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Stereoselective carbon–carbon bond forming reactions of chiral cyclopent-2-enone and cyclopentene-1-methanol, both spiro-connecting a 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl ring

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Abstract

The conjugate additions of a variety of organocopper reagents or dimethyl malonate anion to a spirocyclic cyclopent-2-enone connecting a 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranosyl ring as a constituent of the spiro structure, namely (1*S*,3*R*,4*R*,5*R*)-3,4-(isopropylidenedioxy)-1-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-2-oxaspiro[4.4]non-6-en-8-one, proceeded stereoselectively in some cases affording a variety of β-functionalized cyclopentanone derivatives. The thermal treatment of (1*S*,3*R*,4*R*,5*R*)-7-(hydroxymethyl)-3,4-(isopropylidenedioxy)-1-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-2-oxaspiro[4.4]non-6-ene, another D-glucose-derived spirocyclic substrate, with triethyl orthoacetate in the presence of a catalytic amount of acid afforded the Claisen rearrangement product with a high level of diastereoselectivity.

1. Introduction

Spirocyclic compounds are frequently found in nature as core skeletons of a variety of natural terpenoids, represented by spirovetivane, acorane, vetispirane, and chamigrane-type sesquiterpenoids.[1] A number of synthetic approaches to the spirocyclic compounds including natural products have been reported so far.[2] Quite recently Meyers and co-workers reported an asymmetric route to chiral cyclohexenones with spiro-connected cyclopentanes.[3] Florent and Kuhn reported a novel synthetic approach to the antitumor prostanoid punaglandin IV using the 'intramolecular spirocyclization' of a D-glucose-derived substrate.[4] As part of our continuing interest in the transformation of carbohydrates into a variety of multifunctionalized carbocyclic building blocks, we have reported some efficient approaches to spirocyclic compounds carrying a 1,2:5,6-di-*O*-isopropylidene-α-

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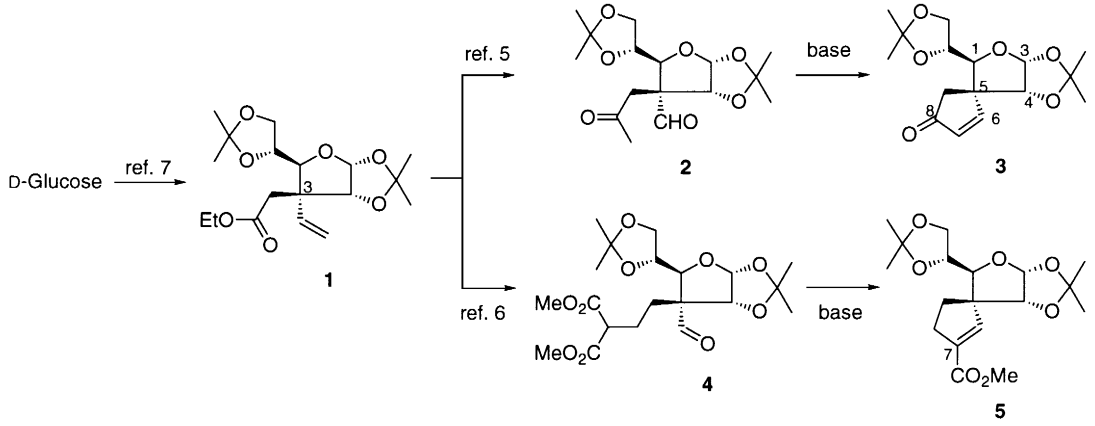
D-glucofuranosyl moiety, which constitutes one ring of the spirocyclic structure, in enantiomerically pure form.[5,6] The two previous approaches are summarized in Scheme 1. The asymmetric quaternary carbon center (C-3 of the so-called diacetone-glucose) in compound **1** was efficiently introduced by the orthoester Claisen rearrangement of a D-glucose-derived allylic alcohol.[7,8] The rearrangement product **1** was converted into **2**, which underwent an intramolecular aldol condensation to afford (1*S*,3*R*,4*R*,5*R*)-3,4-(isopropylidenedioxy)-1-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-2-oxaspiro[4.4]non-6-en-8-one **3**.[5] On the other hand, the Knoevenagel-like ring forming reaction of **4**,[9] followed by demethoxycarbonylation and β-elimination, gave (1*S*,3*R*,4*R*,5*R*)-7-methoxycarbonyl-3,4-(isopropylidenedioxy)-1-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-2-oxaspiro[4.4]non-6-ene **5**.[6] We have recently investigated the 1,4-conjugate additions of a variety of organocopper reagents to the cyclopent-2-enone derivative **3** and the orthoester Claisen rearrangement of an allylic alcohol **11** prepared from **5**.[10] As a result, synthetically useful stereoselective reactions were observed in some cases. In this paper, we describe the results and rationales for the stereochemical outcomes of these reactions.



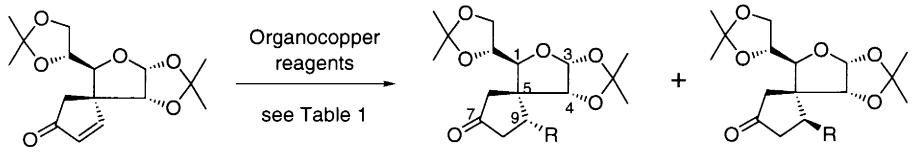
Scheme 1.

2. Results and discussion

*2.1. The 1,4-conjugate addition of organocopper reagents to **3***

We investigated first the conjugate addition of a variety of organocopper reagents to the cyclopent-2-enone **3** (Scheme 2). We anticipated that a carbon nucleophile such as organocopper species would approach the β-carbon of the enone **3** from the less hindered *re*-face (α-side) to avoid the steric interaction between the 3,4-isopropylidene group directly attached to the tetrahydrofuran ring and the nucleophile. The results are summarized in Table 1. The observed stereoselectivity depended on the reaction parameters used. The reaction of **3** with lithium dimethylcuprate (3 molar equiv.), prepared from methyllithium and Cu(I)I, in Et_2O at 0°C gave the two separable adducts, **6α** and **6β**, in a ratio of 84:16 (run 1). As we expected, the α-isomer **6α** was the major product. At −78°C this reaction proceeded with a higher level of diastereoselectivity (run 2). An analogous result was obtained in the presence of chlorotrimethylsilane (TMSCl, 5 molar equiv.) (run 3). It is known that good donor solvents such as THF, DMF, and HMPA diminish the Gilman-type cuprate reactivity in the conjugate addition.[11] In fact, the above reaction did not proceed in THF at −78 to −18°C although the 1,4-adducts were obtained at 0°C virtually nonstereoselectively (run 4). However, the cuprate–TMSCl combination[12] accelerated

the conjugate addition even at −78°C although the β-adduct **6β** was formed in excess, albeit in a moderate combined yield (run 5). The solvent-dependent diastereoselectivity in the conjugate additions of organocopper reagents was reported by other groups.[13] In the case of the methylcuprate, prepared from methylmagnesium bromide (6 molar equiv.) and cuprous bromide–dimethyl sulfide complex (3 molar equiv.), the conjugate addition took place rapidly at −78°C to give 1.7:1 (in Et_2O) or 3.3:1 (in THF–Me_2S) mixtures of the adducts **6α** and **6β** (runs 6 and 7).



