One-Electron Oxidation of Geranyl Acetone Derivatives Using Ceric(IV) Ammonium Nitrate and Manganese(III) Acetate: Carbon–Carbon Bond Formation

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Abstract

Oxidation of geranyl acetone derivatives with ceric ammonium nitrate (CAN) and Mn(OAc)₃ afforded tricyclic and bicyclic compounds as well as hydroxy and nitro compounds as a result of one-electron oxidation followed by carbon–carbon bond formation. This is the first example of radical cyclization (formed by one-electron oxidation) of geranyl acetone derivative 1 and its isomer 4 to give tri- and bicyclic products with carbon–carbon bond formation.

Keywords

oxidation, radical reaction, geranyl acetone derivative, ceric(IV) ammonium nitrate, manganese(III) acetate

Received: April 8th, 2022; Accepted: May 23rd, 2022.

One-electron oxidation¹ as well as one-electron reduction is the interesting reaction via a radical intermediate triggered by a radical initiator, such as AIBN, Bu₃SnH, SmI₂, and so on.¹ Electrolysis has also been studied by many groups,² since it is completely benign to the environment; nowadays generally accepted as green chemistry. On the other hand, single-electron oxidation of carbonyl compounds using ceric (IV) ammonium nitrate (CAN) and Mn(OAc)₃ as an oxidant has been well studied.³⁴⁵ Recently, Thomson⁶ and MacMillan⁷ independently used CAN for the radical coupling reaction of the enolate. Quite recently, Yoshida and Shishido reported a coupling reaction between cyclopentanone carboxylates and alkenes using the CAN and Cu(OAc)₂ system.⁸ And also, Yamashita and Hirama² succeeded in tandem cyclization producing tricyclic rings using Mn(OAc)₃. Other metals, such as Fe, V, and Cu, were used for the generation of a radical by one-electron oxidation.¹⁰⁻¹⁷ We have been investigating one-electron reducing reactions applied to the construction of perhydronaphthalenes, hydrindanes, and perhydroguaiaines.¹⁸⁻²⁵ We are also interested in one-electron oxidation induced by CAN or Mn(OAc)₃ making bicyclic compounds and we now report the results on the one-electron oxidation of geranyl acetone derivative 1 and its isomer 4.²⁶

A solution of methyl 7,11-dimethyl-3-oxo-6,10-dodecadienoate (1) in a certain solvent was treated with CAN (Table 1) and the mixture was purified by silica-gel column chromatography to afford compounds 2 and 3.¹⁵ In MeOH and MeCN (entries 1 and 2), only compound 2 was isolated, although yields were 30% and 27%, respectively. In more polar solvents, yields of compounds 2 and 3 were much lower (entries 3–6). The addition of acid or base did not change the situation very much (entries 7 and 8). Triethyl amine (TEA) caused the reaction very complex and no detectable compound was isolated (entry 9).

Structures of 2 and 3 were determined as follows. Compound 2 (see online Supplementary material), mp. 94–95 °C, showed a quasi molecular ion peak at m/z 235 and its molecular formula was determined to be C₁₄H₁₈O₃ by HR-CIMS and ¹³C NMR data. The IR spectrum exhibited the presence of two kinds of carbonyl groups (1759 and 1734 cm⁻¹). The ¹H NMR spectrum showed the presence of two singlet methyl groups at δ 1.48 and 1.54, and an exomethylene group at δ 4.87 and 4.97. Fourteen signals appeared in the ¹³C NMR spectrum and two were due

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to the carbonyl groups at δ 212.1 and 173.4. The 6 degrees of unsaturation was inferred from the fact that there were two carbonyls and one double bond. Hence, compound 2 should be tricyclic. The selected correlations of HMBC and COSY spectra were displayed in Figure 1. The proton connectivity H2-8/H2-9/H-10 and H2-4/H2-5/H-6 were detected in the COSY. The methine proton at C-6 and C-10 had correlations with both carbonyl carbons, at C-1 and C-3, as well as the quaternary carbon at C-2. The planar structure was thus assumed as depicted in the formula.

