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Synthesis of the ABCDG ring skeleton of communesin F based on carboxoborylation of 1,3-diene and Bi(OTf)$_3$-catalyzed cyclizations

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ABSTRACT: Communesins, isolated from the mycelium of a strain of *Penicillium* sp., are cytotoxic heptacyclic indole alkaloids bearing a bis-aminal structure and two contiguous quarternary carbon centers. Towards a total synthesis of communesin F, we synthesized a pentacyclic ABCDG ring skeleton via carboxoborylation of 1,3-diene and a Friedel-Crafts-type cyclization, resulting in the formation of azepine ring through a Bi(OTf)$_3$-catalyzed S$_{N}2'$ reaction.

Keywords: communesin/ carboxoborylation/ amidine/ Bi(OTf)$_3$
Introduction

Communesins A and B, which were originally isolated by Numata and co-workers from the mycelium of a strain of *Penicillium* sp. attached to the marine alga *Enteromorpha intestinalis*, are heptacyclic indole alkaloids (Figure 1). Spectroscopic analyses, including nuclear magnetic resonance (NMR) spectroscopy (1H NMR, 13C NMR including 2D NMR) and high-resolution mass spectrometry, have revealed that their structures are quite unique. They are characterized by a heptacyclic skeleton bearing two aminals and two contiguous quaternary carbon centers. To date, nine congeners have been reported, and perophoramidine is also known as a structurally related bis-amidine indole alkaloid. Recently, Tang and co-workers confirmed that communesins can be biosynthetically produced through the coupling of aurantioclavine and tryptamine based on genetic inactivation studies. Communesins show cytotoxicity against P388 lymphocytic leukemia cells (ED$_{50}$ A: 3.5 µg/mL, B: 0.45 µg/mL) and potent insecticidal activity towards silkworms (LD$_{50}$ D: 300 µg/g, E: 80 µg/g). Because of their unique structure and biological activity, many research groups have conducted synthetic studies of communesins in which various synthetic methods were developed. The first racemic total synthesis of communesin F was achieved by Qin and co-workers based on an intramolecular cyclopropanation strategy. Weinreb and Funk also reported total synthesis of communesin F, independently. The first asymmetric total syntheses of communesins A, B and F were accomplished by Ma and co-workers. Asymmetric total syntheses were also reported by Stoltz, Movassaghi, Yang, and Chen, independently. We have also engaged in the development of synthetic strategies for this class of alkaloids including communesins, perophoramidine and aurantioclavine.

Figure 1. Communesins and related alkaloids.
Results and Discussion

Recently, we have developed palladium(Pd)-catalyzed carbosilylation of 1,3-diene with carbamoyl chloride for the synthesis of several spirooxindoles. Extending this reaction, a Pd-catalyzed carboborylation of 1,3-diene was developed for a synthesis of iminoindoline. Considering our developed method, it was envisioned that communesin F would be accessed from a pentacyclic skeleton II through intermediate I by the introduction of an aminoethyl unit and the formation of amidine. The pentacyclic skeleton II would be constructed from a tetracyclic compound IV via III by the introduction of an allyl alcohol unit, resulting in an S_N2’ reaction for the formation of an azepine ring and a reduction of amidine. The tetracyclic compound IV can be synthesized by a carboborylation of 1,3-diene VI and an intramolecular Friedel-Crafts-type reaction of a resultant iminoindoline V. Following this retrosynthetic analysis, we have recently succeeded in the construction of tetracyclic skeleton IV (R = OMe) from diene VI (R = OMe) through iminoindoline V (R = OMe). However, compound 1 could not be converted to compound 2 through removal of the methyl group, although we tried various conditions including BBr_3, BCl_3, AlCl_3, LiCl, Ph_3PLi and pMe_C_6H_4SLi (Scheme 1b). These reaction conditions resulted in the removal of a Cbz group or the decomposition of compound 1. Therefore, we needed to revise our initial synthetic route and planned to employ a 1,3-diene-containing triflate (R = OTf) to avoid a protecting group manipulation. The use of a substrate bearing a triflate group for Pd-catalyzed carboborylation would extend its reaction scope, and it might react itself under the reaction conditions. In the current manuscript, we report the construction of a pentacyclic skeleton of communesin F by extending our strategy based on carboborylation of 1,3-diene.
Scheme 1. (a) Retrosynthesis of communesin F and (b) failed attempt at removing a methyl group from compound 1.

The synthesis started with a removal of a methyl group on a phenolic hydroxyl group. A methoxy aniline derivative 3, which was prepared from t-butyl(3-methoxyphenyl)carbamate in four steps,[30] was treated using BBr₃ to give a phenol (Scheme 2). The resultant phenolic hydroxy group was silylated with tert-butyldimethylsilyl (TBS) chloride and imidazole to give compound 4. A half reduction of a lactone with diisobutylaluminum hydride (DIBAL-H) was followed by Wittig olefination, which gave diene 5 through internal transfer of a TBS group. After the formation of urea by a treatment of phenyl isocyanate, a phenolic hydroxy group was protected as a triflate. A removal of a TBS group was followed by a Mitsunobu reaction with pNsNHBoc[34] to give compound 8, which was converted to carbodiimide 9 through dehydration with CBr₄, PPh₃ and Et₃N.

With carbodiimide 9 containing a diene moiety, we investigated whether the triflate is intact under the reaction conditions of Pd-catalyzed carboxoborylation of 1,3-diene. In the previous literature, there is no report concerning
Pd(II)-catalyzed Miyaura borylation of triflates and diborone without a ligand, but reactions using diphenylphosphinoferrocene\textsuperscript{35} or the reaction of arylbromide have been reported.\textsuperscript{36} Therefore, it was expected that a triflate group would be intact during the carboborylation of 1,3-diene. As expected, the reaction of 9 proceeded smoothly under the established conditions (Pd(OAc)_2, (pinB)_2, xylene, 50°C) to give an allyl borane, which was treated with NaBO_3·4H_2O to give allyl alcohol 10. After silylation of allyl alcohol 10, a tert-butoxyxycarbonyl (Boc) group was introduced to an amidine nitrogen for further transformation. The treatment of compound 11 using tetrabutylammonium fluoride gave an allyl alcohol along with the removal of a triflate group, which was converted to allyl bromide 12 under standard conditions. Unfortunately, the resultant allyl bromide 12 could not be converted to compound 13 through a treatment of Tf_2O and pyridine. On the other hand, when HF·pyridine was used, a triethylsilyl group was selectively removed with the triflate group intact. The resultant allyl alcohol was also converted to allyl bromide 13 containing a triflate group, while a small amount of compound 14 was also obtained through the removal of a Boc group.

