An unexpected synthesis of an α,β,γ,δ-unsaturated ketone due to an abnormal opening of benzylidene acetal by bromide anion

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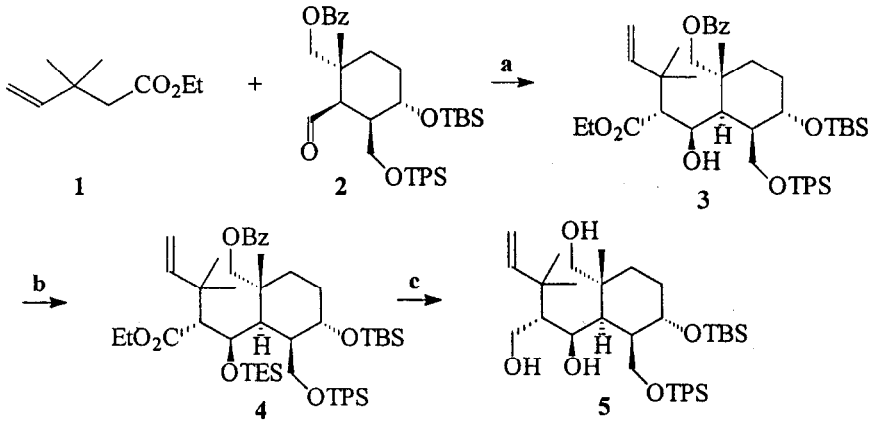
An unexpected synthesis of an α,β,γ,δ-unsaturated ketone, which embodies a new type of oxy-carbon cyclic structure, was achieved, while we tried to construct the taxane CB-ring system. Also, a series of abnormal reaction phenomena was found to be related to the formation and reaction of seven membered cyclic benzylidene acetal.

Keywords Synthesis, unsaturated ketone, seven membered cyclic benzylidene acetal

Recently, we accomplished the stereoselective synthesis of a taxane CB-ring skeleton.[1] Herein we would like to report an unexpected synthesis of α,β,γ,δ-unsaturated cyclopentenone in our research on the synthesis of taxane CB-ring skeleton. We started the synthesis from our C-ring synthon **2**[1] (Scheme 1).

According to our strategy the aldol reaction between **1** and **2** took place smoothly in the presence of $ZnCl_2$ to furnish desired β-hydroxyester **3** in 88% yield with good stereoselectivity.[2] Protection of compound **3** as its triethyl silyl ether **4** was achieved in 95% yield upon treatment with TESOTf and 2,6-lutidine. LAH reduction of compound **4** gave triol **5** in 86% yield. The direct reducion of **3** with LAH gave poor yield.

Scheme 1



Reagents and conditions: a, LDA, THF, −78℃, 1 h; $ZnCl_2$, −78℃, 1 h, 88%; b, TESOTf, 2,6-lutidine, 0℃, 10 h, 95%; c, LAH, Et_2O, 0℃, 86%.

The next selective protection of 1, 3-dihydroxyl group in compound **5** proved to be unsatisfactory (Scheme 2). Two kinds of diol protection groups, *i.e.* isopropylidene acetal and benzylidene acetal were tried,

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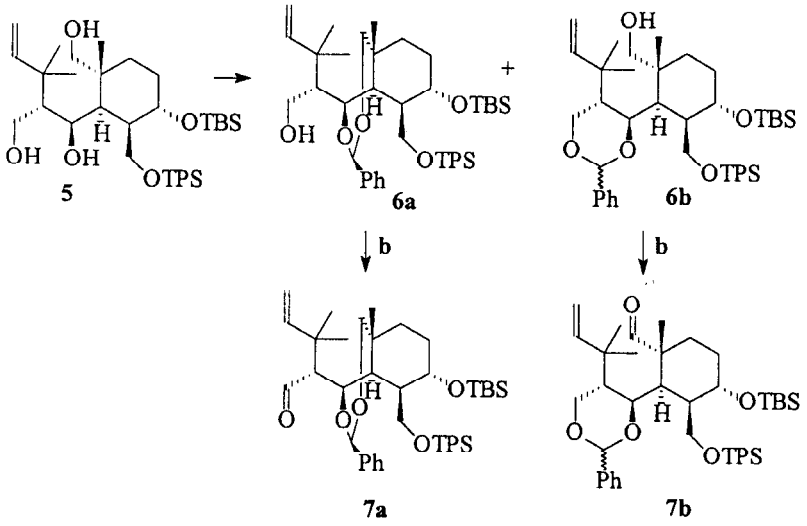
but in both cases a mixture of two products due to 1,3- and 1,4-dihydroxyl group protection was produced. In the case of isopropylidene acetal, the ratio was about 1.5:1.0, that of the latter was relatively enriched to 2.2:1.0. At this stage we did not know the exact structure of two products in both cases, so we continued the following transformations. Two hydroxyl groups in compound **5** were protected with the benzylidene acetal to produce **6a** and **6b**. Oxidation of the unmasked hydroxyl group in **6a** and **6b** with TPAP/NMO combined system[3] took place rapidly to afford aldehydes **7a** and **7b** respectively. The ^{1}H NMR spectrum showed that the proton corresponding to the aldehyde group appears to be a "d" peak while that of **7b** displayed an "s" peak. Hence we deduced easily that in the case of selective protection of hydroxyl groups in compound **5**, the major product was the thermodynamically less stable seven-membered cyclic 1,4-dihydroxyl benzylidene acetal **6a**, while the minor was the thermodynamically more stable six-membered cyclic 1,3-dihydroxyl **6b**. This result may be due to the steric effects of the rigid molecule.

