# Accepted Manuscript


Palladium-catalyzed highly regio- and stereoselective carbon–carbon bond formation reaction of γ-substituted vinylaziridines with a silylated masked acyl cyanide reagent

Tomoyuki Kawamura, Nanae Matsuo, Daisuke Yamauchi, Yoo Tanabe, Hisao Nemoto

PII: S0040-4020(13)00703-5

DOI: 10.1016/j.tet.2013.04.129

Reference: TET 24329

To appear in: *Tetrahedron*

Received Date: 1 March 2013

Revised Date: 24 April 2013

Accepted Date: 26 April 2013

Please cite this article as: Kawamura T, Matsuo N, Yamauchi D, Tanabe Y, Nemoto H, Palladium-catalyzed highly regio- and stereoselective carbon–carbon bond formation reaction of γ-substituted vinylaziridines with a silylated masked acyl cyanide reagent, *Tetrahedron* (2013), doi: 10.1016/j.tet.2013.04.129.

## Graphical Abstract

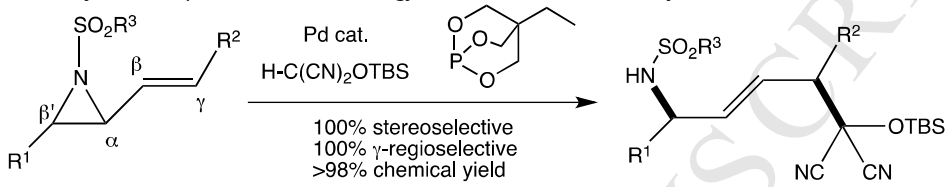
**Palladium-catalyzed highly regio- and stereoselective carbon–carbon bond formation reaction of γ-substituted vinylazrlidines with a silylated masked acyl cyanide reagent**

Leave this area blank for abstract info.

Tomoyuki Kawamura,[a] Nanae Matsuo,[b] Daisuke Yamauchi,[a] Yoo Tanabe,[b] Hisao Nemoto [a]

[a] *Department of Pharmaceutical Chemistry, Division of Heath Biosciences, Graduate School of The University of Tokushima, 1-78-1, Sho-machi, Tokushima 770-8505, Japan*

[b] *Department of Chemistry, School of Science and Technology, Kwansei Gakuin University, 2-1, Gakuen, Sanda 669-1337, Japan*



Tetrahedron
journal homepage: www.elsevier.com

# Palladium-catalyzed highly regio- and stereoselective carbon–carbon bond formation reaction of γ-substituted vinylaziridines with a silylated masked acyl cyanide reagent

Tomoyuki Kawamura[a] , Nanae Matsuo[b], Daisuke Yamauchi[a], Yoo Tanabe[b], and Hisao Nemoto[a]*

[a] *Department of Pharmaceutical Chemistry, Division of Heath Biosciences, Graduate School of The University of Tokushima, 1-78-1, Sho-machi, Tokushima 770-8505, Japan*
[b] *Department of Chemistry, School of Science and Technology, Kwansei Gakuin University, 2-1, Gakuen, Sanda 669-1337, Japan*

Corresponding author: Tel & FAX: +81 88-633-7284; e-mail address: nem@ph.tokushima-u.ac.jp

ARTICLE INFO

*Article history:*
Received
Received in revised form
Accepted
Available online

*Keywords:*
Keyword_1
Keyword_2
Keyword_3
Keyword_4
Keyword_5
palladium, aziridine, π-allyl complex, masked acyl cyanide

ABSTRACT

Highly regio- and stereoselective carbon–carbon bond formation reaction of vinylaziridines using a masked acyl cyanide reagent possessing a *tert*-butyldimethylsilyl group occurred in the presence of a catalytic amount of palladium complex in excellent yield. It is considered that these excellent selectivities are the result of three simultaneous conditions, strained leaving group, small nucleophile, and ligand with small cone-angle.



## 1. Introduction

A number of reactions via η -allylpalladium complexes have been reported,[1] and the reaction mechanism for the stereochemistry (double inversion mechanism involving intermolecular attack of nucleophile) is now broadly accepted. In contrast, a consensus on the α- versus γ-regioselectivity based on the position of the leaving group (X of **1** in Figure 1) has not yet been established.[2]

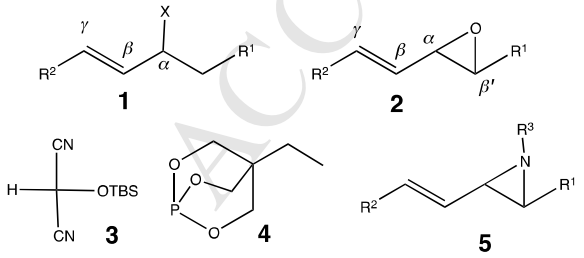



**Figure 1**. Structures of an allylic compound **1**, a β',γ-disubstituted vinyloxirane **2**, a silylated masked acyl cyanide **3** (TBS = *tert*-butyldimethylsilyl), conformationally fixed ligand **4**, and a β',γ-disubstituted vinylaziridine **5**.

One reason for this may be due to the use of molecules with different steric factor in the α- and γ-regions, which gives unequal opportunity to the regioselectivity. Another may be the presence of a bond reforming process between the resulting $\eta^3$-allylpalladium system and a leaving group to generate a mixture of original allylic compounds and the corresponding regio isomer *in situ*. As far as we have surveyed, Tsuji[3] and Takahashi[4] reported the sole suggestible examples for the consensus, which was the palladium-catalyzed intermolecular carbon–carbon bond formation reaction between active methylene compounds and acyclic vinyloxiranes bearing alkyl groups at both α- and γ-positions such as **2** to afford the product with >90% γ-regioselectivity. We also examined the reaction of sorbic amide 4,5-monoxide with a masked acyl cyanide reagent (MAC) possessing a *tert*-butyldimethylsilyl (TBS) group (**3**)[5] to afford the adduct in 100% γ-regioselectivity.[6] Highly selective formation of one diastereomer was also observed.[6] In these cases,[3,4,6] use of conformationally fixed tricyclic ligands[7] such as phosphite **4** was very effective for the improvement of both chemical yield and selectivity.

Based on the above-mentioned examples, we hypothesized that γ-regioselectivity was due to the nature of the palladium-catalyzed carbon–carbon bond formation of $\eta^3$-allyl system by the nucleophilic attack far from the out of ligand field. High γ-selectivity was the result of the two following factors. The first is the exhaustive reduction of steric factors of both ligands[8] and nucleophiles to observe as pure orbital control as possible. The second is the use of

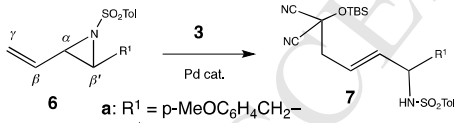
highly strained leaving group such as an oxirane, which prohibits the bond formation between a $\eta^3$-allyl system and a leaving group. To verify this hypothesis, additional examples with high γ-regioselectivity must be demonstrated. As an alternative strained leaving group, an aziridine is a suitable candidate. Although a palladium-catalyzed *hydrogen–carbon* bond formation reaction of alkenylated aziridines by Shimizu et al[9] and Ibuka et al,[10] and a carbon–carbon bond formation reaction of aziridine possessing *terminal alkene* by Sweeney et al[11] have been reported, these examples are unsuitable to explain the regioselective nature of palladium-catalyzed *carbon–carbon* bond formation reaction.[12]

## 2. Results and discussion

In this paper, we report a highly γ-regioselective and stereoselective palladium-catalyzed carbon–carbon bond formation reaction of a vinylaziridine possessing alkyl groups at both β'- and γ-positions **5** with a MAC reagent such as **3**. Because of the two electron withdrawing groups possessing *sp*-hybridized orbital (–CN), MAC reagents including **3** are very small carbon nucleophiles of palladium-affinitive active *methyne* compound.[13] Accordingly, the combination of **5** and **3** is a suitable example for the demonstration of expected high γ-regioselectivity.

As substrates for the palladium-catalyzed reactions, we chose *N*-arylsulfonylated derivatives of **5** ($R^3$ = $ArSO_2$–) because the corresponding N-diphenylphosphinyl derivatives of **5**[11] [$R^3$ = $P(O)Ph_2P(O)$–] possessing aliphatic group $R^1$ cannot be easily prepared, and the corresponding *N*-*tert*-butyloxycarbonylated derivative of **5** ($R^3$ = $^t$BuOCO–) was too unstable to purify by silica gel column chromatography based on our preliminary attempts. Since Sweeney's reaction conditions using an aziridine possessing a terminal alkene were not specified[11,14] and may be in discord with the optimized conditions for vinyloxiranes reported by Tsuji,[3] Takahashi[4] and us,[6] we first optimized the reaction conditions by using aziridines possessing terminal alkene **6** (Table 1).

**Table 1** Palladium-catalyzed reaction of **3** and **6** (Tol = 4-$MeC_6H_4$–)




**6** **7**

**a**: $R^1$ = p-$MeOC_6H_4CH_2$–
**b**: $R^1$ = $Me_2CH$–
**c**: $R^1$ = $Me_2CHCH_2$–

| entry | **6** | ligand | time (min) | Yield of **7** (%) | *E*/*Z* |
|---|---|---|---|---|---|
| 1 | **6a** | $PPh_3$ | 5 | 93 | 95:5 |
| 2 | **6a** | dppe | 30 | 91 | >99:1 |
| 3 | **6a** | **4** | 5 | 99 | >99:1 |
| 4 | **6a** | $P^nBu_3$ | 60 | 0 | - |
| 5 | **6b** | **4** | 15 | 97 | >99:1 |
| 6 | **6c** | **4** | 15 | 89 | >99:1 |
| 7 | **6d**[a] | **4** | 5 | 89 | >99:1 |

a: diastereomer of **6a** (α,β'-*cis*-isomer)

The reaction of **6a** was examined using **3** (1.2 equiv.) in THF for 5–60 min at room temperature in the presence of a catalytic amount of ligand (0.6 mol% in the case of monodentate ligand, 0.3 mol% in the case of bidentate ligand) and tris(dibenzylideneacetone)dipalladium–chloroform complex [$(dba)_3Pd_2$•$CHCl_3$] (0.1 mol%, 0.2 mol% based on Pd atom). In entries 1–3 [use of triphenylphosphine ($PPh_3$), 1,2-bis(diphenylphosphino)ethane (dppe) and **4**, respectively], adduct **7a** was smoothly afforded in over 90% yield without addition of base.[14] In contrast, when tributylphosphine ($P^nBu_3$) was used, the desired product was undetected although complete consumption of **6a** was observed (entry 4). This negative result was probably due to the large cone angle of the ligand,[2] which prohibited the approach of the nucleophile to the allylpalladium species.

Based on the reaction time and the E/Z selectivity, the conditions for entry 3 were applied to the aliphatic derivatives **6b** and **6c** to afford the desired adducts **7b** and **7c** in 97% and 89% yields, respectively (entries 5 and 6). Finally, the same conditions were applied to **6d** (the α,β'-*cis*-isomer of **6a**) to afford **7a** in 89% yield with E-geometry (>99:1).

Incidentally, we have examined the reaction of **6a** with three equivalents of *diethyl malonate* instead of **3** under the conditions for entry 3 to afford the corresponding adducts (a mixture of mono- and diallylated malonates) in ca. 60% yield. This yield was consistent with that reported by Sweeney.[11] Attempt of diethyl 2-methylmalonate instead of **3** gave no carbon–carbon bond adducts. Accordingly, it showed that ***3** was more suitable than malonates* to explore the palladium-catalyzed reaction with vinylaziridine.[13,15]

We next examined the regioselectivity using eight γ-substituted vinylaziridines **8**, reasonable substrates for the fare assessment of regioselectivity, which were prepared as shown in Scheme 1. Because of the higher overall yield from α-amino esters **9** to **8**, and more efficient diastereomeric separation of **13** and **14** by silica gel flash column chromatography, the 2,4,6-trimethylbenzenesulfonyl group ($MesSO_2$–) rather than $TolSO_2$ group was chosen as the *N*-protecting group.

**Scheme 1**

Thus, commercially available amino acid methyl ester hydrochloride salt (±)-**9e** was sulfonylated at 0 ˚C with $MesSO_2Cl$ in pyridine in the presence of a catalytic amount of 4-(dimethylamino)pyridine (DMAP) to afford (±)-**10e** in 99% yield. Horner-Emmons agent (±)-**11e** was prepared from (±)-**10e** and the carbanion generated from dimethyl methylphosphonate [$CH_3P(O)(OMe)_2$] and butyllithium (BuLi) at –78 ˚C in THF in 99% yield. Condensation of (±)-**11e** and acetaldehyde in ethanol with anhydrous potassium carbonate ($K_2CO_3$) at room temperature gave (±)-**12g** in 85% yield. Reduction of the ketone (±)-**12g** by sodium borohydride ($NaBH_4$) and cerium chloride heptahydrate ($CeCl_3$•$7H_2O$) in methanol at 0 ˚C afforded **13g** and **14g** as a diastereomeric mixture in 96% chemical yield. Mixtures of **13h**/**14h**, **13i**/**14i**, and **13j**/**14j** were also obtained in similar manner as illustrated in Scheme 1. All four diastereomers of (±)-**13** were separable from (±)-**14** by flash column chromatography. Finally, each amino alcohol **13** or

**14** was transformed to the corresponding (±)-**8** in excellent yield with diethyl diazene 1,2-dicarboxylate (DEAD) and $PPh_3$ in THF at 0 ˚C.[10]

Coupling constant between the α and β' hydrogens of $\mathbf{8^t}$ was clearly smaller than those of the corresponding $\mathbf{8^c}$ (Table 2). Thus, $\mathbf{8^t}$ was assigned as *trans*-aziridine and $\mathbf{8^c}$ was assigned as *cis*-aziridine.[16] Relative stereochemistries of **13** and **14** were assigned based on the mechanism of Mitsunobu reaction,[16] as illustrated in Scheme 1.

Results of the reaction of **3** and $\mathbf{8^t}$ are illustrated in Scheme 2. Under the optimized conditions (entry 3 in Table 1), $\mathbf{8^t g}$–$\mathbf{8^t j}$ exclusively gave γ-adducts **15g**–**15j**, respectively, in >98% chemical yield. Incidentally, the double inversion mechanism[17] was also confirmed because not even a trace amount of the corresponding diastereomer **16**, illustrated in Scheme 3, was observed in the crude mixture. It is further noted that $PPh_3$ instead of **4** did not work for the carbon–carbon bond formation. When the reaction was prolonged or carried out at higher temperature with $PPh_3$, a small amount of unidentified compounds (probably something like a complicated mixture of dienes via β-elimination process) was detected.

**Table 2.** Coupling constants between α and β' hydrogens of **8**

| Compounds | Coupling Constant |
|---|---|
| $\mathbf{8^t g}$ / $\mathbf{8^c g}$ | 4.5 / 5.5 |
| $\mathbf{8^t h}$ / $\mathbf{8^c h}$ | 4.0 / 5.5 |
| $\mathbf{8^t i}$ / $\mathbf{8^c i}$ | - / 5.5 |
| $\mathbf{8^t j}$ / $\mathbf{8^c j}$ | 4.5 / 7.6 |

**Scheme 2**

In Scheme 3, results of the reaction of $\mathbf{8^c}$ are illustrated. When either $R^1$ or $R^2$ was not an isopropyl group (iPr) ($\mathbf{8^c g}$ and $\mathbf{8^c h}$), the desired reaction proceeded smoothly to afford γ-adduct **16** in excellent yield. The corresponding diastereomer **15** was not detected at all. In the case of $\mathbf{8^c i}$, however, a small amount of α-isomer **17i** was detected. In the case of $\mathbf{8^c j}$, α-isomer **17j** was produced with 42% selectivity.

**Scheme 3**

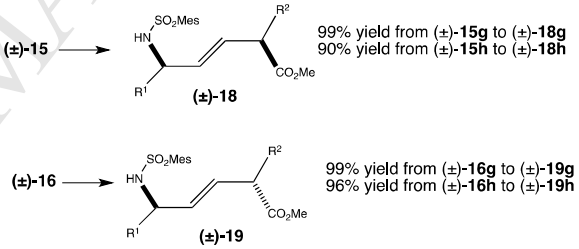
Except $\mathbf{8^c j}$, all the substrates illustrated in Schemes 2 and 3 were successfully converted to the products with excellent γ-regioslelectivity by the use of palladium-affinitive small nucleophile, small ligand, and strained leaving group.