Scheme 2. Synthesis of 3,3-disubstituted iminoindoline 10 based on the Pd-catalyzed carboborylation of 1,3-diene.
and its derivatization.

Next, we investigated Friedel-Crafts-type cyclization of allyl bromides 12 and 13 to construct a tetracyclic ABCD ring skeleton. Previously, we have reported the cyclization of compound 15 containing a methoxy group using 10 mol% of Bi(OTf)₃ and 3.5 equivalents of AgOTf (Table 1, entry 1). The reaction gave compound 16a in 49% yield along with 16b in 30% yield. We initially applied these conditions to a cyclization of compound 13 containing a triflate group. However, the reaction gave a complex mixture instead of any cyclized products 17a and 17b (entry 2). On the other hand, the cyclization of compound 12 containing a phenolic hydroxy group proceeded under the same conditions to give compounds 18a and 18b in 63% and 30% yields with excellent stereochemistry, respectively (entry 3). The stereochemistry was determined by a comparison with our previous results and a NOESY experiment of a derivatized compound 28 (Scheme 4, vide infra). When 3.5 equivalents of AgOTf was reduced to 1.2 equivalents, the formation of byproduct 18b was suppressed to 17% yield (entry 4). Finally, the yield of the desired product 18a was improved to 80% yield using 1.05 equivalents of AgOTf (entry 5). AgOTf was essential for this Friedel-Crafts-type reaction (entry 6).

![Diagram of chemical reactions](image)

Table 1. Formation of a tetracyclic ABCD skeleton through a Friedel-Crafts-type reaction.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Starting Material</th>
<th>X equiv</th>
<th>Product 16a (%)</th>
<th>Product 16b (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15 (R = OMe)</td>
<td>3.5</td>
<td>16a: 49%</td>
<td>16b: 30%</td>
</tr>
<tr>
<td>2</td>
<td>13 (R = OTf)</td>
<td>3.5</td>
<td>17a: 0%</td>
<td>17b: 0%*</td>
</tr>
<tr>
<td>3</td>
<td>12 (R = OH)</td>
<td>3.5</td>
<td>18a: 63%</td>
<td>18b: 30%</td>
</tr>
<tr>
<td>4</td>
<td>12 (R = OH)</td>
<td>1.2</td>
<td>18a: 74%</td>
<td>18b: 17%</td>
</tr>
<tr>
<td>5</td>
<td>12 (R = OH)</td>
<td>1.05</td>
<td>18a: 80%</td>
<td>18b: 13%</td>
</tr>
<tr>
<td>6</td>
<td>12 (R = OH)</td>
<td>0</td>
<td>18a: 0%</td>
<td>18b: 0%**</td>
</tr>
</tbody>
</table>

*Complex mixture. **Starting material 12 was recovered in 77% yield.

After the construction of a tetracyclic ABCD ring skeleton containing an amidine, we turned our attention to the
formation of an azepine ring (G ring). A treatment of compound 18a with Tf2O and pyridine gave compound 17a in 91% yield (Scheme 3). To introduce an allyl alcohol unit, Suzuki-Miyaura coupling with vinyl boronic ester 19 was examined. When compound 17a and vinyl boronic ester 19 were treated with a catalytic amount of Pd(dba)2, SPhos and K3PO4, or Pd(PPh3)4 and Na2CO3 in N,N-dimethylformamide (DMF) at 100°C, respectively, these reactions gave the desired product 20 in low yields (Table 2, entries 1 and 2). However, conditions involving Pd(PPh3)4 and Na2CO3 in toluene and ethanol at 100°C improved the yield to 56% (entry 3). The removal of the pNs and trimethylsilyl (TMS) group gave allyl alcohol 21 in 66% yield over two steps. To construct the azepine ring, mesylation of a tertiary alcohol was initially attempted through a treatment using methanesulfonyl chloride (MsCl) and Et3N. However, a dehydration occurred to give diene 23 instead of the desired cyclized product 22. Interestingly, when compound 21 was treated with pyridinium p-toluenesulfonate (PPTS),15 ortho-amide 24 was observed (as assessed using 1H NMR analysis). A related structure was observed in synthetic studies of dehaloperophoramidine reported by Somfai and co-workers.13,14 We considered the thermodynamic stability of possible equilibrium products such as simplified compounds 25, 26 and 27 through density functional theory (DFT) calculations (Figure 2). These calculations revealed that ortho-amide 26 was the most stable isomer among these compounds. These results indicate that the formation of the ortho-amide through acid activation using PPTS from amidine would be a competitive process with the formation of the azepine ring via the SN2 reaction of the tertiary alcohol, and the equilibrium tends to be biased towards the ortho-amides such as compounds 24 and 26. Therefore, we expected that it would be difficult to achieve the formation of azepine 22 from compound 21 containing the amidine moiety.
Scheme 3. Failed attempt at the formation of an azepine ring.

Table 2. Suzuki-Miyaura coupling of compound 17a and boronic acid 19.

<table>
<thead>
<tr>
<th>entry</th>
<th>cat.</th>
<th>ligand</th>
<th>base</th>
<th>solvent</th>
<th>temp.</th>
<th>yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd(dba)$_2$</td>
<td>SPhos</td>
<td>K$_3$PO$_4$</td>
<td>DMF</td>
<td>100 °C</td>
<td>10%</td>
</tr>
<tr>
<td>2</td>
<td>Pd(PPh$_3$)$_4$</td>
<td>—</td>
<td>aq. Na$_2$CO$_3$</td>
<td>DMF</td>
<td>100 °C</td>
<td>28%</td>
</tr>
<tr>
<td>3</td>
<td>Pd(PPh$_3$)$_4$</td>
<td>—</td>
<td>aq. Na$_2$CO$_3$</td>
<td>toluene/ EtOH</td>
<td>100 °C</td>
<td>56%</td>
</tr>
</tbody>
</table>

Figure 2. Comparison of the thermodynamic stability of formable compounds 25, 26 and 27, calculated using Gaussian ‘09 at the B3LYP/6-31G(d) level of theory (DFT).

