see: (a) Ball-Jones, N. R.; Badillo, J. J.; Tran, N. T.; Franz, A. K. *Angew. Chem., Int. Ed.* **2014**, *53*, 9462. (b) Matsumura, Y.; Suzuki, T.; Sakakura, A.; Ishihara, K. *Angew. Chem., Int. Ed.* **2014**, *53*, 6131.

(5) (a) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293. (b) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, 2000; Chapter 10.

(6) (a) Corriu, R. J. P.; Huynh, V.; Moreau, J. J. E. *J. Organomet. Chem.* **1983**, *259*, 283. (b) Chen, S.-F.; Ho, E.; Mariano, P. S. *Tetrahedron* **1988**, *44*, 7013. (c) Honda, T.; Satoh, S.-I.; Mori, M. *Organometallics* **1995**, *14*, 1548. (d) Parisi, M.; Solo, A.; Wulff, W. D. *Organometallics* **1998**, *17*, 3696. (e) Lin, S.; Yang, Z.-Q.; Kwok, B. H. B.; Koldobskiy, M.; Crews, C. M.; Danishefsky, S. J. *J. Am. Chem. Soc.* **2004**, *126*, 6347. (f) Roy, S.; Spino, C. *Org. Lett.* **2006**, *8*, 939. (g) Ballweg, D. M.; Miller, R. C.; Gray, D. L.; Scheidt, K. A. *Org. Lett.* **2005**, *7*, 1403. (h) Han, X.-J.; Yao, M.; Lu, C.-D. *Org. Lett.* **2012**, *14*, 2906.

(7) (a) Weisenburger, G. A.; Beak, P. *J. Am. Chem. Soc.* **1996**, *118*, 12218. (b) Weisenburger, G. A.; Faibish, N. C.; Pippel, D. J.; Beak, P. *J. Am. Chem. Soc.* **1999**, *121*, 9522.

(8) (a) Sieburth, S. McN.; O'Hare, H. K.; Xu, J.; Chen, Y.; Liu, G. *Org. Lett.* **2003**, *5*, 1859. (b) Liu, G.; Sieburth, S. McN. *Org. Lett.* **2003**, *5*, 4677.

(9) Lauzon, S.; Tremblay, F.; Gagnon, D.; Godbout, C.; Chabot, C.; Mercier-Shanks, C.; Perreault, S.; DeSève, H.; Spino, C. *J. Org. Chem.* **2008**, *73*, 6239.

(10) Kondo, Y.; Sasaki, M.; Kawahata, M.; Yamaguchi, K.; Takeda, K. *J. Org. Chem.* **2014**, *79*, 3601.

(11) Mita, T.; Sugawara, M.; Saito, K.; Sato, Y. *Org. Lett.* **2014**, *16*, 3028.

(12) For a stereoselective approach based on addition of silyl anion to a chiral sulfinyl imine, see ref 6g.

(13) For examples, see: (a) Mutahi, M. W.; Nittoli, T.; Guo, L.; Sieburth, S. McN. *J. Am. Chem. Soc.* **2002**, *124*, 7363. (b) Meanwell, N. A. *J. Med. Chem.* **2011**, *54*, 2529. (c) Min, G. K.; Hernandez, D.; Skrydstrup, T. *Acc. Chem. Res.* **2013**, *46*, 457.

(14) For the first report of this type of rearrangement, see: (a) Christophersen, C.; Holm, A. *Acta Chem. Scand.* **1970**, *24*, 1512. (b) Christophersen, C.; Holm, A. *Acta Chem. Scand.* **1970**, *24*, 1852.

(15) For some recent examples, see: (a) Arbour, M.; Roy, S.; Godbout, C.; Spino, C. *J. Org. Chem.* **2009**, *74*, 3806. (b) Gagnon, D.; Spino, C. *J. Org. Chem.* **2009**, *74*, 6035. (c) Toma, T.; Kita, Y.; Fukuyama, T. *J. Am. Chem. Soc.* **2010**, *132*, 10233. (d) Ichikawa, Y.; Matsuda, Y.; Okumura, K.; Nakamura, M.; Masuda, T.; Kotsuki, H.; Nakano, K. *Org. Lett.* **2011**, *13*, 2520. (e) Boyd, D. R.; Sharma, N. D.; Kaik, M.; M^{c}Intyre, P. B. A.; Stevenson, P. J.; Allen, C. C. R. *Org. Biomol. Chem.* **2012**, *10*, 2774. (f) Umezaki, S.; Yokoshima, S.; Fukuyama, T. *Org. Lett.* **2013**, *15*, 4230. (g) Stecko, S. *J. Org. Chem.* **2014**, *79*, 6342.

