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Asymmetric synthesis of (1*S*,6*R*,7*S*,9*R*)-7,9-bis(*tert*-butyldiphenylsilyloxy)-3-oxabicyclo[4,3,0]nonan-2-one

Xiao-Xin Shi,[a,b,*] Wei He,[a] Qing-Quan Wu,[b] Jie Yin,[a] Feng Ni[a] and Xiao-Zhou Jin[a]

[a]*The Faculty of Chemistry and Pharmaceutical Engineering, East China University of Science and Technology, PO Box 361, 130 Mei-Long Road, Shanghai 200237, PR China*
[b]*Shanghai Institute of Organic Chemistry, Chinese Academy of Science, 354 Feng-Ling Road, Shanghai 200032, PR China*

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Dedicated to Professor Li-Xin Dai in Shanghai Institute of Organic Chemistry on the occasion of his 80th birthday

Abstract—The asymmetric synthesis of (1*S*,6*R*,7*S*,9*R*)-7,9-bis(*tert*-butyldiphenylsilyloxy)-3-oxabicyclo[4,3,0]nonan-2-one **1** from (4*S*)-4-acetoxy-2-methoxycarbonyl-3-methoxycarbonylmethyl-2-cyclopenten-1-one **2** is described in eight steps. Compound **2** was readily prepared from L-malic acid according to a known procedure. The key step of this synthesis is a palladium on charcoal catalyzed hydrogenation of olefinic bicyclic lactone **9**.

1. Introduction

Isoprostanes (IPGs) are a new type of naturally occurring biologically active compounds. It was discovered that these compounds are formed from arachidonic acid (AA), as well as other polyunsaturated fatty acids, via a free-radical peroxidation mechanism rather than by an enzymatic pathway.[1–5] IPGs are actually isomers of prostaglandins (PGs), they possess two characteristic *cis*-dialkyl side chains on the five-membered ring. During the last decade, there has been growing interest in the total syntheses of these bioactive prostanoids[6–16] in order to investigate their physiological role. Recently, we have been engaged in new total syntheses of isoprostanes. Herein we report the preparation of a key chiral synthon, namely (1*S*,6*R*,7*S*,9*R*)-7,9-bis(*tert*-butyldiphenylsilyloxy)-3-oxabicyclo[4,3,0]nonan-2-one **1**. Though some similar bicyclic lactones have appeared in the literature,[8–10,14,17–21] to the best of our knowledge, chiral synthon **1** has not been reported to date. This synthon could be used in the total syntheses of *all-syn* type isoprostanes.

2. Results and discussion

As outlined in Scheme 1, the title compound was synthesized in eight steps starting from compound **2**, which was readily prepared from L-malic acid.[22,23]

Protection of carbonyl group of compound **2** with 1.1 equiv of 1,3-propanedithiol and 1.5 equiv of boron trifluoride etherate in dichloromethane at −20 °C for 3 h afforded compound **3** in 87% yield. Alcoholysis of **3** at −5 °C for 6 h in methanol, with sodium carbonate as a catalyst, followed by silylation of the hydroxyl group with 2 equiv of *tert*-butyldiphenylchlorosilane (TBDPSCl), 3 equiv of imidazole, and 0.1 equiv of 4-dimethylaminopyridine (DMAP) as the catalyst, in dichloromethane afforded compound **4** in 86% yield. Reduction of diester **4** with 5 equiv of diisobutylaluminum hydride (DIBAL-H) in dichloromethane at −78 to −40 °C for 2 h produced the crude product diol **5**, which was contaminated with around 10% α,β-unsaturated lactol. This crude product was treated with sodium borohydride in methanol at 0 °C for 15 min to give pure diol **5** in 90% yield. Compound **5** was mixed and stirred with 10 equiv of acetic anhydride and 15 equiv of pyridine in dichloromethane overnight to furnish diacetate **6** quantitatively. Removal of the dithiane group of compound **6** with 3 equiv of periodic acid[24] under non-aqueous conditions produced enone **7** in 65% yield. It is