Therefore, a reduction of amidine 20 was investigated prior to the formation of the azepine ring to avoid the formation of the ortho-amide (Scheme 4). When compound 20 was treated using NaBH$_4$, the desired product was not obtained. In the case of DIBAL-H, the removal of a Boc group occurred instead of the reduction of the amidine. However, in sharp contrast, treatment using catecholborane$^{40}$ gave the desired product 28 in 65% yield as a 3.3:1 mixture of diastereomers. A NOESY experiment indicated that the stereochemistry of the major isomer was a trans-fused structure, which would be epimerized to a cis-fused structure later. Because a reducing reagent approached from the less hindered face, the trans isomer was obtained as a major product in this reaction. After the removal of Boc and the TMS groups, the formation of an azepine ring was investigated again. When compound 29 was treated using MsCl and Et$_3$N,$^{18}$ the reaction gave diene 31 in 48% yield and the desired cyclized product 30 was not detected at all (Table 3, entry 1). When Bi(OTf)$_3$ was employed at $-15^{\circ}$C as a Lewis acid, the reaction proceeded to give the desired product 30 as a major product albeit in low yield (entry 2).$^{41,42}$ The reaction using Bi(OTf)$_3$ at $-40^{\circ}$C gave the desired product 30 in 17% yield with recovery of the starting material (entry 3). However, under room temperature reaction
conditions the starting material 29 was consumed completely to give the desired azepine 30 in 55% yield, while diene 31 was obtained in 34% yield (entry 4). The obtained pentacyclic compound 30 would be useful for further derivatization, and now we are investigating further transformations to achieve a total synthesis of communesin F.


Table 3. Investigation of the formation of the azepine ring.

<table>
<thead>
<tr>
<th>entry</th>
<th>conditions</th>
<th>yields</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MsCl, Et,N, CH₂Cl₂, 0 °C</td>
<td>30: 0%, 31: 48%</td>
</tr>
<tr>
<td>2</td>
<td>Bi(OTf)³ (10 mol%), MS4A, CH₂Cl₂, −15 °C</td>
<td>30: 23%, 31: trace</td>
</tr>
<tr>
<td>3</td>
<td>Bi(OTf)³ (10 mol%), MS4A, CH₂Cl₂, −45 °C</td>
<td>30: 17%, 31: 0%, starting material 29 67%</td>
</tr>
<tr>
<td>4</td>
<td>Bi(OTf)³ (10 mol%), MS4A, CH₂Cl₂, 0 °C to n</td>
<td>30: 55%, 31: 34%</td>
</tr>
</tbody>
</table>

In summary, we have investigated the synthesis of a pentacyclic ABCDG ring skeleton of communesin F based on carboborylation of 1,3-diene, a Bi(OTf)³-catalyzed Friedel-Crafts-type reaction and azepine ring formation. It is interesting that a triflate group was intact under the conditions required for Pd-catalyzed carboborylation of 1,3-diene. Additionally, it was essential that the resultant amidine was reduced prior to the formation of the azepine ring through Bi(OTf)³-catalyzed cyclization to avoid an undesired formation of ortho-amide. We are currently investigating further transformation of the pentacyclic compound to complete the synthesis of communesin F.

Experimental Procedure
**General.** All non-aqueous reactions were carried out under a positive pressure of argon in over-dried glassware. Analytical thin-layer chromatography was performed using Silica gel 60 plates (Merck, Darmstadt, Germany). Silica gel column chromatography was performed using Kanto silica gel 60 (particle size 63–210 μm, Kanto, Tokyo, Japan) and Chromatorex BW-300 (Fuji syliesia, Aichi, Japan). Proton nuclear magnetic resonance (1H NMR) spectra were recorded using a JNM-ECA 500 (JEOL, Tokyo, Japan) at 500 MHz or a JNM-AL 400 (JEOL) at 400 MHz. Chemical shifts were reported relative to Me4Si (δ 0.00) in CDCl3 or the residual solvent peak in C6D6 (δ 7.16). Multiplicity was indicated by one or more of the following: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); br (broad). Carbon nuclear magnetic resonance (13C NMR) spectra were recorded using a JNM-ECA 500 at 126 MHz or a JNM-AL 400 at 100 MHz. Chemical shifts were reported relative to CDCl3 (δ 77.0) or C6D6 (δ 128.0). Infrared spectra were recorded using a FT/IR-4100 Fourier-transform infrared spectrometer (JASCO, Tokyo, Japan) with ATR (attenuated total reflectance). Low and high resolution mass spectra were recorded using a JMS-700 mass spectrometer (JEOL) for FAB-MS and a LCMS-IT-TOF (Shimadzu, Kyoto, Japan) for ESI-MS.

**Experimental procedures and spectroscopic data.**

![Diagram](image)

Silyl ether 4: To a solution of aniline 3 (2.06 g, 9.40 mmol) in CH2Cl2 (94.0 mL) was added a solution of BBr3 (25.0 g, 94.0 mmol) in CH2Cl2 (94.0 mL) at −78 °C. The mixture was stirred at −78 °C for 20 min, and then warmed to room temperature. After 2 h, saturated aqueous NaHCO3 and 1M aqueous NaOH were added to the reaction mixture until the mixture became basic. The mixture was extracted with EtOAc. The combined organic layers were washed with brine, and dried over Na2SO4. Concentration under reduced pressure gave a crude demethylated lactone.

To a solution of the above crude lactone in anhydrous DMF (20.0 mL) were added TBSCI (2.80 g, 18.8 mmol) and imidazole (1.90 g, 28.2 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h. After addition of water, the mixture was extracted with Et2O. The combined organic layers were washed with brine and dried over Na2SO4. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-40% EtOAc/hexane) gave silyl ether 4 (1.88 g, 63% in 2 steps) as a pale yellow solid: 1H NMR (500 MHz, CDCl3) δ 6.99 (dd, 1H, J = 8.0, 8.0 Hz), 6.35 (dd, 1H, J = 8.0, 1.1 Hz), 6.27 (dd, 1H, J = 8.0, 1.1 Hz), 6.06 (dd, 1H, J = 1.7, 1.2 Hz), 4.53 (dd, 2H, J = 6.3, 5.8 Hz), 3.76 (br, 2H), 2.72 (dd, 2H, J = 6.3, 5.7 Hz), 0.94 (s, 9H), 0.21 (s, 6H); 13C NMR (126 MHz, CDCl3) δ 164.4, 156.1, 153.1, 144.0, 129.8, 120.3, 115.5, 108.7, 108.6, 66.5, 28.2, 25.6, 18.1, -4.1; IR (ATR, cm⁻¹) 3369, 2954, 2891, 2857, 2816, 1625, 1580, 1462, 1398, 1302, 1257, 1219, 1081, 1020; MS (FAB) m/z 320 [M + H]+; HRMS caled for C17H26NO3Si [M + H]+ 320.1682; Found: m/z 320.1685.
(E)-Diencyaniline 5: To a solution of silyl ether 4 (1.25 g, 3.91 mmol) in CH₂Cl₂ (40.0 mL) was added DIBAL-H (1M in toluene, 7.80 mL, 7.80 mmol) at −78 °C. After the mixture was stirred at −78 °C for 2 h, saturated aqueous Na/K tartrate was added to the reaction solution. The resultant mixture was stirred vigorously at room temperature for 2 h, and extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. Concentration under reduced pressure gave a crude acetal.

