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SYNTHESIS OF 2-PYRONES BRIDGED AT THE 3- AND 6-POSITIONS BY RING-CLOSING METATHESIS

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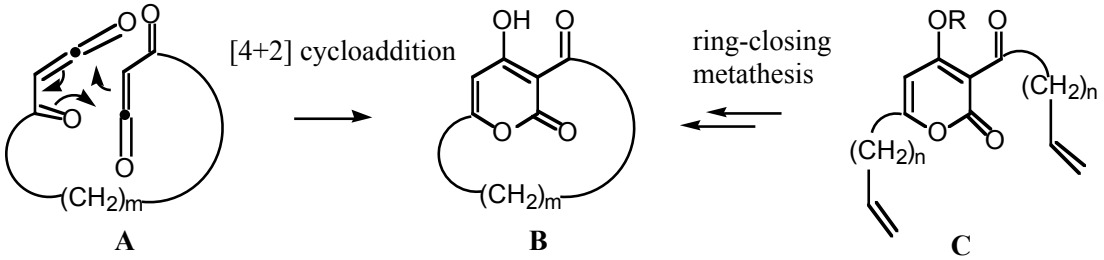
Abstract –Synthesis of 4-hydroxy-2-pyrones bridged at the 3- and 6-positions by ring-closing metathesis was studied. The reaction of 6-(9-decenyl)-4-methoxy-3-(10-undecenoyl)pyran-2-one (**6b**) by the first generation ruthenium catalyst (**7**) gave 3,6-bridged 2-pyrone (**10b**) in 62% yield. The reaction of 3-(6-heptenoyl)-6-(5-hexenyl)-4-methoxypyran-2-one (**6a**) (n = 4) under the same conditions afforded the 3,6-bridged 2-pyrone (**10a**) in 6% yield together with considerable amounts of intermolecular metathesis products.

INTRODUCTION

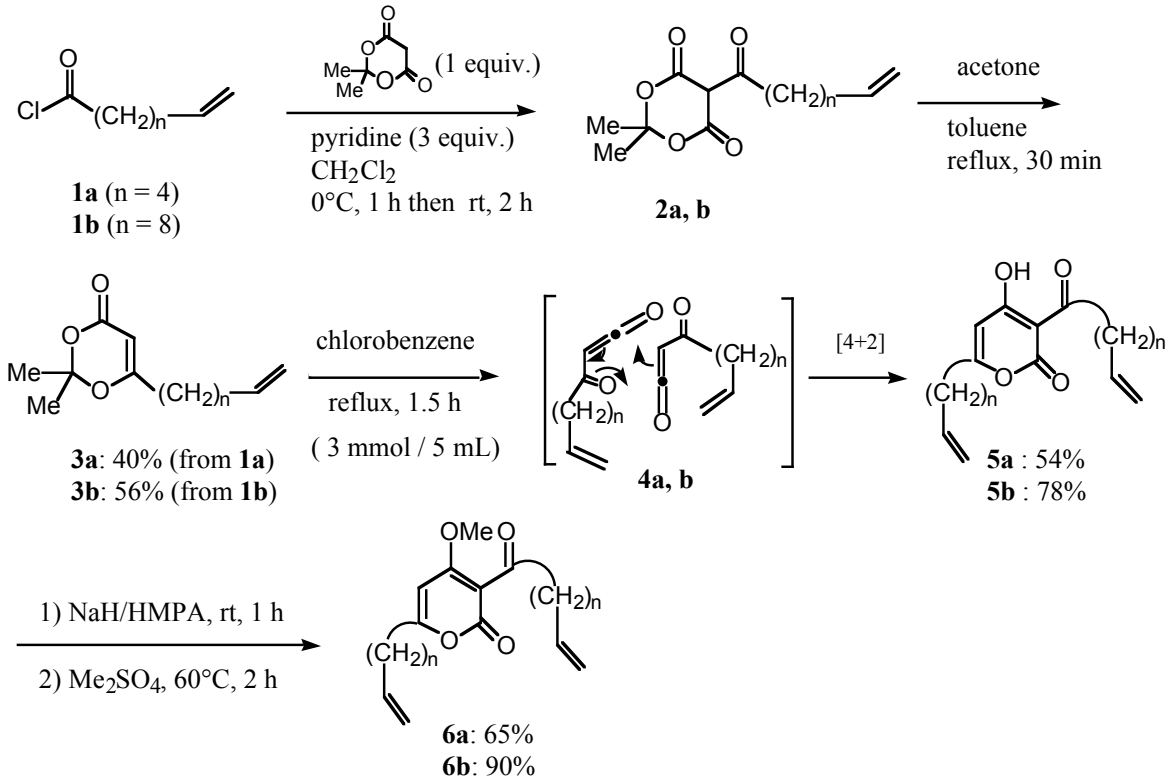
The design and synthesis of cyclophanes, macrocycles containing aromatic or heteroaromatic groups, is a fascinating branch of organic chemistry.[1,2] Previously, we reported a convenient synthesis of cyclophane (**B**) by intramolecular [4+2] cycloaddition of bis(acylketene) (**A**).[3] The heterophane (**B**) having relatively short bridge (m = 7~10) showed planar chirality due to the restricted rotation of pyrone ring. We have demonstrated that enantiomerically pure **B** serve as a new optical resolution reagent.[4] We have also shown that **B** serves as excellent intermediates for 2,6-pyridinophanes.[5] In the recent years, increasing attention has been directed toward the synthesis of medium and large rings including cyclophanes using metal-catalyzed ring-closing metathesis.[6] Here we report the synthesis of heterophane (**B**) by ring-closing metathesis of pyrone derivative (**C**) catalyzed by ruthenium alkylidene complexes (Scheme 1).