The stereochemistry was established by the NOESY spectrum, the selected correlations of which were shown in Figure 1. Fortunately, compound 2 crystallized and its structure was established by the x-ray crystallographic analysis to confirm the above assumption. [X-ray crystallographic analysis of compound 2: All diagrams and calculations were performed using maXus (Bruker Nonius, Delft & MacScience, Japan), C15H19O5; Mo Kα radiation, λ = 0.71073 Å, 3707 measured reflections, 3242 independent reflections, Program(s) used to refine the structure: SHPXL-97 (Sheldrick, 1997); refinement of F2, full matrix least squares refinement. Crystal data: triclinic, P1, a = 6.935(3) Å, b = 9.838(4) Å, c = 10.245(4) Å, α = 74.720(5)°, β = 89.138(5)°, γ = 84.052(4)°, R = 0.0389. Crystallographic data for compound 1 have been deposited in Cambridge Crystallographic Data Center as supplementary publication number CCDC 982800. Copies of the data can be obtained, free of charge, via www.ccdc.cam.ac.uk/data_request/cif, or by mailing the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax. + 44 1223 336033 or e-mail: data_request@ccdc].] The ORTEP drawing was shown in Figure 2.

The spectroscopic data of compound 3 (see online Supplementary material) were very similar to those of compound 2, and the structure was supported by the 2D NMR, IR, and MS spectra.

We have next studied the oxidation of methyl 2-acetyl-5,9-dimethyl-4,8-decadienoate (4), an isomer of compound 1. Oxidation of keto ester 4 was similarly carried out with CAN (3 equiv.) (Table 2). Either in MeOH or MeCN, no product was obtained even after 30 h. However, a cyclized compound 5 (see online Supplementary material) as well as hydroxy

**Table 1. Oxidation of Compound 1 With CAN (3 equiv.).**

| Entry | Additive | Solvent | Time (h) | Yield (%) | Ratio (2:3) |
|-------|----------|---------|----------|-----------|-------------|
| 1     | None     | MeOH    | 3        | 30        | 100:0       |
| 2     | None     | MeCN    | 3        | 27        | 100:0       |
| 3     | None     | DMF     | 24       | 8         | 3:1         |
| 4     | None     | MeCN    | 24       | 9         | 4:5         |
| 5     | H2O      | MeOH    | 3        | 35        | 6:1         |
| 6     | H2O      | MeCN    | 7        | 29        | 5:2         |
| 7     | NaOMe    | MeOH    | 3        | 27        | 7:2         |
| 8     | TsOH     | MeOH    | 3        | 19        | 4:3         |
| 9     | Et3N     | MeOH    | 3        | Complex mixture |

*Isolated yield.

**Figure 1.** Selected HMBC and NOE correlations of compound 2.
and nitro compounds 6 (see online Supplementary material) and 7 (see online Supplementary material) were produced in THF (entry 3). The degraded compound 8 was also obtained in a 9% yield. Although yields were not acceptable, the formation of compound 5 is very interesting.

The structure of compound 5 (see online Supplementary material) was determined by analysis of 1D/2D NMR, IR, and MS (Figure 3). The molecular formula C_{14}H_{21}O_{3} was determined by HR-CIMS and $^{13}$C NMR data, showing the presence of four methyl, three methylene, two methine, and five quaternary carbon atoms. Two signals were due to carbonyl ($\delta$ 172.3 and 200.8) and another two to olefinic carbons ($\delta$ 122.4 and 133.0). Therefore, this molecule should be bicyclic. The HMBC indicated correlations as shown in Figure 3. The stereochemistry was also determined by the NOESY.

Because one-electron oxidation of both compounds 1 and 4 using CAN afforded cyclized products, we next investigated the similar reactions using Mn(OAc)$_3$.

When compound 1 was treated with Mn(OAc)$_3$ (4 equiv) in MeOH at rt for 24 h (Table 3), compound 10 (see online Supplementary material) was formed in 12% (calcd by GC) (entry 1). In MeCN (entry 2), compounds 2 and 9 (see online Supplementary material) as well as 10 (see online Supplementary material) were formed in 5%, 8%, and 8% yields, respectively. Then, in THF at 80 °C, compound 10 was formed in a 59% yield (entry 3). When this reaction was carried out at rt, the yield was dramatically low.