To a suspension of MePPh₃Br (4.89 g, 13.7 mmol) in anhydrous THF (25.0 mL) was added KHMDS (1M solution in THF; 12.0 mL, 11.7 mmol) at 0 °C, and the mixture was stirred at 0 °C for 30 min. To the yellow mixture was then added a solution of the above crude acetal in anhydrous THF (15 mL) via cannula. The reaction mixture was stirred at room temperature for 2 h. After addition of water, the resultant mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-40% EtOAc/hexane) gave (E)-diencyaniline 5 (963.1 mg, 77% in 2 steps) as a yellow oil: ¹H NMR (500 MHz, CDCl₃) δ 6.95 (dd, 1H, J = 8.0, 8.0 Hz), 6.77 (ddd, 1H, J = 16.9, 10.9, 10.3 Hz), 6.36 (dd, 1H, J = 8.0, 0.8 Hz), 6.29 (d,1H, J = 11.1 Hz), 6.25 (dd, 1H, J = 10.3 Hz), 5.27 (dd, 1H, J = 16.9, 1.2 Hz), 5.24 (d, 1H, J = 10.3 Hz), 3.75 (br, 1H), 3.63 (br, 1H), 3.60 (br, 2H), 2.98 (br, 1H), 2.38 (br, 1H), 0.88 (s, 9H), 0.08 (s, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 154.9, 144.7, 136.6, 132.4, 132.1, 128.7, 119.3, 115.8, 106.9, 106.0, 60.6, 33.3, 25.7, 18.1, −5.5; IR (ATR, cm⁻¹) 3332, 2954, 2857, 1659, 1550, 1524, 1446, 1420, 1296, 1250, 1207, 1139, 1054, 962; MS (FAB) m/z 320 [M + H]⁺; HRMS calcd for C₁₄H₂₄NO₂Si [M + H]⁺ 320.2046; Found: m/z 320.2045.

(E)-Diencylaniline 6: To a solution of (E)-diencyaniline 5 (847.9 mg, 2.65 mmol) in CH₂Cl₂ (26.0 mL) was added phenyl isocyanate (317.0 µL, 2.92 mmol) at 0 °C. The mixture was stirred at 0 °C for 13 h. After addition of water, the reaction mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by short column chromatography on silica gel (10-20% EtOAc/hexane) gave a crude urea as a white solid.

To a solution of the above crude urea in CH₂Cl₂ (50.0 mL) were added Et₃N (2.10 mL, 15.1 mmol) and PhNTf₂ (6.15 g, 17.2 mmol) in some portions. The resultant solution was refluxed at 55 °C for 3 days. The reaction mixture was then cooled to room temperature. After addition of saturated aqueous NH₄Cl, the mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-20% EtOAc/hexane) gave (E)-diencylaniline 6 (1.37 g, 90% in 2 steps) as a pale yellow solid: ¹H NMR (500 MHz, CDCl₃) δ 8.21 (dd, 1H, J = 8.3, 0.9 Hz), 7.39 (br, 1H), 7.34-7.30 (m, 5H), 7.13-7.09 (m, 1H), 9.97 (dd, 1H, J = 8.3, 0.9 Hz), 6.69 (ddd, 1H, J = 16.6, 10.9, 10.3 Hz), 6.65 (br, 1H), 6.21 (d, 1H, J = 11.1 Hz), 5.38-5.34 (m, 2H), 3.71-3.69 (m, 1H), 3.55-3.51 (m, 1H), 2.97-2.95 (m, 1H), 2.39-2.36 (m, 1H), 0.83 (s, 9H), 0.02 (s, 6H); ¹³C NMR (126 MHz, CDCl₃) δ 152.6, 147.2, 138.8, 137.6, 137.1, 131.4, 129.7, 129.3, 128.9, 126.8, 124.4, 121.4, 121.1, 120.6, 119.7, 118.4 (q, J = 321 Hz), 115.1, 61.6, 55.0, 25.9, 18.5, −5.5; IR (ATR, cm⁻¹) 3332, 2954, 2857, 1659, 1550, 1524, 1446, 1420, 1296, 1250, 1207, 1139, 1054, 962; MS
(FAB) m/z 571 [M + H]+; HRMS cale for C26H34F3N2O5Si [M + H]+ 571.1910; Found: m/z 570.1910.

(E)-Diennyalcohol 7: To a solution of (E)-diennyurea 6 (42.7 mg, 0.0748 mmol) in THF (1.0 mL) was added TBAF (1M in THF, 83.0 µL, 0.0823 mmol) at 0 °C. The mixture was stirred at 0 °C for 1 h. After addition of saturated aqueous NH4Cl, the mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na2SO4. After concentration under reduced pressure, purification by flash column chromatography on silica gel (10-40% EtOAc/hexane) gave (E)-diennyalcohol 7 (35.3 mg, quant.) as a pale yellow solid: 1H NMR (500 MHz, CDCl3) δ 8.25 (d, 1H, J = 8.6 Hz), 7.77 (br, 1H), 7.32-7.18 (m, 5H), 7.18 (br, 1H), 7.07 (dd, 1H, J = 7.1, 6.9 Hz), 6.94 (d, 1H, J = 8.3 Hz), 6.72 (ddd, 1H, J = 16.9, 10.9, 10.3 Hz), 6.24 (d, 1H, J = 10.9 Hz), 5.39-5.33 (m, 2H), 3.81 (br, 1H), 3.46 (br, 1H), 3.04 (br, 1H), 2.35 (d, 1H, J = 14.6 Hz), 2.23 (br, 1H); 13C NMR (126 MHz, CDCl3) δ 153.2, 147.3, 139.3, 137.9, 137.8, 131.3, 129.2, 129.1, 129.1, 126.1, 124.1, 121.4, 120.9, 119.6, 118.4 (q, J = 321 Hz), 114.8, 60.2, 34.2; IR (ATR, cm⁻¹) 3337, 3010, 2926, 1670, 1579, 1550, 1446, 1420, 1297, 1210, 1138, 1051, 963; MS (FAB) m/z 457 [M + H]+; HRMS cale for C20H28F2N2O5Si [M + H]+ 457.1045; Found: m/z 457.1042.