(16) (a) Touchet, S.; Macé, A.; Roisnel, T.; Carreaux, F.; Bouillon, A.; Carboni, B. *Org. Lett.* **2013**, *15*, 2712. (b) Macé, A.; Touchet, S.; Andres, P.; Cossio, F. P.; Dorcet, V.; Carreaux, F.; Carboni, B. *Angew. Chem., Int. Ed.* **2016**, *55*, 1025.

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(17) DFT calculations on the [3,3]-sigmatropic cyanate-to-isocyanate rearrangement have only been realized using an achiral model such as 3-cyanato-1-propene. See: Koch, R.; Finnerty, J. J.; Murali, S.; Wentrup, C. *J. Org. Chem.* **2012**, *77*, 1749.
(18) (a) Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595. (b) Mohamed, M.; Brook, M. A. *Helv. Chim. Acta* **2002**, *85*, 4165.
(19) (a) Ichikawa, Y. *Synlett* **2007**, *2007*, 2927. (b) Clayden, J.; Donnard, M.; Lefranc, J.; Tetlow, D. J. *Chem. Commun.* **2011**, *47*, 4624. (c) Szcześniak, P.; Pieczykolan, M.; Stecko, S. *J. Org. Chem.* **2016**, *81*, 1057.
(20) After evaporation of solvent under controlled reduced pressure, the allyl isocyanate **4** can be stored at −20 °C for several weeks without any degradation.
(21) Ichikawa, Y. *Synlett* **1991**, *1991*, 238.
(22) The thermal stability of this new compound was tested since it was described that α-silylallyl amides undergo a rearrangement−hydrolysis at higher temperature to form the corresponding *cis*-enamides, see ref 6e. After 3 days at reflux in toluene, no product resulting from this transformation was detected by ^{1}H NMR.
(23) The allyl cyanate intermediates have a short-lived nature, except one highly substituted example which has been isolated. See: Banert, K.; Melzer, A. *Tetrahedron Lett.* **2001**, *42*, 6133.
(24) For this study, the ^{1}H NMR spectrum was recorded at −70 °C every 2 min for 8 h.
(25) (a) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129. (b) Marshall, J. A.; Chobanian, H. *Org. Synth.* **2005**, *82*, 43.
(26) CCDC 1446908 and 1446907 contain the supplementary crystallographic data for compounds **5b** and **13a**, respectively. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.com.ac.uk/data_request/cif.
(27) For the first time, the stereospecificity of this domino reaction was confirmed by a X-ray crystallographic structure. Chiral derivatizing agents are generally used in the literature, see: (a) Ichikawa, Y.; Tsuboi, K.; Isobe, M. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2791. (b) Ichikawa, Y.; Yamauchi, E.; Isobe, M. *Biosci., Biotechnol., Biochem.* **2005**, *69*, 939.
(28) (a) Weinhold, F.; Landis, C. *Valency and Bonding − A Natural Bond Orbital Donor-Acceptor Perspective*; Cambridge University Press: Cambridge, UK, 2005; pp 31, 182−215. (b) Landis, C. R.; Weinhold, F. The NBO View of Chemical Bonding. In *The Chemical Bond − Fundamental Aspects of Chemical Bonding*; Frenking, G., Shaik, S., Eds.; Wiley−VCH: Weinheim, 2014; pp 91−119.
(29) (a) Anslyn, E. V.; Dougherty, D. A. *Modern Physical Organic Chemistry*; University Science Books: Sausalito, CA, 2006; pp 378−379. (b) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83.
(30) Wiberg, K. B. *Tetrahedron* **1968**, *24*, 1083.
(31) (a) Dewar, M. J. S. *J. Am. Chem. Soc.* **1984**, *106*, 209. (b) Borden, W. T.; Loncharich, R. J.; Houk, K. N. *Annu. Rev. Phys. Chem.* **1988**, *39*, 213.
