Efficient Synthesis of Bicyclic Lactones via Tungsten-Mediated Intramolecular Cycloalkenation

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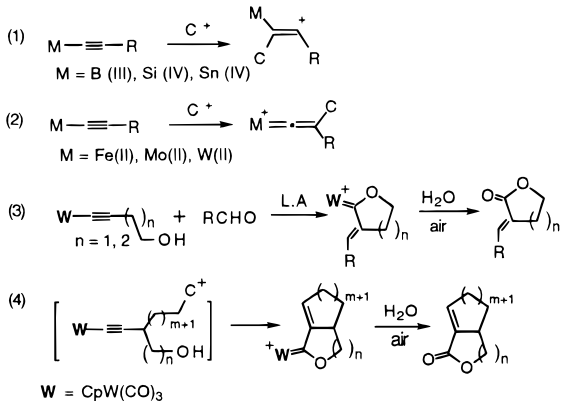
A series of tungsten-η^1-alkynols tethered with a dimethylacetal, methyl ketone, or trimethoxymethane group are prepared. Treatment of these functionalized tungsten-alkynols with $BF_3{\cdot}Et_2O$ leads to intramolecular cycloalkenation, producing bicyclic tungsten-oxacarbeniums in high yields. Air oxidation of these oxacarbenium salts produces unsaturated bicyclic lactones in good yields. The lactone products include δ- and ϵ-lactones fused with five-, six- and seven-membered carbocyclic rings. The preceding bicyclic tungsten-η^1-oxacarbeniums are highly reactive toward organocuprates, Grignard reagents, and diazomethane, leading to demetalation to give various derivatives of bicyclic lactones. A short synthesis of (±)-mitsugashiwalactone is developed based on this method.

Introduction

Transition-metal alkynyl compounds[1−3] show a reaction pathway distinct from that of their main group metal analogues in electrophilic addition.[4−6] In reaction with carbon electrophiles, the regiochemistry occurs at the alkynyl C_α carbon for alkynylsilanes and -stannanes[4−6] but at the C_β carbon for iron- and tungsten-alkynyl compounds, as depicted in Scheme 1 (eqs 1 and 2).[1−3] Previously, we reported cycloalkenation of tungsten-alkynol compounds via treatment with aldehydes and Lewis acid;[3] the reaction intermediate involved a tungsten-η^1-oxacarbenium species, as shown in Scheme 1 (eq 3). Further treatment of these salts with water and air delivered unsaturated lactones in high yields.[3a] A drawback in this reaction is that the scope of products mainly consists of unsaturated γ- and δ-lactones generated from organic aldehydes. Bicyclic lactones are common structural substituents for many naturally occurring substances.[7−9] We herein report a facile construction of such

Scheme 1. Electrophilic Additions of Metal Alkynyl Complexes



constituents via intramolecular cycloalkenation with a protocol shown in Scheme 1 (eq 4) and involving generation of tungsten-η^1-alkynol tethered with a carbon electrophile, ultimately yielding the desired bicyclic lactones according to the same principle. The types of lactone products as well as the scope of electrophiles constitute the focus of this investigation.

Results and Discussion

Syntheses of Tungsten-η^1-alkynol Substrates. Scheme 2 shows the synthesis of substrate **1** that is easily prepared from 4-pentyn-1-ol according to the literature procedure.[10] Treatment of this terminal alkynol with BuLi (3.5 equimolar) in cold THF (−78 °C), followed by alkylation with bromopropionaldehyde dimethylacetal, delivered compound **1** in 61% yield after workup. Scheme 2 also shows all substrates **2**−**12** used in this work; the yields are reported based on starting alkynols (51−67%). The alkylation is applicable to 4-pentyn-1-ol, 5-hexyn-1-ol, and 6-heptyn-1-ol but not to 3-butyn-1-ol;[10] we also prepare the substrates **8**−**12** that are tethered with either a ketone or a trimethoxymethane group.