Scheme 1

RESULTS AND DISCUSSION

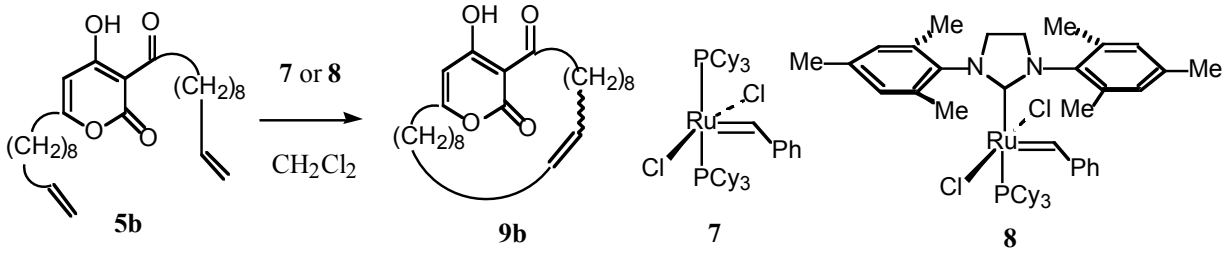
The substrates for ring-closing metathesis were synthesized by [4+2] cycloaddition of acylketene. Meldrum's acid was condensed with 6-heptenoyl chloride (**1a**) and 10-undecenoyl chloride (**1b**) by Yonemitsu method[7] to produce the corresponding acylated Meldrum's acids (**2a**) and (**2b**). These compounds were transformed into 6-(ω-alkenyl)-1,3-dioxin-4-ones (**3a**) and (**3b**) in refluxing toluene.[8] Heating **3a** and **3b** in refluxing chlorobenzene generated acylketenes (**4a**) and (**4b**), which *in situ* underwent intermolecular cycloaddition to produce 4-hydroxy-2-pyrone derivatives (**5a**) (54%) and (**5b**) (78%), respectively.[9,10] Heating sodium salts of (**5a**) or (**5b**) with dimethyl sulfate in HMPA[11] gave the methyl ether (**6a**) or (**6b**) (Scheme 2).



Scheme 2

First, we examined ring-closing metathesis of 4-hydroxy compound (**5b**) (n = 8) because the reaction with ruthenium alkylidene catalysts has functional group tolerance[6,12] and the 4-hydroxy hydorogen is strongly hydrogen bonded to acyl oxygen. The reaction was conducted in dichloromethane (3 mmol) under the first-generation catalyst **7** or the second-generation catalyst **8**. The results are summarized in Table 1. When the reaction was conducted under catalyst (**7**) (5 or 10 mol%), the desired heterophane (**9b**) was obtained in 13~18% yields together with starting **5b** (10~12%, Entries 1~3). The reaction of higher

concentration (20 mmol) gave lower yield of **9b** (Entry 4). Use of catalyst (**8**) resulted in the formation of rather complex mixture, from which **9b** was isolated in 7% yield (Entry 5). Compound (**9b**) was obtained as an inseparable mixture of *E*- and *Z*-isomers at the alkenylene bridge as indicated by ^{1}H- and ^{13}C-NMR spectroscopic studies. For example, hydroxy protons appeared at 16.9 and 17.0 ppm in 7 : 3 ratio in the ^{1}H-NMR spectra. The geometry of the major component is not clear.