The structure of each product was determined by spectroscopic analysis. The molecular formula of compound 9 (see online Supplementary material) was determined to be C_{15}H_{20}O_{3} by HR-CIMS and $^{13}$C NMR data. The IR spectrum indicated the presence of ester (1720 cm$^{-1}$) and a five-membered ketone (1750 cm$^{-1}$), which was supported by the signals at $\delta$C 169.4 and 211.4. The 2D correlations shown in Figure 4 indicated the presence of a bicyclic system with cis-fused cyclopentanone. The stereochemistry was suggested by the NOESY as shown in Figure 4.

Keto ester 4 was similarly treated with Mn(OAc)$_3$ (Table 4). In any case, only compound 11 (see online Supplementary material) was isolated. In MeOH (entry 1), the yield was 15% and in MeCN 45% (entry 2). The yield in THF at rt was raised to 71%.

The molecular formula of compound 11 (see online Supplementary material) was determined to be C_{13}H_{20}O_{4} by HR-MS and $^{13}$C NMR data. The IR spectrum indicated the presence of a hydroxy (3500 cm$^{-1}$) and ester (1720 cm$^{-1}$) peak at $m/z$ 250 and its molecular formula was determined to be C_{15}H_{22}O_{3} by HR-MS and $^{13}$C NMR data. The IR spectrum indicated the presence of an ester (1715 cm$^{-1}$) and a five-membered ketone (1750 cm$^{-1}$), supported by the signals at $\delta$C 172.1 and 217.8. Therefore, this molecule should be tricyclic. Analysis of 2D NMR led to the conclusion that compound 10 had the structure further cyclized from compound 9 as shown in Figure 5. The stereochemistry was also determined by NOESY.

Table 2. Oxidation of Compound 4 With CAN (3 equiv).

| Entry | Additive | Solvent | Time (h) | Yield (%)$^a$ |
|-------|----------|---------|----------|--------------|
| 1     | None     | MeOH    | 4        | 0            |
| 2     | None     | MeCN    | 30       | 0            |
| 3     | None     | THF     | 24       | 5 (10), 6 (8), 7 (1), 8 (9) |

$^a$Isolated yield.
Figure 3. Selected 2D correlations of compounds 5 and 6.

Table 3. Oxidation of Compound 1 With Mn(OAc)₃ (4 equiv.).

| Entry | Solvent | Time (h) | Yield (%)<sup>a</sup>  |
|-------|---------|----------|------------------------|
| 1     | MeOH    | 24       | 10 (12)                |
| 2     | MeCN    | 24       | 2 (5), 9 (8), 10 (8)   |
| 3<sup>b</sup> | THF    | 24       | 10 (59)                |

<sup>a</sup>Isolated yield.

<sup>b</sup>At 80 °C.

Figure 4. Selected 2D correlations of compound 9.

Figure 5. Selected 2D correlations of compound 10.
functionalities. The $^{13}$C NMR spectrum indicated the presence of two sp$^2$ carbons ($\delta_C$ 146.0 and 106.5) as well as two quaternary oxidized carbon atoms ($\delta_C$ 76.6 and 79.9). Therefore, this molecule should be bicyclic. The structure was suggested by the analysis of 2D NMR spectra (Figure 6). The rings were shown to be cis-fused by the NOESY.

The formation of these products was explained by the mechanism shown in Scheme 1. Treatment of compound 1 with CAN or Mn(OAc)$_3$ resulted in oxidation of the C-2 carbon to form a radical. It attacked the nearby double bond forming a five-membered carbocycle and the resulting radical was further oxidized to a cation, which lost a proton to form an exomethylene intermediate. This intermediate was oxidized by the reagent to form a radical cation, which attacked the other double bond forming a six-membered ring. The resulting radical was once more oxidized to a cation and finally, the lactone was formed to give compound 2.

In the case of compound 4 shown in Scheme 2, the radicals attacked the carbon C-4 producing a cyclopropane ring followed by hydroxylation or lactonization to afford 5 and 6. When Mn$^{3+}$ was employed acetyl group was lost and further oxidation to give dienol radical e, which attacked the carbon C-9, and the resulting radical made a C–C bond with C-4. Thus, compound 11 was formed. The other products can also be well explained by a similar mechanism.