(32) (a) Moyano, A.; Pericás, M. A.; Valentí, E. *J. Org. Chem.* **1989**, *54*, 573. (b) Lecea, B.; Arrieta, A.; Roa, G.; Ugalde, J. M.; Cossío, F. P. *J. Am. Chem. Soc.* **1994**, *116*, 9613. (c) Lecea, B.; Arrieta, A.; López, X.; Ugalde, J. M.; Cossío, F. P. *J. Am. Chem. Soc.* **1995**, *117*, 12314.
(33) Spino, C.; Joly, M.-A.; Godbout, C.; Arbour, M. *J. Org. Chem.* **2005**, *70*, 6118.
(34) For a racemic version of this reaction, see: McLaughlin, M. G.; Cook, M. J. *Chem. Commun.* **2011**, *47*, 11104.
(35) A small quantity of the α-isomer was also observed with a ratio around 91/9 in favor of the β-isomer with the *E*-geometry.
(36) For examples, see: (a) Bassindale, A. R.; Stout, T. *J. Organomet. Chem.* **1984**, *271*, C1. (b) Uhlig, W. *Chem. Ber.* **1996**, *129*, 733. (c) Tacke, R.; Schmid, T.; Merget, M. *Organometallics* **2005**, *24*, 1780. (d) Singh, R.; Singh, G. C.; Gosh, S. K. *Eur. J. Org. Chem.* **2007**, *2007*, 5376. (e) Nielsen, L.; Lindsay, K. B.; Faber, J.; Nielsen, N. C.; Skrydstrup, T. *J. Org. Chem.* **2007**, *72*, 10035. (f) Kundu, P. K.; Singh, R.; Ghosh, S. K. *J. Organomet. Chem.* **2009**, *694*, 382. (g) Singh, S.; Sieburth, S. McN. *Org. Lett.* **2012**, *14*, 4422.
(37) (a) Desvergne, J.-P.; Bonneau, R.; Dörr, G.; Bouas-Laurent, H. *Photochem. Photobiol. Sci.* **2003**, *2*, 289. (b) Werle, S.; Robert, F.; Bouas-Laurent, H.; Landais, Y. *Tetrahedron Lett.* **2007**, *48*, 8909.
(38) The chemical composition of one batch of platinum oxide was determined by analytical electron microscopy, indicating the presence of chlorine atoms (average of 1.30%) with the other expected elements (Pt, O).
(39) No reaction without hydrogen. The use of different hydrogen purities has no influence on the yield.
(40) Treatment of **14** under conventional conditions for the protodesilylation of arylsilane (CF_3SO_3H, 5 equiv, 0 °C) led to a complex mixture of compounds, probably due to the presence of carbamate protecting group. When trifluoroacetic acid at room temperature (15 equiv) is used, disiloxane **15** is formed but in the presence of the corresponding silanol (ratio around 6:4).
(41) Under the same hydrogenation conditions, the saturated compound was obtained exclusively from (*S*,*E*)-**8a**.
(42) Sieburth, S. McN.; Nittoli, T.; Mutahi, A. M.; Guo, L. *Angew. Chem., Int. Ed.* **1998**, *37*, 812.
(43) Mohamed, M.; Brook, M. A. *Helv. Chim. Acta* **2002**, *85*, 4165.
(44) Beresis, R.; Solomon, J.; Yang, M.; Jain, N.; Panek, J. *Org. Synth.* **1998**, *75*, 78.
(45) Murphy, P. J.; Spencer, J. L.; Procter, G. *Tetrahedron Lett.* **1990**, *31*, 1051.
(46) Gaussian 09, Revision D.01: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford, CT, 2009.
(47) (a) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215. (b) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157.
(48) Weigend, F.; Alhrichs, R. *Phys. Chem. Chem. Phys.* **2005**, *7*, 3297.
(49) Cammi, R.; Mennucci, B.; Tomasi, J. *J. Phys. Chem. A* **2000**, *104*, 5631.
(50) (a) Foster, J. P.; Weinhold, F. *J. Am. Chem. Soc.* **1980**, *102*, 7211. (b) Reed, A. E.; Weinstock, R. B.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 735. (c) Reed, A. E.; Weinhold, F. *J. Chem. Phys.* **1985**, *83*, 1736. (d) Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

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