Scheme 2

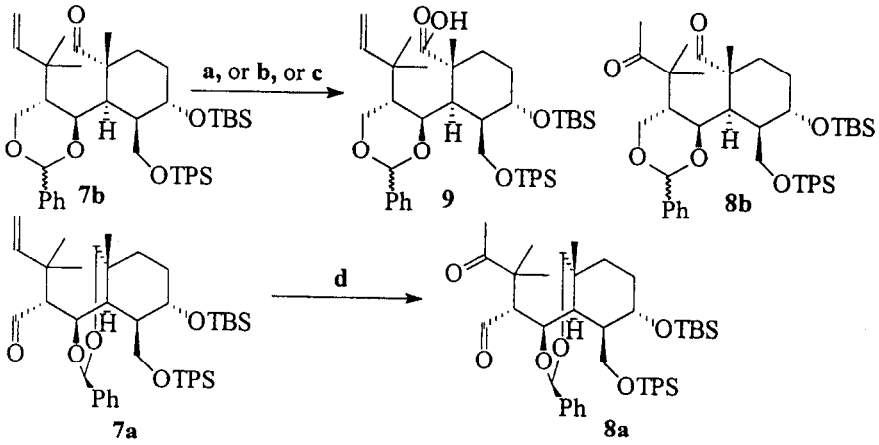


Reagents and conditions: a, $PhCH(OMe)_2$, cat. CSA, CH_2Cl_2, rt, 12 h, 98% (**6a**:**6b** = 2.2:1); b, TPAP, NMO, 4Ams, CH_2Cl_2, rt, 2 h, 98%.

Difficulties were encountered while we tried to convert the terminal double bond in compound **7b** to the methyl ketone unit to generate the ideal B-ring closure precursor **8b**, using various traditional Wacker's oxidation condition, which was used in the synthesis of many complex natural products.[4-7] To our surprise, no expected methyl ketone product **8b** was obtained, but the by-product carboxyl acid **9** which was produced due to the oxidation of aldehyde group in **7b**. While in the case of compound **7a**, we got the desired methyl ketone product **8a** in good yield (Scheme 3). The different behaviors between **7a** and **7b** in Wacker oxidation may stem from their structure characteristics.

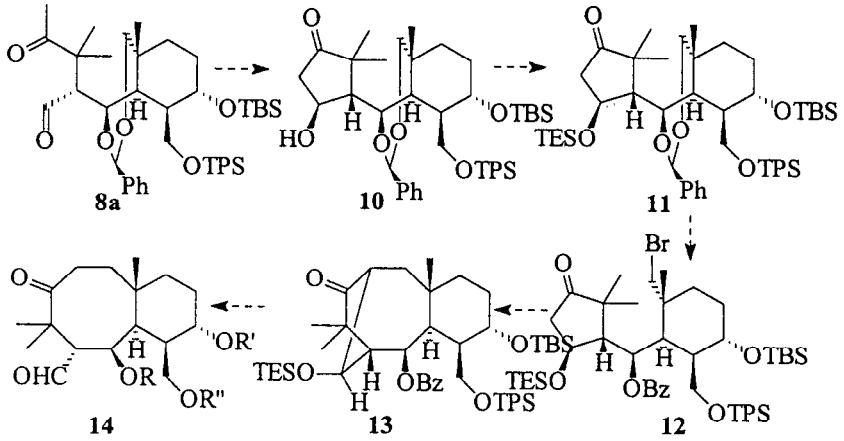
Since compound **8a** is easily available in our laboratory we tried to use **8a** as starting material for the synthesis of taxane CB-ring or its analogs which may lead to new bioactive compounds. Therefore, we had to modify the previous synthetic strategy as shown in Scheme 4. Compound **8a** undergoing an intramolecular aldol reaction could give compound **10**. Hydroxyl group protection of compound **10** would give rise to triethyl silyl ether **11**. After opening of the benzylidene acetal in compound **11** from the less hindered side using NBS/$BaCO_3$ condition, we could get the bromide **12**. Upon treatment with aldol-type condition, compound **12** could be converted to the B-ring closure bridged-fused compound **13**. Compound **13** undergoing a Retro-aldol reaction induced by a strong base would generate the CB-ring skeleton **14** which was similar to our target structure.