In conclusion, we have developed the oxidative cyclization of geranyl acetone derivative 1 and its isomer 4 to tricyclic and bicyclic compounds as well as hydroxy and nitro substituted compounds induced by CAN and Mn(OAc)$_3$, although the yields were not very high. However, this type of cyclization has never been reported so far. We are currently investigating these reactions to get better yields using other substrates.

**Experimental**

**Oxidation of compound 1 using CAN:** To a stirred solution of compound 1 (508.4 mg, 2.01 mmol) in MeOH (16 mL), CAN (3.29 g, 6.03 mmol) and H$_2$O (72.4 mg, 4.02 mmol) in one portion at rt and the mixture was stirred for 3 h. The mixture was cooled to 0 °C and water was added. The mixture was extracted with ether and the organic layer was washed with brine. After drying (MgSO$_4$), the solvent was evaporated in vacuo to afford a residue. The residue was separated by silica-gel column chromatography to afford compounds 2 (141.5 mg, 0.60 mmol, 30%) and 3 (23.6 mg, 0.10 mmol, 5%), respectively.

**Compound 2**

Crystals.

mp. 94–95 °C.

FTIR: 1759, 1734 cm$^{-1}$.

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**Table 4. Oxidation of Compound 4 With Mn(OAc)$_3$ (3 Equiv.).**

| Entry | Solvent | Time (h) | Yield (%)$^a$ of 11 |
|-------|---------|----------|------------------|
| 1     | MeOH    | 24       | 15               |
| 2     | MeCN    | 72       | 45               |
| 3     | THF     | 24       | 71               |

$^a$Isolated yield.
A plausible mechanism of one-electron oxidation of 1 using CAN to give compounds 2, 9, and 10.

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 1.48 (3H, s), 1.54 (3H, s), 1.59–1.65 (1H, m), 1.72 (1H, dq, $J$ = 14.6, 5.1 Hz), 2.16 (1H, dt, $J$ = 14.3, 5.5 Hz), 2.23–2.29 (1H, m), 2.30 (1H, s), 2.34 (1H, br q, $J$ = 9.1 Hz), 2.53–2.59 (1H, m), 2.67–2.73 (1H, m), 2.75 (1H, dd, $J$ = 7.1, 4.4 Hz), 3.20 (1H, br d, $J$ = 6.3 Hz), 4.87 (1H, br s), 4.97 (1H, br s).

$^{13}$C NMR (150 MHz, CDCl$_3$) $\delta$ 21.4 (CH$_2$), 23.4 (CH$_2$), 25.2 (CH$_3$), 28.6 (CH$_3$), 30.6 (CH$_2$), 34.0 (CH$_2$), 43.5 (CH), 44.3 (CH), 63.8 (C), 86.3 (C), 110.3 (CH$_2$), 143.9 (C), 173.4 (C), 212.1 (C).

MS (Cl) $m/z$ 235 [M + H]$^+$ (base), 217, 191, 189, 179, 161, 147, 129, 89.
HR-MS Found \( m/z \) 235.1329 \([M + H]^+\), Calcd for C\(_{14}\)H\(_{19}\)O\(_3\) 235.1334.

Compound 3

Oil.

\( ^1\)H NMR (600 MHz, C\(_6\)D\(_6\)) \( \delta \) 0.83 (3H, s), 1.04 (3H, s), 1.26–1.29 (1H, m), 1.30 (3H, br s), 1.44 (1H, ddt, \( J = 12.9, 8.8, 3.7 \) Hz), 1.60–1.66 (1H, m), 1.76 (br dt, \( J = 18.1, 8.5 \) Hz), 2.15–2.22 (1H, m), 2.25–2.30 (1H, m), 2.54 (1H, br d, \( J = 5.8 \) Hz), 2.86 (1H, d, \( J = 8.2 \) Hz), 5.03 (1H, br s).

\( ^{13}\)C NMR (150 MHz, C\(_6\)D\(_6\)) \( \delta \) 20.8 (CH\(_2\)), 21.2 (CH\(_3\)), 23.3 (CH\(_3\)), 23.5 (CH\(_2\)), 27.9 (CH\(_3\)), 35.7 (CH\(_2\)), 42.1 (CH), 43.7 (CH), 59.8 (C), 85.3 (C), 122.1 (CH), 132.7 (C), 174.3 (C), 212.5 (C).