Thus, it cannot be simply concluded that iPr as $R^2$ is too bulky to undergo a palladium-catalyzed reaction. This is because carbon–carbon bond formation at the γ-position was successful in excellent yield even when $R^2$ was a bulky iPr (in the cases of $\mathbf{8^t i}$ and $\mathbf{8^t j}$). Furthermore, low γ-selectivity was observed by the influence of iPr at the β'-position ($R^1$) rather than the γ-position ($R^2$) ($\mathbf{8^c j}$ versus $\mathbf{8^c i}$).

By our preliminary conformational analysis (ground state using MM2 calculations) of four compounds $\mathbf{8^c g}$–$\mathbf{8^c j}$, a proposal for the regioselectivity is as follows (Figure 2). For the initial xyz-coordinates of all $\mathbf{8^c}$, the Cα–Cβ=Cγplane was orthogonally drawn to the σ-Cα–N bond for the smooth generation of the $\eta^3$-allylpalladium complex. After energy minimization using MM2, the Cα–Cβ=Cγplane was still approximately orthogonal to the σ-Cα–N bond in the cases of $\mathbf{8^c g}$, $\mathbf{8^c h}$ and $\mathbf{8^c i}$ (conformation **A**). In contrast, in the case of $\mathbf{8^c j}$, the relationship between the Cα–Cβ=Cγplane and σ-Cα–N bond was not orthogonal any more, probably due to the distortion caused by the steric repulsion between the Cβ hydrogen and Cβ' iPr (conformations **B** or **C**). In fact, as listed in Table 2, the coupling constant between the α and β' hydrogens of $\mathbf{8^c j}$ was significantly greater than those of $\mathbf{8^c g}$–$\mathbf{8^c i}$. Accordingly, a distorted palladium complex intermediate such as $\eta^1$-allylpalladium may be generated as a non-trivial conformational possibility to direct nucleophile **3** to the α-position to some extent.

**Figure 2**

The relative stereochemistry of each compound was confirmed or determined as follows. The MAC moiety of **15g**, **15h**, **16g** and **16h** was smoothly transformed to the corresponding methyl ester to afford **18g**, **18h**, **19g** and **19h**, respectively, in excellent yields without a detection of the corresponding diastereomer[6,18] by using tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) as a mild deprotecting agent for TBS group[19] in methanol (Scheme 4). The relative stereochemistries of **18g, 18h, 19g** and **19h** were unambiguously determined by the comparison of known compounds.[10,16] Accordingly, the stereochemistry of **15g**, **15h**, **16g** and **16h** was also determined.




**Scheme 4**. Condition: TASF (1.2 eq), MeOH, 0 ˚C, 35 min.

The relative stereochemistry of **15i**, **15j**, **16i** and **16j** was determined by the value of the coupling constants of the two hydrogens as shown in Table 3. It was clearly observed that $J_{\beta'-\alpha}$ of **15** was smaller than that of **16**.[20]

**Table 3**. Coupling constant of $H_{\beta'}$–$H_{\alpha}$

| Compounds | $J_{\beta-\alpha}$ (Hz) | comparison |
|---|---|---|
| **15g/16g** | *6.3/7.6* | $J_{15} < J_{16}$ |
| **15h/16h** | *5.8/6.8* | $J_{15} < J_{16}$ |
| **15i/16i** | *5.2/7.2* | $J_{15} < J_{16}$ |
| **15j/16j** | *4.8/7.9* | $J_{15} < J_{16}$ |

Thus, it is considered that palladium-catalyzed reactions described in Schemes 2 and 3 proceeded via double inversion mechanism by comparison of the stereochemistry of $\mathbf{8^t}$ and **15** as well as that of $\mathbf{8^c}$ and **16**.[17]

**3. Conclusion**

Highly regio- and stereoselective palladium-catalyzed carbon–carbon bond formation reaction of γ-substituted vinylaziridines was successfully demonstrated under the

three simultaneous conditions: strained leaving group, small nucleophile, and ligand with small cone-angle. Under the conditions that we reported, very high γ-selectivity was observed in many cases, even when a bulky iPr was substituted at the γ-position. Finally, we would like to argue that MAC reagents can be powerful and efficient nucleophiles to probe the regioselective nature of a palladium-catalyzed reaction and also are highly applicable to the synthesis of various dipeptide isoster derivatives.[10,16,21]

## 4. Experimental section

Melting points were determined on YAMAMOTO-MODEL 20 melting point apparatus, and were uncorrected. NMR spectra were recorded on a JEOL FT-NMR AL-400 spectrometer, operating at 400 MHz for $^1$H NMR and 100 MHz for $^{13}$C NMR and JEOL DELTA 300 spectrometer, operating at 300 MHz for $^1$H NMR and 75 MHz for $^{13}$C NMR. Chemical shifts (δ ppm) in $CDCl_3$ were downfield from tetramethylsilane (0.00 ppm) for $^1$H NMR, and were reported in the scale relative to $CDCl_3$ (77.0 ppm) for $^{13}$C NMR. IR spectra were recorded on a JASCO FT-IR 420 spectrometer. Mass spectra were recorded on a JEOL JMS-DX 303 or Waters/Micromass LCT PREMIRE Mass spectrometer. Column chromatography was performed with silica-gel KANTO KAGAKU 60N (spherical, neutral, 63–210 μm). Flash column chromatography was performed with silica-gel KANTO KAGAKU 60N (spherical, neutral, 40–50 μm). TLC analysis was performed on precoated plates (0.25 mm, Silica gel Merk Kieselgel 60 $F_{254}$). All reactions were carried out in oven-dried glassware under an agron atmosphere, unless otherwise noted. Reaction mixtures were stirred magnetically. Ethanol was distilled over sodium. Methanol was distilled over magnesium. Pyridine was distilled from calusium hydride. Anhydrous tetrahydrofuran (THF) was purchased from Kanto Chemical Co., Inc.

**(2*E*)-*N*-(5-(*tert*-Butyldimethylsilyloxy)-5,5-dicyano-1-(4-methoxyphenyl)pent-2-enyl)-4-methylbenzenesulfonamide [(±)-7a]**

Synthesis of (±)-**7a** was carried out starting from (±)-**6a** (50.0 mg, 0.152 mmol, 1.0 eq.) as described for (±)-**15g**. Purified by silica gel column chromatography with hexane and ethyl acetate (3:1) as an eluent to give (±)-**7a** (79 mg, 0.15 mmol, 99% yield) as a pale yellow oil. FT-IR (neat): 3276, 2956, 2933, 2859, 2256, 1513, 1328, 1253, 1159, 1033, 973, 842, 786, 732 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 7.64 (d, J = 8.3 Hz, 2H, aromatic), 7.24 (d, J = 8.3 Hz, 2H, aromatic), 6.99 (d, J = 8.5 Hz, 2H, aromatic), 6.75 (d, J = 8.5 Hz, 2H, aromatic), 5.89 (dd, J = 15.4, 5.6 Hz, 1H, –C*H*=C), 5.56 (dt, J = 15.4, 7.3 Hz, 1H, –C=C*H*CH$_2$), 4.91 (t, J = 6.4 Hz, 1H, –NC*H*), 4.73 (brd, J = 6.4 Hz, 1H, –N*H*), 3.76 (s, 3H, ArOC*H*$_3$), 2.77 (d, J = 7.3 Hz, 2H, –C*H*$_2$), 2.42 (s, 3H, ArC*H*$_3$), 0.87 (s, 9H, –SiC(C*H*$_3$)$_3$), 0.32 (s, 6H, –SiC*H*$_3$ ×2); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 159.2 (C), 143.3 (C), 138.6 (CH), 137.4 (C), 130.7 (C), 129.5 (CH ×2), 128.2 (CH ×2), 127.1 (CH ×2), 121.3 (CH), 114.7 (C), 114.6 (C), 114.1 (CH ×2), 63.4 (C), 58.4 (CH), 55.3 ($CH_3$), 45.1 ($CH_2$), 25.2 ($CH_3$ ×3), 21.6 ($CH_3$), 18.0 (C), –4.5 ($CH_3$ ×2); HRMS (ESI-TOF) *m/z* calcd for $C_{27}H_{35}N_3O_4NaSSi$ $[M+Na]^+$ 548.2015, found 548.2040.

**(4*E*)-*N*-(7-(*tert*-Butyldimethylsilyloxy)-7,7-dicyano-2-methylhept-4-en-3-yl)-4-methylbenzenesulfonamide [(±)-7b]**

Synthesis of (±)-**7b** was carried out starting from **(±)-6b** (40.3 mg, 0.152 mmol, 1.0 eq.) as described for **(±)-15g**. Purified by silica gel column chromatography with hexane and ethyl acetate (3:1) as an eluent to give **(±)-7b** (68 mg, 0.15 mmol, 97% yield) as a solid, which was recrystallized from hexane to give a colorless needle (mp 75˚C). FT-IR (neat): 3278, 2960, 2933, 2861, 2242, 1471, 1328, 1261, 1160, 1047, 973, 842, 786, 734 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, J = 8.3 Hz, 2H, aromatic), 7.29 (d, J = 8.3 Hz, 2H, aromatic), 5.55 (dd, J = 15.4, 7.1 Hz, 1H, –C*H*=C), 5.37 (dt, J = 15.4, 7.8 Hz, 1H, –C=C*H*CH$_2$), 4.66 (brd, J = 8.1 Hz, 1H, –N*H*), 3.67–3.59 (m, 1H, –NC*H*), 2.67 (dd, J = 13.9, 6.6 Hz, 1H, –C*H*$_a$H$_b$), 2.60 (dd, J = 13.9, 8.1 Hz, 1H, –CH$_a$*H*$_b$), 2.43 (s, 3H, ArC*H*$_3$), 1.80–1.71 (m, 1H, –C*H*(CH$_3$)$_2$), 0.91 (s, 9H, –SiC(C*H*$_3$)$_3$), 0.86 (d, J = 6.6 Hz, 3H, –CC*H*$_3$), 0.85 (d, J = 6.6Hz, 3H, –CC*H*$_3$), 0.34 (s, 6H, –SiC*H*$_3$ ×2); $^{13}$C NMR ($CDCl_3$, 100 MHz) δ 143.3 (C), 137.8 (C), 137.3 (CH), 129.5 (CH ×2), 127.1 (CH ×2), 121.2 (CH), 114.7 (C ×2), 63.6 (C), 60.9 (CH), 45.3 ($CH_2$), 32.8 (CH), 25.2 ($CH_3$ ×3), 21.6 ($CH_3$), 18.2 ($CH_3$), 18.0 (C), –4.5 ($CH_3$ ×2); HRMS (ESI-TOF) *m/z* calcd for $C_{23}H_{35}N_3O_3NaSSi$ $[M+Na]^+$ 484.2066, found 484.2080.

**(5*E*)-*N*-(8-(*tert*-Butyldimethylsilyloxy)-8,8-dicyano-2-methyloct-5-en-4-yl)-4-methylbenzenesulfonamide [(±)-7c]**

Synthesis of (±)-**7c** was carried out starting from (±)-**6c** (42.5 mg, 0.152 mmol, 1.0 eq.) as described for (±)-**15g**. Purified by silica gel column chromatography with hexane and ethyl acetate (3:1) to as an eluent give (±)-**7c** (64 mg, 0.14 mmol, 89% yield) as a solid, which was recrystallized from hexane to give a colorless needle (mp 82˚C). FT-IR (neat): 3272, 2956, 2933, 2861, 2242, 1471, 1328, 1261, 1159, 1047, 971, 842, 786 cm$^{-1}$; $^1$H–NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, J = 8.3 Hz, 2H, aromatic), 7.30 (d, J = 8.3 Hz, 2H, aromatic), 5.52 (dd, J = 15.4, 6.6 Hz, 1H, –C*H*=C), 5.43 (dt, J = 15.4, 6.6 Hz, 1H, –C=C*H*CH$_2$), 4.60 (brd, J = 7.3 Hz, 1H, –N*H*), 3.82 (ddd, J = 7.6, 7.3, 7.1 Hz, 1H, –NC*H*), 2.67 (dd, J = 13.7, 6.1 Hz, 1H, –C=CC*H*$_a$H$_b$), 2.58 (dd, J = 13.7, 7.6 Hz, 1H, –C=CC*H*$_a$H$_b$), 2.43 (s, 3H, ArC*H*$_3$), 1.64–1.55 (m, 1H, –C*H*(CH$_3$)$_2$), 1.38–1.25 (m, 2H, –CHC*H*$_2$CH), 0.91 (s, 9H, –SiC(C*H*$_3$)$_3$ ×3), 0.82 (d, J = 6.6Hz, 3H, –CC*H*$_3$), 0.78 (d, J = 6.6Hz, 3H, –CC*H*$_3$), 0.33 (s, 6H, –SiC*H*$_3$ ×2); $^{13}$C–NMR ($CDCl_3$, 100 MHz) δ 143.3 (C), 139.4 (CH), 137.8 (C), 129.5 (CH ×2), 127.1 (CH ×2), 120.2 (CH), 114.6 (C ×2), 63.5 (C), 53.8 (CH), 45.1 ($CH_2$), 44.8 ($CH_2$), 25.2 ($CH_3$ ×3), 24.3 (CH), 22.2 ($CH_3$ ×2), 21.6 ($CH_3$), 18.1 (C), –4.5 ($CH_3$ ×2); HRMS (ESI–TOF) *m/z* calcd for $C_{24}H_{37}N_3O_3NaSSi$ $[M+Na]^+$ 498.2223, found 498.2198.

**Methyl-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-3-phenyl-propionate [(±)-10e]**

To a suspension of $_{DL}$-phenylalanine methyl ester hydrochloride **[(±)-9e]** (3.00 g, 13.9 mmol, 1.00 eq.) and DMAP (0.170 g, 1.39 mmol, 0.100 eq.) in pyridine (11.4 mL, 139 mmol, 10.0 eq.) was added $MesSO_2Cl$ (2.66 g, 16.7 mmol, 1.20 eq.) at 0˚C and the mixture was stirred at room temperature for 20 h. The resulting mixture was acidified with 1N HClaq (300 mL) and extracted with ethyl acetate (200 mL × 3). The combined organic layers were washed with water (100 mL), a saturated aqueous solution of sodium hydrogen carbonate ($NaHCO_3$aq) (100 mL) and brine (100 mL), dried over anhydrous sodium sulfate ($Na_2SO_4$) and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 1:1) to give **(±)-10e** (5.0 g, 14 mmol, 99% yield). Colorless crystal: mp 135–136 ˚C (recrystallized from ethyl acetate); FT-IR (KBr) 3294, 2937, 2364, 1745, 1604, 1160, 1105, 1037, 950, 902, 846, 661 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 2.55 (s, 6H), 2.99 (dd, *J* = 6.0, 13.6 Hz, 1H), 3.03 (dd, *J* = 5.6, 13.6 Hz, 1H), 3.52 (s, 3H), 4.10 (ddd, *J* = 5.6, 6.0, 8.8 Hz, 1H), 5.13 (brd, *J* = 8.8 Hz, 1H, –N*H*), 6.89 (s, 2H), 6.99–7.06 (m, 2H), 7.19–7.24 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 20.9 ($CH_3$), 22.9 ($CH_3$ × 2), 39.2 ($CH_2$), 52.4 ($CH_3$), 56.4 (CH), 127.0 (CH), 128.4 (CH × 2), 129.1 (CH × 2), 131.8 (CH × 2), 133.1 (C),

135.0 (C), 139.2 (C × 2), 142.2 (C), 171.4 (C=O); HRMS (ESI-HRMS) m/z calcd for $C_{19}H_{23}NO_4NaS$ $[M+Na]^+$ 384.1245, found 384.1249.

