Stereocontrolled Synthesis of the Oxabicyclo[2.2.1]heptane Segment of Solanoeclepin A
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Received 22 December 2004; revised 17 January 2005

SYNTHESIS 2005, No. 8, pp 1237–1244
Advanced online publication: 07.04.2005
DOI: 10.1055/s-2005-865291; Art ID: F18604SS
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Abstract: An asymmetric synthesis of the oxabicyclo[2.2.1]heptane segment of Solanoeclepin A, which shows significant hatch-stimulating activity for the potato cyst nematode, is described. The oxabicyclo framework was constructed by iodoetherification with bis(collidine)iodine(I) hexafluorophosphate in acetonitrile. The oxabicyclo segment was further synthesized by the following stereoselective dihydroxylation and dimethyl group introduction.

Key words: solanoeclepin A, hatch-stimulating activity, oxabicyclo[2.2.1]heptane, iodoetherification

Potato is one of the most important agricultural products in the world. Potato cyst nematode is well known as an insect that causes significant damage to potatoes, and is extremely difficult to exterminate using the existing agricultural chemicals or the rotation of crops. Solanoeclepin A (1), which was isolated from a large quantity of potato cultivation, shows significant hatch-stimulating activity toward the potato cyst nematode.1a Therefore, 1 has received much attention regarding the relationship of its structure and activity, and is expected to be a new agricultural chemical. The related configuration was characterized by X-ray crystallography,1b however, the absolute configuration has not yet been determined. The absolute configuration was only assumed, as shown in Figure 1, on the basis of the similarity of the oxabicyclo[2.2.1]heptane moiety to glycinoeclepin A (2), another hatching stimulant toward the soybean cyst nematode.2,3 The structure of 1 contains a heptacyclic compound consisting of five different ring sizes ranging from three to seven, and including an oxabicyclo[2.2.1]heptane unit and a highly strained bicyclo[2.1.1]hexanone unit. Although Hemstra’s group has already reported some synthetic studies of 1,4 its total synthesis has not yet been achieved.

Figure 1 Hatch-stimulating agents

Our retrosynthetic analysis of 1 is shown in Scheme 1. The six-membered ring would be closed through an equivalent of the enolate 3 in the last step. Nicholas reaction5 of the acetylene dicobalthexacarbonyl complex 4 may construct the seven-membered ring as a key step to 3. The precursor 4 should be prepared by coupling between the oxabicyclo segment 5 and the bicyclo[2.1.1]hexanone segment 6. This segment 5 would be converted from the vinyl ether 7 via stereoselective dihydroxylation and the dimethylation. The oxabicyclo framework of 7 should be constructed through iodoetherification3a,b of the alcohol 8, and the latter would be obtained from the known enone 9 prepared from (−)-quinic acid. Herein, we describe in detail the synthesis of the oxabicyclo segment 5.