* Corresponding author. Fax: +86-21-64252485; e-mail: xxshi@ecust.edu.cn

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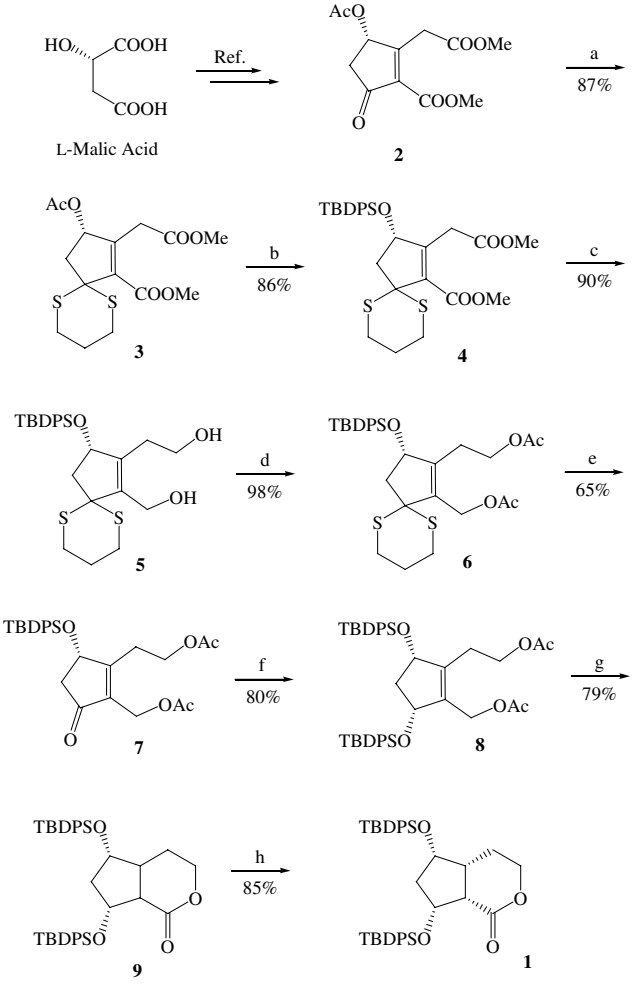
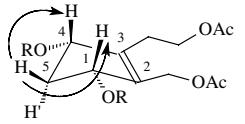


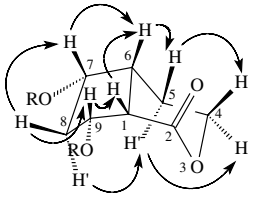
Scheme 1. Reagents and conditions: (a) 1,3-propandithiol (1.1 equiv), $BF_3{\cdot}OEt_2$ (1.5 equiv), CH_2Cl_2, −20 °C, 3 h; (b) Na_2CO_3 (0.1 equiv), in methanol, −5 °C, 6 h; then DMAP (0.1 equiv), *tert*-butyldiphenylchlorosilane (2 equiv), imidazole (3 equiv), CH_2Cl_2, 0 °C to rt, overnight; (c) DIBAL-H (5 equiv), CH_2Cl_2, −78 to −40 °C, 2 h; then $NaBH_4$ (1 equiv), in methanol, 0 °C, 15 min; (d) Ac_2O (10 equiv), pyridine (15 equiv), CH_2Cl_2, 0 °C to rt, overnight; (e) H_5IO_6 (3 equiv), THF, 0 °C, 3 min; (f) $NaBH_4$ (5 equiv), $CeCl_3{\cdot}7H_2O$ (3 equiv), in methanol, −20 °C, 1 h; then *tert*-butyldiphenylchlorosilane (3 equiv), imidazole (3 equiv), triethylamine (3 equiv), CH_2Cl_2, rt, 32 h; (g) $LiOH{\cdot}H_2O$ (4 equiv), in aqueous methanol (CH_3OH–H_2O = 9:1), rt, 30 min; then PCC (10 equiv), triethylamine (5 equiv), CH_2Cl_2, rt, 3 h; (h) Pd/C (5%), triethylamine (0.2 equiv), EtOAc, rt, overnight.