Intramolecular Cycloalkenations of Tungsten-η^1-alkynols. Metalation of **1** with $CpW(CO)_3Cl$ (1.0 equiv)

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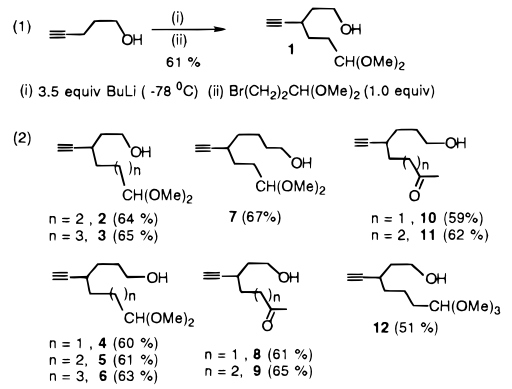
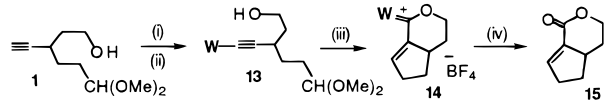
Scheme 2. Preparation of Functionalized Alkynols

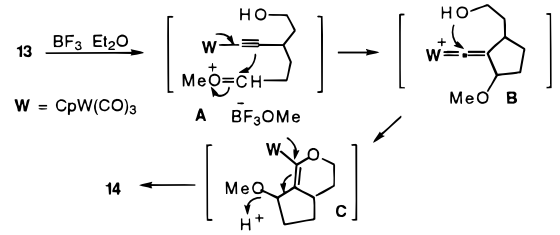


Scheme 3[a]

(1) Formation of bicyclic lactones



(2) Proposed Formation Mechanism of Bicyclic Lactones



[a] W = $CpW(CO)_3$; (i) W−Cl (1.0 equiv), Et_2NH; (ii) CuI (7 mol %); (iii) BF_3 Et_2O (2.0 equiv); (iv) H_2O/air.

in Et_2NH in the presence of a CuI catalyst[11] (7 mol %) delivered functionalized tungsten-η^1-alkynol **13** in 70% yield. The slow addition of $BF_3{\cdot}Et_2O$ (2.0 equimolar) to a diethyl ether solution of **13** at −40 °C yielded an orange precipitate in 91% yield, which was characterized as a bicyclic tungsten-oxacarbenium **14** (as BF_4^- salt) according to X-ray diffraction studies.[12] The treatment of this oxacarbenium salt **14** in CH_2Cl_2 with water and air caused demetalation to give unsaturated bicyclic lactone **15** in 81% yield. A proposed mechanism of formation of **14** is shown in Scheme 3 and involves attack of the η^1-alkynyl C_β carbon at the oxonium carbon of **A** to generate the tungsten-η^1-allenylidenium cation[13] **B**. The intramolecular addition of the hydroxyl group of **B** at its W=C_α=C carbon releases a proton to cleave the C−OMe bond of species **C**, ultimately generating the observed product **14**. Here the BF_3OMe^- counteranion of **A** undergoes anion exchange with remaining BF_3 to form a more stable BF_4^- species.[14]

This intramolecular cycloalkenation has been proven useful for a short synthesis of [4.3.0]-bicyclic lactone such as **15** as only three steps are required from 4-pentyn-1-ol to **15**. Table 1 lists cyclization results for the tungsten-alkynols **16**−**26** derived from the substrates. The preparation of these tungsten-alkynol species **16**−**26** followed

Table 1. Isolated Yields of Tungsten-η^1-alkynols and Bicyclic Lactones

entry	alkynol	tungsten-alkynol[a−c]	bicyclic lactone[d,e]
1	**2**	**16** (71%)	**27** (81%)
2	**3**	**17** (69%)	**28** (67%)
3	**4**	**18** (78%)	**29** (68%)
4	**5**	**19** (77%)	**30** (61%)
5	**6**	**20** (78%)	**31** (54 %)
6	**7**	**21** (76%)	—
7	**8**	**22** (74%)	**32** (58%)
8	**9**	**23** (68%)	**33** (61%)
9	**10**	**24** (72%)	**34** (40%)
10	**11**	**25** (67%)	—
11	**12**	**26** (70%)	**35** (61%)

[a] Equimolar ratios of $CpW(CO)_3Cl$ and organic substrates were used. [b] These organometallic compounds were purified on a silica column. [c] Isolated yields after chromatographic purification. [d] Isolated yields after purification by preparative silica TLC. [e] Yields are estimated based on tungsten-η^1-alkynol compounds.