The oxabicyclo[2.2.1]heptane moiety was constructed by the following steps (Scheme 2). The enone 9, which was easily prepared from the commercially available (−)-quinic acid in four steps,5 was regioselectively reduced by treating with Wilkinson’s catalyst and triethylsilane7 to afford the vinyl silyl ether 10 in 86% yield. Another attempt using Birch reduction condition (Li, NH3, THF) was unsuccessful, because 9 was immediately decomposed under the basic condition. The Mukaiyama aldol reaction8 of 11 was successful with acetaldehyde and ZnCl2 in CH2Cl2–Et2O to obtain the aldol products as a mixture of diastereomers in a ratio of ca. 1:1 in 71% yield. Mesylation of the alcohol and subsequent treatment with DBU in one-pot afforded the E-enone 12 in 74% yield. The reduction of 12 under Luche condition9 at −20 °C provided largely the alcohol 13 together with a minor a-isomer in a ratio of ca. 15:1, which was purified by silica gel flash column chromatography. It was protected with benzyl chloride to give 14. The acetonide group was removed with aqueous AcOH in THF at 25 °C to afford the diol 15 in 85% yield in 3 steps. The stereochemistry of the alcohol and the geometry of the alkene were confirmed by the NOESY spectra of 15 as shown in Figure 2. Formation of the oxabicyclo system was accomplished by iodoetherification3a,b with bis(collidine)iodine(I) hexafluorophosphate [I(collidine),PF6]11 in acetonitrile to give the iodide 16 in 96% yield. When N-iodosuccinimide (NIS) was employed as the I+ source, this reaction was very slow at room temperature to give 16 in lower yields. Elimination of the iodine was facilitated by heating 16 with DBU in toluene to afford the alcohol 17, which was further protected with TBDPSCl to obtain the silyl ether 18 in 86% yield in two steps.
Next, in order to introduce the secondary hydroxyl group, we examined the stereoselective dihydroxylation of 18 under various conditions as listed in Scheme 3. We first used AD-mix reagents\(^{12}\) as the reagent control conditions. The olefin 18 was initially treated with AD-mix-b, expecting the desired diol with an \(S\) configuration, however, the reaction was extremely slow and afforded a mixture of the diols 19 and 20 in only trace yields (entry 1). On the other hand, the treatment with AD-mix-a gave the desired diol 19 as the major isomer. However, the yield was very low because of the major products were mixtures of the migrated benzoyl group (entry 2). The attempted reagent control turned out to be a mismatched pair due to the existing functional groups in 18. Therefore, the substrate control conditions were examined with OsO\(_4\) (cat.) and NMO in various solvents. All the reactions smoothly proceeded and gave the diols with moderate selectivity but in high yields, and the major product was proved to have the desired stereochemistry (entries 3, 4, and 5). After several trials, we found that the treatment of 18 with a mixture of OsO\(_4\) (cat.), (DHQ)\(_2\)PHAL (cat.), and NMO in THF–H\(_2\)O at 0 °C afforded 19 in the ratio of ca. 7.1:1 in 99% yield without any migration of the benzoyl group (entry 7). (DHQ)\(_2\)PHAL was added for the purpose of increasing the steric hindrance of OsO\(_4\). It was important that the combination of OsO\(_4\) and NMO was effective for avoiding the benzoate migration, because this migration was observed under the basic conditions with K\(_2\)OsO\(_2\)(OH)\(_4\) and NMO in THF–H\(_2\)O.
Selective protection of 19 with benzoyl chloride in the presence of pyridine 0 °C produced the primary benzoate 21, followed by protection of the secondary alcohol with TESOTf to obtain 22. Both benzoyl groups were then removed with DIBAL–H to afford the diol 23 in 85% yield in 3 steps (Scheme 4). At this step, the mixture of the diastereomers could be easily separated by silica gel column chromatography.

Selective oxidation of the primary alcohol of 23 smoothly proceeded with IBX (2-iodoxybenzoic acid) under neutral condition to afford the lactol 24 as a mixture in a ratio of ca. 1:1 in 86% yield. In order to confirm the configuration of the secondary alcohol (introduced at the dihydroxylation step of 18), a part of 24 was oxidized with TPAP to produce the lactone 25. The stereochemistry was determined from the NOESY spectra (Scheme 5). The Wittig reaction of the remaining amount of 24 provided the E-ester 26 in 99% yield, which was reduced with DIBAL–H in toluene–THF (5:1) at −78 °C to give the allyl alcohol 27 in 97% yield. The primary alcohol group of 27 was selectively converted to the phenyl sulfide 28 with N-(phenylthio)phthalimide and Bu3P in CH2Cl2 at −20 °C in 99% yield. The ring alcohol was then oxidized to the ketone 29 by Swern oxidation in 92% yield. Finally, introduction of the gem-dimethyl groups to the ketone 29 was achieved with MeI and t-BuOK in THF at −78 °C to afford the dimethyl compound 30 in 94% yield.

In conclusion, we have achieved the efficient synthesis of the oxabicyclic 30 in 19 steps from the enone 9. The oxabicyclo framework was constructed by iodoetherification with I(collidine)2PF6, and the introduction of the hydroxyl group was accomplished by the diastereoselective reaction of the remaining amount of 24 provided the E-ester 26 in 99% yield, which was reduced with DIBAL–H in toluene–THF (5:1) at −78 °C to give the allyl alcohol 27 in 97% yield. The primary alcohol group of 27 was selectively converted to the phenyl sulfide 28 with N-(phenylthio)phthalimide and Bu3P in CH2Cl2 at −20 °C in 99% yield. The ring alcohol was then oxidized to the ketone 29 by Swern oxidation in 92% yield. Finally, introduction of the gem-dimethyl groups to the ketone 29 was achieved with MeI and t-BuOK in THF at −78 °C to afford the dimethyl compound 30 in 94% yield.