Scheme 3

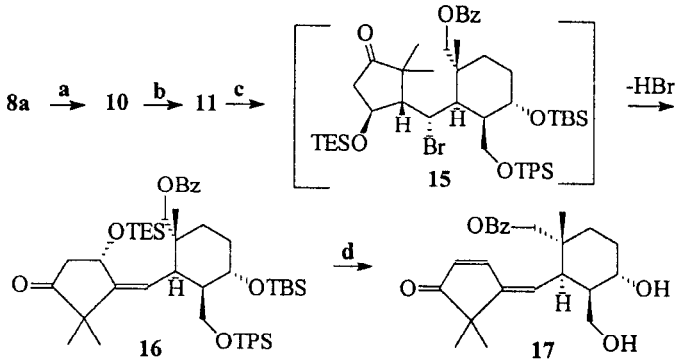


Reagents and conditions: a, $PdCl_2/CuCl/O_2$, DMF/H_2O, rt, 2 d, **9** (65%), **8b** (no); b, $Pd(OAc)_2$/benzoquinone, CH_3CN/H_2O, 70% $HClO_4$, rt, 2 h, no reaction; c, $PdCl_2/Cu(OAc)_2/O_2$, $AcNMe_2/H_2O$, rt, 2 d, **9** (62%), **8b** (trace); d, $PdCl_2/CuCl/O_2$, DMF/H_2O, rt, 2 d, 82%.

Scheme 4



Scheme 5



Reagents and conditions: a, LDA, THF, -78℃, 1 h, 91%; b, TESOTf, 2,6-lutidine, 10 h, 92%; c, NBS, $BaCO_3$, CCl_4, reflux, 2 h, 81%; d, TBAF, THF, rt, 12 h, 86%.

But when we started our new expedition based on Scheme 5 still unexpected result emerged. As we expected, the intramolecular aldol reaction of **8a** took place smoothly to afford a single adduct **10** in high yield. The structure of compound **10** was confirmed by an X-ray crystallographic analysis (Fig. 1).[8] Next hydroxyl group protection of **10** gave its triethyl silyl ether **11** in 92% yield. Unexpectedly, while we tried the NBS/$BaCO_3$ condition[9] to open the benzylidene acetal in compound **11**, we did not get the desired bromide **12**, but compound **16**. We thought that the benzylidene acetal was attacked by bromide anion not from the less hindered face but from the opposite face to give the intermediate **15**, which eliminated a molecule of HBr later to give compound **16**. The structure of **16** was established by ^{1}H NMR, ^{13}C NMR, ^{1}H-^{1}H COSY and NOESY analysis. Further deprotection of all three silyl protected hydroxyl groups in compound **16** followed by simultaneous dehydration furnished the α,β,γ,δ-unsaturated ketone **17** in 86% yield. The ^{1}H NMR spectrum of compound **17** was assigned by a ^{1}H-^{1}H COSY analysis. Thus generated compound **17** which embodies a new type of cyclic structure will be submitted for further bioactivity determination and can be further transformed.

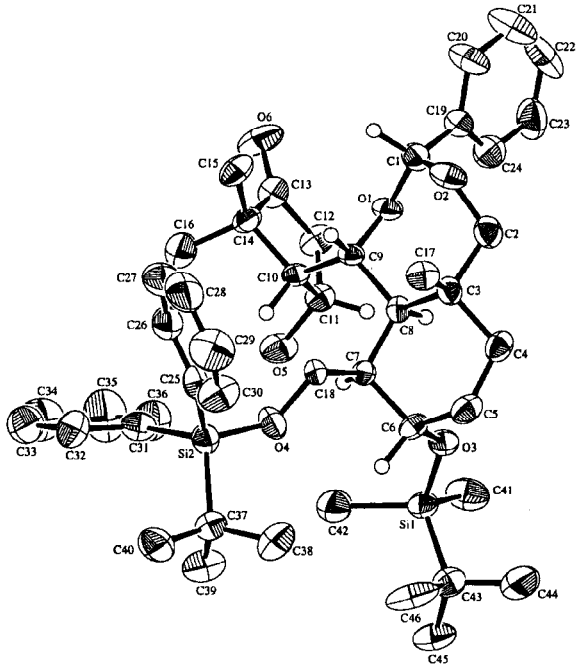


Fig. 1 The ORTEP view of compound **10**.