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(12) Crystal data for the **14** monoclinic space group, *C*2/*c*, a = 17.9293(6) Å, b = 12.6096(4) Å, c = 16.9748(4) Å, V = 3741.0(8) Å^3, Z = 8. Final R = 0.037, and R_w = 0.036. The X-ray data of **14** is provided in Supporting Information.

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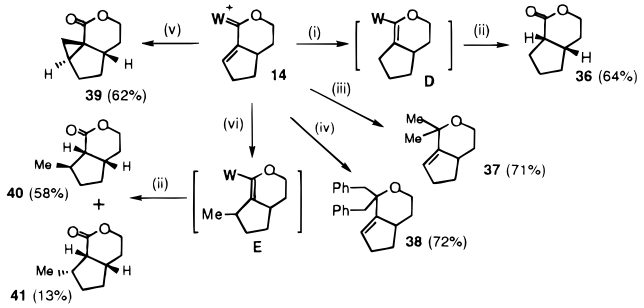
Scheme 4. Reaction Sequence of Bicyclic Tungsten-oxacarbenium[a]

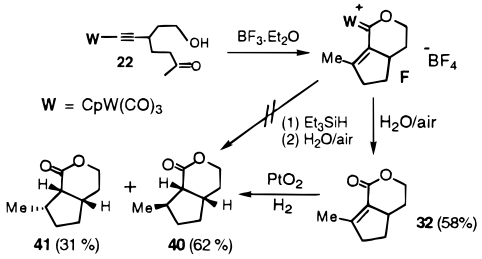


[a] W = CpW(CO)$_3$; (i) Et_3SiH (3.0 equiv), CH_2Cl_2, 23 °C, 36 h; (ii) H_2O, air, 8 h; (iii) MeMgBr (5.0 equiv), CH_2Cl_2, −40 °C, 2 h; (iv) $PhCH_2MgBr$ (5.0 equiv), CH_2Cl_2, −40 °C, 2 h; (v) (a) CH_2N_2, 0 °C, 8 h; (b) H_2O, air; (vi) ME_2CuLi (5.0 equiv), CH_2Cl_2, −40 °C → 23 °C.

that of **13**, and product yields exceeded 67−78%. For the cyclization of these tungsten-η^1-alkynols, as shown in entries 1−9, $BF_3{\cdot}Et_2O$ in two equimolar proportions was used to generate the corresponding tungsten-η^1-oxacarbenium salts in cold diethyl ether (−40 °C). The salts were filtered and redissolved in CH_2Cl_2 for water demetalation in air to release the bicyclic lactones **27**−**35**. Entries 1−5 show the syntheses of δ- and ϵ-lactones fused with five-, six-, and seven-membered carbocyclic rings such as **27**−**31**; the isolated yields are reported based on starting tungsten-η^1-alkynols. Entries 1−5 illustrate results for substrates **2**−**6** having a tethered dimethoxymethane group; yields are 54−81% depending on the ring sizes of the products. The yields decreased as ring sizes of bicyclic lactones increased. A medium ring product such as [5.5.0]-ϵ-lactone **31** was obtained in 54% yield. We attempted to cyclize tungsten-η^1-hept-1-yn-7-ol **21** intramolecularly (entry 6) but formed a complicated mixture of products from which we cannot isolate the corresponding [6.4.0]-λ-lactone. Intermolecular cycloalkenation fails to work for common organic ketones. Entries 7 and 8 show two instances for annulations of the functionalized tungsten-η^1-pent-1-yn-5-ols **22** and **23** possessing a tethered ketone; these yielded the corresponding bicyclic δ-lactones **32** (58%) and **33** (61%), respectively, after water demetalation. The reaction on the analogous tungsten-η^1-hex-1-yn-6-ol **24** proceeded less efficiently, and the yield of the corresponding ϵ-lactone **34** was 40%. Unfortunately, the same reaction did not work for tungsten-η^1-hex-1-yn-6-ol **25**, and the desired [7.6.0]-ϵ-lactone cannot be found among the reaction products. This $BF_3{\cdot}Et_2O$-promoted intramolecular alkylation also works for tungsten-η^1-pent-1-yn-5-ol **26** tethered with a trimethoxymethane group, affording the β-keto δ-lactone **35** in 61% yield.