Scheme 2.

Table 1
The 1,4-conjugate additions of a variety of organocopper reagents to enone **3**

run	reagents	solvent	temp. (°C)	product	isolated yields (%) α	β	(**3**)	selectivity α : β
1	MeLi, CuI	Et_2O	0	**6**	53	10		84:16
2	MeLi, CuI	Et_2O	–78	**6**	70	6		92:8
3	MeLi, CuI, TMSCl	Et_2O	–78	**6**	68	8		89:11
4	MeLi, CuI	THF	0	**6**	16	24	(38)	40:60
5	MeLi, CuI, TMSCl	THF	–78	**6**	17	30		36:64
6	MeMgBr, CuBr·Me_2S	Et_2O	–78	**6**	41	23		64:36
7	MeMgBr, CuBr·Me_2S	THF–Me_2S (2:1)	–78	**6**	43	13		77:23
8	*n*-BuLi, CuI	Et_2O	–78 to –18	**7**	34	24		59:41
9	*n*-BuLi, CuI, TMSCl	Et_2O	–78	**7**	23	47		33:67
10	*n*-BuLi, CuI	THF	–78 to –18	**7**	47	6	(28)	89:11
11	*n*-BuLi, CuI, TMSCl	THF	–78	**7**	56	30		65:35
12	*i*-PrMgBr, CuBr·Me_2S	Et_2O	–78	**8**	21	12	(36)	64:36
13	*i*-PrMgBr, CuBr·Me_2S	Et_2O	–78 to rt	**8**	13	55		19:81
14	*i*-PrMgBr, CuBr·Me_2S	THF–Me_2S (2:1)	–78	**8**	18	65		22:78
15	*i*-PrMgBr, CuBr·Me_2S, TMSCl	THF–Me_2S (2:1)	–78	**8**	50	8	(21)	86:14
16	vinylMgBr, CuBr·Me_2S	Et_2O	–78	**9**	9	6		60:40
17	vinylMgBr, CuBr·Me_2S	THF–Me_2S (2:1)	–78	**9**	19	13		59:41
18	vinylMgBr, CuBr·Me_2S, TMSCl	THF–Me_2S (2:1)	–78	**9**	31	20		61:39

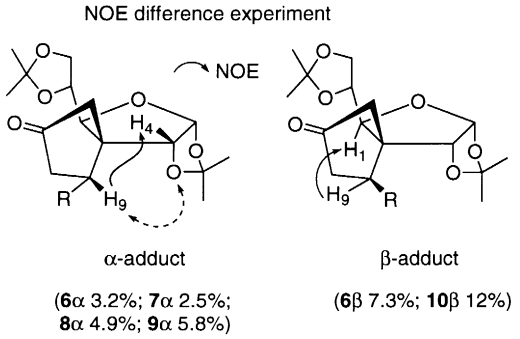
As shown in runs 8–11, the conjugate addition of lithium di-*n*-butylcuprate (3 molar equiv.) to **3** provided the adducts **7α** and **7β**. The reaction in Et_2O proceeded nonstereoselectively (run 8). In the presence of TMSCl, the reaction gave a 1:2 mixture of **7α** and **7β** (run 9). On the other hand, a high α-selectivity was observed in THF (run 10) although the combined yield was moderate. The solvent effect on stereoselectivity was apparent, while these stereochemical outcomes were opposite to those obtained in the cases using lithium dimethylcuprate.

The reaction of **3** with *i*-propylmagnesium bromide (6 molar equiv.) and cuprous bromide–dimethyl sulfide (3 molar equiv) in Et_2O at −78°C gave a separable mixture of **8α** (21%) and **8β** (12%) (run 12). When the reaction was initiated at −78°C then gradually warmed to ambient temperature, the

stereochemical outcome reversed and the β-isomer **8β** was obtained in a yield of 55% (run 13). These results suggest that an equilibrium between intermediary α-oriented copper–enone (d–π*) complexes and the β-oriented one formed at an early stage of the reaction.[12a,13] In this case, it is likely that the rate of the product formation from the β-oriented d–π* complex is faster than that from the α-oriented one at ambient temperature. The similar β-selectivity was observed in the reaction using THF–dimethyl sulfide (2:1) as the solvent (run 14). Interestingly, the addition of TMSCl to the above system resulted in the preferential formation of the α-adduct **8α** (run 15).[14] This phenomenon may be attributable to: (1) the change of the steric environment at the reaction site by coordination of TMSCl to the carbonyl oxygen; and (2) the intervention of TMSCl in the aforementioned equilibrium of d–π* complexes.[15]

The introduction of a vinyl group to **3** was conducted less effectively by using vinylmagnesium bromide (6 molar equiv.) and cuprous bromide–dimethyl sulfide (3 molar equiv.) in Et_2O. A 15% combined yield of the 1,4-adducts **9α** and **9β** was obtained (run 16). In a mixture of THF–dimethyl sulfide (2:1), the yield was slightly improved (run 17). As expected, the addition of TMSCl improved yields of the conjugate addition products although the combined yield was not sufficient (run 18).

Assignment of the stereochemistry to the newly introduced stereogenic center (C-9) in the 1,4-adducts **6α,β**–**9α,β** was achieved based on the ^{1}H NMR analysis including NOE experiments as depicted in Fig. 1. In the case of each α-adduct, a signal enhancement at H-4 was observed when H-9 was irradiated, whereas an NOE was observed between H-1 and H-9 in each β-adduct. Furthermore, the H-9 signal of each α-adduct appeared at lower field than that of the β-adduct, due to the proximity of H-9 to the isopropylidene oxygen at C-4 in the α-adducts.



Chemical shifts (δ) of H-9 in **6–10**

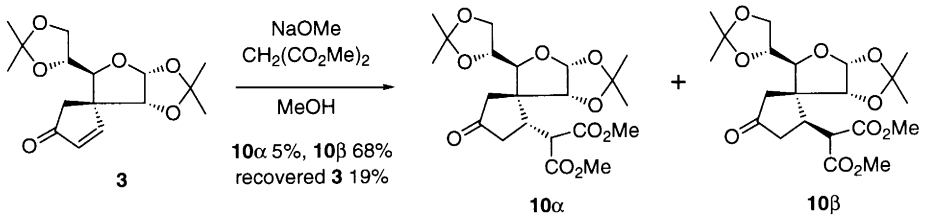
	6	7	8	9	10
α	2.80	2.64	2.66	3.41	3.53
β	2.61	2.46	2.40	3.26	3.18

Fig. 1.