**Methyl-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-3-methyl-butanoate [(±)-10f]**

Preparation of (±)-**10f** was carried out starting from DL-valine methyl ester hydrochloride [(±)-**9f**] (1.68 g, 10.0 mmol) as described for (±)-**10e** from (±)-**9e**. Purified by silica gel column chromatography (hexane : ethyl acetate = 1:1) to give (±)-**10f** (3.1 g, 10 mmol, 99% yield from (±)-**9f**). Colorless crystal: mp 120–121 ˚C (recrystallized from ethyl acetate); FT-IR (KBr) 3309, 3247, 2971, 2358, 1757, 1740, 1470, 1397, 1375, 1346, 1260, 1206, 1185, 1140, 1059, 941, 884, 851, 657 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.87 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H), 1.91–2.02 (m, 1H), 2.29 (s, 3H), 2.64 (s, 6H), 3.46 (s, 3H), 3.61 (dd, *J* = 5.5, 10.0 Hz, 1H), 5.14 (brd, *J* = 10.0 Hz, 1H, –N*H*), 6.94 (s, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 17.7 ($CH_3$), 18.8 ($CH_3$), 20.9 ($CH_3$), 23.0 ($CH_3$ × 2), 31.6 (CH), 52.1 ($CH_3$), 60.1 (CH), 131.8 (CH × 2), 133.4 (C), 139.3 (C × 2), 142.3 (C), 171.9 (C=O); HRMS (ESI-HRMS) m/z calcd for $C_{15}H_{23}NO_4NaS$ $[M+Na]^+$ 336.1245, found 336.1260.

**Dimethyl-{3-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-2-oxo-4-phenyl-butyl}-phosphonate [(±)-11e]**

To a solution of dimethyl methylphosphate (3.6 mL, 33.2 mmol, 4.00 eq.) in anhydrous THF (50 mL) was added a solution of BuLi in hexane (2.77 M, 12 mL, 33.2 mmol, 4.0 eq) dropwise over 15 min at –78 ˚C. After 30 min, to the mixture was added a solution of (±)-**10e** (3.00 g, 8.30 mmol, 1.00 eq.) in THF (30 mL) dropwise over 15 min at –78 ˚C. The resulting mixture was stirred for 1 h at –78 ˚C, for 4 h at 0 ˚C, quenched with acetic acid (10% aqueous solution) at 0 ˚C, and extracted with ethyl acetate (100 mL × 3). The combined organic layers were washed with water (100 mL), $NaHCO_3$aq (100 mL), brine (100 mL), dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 1:9) to give [(±)-**11e**] (3.7 g, 8.2 mmol, 99% yield). Colorless crystal: mp 130–131˚C (recrystallized from ethyl acetate); FT-IR (KBr) 3183, 2950, 2360, 1733, 1604, 1457, 1299, 1224, 1162, 1029, 952, 919, 842, 703, 665 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 2.41 (s, 6H), 2.85 (dd, *J* = 8.8, 14.1 Hz, 1H), 3.06 (dd, *J* = 14.0, $J_{H-P}$ = 29.0 Hz, 1H), 3.09 (dd, *J* = 6.0, 14.1 Hz, 1H), 3.72 (d, $J_{H-P}$ = 11.4 Hz, 3H), 3.73 (dd, *J* = 14.0, $J_{H-P}$ = 29.0 Hz, 1H), 3.78 (d, $J_{H-P}$ = 11.4 Hz, 3H), 4.13 (ddd, *J* = 6.0, 8.0, 8.8 Hz, 1H), 5.96 (brd, *J* = 8.0 Hz, 1H, –N*H*), 6.81 (s, 2H), 6.90–6.94 (m, 2H), 7.06–7.15 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 20.9 ($CH_3$), 22.8 ($CH_3$ × 2), 37.6 ($CH_2$), 38.3 (d, $J_{C-P}$ = 127.8 Hz, –*C*$H_2$P), 53.2 (d, $J_{C-P}$ = 6.6 Hz, –POC$H_3$), 53.3 (d, $J_{C-P}$ = 6.6 Hz, –POC$H_3$), 63.5 (CH), 126.8 (CH), 128.4 (CH × 2), 128.8 (CH × 2), 131.8 (CH × 2), 133.2 (C), 135.5 (C), 138.8 (C × 2), 142.1 (C), 201.0 (d, $J_{C-P}$ = 5.7Hz, C=O); HRMS (ESI-HRMS) m/z calcd for $C_{21}H_{29}NO_6NaPS$ $[M+H]^+$ 454.1453, found 454.1409.

**Dimethyl-{3-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-4-methyl-2-oxo-pentyl}-phosphonate [(±)-11f]**

Preparation of (±)-**11f** was carried out starting from (±)-**10f** (6.20 g, 19.8 mmol) as described for (±)-**11e** from (±)-**10e**. Purified by silica gel column chromatography (hexane : ethyl acetate = 1:4) to give (±)-**11f** (7.8 g, 19 mmol, 97% yield from (±)-**10f**). Colorless crystal: mp 129–131 ˚C (recrystallized from ethyl acetate); FT-IR (KBr) 3253, 2971, 2938, 1727, 1467, 1450, 1287, 1187, 1095, 931, 880, 850, 662, 584, 537, 497, 463 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.71 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H), 2.19–2.31 (m, 1H), 2.28 (s, 3H), 2.67 (s, 6H), 2.98 (dd, *J* = 14.1, $J_{H-P}$ = 21.7 Hz, 1H), 3.38 (dd, *J* = 14.1, $J_{H-P}$ = 23.4 Hz, 1H), 3.70 (d, $J_{H-P}$ = 11.4 Hz, 3H), 3.75 (d, $J_{H-P}$ = 11.4 Hz, 3H), 3.96 (dd, *J* = 3.8, 9.3 Hz, 1H), 6.02 (brd, *J* = 9.3 Hz, 1H, –N*H*), 6.94 (s, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 16.3 ($CH_3$), 19.7 ($CH_3$), 20.9 ($CH_3$), 22.9 ($CH_3$ × 2), 29.6 (CH), 38.6 (d, $J_{C-P}$ = 128.6 Hz, –*C*$H_2$P), 53.0 (d, $J_{C-P}$ = 6.5 Hz, –POC$H_3$), 53.3 (d, $J_{C-P}$ = 6.5 Hz, –POC$H_3$), 67.3 (CH), 131.9 (CH × 2), 134.2 (C), 138.9 (C × 2), 142.2 (C), 200.6 (d, $J_{C-P}$ = 5.8 Hz, C=O); HRMS (ESI-HRMS) m/z calcd for $C_{17}H_{28}NO_6NaSP$ $[M+Na]^+$ 428.1273, found 428.1281.

**(4*E*)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-phenyl-4-hexen-3-one [(±)-12g]**

To a solution of (±)-**11e** (1.00 g, 2.21 mmol, 1.00 eq.) and acetoaldehyde (0.15 mL, 2.65 mmol, 1.20 eq.) in ethanol (10 mL) was added oven-dried potassium carbonate (0.305 g, 2.21 mmol, 1.00 eq.) portionwise over 15 min at room temperature, and the mixture was stirred for 5 h at room temperature. The resulting suspension was filtered and the residue was washed with ethyl acetate (20 mL). The combined filtrates were neutralized with glacial acetic acid and concentrated in vacuo. The residue was diluted with ethyl acetate (30 mL), and washed with water (30 mL). The aqueous phase was extracted with ethyl acetate (30 mL × 2). The combined organic layers were washed with water (30 mL), $NaHCO_3$aq (30 mL), brine (30 mL), dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 9:1) to give (±)-**12g** (0.70 g, 1.9 mmol, 85% yield). Colorless crystal: mp 125–126 ˚C (recrystallized from hexane); FT-IR (KBr) 3250, 3026, 2972, 2920, 1699, 1631, 1605, 1497, 1454, 1425, 1325, 1295, 1158, 1114, 1072, 1059, 968, 950, 918, 846, 757, 741, 702, 657, 588 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 1.82 (dd, *J* = 1.7, 6.9 Hz, 3H), 2.26 (s, 3H), 2.53 (s, 6H), 2.90 (dd, *J* = 6.2, 14.1 Hz, 1H), 3.00 (dd, *J* = 6.5, 14.1 Hz, 1H), 4.28 (ddd, *J* = 6.2, 6.5, 7.6 Hz, 1H), 5.45 (brd, *J* = 7.6 Hz, 1H, –N*H*), 6.07 (dq, *J* = 1.7, 15.5 Hz, 1H), 6.80 (dq, *J* = 6.9, 15.5 Hz, 1H), 6.86 (s, 2H), 6.96–7.02 (m, 2H), 7.16–7.20 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 18.5 ($CH_3$), 20.9 ($CH_3$), 22.8 ($CH_3$ × 2), 39.1 ($CH_2$), 60.2 (CH), 127.0 (CH), 127.9 (CH), 128.4 (CH × 2), 129.4 (CH × 2), 131.9 (CH × 2), 133.6 (C), 135.3 (C), 139.0 (C × 2), 142.2 (C), 145.6 (CH), 196.0 (C=O); HRMS (ESI-HRMS) m/z calcd for $C_{21}H_{26}NO_3S$ $[M+H]^+$ 372.1633, found 372.1624.

**(4*E*)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-7-methyl-1-phenyl-4-octen-3-one [(±)-12h]**

Preparation of (±)-**12h** was carried out starting from (±)-**11e** (1.00 g, 2.21 mmol) and isovaleraldehyde as described for (±)-**12g** from (±)-**11e** and acetoaldehyde. Purified by silica gel column chromatography (hexane : ethyl acetate = 9:1) to give (±)-**12h** (0.79 g, 1.9 mmol, 87% yield from (±)-**11e**). Colorless oil; FT-IR (neat) 3299, 3029, 2956, 1693, 1625, 1565, 1495, 1454, 1334, 1159, 1078, 1031, 983, 904, 852, 750, 770, 655 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H), 1.63–1.73 (m, 1H), 1.98–2.02 (m, 2H), 2.26 (s, 3H), 2.55 (s, 6H), 2.93 (dd, *J* = 6.4, 14.0 Hz, 1H), 3.00 (dd, *J* = 6.4, 14.0 Hz, 1H), 4.31 (ddd, *J* = 6.4, 6.4, 7.2 Hz, 1H), 5.50 (brd, *J* = 7.2 Hz, 1H, –N*H*), 5.97 (dt, *J* = 1.2, 15.6 Hz, 1H), 6.73 (dt, *J* = 7.6, 15.6 Hz, 1H), 6.87 (s, 2H), 6.97–7.04 (m, 2H), 7.15–7.21 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 21.0 ($CH_3$), 22.39 ($CH_3$), 22.42 ($CH_3$), 22.9 ($CH_3$ × 2), 27.8 (CH), 39.5 ($CH_2$), 41.9 ($CH_2$), 60.0 (CH), 127.0 (CH), 127.4 (CH), 128.4 (CH × 2), 129.3 (CH × 2), 131.8 (CH × 2), 133.6 (C), 135.2 (C), 138.9 (C × 2), 142.1 (C), 149.3 (CH), 196.0 (C=O); HRMS (ESI-HRMS) m/z calcd for $C_{24}H_{31}NO_3NaS$ $[M+Na]^+$ 436.1922, found 436.1952.

**(4*E*)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-6-methyl-1-phenyl-4-hepten-3-one [(±)-12i]**

Preparation of (±)-**12i** was carried out starting from (±)-**11e** (1.00 g, 2.21 mmol) and isobutyraldehyde as described for (±)-**12g** from (±)-**11e** and acetoaldehyde. Purified by silica gel column chromatography (hexane : ethyl acetate = 9:1) to give (±)-**12i** (0.65 g, 1.6 mmol, 73% yield). Colorless oil; FT-IR (neat) 3297, 3029, 2965, 2871, 1694, 1624, 1566, 1497, 1455, 1336, 1157, 1059, 984, 851, 700, 656 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.94 (d, *J* = 6.5 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H), 2.26 (s, 3H), 2.26–2.38 (m, 1H), 2.56 (s, 6H), 2.96 (d, *J* = 6.5 Hz, 2H), 4.34 (dt, *J* = 6.5, 7.6 Hz, 2H), 5.53 (brd, *J* = 7.6 Hz, 1H, –N*H*), 5.85 (dd, *J* = 1.4, 15.8 Hz, 1H), 6.65 (dd, *J* = 6.5, 15.8 Hz, 1H), 6.87 (s, 2H), 7.00–7.03 (m, 2H), 7.17–7.20 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 22.8 ($CH_3$), 20.9 ($CH_3$ × 2), 22.8 ($CH_3$ × 2), 31.2 (CH), 39.6 ($CH_2$), 59.9 (CH), 123.8 (CH), 127.0 (CH), 128.4 (CH × 2), 129.4 (CH × 2), 131.9 (CH × 2), 133.7 (C), 135.4 (C), 139.0 (C × 2), 142.2 (C), 156.3 (CH), 196.9 (C=O); HRMS (ESI-HRMS) m/z calcd for $C_{23}H_{29}NO_3NaS$ $[M+Na]^+$ 422.1766, found 422.1750.

**(5*E*)-3-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-2,7-dimethyl-5-octen-4-one [(±)-12j]**

Preparation of (±)-**12j** was carried out starting from (±)-**11f** (2.00 g, 4.93 mmol) and isobutyraldehyde as described for (±)-**12g** and acetoaldehyde. Purified by silica gel column chromatography (hexane : ethyl acetate = 9:1) to give (±)-**12j** (1.6 g, 4.5 mmol, 91% yield). Colorless oil; FT-IR (neat) 3298, 2968, 2874, 1694, 1624, 1605, 1566, 1455, 1328, 1159, 1059, 980, 891, 852, 725, 656 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.77 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 6H), 1.90–2.01 (m, 1H), 2.25 (s, 3H), 2.32–2.43 (m, 1H), 2.64 (s, 6H), 3.97 (dd, *J* = 4.2, 8.9 Hz, 1H), 5.56 (brd, *J* = 8.9 Hz, 1H, –N*H*), 5.86 (dd, *J* = 1.2, 15.8 Hz, 1H), 6.66 (dd, *J* = 6.5, 15.8 Hz, 1H), 6.89 (s, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 16.7 ($CH_3$), 19.8 ($CH_3$), 20.8 ($CH_3$), 20.9 ($CH_3$), 21.0 ($CH_3$), 22.9 ($CH_3$ × 2), 31.0 (CH), 31.2 (CH), 63.5 (CH), 124.3 (CH), 131.9 (CH × 2), 133.8 (C), 138.9 (C × 2), 142.1 (C), 155.7 (CH), 197.5 (C=O); HRMS (ESI-HRMS) m/z calcd for $C_{19}H_{29}NO_3NaS$ $[M+Na]^+$ 374.1766, found 374.1771.

**(4*E*)(2*R**,3*S**)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-3-hydroxy-1-phenyl-4-hexene [(±)-13g] and (4*E*)(2*R**,3*R**)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-3-hydroxy-1-phenyl-4-hexene [(±)-14g]**

To a solution of (±)-**12g** (500 mg, 1.35 mmol, 1.00 eq.) and cerium(III) chloride heptahydrate (503 mg, 1.35 mmol, 1.00 eq.) in methanol (6.8 mL) was added sodium borohydride (51.1 mg, 1.35 mmol, 1.00 eq.) in small portions over 15 min at 0 ˚C, and stirred for 30 min at 0 ˚C. The resulting mixture was neutralized with glacial acetic acid and concentrated in vacuo. The residue was diluted with ethyl acetate (10 mL), and washed with $H_2O$ (10 mL). The aqueous phase was extracted with ethyl acetate (10 mL × 2). The combined organic layers were washed with water (10 mL), $NaHCO_3$aq (10 mL), brine (10 mL), dried over $Na_2SO_4$ and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 4:1) to give a mixture of diastereomers (483 mg, 1.29 mmol, 96% yield, (±)-**13g** : (±)-**14g** = 61 : 39). These diastereomers were separated by flash column chromatography (hexane : diethyl ether = 1 : 1).

(±)-**13g**: Colorless oil; FT-IR (neat) 3733, 3308, 3027, 2938, 1604, 1567, 1497, 1455, 1319, 1188, 1152, 1057, 967, 850, 743, 698, 652 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 1.73 (brd, *J* = 6.5 Hz, 3H), 2.28 (s, 3H), 2.35 (brd, *J* = 5.5 Hz, 1H, –O*H*), 2.45 (s, 6H), 2.65 (dd, *J* = 8.3, 14.1 Hz, 1H), 2.78 (dd, *J* = 5.6, 14.1 Hz, 1H), 3.40–3.48 (m, 1H), 4.17–4.24 (m, 1H), 4.65 (brd, *J* = 7.9 Hz, 1H, –N*H*), 5.46 (ddq, *J* = 1.5, 6.3, 15.5 Hz, 1H), 5.77 (ddq, *J* = 1.2, 6.6, 15.5 Hz, 1H), 6.83 (s, 2H), 6.88–6.94 (m, 2H), 7.08–7.16 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 17.9 ($CH_3$), 20.8 ($CH_3$), 22.9 ($CH_3$ × 2), 36.0 ($CH_2$), 59.5 (CH), 73.2 (CH), 126.3 (CH), 128.4 (CH × 2), 128.8 (CH × 2), 129.0 (CH), 129.4 (CH), 131.9 (CH × 2), 133.2 (C), 137.0 (C), 138.9 (C × 2), 142.0 (C); HRMS (ESI-HRMS) m/z calcd for $C_{21}H_{27}NO_3NaS$ $[M+Na]^+$ 396.1609, found 396.1583.