In conclusion, in our synthetic trials to construct the target CB-ring system we got a new type of α,β,γ,δ-unsaturated ketone unexpectedly and found several interesting abnormal reaction phenomena which must relate with steric structure characteristics.

Experimental

All ^{1}H NMR spectrum data are reported in δ units, parts per million. Infrared (IR) spectra are reported in wave numbers (cm^{-1}). Flash column chromatography was performed on silica gel H (10—40 μm). THF and Et_2O were distilled from sodium/benzophenone ketyl. CH_2Cl_2 was distilled from CaH_2. DMF was distilled before use. Other reagents were obtained commercially and used as received unless otherwise specified. All reactions were performed under a static nitrogen or argon atmosphere in flame-dried glassware.

Adduct **3** Butyllithium (0.075 mL, 0.12 mmol) was added to a solution of *i*-Pr_2NH (0.017 mL, 0.12 mmol) in THF (2 mL) at 0℃, then the mixture was allowed to warm to room temperature and stirred for 20 minutes. The mixture was then cooled to −78℃, $ZnCl_2$ (0.017 g, 0.12 mmol) was added and stirred for 1 h. **1** (0.017 g, 0.11 mmol) was added and stirred for 1 h, then **2** (0.066 g, 0.1 mmol) was added and stirred for another 1 h. Saturated aqueous NH_4Cl was added and the mixture was warmed to room temperature. The aqueous layer was extracted with CH_2Cl_2 (10 mL × 3), the combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, then dried over Na_2SO_4. Removal of solvent and purification by flash column chromatography (petroleum: ethyl acetate = 20: 1) gave the title compound **3** (0.072 g, 88%) as a colorless oil. ν_{max} (neat): 3497, 3072, 1720, 1640, 1472, 775, 741, 709. ^{1}H NMR (300 MHz, $CDCl_3$): 0.02(3H, s), 0.08(3H, s), 0.72(3H, s), 0.88 (9H, s), 1.02(3H, s), 1.10(12H, s), 1.15—1.50 (3H, m), 1.28(3H, t, J = 7.2 Hz), 1.98—2.20 (2H, m), 2.40(1H, dd, J = 10.4, 5.2 Hz), 2.52 (1H, s), 3.48—3.51(2H, m), 3.65(1H, d, J = 11.0 Hz), 3.85—4.05(3H, m), 4.15—4.21(1H, m), 4.24—4.27(1H, m), 4.59(1H, d, J = 10.4 Hz), 4.82(1H, d, J = 10.7 Hz), 4.90(1H, d, J = 17.5 Hz), 5.70(1H, dd, J = 17.5, 10.7 Hz), 7.30—7.70(13H, m), 8.07(2H, d, J = 7.1 Hz).

EIMS(m/z): 814(M^+ - 1). E.A. $C_{48}H_{70}O_7Si_2$. Calcd.: C, 70.72; H, 8.66. Found: C, 70.80; H, 8.87. Spectral data of the diastereoisomer: IR (neat): 3560, 3072, 1722, 1640, 1473, 775, 740, 709. ^1H NMR (300 MHz, $CDCl_3$): 0.05(3H, s), 0.07(3H, s), 0.90(12H, s), 0.98—1.20(18H, m), 1.20—1.50(3H, m), 2.04—2.06(1H, m), 2.20(1H, d, J = 3.5 Hz), 2.28(1H, m), 2.73—2.76(1H, m), 3.70—3.77(1H, m), 3.79—3.91(2H, m), 3.97—4.01(1H, m), 4.12—4.16(3H, m), 4.41—4.44 (1H, m), 4.95(1H, d, J = 10.9 Hz), 5.02(1H, d, J = 17.7 Hz), 6.15(1H, dd, J = 17.7, 10.9 Hz), 7.30—7.80(13H, m), 8.10(2H, d, J = 7.1 Hz). ESI(m/z) 816(M^+ + 1), 838(M^+ + Na), 861(M^+ + 2Na).