(E)-Diennyurea 8: To a solution of (E)-diennyalcohol 7 (992.0 mg, 2.17 mmol), pNsNHBOc (786.0 mg, 2.60 mmol) and PPh3 (682.0 mg, 2.60 mmol) in THF (12.0 mL) was added a solution of di-tert-butyl azodicarboxylate (598.7 mg, 2.60 mmol) in THF (10.0 mL). The mixture was stirred at room temperature for 13.5 h. After addition of saturated aqueous NH4Cl, the mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na2SO4. After concentration under reduced pressure, purification by flash column chromatography on silica gel (10-40% EtOAc/hexane) gave the mixture of (E)-diennyurea 8 and pNsNHBOc. The mixture was dissolved in CHCl3, washed with 1M aqueous NaOH and brine, dried over Na2SO4. Concentration under reduced pressure gave (E)-diennyurea 8 (1.43 g, 89%) as a pale yellow solid: 1H NMR (500 MHz, CDCl3) δ 8.35-8.32 (m, 3H), 8.04 (d, 2H, J = 9.1 Hz), 7.47 (br, 1H), 7.37-7.29 (m, 5H), 7.17 (br, 1H), 7.13-7.09 (m, 1H), 6.98 (d, 1H, J = 8.3 Hz), 6.79 (ddd, 1H, J = 16.3, 10.9, 10.6 Hz), 6.24 (d, 1H, J = 10.9 Hz), 5.42-5.38 (m, 2H), 3.88-3.78 (m, 2H), 3.15-3.09 (m, 1H), 2.76-2.70 (m, 1H), 1.32 (s, 9H); 13C NMR (126 MHz, CDCl3) δ 152.6, 150.9, 150.5, 147.3, 145.1, 138.5, 138.4, 137.7, 131.3, 129.4, 129.1, 128.1, 125.9, 124.6, 124.1, 122.6, 121.3, 120.0, 118.4 (q, J = 321 Hz), 115.1, 86.5, 46.2, 33.4, 27.9; IR (ATR, cm⁻¹) 3349, 2929, 2854, 1732, 1668, 1534, 1446, 1420, 1368, 1351, 1291, 1249, 1212, 1139, 1055, 961; MS (FAB) m/z 741 [M + H]+; HRMS cale for C31H32F3N4O10S2 [M + H]+ 741.1512; Found: m/z 741.1512.
(E)-Dienylcarbodiimide 9: To a solution of (E)-dienylurea 8 (62.5 mg, 0.0844 mmol) and PPh₃ (73.5 mg, 0.270 mmol) in CH₂Cl₂ (2.0 mL) were added Et₃N (47.0 µL, 0.338 mmol) and CBr₄ (83.9 mg, 0.253 mmol) at 0 °C. The mixture was stirred at 0 °C for 2.5 h. After concentration of the mixture under reduced pressure, purification of the residue by flash column chromatography on neutral silica gel (5-20% EtOAc/hexane) gave (E)-dienylcarbodiimide 9 (56.4 mg, 92%) as a pale-yellow oil. The product was not stable, thus it was used for the next reaction immediately:

1H NMR (500 MHz, CDCl₃) δ 8.33 (d, 2H, J = 8.9 Hz), 8.07 (d, 2H, J = 8.8 Hz), 7.37-7.27 (m, 4H), 7.19 (dd, 1H, J = 7.5, 7.4 Hz), 7.16-7.13 (m, 3H), 6.80 (ddd, 1H, J = 16.6, 10.6, 10.6 Hz), 6.25 (d, 1H, J = 11.2 Hz), 5.37-5.32 (m, 2H), 3.89 (dd, 2H, J = 7.2, 7.2 Hz), 2.99 (br, 2H), 1.31 (s, 9H); 13C NMR (126 MHz, CDCl₃) δ 150.3, 150.2, 147.6, 145.4, 139.3, 137.3, 137.2, 132.4, 132.1, 131.1, 129.5, 129.3, 129.1, 127.9, 125.9, 124.9, 124.4, 123.9, 121.6, 118.4 (q, J = 321 Hz), 118.2, 85.2, 45.9, 33.4, 27.7; IR (ATR, cm⁻¹) 3105, 2938, 2857, 2141, 1731, 1591, 1563, 1533, 1476, 1452, 1421, 1366, 1351, 1285, 1250, 1213, 1137, 909. (Compound 9 was too unstable to measure HRMS)

2-Iminoindoline 10: To a solution of carbodiimide 9 (56.4 mg, 0.0780 mmol) in anhydrous xylene (1.0 mL) were added bis(pinacolato)diboron (39.6 mg, 0.156 mmol) and Pd(OAc)₂ (3.5 mg, 0.0156 mmol) and the reaction atmosphere was replaced by the Ar atmosphere. After addition of water (1.0 mL) and sodium perborate tetrahydrate (72.0 mg, 0.468 mmol), the mixture was stirred vigorously at room temperature for 1 h. The mixture was then extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (20-60% EtOAc/hexane) gave 2-iminoindoline 10 (42.4 mg, 73%) as a yellow oil: 1H NMR (500 MHz, CDCl₃) δ 8.26 (d, 2H, J = 8.9 Hz), 7.94 (d, 2H, J = 8.9 Hz), 7.79 (d, 2H, J = 8.0 Hz), 7.40-7.34 (m, 4H), 7.13 (dd, 1H, J = 7.5, 7.4 Hz), 6.98 (br, 1H), 6.93-6.90 (m, 1H), 6.07 (ddd, 1H, J = 15.8, 5.2, 4.8 Hz), 5.78 (d, 1H, J = 16.0 Hz), 4.23 (d, 2H, J = 4.9 Hz), 3.45 (ddd, 1H, J = 14.0, 11.8, 4.0 Hz), 3.22 (ddd, 1H, J = 14.3, 12.0, 4.3 Hz), 2.89 (ddd, 1H, J = 12.6, 12.6, 4.3 Hz), 2.54 (ddd, 1H, J = 12.6, 12.4, 4.0 Hz), 1.94 (br, 1H), 1.31 (s, 9H); 13C NMR (126 MHz, CDCl₃) δ 170.5, 158.9, 150.3, 150.0, 145.1, 144.9, 138.6, 133.2, 131.1, 129.2, 129.1, 127.6, 127.5, 124.1, 123.9, 120.0, 118.5 (q, J = 320 Hz), 117.9, 114.4, 85.7, 62.8, 59.0, 43.4, 33.0, 27.7; IR (ATR, cm⁻¹) 3380, 3106, 2936, 2877, 1732, 1561, 1534, 1439, 1420, 1349, 1247, 1213, 1138, 1083, 1014, 907; MS (FAB) m/z 741 [M + H]⁺; HRMS calcd for C₂₃H₂₅F₃NaO₁₀S₂ [M + H]⁺ 741.1512; Found: m/z 741.1508.
N-Boc-iminoindoline 11: To a solution of 2-iminoindoline 10 (39.4 mg, 0.0532 mmol) in CH₂Cl₂ (1.0 mL) were added Et₃N (23.0 µL, 0.160 mmol) and TESCl (16.0 µL, 0.106 mmol) at 0 °C. The mixture was stirred at room temperature for 2 h. After addition of water, the mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by short column chromatography on neutral silica gel (10-30% EtOAc/hexane) gave a crude TES-protected iminoindoline. To a solution of the above crude iminoindoline in CH₂Cl₂ (1.0 mL) were added TBAF (48.1 µL, 0.0481 mmol) at 0 °C. The mixture was stirred at room temperature for 1.5 h. After concentration of the resultant mixture under reduced pressure, purification of the residue by flash column chromatography on silica gel (10-30% EtOAc/hexane) gave N-Boc-iminoindoline 11 (33.7 mg, 84% in 2 steps) as a colorless oil: ¹H NMR (500 MHz, CDCl₃) δ 8.26 (d, 2H, J = 8.9 Hz), 8.05 (d, 2H, J = 8.8 Hz), 7.73 (d, 1H, J = 8.0 Hz), 7.41 (dd, 1H, J = 8.6, 8.3 Hz), 7.31 (dd, 2H, J = 7.8, 7.7 Hz) 7.12 (d, 1H, J = 8.3 Hz), 7.06-7.02 (m, 3H), 5.93 (d, 1H, J = 15.5 Hz), 5.66 (d, 1H, J = 15.5 Hz), 4.17 (d, 2H, J = 4.3 Hz), 3.85-3.79 (m, 1H), 3.65-3.62 (m, 1H), 2.70-2.63 (m, 2H), 1.27 (s, 9H), 1.18 (s, 9H), 0.92 (dd, 9H, J = 8.0, 7.8 Hz), 0.57 (q, 6H, J = 7.8 Hz); ¹³C NMR (126 MHz, CDCl₃) δ 153.2, 150.2, 150.1, 149.0, 147.9, 145.9, 145.6, 143.5, 131.5, 130.5, 129.4, 129.1, 128.7, 123.9, 123.8, 122.1, 120.5, 118.3 (q, J = 321 Hz), 115.8, 114.1, 85.3, 84.8, 62.6, 54.0, 43.2, 34.7, 27.7, 27.4, 6.7, 4.3; IR (ATR, cm⁻¹) 2955, 2876, 1731, 1698, 1617, 1594, 1535, 1456, 1421, 1370, 1348, 1287, 1251, 1218, 1141, 1046, 1014, 917, 822; MS (FAB) m/z 955 [M + H]⁺; HRMS calcd for C₃₅H₄₆F₄N₂O₁₂S₂Si [M + H]⁺ 955.2901; Found: m/z 955.2900.