MS (EI) \( m/z \) 234 \([M + H]^+\), 216, 203, 191, 177, 153, 123 (base).

HR-MS (EI) Found \( m/z \) 234.1222 \([M^+]\), Calcd for C\(_{14}\)H\(_{18}\)O\(_3\) 234.1256.

Scheme 2. A plausible mechanism of one-electron oxidation of 4 using CAN or Mn(OAc)\(_3\) to give compounds 5, 6, and 11.

Oxidation of compound 4 using CAN: To a stirred solution of compound 4 (580.4 mg, 2.30 mmol) in THF (18.4 mL), CAN (3.78 g, 6.90 mmol) in one portion at rt and the mixture was stirred for 24 h. The mixture was cooled to 0°C and water was added. The mixture was extracted with ether and the organic layer was washed with brine. After drying (MgSO\(_4\)), the solvent was evaporated in \textit{vacuo} to afford a residue. The residue was separated by a silica-gel column chromatography to afford compounds 5 (54.3 mg, 0.23 mmol, 10%), 6 (51.0 mg, 0.19 mmol, 8%), 7 (8.9 mg, 0.03 mmol, 1%) and 8 (53.6 mg, 0.21 mmol, 9%), respectively.

Compound 5

Oil.

\( ^1\)H NMR (600 MHz, CDCl\(_3\)) \( \delta \) 1.37 (3H, s), 1.47 (1H, dd, \( J = 5.6, 4.3 \) Hz), 1.59 (3H, br s), 1.68 (3H, br s), 1.69–1.72 (1H, m), 1.76–1.82 (1H, m), 1.96 (1H, dd, \( J = 8.0, 4.3 \) Hz), 2.06 (2H, br q, \( J = 7.2 \) Hz), 2.57 (3H, s), 2.58 (1H, dd, \( J = 5.6 \) Hz), 5.05–5.07 (1H, m).

\( ^{13}\)C NMR (150 MHz, CDCl\(_3\)) \( \delta \) 17.7 (CH\(_3\)), 21.7 (CH\(_2\)), 22.5 (CH\(_3\)), 22.6 (CH\(_3\)), 25.6 (CH\(_3\)), 29.3 (CH\(_3\)), 38.5 (CH), 39.4 (C), 41.9 (CH\(_2\)), 83.1 (C), 122.4 (CH), 133.0 (C), 172.3 (C = O), 200.8 (C = O).

MS (Cl) \( m/z \) 237 \([M + H]^+\), 219, 203, 191, 177, 153, 123 (base).

HR-MS (Cl) Found \( m/z \) 237.1464 \([M + H]^+\), Calcd for C\(_{14}\)H\(_{23}\)O\(_3\) 237.1491.
Compound 6

Oil.

FTIR: 3470, 1740 cm⁻¹.

¹H NMR (600 MHz, CDCl₃) δ 1.59 (3H, br s), 1.64 (3H, br s), 1.68 (3H, br s), 2.00–2.10 (4H, m), 2.27 (3H, s), 2.65–2.87 (2H, m), 3.79 (3H, s), 4.12 (1H, s), 4.95–5.10 (2H, m).

¹³C NMR (50 MHz, CDCl₃) δ 16.4 (CH₃), 17.7 (CH₃), 24.8 (CH₃), 25.7 (CH₂), 26.4 (CH₂), 34.1 (CH₂), 39.8 (CH₂), 53.3 (CH₃), 84.0 (C), 115.9 (CH), 123.9 (CH), 131.7 (C), 140.4 (C), 171.2 (C = O), 204.6 (C = O).

MS (EI) m/z 268 [M]+, 250, 235, 225, 218, 207, 199, 191, 181 167, 81, 69 (base).

HR-MS (EI) Found m/z 268.1679 [M]+, Calcd for C₁₅H₂₀O₅N 296.1498.

Compound 7

Oil.

FTIR: 1760, 1730 cm⁻¹.

¹H NMR (600 MHz, CDCl₃) δ 1.59 (3H, br s), 1.63 (3H, br s), 1.67 (3H, br s), 1.98–2.08 (4H, m), 2.38 (3H, s), 3.05–3.12 (2H, m), 3.87 (3H, s), 5.01–5.04 (1H, m), 5.13–5.16 (1H, m).