noteworthy that enone **7** is unstable and should be used immediately for the next step. Luche reduction of compound **7** with 3 equiv of cerium chloride hydrate and 5 equiv of sodium borohydride in methanol gave a mixture (*cis:trans* = 92:8) of chiral alcohols, which were silylated by 3 equiv of *tert*-butyldiphenylchlorosilane, 3 equiv of imidazole, and 3 equiv of triethylamine to give pure *bis*-silylated compound **8** after chromatography in 80% yield. It should be noted that both imidazole and triethylamine were used here to give the best yield. Analysis of ^1H–^1H NOESY spectra of compound **8** showed two silyloxyl groups with *cis* stereochemistry, (Scheme 2), both H-1β and H-4β have correlation spots with the same proton H-5β. With compound **8** in hand,



Scheme 2. NOE of compound **8** (R = TBDPS).

we attempted hydrogenation on **8** to reduce the double bond with Pd/C as catalyst. However this failed to give the desired product. High pressure (60 atms) and warming made no impact on the tetrasubstituted double bond of **8** due to low activity and bulkiness of the substituents. We next tried to hydrogenate α,β-unsaturated lactone **9**. Fortunately, the hydrogenation reaction of the unsaturated lactone **9** smoothly afforded the desired product because of electron deficiency of the conjugate double bond. Saponification of diester **8** with 4 equiv of lithium hydroxide in aqueous methanol produced quantitatively a diol, which was used without purification and was immediately transformed into compound **9** in 79% yield by oxidation with 10 equiv of pyridinum chromium chloride (PCC) in the presence of triethylamine.[25] Addition of triethylamine was crucial for the oxidation otherwise desilylation occurred. Palladium on charcoal catalyzed hydrogenation of compound **9** under 1 atm of hydrogen gas at room temperature (done by adding a small amount of triethylamine) smoothly gave the saturated lactone **1** in 85% yield. During this heterogeneous catalytic hydrogenation, the palladium atom preferentially approaches the double bond on the face opposite to the silyloxy groups of **9**, so that hydrogenation of the double bond should give a desired *all-syn* product, with no other stereoisomers observed at all. Structure and stereochemistry of the bicyclic lactone **1** was unequivocally identified by ^1H NMR, ^{13}C NMR, ^1H–^1H COSY, and ^1H–^1H NOESY spectra. It is noteworthy that there is obvious NOE between H-5α(5-H′) and H-8α(8-H′), which coincides with the conformation of **1** drawn in Scheme 3.



Scheme 3. NOE of compound **1** (R = TBDPS).

3. Conclusion

In summary, the work described herein provides an approach to the useful chiron **1**. It can be used in the total syntheses of *all-syn* type isoprostanes, which are ongoing in our laboratory. In this eight-step synthesis, title compound **1** can be obtained in around 23%

overall yield from the readily available compound **2**, which can be prepared from L-malic acid in a one-pot reaction.[22,23]

4. Experimental

4.1. General methods

NMR spectra were acquired on a Varian 368A spectrometer or a BFX-5300 spectrometer. Chemical shifts were given on the delta scale as parts per million (ppm) with TMS as the internal standard. Mass spectra were recorded on a Finnigan 4021 spectrometer. IR spectra were recorded on a Bio-Rid FT20E spectrometer. Optical rotations of chiral compounds were measured with a WZZ-1S polarimeter. All solvents were purified by standard procedures. In particular, methylene chloride was distilled over CaH_2 and THF distilled from sodium prior to use. All chemicals were analytically pure and used as received. Starting compound **2** was prepared according to a known procedure.[22,23]

4.2. (9*S*)-9-Acetoxy-7-methoxycarbonyl-8-methoxycarbonylmethyl-1,5-dithiaspiro[5,4]dec-7-ene 3

