HETEROCYCLES, Vol. 103, No.1, 2021, pp. 311 - 321. © 2021 The Japan Institute of Heterocyclic Chemistry
Received, 19th May, 2020, Accepted, 3rd July, 2020, Published online, 17th July, 2020
DOI: 10.3987/COM-20-S(K)15

# SELECTIVE REDUCTION AND DIHYDROXYLATION OF α,β-UNSATURATED ESTERS IN THE PRESENCE OF ENALS: ONE-POT SYNTHESIS OF A 2,5-DISUBSTITUTED TETRAHYDROFURAN†

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**Abstract** – Two-way discriminative conversion, reduction and dihydroxylation of α,β-unsaturated esters were achieved in the presence of enals using two phosphonium salts as *in situ* protecting groups. Furthermore, a pot-economical one-pot synthesis of a tetrahydrofuran derivative was achieved.

## INTRODUCTION

*In situ* protection methods are powerful tools in the chemoselective conversion of functional groups. We can convert the less reactive functions in the presence of more reactive ones in a one-pot reaction.[1,2] In our effort to develop practical *in situ* protection methods using phosphonium salts as protecting groups, we have developed the reversal and control of the reactivities of many carbonyl groups.[3,4] Among those, the control of the reactivity of two α,β-unsaturated carbonyl groups, enones and α,β-unsaturated esters, are of interest because bidirectional discriminative transformations of α,β-unsaturated esters, conversion of the ester moiety and electrophilic addition to the olefin moiety, are possible in the presence of enone.[3e] This time, we applied our *in situ* protection method to the combination of enals (α,β-unsaturated aldehydes) and α,β-unsaturated esters.

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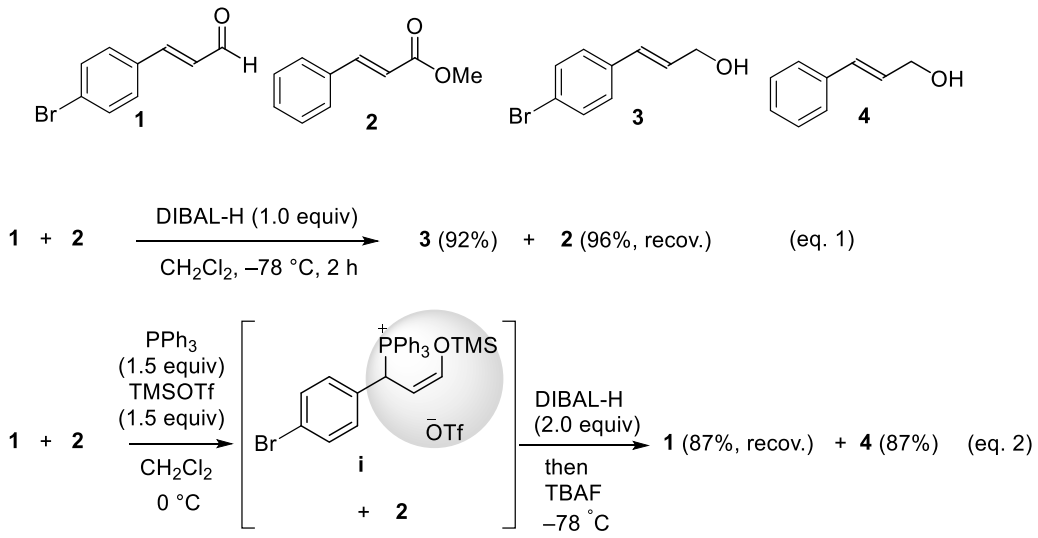
†This paper is dedicated to Professor Yasuyuki Kita on the occasion of his 77th birthday.