We next examined the conjugate addition of the anion of dimethyl malonate to **3** (Scheme 3). A mixture of **3** and dimethyl malonate was treated with sodium methoxide (1 molar equiv.) in methanol at ambient temperature. The reaction proceeded with a high level of diastereoselectivity (dr=7:93) providing the 1,4-adducts **10α** and **10β** in 5% and 68% yields, respectively, along with 19% recovery of **3**. Exposure of the major adduct **10β** to the same reaction conditions (NaOMe, $CH_2(CO_2Me)_2$/MeOH) resulted in the formation of **3** (11%) and **10α** (6%), and also 63% of **10β** was recovered. The fact that **3** and **10α** were reproduced from **10β** indicates that the reaction is reversible. Consequently, the major isomer **10β** might be a thermodynamically controlled product. The stereochemical assignment of the major adduct **10β** was also secured by the ^{1}H NMR analysis including NOE experiments (Fig. 1).

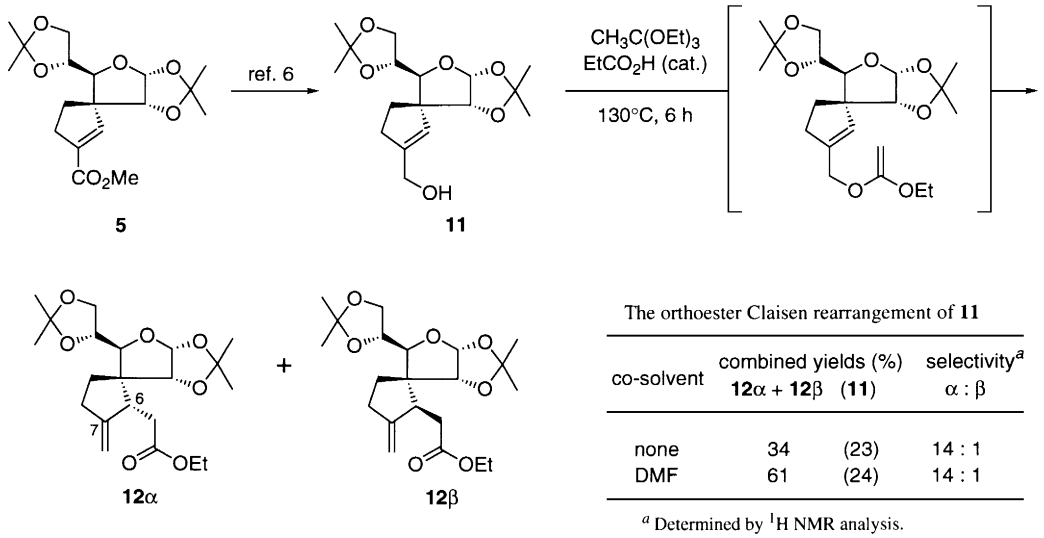
*2.2. Orthoester Claisen rearrangement of **11***

We examined the 1,4-conjugate addition of organocuprates to the cyclopentene-1-carboxylate **5**. However, the conjugate additions did not proceed and **5** was recovered almost quantitatively. We turned our



Scheme 3.

attention to the Claisen rearrangement of allylic alcohol **11**[6] which was prepared by diisobutylaluminum hydride reduction of **5** (Scheme 4).[16] Treatment of **11** with triethyl orthoacetate in the presence of a catalytic amount of propanoic acid at 130°C for 6 h provided an inseparable mixture of the rearrangement products **12α** and **12β** (14:1) in a combined yield of 34% (23% recovery of **11**). With DMF as a co-solvent, the combined yield of the products increased to 61% and the similar high level of diastereoselectivity was observed. As anticipated, the σ-bond formation in the Claisen rearrangement proceeded predominantly from the less hindered α-side of the cyclopentene ring in the intermediary allyl vinyl ether.



The orthoester Claisen rearrangement of **11**

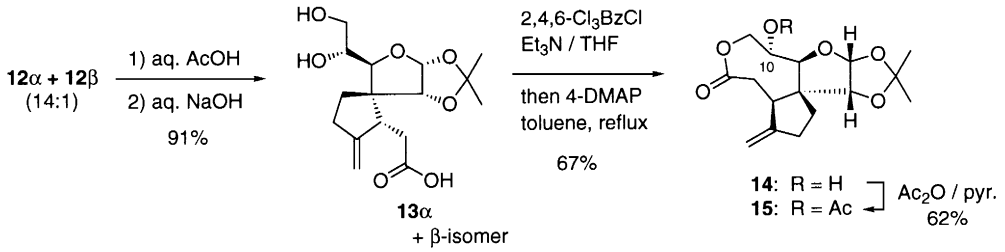
co-solvent	combined yields (%) **12α** + **12β** (**11**)		selectivity[a] α : β
none	34	(23)	14 : 1
DMF	61	(24)	14 : 1

[a] Determined by ^{1}H NMR analysis.

Scheme 4.

To confirm the structural assignment of the rearrangement products **12α**, we carried out the following chemical transformation (Scheme 5). Mild acid hydrolysis of the 14:1 mixture of **12α** and **12β** followed by saponification of the resulting diol gave a mixture of dihydroxy-carboxylic acid **13α** and its β-isomer. Using the modified Yamaguchi method,[17] **13α** was macrolactonized to give the eight-membered lactone **14** in 67% yield. We could not isolate a compound derived from the minor product **12β**. Compound **14** was acetylated as usual to give **15**. In the ^{1}H NMR spectrum of **15**, a doublet (J=2.4 Hz) attributable to H-10 shifted from δ 4.52 (for **14**) to 5.51 (for **15**). Consequently, the macrolactone **14** is an eight-membered one but not a seven-membered one. By the reason that the minor product **13β** derived from **12β** cannot be macrolactonized sterically, the structure of **13α** and also that of the major rearrangement product **12α** was established.

In conclusion, the 1,4-conjugate additions to **3** with a variety of carbon nucleophiles provided the adducts **6**–**10** with high diastereoselectivity in some cases. The Claisen rearrangement of **11** with triethyl orthoacetate proceeded with a quite high level of diastereoselectivity providing the rearrangement product



Scheme 5.

12α. Further manipulation of **6**–**10** and **12α** would provide enantiomerically pure multifunctionalized spirocyclic compounds such as entirely carbocyclic spiro[4.4]nonanes and spiro[4.5]decanes, the skeletal characteristics of a number of spiro type sesquiterpenoids.

3. Experimental

3.1. General methods

Melting points are uncorrected. Specific rotations were measured in a 10 mm cell. ^{1}H NMR spectra were recorded by a Jeol JNM-GSX 270 (at 270 MHz) in $CDCl_3$ solution with tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded at 68 MHz in $CDCl_3$ solution. High-resolution mass spectra (HRMS) were measured by a Jeol JMS-GCMATE spectrometer (EI, 70 eV). Thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 F_{254} plates. The crude reaction mixtures and extractive materials were purified by chromatography on silica gel 60 K070 (Katayama Chemical) or Wakogel C-300 (Wako). Unless described otherwise, reactions were carried out at ambient temperature. Combined organic extracts were dried over anhydrous Na_2SO_4. Solvents were removed from the reaction mixture or combined organic extracts by concentration under reduced pressure using an evaporator with bath at 35–45°C.