(±)-**14g**: Colorless crystal: mp 72–74 ˚C (recrystallized from hexane); FT-IR (KBr) 3510, 3335, 3027, 2936, 1604, 1563, 1454, 1420, 1336, 1236, 1187, 1160, 1149, 1123, 1058, 968, 850, 749, 702, 662, 574, 540, 469 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 1.54 (ddd, *J* = 0.7, 1.7, 6.5 Hz, 3H), 1.72–1.76 (brm, 1H, –O*H*), 2.28 (s, 3H), 2.58 (s, 6H), 2.72 (dd, *J* = 6.2, 13.4 Hz, 1H), 2.93 (dd, *J* = 8.3, 13.4 Hz, 1H), 3.34–3.43 (m, 1H), 3.98–4.04 (m, 1H), 4.93 (brd, *J* = 8.6 Hz, 1H, –N*H*), 5.24 (ddq, *J* = 1.7, 6.9, 15.5 Hz, 1H), 5.58 (ddq, *J* = 1.0, 6.5, 15.5 Hz, 1H), 6.88 (s, 2H), 7.04–7.07 (m, 2H), 7.10–7.21 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 17.6 ($CH_3$), 20.8 ($CH_3$), 23.1 ($CH_3$ × 2), 38.4 ($CH_2$), 59.2 (CH), 71.8 (CH), 126.4 (CH), 128.4 (CH × 2), 129.0 (CH), 129.1 (CH × 2), 130.3 (CH), 131.9 (CH × 2), 134.5 (C), 137.6 (C), 138.6 (C × 2), 141.8 (C); HRMS (ESI-HRMS) m/z calcd for $C_{21}H_{27}NO_3NaS$ $[M+Na]^+$ 396.1609, found 396.1613.

**(4*E*)(2*R**,3*S**)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-3-hydroxy-7-methyl-1-phenyl-4-octene [(±)-13h] and (4*E*)(2*R**,3*R**)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-3-hydroxy-7-methyl-1-phenyl-4-octene [(±)-14h]**

Preparation of (±)-**13h** and (±)-**14h** was carried out starting from enone (±)-**12h** (500 mg, 1.21 mmol) as described for (±)-**13g** and (±)-**14g** from (±)-**12g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 4:1) to give the mixture of diastereomers (461 mg, 1.11 mmol, 92% yield, (±)-**13h** : (±)-**14h** = 65 : 35). These diastereomers were separated by flash column chromatography (hexane : diethyl ether = 3 : 2).

(±)-**13h**: Colorless oil; FT-IR (neat) 3500, 3305, 2952, 2360, 1604, 1454, 1317, 1151, 1056, 970, 914, 848, 742, 698, 649 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 0.91 (d, *J* = 6.8 Hz, 6H), 1.59–1.71 (m, 1H), 1.48–1.82 (brm, 1H, –O*H*), 1.93 –1.99 (m, 2H), 2.28 (s, 3H), 2.44 (s, 6H), 2.64 (dd, *J* = 8.8, 14.3 Hz, 1H), 2.78 (dd, *J* = 5.8, 14.3 Hz, 1H), 3.40–3.50 (m, 1H), 4.23–4.29 (m, 1H), 4.65 (brd, *J* = 7.6 Hz, 1H, –N*H*), 5.46 (ddt, *J* = 0.8, 6.2, 15.5 Hz, 1H), 5.74 (ddt, *J* = 0.8, 7.0, 15.5 Hz, 1H), 6.82 (s, 2H), 6.87–6.93 (m, 2H), 7.07–7.16 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 21.0 ($CH_3$), 22.38 ($CH_3$), 22.41 ($CH_3$), 23.1 ($CH_3$ × 2), 28.6 (CH), 36.2 ($CH_2$), 41.8 ($CH_2$), 59.7 (CH), 73.2 (CH), 126.4 (CH), 128.4 (CH × 2), 128.6 (CH), 128.8 (CH × 2), 131.9 (CH × 2), 133.2 (C), 133.5 (CH), 136.9 (C), 138.9 (C × 2), 142.0 (C); HRMS (ESI-HRMS) m/z calcd for $C_{24}H_{33}NO_3NaS$ $[M+Na]^+$ 438.2079, found 438.2076.

(±)-**14h**: Colorless crystal mp 84–85 ˚C (recrystallized from hexane); FT–IR (KBr) 3448, 3164, 2952, 2360, 1602, 1434, 1313, 1147, 1058, 931, 850, 744, 700 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 0.81 (d, *J* = 6.8 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H), 1.46–1.60 (m, 1H), 1.50–1.67 (brm, 1H, –O*H*), 1.67–1.82 (m, 2H), 2.28 (s, 3H), 2.57 (s, 6H), 2.71 (dd, *J* = 5.8, 13.7 Hz, 1H), 2.94 (dd, *J* = 8.4, 13.7 Hz, 1H), 3.34–3.45 (m, 1H), 3.98–4.07 (m, 1H), 4.89 (brd, *J* = 8.4 Hz, 1H, –N*H*), 5.28 (ddt, *J* = 1.2, 7.2, 15.4 Hz, 1H), 5.56 (dt, *J* = 7.2, 15.4 Hz, 1H), 6.88 (s, 2H), 7.02–7.08 (m, 2H), 7.12–7.22 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 20.9 ($CH_3$), 22.32 ($CH_3$), 22.37 ($CH_3$), 23.2 ($CH_3$ × 2), 28.1 (CH), 38.4 ($CH_2$), 41.6 ($CH_2$), 59.2 (CH), 72.1 (CH), 126.4 (CH), 128.4 (CH × 2), 129.1 (CH × 2), 130.1 (CH), 131.8 (CH × 2), 133.4 (CH), 134.5 (C), 137.4 (C), 138.5 (C × 2), 141.7 (C); HRMS (ESI-HRMS) m/z calcd for $C_{24}H_{33}NO_3NaS$ $[M+Na]^+$ 438.2079, found 438.2019.

**(4*E*)(2*R**,3*S**)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-3-hydroxy-6-methyl-1-phenyl-4-heptene [(±)-13i] and (4*E*)(2*R**,3*R**)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-3-hydroxy-6-methyl-1-phenyl-4-heptene [(±)-14i]**

Preparation of (±)-**13i** and (±)-**14i** was carried out starting from (±)-**12i** (500 mg, 1.25 mmol) as described for (±)-**13g** and (±)-**14g** from (±)-**12g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 5:1) to give the mixture of diastereomers (497 mg, 1.23 mmol, 99% yield, (±)-**13i** and (±)-**14i** = 59 : 41). These diastereomers were separated by flash column chromatography (hexane : diethyl ether = 2 : 1).

(±)-**13i**: Colorless oil; FT-IR (neat) 3307, 3028, 2956, 1738, 1666, 1605, 1566, 1497, 1455, 1150, 1058, 971, 851, 743 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.99 (d, *J* = 6.9 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 2.25 (brd, *J* = 5.5 Hz, 1H, –O*H*), 2.28 (s, 3H), 2.29–2.35 (m, 1H), 2.46 (s, 6H), 2.64 (dd, *J* = 8.6, 14.1 Hz, 1H), 2.78 (dd, *J* = 5.9, 14.1 Hz, 1H), 3.42–3.50 (m, 1H), 4.20–4.25 (m, 1H), 4.65 (brd, *J* = 7.6 Hz, 1H, –N*H*), 5.40 (ddd, *J* = 1.3, 6.2, 15.5 Hz, 1H), 5.72 (ddd, *J* = 1.4, 6.5, 15.5 Hz, 1H), 6.83 (s, 2H), 6.90–6.93 (m, 2H), 7.09–7.13 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 20.9 ($CH_3$), 22.2 ($CH_3$ × 2), 23.0 ($CH_3$ × 2), 30.9 (CH), 35.8 ($CH_2$), 59.8 (CH), 73.4 (CH), 124.8 (CH), 126.3 (CH), 128.4 (CH × 2), 128.9 (CH × 2), 131.9 (CH × 2), 133.3 (C), 137.2 (C), 138.9 (C × 2), 141.5 (CH), 142.0 (C); HRMS (ESI-HRMS) m/z calcd for $C_{23}H_{31}NO_3SK$ $[M+K]^+$ 440.1662, found 440.1657.

(±)-**14i**: Colorless crystal mp 85–87 ˚C (recrystallized from hexane); FT-IR (KBr) 3490, 3307, 3029, 2961, 2870, 1604, 1567, 1454, 1381, 1337, 1225, 1155, 1059, 971, 932, 852, 747, 702, 662, 575, 543, 475 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 3H), 1.70 (brd, *J* = 3.1 Hz, 1H, –O*H*), 2.06–2.18 (m, 1H), 2.27 (s, 3H), 2.59 (s, 6H), 2.74 (dd, *J* = 5.4, 13.4 Hz, 1H), 2.94 (dd, *J* = 8.3, 13.4 Hz, 1H), 3.34–3.43 (m, 1H), 3.98–4.01 (m, 1H), 4.90 (brd, *J* = 8.6 Hz, 1H, –N*H*), 5.23 (ddd, *J* = 1.4, 7.2, 15.5 Hz, 1H), 5.54 (ddd, *J* = 1.0, 6.5, 15.5 Hz, 1H), 6.88 (s, 2H), 7.04–7.07 (m, 2H), 7.13–7.22 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 20.8 ($CH_3$), 21.8 ($CH_3$), 21.9 ($CH_3$), 23.1 ($CH_3$ × 2), 30.6 (CH), 59.3 ($CH_2$), 72.0 (CH), 126.2 (CH), 126.4 (CH), 128.4 (CH × 2), 129.2 (CH × 2), 131.9 (CH × 2), 134.5 (C), 137.6 (C), 138.6 (C × 2), 141.4 (CH), 141.8 (C); HRMS (ESI-HRMS) m/z calcd for $C_{23}H_{31}NO_3SK$ $[M+K]^+$ 440.1662, found 440.1678.

**(5*E*)(2*R**,3*S**)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-4-hydroxy-2,7-dimethyl-5-octene [(±)-13j] and (5*E*)(2*R**,3*R**)-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-4-hydroxy-2,7-dimethyl-5-octene [(±)-14j]**

Preparation of (±)-**13j** and (±)-**14j** was carried out starting from (±)-**12j** (600 mg, 1.71 mmol) as described for (±)-**13g** and (±)-**14g** from (±)-**12g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 5:1) to give the mixture of diastereomers (588 mg, 1.66 mmol, 97% yield, (±)-**13j** : (±)-**14j** = 35 : 65). These diastereomers were separated by flash column chromatography (hexane : diethyl ether = 20 : 1).

(±)-**13j**: Colorless oil; FT-IR (neat) 3051, 3297, 2961, 2872, 1716, 1605, 1566, 1465, 1324, 1187, 1155, 1059, 972, 928, 851, 756, 719, 657 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.79 (d, *J* = 6.9 Hz, 3H), 0.80 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 6H), 1.64–1.76 (m, 1H), 2.17 (brd, *J* = 6.5 Hz, 1H, –O*H*), 2.24–2.35 (m, 1H), 2.30 (s, 3H), 2.66 (s, 6H), 3.12 (ddd, *J* = 3.8, 6.2, 10.0 Hz, 1H), 4.11–4.19 (m, 1H), 4.63 (brd, *J* = 10.0, 1H, –N*H*), 5.36 (ddd, *J* = 1.4, 6.2, 15.5 Hz, 1H), 5.68 (ddd, *J* = 1.4, 6.6, 15.5 Hz, 1H), 6.95 (s, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 18.6 ($CH_3$), 20.4 ($CH_3$), 20.9 ($CH_3$), 22.2 ($CH_3$ × 2), 23.2 ($CH_3$ × 2), 29.5 (CH), 30.8 (CH), 63.7 (CH), 72.9 (CH), 124.9 (CH), 132.0 (CH × 2), 134.8 (C), 138.6 (C × 2), 141.2 (CH), 142.1 (C); HRMS (ESI-HRMS) m/z calcd for $C_{19}H_{31}NO_3NaS$ $[M+Na]^+$ 376.1922, found 376.1910.

(±)-**14j**: Colorless crystal: mp 108–109 ˚C (recrystallized from hexane); FT-IR (KBr) 3496, 3343, 3281, 2938, 1604, 1457, 1399, 1382, 1345, 1305, 1267, 1161, 1148, 1071, 1054, 972, 945, 852, 689, 648, 569, 540, 514 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.78 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 6H), 0.89 (d, *J* = 6.9 Hz, 6H), 1.78–1.91 (m, 2H), 2.02–2.13 (m, 1H), 2.28 (s, 3H), 2.65 (s, 6H), 2.99–3.06 (m, 1H), 4.03–4.08 (m, 1H), 4.93 (brd, *J* = 8.9 Hz, 1H, –N*H*), 5.11 (ddd, *J* = 1.4, 7.6, 15.5 Hz, 1H), 5.58 (dd, *J* = 6.5, 15.5 Hz, 1H), 6.94 (s, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 17.9 ($CH_3$), 19.7 ($CH_3$), 20.8 ($CH_3$), 20.87 ($CH_3$), 21.95 ($CH_3$), 23.2 ($CH_3$ × 2), 30.5 (CH), 30.6 (CH), 63.5 (CH), 72.9 (CH), 127.1 (CH), 131.9 (CH × 2), 135.6 (C), 138.3 (C × 2), 141.0 (CH), 141.7 (C); HRMS (ESI-HRMS) m/z calcd for $C_{19}H_{31}NO_3NaS$ $[M+Na]^+$ 376.1922, found 376.1927.

**(2*R**,3*R**)-2-phenylmethyl-3-[(1*E*)-1-propenyl]-1-[*N*-(2,4,6-trimethylbenzenesulfonyl)]aziridine [(±)-8$^t$g]**

To a solution of amino alcohol (±)-**13g** (93.4 mg, 0.250 mmol, 1.00 eq.) and $PPh_3$ (163 mg, 0.625 mmol, 2.50 eq.) in THF (2.5 mL) was added a solution of diethyl azodicarboxylate in toluene (40%, 0.29 mL, 0.625 mmol, 2.50 eq.) dropwise over 5 min at 0 ˚C, and the mixture was stirred for 5 h at 0 ˚C. The resulting mixture was concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane : diethyl ether : triethylamine = 95 : 5 : 1) to give (±)-**8$^t$g** (80.9 mg, 0.228 mmol, 91% yield). Colorless oil: FT-IR (neat) 3029, 2853, 1737, 1666, 1604, 1567, 1496, 1380, 1232, 1187, 1152, 1033, 920, 851, 807, 772, 746, 721 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 1.75 (dd, *J* = 1.4, 6.5 Hz, 3H), 2.30 (s, 3H), 2.54 (s, 6H), 2.63 (dd, *J* = 7.2, 14.5 Hz, 1H), 2.96 (dd, *J* = 4.8, 14.5 Hz, 1H), 3.12 (ddd, *J* = 4.5, 4.8, 7.2 Hz, 1H), 3.17 (dd, *J* = 4.5, 8.9 Hz, 1H), 5.72 (ddq, *J* = 1.4, 8.9, 15.1 Hz, 1H), 5.95 (dq, *J* = 6.5, 15.1 Hz, 1H), 6.84 (s, 2H), 6.89–6.93 (m, 2H), 7.03–7.14 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 18.0 ($CH_3$), 20.9 ($CH_3$), 22.7 ($CH_3$ × 2), 37.3 ($CH_2$), 48.8 (CH), 50.8 (CH), 124.9 (CH), 126.2 (CH), 128.2 (CH × 2), 128.5 (CH × 2), 131.5 (CH × 2), 133.2 (CH), 134.4 (C), 137.2 (C), 139.6 (C × 2), 142.2 (C); HRMS (ESI-HRMS) *m/z* calcd for $C_{21}H_{26}NO_2S$ $[M+H]^+$ 356.1684, found 356.1703.