To a stirred solution of compound **2** (6.20 g, 23 mmol) and 1,3-propandithiol (2.74 g, 25 mmol) in CH_2Cl_2 (60 mL) at −20 °C was added dropwise $BF_3{\cdot}OEt_2$ (5.14 g, 36 mmol) over 5 min. After addition, stirring was continued at −20 °C for 3 h, with the reaction monitored by TLC. The mixture was then quenched by saturated $NaHCO_3$ aqueous solution (50 mL). The organic layer was separated and the aqueous layer extracted twice with CH_2Cl_2 (2×30 mL). The organic extracts were combined and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude oil, which was purified by chromatography on silica gel to give (9*S*)-9-acetoxy-7-methoxycarbonyl-8-methoxycarbonylmethyl-1,5-dithiaspiro[5,4]dec-7-ene **3** (7.20 g, 20.0 mmol) in 87% yield. $[\alpha]_D = -14.1$ (*c* 6.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 1.95–2.11 (m, 2H), 2.40 (dd, $J = 6.0$ Hz; 13.7 Hz, 1H), 2.86–3.11 (m, 4H), 3.36 (dd, $J = 7.2$ Hz; 13.7 Hz, 1H), 3.38 (d, $J = 16.6$ Hz, 1H), 3.67 (d, $J = 16.4$ Hz, 1H), 3.69 (s, 3H), 3.84 (s, 3H), 5.84 (t, $J = 6.6$ Hz, 1H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 20.69, 23.67, 27.75, 28.44, 32.87, 48.83, 51.74, 52.01, 57.00, 77.37, 138.08, 145.98, 163.95, 169.10, 170.13. MS (*m*/*z*) 360 (M^+). IR (neat) 1741 (br), 1232 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_6S_2$: C, 49.98; H, 5.59. Found: C, 50.10; H, 5.46.

4.3. (9*S*)-9-(*tert*-Butyldiphenylsilyloxy)-7-methoxycarbonyl-8-methoxycarbonylmethyl-1,5-dithiaspiro[5,4]-dec-7-ene 4

To a stirred solution of compound **3** (7.02 g, 19.5 mmol), in anhydrous CH_3OH (60 mL) was added solid Na_2CO_3 (206 mg, 1.96 mmol). The solution was stirred at −5 °C for 6 h. The solvent CH_3OH was removed under a vacuum and the residue dissolved in EtOAc (60 mL). The organic phase was washed with a buffer solution of Na_2HPO_4–NaH_2PO_4 (20 mL, pH = 6.5), and then dried over anhydrous Na_2SO_4. The solvent was removed and the oily residue dissolved in CH_2Cl_2 (20 mL). To this solution were added *tert*-butyldiphenylchlorosilane (10.72 g, 39.0 mmol), 4-dimethylaminopyridine (250 mg, 2 mmol), and imidazole (3.98 g, 58.5 mmol) at 0 °C. The mixture was then stirred overnight at 0 °C to rt. The reaction mixture was diluted with EtOAc (60 mL) and washed with 1 M HCl (30 mL). The aqueous solution was then extracted once more with EtOAc (30 mL). The combined extracts were washed with brine (30 mL) and dried over $MgSO_4$. Evaporation of solvents gave a crude product, which was purified by chromatography to give (9*S*)-9-(*tert*-butyldiphenylsilyloxy)-7-methoxycarbonyl-8-methoxycarbonylmethyl-1,5-dithiaspiro[5,4]dec-7-ene **4** (9.33 g, 16.77 mmol) in 86% yield. $[\alpha]_D = -6.5$ (*c* 3.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.90–1.95 (m, 2H), 2.20 (dd, $J = 7.3$ Hz; 12.9 Hz, 1H), 2.67 (dd, $J = 7.2$ Hz; 12.9 Hz, 1H), 2.65–2.85 (m, 3H), 2.95–3.01 (m, 1H), 3.51 (d, $J = 16.5$ Hz, 1H), 3.59 (s, 3H), 3.68 (d, $J = 16.6$ Hz, 1H), 3.79 (s, 3H), 4.97 (t, $J = 6.9$ Hz, 1H), 7.30–7.50 (m, 6H), 7.60–7.75 (m, 4H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 19.15, 23.92, 26.84, 27.65, 28.57, 32.55, 50.99, 51.63, 51.93, 56.26, 76.85, 127.66, 127.73, 129.88, 129.91, 132.89, 133.60, 134.84, 135.81, 135.93, 151.97, 164.46, 169.54. MS (*m*/*z*) 556 (M^+). IR (neat) 1742 (br), 1106 cm^{-1}. Anal. Calcd for $C_{29}H_{36}O_5S_2Si$: C, 62.56; H, 6.52. Found: C, 62.38; H, 6.59.