Elaboration of Tungsten-η^1-oxacarbeniums. One important feature of tungsten-mediated cycloalkenation is the generation of a tungsten-η^1-oxacarbenium such as **14** that can easily be demetalated with a suitable nucleophile; the salt can function as a mono- or dication equivalent depending on the nucleophilic reagents.[3a] Further elaboration of such chemical versatility leads to the formation of various fused oxygen heterocyclics, particularly as the oxacarbenium salts are readily isolated from the reaction mixture. Representative compounds in Scheme 4 illustrate the demetalation products obtained from cation **14**. The C═C bond of **14** was readily

Scheme 5. A Sort Synthesis of Natural Bicyclic Lactones



reduced with Et_3SiH[15] and then hydrolyzed to yield saturated lactone **36** in 64% yield; the intermediate is presumably the tungsten-η^1-pyranyl species **D**. The treatment of this salt with MeMgBr and $PhCH_2MgBr$ in CH_2Cl_2 led to dialkylation at the W═C carbon, yielding **37** and **38** in 71% and 72% yields, respectively. The slow addition of dry CH_2N_2 to **14** in cold CH_2Cl_2 (0 °C) led to a cyclopropanation reaction, which afforded the lactone **39** in 62% yield after hydrolysis of its carbenium salt. Only single diastereomer was found for **39**; its stereochemistry was determined by proton−NOE−difference spectroscopy. In this case, CH_2N_2 preferably attacks the C═C bond of **14** from the less hindered face to generate a cyclopropane ring. The formation mechanism has been elucidated in our previous paper.[3] Our approach is applicable to the syntheses of naturally occurring bicyclic lactones such as mitsugashiwalactone **40** and onikulactone **41**.[8a−c,16−18] Syntheses of these lactones were attempted through treatment of this salt with Me_2CuLi, followed by hydrolysis and yielded **40** and **41** in 58% and 13% yields, respectively. The stereochemistries of **40** and **41** are established by proton−NOE effect and further confirmed by comparison of their ^1H and ^{13}C NMR spectra with those of authentic samples.[8a−c,16−18] In principle, the synthesis of onikulactone **41** can be achieved by Et_3SiH reduction[15] of the tungsten-η^1-oxacarbenium **F** derived from **22** (Scheme 5). Unfortunately, we found that the cation was very stable toward excess Et_3SiH (5.0 equiv) under reflux in CH_3CN. Attempts to reduce this cation with Bu_3SnH, $PhSiH_3$,[19] and $[HCu(PPh_3)]_6$[20−22] in refluxing CH_3CN were unsuccessful. We therefore demetalated this oxacarbenium salt, and the resulting lactone **32** was hydrogenated over a PtO_2 catalyst (1.0 atom, 10 mol %) in MeOH, yielding onikulactone **41** in 31% yield with mitsugashiwalactone **40** as the major isomer (62%). Attempts to increase stereoselection for onikulactone **41** via conjugated addition of **32** with $[HCu(PPh_3)]_6$[20−22] were unsuccessful, and compound **32** was recovered in 91% yield.

Summary. Bicyclic lactones are important structural units for many organic substances. Syntheses of these lactones can be achieved through $BF_3{\cdot}Et_2O$-promoted intramolecular cycloalkenation of tungsten-η^1-alkynol

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compounds tethered with a dimethylacetal, ketone, or trimethoxymethane group. Fused lactones of various sizes and types were prepared based on this method, including [5.5.0]-δ-lactone. In the course of cyclization, tungsten-oxacarbenium salts can be isolated; these salts can function as a mono- or dication equivalent. Examples to illustrate the synthetic utility of this salt were provided; one instance is a short synthesis of racemic (±)-mitsugashiwalactone.