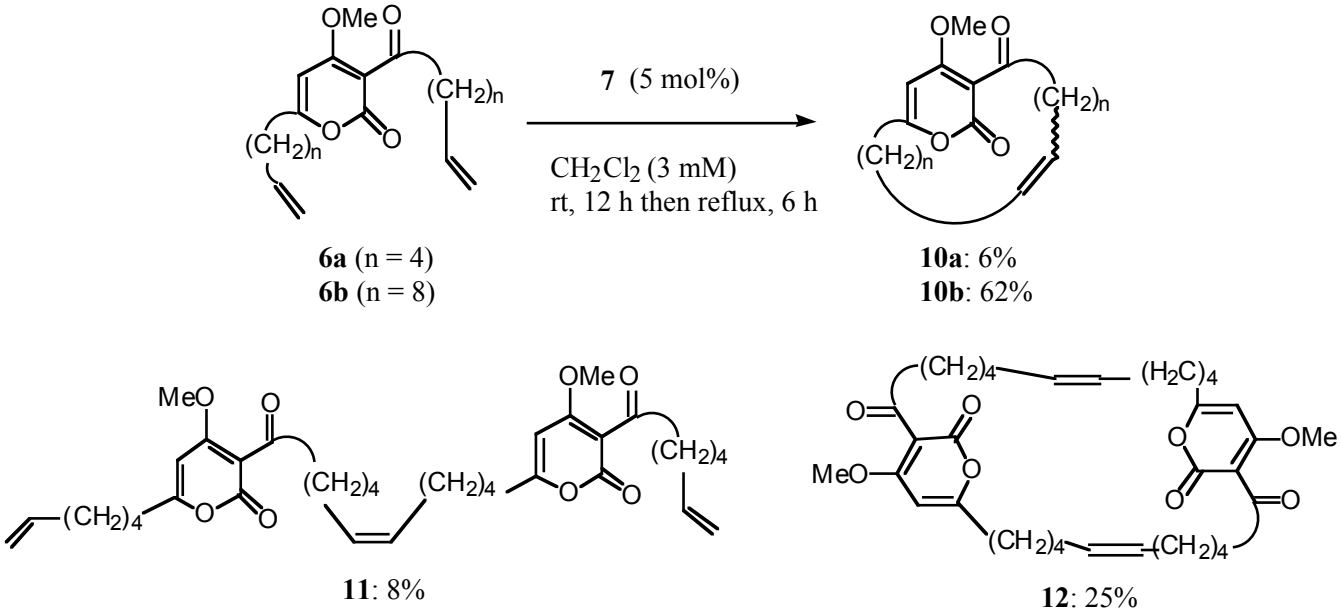
Scheme 3

Table 1. Ring-closing metathesis of **5b** to give **9b**

Entry	Concentration	Catalyst	Condition	**9b** (%)	**5b** (%)
1	3 mM	**7** (5 mol%)	reflux, 16 h	15	10
2	3 mM	**7** (5 mol%)	rt, 12 h then reflux, 6 h	18	12
3	3 mM	**7** (10 mol%)	rt, 12 h then reflux, 6 h	13	12
4	20 mM	**7** (5 mol%)	reflux, 5 h	5	2
5	3 mM	**8** (5 mol%)	reflux, 6 h	7	10

Next, ring-closing metathesis of 4-methoxy compound (**6b**) was studied. Heating **6b** with catalyst (**7**) in dichloromethane afforded heterophane (**10b**) in 62% yield proving that the free 4-hydroxy group causes the low efficiency for formation of **9b** from **5b**. Heterophane (**10b**) was obtained as an inseparable mixture of *E*- and *Z*-isomers. The ratio of geometrical isomers was again 7 : 3 as indicated by the ^{13}C-NMR spectrum, though the geometry of the major component is not clear.