4.4. (9*S*)-9-(*tert*-Butyldiphenylsilyloxy)-8-(2-hydroxyethyl)-7-hydroxymethyl-1,5-dithiaspiro[5,4]dec-7-ene 5

A solution of compound **4** (2.6 g, 4.67 mmol) in CH_2Cl_2 (20 mL) was cooled to −78 °C, and then a solution of DIBAL-H (1 M, 23.5 mL, 23.5 mmol) in toluene was added dropwise over a period of 5 min maintaining the temperature below −60 °C. After addition, the mixture was stirred at −78 to −40 °C for 2 h, and then the reaction quenched by adding dilute HCl solution (1 M, 20 mL). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2×20 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. Evaporation of solvents gave a crude product, which was further reduced by $NaBH_4$ as follows: The crude product was dissolved in CH_3OH (10 mL) and cooled to 0 °C. After addition of $NaBH_4$ (178 mg, 4.70 mmol), the solution was stirred for 15 min and then diluted with CH_2Cl_2 (30 mL). The organic solution was washed with water (30 mL) and separated. The aqueous phase was extracted with CH_2Cl_2 (2×20 mL). Extracts were combined and dried with anhydrous Na_2SO_4. Removal of the solvent gave a pale yellow oil, which was purified by chromatography to afford pure (9*S*)-9-(*tert*-butyldiphenylsilyloxy)-8-(2-hydroxyethyl)-7-hydroxymethyl-1,5-dithiaspiro[5,4]dec-7-ene **5** (2.1 g, 4.2 mmol) in 90% yield. $[\alpha]_D = +18.0$ (*c* 3.2, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (s, 9H), 1.75–1.85 (m, 1H), 1.95–2.05 (m, 1H), 2.32 (dd, $J = 6.3$ Hz; 13.0 Hz, 1H), 2.35–2.42 (m, 1H), 2.48–2.55 (m, 1H), 2.60–2.91 (m,

5H), 3.09 (br s, 2H), 3.28–3.34 (m, 1H), 3.55–3.61 (m, 1H), 4.26 (AB quartet, $J = 12.6$ Hz, 2H), 4.86 (t, $J = 6.5$ Hz, 1H), 7.30–7.50 (m, 6H), 7.61–7.72 (m, 4H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 19.21, 24.39, 27.05, 27.52, 29.11, 51.24, 55.83, 59.51, 59.55, 77.34, 127.66, 127.78, 129.86, 129.95, 133.36, 134.02, 135.94, 136.08, 141.48, 145.52. MS (m/z) 500 (M^+). IR (neat) 3333 (br), 1111 cm^{-1}.