*3.2. 1,4-Addition of a methyl group to enone **3** (Table 1, run 2). (1S,3R,4R,5R,9R)- **6α** and (1S,3R,4R,5R,9S)-3,4-(Isopropylidenedioxy)-1-[(1R)-1,2-(isopropylidenedioxy)ethyl]-9-methyl-2-oxaspiro-[4.4]nonan-7-one **6β***

The following reaction was carried out under argon. To a cooled (0°C) stirred suspension of CuI (297 mg, 1.56 mmol) in Et_2O (3 ml) was added MeLi (1.14 M solution in Et_2O, 2.7 ml, 3.10 mmol). After being stirred at 0°C for 15 min, the resulting colorless solution was cooled to −78°C, and a solution of **3** (161 mg, 0.52 mmol) in Et_2O (2 ml) was added. The mixture was stirred at −78°C for 1 h, quenched with saturated aqueous NH_4Cl (1 ml), and diluted with H_2O (20 ml). The whole was extracted with CH_2Cl_2 (3×10 m1), and the combined extracts were dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 1:6) to afford 118 mg (70%) of **6α** and 9.8 mg (6%) of **6β**. Compound **6α** as colorless crystals; mp 72–74°C; TLC, R_f 0.32 (EtOAc:hexane, 1:2); $[\alpha]_D^{24}$ –15.4 (*c* 1.54, $CHCl_3$); IR (neat) 2980, 2960, 2940, 1750, 1460, 1400, 1380 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.29, 1.33, 1.41, 1.57 (4s, 3H×4, $C(CH_3)_2$×2), 1.33 (d, *J*=7.0 Hz, 3H, CH_3-9), 1.93 (d, *J*=18.5 Hz, 1H, H-6), 2.41 (d, *J*=10.3 Hz, 2H, H-8, 8), 2.51 (d, *J*=18.5 Hz, 1H, H-6), 2.80 (tq, *J*=10.3, 7.0 Hz, 1H, H-9), 3.80–4.21 (m, 4H, H-1, H-1′, 2′, 2′), 4.36 (d, *J*=3.7 Hz, 1H, H-4), 5.63 (d, *J*=3.7 Hz, 1H, H-3); ^{13}C NMR (68 MHz) δ 16.5, 25.0, 26.2, 26.2, 26.7, 33.9, 45.1, 45.5, 54.3, 69.2, 72.7, 79.8, 91.1, 103.1, 109.7,

112.4, 216.5; HRMS calcd for $C_{16}H_{23}O_6$ [$(M–CH_3)^+$]: *m/z* 311.1494; found: 311.1497. Compound **6β** as colorless crystals; mp 76–78°C; TLC, R_f 0.44 (EtOAc:hexane, 1:2); $[\alpha]_D^{26}$ +18.7 (*c* 1.30, $CHCl_3$); IR (neat) 2980, 2940, 2880, 1740, 1460, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 1.25 (d, *J*=7.0 Hz, 3H, CH_3-9), 1.30, 1.33, 1.40, 1.55 (4s, 3 H×4, $C(CH_3)_2$×2), 1.96 (dd, *J*=3.9, 19.1 Hz, 1H, H-8), 2.00 (d, *J*=18.7 Hz, 1H, H-6), 2.35 (d, *J*=18.7 Hz, 1H, H-6), 2.61 (m, 1H, H-9), 3.03 (dd, *J*=8.1, 19.1 Hz, 1H, H-8), 3.84 (dt, *J*=9.0, 5.8 Hz, 1H, H-1′), 3.92 (dd, *J*=8.4, 5.8 Hz, 1H, H-2′), 4.03 (d, *J*=9.0 Hz, 1H, H-1), 4.12 (dd, *J*=8.4, 5.8 Hz, 1H, H-2′), 4.38 (d, *J*=3.3 Hz, 1H, H-4), 5.58 (d, *J*=3.3 Hz, 1H, H-3); ^{13}C NMR (68 MHz) δ 18.1, 25.3, 26.4, 26.6, 27.0, 32.9, 41.6, 46.3, 55.6, 68.9, 72.6, 83.0, 86.7, 103.3, 109.8, 112.5, 217.2; HRMS calcd for $C_{16}H_{23}O_6$ [$(M–CH_3)^+$]: *m/z* 311.1494; found: 311.1491.

3.3. 1,4-Addition of an n*-butyl group to enone* ***3*** *(Table 1, run 10). (1*S*,3*R*,4*R*,5*R*,9*R*)-7α and (1*S*, 3*R*,4*R*,5*R*,9*S*)-9-Butyl-3,4-(isopropylidenedioxy)-1-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-2-oxaspiro-[4.4]nonan-7-one* ***7β***