In conclusion, we have achieved the efficient synthesis of the oxabicyclic segment 30 in 19 steps from the enone 9. The oxabicyclo framework was constructed by iodoetherification with I(collidine)2PF6, and the introduction of the hydroxyl group was accomplished by the diastereoselective reaction of the remaining amount of 24 provided the E-ester 26 in 99% yield, which was reduced with DIBAL–H in toluene–THF (5:1) at −78 °C to give the allyl alcohol 27 in 97% yield. The primary alcohol group of 27 was selectively converted to the phenyl sulfide 28 with N-(phenylthio)phthalimide and Bu3P in CH2Cl2 at −20 °C in 99% yield. The ring alcohol was then oxidized to the ketone 29 by Swern oxidation in 92% yield. Finally, introduction of the gem-dimethyl groups to the ketone 29 was achieved with MeI and t-BuOK in THF at −78 °C to afford the dimethyl compound 30 in 94% yield.

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tive dihydroxylation of the vinyl ether 18. The diol 19 was converted into the oxabicyclo[2.2.1]heptane segment 30 via the extension of the side chain and the dimethylation. An additional synthetic study, including the investigation of the seven-membered ring on solanoeclepin A, is now under way in our laboratory.

Solvents and reagents were dried and distilled before use. THF was distilled from sodium benzophenone ketyl. CH₂Cl₂, MeCN, pyridine, and Et₂N were distilled from CaH₂. Normal reagent-grade solvents were used for the flash chromatography and extraction. I(2-collidine),PPh₃, and IBX were prepared by literature methods.¹⁵ All other reagents were commercially available and used without further purification. All reactions were monitored by TLC analysis using precoated SiO₂ plates (Merck, silica gel 60 F254 Art. 5715). Visualization was achieved via UV light and the appropriate spray reagents were as follows: a 2.5% ethanolic diacid solution, and I₂ on SiO₂. SiO₂ (Merck, silica gel 60, 230–400 mesh ASTM and NACALAI TESQUE, silica gel 60, spherical, neutral, 105–210 μm) was used for the flash chromatography. Melt points were measured using a Yanagimoto MP-S3 micro-melting point apparatus and are uncorrected. IR spectra were recorded using a JASCO P-1010-GT digital polarimeter with CHCl₃ as the solvent. High-resolution mass spectra (HRMS) were obtained using a JASCO FT/IR-8300 spectrophotometer. ¹H NMR (CDCl₃, 270 MHz): δ = 3.6, 4.9, 6.9 Hz, H-4), 2.40 (1 H, ddd, J = 3.3, 16.5 Hz, H-6), 2.35–2.25 (1 H, m, H-3), 2.16 (1 H, ddd, J = 1.3, 5.6, 16.5 Hz, H-6), 2.03–1.93 (1 H, m, H-3), 1.49 (3 H, s, CH₃, acetoneide), 1.25 (3 H, s, CH₃, acetoneide), 1.00 (9 H, t, J = 7.9 Hz, CH₃, TES), 0.67 [6 H, q, J = 7.9 Hz, CH₂, TES].

¹³C NMR (CDCl₃, 67.8 MHz): δ = 149.9, 107.9, 98.4, 74.5, 73.2, 34.5, 28.0, 27.5, 25.0, 7.1, 5.5.

FAB-HRMS: m/z calcd for C₁₁H₁₇O₃Si (M + Na)+: 370.1705; found: 370.1696.

(2E,4S,5R)-2-Ethyline-4,5-(dimethylenediethoxy)cyclohexan-1-one (12)