¹³C NMR (150 MHz, CDCl₃) δ 16.1 (CH₃), 17.7 (CH₃), 25.6 (CH₃), 26.3 (CH₂), 27.1 (CH₃), 32.7 (CH₂), 39.8 (CH₂), 53.9 (CH₃), 100.9 (C), 114.7 (CH), 123.6 (CH), 131.8 (C), 142.2 (C), 163.7 (C = O), 194.3 (C = O).

MS (CI) m/z 296 [M + H-2]⁺, 252, 219, 186, 167, 137, 129, 69 (base).

HR-MS (CI) Found m/z 296.1471 [M + H-2]⁺, Calcd for C₁₅H₂₂O₄N 296.1498.

Compound 8

Oil.

FTIR: 1750, 1560 cm⁻¹.

¹H NMR (600 MHz, CDCl₃) δ 1.59 (3H, br s), 1.65 (3H, br s), 1.67 (3H, br s), 1.98–2.01 (2H, m), 2.04–2.06 (2H, m), 2.84 (1H, dt, J = 14.5, 5.6 Hz), 3.02 (1H, dt, J = 14.5, 9.2 Hz), 3.83 (3H, s), 5.02–5.03 (1H, m), 5.04–5.05 (1H, m), 5.08 (1H, dd, J = 9.2, 5.6 Hz).

¹³C NMR (150 MHz, CDCl₃) δ 16.1 (CH₃), 17.6 (CH₃), 25.6 (CH₃), 26.3 (CH₂), 29.2 (CH₂), 39.6 (CH₂), 53.5 (CH₃), 87.7 (CH), 115.6 (CH), 123.6 (CH), 131.8 (C), 141.7 (C), 164.8 (C = O).

MS (CI) m/z 254 [M + H-2]⁺, 238, 208, 207, 141, 137, 81, 69 (base).

HR-MS (CI) Found m/z 254.1383 [M + H-2]⁺, Calcd for C₁₃H₁₂O₄N 254.1392.

Oxidation of compound 1 using Mn(OAc)₃: To a stirred solution of compound 1 (164.0 mg, 0.65 mmol) in MeCN (5.2 mL), Mn(OAc)₃ (702.4 mg, 2.62 mmol) in one portion at rt and the mixture was stirred for 24 h. The mixture was cooled to 0 °C and water was added. The mixture was extracted with ether and the organic layer was washed with brine. After drying (MgSO₄), the solvent was evaporated in vacuo to afford a residue. The residue was separated by silica-gel column chromatography to afford compounds 2 (8.0 mg, 0.03 mmol, 5%), 9 (12.4 mg, 0.05 mmol, 8%), and 10 (12.6 mg, 0.05 mmol, 8%), respectively.

Compound 9

Oil.

FTIR: 1750, 1720 cm⁻¹.

¹H NMR (600 MHz, CDCl₃) δ 1.42 (1H, dddd, J = 13.5, 10.2, 4.9, 4.1 Hz), 1.77 (3H, br s), 1.83 (1H, dddd, J = 13.5, 6.6, 5.5, 4.0 Hz), 2.10–2.16 (2H, m), 2.25–2.37 (4H, m), 2.96 (1H, br, J = 5.2 Hz), 3.50 (1H, br, j = 5.2 Hz), 3.63 (3H, s), 4.72 (1H, br s), 4.86 (1H, br s), 4.91 (2H, m).

¹³C NMR (150 MHz, CDCl₃) δ 22.8 (CH₂), 23.6 (CH₃), 27.7 (CH₂), 29.8 (CH₂), 35.0 (CH₂), 43.5 (CH), 45.6 (CH), 52.3 (CH₂), 66.8 (C), 110.0 (CH₂), 113.5 (CH₂), 145.2 (C), 145.4 (C), 169.4 (C), 211.4 (C).

MS (CI) m/z 248 [M]+, 216 (base), 188, 161, 147, 91.

HRMS (CI) Found m/z 248.1411 [M]+, Calcd for C₁₅H₂₀O₃ 248.1412.