The following reaction was carried out under argon. To a cooled (−18°C) stirred suspension of CuI (115 mg, 0.60 mmol) in THF (1 m1) was added *n*-BuLi (1.64 M solution in hexane, 0.74 m1, 1.2 mmol). After being stirred at −18°C for 1 h, the resulting black solution was cooled to −78°C, and a solution of **3** (62.4 mg, 0.20 mmol) in THF (1 ml) was added. The mixture was stirred at −78°C for 1 h and then at −18°C for 1 h, quenched with saturated aqueous NH_4Cl (1 ml), and diluted with H_2O (20 ml). The whole was extracted with CH_2Cl_2 (3×10 mL), and the combined extracts were dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 1:6) to afford 35.1 mg (47%) of **7α**, 4.2 mg (6%) of **7β** and 17.2 mg (28%) of **3**. Compound **7α** as a colorless oil; TLC, R_f 0.44 (EtOAc:hexane, 1:2); $[\alpha]_D^{30}$ –34.0 (*c* 1.43, $CHCl_3$); IR (neat) 2980, 2960, 2880, 1750, 1460, 1400, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 0.91 (t, *J*=7.0 Hz, 3H, CH_3 of *n*-Bu), 1.24–1.37 (m, 5H, CH_2×2 and CH of *n*-Bu), 1.28, 1.32, 1.41, 1.56 (4s, 3 H×4, $C(CH_3)_2$×2), 1.93 (d, *J*=17.9 Hz, 1H, H-6), 2.03 (m, 1H, CH of *n*-Bu), 2.36 (ddd, *J*=1.5, 11.4, 19.1 Hz, 1H, H-8), 2.45 (dd, *J*=1.5, 17.9 Hz, 1H, H-6), 2.50 (dd, *J*=8.1, 19.1 Hz, 1H, H-8), 2.64 (m, 1H, H-9), 3.79–4.21 (m, 4H, H-1, H-1′, 2′, 2′), 4.36 (d, *J*=3.5 Hz, 1H, H-4), 5.62 (d, *J*=3.5 Hz, 1H, H-3); ^{13}C NMR (68 MHz) δ 13.9, 22.8, 25.0, 26.3, 26.3, 26.8, 31.0, 31.3, 39.4, 43.6, 45.4, 54.4, 69.3, 72.8, 80.0, 91.2, 103.2, 109.7, 112.4, 216.6; HRMS calcd for $C_{19}H_{29}O_6$ [$(M–CH_3)^+$]: *m/z* 353.1964; found: 353.1963. Compound **7β** as a colorless oil; TLC, R_f 0.56 (EtOAc:hexane, 1:2); $[\alpha]_D^{30}$ +59.1 (*c* 2.55, $CHCl_3$); IR (neat) 2980, 2960, 2940, 1750, 1460, 1410, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 0.91 (t, *J*=6.3 Hz, 3H, CH_3 of *n*-Bu), 1.26–1.39 (m, 5H, CH_2×2 and CH of *n*-Bu), 1.31, 1.32, 1.40, 1.54 (4s, 3 H×4, $C(CH_3)_2$×2), 1.95 (d, *J*=18.1 Hz, 1H, H-6), 1.96 (m, 1H, CH of *n*-Bu), 2.10 (dd, *J*=6.2, 19.1 Hz, 1H, H-8), 2.37 (d, *J*=18.1 Hz, 1H, H-6), 2.46 (m, 1H, H-9), 2.86 (dd, *J*=8.4, 19.1 Hz, 1H, H-8), 3.86 (dt, *J*=8.8, 5.9 Hz, 1H, H-1′), 3.93 (dd, *J*=5.9, 8.4 Hz, 1H, H-2′), 4.07 (d, *J*=8.8 Hz, 1H, H-1), 4.13 (dd, *J*=5.9, 8.4 Hz, 1H, H-2′), 4.37 (d, *J*=3.3 Hz, 1H, H-4), 5.59 (d, *J*=3.3 Hz, 1H, H-3); ^{13}C NMR (68 MHz) δ 14.0, 22.6, 25.3, 26.4, 26.6, 26.9, 30.4, 30.4, 38.9, 42.7, 43.1, 55.8, 68.9, 73.0, 82.2, 86.0, 103.5, 109.8, 112.5, 216.8; HRMS calcd for $C_{20}H_{32}O_6$ (M^+): *m/z* 368.2199; found: 368.2200.

3.4. 1,4-Addition of an isopropyl group to enone ***3*** *(Table 1, run 13). (1*S*,3*R*,4*R*,5*R*,9*S*)-8α and (1*S*,3*R*, 4*R*,5*R*,9*R*)-9-Isopropyl-3,4-(isopropylidenedioxy)-1-[(1*R*)-1,2-(isopropylidenedioxy)ethyl]-2-oxaspiro-[4.4]nonan-7-one* ***8β***

The following reaction was carried out under argon. To a cooled (−78°C) stirred suspension of $CuBr·Me_2S$ (86.2 mg, 0.42 mmol) in Et_2O (3 ml) was added isopropylmagnesium bromide (0.67 M

solution in THF, 1.25 ml, 0.84 mmol). The mixture was stirred at −78°C for 30 min and a solution of **3** (43.4 mg, 0.14 mmol) in Et_2O (2 ml) was added. After being stirred at −78°C for 30 min and then at ambient temperature for 20 min, the mixture was quenched with saturated aqueous NH_4Cl (1 ml) and diluted with H_2O (20 ml). The whole was extracted with CH_2Cl_2 (3×10 ml), and the combined extracts were dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 1:6) to provide 6.3 mg (13%) of **8α** and 27.1 mg (55%) of **8β**. Compound **8α** as a colorless oil; TLC, R_f 0.45 (EtOAc:hexane, 1:2); $[\alpha]_D^{28}$ +22.0 (*c* 1.30, $CHCl_3$); IR (neat) 2980, 2960, 2940, 1750, 1460, 1410, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 0.89, 1.01 (2d, *J*=6.8 Hz, 3 H×2, $CH(CH_3)_2$), 1.30, 1.33, 1.40, 1.56 (4s, 3 H×4, $C(CH_3)_2$×2), 1.87 (d, *J*=18.8 Hz, 1H, H-6), 2.28 (dd, *J*=8.6, 18.8 Hz, 1H, H-8), 2.45 (m, 1H, $CH(CH_3)_2$), 2.51 (d, *J*=18.8 Hz, 1H, H-6), 2.53 (dd, *J*=8.6, 18.8 Hz, 1H, H-8), 2.66 (dt, *J*=2.5, 8.6 Hz, 1H, H-9), 3.83 (dd, *J*=7.3, 7.8 Hz, 1H, H-2′), 3.93 (dt, *J*=5.9, 7.3 Hz, 1H, H-1′), 4.14 (dd, *J*=5.9, 7.8 Hz, 1H, H-2′), 4.25 (d, *J*=3.4 Hz, 1H, H-4), 4.35 (d, *J*=7.3 Hz, 1H, H-1), 5.66 (d, *J*=3.4 Hz, 1H, H-3); ^{13}C NMR (68 MHz) δ 19.2, 24.6, 25.1, 26.1, 26.3, 27.0, 27.1, 38.9, 44.7, 45.1, 55.6, 68.8, 73.8, 80.6, 90.3, 103.0, 109.6, 112.5, 216.3; HRMS calcd for $C_{18}H_{27}O_6$ $[(M–CH_3)^+]$: *m/z* 339.1807; found: 339.1807. Compound **8β** as a colorless oil; TLC, R_f 0.52 (EtOAc:hexane, 1:2); $[\alpha]_D^{26}$ +18.6 (*c* 1.33, $CHCl_3$); IR (neat) 2980, 2960, 2940, 1740, 1460, 1410, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 0.85, 0.95 (2d, *J*=6.8 Hz, 3 H×2, $CH(CH_3)_2$), 1.31, 1.35, 1.41, 1.56 (4s, 3 H×4, $C(CH_3)_2$×2), 1.99 (dd, *J*=1.1, 18.9 Hz, 1H, H-6), 2.19 (dd, *J*=3.5, 19.4 Hz, 1H, H-8), 2.33 (d, *J*=18.9 Hz, 1H, H-6), 2.40 (dt, *J*=3.5, 9.2 Hz, 1H, H-9), 2.58 (m, 1H, $CH(CH_3)_2$), 2.83 (ddd, *J*=1.1, 9.2, 19.4 Hz, 1H, H-8), 3.81 (m, 1H, H-1′), 3.88 (dd, *J*=6.6, 8.1 Hz, 1H, H-2′), 4.08 (d, *J*=8.8 Hz, 1H, H-1), 4.12 (dd, *J*=5.9, 8.1 Hz, 1H, H-2′), 4.48 (d, *J*=3.1 Hz, 1H, H-4), 5.57 (d, *J*=3.1 Hz, 1H, H-3); ^{13}C NMR (68 MHz) δ 18.5, 22.9, 25.4, 26.4, 26.5, 27.0, 27.8, 39.2, 42.9, 43.5, 55.8, 69.0, 72.4, 84.1, 86.0, 103.6, 109.9, 112.6, 217.8; HRMS calcd for $C_{18}H_{27}O_6$ $[(M–CH_3)^+]$: *m/z* 339.1807; found: 339.1805.