Allyl bromide 12: To a solution of N-Boc-iminoindoline 11 (21.9 mg, 0.0229 mmol) in THF (0.5 mL) was added TBAF (48.1 µL, 0.0481 mmol) at 0 °C. The mixture was stirred at room temperature for 30 min. After addition of saturated aqueous NH₄Cl, the mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (20-60% EtOAc/hexane) gave an allyl alcohol (15.1 mg, 93%) as a pale yellow oil: ¹H NMR (500 MHz, CDCl₃) δ 8.24 (d, 2H, J = 8.8 Hz), 8.07 (d, 2H, J = 8.8 Hz), 7.29 (dd, 2H, J = 7.5, 7.2 Hz), 7.19 (d, 1H, J = 7.7 Hz), 7.13-7.09 (m, 1H) 7.04-6.99 (m, 3H), 6.59 (d, 1H, J = 8.0 Hz), 6.03 (d, 1H, J = 15.1 Hz), 5.77 (d, 1H, J = 15.4 Hz), 4.09 (br, 2H), 3.86-3.80 (m, 1H), 3.69-3.83 (m, 1H), 2.78 (ddd, 1H, J = 12.3, 12.1, 4.6 Hz), 2.58 (ddd, 1H, J = 12.1, 12.0, 4.3 Hz), 1.27 (s, 9H), 1.21 (s, 9H); ¹³C NMR (126 MHz, CDCl₃) δ 156.0, 152.7, 150.3, 156.0, 152.7, 150.3.
The combined organic layers were washed with brine, was stirred at room temperature for 15 min. After addition of water, the mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (10-40% EtOAc/hexane) gave allylbromide 12 (180.3 mg, 98%) as a white solid: ¹H NMR (500 MHz, CDCl₃) δ 8.26 (d, 2H, J = 8.6 Hz), 8.08 (d, 2H, J = 8.8 Hz), 7.32 (dd, 2H, J = 8.0, 7.7 Hz), 7.32-7.27 (m, 1H), 7.21-7.17 (m, 1H) 7.07-7.02 (m, 3H), 6.63 (d, 1H, J = 8.0 Hz), 6.05 (d, 1H, J = 15.2 Hz), 5.87-5.81 (m, 1H), 3.96-3.89 (m, 2H), 3.82 (ddd, 1H, J = 14.7, 11.1, 4.6 Hz), 3.67 (dd, 1H, J = 12.0, 11.2 Hz), 2.77 (dd, 1H, J = 12.3, 10.9 Hz), 2.58 (ddd, 1H, J = 12.3, 12.0, 4.3 Hz), 1.29 (s, 9H), 1.20 (s, 9H); ¹³C NMR (126 MHz, CDCl₃) δ 154.8, 152.2, 150.3, 150.2, 149.2, 148.3, 145.5, 142.4, 134.6, 130.1, 129.4, 129.1, 126.8, 123.8, 120.5, 114.8, 112.8, 107.4, 107.3, 85.3, 84.2, 53.5, 43.8, 34.8, 32.1, 27.8, 27.4; IR (ATR, cm⁻¹) 3445, 2980, 1729, 1695, 1535, 1450, 1360, 1352, 1270, 1085, 891, 709, 691. The mixture was stirred at 0 °C for 30 min. After addition of water, the mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (10-60% EtOAc/hexane) gave a tetracyclic compound 18a (215.8 mg, 80%) as a yellow oil: ¹H NMR (500 MHz, CDCl₃) δ 8.21 (d, 2H, J = 8.8 Hz), 7.89 (d, 2H, J = 8.9 Hz), 7.52 (d, 1H, J = 8.3 Hz), 7.41 (dd, 1H, J = 7.8, 1.1 Hz), 7.36 (dd, 1H, J = 7.5, 7.4 Hz), 7.24 (ddd, 1H, J = 8.3, 8.3, 0.8 Hz), 7.18 (dd, 1H, J = 7.5, 7.4 Hz), 7.13 (d, 1H, J = 7.4 Hz), 6.69 (d, 1H, J = 8.0 Hz), 6.48 (ddd, 1H, J = 17.4, 10.0, 9.1 Hz), 5.81 (d, 1H, J = 9.1 Hz), 5.67 (d, 1H, J = 17.5 Hz), 4.00 (d, 1H, J = 9.7 Hz), 3.57-3.50 (m, 1H), 3.26-3.20 (m, 1H), 2.19-2.11 (m, 2H), 1.70 (s, 9H), 1.26 (s, 9H); ¹³C NMR (126 MHz, CDCl₃) δ 163.0, 152.9, 150.2, 149.9, 149.3, 145.0, 143.6, 142.9, 136.2, 130.7, 129.5, 128.6, 126.5, 126.0, 125.8, 125.1, 124.7, 123.8, 114.5, 114.2, 108.0, 85.1, 84.2, 50.1, 47.9, 43.8, 28.2, 27.7, 27.3; IR (ATR, cm⁻¹) 3449, 2979, 2919, 1731, 1654, 1599, 1533, 1460, 1368, 1348, 1282, 1236, 1148, 1088, 889; MS (FAB) m/z 691 [M + H]⁺; HRMS calcd for C₃₅H₃₉N₄O₇S [M + H]⁺ 691.2438; Found: m/z 691.2439.
Triflate 17a: To a solution of tetracyclic compound 18a (213.0 mg, 0.308 mmol) in CH₂Cl₂ (5.0 mL) were added pyridine (87.3 µL, 1.08 mmol) and Tf₂O (103.5 µL, 0.616 mmol) at 0 °C. The mixture was stirred at 0 °C for 2.5 h. After addition of water, the mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-20% EtOAc/hexane) gave triflate 17a (230.3 mg, 91%) as a yellow oil: 1H NMR (500 MHz, CDCl₃) δ 8.24 (d, 2H, J = 8.6 Hz), 7.97 (d, 1H, J = 8.3 Hz), 7.91 (d, 2H, J = 8.9 Hz), 7.45 (dd, 1H, J = 8.6, 8.3 Hz), 7.37-7.32 (m, 2H), 7.23-7.14 (m, 3H), 6.28 (ddd, 1H, J = 16.9, 10.0, 9.8 Hz), 5.55 (d, 1H, J = 10.0 Hz), 5.30 (d, 1H, J = 16.9 Hz), 3.88 (d, 1H, J = 9.7 Hz), 3.53-3.49 (m, 1H), 3.38-3.32 (m, 1H), 2.26-2.22 (m, 2H), 1.70 (s, 9H), 1.27 (s, 9H); 13C NMR (126 MHz, CDCl₃) δ 162.3, 150.2, 149.7, 149.1, 147.1, 145.2, 144.5, 143.4, 133.6, 131.0, 129.5, 128.4, 126.8, 126.3, 125.7, 125.5, 123.8, 121.5, 119.5, 118.2 (q, J = 318 Hz), 114.9, 114.3, 85.3, 84.8, 51.0, 48.1, 43.2, 28.1, 27.8, 27.6; IR (ATR, cm⁻¹) 2982, 2933, 1729, 1661, 1534, 1455, 1423, 1369, 1364, 1291, 1217, 1143, 1086, 1033, 922; MS (FAB) m/z 823 [M + H]^+; HRMS calcd for C₃₆H₃₆F₃N₄O₁₅S₂ [M + H]^+ 823.1931; Found: m/z 823.1929.