## RESULT AND DISCUSSION

First, the relative reactivities of enal and α,β-unsaturated ester substrates were investigated (Scheme 1, eq. 1). That is, 1 equiv of DIBAL-H (the same mole as **1**) was added to a 1:1 mixture of enal **1** and α,β-unsaturated ester **2** in $CH_2Cl_2$ at –78 °C. As a result, ally alcohol **3** was obtained from **1** in 92% yield along with 96% of recovered **2**. That is, it was found that the reactivity of the enal toward reduction was much higher than that of the α,β-unsaturated ester. Therefore, the selective conversion of an α,β-unsaturated ester in the presence of an enal usually requires a three-step sequence: 1) protection of the enal, 2) reduction of the α,β-unsaturated ester, and 3) rebirth of the enal by deprotection.[5]

Next, an *in situ* protection method was applied to the selective conversion of an α,β-unsaturated ester in the presence of an enal to achieve pot- and step-economy reactions. That is, $PPh_3$ and TMSOTf (1.5 equiv of each to enal) were added to a 1:1 mixture of enal **1** and α,β-unsaturated ester **2** in $CH_2Cl_2$ followed by DIBAL-H reduction and TBAF treatment afforded 87% of allyl alcohol **4** from α,β-unsaturated ester **2** and the recovered enal **1** (87%; Scheme 1, eq. 2). This result indicated that enal **1** was selectively protected *in situ* as a phosphonium silyl enol ether **i**[6] and their relative reactivities were completely reversed.

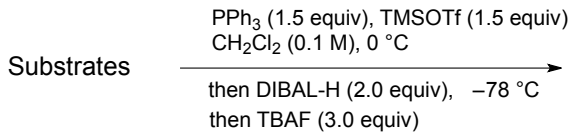


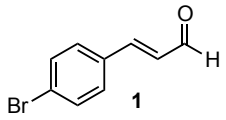
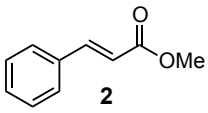
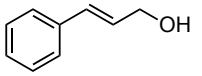
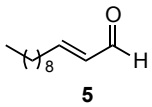
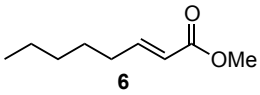
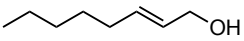
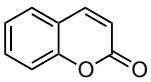
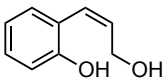

Scheme 1. Reduction of a 1:1 mixture of enal **1** and α,β-unsaturated ester **2** with DIBAL-H in $CH_2Cl_2$: Without (eq. 1) and with (eq. 2) *in situ* protection

Table 1 shows the results of selective reduction of α,β-unsaturated esters in the presence of enal. The selective *in situ* protection was effective both for enal **5** with terminal aliphatic chain and enal **2** with a terminal aromatic ring. As a result, α,β-unsaturated esters with either an aromatic ring (**2**) or an aliphatic side chain (**6**) at the β-position were selectively converted in the presence of enal, and the corresponding

allyl alcohols **4** and **7** were obtained in high yields (entries 1–4). In addition, a cyclic unsaturated ester, coumarin **8**, was selectively reduced, yielding diol **9** in 90% yield (entry 5).