TES *ether* **4** To a solution of **3** (0.081 g, 0.1 mmol) and 2,6-lutidine (0.023 mL, 0.2 mmol) in CH_2Cl_2 (2mL) was added TESOTf (0.034 mL, 0.15 mmol) at 0℃. Then the mixture was allowed to stand overnight at room temperature. Saturated aqueous $NaHCO_3$ was added to quench the reaction and the aqueous layer was extracted with CH_2Cl_2(10 mL × 3), the combined organic layers were washed with brine, then dried over Na_2SO_4. Removal of solvent and purification by flash column chromatography (petroleum: ethyl acetate = 30:1) gave the title compound **4** (0.089 g, 95%) as a colorless oil. IR (neat): 3073, 1728, 1638, 1473, 740, 709. ^1H NMR (300 MHz, $CDCl_3$) 0.06 (3H, s), 0.10(3H, s), 0.40(6H, q, J = 7.5 Hz), 0.72(12H, t, J = 7.5 Hz), 0.85(3H, s), 0.93 (12H, s), 1.08(9H, s), 1.12(3H, t, J = 6.3 Hz), 1.25—1.92 (4H, m), 2.08—2.21(2H, m), 2.50 (1H, d, J = 5.0 Hz), 2.99(1H, d, J = 6.8 Hz), 3.75—3.92(3H, m), 4.00—4.18(2H, m), 4.29 (1H, s), 4.38(1H, d, J = 11.3), 4.94(1H, d, J = 17.5 Hz), 6.05(1H, dd, J = 17.5, 10.7 Hz), 7.35—7.75(13H, m), 8.11(2H, d, J = 6.5 Hz). EIMS(m/z) 901(M^+ - CH_2 = CH). E.A. $C_{54}H_{84}O_7Si_3$. Calcd.: C, 69.78; H, 9.11. Found: C, 70.18; H, 9.36.

Triol **5** To the suspension of LAH (0.01 g, 0.25 mmol) in ether (5 mL) was added **4** (0.046 g, 0.05 mol) at 0℃, then the suspension was allowed to warm to room temperature and stirred for 4 h. Aqueous NaOH was added to quench the reaction. The mixture was filtered through a pad of celite and the solid was washed with ethyl acetate, the combined organic fractions were washed with brine, dried over Na_2SO_4. After removal of solvent, the residue was purified by flash column chromatography (petroleum: ethyl acetate = 5:1) to give the title compound **5** (0.029 g, 86%) as a colorless solid. mp 218—219℃. IR (film): 3252, 3072, 1637, 1472, 774, 740, 701. ^1H NMR (300 MHz, $CDCl_3$): 0.04(3H, s), 0.07(3H, s), 0.58(3H, s), 0.91(9H, s), 0.99(3H, s), 1.06(9H, s), 1.11 (3H, s), 1.20—1.50(4H, m), 1.76(1H, ddd, J = 11.5, 11.5, 4.3 Hz), 1.74—1.88(1H, m), 2.24 (1H, dd, J = 9.9, 4.7 Hz), 3.19(2H, s), 3.37 (1H, d, J = 10.6 Hz), 3.49(1H, dd, J = 10.1, 10.1 Hz), 3.66(3H, br.s), 4.00—4.15(4H, m), 4.92(1H, d, J = 10.7 Hz), 5.02(1H, d, J = 17.7 Hz), 6.07(1H, dd, J = 17.7, 10.7 Hz), 7.35—7.70(10H, m). FABMS: 669(M^+), 670(M^+ + 1), E.A. $C_{39}H_{64}O_5Si_2$. Calcd.: C, 70.01; H, 9.64. Found: C, 70.06; H, 10.22.

Benzylidene acetal alcohols **6a** *and* **6b** To a solution of **5** (0.054 g, 0.08 mmol) in CH_2Cl_2 (1.5 mL) were added $PhCH(OMe)_2$(0.03 mL, 0.2 mmol) and CSA (3.75 mg, Cat.). The mixture was allowed to stand overnight at room temperature. Saturated aqueous $NaHCO_3$ was added to quench the reaction and the aqueous layer was extracted with CH_2Cl_2(10 mL × 3), the combined organic layers were washed with brine, then dried over Na_2SO_4. Removal of solvent and purification by flash column chromatography (petroleum: ethyl acetate = 20:1) gave the 1,4-dihydroxyl benzylidene acetal **6a** and the 1,3-dihydroxyl benzylidene acetal **6b** (0.06 g, overall 98%) as a colorless solid. (**6a**:**6b** = 2.2:1). Spectral data of compound **6a**: IR(film): 3562, 3072, 1636, 1472, 775, 739, 701. ^1H NMR (300 MHz, $CDCl_3$): 0.05(3H, s), 0.10(3H, s), 0.76(3H, s), 0.93(9H, s), 1.04(3H, s), 1.09(9H, s), 1.12 (3H, s), 1.20—1.55(4H, m), 2.00—2.02(1H, m), 2.19(1H, dd, J = 9.3, 4.9 Hz), 2.56—2.59 (1H, m), 2.91(1H, d, J = 11.5 Hz), 3.36(1H, dd, J = 10.7, 1.7 Hz), 3.50—3.55(2H, m), 3.99—4.18(4H, m), 4.81(1H, d, J = 10.6 Hz), 4.91(1H, d, J = 17.4 Hz), 5.65(1H, s), 5.88 (1H, dd, J = 17.4, 10.6 Hz), 7.25—7.70(15H, m). ESI(m/z): 780(M^+ + Na), 802(M^+ - 1 + 2Na). E.A. $C_{46}H_{68}O_5Si_2$. Calcd.: C, 72.97; H, 9.05. Found: C, 73.27; H, 9.32. Spectral data of compound **6b**: IR (film): 3501, 3072, 1637, 1472,