To a solution of 11 (55.9 mg, 0.197 mmol) and MeCHO (ca. 220 μL, 3.92 mmol) in CH₂Cl₂ (2.4 mL) at –20 °C was added ZnCl₂ (1.0 M solution in Et₂O, 240 μL, 0.24 mol). After stirring for 2.5 h, the mixture was allowed to warm to 0 °C. The reaction was quenched with sat. aq NaHCO₃ (2 mL), and extracted with Et₂O (4 × 3 mL). The combined extracts were dried (MgSO₄) and concentrated, and the residue was purified by flash chromatography (SiO₂, hexane–EtOAc, 5:2, 2.1:1) to furnish a mixture of the aldol products (ca. 1:1) (31.7 mg, 71%) as white solids. To a solution of the aldol compounds (19.7 mg, 92.4 μmol) and Et₃N (65 μL, 0.466 mmol) in CH₂Cl₂ (0.5 mL) was added dropwise a solution of MsCl (9 μL, 0.114 mmol) in CH₂Cl₂ over 10 min at 0 °C. After stirring at 27 °C for 1.5 h, an additional amount of DBU (20 μL, 0.134 mmol) was added, and the mixture was stirred at the same temperature for 12.5 h. Again DBU (5 μL, 33.5 μmol) was added, and the stirring was continued for an additional 2 h. The reaction was quenched with sat. aq NH₄Cl (10 mL), and extracted with CH₂Cl₂ (2 mL), and the mixture was extracted with Et₂O (3 × 2 mL). Drying (MgSO₄), concentration, and flash chromatography (SiO₂, hexane–EtOAc, 7:1, 6:1, 5:1, 4:1) gave the enone 12 (13.4 g, 74%) as a colorless liquid; [α]₂₃^25+4.2 (c = 0.98, CHCl₃).

IR (neat): 2956, 2913, 2878, 1663, 1457, 1379, 1242, 1188, 1131, 1054, 983, 848, 700, 545, 513 cm⁻¹.

¹H NMR (CDCl₃, 270 MHz): δ = 6.90 (1 H, dq, J = 2.0, 7.3 Hz, =CH₂, ethyleneidene), 4.68–4.57 (2 H, m, H-4, H-5), 2.98 (1 H, dd, J = 2.8, 15.5 Hz, H-3), 2.73 (1 H, dd, J = 3.0, 15.8 Hz, H-6), 2.53 (1 H, dd, J = 3.5, 15.8 Hz, H-6), 2.37 (1 H, ddd, J = 2.0, 2.6, 2.8, 15.5 Hz, H-3), 1.80 (3 H, dd, J = 2.6, 7.3 Hz, =CH₂H₂, ethyleneidene), 1.32 (3 H, s, CH₃, acetoneide), 1.32 (3 H, s, CH₃, acetoneide).

¹³C NMR (CDCl₃, 100 MHz): δ = 197.1, 135.8, 132.5, 108.0, 72.9, 72.8, 42.1, 28.7, 26.1, 12.4, 13.6.

El-HRMS: m/z calcd for C₁₁H₁₇O₃Si (M + H)+: 197.1178; found: 197.1183.

(1E,2E,4S,5R)-2-Ethyline-4,5-(dimethylenediethoxy)cyclohexan-1-ol (13)

To a solution of 12 (3.17 g, 16.2 mmol) and CeCl₃·7H₂O (8.13 g, 21.8 mmol) in MeOH (100 mL) was added NaNb₄H₆ (795 mg, 2.0 mol) at –78 °C, and the reaction mixture was stirred at the same temperature for 50 min. Brine (100 mL) was added and the mixture was extracted with Et₂O (3 × 200 mL). Drying (MgSO₄), concentration, and flash chromatography (SiO₂, hexane–EtOAc, 6:1, 5:1, 4:3) afforded the alcohol 13 (2.97 g, 93%) as a white solid; [α]₂₃^25+21.6 (c = 1.00, CHCl₃).

IR (neat): 3447, 2985, 2935, 1456, 1381, 1217, 1155, 1046, 843, 590, 514 cm⁻¹.

¹H NMR (CDCl₃, 600 MHz): δ = 5.70 (1 H, br q, J = 6.6 Hz, =CH₂, ethyleneidene), 4.38–4.35 (1 H, m, H-5), 4.25–4.22 (1 H, m, H-4), 4.16–4.13 (1 H, m, H-1), 2.79 (1 H, dd, J = 9.6 Hz, OH), 2.57 (1 H, dd, J = 6.6, 14.4 Hz, H-3), 2.40 (1 H, dd, J = 6.0, 14.4 Hz, H-3), 2.27 (1 H, td, J = 3.6, 15.6 Hz, H-6), 1.93 (1 H, ddd, J = 3.6, 4.2, 15.6 Hz, H-6), 1.65 (3 H, d, J = 6.6 Hz, =CH₂H₂, ethyleneidene), 1.51 (3 H, s, CH₃, acetoneide), 1.34 (3 H, s, CH₃, acetoneide).
13C NMR (CDCl3, 67.8 MHz); δ = 136.2, 121.6, 108.3, 74.3, 73.6, 70.6, 34.3, 28.0, 27.6, 25.5, 13.0.