Experimental Section

Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere in oven-dried glassware using standard syringe, cannula, and septa apparatus. Benzene, diethyl ether, tetrahydrofuran, and hexane were dried with sodium benzophenone and distilled before use. Dichloromethane and acetonitrile were dried over CaH_2 and distilled before use. $W(CO)_6$, dicyclopentadiene, propargyl alcohol, and sodium were obtained commercially and used without purification. The syntheses and the spectral data of compounds of the same family (i.e., **2**−**12**, **16**−**26**, and **27**−**35**) in repetitive operations are listed in Supporting Information.

Elemental analyses were performed at National Cheng Kung University, Taiwan. Mass spectral data of tungsten compounds are reported based on ^{184}W isotopes.

General Procedure for the Synthesis of Functionalized Alkynols. **Synthesis of Compound 1**. To a THF solution (150 mL) of 4-pentyn-1-ol (2.10 g, 25.0 mmol) was added BuLi in hexane (1.6 M, 54.7 mL) at −78 °C; the resulting solution was brought to 23 °C and stirred for 8 h. The resulting yellow suspension was warmed to 40 °C for 1 h and then cooled to −40 °C. To this solution was slowly added bromopropionaldehyde dimethylacetal in THF (4.58 g, 25.0 mmol); the mixture was stirred for 8 h before a saturated aqueous NH_4Cl solution (20 mL) was added. The solution was concentrated, and the organic layer was extracted with diethyl ether (3 × 20 mL). The extract was dried and chromatographed through a short silica column to yield compound **1** as a colorless oil (2.84 g, 15.3 mmol, 61%). IR (Nujol, cm^{-1}): υ(OH) 3410 (br s), υ(C≡C) 2110 (w). ^1H NMR (300 MHz, $CDCl_3$): δ 4.23 (1H, t, J = 5.7 Hz), 3.66 (2H, t, J = 6.5 Hz), 3.20 (6H, s), 2.74 (1H, br s), 2.44 (1H, m), 2.01 (1H, d, J = 2.4 Hz), 1.86−1.30 (6H, m). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 104.0, 86.5, 70.1, 60.1, 52.6, 52.3, 37.4, 29.8, 29.5, 27.7. HRMS calcd for $C_{10}H_{18}O_3$: 186.1256. Found: 186.1264.

General Procedure for the Synthesis of Tungsten-η^1-alkynols. Synthesis of Compound 13. To a Et_2NH solution (40 mL) of $CpW(CO)_3Cl$ (3.69 g, 10.0 mmol) and CuI (133.3 mg, 0.7 mmol) was added alkynol **1** (1.86 g, 10.0 mmol) at 23 °C in the absence of light. The mixture was stirred for 30 min before it was concentrated to ca. 2 mL. The residues were chromatographed through a silica column (diethyl ether/hexane = 1/1) to yield a yellow band that afforded **13** (R_f = 0.12) as a dark orange oil (3.26 g, 6.3 mmol, 70%). IR (Nujol, cm^{-1}): υ(OH) 3408 (br s), υ(C≡C) 2113 (w), υ(CO) 2033 (s), 1937 (s). ^1H NMR (300 MHz, $CDCl_3$): δ 5.52 (5H, s), 4.33 (1H,t, J = 5.7 Hz), 3.74 (2H, m), 3.26 (3H, s), 3.25 (3H, s), 3.00 (1H, br s), 2.59 (1H, m), 1.90−1.75 (1H, m), 1.72−1.50 (3H, m), 1.48−1.32 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 229.4, 211.7, 132.1, 104.3, 91.3, 62.2, 59.7, 52.7, 52.2, 38.4, 32.5, 31.2, 30.1. MS (75 eV, m/e): 518 (M^+). Anal. Calcd for $C_{18}H_{22}WO_6$: C, 41.72; H, 4.28. Found: C, 41.80; H, 4.23.