774, 740, 701. ^{1}H NMR(300 MHz, $CDCl_3$): 0.06 (3H, s), 0.11(3H, s), 0.58(3H, s), 0.98(9H, s), 1.09(9H, s), 1.13(3H, s), 1.23(3H, s), 1.15—1.50(4H,m), 1.72(1H,ddd,J = 12.1,12.1, 4.8 Hz), 1.88—1.91(1H, m), 2.94—3.23(3H, m), 3.41(1H, d, J = 9.7 Hz), 3.54(1H, dd, J = 9.1, 9.1 Hz), 3.98—4.02(2H, m), 4.36—4.41 (2H, m), 4.85(1H, d, J = 10.7 Hz), 4.99(1H, d, J = 17.3 Hz), 5.56(1H, dd, J = 17.3, 10.7 Hz), 5.88(1H, s), 7.30—7.70(15H, m). FABMS (MW = 757): 651(M^+ - PhCHO). E.A. $C_{46}H_{68}O_5Si_2$. Calcd.: C, 72.97; H, 9.05. Found: C, 73.72; H, 9.45.

Benzylidene acetal aldehyde **7a** To a solution of **6a** (0.076 g, 0.1 mmol) in CH_2Cl_2(2 mL) was added 4Å ms (50 mg), NMO (17.6 mg, 0.15 mmol), TPAP (1.76 mg, Cat.). The mixture was stirred for 2 h at room temperature, then diluted with CH_2Cl_2, filtered through a pad of celite and the solid was washed with CH_2Cl_2. After removal of solvent, the residue was purified by flash column chromatography (petroleum: ethyl acetate = 20:1) to give the title compound **7a** (0.075 g, 98%) as a colorless oil. IR (neat): 3072, 1718, 1638, 1472, 776, 740, 701. ^{1}H NMR (300 MHz, $CDCl_3$): 0.06(3H, s), 0.15(3H, s), 0.73 (3H, s), 0.88(9H, s), 0.99(3H, s), 1.09(9H, s), 1.11(3H, s), 1.20—1.55(4H, m), 1.99—2.03(1H, m), 2.24—2.29(1H, m), 2.30(1H, d, J = 5.0 Hz), 2.86(1H,d,J = 11.6 Hz),3.24—2.29 (1H, d, J = 10.9 Hz), 3.41(1H, d, J = 11.9 Hz), 3.50(1H, dd, J = 10.2, 10.2 Hz), 4.10(1H, s), 4.18(1H, d, J = 9.6 Hz), 4.86(1H, d, J = 10.9 Hz), 4.91(1H,d, J = 17.8 Hz), 5.67(1H,dd,J = 17.8, 10.9 Hz), 5.69(1H, s), 7.25—7.70(15H, m), 10.09(1H, d, J = 4.1 Hz). EIMS(m/z) (MW = 754): 591 (M^+ - PhCHO - ^{t}Bu). FABMS: 591 (M^+ - PhCHO - ^{t}Bu). E.A. $C_{46}H_{66}O_5Si_2$. Calcd.: C, 73.16; H, 8.81. Found: C, 73.33; H, 9.08.

Ketoaldehyde **8a** O_2 was bubbled through a stirred solution of $PdCl_2$(3.54 mg, Cat.), CuCl (10 mg, 0.1 mmol) in 3.5 mL of DMF and 0.5 mL of H_2O for 2 h. Compound **7a** (0.075 g, 0.1 mmol) was added to the solution and O_2 was bubbled through for additional 24 h at room temperature. Water was added to dilute the reaction mixture and the aqueous layer was extracted with ether (10 mL × 3), the combined organic layers were concentrated and purified by flash column chromatography (petroleum: ethyl acetate = 20: 1) to give the title compound **8a** (0.062 g, 82%) as a colorless oil. IR (neat): 3072, 1707, 1472, 757, 702. ^{1}H NMR(300 MHz, $CDCl_3$): 0.04(3H, s), 0.10(3H, s), 0.77(3H, s), 0.88(9H, s), 1.01(3H, s), 1.10(9H, s), 1.19(3H, s), 1.24—1.50(4H, m), 2.08(3H, s), 2.17—2.20(1H, m), 2.30(1H, dd, J = 8.6, 5.5 Hz), 2.88(1H, d, J = 11.8 Hz), 3.04(1H, s), 3.38—3.44(2H, m), 3.55(1H, dd, J = 10.2 Hz), 4.11(1H, d, J = 2.1 Hz), 4.18(1H, d, J = 9.9 Hz), 5.61(1H, s), 7.25—7.70(15H, m), 10.01(1H, d, J = 1.7 Hz). ESI (m/z): 771 (M^+), 794(M^+ + Na), 817(M^+ + 2Na). E.A. $C_{46}H_{66}O_6Si_2$. Calcd.: C, 71.64; H, 8.63. Found: C, 71.37; H, 8.47.