EI-MS: m/z cale for C11H18O3 (M+): 198.1256; found: 198.1251.

(1S,2E,4S,5R)-1-Benzoyloxy-2-ethylidene-4,5-dimethylmethyleneenediolocyclohexane (14)

To a solution of 13 (513 mg, 2.59 mmol) in CH2Cl2 (20 mL) were added DMAP (794 mg, 6.50 mmol) and BzCl (360 mL, 3.10 mmol) at 0 °C, and the mixture was stirred at 24 °C for 2 h. The reaction was quenched with sat. aq NaHCO3 (15 mL), and extracted with Et2O (3 × 20 mL). The combined extracts were dried (MgSO4) and concentrated. The residue was purified by flash chromatography (SiO2, hexane–EtOAc, 3:2) to furnish the iodide 17 (781 mg, ca. 100%) as a colorless amorph. Anal. Calcd for C15H17O4I: C, 46.41; H, 4.41. Found: C, 46.45; H, 4.08.

FAB-MS: m/z cale for C15H17O4 (M+): 261.1127; found: 261.1127.

(1S,2E,4S,5R)-1-Benzoyloxy-2-ethylidene-4,5-cyclohexadiol (15)

To a solution of 14 (98.9 mg, 0.327 mmol) in THF (0.3 mL) and H2O (0.5 mL) was added AcOH (0.9 mL) at 0 °C, and the mixture was stirred at 25 °C for 9.5 h. The reaction mixture was neutralized with sat. aq NaHCO3, and extracted with EtOAc (3 × 20 mL). The combined extracts were dried (MgSO4) and concentrated. The residue was purified by flash chromatography (SiO2, hexane–EtOAc, 10:1) to furnish the iodide 17 (736 mg, ca. 100%) as a colorless amorph. FAB-MS: m/z cale for C15H17O4 (M+): 261.1127; found: 261.1127.
CH₂=CH₂), 5.27 (1 H, dd, J = 1.8, 10.8 Hz, CH₂=CH₂), 4.92 (1 H, dd, J = 2.4, 7.2 Hz, H-2), 4.38 (1 H, br, d, J = 6.0 Hz, H-4), 3.99 (1 H, dd, J = 2.4, 6.6 Hz, H-5), 1.94 (1 H, dd, J = 6.6, 13.2 Hz, H-6), 1.80 (1 H, dd, J = 7.2, 13.8 Hz, H-3), 1.75–1.72 (1 H, m, H-6), 1.68 (1 H, ddd, J = 2.4, 6.0, 13.8 Hz, H-3), 1.07 [9 H, s, Si(CH₃)₃].

1¹C NMR (CDCl₃, 67.8 MHz): δ = 165.8, 135.6, 135.6, 133.8, 133.6, 132.9, 132.7, 130.0, 129.7, 129.6, 128.2, 127.8, 127.6, 117.2, 87.3, 81.2, 76.6, 75.9, 43.1, 36.1, 26.9, 19.1.

FAB-HRMS: m/z calc'd for C₁₁H₃O₅Si (M + H)⁺: 499.2305; found: 499.2310.

(1R,2S,4R,5S)-5-(tert-Butyldiphenylsilyloxy)-1-[(1S,2E,4S)-4-(ethoxy carbonyl)-1’-(tritylsilyloxy)prop-2’-enyl]-7-oxabicyclo[2.2.1]heptan-2-ol (26)

To a solution of 23 (226 mg, 0.417 mmol) in THF (3 mL) and DMSO (3 mL) was added IBX (349 mg, 1.25 mmol), and the mixture was stirred at 16 °C for 11 h. The mixture was diluted with H₂O (4 mL), and stirred at 0 °C for 10 min. The resulting suspension was filtered through a Celite pad, which was washed with EtOAc.

The filtrate was diluted with brine (5 mL), followed by extraction with Et₂O (3 × 15 mL). The combined extracts were dried (MgSO₄) and concentrated.

The residue was purified by flash chromatography (SiO₂, hexane–EtOAc, 6:1, 4:1) to provide a mixture of the lactols 24 (ca. 1:1) (193 mg, 86%) as a colorless oil. To a solution of 24 (29.0 mg, 53.6 μmol) in toluene (1 mL) at 22 °C was added ethyl triphenylphosphoranylideneacetate (58.9 mg, 0.161 mmol).