*3.5. 1,4-Addition of a vinyl group to enone **3** (Table 1, run 18). (1S,3R,4R,5R,9S)-**9α** and (1S,3R,4R,5R,9R)-3,4-(Isopropylidenedioxy)-1-[(1R)-1,2-(isopropylidenedioxy)ethyl]-9-vinyl-2-oxaspiro-[4.4]nonan-7-one **9β***

The following reaction was carried out under argon. To a cooled (−78°C) stirred solution of $CuBr·Me_2S$ (57.1 mg, 0.28 mmol) in THF (1 ml) and Me_2S (0.5 ml) was added vinylmagnesium bromide (0.95 M solution in THF, 0.59 ml, 0.56 mmol). After stirring at −78°C for 30 min, chlorotrimethylsilane (59 μl, 0.47 mmol) and a solution of **3** (28.7 mg, 0.093 mmol) in THF (1 ml) were added successively. The mixture was stirred at −78°C for 20 min, quenched with 1 M aqueous HCl (0.1 ml), and diluted with H_2O (20 ml). The whole was extracted with CH_2Cl_2 (3×10 ml), and the combined extracts were dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 1:6) to provide 9.6 mg (31%) of **9α** and 6.3 mg (20%) of **9β**. Compound **9α** as a colorless oil; TLC, R_f 0.31 (EtOAc:hexane, 1:2); $[\alpha]_D^{27}$ +6.0 (*c* 1.58, $CHCl_3$); IR (neat) 3080, 2980, 2940, 2900, 1750, 1640, 1460, 1400, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 1.27, 1.32, 1.39, 1.53 (4s, 3 H×4, $C(CH_3)_2$×2), 1.98 (d, *J*=18.7 Hz, 1H, H-6), 2.42 (dd, *J*=9.2, 19.1 Hz, 1H, H-8), 2.56 (dd, *J*=1.1, 18.7 Hz, 1H, H-6), 2.73 (ddd, *J*=1.1, 10.3, 19.1 Hz, 1H, H-8), 3.41 (m, 1H, H-9), 3.81–4.19 (m, 4H, H-1, H-1′, 2′, 2′), 4.40 (d, *J*=3.7 Hz, 1H, H-4), 5.11 (dt, *J*=17.6, 1.5 Hz, 1H, –CH=CH*H*), 5.12 (dt, *J*=10.3, 1.5 Hz, 1H, –CH=C*H*H), 5.67 (d, *J*=3.7 Hz, 1H, H-3), 6.15 (ddd, *J*=7.2, 10.3, 17.6 Hz, 1H, –C*H*=CHH); ^{13}C NMR (68 MHz) δ 25.0, 25.9, 26.2, 26.6, 42.6, 44.3, 44.5, 54.6, 68.9, 73.3, 80.2, 90.9, 103.3, 109.7, 112.6, 116.5, 137.3, 215.6; HRMS calcd for $C_{18}H_{26}O_6$ (M^+): *m/z* 338.1729; found: 338.1715. Compound **9β** as a colorless oil; TLC, R_f 0.45 (EtOAc:hexane, 1:2); $[\alpha]_D^{27}$ +66.7 (*c* 1.06, $CHCl_3$); IR (neat) 3080, 2980, 2940, 1750, 1640, 1460, 1380 cm^{-1}; ^1H NMR (270 MHz) δ 1.31, 1.33, 1.43, 1.54 (4s, 3 H×4, $C(CH_3)_2$×2), 1.98 (dd,

J=1.1, 17.8 Hz, 1H, H-6), 2.37 (dd, *J*=9.0, 18.7 Hz, 1H, H-8), 2.39 (d, *J*=17.8 Hz, 1H, H-6), 2.87 (ddd, *J*=1.1, 8.1, 18.7 Hz, 1H, H-8), 3.26 (m, 1H, H-9), 3.84–4.20 (m, 4H, H-1, H-1′, 2′, 2′), 4.34 (d, *J*=3.3 Hz, 1H, H-4), 5.06 (dt, *J*=17.4, 1.5 Hz, 1H, –CH=CH*H*), 5.10 (dt, *J*=10.6, 1.5 Hz, 1H, –CH=C*H*H), 5.62 (d, *J*=3.3 Hz, 1H, H-3), 6.25 (ddd, *J*=7.7, 10.6, 17.4 Hz, 1H, –C*H*=CHH); ^{13}C NMR (68 MHz) δ 25.3, 26.4, 26.6, 26.9, 42.5, 42.5, 42.6, 55.9, 69.0, 73.2, 81.8, 86.3, 103.7, 109.9, 112.8, 115.6, 137.9, 215.6; HRMS calcd for $C_{17}H_{23}O_6$ [(M–CH_3)$^+$]: *m/z* 323.1494; found: 323.1500.

*3.6. 1,4-Addition of sodio dimethyl malonate to enone **3**. (1S,3R,4R,5R,9S)-**10α** and (1S,3R,4R,5R,9R)-9-[Bis(methoxycarbonyl)]methyl-3,4-(isopropylidenedioxy)-1-[(1R)-1,2-(isopropylidenedioxy)ethyl]-2-oxa-spiro-[4.4]nonan-7-one **10β***