Adduct **10** Butyllithium (0.075 mL, 0.12 mmol) was added to a solution of i-Pr_2NH (0.017 mL, 0.12 mmol) in THF (2 mL) at 0℃, then the mixture was allowed to warm to room temperature and stirred for 20 minutes. The mixture was then cooled to - 78℃, **8a**(0.077 g, 0.1 mmol) was added and stirred for 1 h. Saturated aqueous NH_4Cl was added and the mixture was warmed to room temperature. The aqueous layer was extracted with CH_2Cl_2(10 mL × 3), the combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, then dried over Na_2SO_4. Removal of solvent and purification by flash column chromatography (petroleum: ethyl acetate = 10: 1) gave the title compound **10** (0.07 g, 91%) as a colorless solid. mp 120—121℃. IR(film): 3418, 3070, 1729, 1471, 783, 739, 702. ^{1}H NMR (300 MHz, $CDCl_3$): 0.08 (3H, s), 1.02(3H, s), 0.77(3H, s), 0.89(9H, s), 0.96(3H, s), 1.07(9H,s), 1.16(3H,s),1.25—1.50(2H, m), 1.50—1.60(1H, br.s), 1.55 (1H, s), 1.65(1H, d, J = 4.3 Hz), 2.16(1H, dd, J = 9.3, 4.9 Hz), 2.22(1H, s), 2.28—2.30(1H, m), 2.44(1H, dd, J = 19.2, 3.3 Hz), 2.78(1H, dd, J = 19.2, 7.8 Hz), 2.96(1H, d, J = 11.7 Hz), 3.38(1H, d, J = 9.8 Hz), 3.46(1H, d, J = 11.6 Hz), 3.52(1H, dd, J = 9.8, 9.8 Hz), 3.94 (1H, d, J = 9.4 Hz), 4.18(1H, d, J = 1.9 Hz), 4.79—4.82(1H, m), 5.62(1H, s), 7.25—7.70 (15H, m). ESI(m/z): 771(M^+), 794(M^+ + Na), 817(M^+ + 2Na). E.A. $C_{46}H_{66}O_6Si_2$. Calcd.: C, 71.64; H, 8.63. Found: C, 71.62; H, 8.89.

TES *ether* **11** To a solution of **10** (0.04 g, 0.05 mmol) and 2,6-lutidine (0.018 mL, 0.15 mmol)

in CH_2Cl_2 (2 mL) was added TESOTf (0.024 mL, 0.1 mmol) at 0℃. Then the reaction mixture was allowed to stand overnight at room temperature. Saturated aqueous $NaHCO_3$ was added to quench the reaction and the aqueous layer was extracted with CH_2Cl_2 (10 mL × 3), the combined organic layers were washed with brine, then dried over Na_2SO_4. Removal of solvent and purification by flash column chromatography (petroleum: ethyl acetate = 30: 1) gave the title compound **11** (0.04 g, 92%) as a colorless oil. IR(neat): 3072, 1740, 1472, 740, 702. ^{1}H NMR(300 MHz, $CDCl_3$): 0.11(3H, s), 0.13(3H, s), 0.66(6H, q, J = 7.3 Hz), 0.72(3H, s), 0.92(9H, s), 0.95 (9H, t, J = 7.3 Hz), 0.99(3H, s), 1.08(9H, s), 1.25—1.55(4H, m), 1.30(3H, s), 2.12(1H, dd, J = 9.4, 5.1 Hz), 2.28—2.30(1H, m), 2.30—2.40(2H, m), 2.73(1H, dd, J = 19.0, 6.5 Hz), 2.98(1H, d, J = 11.6), 3.35—3.50(2H, m), 3.53(1H, d, J = 11.6 Hz), 3.93(1H, d, J = 9.4 Hz), 4.24(1H, d, J = 1.8 Hz), 4.69(1H, d, J = 6.4 Hz), 5.62(1H, s), 7.25—7.70(15H, m). ESI (m/z): 908(M^+ + Na), 931(M^+ + 2Na). E.A. $C_{52}H_{80}O_6Si_3$. Calcd.: C, 70.54; H, 9.11. Found: C, 70.69; H, 9.40.