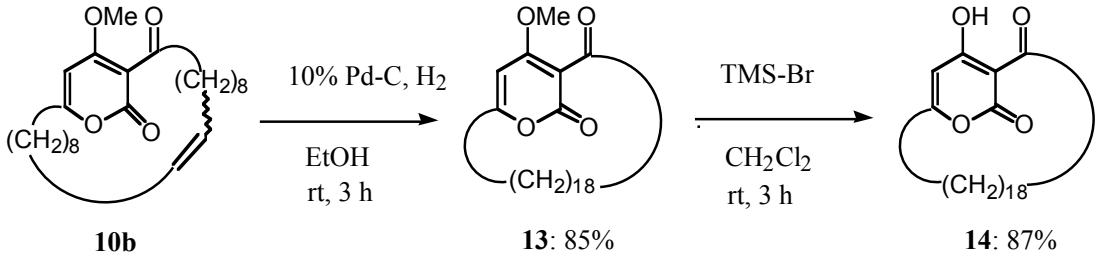
The results prompted us to study the ring-closing of **6a** to heterophane (**10a**) that is expected to show planar chirality owing to the short alkenylene bridge. However, the reaction of (**6a**) under the same conditions as for (**6b**) gave rise to a rather complex mixture. Purification by chromatography afforded heterophane (**10a**) only in 6% yield as an inseparable mixture of *E*- and *Z*-isomers. Considerable amounts of oily products (**11**) (8%) and (**12**) (25%) were obtained from this reaction. These products are assigned to intermolecular metathesis products. ^{1}H-NMR spectroscopic studies indicated that both of these are mixtures of *E,Z*-isomers and regioisomers. As the regioisomers, head-to-tail, head-to-head, and tail-to-tail products are possible. In Scheme 4, only head-to-tail products (**11**) and (**12**) are shown.



Scheme 4

The results show clearly that efficiency for ring-closing metathesis is much dependent upon the bridge length of products. Heterophane (**10b**) having long bridge is formed in satisfactory yield, while **10a** having short bridge are formed in low yield. It should be noted that intramolecular cycloaddition of bis(acylketene) (**A**) to produce heterophane (**B**) (m = 10) proceeds highly efficiently.[3]

Finally, we examined conversion of **10b** to heterophane of type (**B**). Hydrogenation of **10b** with 5% Pd-C gave heterophane (**13**) as a sole product in 85% yield. Treatment of **13** with bromotrimethylsilane at room temperature afforded 4-hydroxy compound (**14**)[5] in 87% yield (Scheme 5).



Scheme 5

CONCLUSION

Synthesis of 4-hydroxy-2-pyrone bridged at the 3- and 6-positions by ring-closing metathesis was studied. The key compound (**5**) for this ring-closing was readily synthesized by intermolecular [4+2] cycloaddition of alkenoylketene. Ring-closing metathesis of 4-hydroxy compound (**5b**) under ruthenium catalyst (**7**) afforded heterophane (**9b**) in low yield, while that of and 4-methoxy compound (**6b**) produced

the corresponding heterophane (**10b**) in satisfactory yield. Compound (**10b**) was successfully transformed into 3,6-bridged 4-hydroxy-2-pyrone (**14**). The reaction of 4-methoxy compound (**6a**) having short □-alkenyl groups resulted in low yield of heterophane (**10a**) due to the preferential formation of intermolecular metathesis products, indicating a limitation of this useful cyclization method in strained heterophane synthesis.

EXPERIMENTAL

General. Melting points were determined with a Yazawa Micro Melting Point Apparatus without correction. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a JEOL JNM-GSX 270, 400 or 500 spectrometers with tetramethylsilane as an internal standard. IR spectra were determined on a JASCO FT/IR-8000 spectrophotometer. MS spectra were recorded on a JEOL JMS-700 Mstation spectrometer by using *m*-nitrobenzyl alcohol matrix. Column chromatography was done with Silica Gel 60 N (Kanto Chemical Co., Inc.). Preparative thin layer chromatography (PTLC) was done on Merck Silica Gel 60 F_{254}. The ratios of solvent mixtures for chromatography are shown as volume/volume. Ruthenium alkylidene complexes (**7**) and (**8**) were purchased from Aldrich Chemical Company, Inc.