To a cooled (0°C) stirred solution of **3** (63.2 mg, 0.20 mmol) in MeOH (3 ml) were added dimethyl malonate (69 μL, 0.60 mmol) and sodium methoxide (1.0 M solution in MeOH, 0.20 ml, 0.20 mmol). The mixture was stirred at ambient temperature for 23 h, quenched with saturated aqueous NH_4Cl (1 ml), and diluted with H_2O (20 ml). The whole was extracted with CH_2Cl_2 (3×10 ml), and the combined extracts were dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 1:5) to provide 4.2 mg (5%) of **10α**, 60.5 mg (68%) of **10β** and 11.9 mg (19%) of **3** was recovered. Compound **10α** as a colorless oil; TLC, R_f 0.30 (EtOAc:hexane, 1:2); $[\alpha]_D^{27}$ −1.2 (*c* 0.53, $CHCl_3$); IR (neat) 2980, 2960, 2940, 1740, 1440, 1410, 1380 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.29, 1.30, 1.46, 1.54 (4s, 3H×4, C(CH_3)$_2$×2), 1.96 (d, *J*=18.3 Hz, 1H, H-6), 2.50 (dd, *J*=9.2, 19.1 Hz, 1H, H-8), 2.61 (dd, *J*=1.4, 18.3 Hz, 1H, H-6), 2.72 (ddd, *J*=1.4, 9.2, 19.1 Hz, 1H, H-8), 3.53 (dt, *J*=7.3, 9.2 Hz, 1H, H-9), 3.71, 3.75 (2s, 3H×2, OCH_3×2), 3.80–3.90 (m, 2H, H-1′, 2′), 4.11 (d, *J*=7.3 Hz, 1H, C*H*(CO_2Me)$_2$), 4.16 (m, 1H, H-2′), 4.22 (d, *J*=8.4 Hz, 1H, H-1), 4.28 (d, *J*=3.1 Hz, 1H, H-4), 5.59 (d, *J*=3.1 Hz, 1H, H-3); ^{13}C NMR (68 MHz) δ 25.2, 26.1, 26.5, 26.8, 37.8, 41.4, 44.3, 52.3, 52.5, 52.7, 55.3, 69.0, 72.4, 80.0, 88.6, 102.9, 110.1, 113.1, 168.9, 168.9, 213.5; HRMS calcd for $C_{20}H_{27}O_{10}$ [(M–CH_3)$^+$]: *m/z* 427.1604; found: 427.1603. Compound **10β** as a colorless oil; TLC, R_f 0.37 (EtOAc:hexane, 1:2); $[\alpha]_D^{27}$ +30.2 (*c* 0.775, $CHCl_3$); IR (neat) 2980, 2960, 2940, 1740, 1440, 1410, 1380 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.30, 1.33, 1.42, 1.55 (4s, 3H×4, C(CH_3)$_2$×2), 2.10 (dd, *J*=1.1, 19.1 Hz, 1H, H-6), 2.34 (d, *J*=19.1 Hz, 1H, H-6), 2.66 (dd, *J*=3.9, 19.4 Hz, 1H, H-8), 2.91 (ddd, *J*=1.1, 9.9, 19.4 Hz, 1H, H-8), 3.18 (dt, *J*=9.9, 3.9 Hz, 1H, H-9), 3.74, 3.76 (2s, 3 H×2, OCH_3×2), 3.78–3.92 (m, 2H, H-1′, 2′), 4.02 (d, *J*=8.8 Hz, 1H, H-1), 4.13 (m, 1H, H-2′), 4.41 (d, *J*=3.1 Hz, 1H, H-4), 4.44 (d, *J*=3.9 Hz, 1H, C*H*(CO_2Me)$_2$), 5.58 (d, *J*=3.1 Hz, 1H, H-3); ^{13}C NMR (68 MHz) δ 25.1, 26.2, 26.5, 26.9, 37.7, 41.1, 42.1, 51.7, 52.4, 52.8, 54.4, 68.8, 72.5, 83.9, 86.0, 103.8, 110.0, 112.9, 169.3, 170.1, 215.2; HRMS calcd for $C_{20}H_{27}O_{10}$ [(M–CH_3)$^+$]: *m/z* 427.1604; found: 427.1601.

*3.7. Orthoester Claisen rearrangement of allylic alcohol **11**. Mixture of (1S,3R,4R,5R,6R)-**12α** and (1S,3R,4R,5R,6S)-6-(ethoxycarbonyl)methyl-3,4-(isopropylidenedioxy)-1-[(1R)-1,2-(isopropylidenedioxy)-ethyl]-7-methylene-2-oxaspiro[4.4]nonane **12β***

To a stirred solution of **11** (106 mg, 0.325 mmol) in DMF (2 ml) were added triethyl orthoacetate (1 ml) and propionic acid (2% solution in DMF, 12 μl, 3.2 μmol). The mixture was stirred at 130°C for 6 h and concentrated in vacuo with aid of toluene. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 1:10) to provide 78.1 mg (61%) of an inseparable mixture of **12α** and **12β**, and 25.0 mg (24%) of **11** was recovered. The diastereomeric mixture (14:1) of **12α** and **12β** as a colorless oil: TLC, R_f 0.50 (EtOAc:hexane, 1:2); $[\alpha]_D^{25}$ +47.8 (*c* 1.63, $CHCl_3$); IR (neat) 2985, 2940, 2880, 1735, 1660, 1460 cm^{-1}; ^{1}H NMR (270 MHz) for the major isomer **12α** δ 1.27 (t, *J*=7.1 Hz, 3H,

OCH_2CH_3), 1.27, 1.32, 1.39, 1.51 (4s, 3 H×4, $C(CH_3)_2$×2), 1.47–1.53 (m, 1H, H-9), 1.85–1.97 (m, 1H, H-9), 2.42–2.54 (m, 2H, H-8, 8), 2.62 (dd, *J*=9.9, 16.5 Hz, 1H, –C*H*HCO_2Et), 2.84 (dd, *J*=3.3, 16.5 Hz, 1H, –CH*H*CO_2Et), 3.33–3.37 (m, 1H, H-6), 3.96–4.17 (m, 6H, H-1, H-1′, 2′, 2′, OCH_2CH_3), 4.22 (d, *J*=3.3 Hz, 1H, H-4), 4.78 (q, *J*=2.2 Hz, 1H, C=C*H*H), 4.87 (q, *J*=2.2 Hz, 1H, C=CH*H*), 5.65 (d, *J*=3.3 Hz, 1H, H-3); ^{13}C NMR (68 MHz) for **12α** δ 14.3, 25.2, 26.3, 26.4, 27.1, 27.6, 28.9, 34.4, 43.6, 57.0, 60.2, 68.4, 74.1, 80.6, 85.6, 104.2, 105.5, 109.5, 112.4, 152.3, 173.3; HRMS calcd for $C_{20}H_{29}O_7$ [$(M–CH_3)^+$]: *m/z* 381.1914; found: 381.1913.

*3.8. Acid hydrolysis of the mixture **12α** and **12β** and successive saponification. Mixture of (1S,3R,4R,5R,6R)-6-carboxymethyl-1-[(1R)-1,2-dihydroxyethyl]-3,4-(isopropylidenedioxy)-7-methylene-2-oxaspiro[4.4]nonane **13α** and the 6R isomer **13β***