Coupling product 20: To a solution of triflate 17a (30.0 mg, 0.0365 mmol) and vinyl boronate 19 (20.8 mg, 0.0730 mmol) in toluene (1.0 mL) and EtOH (0.1 mL) were added 0.5 M aqueous Na₂CO₃ (220.0 µL, 0.110 mmol) and Pd(PPh₃)₄ (4.2 mg, 3.65×10⁻³ mmol). The reaction atmosphere was replaced by the Ar atmosphere, and the mixture was stirred at 100 °C for 7 h. After the reaction mixture was then cooled to room temperature, the resultant mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-20% EtOAc/hexane) gave coupling product 20 (16.9 mg, 56%) as a yellow oil: 1H NMR (500 MHz, CDCl₃) δ 8.21 (d, 2H, J = 8.9 Hz), 7.86 (d, 2H, J = 9.2 Hz), 7.35-7.31 (m, 5H), 7.18-7.17 (m, 2H), 6.90 (d, 1H, J = 15.5 Hz), 6.30 (ddd, 1H, J = 16.9, 10.1, 10.0 Hz), 6.13 (d, 1H, J = 15.7 Hz), 5.48 (dd, 1H, J = 10.0, 1.5 Hz), 5.27 (d, 1H, J = 16.9 Hz), 3.85 (d, 1H, J = 10.0 Hz), 3.41 (ddd, 1H, J = 14.3, 13.7, 4.0 Hz), 3.26-3.19 (m, 1H), 2.29 (ddd, 1H, J = 12.9, 12.8, 5.5 Hz), 2.16 (ddd, 1H, J = 12.9, 12.0, 4.0 Hz), 1.67 (s, 9H), 1.68 (s, 3H), 1.30 (s, 3H), 1.29 (s, 9H), 0.15 (s, 9H); 13C NMR (126 MHz, CDCl₃) δ 164.3, 149.8, 149.6, 149.7, 145.2, 144.1, 142.6, 139.0, 136.1, 134.6, 129.4, 129.0, 128.2, 126.7, 126.3, 125.7, 125.3, 125.0, 123.8, 123.7, 122.5, 122.4, 113.5, 85.1, 84.0, 74.0, 51.5, 48.1, 44.3, 30.1,
30.1, 28.2, 27.9, 2.6; IR (ATR, cm−1) 2978, 1727, 1655, 1575, 1533, 1474, 1452, 1368, 1347, 1291, 1249, 1150, 1087, 1034, 840, 748, 713, 685, 628, 602; MS (FAB) m/z 831 [M + H]+; HRMS calcd for C_{43}H_{55}N_{4}O_{9}SSi [M + H]+ 831.3459; Found: m/z 831.3448.