Table 1. Selective reduction of α,β-unsaturated ester in the presence of enal

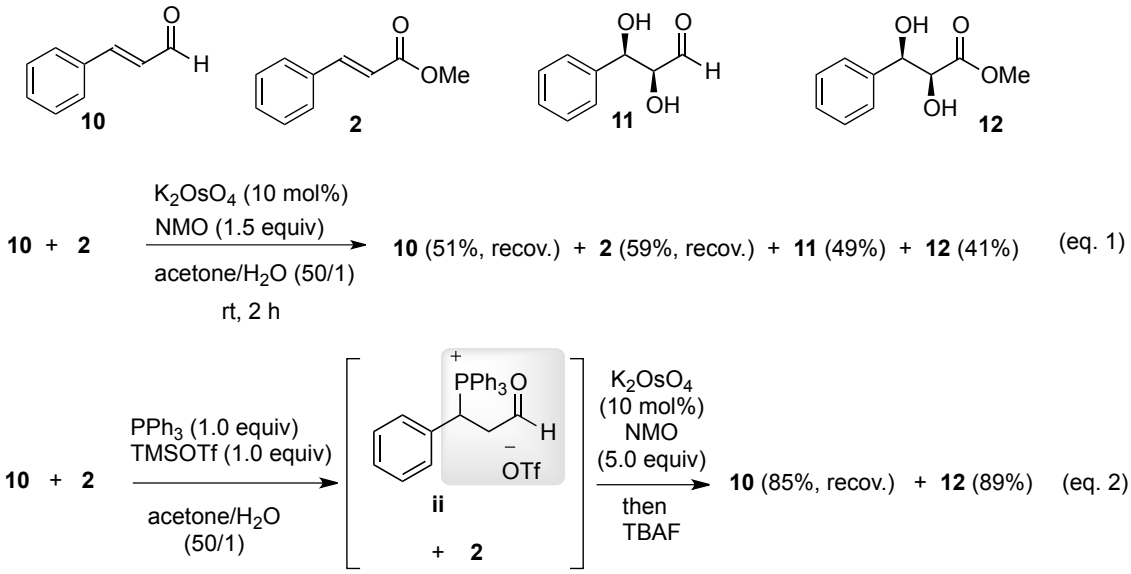



| Entry | Substrates | | Products | |
|---|---|---|---|---|
| | enal | α,β-unsaturated ester | recovered enal | product from α,β-unsaturated ester |
| 1[a] |  **1** |  **2** | **1** (87%) |  **4** (87%) |
| 2 |  **5** | **2** | **5** (88%) | **4** (91%) |
| 3 | **1** |  **6** | **1** (89%) |  **7** (85%) |
| 4 | **5** | **6** | **5** (73%) | **7** (80%) |
| 5 | **1** |  **8** | **1** (88%) |  **9** (90%) |

[a] Entry 1 is the same as Scheme 1, eq. 2.

Next, selective dihydroxylation of the olefin moieties of enal and α,β-unsaturated ester was examined. Such a conversion between enone and α,β-unsaturated ester together has been achieved.[3e] However, in those cases, the reactivity of both compounds toward reduction was very similar. On the other hand, the reductions of enal and α,β-unsaturated ester are completely different from each other: reduction of the enal proceeds much faster than that of the α,β-unsaturated ester. Thus we first investigated the relative reactivities of enals and α,β-unsaturated esters in the dihydroxylation of the olefin moieties (Scheme 2). That is, a 1:1 mixture of enal **10** and α,β-unsaturated ester **2** in acetone/$H_2O$ (50:1) was dihydroxylated (10 mol% of $K_2OsO_4$, 1.5 equiv of NMO, 2 h) to afford a mixture of recovered **10** (51%), recovered **2** (59%) and dihydroxy esters **11** (49%) from **10** and **12** (41%) from **2** (Scheme 2, eq. 1). This result indicated that the reactivities of the two olefins toward dihydroxylation was similar. However, when $PPh_3$ and TMSOTf (1.0 equiv of each to enal) were added to a 1:1 mixture of enal **10** and α,β-unsaturated ester

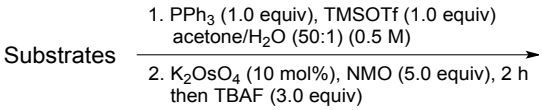
**2** in acetone/$H_2O$ (50:1) before dihydroxylation, dihydroxy ester **12** was obtained from α,β-unsaturated ester **2** in 89% yield along with the recovered enal **10** (85%; Scheme 2, eq. 2). This result indicated that enal **10** was selectively protected *in situ* as phosphonium aldehyde **ii**[6] and the reactivities of the two olefins were completely controlled.