Synthesis of the Tungsten-η^1-oxacarbenium 14. To a diethyl ether solution (10 mL) of tungsten-η^1-alkynol **13** (260 mg, 0.5 mmol) was added $BF_3{\cdot}Et_2O$ (0.13 mL, 1.0 mmol) at −40 °C, immediately depositing an orange precipitate that was collected by filtration. The precipitate was recrystallized in a saturated CH_2Cl_2/diethyl ether solution to yield dark red crystals of **14** (208 mg, 0.38 mmol, 77%). IR (Nujol, cm^{-1}): υ(W−CO) 2055 (s), 1944 (s), υ(C=C) 1658 (w). ^1H NMR (300 MHz, $CDCl_3$): δ 7.38 (1H, m), 5.99 (5H, s), 5.12 (1H, dd, J = 12.2, 4.8 Hz), 4.87 (1H, td, J = 12.4, 3.3 Hz), 3.03 (1H, m), 2.62 (2H, m), 2.49−2.35 (1H, m), 2.33−2.21 (1H, m), 1.78−1.51 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 282.1, 216.8, 214.5, 171.2, 152.9, 96.4, 81.3, 36.9, 33.5, 32.0, 29.0. Anal. Calcd for $C_{16}H_{15}WO_4BF_4$: C, 35.46; H, 2.79. Found: C, 35.49; H, 2.82.

General Procedure for the Synthesis of Fused Bicyclic Lactones. **Synthesis of 15.** To a CH_2Cl_2 solution (10 mL) of carbenium salt **14** (200 mg, 0.37 mmol) was added H_2O (2 mL); the mixture was stirred for 12 h in the presence of air. The organic layer was concentrated and chromatographed by preparative silica TLC to yield **15** as a colorless solid (41.3 mg, 0.30 mol, 81%). IR (neat, cm^{-1}): υ(C=O) 1727 (s), υ(C=C) 1658 (w). ^1H NMR (300 MHz, $CDCl_3$): δ 6.9 (1H, t, J = 2.2 Hz), 4.40 (1H, m), 4.25 (1H, m), 2.93 (1H, m), 2.51−2.24 (3H, m), 2.11−1.98 (1H, m), 1.71−1.47 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.4, 145.4, 134.6, 69.5, 41.8, 32.5, 31.5, 30.6. HRMS calcd for $C_8H_{10}O_2$: 138.0681. Found: 138.0688.

Demetalation of 14 with Et_3SiH. To a CH_2Cl_2 solution of **14** (200 mg, 0.37 mmol) was added Et_3SiH (129 mg, 1.11 mol); the mixture was refluxed for 36 h before the addition of water (2 mL). The solution was further stirred for 8 h in the presence of air, and the organic layer was concentrated and chromatographed by preparative silica TLC to yield **36** as a colorless oil (33.2 mg, 0.24 mol, 64%). IR (neat, cm^{-1}): 1730 (s). ^1H NMR (400 MHz, $CDCl_3$): δ 4.24 (1H, m), 4.14 (1H, m), 2.87 (1H, m), 2.45 (1H, m), 2.10−1.98 (4H, m), 1.75−1.59 (1H, m), 1.57−1.38 (2H, m), 1.32−1.12 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 67.3, 42.7, 36.2, 33.5, 29.7, 29.1, 25.1. HRMS calcd for $C_8H_{12}O_2$: 140.0837. Found: 140.0830.

Demetalation of 14 with MeMgBr. To a CH_2Cl_2 solution (10 mL) of **14** (200 mg, 0.37 mmol) was added MeMgBr (1.85 mmol) at −40 °C, and the mixture was stirred for 2 h before being quenched with water (3 mL). To the solution was added diethyl ether (3 × 10 mL), and the organic layer was separated and chromatographed by preparative silica TLC to yield **37** as a colorless oil (54.0 mg, 0.36 mol, 71%). IR (neat, cm^{-1}): υ(C=C) 1649 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 5.35 (1H, t, J = 2.0 Hz), 3.72 (2H, m), 2.67 (1H, m), 2.32−2.09 (3H, m), 1.90−1.81 (1H, m), 1.37 (3H, s), 1.38−1.26 (2H, m), 1.27 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5, 120.6, 73.2, 61.0, 40.3, 36.3, 31.0, 30.6, 27.9, 23.8. HRMS calcd for $C_{10}H_{16}O$: 152.1201. Found: 152.1206.