Aminal 28: To a solution of coupling product 20 (50.0 mg, 0.0602 mmol) in THF (6.0 mL) was added catechol borane solution (1M in THF, 75.3 µL, 0.0753 mmol) at 0 °C. The mixture was stirred at 0 °C for 2 h. After addition of water, the resultant mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-20% EtOAc/hexane) gave aminal 28 (32.6 mg, 65%, dr = 3.3:1) as a yellow oil: (major diastereomer) 1H NMR (500 MHz, CDCl₃) δ 8.14 (d, 2H, J = 8.9 Hz), 7.93 (d, 2H, J = 8.9 Hz), 7.75 (br, 1H), 7.30 (d, 1H, J = 15.8 Hz), 7.27-7.24 (m, 1H), 7.20-7.14 (m, 2H), 7.06 (d, 1H, J = 15.8 Hz), 6.89 (dd, 1H, J = 7.8, 7.4 Hz), 6.83 (d, 1H, J = 8.0 Hz), 6.07 (d, 1H, J = 15.8 Hz), 6.05-5.98 (m, 2H), 5.61 (dd, 1H, J = 10.0, 1.7 Hz), 5.35 (dd, 1H, J = 16.9, 1.5 Hz), 4.89 (s, 1H), 4.15 (d, 1H, J = 10.3 Hz), 4.13-4.08 (m, 1H), 3.29 (dd, 1H, J = 14.1, 14.1, 4.0 Hz), 2.08 (dd, 1H, J = 12.6, 12.6, 4.3 Hz), 1.86 (dd, 1H, J = 12.9, 12.9, 4.3 Hz), 1.65 (s, 9H), 1.64 (s, 3H), 1.28 (s, 3H), 1.25 (s, 9H), 0.15 (s, 9H); 13C NMR (126 MHz, CDCl₃) δ 150.4, 150.2, 145.7, 144.7, 140.6, 137.8, 137.1, 131.5, 129.5, 129.2, 128.9, 127.8, 127.7, 127.0, 125.4, 123.8, 123.7, 123.5, 121.9, 120.1, 116.9, 113.7, 84.6, 83.3, 78.3, 74.1, 54.8, 50.6, 44.8, 30.6, 30.4, 28.6, 27.9, 2.8; IR (ATR, cm⁻¹) 2997, 2918, 1731, 1696, 1534, 1467, 1370, 1347, 1235, 1089, 887, 627; MS (FAB) m/z 833 [M + H]+; HRMS calcd for C_{43}H_{55}N_{4}O_{9}SSi [M + H]+ 833.3616; Found: m/z 833.3616.

Aminal 29: To a solution of aminal 28 (10.8 mg, 0.0130 mmol) in THF (1.3 mL) was added TBAF (1M in THF, 15.6 µL, 0.0156 mmol) at 0 °C. The mixture was stirred at 0 °C for 4 h. After addition of saturated aqueous NH₄Cl, the resultant mixture was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-30% EtOAc/hexane) gave an alcohol (7.6 mg, 77%) as a yellow oil.

To a solution of the above alcohol (7.6 mg, 9.99×10⁻³ mmol) in MeCN (1.0 mL) were added K₂CO₃ (9.6 mg, 0.0695 mmol) and PhSH (6.3 µL, 0.0614 mmol). The mixture was stirred at room temperature for 12 h, and then diluted with EtOAc. The organic layer was washed with water and brine, and then dried over Na₂SO₄. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-30% EtOAc/hexane) gave
aminal 29 (4.0 mg, 70%) as a yellow oil: 1H NMR (500 MHz, CDCl3) δ 7.70 (br, 1H), 7.33-7.26 (m, 2H), 7.21 (dd, 1H, J = 8.0, 8.0 Hz), 7.14-7.03 (m, 2H), 6.84 (ddd, 1H, J = 7.8, 7.8, 1.2 Hz), 6.78 (d, 1H, J = 7.7 Hz), 6.14-6.07 (m, 2H), 5.97 (br, 1H), 5.61 (dd, 1H, J = 10.0, 1.7 Hz), 5.40 (dd, 1H, J = 17.2, 1.8 Hz), 4.85 (s, 1H), 4.40 (br, 1H), 4.15 (d, 1H, J = 9.7 Hz), 2.94 (br, 1H), 2.73 (br, 1H), 1.93 (br, 1H), 1.86 (br, 1H), 1.63 (s, 9H), 1.44 (s, 3H), 1.40 (s, 3H), 1.32 (s, 9H); 13C NMR (126 MHz, CDCl3) δ 155.6, 144.7, 142.9, 140.7, 139.3, 137.2, 131.3, 129.9, 129.1, 127.6, 127.3, 124.0, 122.9, 120.9, 120.1, 117.2, 113.9, 83.2, 78.9, 78.4, 71.2, 55.5, 50.8, 37.1, 30.2, 29.3, 28.5; IR (ATR, cm−1) 2978, 2916, 1469, 1384, 1283, 1234, 1089, 888, 628; MS (FAB) m/z 576 [M + H]+; HRMS calcd for C34H45N3O5 [M]+ 575.3359; Found: m/z 575.3359.

Pentacyclic compound 30: To a mixture of aminal 29 (6.9 mg, 0.0120 mmol) and MS4Å (7.0 mg) in CH2Cl2 (1.2 mL) was added Bi(OTf)3 (0.8 mg, 1.2×10−3 mmol) at 0 °C. The mixture was stirred at 0 °C for 2 h, and then warmed to room temperature and stirred for 1 h. After addition of saturated aqueous NaHCO3, and the mixture was diluted with EtOAc. The organic layer was washed with brine and dried over Na2SO4. After concentration under reduced pressure, purification by flash column chromatography on silica gel (5-20% EtOAc/hexane) gave a pentacyclic compound 30 (3.7 mg, 55%) as a yellow oil: 1H NMR (500 MHz, CDCl3) δ 7.74 (br, 1H), 7.23-7.18 (m, 2H), 7.11 (dd, 1H, J = 7.2, 7.1 Hz), 7.00 (d, 1H, J = 7.8 Hz), 6.81 (dd, 1H, J = 8.3, 7.9 Hz), 6.75 (d, 1H, J = 8.0 Hz), 5.94 (d, 1H, J = 9.2 Hz), 5.92-5.88 (m, 1H), 5.84 (br, 1H), 5.42 (dd, 1H, J = 16.6, 2.3 Hz), 5.38 (dd, 1H, J = 9.5, 2.3 Hz), 5.05 (s, 1H), 5.00 (d, 1H, J = 8.3 Hz), 4.10 (d, 1H, J = 10.0 Hz), 3.90 (dd, 1H, J = 14.0, 4.0 Hz), 2.10 (ddd, 1H, J = 14.6, 11.4, 5.4 Hz), 2.03-1.96 (m, 2H), 1.85 (s, 3H), 1.65 (s, 3H), 1.63 (s, 3H), 1.46 (s, 9H); 13C NMR (126 MHz, CDCl3) δ 155.4, 153.8, 144.7, 142.8, 138.5, 137.7, 132.7, 131.2, 130.7, 128.2, 127.6, 126.0, 124.7, 122.8, 120.0, 118.2, 116.7, 114.6, 82.8, 79.2, 78.7, 58.7, 58.2, 50.7, 41.0, 28.5, 28.4, 25.2, 23.5, 18.4; IR (ATR, cm−1) 2977, 2916, 1691, 1466, 1391, 1341, 1279, 1235, 1089, 889, 756, 628, 523; MS (FAB) m/z 558 [M + H]+; HRMS calcd for C34H44N3O4 [M−H−]− 556.3175; Found: m/z 556.3177. (ESI) HRMS calcd for C34H44N3O4 [M + H]+ 558.3311; Found: m/z 558.3311.

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