After stirring at 80 °C for 6.5 h, the mixture was diluted with sat. aq NaHCO₃ (1 mL), followed by extraction with Et₂O (3 × 2 mL). Drying (MgSO₄), concentration, and flash chromatography (SiO₂, hexane–EtOAc, 10:1, 7:1) afforded the ether ester 26 (32.4 mg, 99%) as white needles; mp 101.8–102.6 °C; [α]D²ⁿ –0.7 (c = 0.93, CHCl₃).

IR (KBr): 3459, 2958, 2878, 1725, 1659, 1429, 1369, 1276, 1158, 1112, 1031, 739, 701, 692, 508 cm⁻¹.

1H NMR (CDCl₃, 600 MHz): δ = 7.67–7.65 (2 H arom, m, TDBPS), 7.61–7.59 (2 H arom, m, TDBPS), 7.45–7.35 (6 H arom, m, TDBPS), 7.09 (1 H, dd, J = 4.5, 15.6 Hz, H-2), 6.16 (1 H, dd, J = 1.8, 15.6 Hz, H-3), 4.94 (1 H, dd, J = 1.8, 4.5 Hz, H-1'), 4.26 (1 H, d, J = 6.6 Hz, H-4), 4.25–4.16 (2 H, m, OCH₂CH₃), 3.83 (1 H, dd, J = 1.8, 6.6 Hz, H-5), 3.74 (1 H, dd, J = 1.2, 6.3, 7.2 Hz, H-2), 2.93 (1 H, d, J = 7.2 Hz, OH), 1.53 (1 H, dd, J = 6.6, 13.8 Hz, H-3), 1.49 (1 H, ddd, J = 6.6, 14.4 Hz, H-6), 1.46 (1 H, br, d, J = 14.4 Hz, H-6), 1.40 (1 H, ddd, J = 1.2, 6.3, 13.8 Hz, H-3), 1.30 (3 H, t, J = 7.2 Hz, OCH₂CH₂), 1.02 (9 H, s, t-C₃H₉), TDBPS, 0.97 (9 H, t, J = 7.8 Hz, CH₃), TES. 0.68 (6 H, q, J = 7.8 Hz, CH₂, TES).

1¹C NMR (CDCl₃, 125 MHz): δ = 166.2, 146.7, 135.7, 135.6, 134.0, 133.7, 129.7, 129.6, 127.7, 127.6, 122.3, 87.6, 80.7, 75.4, 73.3, 71.7, 60.4, 39.3, 38.3, 26.7, 19.0, 14.2, 6.7, 4.7.

Anal. Calc'd for C₃₄H₅₀O₆Si₃: C, 66.84; H, 8.25, found: C, 66.85; H, 8.27.

FAB-HRMS: m/z calc'd for C₃₄H₅₀O₆Si₃Na (M + Na)⁺: 633.3044; found: 633.3052.

(1R,2R,4S,5S)-8-(tert-Butyldiphenylsilyloxy)-2-(tritylsilyloxy)-4,10-dioxatricyclo[5.2.1.0²⁻][2.3.1.0⁶⁻]decan-3-one (25)

To a suspension of 24 (4.4 mg, 8.1 μmol) and MS 4Å (10.0 mg) in CH₂Cl₂, 1.0 mL were added TPAP (1.2 mg, 3.4 μmol) and NMO (4.1 mg, 35 μmol) at 20 °C. After stirring at the same temperature for 2.5 h, the reaction mixture was filtered through a short column of SiO₂, and the filtrate was concentrated.

The residue was purified by PTLC (hexane–EtOAc, 5:1) to afford the lactone 25 (3.8 mg, 86%) as white needles; mp 82.0–83.0 °C; [α]D²ⁿ–12.2 (c = 0.36, CHCl₃).

IR (KBr): 2960, 2881, 1801, 1139, 1087, 964, 824, 743, 705, 512 cm⁻¹.