Ketone **16** To a solution of **11** (0.026 g, 0.03 mmol) in CCl_4 (2 mL) were added NBS (10.5 mg, 0.06 mmol) and $BaCO_3$ (5.8 mg, 0.03 mmol). The reaction mixture was refluxed for 2 h, then diluted with CCl_4, filtered through a pad of celite and the solid was washed with CCl_4. After removal of solvent, the residue was purified by flash column chromatography (petroleum: ethyl acetate = 30: 1) to give the title compound **16** (0.021 g, 81%) as a colorless oil. IR (neat): 3072, 2958, 2859, 1750, 1720, 1472. ^{1}H NMR (300 MHz, $CDCl_3$): 0.14(3H, s), 0.16(3H, s), 0.45(6H, q, J = 7.8 Hz), 0.71(3H, s), 0.79 (9H, t, J = 7.8 Hz), 1.00(12H, s), 1.03(9H, s), 1.05—1.28(2H, m), 1.18(3H, s), 1.57—1.71 (1H, m), 2.16(1H, s), 2.19(1H, d, J = 3.8 Hz), 2.26—2.28(1H, m), 2.36(1H, ddd, J = 12.8, 12.8, 4.5 Hz), 3.37(1H, dd, J = 11.3, 6.1 Hz), 3.50 (1H, d, J = 11.0 Hz), 3.62(1H, dd, J = 10.7, 10.7 Hz), 3.85(1H, dd, J = 10.0, 3.6 Hz), 3.92 (1H, d, J = 11.0 Hz), 4.42(1H, s), 4.79(1H, d, J = 3.8 Hz), 5.21(1H, d, J = 11.6 Hz), 7.31—7.73(13H, m), 8.08(2H, d, J = 11.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 221.0, 166.4, 151.1, 135.7, 135.6, 135.5, 133.7, 133.4, 133.1, 130.2, 129.8, 129.7, 129.6, 128.6, 127.8, 122.4, 77.5, 77.1, 76.7, 71.9, 67.6, 67.3, 62.2, 49.9, 48.6, 47.7, 36.8, 34.1, 28.4, 28.0, 26.8, 26.3, 25.4, 24.7, 19.2, 18.7, 18.3, 6.9, 5.2, −4.1, −4.8. EIMS(m/z): 882(M^+), 867(M^+ − CH_3). ESIMS (m/z): 906(M^+ + Na), 929(M^+ + 2Na). HREIMS Calcd. for $C_{52}H_{78}O_6Si_3$: 882.5106, Found: 882.5101.

α,β,γ,δ-*Unsaturated ketone* **17** To a solution of **16** (0.088 g, 0.1 mmol) in THF (2 mL) was added TBAF (1M in THF, 0.6 mL, 0.6 mmol). Then the mixture was allowed to stand overnight at room temperature. H_2O was added to quench the reaction and the aqueous layer was extracted with CH_2Cl_2 (10 mL × 3), the combined organic layers were washed with brine, then dried over Na_2SO_4. Removal of solvent and purification by flash column chromatography (petroleum: ethyl acetate = 2: 1) gave the title compound **17** (0.035 g, 86%) as colorless solid. mp 179—180℃. IR(film): 3418, 2927, 1706, 1622, 1602, 1275, 1116, 757, 713. ^{1}H NMR (400 MHz, $CDCl_3$): 0.90(3H, s), 1.16(6H, s), 1.50—1.75(3H, m), 1.97—1.99 (1H, m), 2.12—2.16(1H, m), 2.95(1H, dd, J = 3.9, 11.9 Hz), 3.48(1H, dd, J = 3.9, 10.9 Hz), 3.69(1H, dd, J = 8.9, 10.6 Hz), 3.94—3.97(1H, m), 4.39, 4.52(2H, AB, J = 11.1 Hz), 5.59(1H, d, J = 11.9 Hz), 6.22(1H, dd, J = 1.2, 5.7 Hz), 7.48(2H, t, J = 7.5 Hz), 7.59—7.63(1H, m), 7.96(1H, d, J = 5.7 Hz), 8.05(2H, d, J = 7.2 Hz). EIMS (MW = 398): 398(M^+), 380(M^+ − H_2O), 362(M^+ − $2H_2O$), 227, 105. HREIMS Calcd. for $C_{24}H_{30}O_5$: 398.2093, Found: 398.2107.

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