**(2*R**,3*R**)-2-phenylmethyl-3-[(1*E*)-4-methyl-1-pentenyl]-1-[*N*-(2,4,6-trimethylbenzenesulfonyl)]aziridine [(±)-8$^t$h]**

Preparation of (±)-**8$^t$h** was carried out starting from amino alcohol (±)-**13h** (100 mg, 0.241 mmol) as described for (±)-**8$^t$g from** (±)-**13g**. Purified by silica gel column chromatography (hexane : diethyl ether : triethylamine = 95 : 5 : 1) to give (±)-**8$^t$h** (80.5 mg, 0.202 mmol, 84% yield). Colorless oil; FT-IR (neat) 3029, 2954, 1662, 1604, 1565, 1494, 1454, 1382, 1322, 1320, 1186, 1155, 1054, 1031, 925, 850, 769, 746, 721, 684 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 0.87 (d, *J* = 6.4 Hz, 3H), 0.89 (d, *J* = 6.4 Hz, 3H), 1.58–1.69 (m, 1H), 1.90–2.04 (m, 2H), 2.29 (s, 3H), 2.54 (s, 6H), 2.66 (dd, *J* = 6.8, 14.4 Hz, 1H), 2.99 (dd, *J* = 5.2, 14.4 Hz, 1H), 3.19–3.16 (m, 1H), 3.18 (dd, *J* = 4.0, 9.2 Hz, 1H), 5.68 (dd, *J* = 9.2, 15.2 Hz, 1H), 5.90 (dt, *J* = 7.2, 15.2 Hz, 1H), 6.84 (s, 2H), 6.89–6.95 (m, 2H), 7.02–7.14 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 21.0 ($CH_3$) 22.29 ($CH_3$), 22.33 ($CH_3$), 23.0 ($CH_3$ × 2), 28.2 (CH), 37.3 ($CH_2$), 41.7 ($CH_2$), 48.9 (CH), 51.0 (CH), 124.7 (CH), 126.2 (CH), 128.2 (CH × 2), 128.5 (CH × 2), 131.5 (CH × 2), 134.4 (C), 137.2 (C), 137.3 (CH), 139.6 (C × 2), 142.2 (C); HRMS (ESI-HRMS) *m/z* calcd for $C_{24}H_{31}NO_2NaS$ $[M+Na]^+$ 420.1973, found 420.1948.

**(2*R**,3*R**)-2-phenylmethyl-3-[(1*E*)-3-methyl-1-butenyl]-1-[*N*-(2,4,6-trimethylbenzenesulfonyl)]aziridine [(±)-8$^{t}$i]**

Preparation of (±)-**8$^{t}$i** was carried out starting from amino alcohol (±)-**13i** (100 mg, 0.250 mmol) as described for (±)-**8$^{t}$g** from (±)-**13g**. Purified by silica gel column chromatography (hexane : diethyl ether : triethylamine = 95 : 5 : 1) to give (±)-**8$^{t}$i** (87.3 mg, 0.228 mmol, 91% yield). Colorless oil; FT-IR (neat) 3029, 2959, 2869, 1604, 1467, 1496, 1455, 1382, 1323, 1229, 1187, 1154, 1056, 1033, 925, 851, 773, 748, 721, 688, 602 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 0.98 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 2.26–2.40 (m, 1H), 2.29 (s, 3H), 2.54 (s, 6H), 2.64 (dd, *J* = 6.9, 14.1 Hz, 1H), 2.98 (dd, *J* = 4.1, 14.1 Hz, 1H), 3.10–3.16 (m, 2H), 5.64 (ddd, *J* = 1.4, 8.9, 15.5 Hz, 1H), 5.87 (dd, *J* = 6.5, 15.5 Hz, 1H), 6.83 (s, 2H), 6.90–6.94 (m, 2H), 7.03–7.13 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 20.9 ($CH_3$), 21.8 ($CH_3$), 21.9 ($CH_3$), 22.8 ($CH_3$ × 2), 30.9 (CH), 37.3 ($CH_2$), 48.7 (CH), 51.1 (CH), 120.9 (CH), 126.2 (CH), 128.2 (CH × 2), 128.5 (CH × 2), 131.5 (CH × 2), 134.5 (C), 137.2 (C), 139.5 (C × 2), 142.2 (C), 145.2 (CH); HRMS (ESI-HRMS) *m/z* calcd for $C_{23}H_{30}NO_2S$ $[M+H]^+$ 384.1997, found 384.2011.

**(2*R**,3*R**)-2-methylethyl-3-[(1*E*)-3-methyl-1-butenyl]-1-[*N*-(2,4,6-trimethylbenzenesulfonyl)]aziridine [(±)-8$^{t}$j]**

Preparation of (±)-**8$^{t}$j** was carried out starting from amino alcohol (±)-**13j** (106 mg, 0.300 mmol) as described for (±)-**8$^{t}$g from** (±)-**13g**. Purified by silica gel column chromatography (hexane : diethyl ether : triethylamine = 95 : 5 : 1) to give (±)-**8$^{t}$j** (87.9 mg, 0.262 mmol, 87% yield). Colorless oil; FT-IR (neat) 2962, 2868, 1605, 1470, 1382, 1312, 1232, 1188, 1156, 1054, 1032, 978, 945, 907, 849, 797, 719, 696, 659, 620 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 0.71 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 6H), 1.43–1.59 (m, 1H), 2.28–2.40 (m, 1H), 2.29 (s, 3H), 2.70 (s, 6H), 2.77 (dd, *J* = 4.5, 7.2 Hz, 1H), 3.06 (dd, *J* = 4.5, 8.9 Hz, 1H), 5.71 (ddd, *J* = 1.0, 8.9, 15.5 Hz, 1H), 5.84 (dd, *J* = 6.2, 15.5 Hz, 1H), 6.92 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 19.1 ($CH_3$), 19.3 ($CH_3$), 21.0 ($CH_3$), 21.8 ($CH_3$), 21.9 ($CH_3$), 23.0 ($CH_3$ × 2), 30.1 (CH), 31.0 (CH), 51.1 (CH), 53.1 (CH), 121.2 (CH), 131.6 (CH × 2), 134.5 (C), 139.7 (C × 2), 142.3 (C), 145.1 (CH); HRMS (ESI-HRMS) m/z calcd for $C_{19}H_{29}NO_2NaS$ $[M+Na]^+$ 358.1817, found 358.1789.

**(2*R**,3*S**)-2-phenylmethyl-3-[(1*E*)-1-propenyl]-1-[*N*-(2,4,6-trimethylbenzenesulfonyl)]aziridine [(±)-8$^{c}$g]**

Preparation of (±)-**8$^{c}$g** was carried out starting from amino alcohol (±)-**14g** (93.4 mg, 0.250 mmol) as described for (±)-**8$^{t}$g from** (±)-**13g**. Purified by silica gel column chromatography (hexane : diethyl ether : triethylamine = 95 : 5 : 1) to give (±)-**8$^{c}$g** (87.1 mg, 0.245 mmol, 98% yield). Colorless oil; FT-IR (neat) 3029, 2938, 1604, 1567, 1497, 1454, 1406, 1380, 1321, 1233, 1187, 1155, 1056, 1033, 963, 922, 875, 788, 729, 699, 669 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 1.76 (dd, *J* = 1.7, 6.5 Hz, 3H), 2.29 (s, 3H), 2.57 (s, 6H), 2.63 (dd, *J* = 7.5, 14.5 Hz, 1H), 2.76 (dd, *J* = 5.5, 14.5 Hz, 1H), 3.03 (dt, *J* = 5.5, 7.5 Hz, 1H), 3.47 (t, *J* = 7.5 Hz, 1H), 5.41 (ddq, *J* = 1.7, 7.5, 15.5 Hz, 1H), 5.96 (dq, *J* = 6.5, 15.5 Hz, 1H), 6.84 (s, 2H), 6.94–6.98 (m, 2H), 7.03–7.13 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 18.0 ($CH_3$), 20.9 ($CH_3$), 22.8 ($CH_3$ × 2), 33.4 ($CH_2$), 43.4 (CH), 46.3 (CH), 123.0 (CH), 126.1 (CH), 128.26 (CH × 2), 128.34 (CH × 2), 131.6 (CH × 2), 132.6 (C), 132.9 (CH), 137.6 (C), 139.8 (C × 2), 142.5 (C); HRMS (ESI-HRMS) *m/z* calcd for $C_{21}H_{26}NO_2S$ $[M+H]^+$ 356.1684, found 356.1710.

**(2*R**,3*S**)-2-phenylmethyl-3-[(1*E*)-4-methyl-1-pentenyl]-1-[*N*-(2,4,6-trimethylbenzenesulfonyl)]aziridine [(±)-8$^{c}$h]**

Preparation of (±)-**8$^{c}$h** was carried out starting from amino alcohol (±)-**14h** (100 mg, 0.241 mmol) as described for (±)-**8$^{t}$g from** (±)-**13g**. Purified by silica gel column chromatography (hexane : diethyl ether : triethylamine = 95 : 5 : 1) to give (±)-**8$^{c}$h** (89.1 mg, 0.224 mmol, 93% yield). Colorless oil; FT-IR (neat): 3027, 2954, 2869, 1604, 1565, 1496, 1454, 1405, 1382, 1322, 1232, 1186, 1155, 1056, 1033, 966, 933, 850, 786, 730, 700, 671 cm$^{-1}$; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.4 Hz, 6H), 1.58–1.69 (m, 1H), 1.19–2.03 (m, 2H), 2.29 (s, 3H), 2.58 (s, 6H), 2.68 (dd, *J* = 7.6, 14.4 Hz, 1H), 2.76 (dd, *J* = 5.6, 14.4 Hz, 1H), 3.03–3.10 (m, 1H), 3.44 (dd, *J* = 7.2, 7.2 Hz, 1H), 5.37 (ddt, *J* = 1.2, 7.2, 15.4 Hz, 1H), 5.89 (dt, *J* = 7.2, 15.4 Hz, 1H), 6.85 (s, 2H), 6.96–7.01 (m, 2H), 7.05 –7.14 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 21.0 ($CH_3$), 22.6 ($CH_3$ × 2), 23.0 ($CH_3$ × 2), 28.2 (CH), 33.5 ($CH_2$), 41.8 ($CH_2$), 43.8 (CH), 46.3 (CH), 122.7 (CH), 126.2 (CH), 128.3 (CH × 2), 128.4 (CH × 2), 131.6 (CH × 2), 132.7 (C), 137.0 (CH), 137.6 (C), 139.8 (C × 2), 142.5 (C); HRMS (ESI-HRMS) *m/z* calcd for $C_{24}H_{32}NO_2S$ $[M+H]^+$ 398.2154, found 398.2128.

**(2*R**,3*S**)-2-phenylmethyl-3-[(1*E*)-3-methyl-1-butenyl]-1-[*N*-(2,4,6-trimethylbenzenesulfonyl)]aziridine [(±)-8$^{c}$i]**

Preparation of (±)-**8$^{c}$i** was carried out starting from amino alcohol (±)-**14i** (100 mg, 0.250 mmol) as described for (±)-**8$^{t}$g from** (±)-**13g**. Purified by silica gel column chromatography (hexane : diethyl ether : triethylamine = 95 : 5 : 1) to give (±)-**8$^{c}$i** (95.1 mg, 0.248 mmol, 99% yield). Colorless oil; FT-IR (neat) 3027, 2974, 1696, 1604, 1566, 1497, 1455, 1382, 1323, 1217, 1187, 1154, 1057, 969, 852, 752, 700, 658 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 1.00 (d, *J* = 6.5 Hz, 6H), 2.29 (s, 3H), 2.28, (m, 1H), 2.57 (s, 6H), 2.64 (dd, *J* = 7.6, 14.5 Hz, 1H), 2.74 (dd, *J* = 5.5, 14.5 Hz, 1H), 3.04 (dt, *J* = 7.2, 5.5 Hz, 1H), 3.45 (t, *J* = 7.2 Hz, 1H), 5.31 (ddd, *J* = 1.4, 7.2, 15.5 Hz, 1H), 5.89 (ddd, *J* = 0.6, 6.5, 15.5 Hz, 1H), 6.84 (s, 2H), 6.94–6.98 (m, 2H), 7.04–7.11 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 20.1 ($CH_3$), 22.0 ($CH_3$ × 2), 22.9 ($CH_3$ × 2), 31.1 (CH), 33.4 ($CH_2$), 43.7 (CH), 46.4 (CH), 118.9 (CH), 126.2 (CH), 128.3 (CH × 2), 128.4 (CH × 2), 131.6 (CH × 2), 132.8 (C), 137.7 (C), 139.8 (C × 2), 142.6 (C), 145.1 (CH); HRMS (ESI-HRMS) *m/z* calcd for $C_{23}H_{30}NO_2S$ $[M+H]^+$ 384.1997, found 384.1996.

**(2*R**,3*S**)-2-methylethyl-3-[(1*E*)-3-methyl-1-butenyl]-1-[*N*-(2,4,6-trimethylbenzenesulfonyl)]aziridine [(±)-8$^{c}$j]**

Preparation of (±)-**8$^{c}$j** was carried out starting from amino alcohol (±)-**14j** (106 mg, 0.300 mmol) as described for (±)-**8$^{t}$g from** (±)-**13g**. Purified by silica gel column chromatography (hexane : diethyl ether : triethylamine = 95 : 5 : 1) to give (±)-**8$^{c}$j** (96.0 mg, 0.286 mmol, 95% yield). Colorless oil; FT-IR (neat) 2960, 2871, 1604, 1567, 1468, 1384, 1323, 1237, 1187, 1156, 1057, 1007, 968, 944, 884, 842, 807, 747, 671, 583 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 0.74 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 6H), 1.34–1.51 (m, 1H), 2.22–2.34 (m, 1H), 2.30 (s, 3H), 2.49 (dd, *J* = 7.6, 10.0 Hz, 1H), 2.70 (s, 6H), 3.38 (dd, *J* = 7.6, 7.6 Hz, 1H), 5.18 (ddd, *J* = 1.4, 7.6, 15.5 Hz, 1H), 5.81 (dd, *J* = 6.5, 15.5 Hz, 1H), 6.94 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 18.8 ($CH_3$), 20.5 ($CH_3$), 21.0 ($CH_3$), 22.0 ($CH_3$ × 2), 23.1 ($CH_3$ × 2), 26.9 (CH), 31.0 (CH), 44.8 (CH), 51.3 (CH), 119.2 (CH), 131.6 (CH × 2), 133.0 (C), 139.9 (C × 2), 142.7 (C), 144.7 (CH); HRMS (ESI-HRMS) m/z calcd for $C_{19}H_{29}NO_2NaS$ $[M+Na]^+$ 358.1817, found 358.1790.

**(3*E*)(2*R**,5*R**)-5-[18-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-phenyl-3-hexene [(±)-15g]**

To a solution of $(dba)_3Pd_2$•$CHCl_3$ (15.5 mg, 0.0150 mmol, 0.100 eq.) and **4** (14.6 mg, 0.0900 mmol, 0.600 eq.) in THF (1.0 mL) was added

to a mixture of (±)-**8$^{t}$g** (53.3 mg, 0.150 mmol, 1.00 eq.) and **3** (35.3 mg, 0.180 mmol, 1.20 eq.) in THF (1.0 mL), and the mixture was stirred for 1 h at room temperature. The resulting mixture was filtered through a celite™ pad, and the residue was washed with ethyl acetate (5.0 mL). The combined eluents were concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 19 : 1) to give (±)-**15g** (82.5 mg, 0.150 mmol, 99% yield). Colorless oil; FT-IR (neat) 3308, 2933, 2860, 2242, 1739, 1605, 1455, 1327, 1259, 1156, 1057, 974, 844, 787, 750, 700, 658 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 0.34 (s, 6H), 0.91 (s, 9H), 1.05 (d, *J* = 6.9 Hz, 3H), 2.29 (s, 3H), 2.49 (s, 6H), 2.61–2.70 (m, 1H), 2.78 (dd, *J* = 6.9, 13.5 Hz, 1H), 2.85 (dd, *J* = 6.6, 13.5 Hz, 1H), 3.97–4.06 (m, 1H), 4.46 (brd, *J* = 6.9 Hz, 1H, –N*H*), 5.45 (ddd, *J* = 0.7, 7.2, 15.5 Hz, 1H), 5.62 (dd, *J* = 6.3, 15.5 Hz, 1H), 6.89 (s, 2H), 7.05–7.08 (m, 2H), 7.20–7.25 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ –4.72 ($CH_3$), –4.69 ($CH_3$), 13.3 ($CH_3$), 18.1 (C), 20.8 ($CH_3$), 22.9 ($CH_3$ × 2), 25.2 ($CH_3$ × 3), 42.0 ($CH_2$), 47.0 (CH), 56.1 (CH), 67.6 (C), 114.2 (CN), 114.5 (CN), 126.7 (CH), 127.0 (CH), 128.7 (CH × 2), 129.3 (CH × 2), 131.9 (CH × 2), 134.1 (CH), 135.78 (C), 135.82 (C), 138.9 (C × 2), 142.1 (C); HRMS (ESI-HRMS) m/z calcd for $C_{30}H_{41}N_3O_3NaSSi$ $[M+Na]^+$ 574.2536, found 574.2536.