A solution of the 14:1 mixture of **12α** and **12β** (21.9 mg, 0.055 mmol) in 60% aqueous AcOH (1 ml) was stirred for 16 h and concentrated in vacuo with aid of toluene and EtOH to afford crude diol (18.9 mg), which was used directly in the next step. The crude diol (18.9 mg) was dissolved in EtOH (1 ml) and 1 M aqueous NaOH (1 ml) was added. The solution was stirred for 1 h, acidified with 1 M aqueous HCl (2 ml), diluted with H_2O (20 ml), and extracted with CH_2Cl_2 (3×10 ml). The combined extracts were dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOH:toluene, 1:5) to provide 16.5 mg (91%) of a 14:1 mixture of **13α** and **13β** as a colorless oil: TLC, R_f 0.43 (EtOH:toluene, 1:2); $[\alpha]_D^{27}$ +14.7 (*c* 1.15, $CHCl_3$); IR (neat) 3420, 2990, 2930, 2850, 1725, 1660, 1460 cm^{-1}; ^{1}H NMR (270 MHz) for the major isomer **13α** δ 1.27, 1.51 (2s, 3 H×2, $C(CH_3)_2$), 1.27–1.39 (m, 1H, H-9), 1.92–2.04 (m, 1H, H-9), 2.39–2.57 (m, 2H, H-8, 8), 2.63 (dd, *J*=8.2, 16.9 Hz, 1H, –C*H*HCO_2H), 3.07 (dd, *J*=6.0, 16.9 Hz, 1H, –CH*H*CO_2H), 3.33–3.38 (m, 1H, H-6), 3.70–3.82 (m, 3H, H-1′, 2′, 2′), 4.22 (d, *J*=10.3 Hz, 1H, H-1), 4.25 (d, *J*=3.5 Hz, 1H, H-4), 4.75–5.07 (br, 3H, CO_2H, OH×2), 4.86 (q, *J*=1.6 Hz, 1H, C=C*H*H), 4.93 (q, *J*=1.6 Hz, 1H, C=CH*H*), 5.65 (d, *J*=3.5 Hz, 1H, H-3); ^{13}C NMR (68 MHz) for **13α** δ 26.2, 26.5, 26.9, 28.2, 33.5, 43.5, 57.3, 65.0, 70.8, 77.3, 85.0, 103.7, 105.7, 112.4, 151.7, 178.5; HRMS calcd for $C_{15}H_{21}O_7$ [$(M–CH_3)^+$]: *m/z* 313.1287; found: 313.1294.

*3.9. Lactonization of acid **13α**. (1R,5R,10R,11S,13R,17R)-10-Hydroxy-15,15-dimethyl-4-methylene-8,12,14,16-tetraoxatetracyclo[9.6.0.0^{1,5}.0^{13,17}]heptadecan-7-one **14***

The following reaction was carried out under argon. To a cooled (0°C) stirred solution of the diastereomeric mixture (14:1) of **13α** and **13β** (16.5 mg, 0.050 mmol) in THF (2 ml) were added triethylamine (28 μl, 0.20 mmol) and 2,4,6-trichlorobenzoyl chloride (16 μl, 0.10 mmol). The mixture was stirred for 5 h. The precipitated solids were removed by filtration and washed well with toluene. The combined filtrate and washings were diluted with toluene (25 ml) and added to a refluxing suspension of 4-dimethylaminopyridine (74 mg, 0.60 mmol) in toluene (5 ml) dropwise over 3 h. After being refluxed for an additional 30 min, the mixture was cooled to ambient temperature and concentrated in vacuo. The residue was diluted with EtOAc (30 ml) and washed with 1 M aqueous HCl (10 ml), saturated aqueous $NaHCO_3$ (10 ml), and saturated brine (10 ml), successively. The organic layer was dried and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 1:1) to provide 10.5 mg (67%) of **14** as colorless crystals: mp 165–167°C; TLC, R_f 0.50 (EtOH:toluene, 1:2); $[\alpha]_D^{28}$ +20.2 (*c* 1.58, $CHCl_3$); IR (neat) 3480, 2990, 2960, 2935, 1750, 1660, 1455 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.25, 1.50 (2s, 3 H×2, CH_3-15,15), 1.26–1.34 (m, 1H, H-2), 2.35–2.57 (m, 3H, H-2, 3, 3), 2.74 (dd, *J*=11.0, 15.6 Hz, 1H, H-6), 2.82 (dd, *J*=5.9, 15.6 Hz, 1H, H-6), 3.47–3.51 (m, 1H, H-5), 4.00 (s, 1H, H-11), 4.11 (d, *J*=12.6 Hz, 1H, H-9), 4.19 (d, *J*=3.7 Hz, 1H, H-17), 4.52 (d, *J*=2.4 Hz, 1H, H-10), 4.76

(q, *J*=2.2 Hz, 1H, C=C*H*H), 4.86 (q, *J*=2.2 Hz, 1H, C=CH*H*), 5.05 (dd, *J*=2.4, 12.6 Hz, 1H, H-9), 5.68 (d, *J*=3.7 Hz, 1H, H-13); ^{13}C NMR (68 MHz) δ 25.8, 26.0, 27.0, 27.4, 33.4, 46.7, 57.2, 73.4, 76.5, 77.3, 83.7, 103.1, 103.2, 112.2, 148.9, 176.8; HRMS calcd for $C_{15}H_{19}O_6$ [$(M–CH_3)^+$]: *m/z* 295.1181; found: 295.1176.

3.10. Acetylation of ***14****. (1*R,*5*R,*10*R,*11*S,*13*R,*17*R*)-10-Acetoxy-15,15-dimethyl-4-methylene-8,12,14,16-tetraoxatetracyclo[9.6.0.0^{1,5}.0^{13,17}]heptadecan-7-one* ***15***

A solution of **14** (8.8 mg, 0.028 mmol) in Ac_2O (0.5 ml) and pyridine (0.5 ml) was stirred for 1 h and concentrated in vacuo with aid of toluene. The residue was purified by column chromatography on silica gel (EtOAc:hexane, 1:3) to provide 6.2 mg (62%) of **15** as colorless crystals: mp 141–143°C; TLC, R_f 0.67 (EtOAc:hexane, 1:1); $[\alpha]_D^{27}$ −14.5 (*c* 0.51, $CHCl_3$); IR (neat) 2990, 2960, 2935, 1750, 1660, 1460 cm^{-1}; ^{1}H NMR (270 MHz) δ 1.25, 1.51 (2s, 3 H×2, CH_3-15,15), 1.26–1.35 (m, 1H, H-2), 2.13 (s, 3H, $COCH_3$), 2.28–2.55 (m, 3H, H-2, 3, 3), 2.76 (dd, *J*=10.3, 15.8 Hz, 1H, H-6), 2.82 (dd, *J*=8.8, 15.8 Hz, 1H, H-6), 3.44–3.50 (m, 1H, H-5), 4.10 (s, 1H, H-11), 4.11 (d, *J*=13.2 Hz, 1H, H-9), 4.19 (d, *J*=3.7 Hz, 1H, H-17), 4.79 (q, *J*=2.2 Hz, 1H, C=C*H*H), 4.89 (q, *J*=2.2 Hz, 1H, C=CH*H*), 5.06 (dd, *J*=2.4, 13.2 Hz, 1H, H-9), 5.51 (d, *J*=2.4 Hz, 1H, H-10), 5.66 (d, *J*=3.7 Hz, 1H, H-13); ^{13}C NMR (68 MHz) δ 21.1, 26.0, 26.0, 27.0, 27.5, 33.4, 46.6, 57.3, 70.5, 74.3, 75.6, 83.4, 103.0, 103.9, 112.3, 148.6, 169.9, 176.4; HRMS calcd for $C_{17}H_{21}O_7$ [$(M–CH_3)^+$]: *m/z* 337.1286; found: 337.1287.

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