Compound 10

Oil.

FTIR: 1750, 1715 cm⁻¹.

¹H NMR (600 MHz, CDCl₃) δ 0.81, 3H, s), 0.87 (3H, s), 0.90 (3H, s), 1.18 (1H, qj, J = 7.2 Hz), 1.39 (2H, t, J = 7.2 Hz), 1.68–1.74 (1H, m), 1.81–1.86 (1H, m), 2.16 (1H, d, J = 14.0, 10.2 Hz), 2.41 (1H, dt, J = 19.5, 10.2 Hz), 2.56 (1H, dddd, J = 19.5, 10.2, 2.4 Hz), 2.57 (1H, d, J = 4.8 Hz), 3.03 (1H, br d, J = 10.2 Hz), 3.70 (3H, s).

¹³C NMR (150 MHz, CDCl₃) δ 14.4 (CH₃), 19.2 (CH₃), 19.3 (CH₃), 19.4 (CH₃), 23.2 (CH₂), 28.2 (CH₂), 41.0 (CH₂), 50.5 (C), 51.5 (C), 52.4 (CH₂), 52.5 (CH₃), 53.3 (CH), 68.1 (C), 172.1 (C), 217.8 (C).

MS (CI) m/z 250 [M]+, 219 (base), 191, 175, 141.

HRMS (CI) Found m/z 250.1571 [M]+, Calcd for C₁₅H₂₀O₃ 250.1569.

Oxidation of compound 4 using Mn(OAc)₃: To a stirred solution of compound 4 (164.0 mg, 0.65 mmol) in THF (5.2 mL), Mn(OAc)₃ (697.1 mg, 2.60 mmol) in one portion at rt and the mixture was stirred for 24 h. The mixture was cooled to 0 °C and water was added. The mixture was extracted with ether and the organic layer was washed with brine. After drying (MgSO₄), the solvent was evaporated in vacuo to afford a residue. The residue was separated by silica-gel column chromatography to afford compound 11 (110.4 mg, 0.46 mmol, 71%).

Compound 11

Oil.

FTIR: 3500, 1720 cm⁻¹.

¹H NMR (600 MHz, CDCl₃) δ 0.76 (1H, qd, J = 12.0, 7.0 Hz), 0.95 (3H, s), 1.04 (3H, s), 1.27 (3H, s), 1.35–1.40 (1H,
m), 1.52 (1H, ddd, J = 14.0, 12.0, 2.9), 1.57 (1H, dd, J = 12.0, 2.1 Hz), 1.74 (1H, ddd, J = 14.0, 9.2, 7.0 Hz), 2.18 (1H, td, J = 12.0, 7.0 Hz), 3.43 (3H, s), 6.17 (1H, br d, J = 2.1 Hz), 1.74 (1H, ddd, J = 14.0, 9.2, 7.0 Hz), 2.18 (1H, td, J = 12.0, 7.0 Hz), 3.43 (3H, s), 6.17 (1H, br d, J = 2.1 Hz).

$^1$C NMR (150 MHz, C6D6) δ 19.7 (CH3), 23.4 (CH2), 26.8 (CH3), 28.3 (CH3), 40.7 (CH2), 47.4 (CH), 47.7 (CH), 51.3 (CH3), 76.6 (C), 79.9 (C), 106.5 (CH), 146.0 (C), 163.7 (C).

MS (Cl) m/z 240 [M$^+$], 223 (base), 205, 163, 121.

HRMS (Cl) Found m/z 240.1391 [M$^+$], Calcd for C13H20O4 $^+$, 240.1362.

Acknowledgments
We thank Dr. Yasuko Okamoto, Tokushima Bunri University, for the measurement of MS spectra.

Author Contributions
Project administration and supervision, MS and MT; Reaction, isolation of compounds, and structure analysis, MS, YY, and YN; X-ray analysis, ST; Writing, MS and MT.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval
Not applicable, because this article does not contain any studies with human or animal subjects.

Funding
The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article. This work was supported by the Tokushima Bunri University.

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Informed Consent
Not applicable, because this article does not contain any studies with human or animal subjects.

Trial Registration
Not applicable, because this article does not contain any clinical trials.

Supplemental Material
Supplemental material for this article is available online.

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