**(3*E*)(2*R**,5*R**)-5-[1,1-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-7-methyl-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-phenyl-3-octene [(±)-15h]**

Synthesis of (±)-**15h** was carried out starting from aziridine (±)-**8$^{t}$h** (50.0 mg, 0.126 mmol) as described for (±)-**15g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 19 : 1) to give (±)-**15h** (71.6 mg, 0.123 mmol, 98% yield). Colorless oil; FT-IR (neat) 3305, 3027, 2956, 2933, 2861, 2240, 1604, 1565, 1496, 1469, 1365, 1328, 1261, 1186, 1155, 1056, 971, 937, 904, 844, 786, 748, 700, 657 cm$^{-1}$; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 0.33 (s, 3H), 0.34 (s, 3H), 0.73 (d, *J* = 6.4 Hz, H), 0.83 (d, *J* = 6.8 Hz), 0.91 (s, 9H), 1.10–1.44 (m, 3H), 2.29 (s, 3H), 2.53 (s, 6H), 2.46–2.58 (m, 1H), 2.81 (dd, *J* = 7.8, 13.7 Hz, 1H), 2.90 (dd, *J* = 6.4, 13.7 Hz, 1H), 3.96–4.05 (m, 1H), 4.52 (brd, *J* = 6.8 Hz, 1H, –N*H*), 5.24 (ddd, *J* = 0.8, 9.2, 15.3 Hz, 1H), 5.71 (dd, *J* = 5.8, 15.3 Hz, 1H), 6.09 (s, 2H), 7.01–7.07 (m, 2H), 7.17–7.28 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ –4.45 ($CH_3$), –4.52 ($CH_3$), 18.2 (C), 20.8 ($CH_3$), 21.0 ($CH_3$), 23.1 ($CH_3$ × 2), 23.9 ($CH_3$), 24.7 (CH), 25.3 ($CH_3$ × 3), 36.9 ($CH_2$), 42.3 ($CH_2$), 51.4 (CH), 55.9 (CH), 67.5 (C), 114.2 (CN), 114.8 (CN), 126.1 (CH), 126.8 (CH), 128.6 (CH × 2), 129.2 (CH × 2), 132.0 (CH × 2), 133.8 (C), 136.0 (C), 137.3 (CH), 138.8 (C × 2), 142.1 (C); HRMS (ESI-HRMS) *m/z* calcd for $C_{33}H_{47}N_3NaO_3SSi$ $[M+Na]^+$ 616.3005, found 616.3024.

**(3*E*)(2*R**,5*R**)-5-[1,1-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-6-methyl-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-phenyl-3-heptene [(±)-15i]**

Synthesis of (±)-**15i** was carried out starting from aziridine (±)-**8$^{t}$i** (57.5 mg, 0.150 mmol) as described for (±)-**15g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 19 : 1) to give (±)-**15i** (86.8 mg, 0.150 mmol, 99% yield). Colorless crystal mp 122–124 ˚C (recrystallized from hexane); FT-IR (KBr) 3291, 3027, 2958, 2859, 2240, 1305, 1471, 1454, 1414, 1320, 1263, 1188, 1162, 1121, 1057, 975, 845, 793, 784, 696, 655, 593, 539, 501, 475 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 0.357 (s, 3H), 0.362 (s, 3H), 0.78 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 2.15–2.25 (m, 1H), 2.28 (s, 3H), 2.40 (dd, *J* = 3.4, 10.0 Hz, 1H), 2.54 (s, 6H), 2.81 (dd, *J* = 7.5, 13.7 Hz, 1H), 2.89 (dd, *J* = 6.8, 13.7 Hz, 1H), 4.01–4.11 (m, 1H), 4.47 (brd, *J* = 7.2 Hz, 1H, –N*H*), 5.49 (ddd, *J* = 1.4, 10.0, 15.3 Hz, 1H), 5.73 (dd, *J* = 5.2, 15.3 Hz, 1H), 6.89 (s, 2H), 7.03–7.06 (m, 2H), 7.18–7.24 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ –4.7 ($CH_3$), –4.6 ($CH_3$), 17.3 ($CH_3$), 18.1 (C), 20.9 ($CH_3$), 22.2 ($CH_3$), 23.1 ($CH_3$ × 2), 25.2 ($CH_3$ × 3), 27.7 (CH), 42.3 ($CH_2$), 55.7 (CH), 58.2 (CH), 66.8 (C), 114.8 (CN), 115.3 (CN), 122.7 (CH), 126.9 (CH), 128.7 (CH × 2), 129.3 (CH × 2), 132.1 (CH × 2), 133.9 (C), 136.1 (C), 138.6 (CH), 138.9 (C × 2), 142.1 (C); HRMS (ESI-HRMS) m/z calcd for $C_{32}H_{45}N_3O_3NaSSi$ $[M+Na]^+$ 602.2849, found 602.2869.

**(4*E*)(3*R**,6*R**)-6-[1,1-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-2,7-dimethyl-3-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-4-octene [(±)-15j]**

Synthesis of (±)-**15j** was carried out starting from aziridine (±)-**8$^{t}$j** (67.0 mg, 0.200 mmol) as described for (±)-**15g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 30 : 1) to give (±)-**15j** (104 mg, 0.197 mmol, 98% yield). Colorless oil; FT-IR (neat) 3307, 2961, 2240, 1605, 1567, 1471, 1330, 1260, 1152, 976, 891, 844, 787, 659 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 0.35 (s, 3H), 0.37 (s, 3H), 0.80 (d, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 6H), 0.93 (s, 9H), 1.83–1.94 (m, 1H), 2.15–2.26 (m, 1H), 2.28 (s, 3H), 2.44 (dd, *J* = 3.4, 10.0 Hz, 1H), 2.65 (s, 6H), 3.81–3.87 (m, 1H), 4.48 (brd, *J* = 8.6 Hz, 1H, –N*H*), 5.43 (ddd, *J* = 1.7, 10.0, 15.1 Hz, 1H), 5.70 (dd, *J* = 4.8, 15.1 Hz, 1H), 6.94 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ –4.7 ($CH_3$), –4.6 ($CH_3$), 17.2 ($CH_3$), 17.9 ($CH_3$), 18.0 ($CH_3$), 18.1 (C), 20.8 ($CH_3$), 22.2 ($CH_3$), 23.2 ($CH_3$ × 2), 25.2 ($CH_3$ × 3), 27.6 (CH), 32.8 (CH), 58.4 (CH), 59.6 (CH), 66.9 (C), 114.8 (CN), 115.3 (CN), 122.4 (CH), 132.1 (CH × 2), 134.9 (C), 137.9 (CH), 138.5 (C × 2), 141.9 (C); HRMS (ESI-HRMS) m/z calcd for $C_{28}H_{45}N_3O_3NaSSi$ $[M+Na]^+$ 554.2849, found 554.2845.

**(3*E*)(2*R**,5*S**)-5-[1,1-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-phenyl-3-hexene [(±)-16g]**

Synthesis of (±)-**16g** was carried out starting from (±)-**8$^{c}$g** (53.3 mg, 0.150 mmol) as described for (±)-**15g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 19 : 1) to give (±)-**16g** (82.3 mg, 0.149 mmol, 99% yield). Colorless crystal mp 108–110 ˚C (recrystallized from hexane); FT-IR (KBr) 3302, 3034, 2932, 2860, 2241, 1604, 1497, 1455, 1407, 1318, 1148, 1045, 981, 848, 788, 739, 694, 661, 600, 536, 518 cm$^{-1}$; $^{1}$H NMR (300 MHz, $CDCl_3$) δ 0.33 (s, 3H), 0.34 (s, 3H), 0.91 (s, 9H), 1.15 (d, *J* = 6.9 Hz, 3H), 2.29 (s, 3H), 2.44 (s, 6H), 2.56–2.67 (m, 1H), 2.76 (dd, *J* = 7.6, 13.8 Hz, 1H), 2.89 (dd, *J* = 5.9, 13.8 Hz, 1H), 3.88–3.98 (m, 1H), 4.33 (brd, *J* = 6.0 Hz, 1H, –N*H*), 5.34 (ddd, *J* = 1.0, 8.6, 15.3 Hz, 1H), 5.65 (dd, *J* = 7.6, 15.3 Hz, 1H), 6.88 (s, 2H), 7.07–7.10 (m, 2H), 7.25–7.27 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ –4.8 ($CH_3$), –4.7 ($CH_3$), 14.1 ($CH_3$), 18.0 (C), 20.9 ($CH_3$), 22.8 ($CH_3$ × 2), 25.1 ($CH_3$ × 3), 42.0 ($CH_2$), 47.9 (CH), 56.0 (CH), 67.6 (C), 114.2 (CN), 114.6 (CN), 126.9 (CH), 127.1 (CH), 128.8 (CH × 2), 129.3 (CH × 2), 131.9 (CH × 2), 133.8 (C), 135.5 (C), 136.7 (CH), 138.9 (C × 2), 142.1 (C); HRMS (ESI-HRMS) m/z calcd for $C_{30}H_{41}N_3O_3NaSSi$ $[M+Na]^+$ 574.2536, found 574.2538.

**(3*E*)(2*R**,5*S**)-5-[1,1-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-7-methyl-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-phenyl-3-octene [(±)-16h]**

Synthesis of (±)-**16h** was carried out starting from (±)-**8$^{c}$h** (50.0 mg, 0.126 mmol) as described for (±)-**15g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 14 : 1) to give (±)-**16h** (72.3 mg, 0.125 mmol, 99% yield). Colorless oil; FT-IR (neat) 3291, 3029, 2956, 2861, 2240, 1604, 1565, 1496, 1469, 1328, 1261, 1155, 1058, 970, 939, 904, 844, 786, 748, 700, 657 cm$^{-1}$; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 0.33 (s, 3H), 0.34 (s, 3H), 0.81 (d, *J* = 5.6 Hz, 3H), 0.88–0.98

(m, 12H), 1.21–1.52 (m, 3H), 2.29 (s, 3H), 2.44 (s, 6H), 2.52–2.61 (m, 1H), 2.79 (dd, *J* = 7.0, 13.8 Hz, 1H), 2.92 (dd, *J* = 5.8, 13.8 Hz, 1H), 3.90–3.99 (m, 1H), 4.46 (brd, *J* = 6.4 Hz, 1H, –N*H*), 5.25 (dd, *J* = 9.6, 15.6 Hz, 1H), 5.78 (dd, *J* = 6.8, 15.6 Hz, 1H), 6.88 (s, 2H), 7.02–7.09 (m, 2H), 7.19–7.27 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ –4.6 ($CH_3$), –4.5 ($CH_3$), 18.2 (C), 20.9 ($CH_3$), 21.0 ($CH_3$), 22.9 ($CH_3$ × 2), 23.9 ($CH_3$), 24.8 (CH), 25.3 ($CH_3$ × 3), 37.4 ($CH_2$), 42.1 ($CH_2$), 51.7 (CH), 55.7 (CH), 67.5 (C), 114.3 (CN), 114.7 (CN), 125.8 (CH), 127.1 (CH), 128.7 (CH × 2), 129.3 (CH × 2), 131.9 (CH × 2), 133.4 (C), 135.5 (C), 138.6 (CH), 138.9 (C × 2), 142.1 (C); HRMS (ESI-HRMS) *m/z* calcd for $C_{33}H_{47}N_3NaO_3SSi$ $[M+Na]^+$ 616.3005, found 616.3027.

**(3*E*)(2*R**,5*R**)-5-[1,1-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-6-methyl-2-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-1-phenyl-3-heptene [(±)-16i]**

Synthesis of (±)-**16i** was carried out starting from (±)-**8$^c$i** (57.5 mg, 0.150 mmol) as described for (±)-**15g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 14 : 1) to give (±)-**16i** (85.2 mg, 0.147 mmol, 98% yield). Colorless crystal mp 131–133 ˚C (recrystallized from hexane); FT-IR (KBr) 3276, 3030, 2959, 2860, 2241, 1604, 1496, 1455, 1417, 1131, 1263, 1187, 1115, 1054, 983, 949, 886, 744, 698, 649, 588, 509 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 0.34 (s, 3H), 0.36 (s, 3H), 0.89 (d, *J* = 7.2 Hz, 3H), 0.92 (s, 9H), 0.92 (d, *J* = 7.2 Hz, 3H), 2.20–2.31 (m, 1H), 2.29 (s, 3H), 2.40–2.44 (m, 1H), 2.44 (s, 6H), 2.78 (dd, *J* = 7.6, 13.8 Hz, 1H), 2.93 (dd, *J* = 5.5, 13.8 Hz, 1H), 3.92–4.01 (m, 1H), 4.44 (brd, *J* = 6.5 Hz, 1H, –N*H*), 5.47 (ddd, *J* = 0.7, 10.0, 15.5 Hz, 1H), 5.75 (dd, *J* = 7.2, 15.5 Hz, 1H), 6.87 (s, 2H), 7.02–7.08 (m, 2H), 7.20–7.25 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ –4.7 ($CH_3$), –4.6 ($CH_3$), 17.4 ($CH_3$), 18.1 (C), 20.9 ($CH_3$), 22.4 ($CH_3$), 22.9 ($CH_3$ × 2), 25.2 ($CH_3$ × 3), 27.8 (CH), 42.1 ($CH_2$), 55.9 (CH), 58.3 (CH), 66.9 (C), 114.8 (CN), 115.2 (CN), 122.7 (CH), 127.1 (CH), 128.8 (CH × 2), 129.4 (CH × 2), 132.0 (CH × 2), 133.5 (C), 135.5 (C), 139.0 (C × 2), 139.9 (CH), 142.1 (C); HRMS (ESI-HRMS) m/z calcd for $C_{32}H_{45}N_3O_3NaSSi$ $[M+Na]^+$ 602.2849, found 602.2867.

**(4*E*)(3*R**,6*S**)-6-[1,1-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-2,7-dimethyl-3-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-4-octene [(±)-16j] and (5*E*)-4-[1,1-dicyano-1-(*tert*-butyldimethylsilyloxy)methyl]-2,7-dimethyl-3-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-5-octene [(±)-17j]**

Synthesis of (±)-**16j** was carried out starting from aziridine (±)-**8$^c$j** (503 mg, 1.50 mmol) as described for (±)-**15g**. The corresponding regio-isomer (±)-**17j** was also obtained. Purified by silica gel column chromatography (hexane : ethyl acetate = 30 : 1) to give the mixture of regio-isomers (726 mg, 1.37 mmol, 91% yield, (±)-**16j** : (±)-**17j** = 58 : 42). These isomers were separated flash column chromatography (hexane : ethyl acetate = 30 : 1).

(±)-**16j**: Colorless crystal mp 118–119 ˚C (recrystallized from hexane); FT-IR (KBr) 3275, 2958, 2935, 2860, 2239, 1604, 1565, 1471, 1326, 1268, 1220, 1165, 1053, 991, 954, 909, 846, 789, 722, 660, 581, 538 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 0.34 (s, 3H), 0.36 (s, 3H), 0.80 (d, *J* = 6.9 Hz, 3H), 0.88 (d, *J* = 6.9 Hz, 6H), 0.89 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 1.75–1.86 (m, 1H), 2.18–2.29 (m, 1H), 2.28 (s, 3H), 2.37 (dd, *J* = 3.4, 9.6 Hz, 1H), 2.64 (s, 6H), 3.60 (ddd, *J* = 5.2, 7.9, 7.9 Hz, 1H), 4.48 (brd, *J* = 7.9 Hz, 1H, –N*H*), 5.38 (dd, *J* = 9.6, 15.1 Hz, 1H), 5.59 (dd, *J* = 7.9, 15.1 Hz, 1H), 6.93 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ –4.7 ($CH_3$), –4.6 ($CH_3$), 17.3 ($CH_3$), 18.0 ($CH_3$), 18.1 (C), 18.4 ($CH_3$), 20.9 ($CH_3$), 22.3 ($CH_3$), 23.1 ($CH_3$ × 2), 25.2 ($CH_3$ × 3), 27.8 (CH), 33.3 (CH), 58.4 (CH), 61.0 (CH), 67.0 (C), 114.9 (CN), 115.2 (CN), 123.7 (CH), 132.1 (CH × 2), 134.6 (C), 137.9 (CH), 138.7 (C × 2), 142.0 (C); HRMS (ESI-HRMS) m/z calcd for $C_{28}H_{45}N_3O_3NaSSi$ $[M+Na]^+$ 554.2849, found 554.2840.