6-(5-HEXENYL)-2,2-DIMETHYL-1,3-DIOXIN-4-ONE (3A)

A solution of 6-heptenoyl chloride (**1a**) (0.94 g, 7.3 mmol) in dichloromethane (10 mL) was added dropwise to a stirred solution of Meldrum's acid (1.1 g, 7.3 mmol) and pyridine (1.7 g, 22 mmol) in dichloromethane (10 mL) under ice-cooling over 15 min. The mixture was stirred for 1 h under ice-cooling and then for 1 h at rt. The mixture was acidified with 10% hydrochloric acid and extracted with ether. The organic layer was washed with 10% hydrochloric acid and then with brine. The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude (**2a**) as yellow crystals. A solution of the crude (**2a**) in dry toluene (100 mL) and dry acetone (0.3 mL) was heated under reflux for 1 h. The solution was evaporated *in vacuo* and the residue was purified by silica gel column chromatography using hexane-ethyl acetate (10 : 1) to give (**3a**)[13] as a colorless oil [613 mg, 40% from (**1a**)]. MS (FAB) *m/z*: 211 (M^++1). IR (neat) ν : 2934, 1726, 1632 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.42-1.48 (2H, m), 1.53-1.61 (2H, m), 1.68 (6H, s), 2.05-2.10 (2H, m), 2.22 (2H, t, *J* = 7.5 Hz), 4.96-5.04 (2H, m), 5.23 (1H, s), 5.73-5.82 (1H, m). ^{13}C-NMR (126 MHz, $CDCl_3$) δ : 25.1, 25.2, 28.2, 33.3, 33.5, 93.2, 106.3, 115.0, 138.1, 161.5, 172.0.

6-(9-Decenyl)-2,2-dimethyl-1,3-dioxin-4-one (3b)

Following the procedure given for preparation of (**3a**), 10-undecenoyl chloride (**1b**) (1.8 g, 10 mmol) was condensed with Meldrum's acid to give crude (**2b**). Heating (**2b**) in toluene gave (**3b**) as a colorless oil [1.3 g, 50% from (**1b**)]. HRMS (FAB) Calcd for $C_{16}H_{27}O_3$ (M^++1) 267.1960. Found 267.1927. IR (neat)

ν : 2926, 1728, 1634 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.29-1.40 (10H, m), 1.51-1.57 (2H, m), 1.68 (6H, s), 2.02-2.06 (2H, m), 2.21 (2H, t, *J* = 7.7 Hz), 4.93 (1H, dd, *J* = 9.1, 1.5 Hz), 4.99 (1H, dd, *J* = 17.1, 1.5 Hz), 5.23 (1H, s), 5.77-5.85 (1H, m). ^{13}C-NMR (126 MHz, $CDCl_3$) δ : 25.1, 25.8, 28.9, 29.0, 29.1, 29.2, 29.3, 33.7, 33.8, 93.1, 106.3, 114.3, 139.1, 161.5, 172.2, 209.5.

3-(6-HEPTENOYL)-6-(5-HEXENYL)-4-HYDROXYPYRAN-2-ONE (5A)

A solution of (**3a**) (480 mg, 2.3 mmol) in dry chlorobenzene (5 mL) was refluxed for 4 h. After evaporation of the solvent, the residue was purified by silica gel column chromatography (hexane-ethyl acetate, 10:1) to give **5a** (187 mg, 54%) as colorless solid. Recrystallization from hexane gave prisms of mp 33℃. HRMS (FAB) Calcd for $C_{18}H_{25}O_4$ (M^++1) 305.1753. Found 305.1746. MS (FAB) *m/z*: 305 (M^++1). IR (neat) ν : 2932, 1740, 1638 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.43-1.52 (4H, m), 1.65-1.74 (4H, m), 2.04-2.13 (4H, m), 2.49 (2H, t, *J* = 7.6 Hz), 3.08 (2H, t, *J* = 7.3 Hz), 4.93-5.04 (4H, m), 5.74-5.85 (2H, m), 5.91 (1H, s), 16.8 (1H, s). ^{13}C-NMR (126 MHz, $CDCl_3$) δ : 23.5, 25.8, 28.2, 28.5, 33.3, 33.6, 34.2, 41.6, 99.7, 100.9, 114.7, 115.2, 138.0, 138.6, 161.2, 172.4, 181.3, 207.9.