1H NMR (CDCl₃, 600 MHz): δ = 7.65–7.62 (4 H arom, m, TDBPS), 7.45–7.36 (6 H arom, m, TDBPS), 4.37 (1 H, dd, J = 5.3, 5.6 Hz, H-1'), 4.25 (1 H, d, J = 6.2 Hz, H-4'), 3.89–3.65 (3 H, m, H-2, H-1'–H-2'), 2.8 (1 H, br, d, J = 7.2 Hz, OH), 2.65 (1 H, br, s, OH), 1.63–1.47 (3 H, m, H-3, H-6), 1.39 (1 H, ddd, J = 1.2, 6.6, 13.8 Hz, H-5), 1.05 (9 H, s, t-C₃H₉), TDBPS, 0.98 (9 H, t, J = 7.8 Hz, CH₃, TES), 0.68 (6 H, q, J = 7.8 Hz, CH₂, TES).

FAB-HRMS: m/z calc'd for C₂₉H₄₄O₆Si₄Na (M + Na): 565.2782; found: 565.2775.
(1R,2S,4R,5S)-5-(tert-Butyldiphenylsilyloxy)-1-[(1'S,2'E)]-1’-(triethylsilyloxy)-4’-hydroxybut-2’-enyl]-7-oxacyclo-[2.2.1]heptan-2-one (27)

To a solution of 26 (357 mg, 0.585 mmol) in toluene (7.4 mL) and THF (2.0 mL) at −78 °C was added dropwise DIBAL-H (1.01 M solution in toluene, 2.6 mL, 2.63 mmol) over 5 min. After stirring at the same temperature for 20 min, sat. aq potassium carbonate trihydrate (15 mL) was added. The mixture was vigorously stirred at 25 °C for 5 h, and the aqueous layer was extracted with Et2O (3 × 20 mL). The combined organic extracts were dried (MgSO4) and concentrated. The residue was subjected to flash chromatography (SiO2, hexane–EtOAc, 3:1, 2:1) to furnish the diol 27 (321 mg, 97%) as a colorless amorphous powder; [α]D26 +40.8 (c = 0.65, CHCl3).

FAB-HRMS: m/z calc for C38H52O4Si2Na (M + Na)+: 681.2866; found: 681.2865.

IR (neat): 3071, 2956, 2875, 1762, 1717, 1559, 1473, 1112, 1070, 1023, 967, 740, 702, 612, 502, 484 cm−1.

1H NMR (CDCl3, 600 MHz): δ = 7.67–7.61 (4 H, m, TBDPS), 7.45–7.36 (6 H, m, TBDPS), 7.32–7.29 (2 H, m, SpH), 7.24–7.20 (2 H, m, SpH), 7.15–7.10 (1 H, m, SpH), 5.79 (1 H, ddd, J = 6.6, 7.5, 15.6 Hz, H-3’), 5.70 (1 H, dd, J = 6.3, 15.6 Hz, H-2’), 4.62 (1 H, d, J = 6.3 Hz, H-1’), 4.23 (1 H, br, s, H-4’), 3.96 (1 H, d, J = 5.4 Hz, OH), 3.75 (1 H, br, d, J = 6.3 Hz, H-5’), 3.60 (1 H, dd, J = 7.5, 14.1 Hz, H-4’), 3.57–3.52 (2 H, m, H-2, H-4’), 1.40–1.38 (2 H, m, H-3), 1.20 (1 H, br, d, J = 13.5 Hz, H-6’), 1.11 (1 H, d, J = 6.3, 13.5 Hz, H-6’), 1.03 (9 H, s, t-C6H17, TBDPS), 0.94 (9 H, t, J = 7.8 Hz, CH3, TES), 0.62 (3 H, q, J = 7.8 Hz, CH2, TES) 0.61 (3 H, q, J = 7.8 Hz, CH2, TES).

FAB-HRMS: m/z calc for C38H52O4Si2Na (M + Na)+: 683.3023; found: 683.3040.

PAPER

Partial Synthesis of Solanocepin A

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Synthesis 2005, No. 8, 1237–1244 © Thieme Stuttgart · New York
References


Acknowledgment

This study was supported by a Grant of the 21st Century COE Program and Grant-in-Aid for Specially Promoted Research (16002007) from the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan. We are grateful to Mr. S. Kitamura at Nagoya University for the elemental analyses.

For reviews, see: (a) Nicholas, K. M. Acc. Chem. Res. 1987, 20, 207. (b) Trost, B. L. Tetrahedron 2002, 58, 4133; and references cited therein.


(7) This compound was obtained as a mixture of II and the product of the 1,2-reduction in a ratio of ca. 30:1.