(±)-**17j**: Colorless oil; FT-IR (neat) 3272, 2959, 2218, 1698, 1605, 1471, 1361, 1256, 1158, 1088, 1013, 836, 772, 666 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 0.39 (s, 3H), 0.41 (s, 3H), 0.66 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.9 Hz, 3H), 0.95 (s, 9H), 1.03 (d, *J* = 6.5 Hz, 6H), 1.76–1.87 (m, 1H), 2.29 (s, 3H), 2.38 (dq, *J* = 1.4, 6.9 Hz, 1H), 2.64 (s, 6H), 2.70 (dd, *J* = 3.8, 10.0 Hz, 1H), 3.82 (dt, *J* = 3.8, 10.0 Hz, 1H), 4.46 (brd, *J* = 10.0 Hz, 1H, –N*H*), 5.38 (ddd, *J* = 1.4, 10.0, 15.1 Hz, 1H), 5.81 (dd, *J* = 6.9, 15.1 Hz, 1H), 6.93 (s, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ –4.5 ($CH_3$ × 2), 17.5 ($CH_3$), 18.1 (C), 19.0 ($CH_3$), 20.9 ($CH_3$), 21.8 ($CH_3$), 21.9 ($CH_3$), 23.2 ($CH_3$ × 2), 25.3 ($CH_3$ × 3), 31.6 (CH), 32.9 (CH), 54.8 (CH), 56.8 (CH), 66.9 (C), 114.0 (CN), 115.0 (CN), 118.3 (CH), 132.0 (CH × 2), 136.0 (C), 138.1 (C), 141.9 (C), 149.3 (CH); HRMS (ESI-HRMS) m/z calcd for $C_{28}H_{45}N_3O_3NaSSi$ $[M+Na]^+$ 554.2849, found 554.2858.

**Methyl (3*E*)(2*R**,5*R**)-2-methyl-5-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-6-phenyl-3- hexenoate [(±)-18g]**

To a solution of (±)-**15g** (20 mg, 0.036 mmol, 1.0 eq.) in methanol (0.50 mL) was added a solution of TASF (12 mg, 0.044 mmol, 1.2 eq.) in methanol (0.50 mL) dropwise over 5 min at 0˚C, and the mixture was stirred at 0˚C for 30 min. The resulting mixture was quenched with phosphate buffer (pH 7.0, 5.0 mL) at 0˚C, and the aqueous phase was extracted with diethyl ether (10 mL × 3). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate, concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane : ethyl acetate = 5 : 1) to give (±)-**18g** (15 mg, 0.36 mmol, 99% yield). Colorless oil; FT-IR (neat) 3300, 2939, 1732, 1605, 1497, 1455, 1324, 1155, 1057, 967, 852, 749, 701, 659 cm$^{-1}$; $^1$H NMR (300 MHz, $CDCl_3$) δ 1.03 (d, *J* = 7.2 Hz, 3H), 2.29 (s, 3H), 2.49 (s, 6H), 2.78 (d, *J* = 6.9 Hz, 2H), 2.86–2.96 (m, 1H), 3.64 (s, 3H), 3.88–3.98 (m, 1H), 4.44 (brd, *J* = 6.5 Hz, 1H, –N*H*), 5.27 (dd, *J* = 7.2, 15.5 Hz, 1H), 5.46 (dd, *J* = 7.2, 15.5 Hz, 1H), 6.87 (s, 2H), 7.04 (dd, *J* = 2.1, 7.6 Hz, 2H), 7.20–7.24 (m, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 16.6 ($CH_3$), 20.9 ($CH_3$), 22.8 ($CH_3$ × 2), 41.9 (CH), 42.1 ($CH_2$), 51.8 (CH), 56.3 (CH), 126.8 (CH), 128.5 (CH × 2), 129.4 (CH × 2), 130.4 (CH), 130.9 (CH), 131.8 (CH × 2), 134.3 (C), 136.2 (C), 138.9 (C × 2), 142.0 (C), 174.4 (C=O); HRMS (ESI-HRMS) m/z calcd for $C_{23}H_{29}NO_4NaS$ $[M+Na]^+$ 438.1715, found 438.1702.

**Methyl (3*E*)(2*R**,5*R**)-2-(2-methylpropyl)-5-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-6-phenyl-3- hexenoate [(±)-18h]**

Synthesis of (±)-**18h** was carried out starting from (±)-**15h** (20 mg, 0.034 mmol) as described for (±)-**18g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 5 : 1) to give (±)-**18h** (14 mg, 0.030 mmol, 90% yield). Colorless crystal: mp 76–77˚C (recrystallized from hexane); FT-IR (neat) 3288, 3025, 2952, 1936, 1735, 1604, 1567, 1494, 1455, 1367, 1317, 1259, 1230, 1147, 1108, 1060, 979, 935, 848, 813, 744 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ 0.77 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H), 1.07–1.17 (m, 1H), 1.19–1.30 (m, 1H), 1.35–1.45 (m, 1H), 2.29 (s, 3H), 2.49 (s, 6H), 2.76 (dd, *J* = 7.2, 13.6 Hz, 1H), 2.82 (dd, *J* = 6.4, 13.6 Hz, 1H), 2.84–2.92 (m, 1H), 3.88–3.97 (m, 1H), 4.49 (brd, *J* = 6.4 Hz, 1H, –N*H*), 5.26–5.36 (m, 2H,), 6.87 (s, 2H), 7.00–7.06 (m, 2H), 7.17–7.28 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 21.0 ($CH_3$), 22.0 ($CH_3$), 22.6 ($CH_3$), 22.9 ($CH_3$ × 2), 25.4 (CH), 41.0 ($CH_2$), 42.3 ($CH_2$), 46.6 (CH), 51.7 (CH), 56.3 (CH), 126.8 (CH), 128.5 (CH × 2), 129.3 (CH × 2), 130.1 (CH), 131.3 (CH), 131.8 (CH × 2), 134.1 (C), 136.1 (C), 138.8 (C × 2), 141.9 (C), 174.1 (C); HRMS (ESI-HRMS) *m/z* calcd for $C_{26}H_{35}NNaO_4S$ $[M+Na]^+$ 480.2185, found 480.2164.

**Methyl (3*E*)(2*S**,5*R**)-2-methyl-5-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-6-phenyl-3- hexenoate [(±)-19g]**

Synthesis of (±)-**19g** was carried out starting from (±)-**16g** (20 mg, 0.036 mmol, 1.0 eq.) as described for (±)-**18g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 5 : 1) to give (±)-**19g** (15 mg, 0.36 mmol, 99% yield). Colorless crystal: mp 70–72 ˚C (recrystallized from hexane); FT-IR (neat) 3289, 2977, 2949, 1731, 1496, 1456, 1377, 1319, 1273, 1244, 1190, 1148, 1049, 977, 939, 852, 751, 696, 663, 597, 538, 518, 474 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 1.05 (d, *J* = 7.2 Hz, 3H), 2.28 (s, 3H), 2.48 (s, 6H), 2.65–2.93 (m, 2H), 2.92 (dq, *J* = 7.2, 7.2 Hz, 1H), 3.62 (s, 3H), 3.87–3.96 (m, 1H), 4.45 (brd, *J* = 6.3 Hz, 1H, –N*H*), 5.29 (ddd, *J* = 0.7, 7.2, 15.5 Hz, 1H), 5.41 (dd, *J* = 7.2, 15.5 Hz, 1H), 6.86 (s, 2H), 7.02–7.06 (m, 2H), 7.17–7.26 (m, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) δ 16.6 ($CH_3$), 20.9 ($CH_3$), 22.9 ($CH_3$ × 2), 42.16 (CH), 42.22 ($CH_2$), 51.8 ($CH_3$), 56.3 (CH), 126.9 (CH), 128.6 (CH × 2), 129.5 (CH × 2), 130.8 (CH), 131.0 (CH), 131.9 (CH × 2), 134.2 (C), 136.1 (C), 138.9 (C × 2), 142.0 (C), 174.4 (C=O); HRMS (ESI-HRMS) m/z calcd for $C_{23}H_{29}NO_4NaS$ $[M+Na]^+$ 438.1715, found 438.1706.

**Methyl (3*E*)(2*S**,5*R**)-2-(2-methylpropyl)-5-[*N*-(2,4,6-trimethylbenzenesulfonyl)amino]-6-phenyl-3- hexenoate [(±)-19h]**

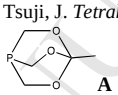
Synthesis of (±)-**19h** was carried out starting from (±)-**16h** (20 mg, 0.034 mmol) as described for (±)-**18g**. Purified by silica gel column chromatography (hexane : ethyl acetate = 5 : 1) to give (±)-**19h** (15 mg, 0.032 mmol, 96% yield). Colorless crystal: mp 105–106 ˚C (recrystallized from hexane); FT-IR (neat) 3297, 2956, 1951, 1733, 1668, 1602, 1558, 1540, 1494, 1455, 1322, 1243, 1151, 1058, 981, 927, 848, 754 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 0.81 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 7.0 Hz, 3H), 1.09–1.18 (m, 1H), 1.30–1.42 (m, 1H), 1.43–1.52 (m, 1H), 2.28 (s, 3H), 2.49 (s, 6H), 2.80 (d, *J* = 6.4 Hz, 1H), 2.89 (dd, *J* = 7.6, 15.6 Hz, 1H), 3.85–3.95 (m, 1H), 4.47 (brd, *J* = 6.4 Hz, 1H, –N*H*), 5.28 (dd, *J* = 8.0, 15.6 Hz, 1H), 5.34 (dd, *J* = 6.8, 15.6 Hz, 1H) 6.88 (s, 2H), 6.99–7.07 (m, 2H), 7.17–7.26 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 21.0 ($CH_3$), 22.3 ($CH_3$), 22.4 ($CH_3$), 23.0 ($CH_3$ × 2), 25.5 (CH), 41.1 ($CH_2$), 42.3 ($CH_2$), 46.8 (CH), 51.7 (CH), 56.2 (CH), 126.8 (CH), 128.5 (CH × 2), 129.4 (CH × 2), 130.2 (CH), 131.5 (CH), 131.8 (CH × 2), 134.1 (C), 136.0 (C), 138.8 (C × 2), 141.9 (C), 174.1 (C=O); HRMS (ESI-HRMS) *m/z* calcd for $C_{26}H_{35}NNaO_4S$ $[M+Na]^+$ 480.2185, found 480.2163.

## Acknowledgement

This work was partly supported by a Grant-in-Aid for Scientific Research of the Ministry of Education of Japan (Grant No. 18550094 in 2006-2007).

## References and notes

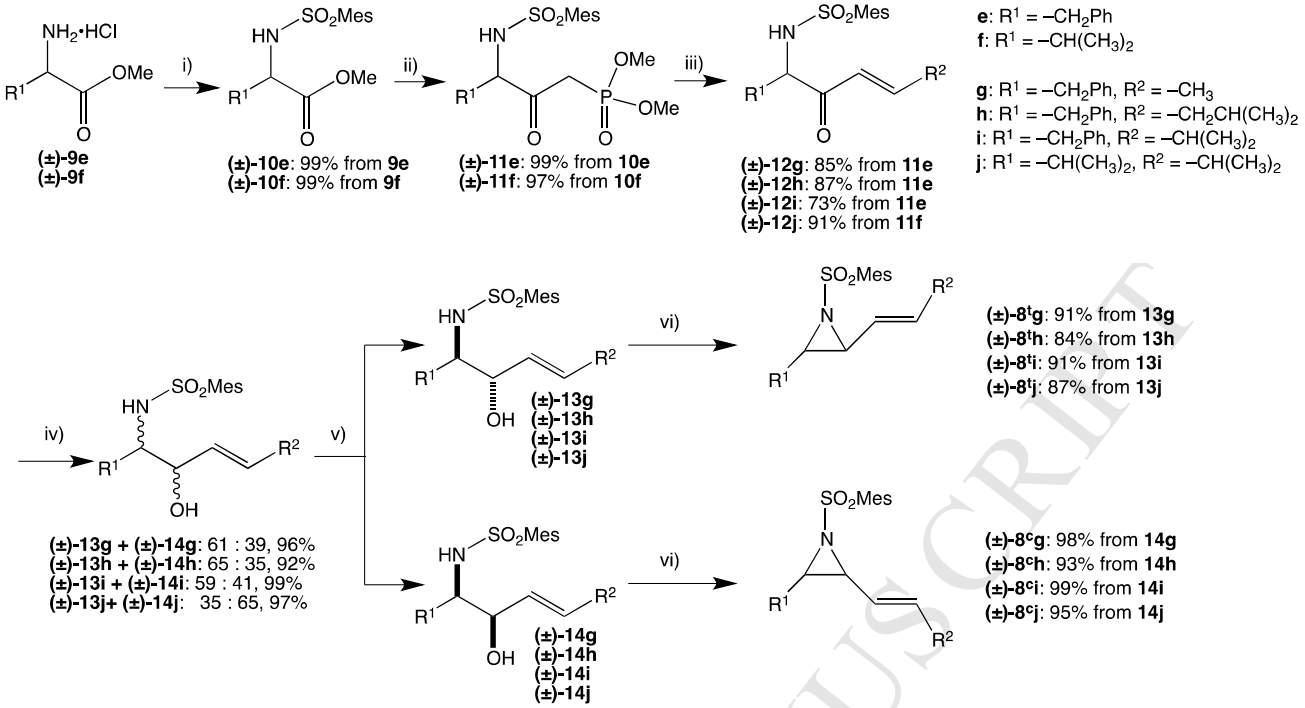

1. (a) Tsuji, J. *"Palladium Reagents and Catalysts"*, John Wiley & Sons, New York, **1995**. (b) Tsuji, J. *"Perspectives in Organopalladium Chemistry for the 21st Century"*, Elsevier, New York, **1999**. (c) Tsuji, J. *"Palladium Reagents and Catalysts: New Perspectives for 21st Century"*, John Wiley & Sons, New York, **2004**. (d) Davies, J. A. in *"Comprehensive Organometallic Chemistry II; Vol.9" (Eds: E. W. Abel, F. G. A. Stone, G. Wilkinson and R. J. Puddephatt)* Elsevier, New York, **1995**, Chapt. 6. (e) Godleski, S. A. in *"Comprehensive Organic Synthesis; Vol.4" (Eds: B. M. Trost and I. Flemming)* Pergamon Press, New York, **1991**, Chapt. 3.3. (f) Tsuji, J. *Tetrahedron* **1986**, *42*, 4361–4401. (g) Trost, B. M. *Acc. Chem. Res*. **1980**, *13*, 385–393.
2. Theoretical studies on the $\eta^3$-allylpalladium complex: (a) Szabó, K. J. *J. Am. Chem. Soc*. **1996**, *118*, 7818–7826. (b) Szabó, K. J. *Chem. Eur. J*. **1997**, *3*, 592–600.
3. Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett*. **1981**, *22*, 2575–2578.
4. (a) Takahashi, T.; Ootake, A.; Tsuji, J.; Tachibana, K. *Tetrahedron* **1985**, *41*, 5747–5754. (b) Takahashi, T.; Miyazawa, M.; Ueno, H.; Tsuji, J. *Tetrahedron Lett*. **1986**, *27*, 3881–3884.
5. Preparation of **3**. (a) Nemoto, H.; Kubota, Y.; Yamamoto, Y. *J. Org. Chem.* **1990**, *45*, 4515–4516. (b) Nemoto, H.; Li, X.; Ma, R.; Suzuki, I.; Shibuya, M. *Tetrahedron Lett*. **2003**, *44*, 73–75. (c) Nemoto, H. Protected Dicyanomethanol (H-MAC-R). *Electronic Encyclopedia of Reagents for Organic Synthesis (e-EROS)* **2007**. (http://onlinelibrary.wiley.com/o/eros/articles/rn00761/frame.html)
   H–MAC–Ac has been commercially available from Sigma-Aldrich since 2013.
6. Nemoto, H.; Ibaragi, T.; Bando, M.; Kido, M.; Shibuya, M. *Tetrahedron Lett*. **1999**, *40*, 1319–1322.
7. When a non-strained (not highly reactive) leaving group such as an alkoxycarbonyl was used, **4** was not effective because the nucleophilicity of a Pd-phosphite complex is generally weaker than that of a phosphine complex. However, 4-methyl-3,5,8-trioxa-1-phosphabicyclo[2.2.2]octane (**A**), a tricyclic phosphine ligand, was effective. Takahashi, T.; Jinbo, Y.; Kitamura, K.; Tsuji, J. *Tetrahedron Lett*. **1984**, *25*, 5921–5924.