6-(9-Decenyl)-4-hydroxy-3-(10-undecenoyl)pyran-2-one (5b)

Following the procedure given for preparation of **5a**, compound (**3b**) (1.2 g, 4.5 mmol) was heated to give **5b** (730 mg, 78%) as a white solid. Recrystallization from hexane gave needles of mp 63℃. HRMS (FAB) Calcd for $C_{26}H_{41}O_4$ (M^++1) 417.3005. Found 417.2966. MS (FAB) *m/z*: 417 (M+1). IR (neat) ν : 2920, 1722, 1634 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.23-1.38 (20H, m), 1.60-1.70 (4H, m), 2.00-2.05 (4H, m), 2.46 (2H, t, *J* = 7.5 Hz), 3.05 (2H, t, *J* = 7.5 Hz), 4.91-4.93 (2H, m), 4.96-5.00 (2H, m), 5.75-5.84 (2H, m), 5.90 (1H, s), 16.8 (1H, s). ^{13}C-NMR (126 MHz, $CDCl_3$) δ : 24.0, 26.4, 28.9, 29.0, 29.1, 29.2, 29.2, 29.3, 29.4, 29.5, 33.8, 33.9, 34.4, 40.2, 99.7, 100.8, 114.2, 114.3, 139.2, 139.3, 161.2, 172.6, 181.4, 208.1.

3-(6-Heptenoyl)-6-(5-hexenyl)-4-methoxypyran-2-one (6a)

To a stirred solution of (**5a**) (150 mg, 0.49 mmol) in anhydrous hexamethylphosphoric triamide (2.7 mL), sodium hydride (60% in mineral oil, 23.6 mg, 0.59 mmol) was added at rt under argon atmosphere and the mixture was stirred for 2 h at rt. Dimethyl sulfate (74 mg, 0.59 mmol) was added to the mixture and the whole was stirred for 2 h at 60℃. The reaction mixture was diluted with diethyl ether, washed with 5% hydrochloric acid and then with brine. The organic layer was dried over $MgSO_4$ and then the solvent was evaporated in vacuo. The residue was purified by silica gel column chromatography (hexane-ethyl acetate, 10:1) to give **6a** as yellow oil (102 mg, 65%). HRMS (FAB) Calcd for $C_{19}H_{27}O_4$ (M^++1)

319.1909. Found 319.1902. MS (FAB) *m/z*: 319 (M^++1). IR (neat) ν : 2932, 1715, 1655 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.38-1.50 (4H, m), 1.62-1.72 (4H, m), 2.03-2.11 (4H, m), 2.53 (2H, t, *J* = 7.7 Hz), 2.82 (2H, t, *J* = 7.3 Hz), 3.92 (3H, s), 4.91-5.04 (4H, m), 5.73-5.84 (2H, m), 6.10 (1H, s). ^{13}C-NMR (126 MHz, $CDCl_3$) δ : 23.5, 26.3, 28.2, 28.5, 33.3, 33.7, 34.5, 43.5, 57.2, 94.4, 105.8, 114.5, 115.2, 138.1, 138.8, 162.0, 169.5, 169.8, 200.2.

6-(9-Decenyl)-4-methoxy-3-(10-undecenoyl)pyran-2-one (6b)

Following the procedure given for preparation of **6a**, **5b** (470 mg, 1.1 mmol) was methylated to give (**6b**) (437 mg, 90%) as yellow oil. HRMS (FAB) Calcd for $C_{27}H_{43}O_4$ (M^++1) 431.3161. Found 431.3173. MS (FAB) *m/z*: 431 (M^++1). IR (neat) ν : 2924, 1713 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.28-1.36 (20H, m), 1.59-1.68 (4H, m), 1.99-2.05 (4H, m), 2.50 (2H, t, *J* = 7.5 Hz), 2.81 (2H, t, *J* = 7.5 Hz), 3.90 (3H, s), 4.89-4.99 (4H, m), 5.75-5.83 (2H, m), 6.04 (1H, s). ^{13}C-NMR (126 MHz, $CDCl_3$) δ : 24.0, 27.0, 28.9, 29.0, 29.1, 29.1, 29.2, 29.2, 29.3, 29.3, 29.4, 29.5, 33.8, 33.9, 43.7, 57.1, 94.3, 105.8, 114.2, 114.3, 139.2, 139.3, 162.0, 169.4, 170.0, 200.4.