4.5. (9*S*)-9-(*tert*-Butyldiphenylsilyloxy)-8-(2-acetoxyethyl)-7-acetoxymethyl-1,5-dithiaspiro[5,4]dec-7-ene 6

Acetic anhydride (4.1 g, 40.2 mmol) and compound **5** (2.0 g, 4.00 mmol) were dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C. Pyridine (4.74 g, 59.9 mmol) was added dropwise into the above solution at 0 °C. After the addition was complete, the ice bath was removed, and the reaction mixture stirred at room temperature overnight. The mixture was diluted with CH_2Cl_2 (60 mL) and the organic phase washed successively with aqueous HCl solution (2 M, 25 mL), aqueous K_2CO_3 solution (10%, 25 mL), and brine (20 mL). The organic solution was dried over anhydrous $MgSO_4$. The solvent was evaporated off, and the residue chromatographed to afford a colorless oil (9*S*)-9-(*tert*-butyldiphenylsilyloxy)-8-(2-acetoxyethyl)-7-acetoxymethyl-1,5-dithiaspiro[5,4]-dec-7-ene **6** (2.31 g, 3.96 mmol) in 98% yield. $[\alpha]_D = +13.2$ (c 2.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.09 (s, 9H), 1.65–1.80 (m, 1H), 1.90–2.05 (m, 1H), 1.98 (s, 3H), 2.08 (s, 3H), 2.31 (dd, $J = 6.4$ Hz; 12.9 Hz, 1H), 2.52–2.90 (m, 7H), 3.81–3.99 (m, 2H), 4.76 (AB quartet, $J = 12.5$ Hz, 2H), 4.84 (t, $J = 6.6$ Hz, 1H), 7.35–7.50 (m, 6H), 7.65–7.73 (m, 4H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 19.17, 20.79, 21.11, 24.33, 25.50, 26.99, 27.35, 29.06, 50.90, 57.55, 59.48, 61.81, 77.10, 127.62, 127.76, 129.82, 129.94, 133.19, 133.93, 135.88, 136.01, 136.50, 147.11, 170.56, 170.63. Anal. Calcd for $C_{31}H_{40}O_5S_2Si$: C, 63.66; H, 6.89. Found: C, 63.60; H, 7.01.

4.6. (4*S*)-3-(2-Acetoxyethyl)-2-acetoxymethyl-4-(*tert*-butyldiphenylsilyloxy)-2-cyclo-penten-1-one 7

Compound **6** (1.6 g, 2.74 mmol) was dissolved in anhydrous THF (8 mL) and the solution cooled to 0 °C. Periodic acid (1.8 g, 7.90 mmol) was then added in one portion. After stirring for 3 min, EtOAc (50 mL) was added. The organic solution was washed successively with cold water (15 mL), aqueous Na_2SO_3 solution (10%, 20 mL), and brine (15 mL). The organic solution was dried over $MgSO_4$ and filtered through a thin layer (5 cm) of Celite. The Celite was then rinsed twice with EtOAc. After removal of the solvents, the residue was purified by flash chromatography to produce pure (4*S*)-3-(2-acetoxyethyl)-2-acetoxymethyl-4-(*tert*-butyldiphenylsilyloxy)-2-cyclopenten-1-one **7** (880 mg, 1.78 mmol) in 65% yield. $[\alpha]_D = +19.5$ (c 0.84, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6) δ 1.08 (s, 9H), 1.59 (s, 3H), 1.65 (s, 3H), 2.17 (dd, $J = 6.0$ Hz; 18.0 Hz, 1H), 2.28 (dd, $J = 2.8$ Hz; 18.0 Hz, 1H), 2.63–2.78 (m, 2H), 3.92 (t, $J = 6.8$ Hz, 2H), 4.53 (dd, $J = 2.6$ Hz; 5.7 Hz, 1H), 4.79 (AB quartet, $J = 12.5$ Hz, 2H), 7.13–7.25 (m, 6H), 7.54–7.67 (m, 4H). ^{13}C NMR (300 MHz, C_6D_6) δ 19.04, 19.97, 20.00, 26.84, 26.96, 44.71, 54.95, 61.22, 71.52, 127.87, 127.97, 130.10, 130.16, 132.95, 133.20, 135.93, 138.14, 169.50, 169,69, 170.79, 200.98.