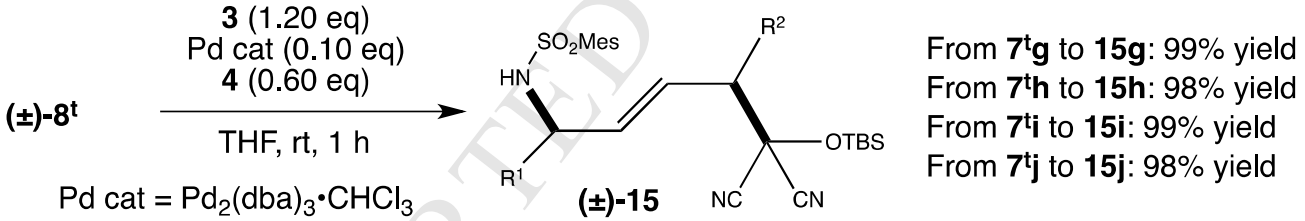
**A**

8. Cone angle for ligands: Bunten, K. A.; Chen, L.; Fernandez, A. L.; Poë A. *J. Coord. Chem. Rev*. **2002**, *233–234*, 41–51.
9. Satake, A.; Shimizu, I.; Yamamoto, A. *Synlett* **1995**, 64–68.
10. Ohno, H.; Mimura, N.; Otaka, A.; Tamamura, H.; Fujii, N.; Ibuka, T. *Tetrahedron* **1997**, *53*, 12933–12946.
11. Sweeney et al mainly reported the reaction of vinylaziridines with copper reagents. Thus, the detail of the palladium-catalyzed reaction such as mol% of tetrakis(triphenylphosphine)palladium, temperature, or equivalents of diethyl malonate were not specified. Cantrill, A. A.; Jarvis, N. A.; Osborn, I. M.; Ouadi, A.; Sweeney, B. J. *Synlett* **1996**, 847.
12. Synthetic application of a MAC reagent with palladium catalyst in high γ-selectivity according to reference 5 was reported. They mentioned that the unmasking step from the MAC moiety to carbonyl functionality proceeded in greater yield under milder conditions than the step for the acidic hydrolysis of the cyanide group. (a) Yamatsugu, K.; Yin, L.; Kamijo, S.; Kimura, Y.; Kanai, M.; Shibasaki, M. *Angew. Chem.* **2008**, *48*, 1070–1076. (b) Yamatsugu, M.; Kanai, M.; Shibasaki, M. *Tetrahedron* **2009**, *65*, 6017–6024.
13. Active methylene and methyne compounds bearing a cyano group as an electron withdrawing group are known to be very palladium-affinitive nucleophiles. (a) Naota, T.; Taki, H.; Mizuno, M.; Murahashi, S.-I. *J. Am. Chem. Soc.* **1989**, *111*, 5954–5955. (b) Nemoto, H.; Kubota, Y.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 1665–1666. (c) Kadota, I.; Shibuya, A.; Gyoung, Y. S.; Yamamoto, Y. *J. Am. Chem. Soc*. **1998**, *120*, 10262–10263. (d) Patil, N. T.; Kadota, I.; Shibuya, A.; Gyoung Y. S.; Yamamoto, Y. *Adv. Synth. Catal*. **2004**, *346*, 800–804.
14. Based on reviews,[1] bases such as sodium hydride might not be essential in the case of Sweeney's reported reaction[11] because the resulting H–NP(O)$Ph_2$ moiety is not highly acidic. Furthermore, they only examined triphenylphosphine but not **4**.
15. The second smallest active methyne compound must be $ROCH(CN)_2$ (MAC reagents), which are smaller than 2-methylmalononitrile. Incidentally, the smallest active methyne must be hydrogen cyanide.
16. Tamamura, H.; Yamashita, M.; Nakajima, Y.; Sakano, K.; Otaka, A.; Ohno, H.; Ibuka, T.; Fujii, N. *J. Chem. Soc., Perkin Trans I* **1999**, 2983–2996.

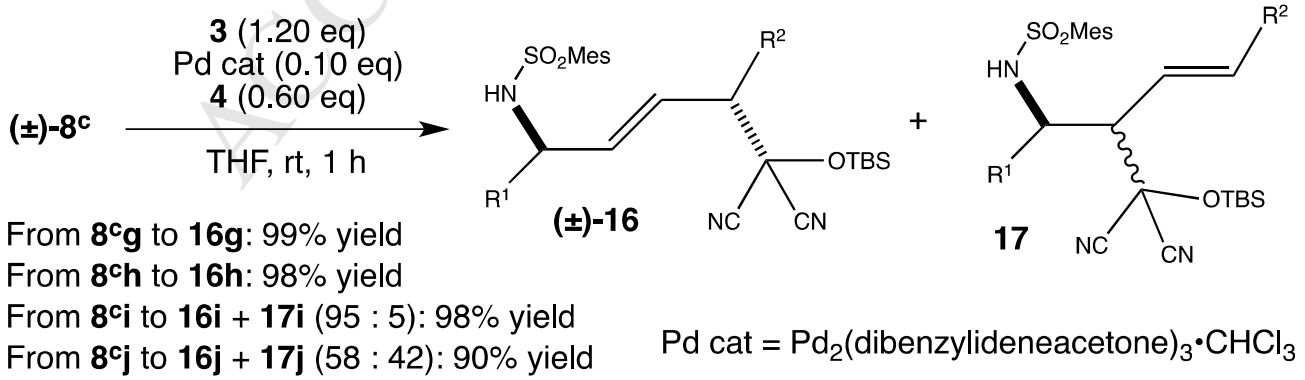
17. Although very high stereoselectivity was observed, the double inversion mechanism has been generally accepted. Therefore, the proposed mechanism for stereochemistry is illustrated in Supplementary Data in order to focus the discussion on the regiochemistry.
18. (a) Nemoto, H.; Ma, R.; Moriguchi, H.; Suzuki, I.; Shibuya, M. *J. Organomet. Chem.* **2000**, *611*, 445–448. (b) Nemoto, H.; Ma, R.; Ibaragi, T.; Suzuki, I.; Shibuya, M. *Tetrahedron* **2000**, *56*, 1463–1468.
19. Scheidt, K. A.; Chen, H.; Follows, B. C.; Chemler, S. R.; Coffey, D. S.; Roush, W. R. *J. Org. Chem.* **1998**, *63*, 6436–6437.
20. Tables for typical $^{1}$H data for **15g–15j** and **16g–16j**, are available in Supplementary Data.
21. Ibuka, T.; Taga, T.; Habashita, H.; Nakai, K.; Tamamura, H.; Fujii, N.; Chounan, Y.; Nemoto, H.; Yamamoto, Y. *J. Org. Chem.* **1993**, *58*, 1207–1214.




**Scheme 1.** Preparation of γ-substituted vinylaziridines. Conditions and reagents: i) $MesSO_2Cl$ (1.2 eq), DMAP (0.10 eq) in pyridine (10 eq), 0 ˚C; ii) BuLi (4.0 eq), $CH_3P(O)(OMe)_2$ (4.0 eq) in THF, –78 ˚C; iii) $R^2CHO$ (1.2 eq), $K_2CO_3$ (1.0 eq) in ethanol, rt; iv) $NaBH_4$ (1.0 eq), $CeCl_3•7H_2O$ (1.0 eq) in methanol, 0 ˚C; v) flash column separation; vi) DEAD (2.5 eq), $PPh_3$ (2.5 eq) in THF, 0 ˚C.




**Scheme 2.** Reaction of γ-substituted *trans*-azidirine $\mathbf{8^t}$ and a masked acyl cyanide reagent **3**




**Scheme 3.** Reaction of γ-substituted *cis*-azidirine $\mathbf{8^c}$ and a masked acyl cyanide reagent **3**

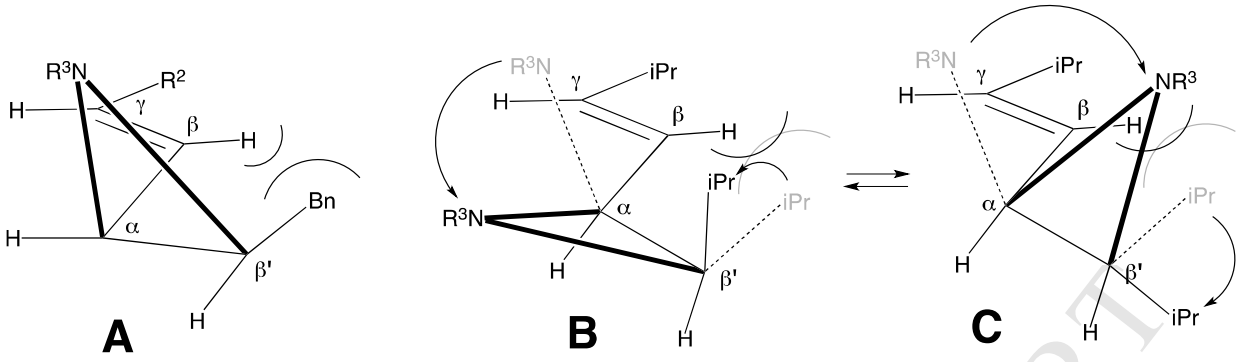



**Figure 2**. Energy minimized conformations **A** (**8$^{c}$g**, **8$^{c}$h** and **8$^{c}$i**) and **B**/**C** (**8$^{c}$j**)

| entry | 6 | ligand | time (min) | Yield of **7** (%) | *E/Z* |
|---|---|---|---|---|---|
| 1 | **6a** | $PPh_3$ | 5 | 93 | 95:5 |
| 2 | **6a** | dppe | 30 | 91 | >99:1 |
| 3 | **6a** | **4** | 5 | 99 | >99:1 |
| 4 | **6a** | $P^nBu_3$ | 60 | 0 | - |
| 5 | **6b** | **4** | 15 | 97 | >99:1 |
| 6 | **6c** | **4** | 15 | 89 | >99:1 |
| 7 | **6d**[a] | **4** | 5 | 89 | >99:1 |

a: diastereomer of **6a** (α,β'-*cis* -isomer)

| Compounds | Coupling Constant |
|---|---|
| **8$^{t}$g / 8$^{c}$g** | 4.5 / 5.5 |
| **8$^{t}$h / 8$^{c}$h** | 4.0 / 5.5 |
| **8$^{t}$i / 8$^{c}$i** | - / 5.5 |
| **8$^{t}$j / 8$^{c}$j** | 4.5 / 7.6 |

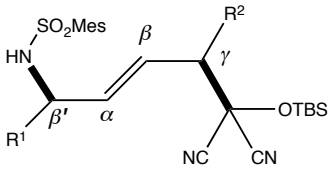
| Compounds | $J_{\beta-\alpha}$ (Hz) | comparison |
|---|---|---|
| **15g/16g** | *6.3/7.6* | $J_{15} < J_{16}$ |
| **15h/16h** | *5.8/6.8* | $J_{15} < J_{16}$ |
| **15i/16i** | *5.2/7.2* | $J_{15} < J_{16}$ |
| **15j/16j** | *4.8/7.9* | $J_{15} < J_{16}$ |

# Palladium-catalyzed highly regio- and stereoselective carbon–carbon bond formation reaction of γ-substituted vinylaziridines with a silylated masked acyl cyanide reagent

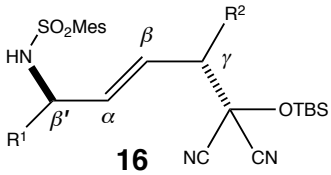
Tomoyuki Kawamura, Nanae Matsuo, Daisuke Yamauchi, Yoo Tanabe, Hisao Nemoto*

E-mail: nem@ph.tokushima-u.ac.jp

Comparison of $^1$H NMR for **15** and **16**




**15**




**16**

**g**: $R^1$ = –$CH_2$Ph, $R^2$ = –$CH_3$
**h**: $R^1$ = –$CH_2$Ph, $R^2$ = –$CH_2CH(CH_3)_2$
**i**: $R^1$ = –$CH_2$Ph, $R^2$ = –$CH(CH_3)_2$
**j**: $R^1$ = –$CH(CH_3)_2$, $R^2$ = –$CH(CH_3)_2$

| Compound | $J_{\beta'-\alpha}$ | $J_{\alpha-\beta}$ | $J_{\beta-\gamma}$ | relative stereochemistry |
|---|---|---|---|---|
| **15g**/**16g** | 6.3/7.6 | 15.5/15.3 | 7.2/8.6 | determined by authentic sample |
| **15h**/**16h** | 5.8/6.8 | 15.3/15.5 | 9.2/9.6 | determined by authentic sample |
| **15i**/**16i** | 5.2/7.2 | 15.3/15.5 | 10.0/10.0 | assumed by mechanism and the value of $J_{\beta'-\alpha}$ |
| **15j**/**16j** | 4.8/7.9 | 15.1/15.1 | 10.0/9.6 | assumed by mechanism and the value of $J_{\beta'-\alpha}$ |
| analysis | $J_{15} < J_{16}$ | trans-olefin | NR | |

NR = no relationship

Typical $^1$H NMR data of **15** and **16**

| | γ | β' | β | α |
|---|---|---|---|---|
| **15g** | 2.61–2.70 (m, 1H) | 3.97–4.06 (m, 1H) | 5.45 (ddd, J = 0.7, 7.2, 15.5 Hz, 1H) | 5.62 (dd, J = 6.3, 15.5 Hz, 1H) |
| **15h** | 2.46–2.58 (m, 1H) | 3.96–4.05 (m, 1H) | 5.24 (ddd, J = 0.8, 9.2, 15.3 Hz, 1H) | 5.71 (dd, J = 5.8, 15.3 Hz, 1H) |
| **15i** | 2.40 (dd, J = 3.4, 10.0 Hz, 1H) | 4.01–4.11 (m, 1H) | 5.49 (ddd, J = 1.4, 10.0, 15.3 Hz, 1H) | 5.73 (dd, J = 5.2, 15.3 Hz, 1H) |
| **15j** | 2.44 (dd, J = 3.4, 10.0 Hz, 1H) | 3.81–3.87 (m, 1H) | 5.43 (ddd, J = 1.7, 10.0, 15.1 Hz, 1H) | 5.70 (dd, J = 4.8, 15.1 Hz, 1H) |
| **16g** | 2.56–2.67 (m, 1H) | 3.88–3.98 (m, 1H) | 5.34 (ddd, J = 1.0, 8.6, 15.3 Hz, 1H) | 5.65 (dd, J = 7.6, 15.3 Hz, 1H) |
| **16h** | 2.52–2.61 (m, 1H) | 3.90–3.99 (m, 1H) | 5.25 (dd, J = 9.6, 15.6 Hz, 1H) | 5.78 (dd, J = 6.8, 15.6 Hz, 1H) |
| **16i** | 2.40–2.44 (m, 1H) | 3.92–4.01 (m, 1H) | 5.47 (ddd, J = 0.7, 10.0, 15.5 Hz, 1H) | 5.75 (dd, J = 7.2, 15.5 Hz, 1H) |
| **16j** | 2.37 (dd, J = 3.4, 9.6 Hz, 1H) | 3.60 (ddd, J = 5.2, 7.9, 7.9 Hz, 1H) | 5.38 (dd, J = 9.6, 15.1 Hz, 1H) | 5.59 (dd, J = 7.9, 15.1 Hz, 1H) |

**Proposed Double Inversion Mechanism**