24-Hydroxy-22-oxabicyclo[19.2.2]pentacosa-1(24),11,21(25)-triene-2,23-dione (9b)

General procedure: To a solution of ruthenium alkylidene catalyst (**7**) (2.8 mg, 5 mol%) in dry dichloromethane (11 mL) was added dropwise a solution of **5b** (30 mg, 0.07 mmol) in dichloromethane (9 mL) over 2 h. The solution was stirred for 12 h at room temperature and then refluxed for 6 h. Solvent was evaporated and the residue was purified by PTLC (hexane-ethyl acetate, 10 : 1) to give starting (**5b**) (3.6 mg, 12%) and *E*/*Z*-mixture of **9b** (4.9 mg, 18%) as a colorless oil. HRMS (FAB) Calcd for $C_{24}H_{37}O_4$ (M^++1) 389.2692. Found 389.2694. MS (FAB) *m/z*: 389 (M^++1). IR (neat) ν : 2926, 1724, 1636 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.26-1.38 (18H, m), 1.52-1.72 (6H, m), 1.90-2.00 (4H, m), 2.51 (2H, t, *J* = 6.1 Hz), 3.07 (2H, t, *J* = 7.0 Hz), 5.30-5.38 (2H, m), 5.93 (1H, s), 16.9 (0.7H, s), 17.0 (0.3H, s). ^{13}C-NMR (126 MHz, $CDCl_3$) δ : 24.3, 25.5, 26.0, 26.2, 26.8, 27.0, 27.8, 27.9, 28.0, 28.1, 28.1, 28.4, 28.4, 28.7, 28.7, 28.8, 28.9, 28.9, 28.9, 29.2, 29.4, 29.5, 32.0, 32.4, 34.3, 34.4, 40.7, 99.6, 101.5, 101.7, 130.0, 130.1, 130.3, 130.7, 161.0, 172.7, 181.4, 181.6, 208.7, 209.1.

16-Methoxy-14-oxabicyclo[11.2.2]heptadeca-1(16),7,13(17)-triene-2,15-dione (10a)

Following the general procedure, **6a** (70 mg, 0.22 mmol) was added to a solution of catalyst (**7**) (9.1 mg, 5 mol%). The solution was stirred for 12 h at rt and then heated under reflux for 6 h. Purification by PTLC (hexane-ethyl acetate, 2 : 1) gave unreacted **6a** (11 mg, 15%), mixture of *E*/*Z*-**10a** (4.1 mg, 6%), (**11**) (5.1 mg, 8%), and cyclic dimer (**12**) (16.2 mg, 25%).

E/Z-(**10a**): HRMS (FAB) Calcd for $C_{17}H_{23}O_4$ (M^++1) 291.1596. Found 291.1604. MS (FAB) *m/z*: 291 (M^++1). IR (neat) ν : 2922, 1736, 1661 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 1.32-1.41 (4H, m), 1.71-1.79 (4H, m), 1.92-1.96 (4H, m), 2.47-2.50 (2H, m), 2.61-2.63 (2H, m), 3.88 (3H, s), 5.28-5.32 (2H, m), 6.12 (1H, s). ^{13}C-NMR (126 MHz, $CDCl_3$) δ : 22.5, 22.7, 22.8, 27.2, 27.6, 29.8, 30.0, 30.1, 31.8, 32.0, 33.6, 52.8, 96.2, 114.9, 122.2, 131.3, 131.6, 165.6, 167.7, 168.0, 173.2, 175.0, 176.0, 201.3.

11: colorless oil. HRMS (FAB) Calcd for $C_{36}H_{49}O_8$ (M^++1) 609.3427. Found 609.3415. MS (FAB) *m/z*: 609 (M^++1). IR (neat) ν : 2930, 1717, 1655 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.38-1.48 (8H, m), 1.62-1.72 (8H, m), 2.00-2.12 (8H, m), 2.50-2.54 (4H, m), 2.79-2.85 (4H, m), 3.91 (6H, s), 4.91-5.04 (4H, m), 5.36-5.40 (2H, m), 5.74-5.84 (2H, m), 6.04 (1H, s), 6.05 (1H, s).