4.7. (1*R*,4*S*)-3-(2-Acetoxyethyl)-2-acetoxymethyl-1,4-bis(*tert*-butyldiphenylsilyloxy)-2-cyclopenten 8

Compound **7** (801 mg, 1.62 mmol) was dissolved in CH_3OH (10 mL), with $CeCl_3{\cdot}7H_2O$ (1.81 g, 4.85 mmol) then added to the solution. After stirring at room temperature for 10 min, the mixture was cooled to −20 °C, and $NaBH_4$ (306 mg, 8.09 mmol) then added. The reaction was continued at −20 °C and monitored by TLC. After the reaction was complete, CH_2Cl_2 (30 mL) and water (20 mL) were added. The organic phase was separated and aqueous phase extracted with CH_2Cl_2 (2×20 mL). Extracts were combined and dried over $MgSO_4$. Evaporation gave a colorless oil, which was immediately dissolved in CH_2Cl_2 (10 mL). *tert*-Butyldiphenylchlorosilane (1.34 g, 4.88 mmol), imidazole (332 mg, 4.88 mmol), and triethylamine (494 mg, 4.88 mmol) were then added. The mixture was stirred at room temperature for 32 h after which TLC showed that the reaction was almost complete. EtOAc (50 mL) was added, and the organic solution washed successively with 1 M HCl (15 mL), saturated $NaHCO_3$ (10 mL), and brine (10 mL). The organic layer was separated and dried over anhydrous $MgSO_4$. Evaporation of solvents gave a crude product, which was carefully purified by chromatography to produce pure (1*R*,4*S*)-3-(2-acetoxyethyl)-2-acetoxymethyl-1,4-bis(*tert*-butyldiphenylsilyloxy)-2-cyclopenten **8** (953 mg, 1.30 mmol) in 80% yield. $[\alpha]_D = -7.4$ (c 0.82, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (s, 18H), 1.54–1.65 (m, 1H), 1.80–1.91 (m, 1H), 1.89 (s, 3H), 1.95 (s, 3H), 2.39–2.50 (m, 1H), 2.55–2.65 (m, 1H), 3.90 (t, $J = 6.9$ Hz, 2H), 4.34 (t, $J = 6.6$ Hz, 1H), 4.47 (t, $J = 6.5$ Hz, 1H), 4.71 (AB quartet, $J = 12.1$ Hz, 2H), 7.23–7.43 (m, 12H), 7.54–7.61 (m, 8H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 19.14, 19.17, 20.79, 20.83, 25.28, 26.97, 27.02, 44.64, 58.04, 62.60, 74.43, 76.03, 127.44, 127.47, 127.50, 127.63, 129.52, 129.58, 129.74, 133.48, 133.68, 134.00, 134.26, 135.88, 135.90, 135.96, 137.54, 142.59, 170.60, 170.65. IR (neat) 1710, 1050 cm^{-1}. Anal. Calcd for $C_{44}H_{54}O_6Si_2$: C, 71.89; H, 7.40. Found: C, 71.60; H, 7.21.

4.8. (7*S*,9*R*)-7,9-Bis(*tert*-butyldiphenylsilyloxy)-3-oxabicyclo[4,3,0]non-1-en-2-one 9

To a solution of compound **8** (950 mg, 1.29 mmol) in solvent (CH_3OH–H_2O = 9:1, 6 mL) was added $LiOH{\cdot}H_2O$ (217 mg, 5.17 mmol). After stirring at room temperature for 30 min, water (20 mL) was added, and the aqueous solution extracted with EtOAc (2×20 mL). The combined organic extracts were then dried with anhydrous Na_2SO_4. Evaporation of solvents gave a pale yellow oil, which was next dissolved in CH_2Cl_2 (50 mL).