Demetalation of 14 with $PhCH_2MgBr$. Compound **14** (200 mg, 0.37 mmol) and $PhCH_2MgBr$ (1.85 mmol) afforded **38** (81 mg, 72%) as a colorless oil. IR (neat, cm^{-1}): υ(C=C) 1653 (w). ^1H NMR (400 MHz, $CDCl_3$): δ 7.42−7.02 (10H, m), 5.18 (1H, t, J = 1.8 Hz), 3.86 (2H, m), 3.05 (2H, dd, J = 24.9, 13.2 Hz), 2.90 (2H, dd, J = 6.4, 13.0 Hz), 2.66 (1H, m), 2.25−2.07 (2H, m), 1.93−1.79 (1H, m), 1.39−1.16 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.0, 138.1, 137.7, 131.2, 130.6, 127.7, 127.5, 127.3, 126.0, 125.6, 124.7, 79.3, 61.0, 43.3, 41.8, 41.2, 34.4, 31.5, 30.6. HRMS calcd for $C_{22}H_{24}O$: 304.1827. Found: 304.1820.

Demetalation of 14 with CH_2N_2. To a CH_2Cl_2 solution (10 mL) of **14** (200 mg, 0.37 mmol) was added CH_2N_2 (77.7 mg, 1.85 mmol) at 0 °C, and the mixture was stirred for 8 h before treatment with water (5 mL). The solution was stirred for 8 h at 23 °C in the presence of air. To the solution was added diethyl ether (3 × 10 mL), and the organic layer was separated and chromatographed by preparative silica TLC to yield **39** as a colorless oil (34.9 mg, 0.23 mol, 62%). IR (neat, cm^{-1}): υ(C=O) 1737 (s). ^1H NMR (400 MHz, $CDCl_3$): δ 4.48−4.22 (2H, m), 2.39−2.27 (1H, m), 1.98−1.81 (2H, m), 1.80−1.61 (4H, m), 1.61−1.43 (2H, m), 0.88 (1H, t, J = 5.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 68.7, 37.2, 34.5, 31.9, 29.0, 28.3, 24.1, 16.6. HRMS calcd for $C_9H_{12}O_2$: 152.0837. Found: 152.0833.

Synthesis of Mitsugashiwalactone 40 and Onikulactone 41. To a CH_2Cl_2 solution (10 mL) of **14** (200 mg, 0.37 mmol) was added a THF solution of Me_2CuLi (ca. 0.38 mmol) at −40 °C; the mixture was stirred for 8 h before treatment with a saturated NH_4Cl solution (5 mL). The solution was stirred for 2 h at 23 °C in the presence of air. To the solution was added diethyl ether (3 × 10 mL), and the organic layer was separated and chromatographed by preparative silica TLC

to yield **40** (33.1 mg, 0.22 mol, 58%) and **41** (7.4 mg, 0.05 mol, 13%), respectively. Spectral data of **40** and **41** are identical to those of the authentic sample.

Spectral data of **40.** IR (neat, cm^{-1}): υ(C═O) 1735 (s). ^1H NMR (600 MHz, $CDCl_3$): δ 4.28 (1H, m), 4.17 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.2, 67.3, 42.7, 36.2, 33.5, 29.7, 29.1, 25.1. HRMS calcd for $C_9H_{14}O_2$: 154.0994. Found: 154.0998.

Spectral data of **41.** IR (neat, cm^{-1}): υ(C═O) 1734 (s). ^1H NMR (600 MHz, $CDCl_3$): δ 4.29 (1H, m), 4.18 (1H, m), 2.96 (1H, dd, J = 10.0, 8.7 Hz), 2.55 (1H, m), 2.41 (1H, m), 1.93 (2H, m), 1.69 (1H, m), 1.58−1.40 (3H, m), 0.90 (d, J = 7.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 67.7, 47.5, 37.6, 35.5, 33.1, 30.8, 29.2, 17.3. HRMS calcd for $C_9H_{14}O_2$: 154.0994. Found: 154.0992.

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Supporting Information Available: ^1H and ^{13}C NMR of all new compounds; syntheses and spectral data of compounds of the same family (i.e., **2**−**12**, **16**−**26**, and **27**−**35**) in the repetitive operations (19 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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