12: colorless oil. HRMS (FAB) Calcd for $C_{34}H_{45}O_8$ (M^++1) 581.3114. Found 581.3097. MS (FAB) *m/z*: 581 (M^++1). IR (neat) ν : 2930, 1705, 1659 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.34-1.42 (8H, m), 1.58-1.72 (8H, m), 1.99-2.06 (8H, m), 2.48-2.54 (4H, m), 2.76-2.83 (4H, m), 3.90-3.93 (6H, m), 5.32-5.42 (4H, m), 6.06-6.11 (2H, m).

24-Methoxy-22-oxabicyclo[19.2.2]pentacosa-1(24),11,21(25)-triene-2,23-dione (10b)

Following the general procedure, a solution of **6b** (30 mg, 0.07 mmol) was added to a solution of catalyst (**7**) (2.8 mg, 5 mol%) over 2 h. The solution was stirred for 12 h at rt and then heated under reflux for 6 h. Purification by PTLC (hexane-ethyl acetate, 5:1) provided unreacted **6b** (2.0 mg, 7%) and **10b** (17.4 mg, 62%) as colorless oil. **10b**: HRMS (FAB) Calcd for $C_{25}H_{39}O_4$ (M^++1) 403.2848. Found 403.2834. MS (FAB) *m/z*: 403 (M^++1). IR (neat) ν : 2922, 1736, 1665 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 1.23-1.35 (18H, m), 1.58-1.77 (6H, m), 1.94-2.00 (4H, m), 2.54-2.57 (2H, m), 2.81-2.84 (2H, m), 3.93 (3H, s), 5.35-5.37 (2H, m), 6.06 (1H, s). ^{13}C-NMR (126 MHz, $CDCl_3$) δ :22.8, 26.8, 26.9, 27.8, 28.0, 28.2, 28.4, 28.9, 29.0, 29.0, 29.1, 29.4, 29.5, 29.8, 31.0, 31.7, 31.8, 31.9, 32.0, 33.3, 52.9, 96.5, 100.0, 109.0, 114.0, 124.5, 131.0, 165.2, 168.2, 168.9, 176.0, 184.0, 207.0.

24-Methoxy-22-oxa-bicyclo[19.2.2]pentacosa-1(24),21(25)-diene-2,23-dione (13)

Compound (**10b**) (120 mg, 0.3 mmol) was hydrogenated with 5% Pd-C (35 mg) under atmospheric pressure in ethanol (8.5 mL) at rt for 3 h. The catalyst was filtered off and the filtrate was evaporated. Purification of the residue by PTLC gave **13** (103 mg, 85%). HRMS (FAB) Calcd for $C_{25}H_{41}O_4$ (M^++1) 405.3005. Found 405.2972. MS (FAB) *m/z*: 405 (M^++1). IR (neat) ν : 2922, 1692 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 1.22-1.31 (28H, m), 1.57 (1H, t, J = 7.5 Hz), 1.60 (1H, t, J = 6.9 Hz), 1.70-1.72 (2H, m), 2.53 (2H, t, J = 6.7 Hz), 2.78 (2H, t, J = 7.4 Hz), 3.91 (3H, s), 6.05 (1H, s). ^{13}C-NMR (126 MHz, $CDCl_3$)

δ : 24.6, 26.3, 28.0, 28.3, 28.4, 28.4, 28.5, 28.5, 28.6, 28.7, 28.8, 28.8, 28.9, 29.2, 34.5, 43.5, 57.2, 94.7, 105.3, 162.0, 169.5, 170.1, 201.1.

24-Hydroxy-22-oxabicyclo[19.2.2]pentacosane-1(24),21(25)-diene-2,23-dione (14)

Bromotrimethylsilane (46 mg, 0.3 mmol) was added to a solution of **13** (25 mg, 0.06 mmol) in dry dichloromethane (1.5 mL) under ice cooling. The mixture was stirred for 3 h at rt. Water was added to the reaction mixture and the whole was extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. Purification of the residue by PTLC (hexane-ethyl acetate, 5 : 1) gave **14** (21 mg, 87%) as a colorless oil. ^{1}H-NMR (270 MHz, $CDCl_3$) δ : 1.21-1.35 (26H, m), 1.40 (2H, m), 1.69 (4H, m), 2.51 (2H, t, *J* = 6.4 Hz), 3.06 (2H, t, *J* = 7.2 Hz), 5.92 (1H, s), 16.96 (1H, s). This compound was identified by the comparison of the ^{1}H-NMR spectrum with that of an authentic sample.[5]

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