Triethylamine (653 mg, 6.45 mmol) was added, followed by PCC (2.78 g, 12.9 mmol) in 10 portions at intervals of 15 min. After addition, the red solution was stirred for one more hour at room temperature. The reaction solution was passed through a column of Celite (15 cm) to remove the colored salts and the Celite column then rinsed several times with EtOAc. All organic solutions were collected and evaporated to dryness. The residue was chromatographed to afford (7*S*,9*R*)-7,9-bis(*tert*-butyldiphenylsilyloxy)-3-oxabicyclo[4,3,0]non-1-en-2-one **9** (663 mg, 1.02 mmol) in 79.4% yield. $[\alpha]_D = -10.2$ (*c* 0.53, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 1.05 (s, 9H), 1.07 (s, 9H), 1.63–1.72 (m, 1H), 1.94–2.04 (m, 1H), 2.12–2.19 (m, 1H), 2.41–2.50 (m, 1H), 4.29–4.42 (m, 3H), 4.73–4.79 (m, 1H), 7.29–7.45 (m, 12H), 7.51–7.62 (m, 4H), 7.67–7.71 (m, 2H), 7.78–7.82 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$) δ 19.21, 19.24, 23.21, 26.98, 27.04, 44.51, 66.69, 72.32, 74.60, 127.48, 127.51, 127.75, 127.85, 129.53, 129.59, 129.97, 130.05, 131.84, 133.25, 133.30, 134.75, 135.80, 135.86, 136.11, 136.44, 160.44, 162.51, 168.42.

4.9. (1*S*,6*R*,7*S*,9*R*)-7,9-Bis(*tert*-butyldiphenylsilyloxy)-3-oxabicyclo[4,3,0]nonan-2-one 1

Compound **9** (350 mg, 0.54 mmol) was dissolved in EtOAc (15 mL), the solution put into a three-necked thick-wall flask, at which point Et_3N (10 mg, 0.1 mmol) and catalyst palladium on charcoal (5%, 100 mg) were added. The flask was purged with hydrogen gas several times, and the reaction mixture stirred under an atmosphere of H_2 for 6 h. Another portion of Pd/C (100 mg) was added, and stirring continued overnight. After the reaction was complete, the mixture was filtered through a thin layer of Celite to remove the catalyst. The thin layer of Celite was also rinsed twice with ethyl acetate. The filtrate was then evaporated to give a crude product, which was purified by chromatography to produce pure (1*S*,6*R*,7*S*,9*R*)-7,9-bis(*tert*-butyldiphenylsilyloxy)-3-oxabicyclo[4,3,0]nonan-2-one **1** (298 mg, 0.46 mmol) in 85% yield. $[\alpha]_D = -15.1$ (*c* 0.67, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 1.02 (s, 9H, *t*-Bu), 1.06 (s, 9H, *t*-Bu), 1.56–1.61 (m, 1H, H-8β), 1.62–1.68 (m, 1H, H-8α), 1.86–1.92 (m, 1H, H-5β), 2.17–2.25 (m, 1H, H-6β), 2.45–2.51 (m, 1H, H-5α), 2.72 (dd, $J = 7.2$ Hz; 7.2 Hz, 1H, H-1β), 4.03 (ddd, $J = 8.1$ Hz; 8.1 Hz; 8.1 Hz, 1H, H-7β), 4.28 (ddd, $J = 10.9$ Hz; 10.9 Hz; 3.4 Hz, 1H, H-4β), 4.44 (ddd, $J = 7.0$ Hz; 7.0 Hz; 4.2 Hz, 1H, H-9β), 4.65 (ddd, $J = 11.2$ Hz; 6.7 Hz; 6.7 Hz, 1H, H-4α), 7.25–7.69 (m, 20H, Ph). ^{13}C NMR (400 MHz, $CDCl_3$) δ 19.04, 19.18, 20.94, 26.86, 26.93, 40.93, 42.71, 48.63, 69.53, 73.42, 74.09, 127.60, 127.72, 129.66, 129.73, 129.75, 129.86, 132.24, 133.53, 133.60, 134.36, 135.51, 135.61, 136.04, 136.33, 170.03 (C=O). MS (*m*/*z*) 649 (M^++1). Anal. Calcd for $C_{40}H_{48}O_4Si_2$: C, 74.03; H, 7.46. Found: C, 74.30; H, 7.51.

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References and notes

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