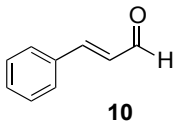
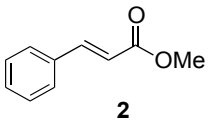
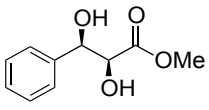
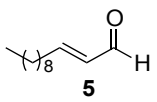
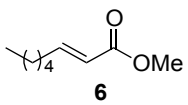
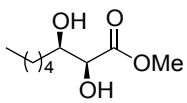



Scheme 2. Dihydroxylation of the 1:1 mixture of enal **10** and α,β-unsaturated ester **2** in acetone/$H_2O$ (50:1): without (eq. 1) and with (eq. 2) *in situ* protection

Table 2 shows the generality of the substrates for selective dihydroxylation. This *in situ* protection method

Table 2. Selective dihydroxylation of α,β-unsaturated esters in the presence of enals

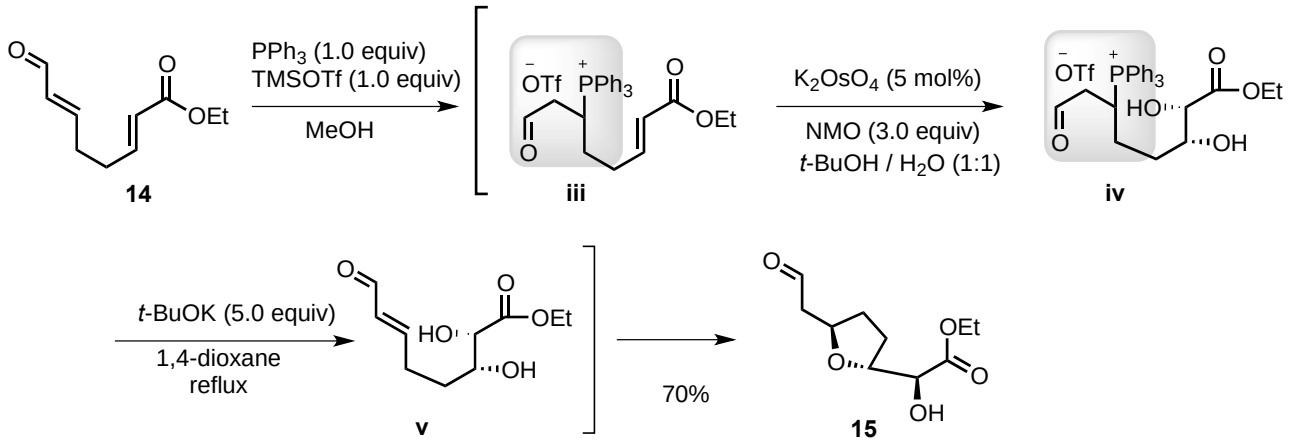



| Entry | Substrates | | Products | |
|---|---|---|---|---|
| | enal | α,β-unsaturated ester | recovered enal | α,β-dihydroxy ester |
| 1[a] |  **10** |  **2** | **10** (85%) |  **12** (89%) |
| 2 |  **5** |  **6** | **5** (84%) |  **13** (83%) |

[a] Entry 1 is the same as Scheme 2, eq. 2.

was effective not only for enal **10** with a β-aromatic ring but also for enal **5** with a β-aliphatic chain, and the corresponding dihydroxy esters **12** and **13** were obtained in high yields.

This selective dihydroxylation was applied to a pot-economical one-pot synthesis of *trans*-2,5-disubsituted tetrahydrofuranyl compound **15** (Scheme 3). That is, compound **14** containing enal and α,β-unsaturated ester units in the same molecule was first converted to β-phosphonium aldehyde **iii**, which was dihydroxylated to obtain dihydroxy ester **iv**. Alkali treatment of **iv** under reflux conditions gave the enal dihydroxyl ester **v**, which was spontaneously cyclized by the oxa-Michael reaction to yield **15**[7] in one-pot with 70% yield.




Scheme 3. One-pot synthesis of *trans*-2,5-disubsituted tetrahydrofuranyl compound **15**

In conclusion, we have succeeded in bidirectional discriminative conversions, reduction and dihydroxylation, of α,β-unsaturated esters in the presence of enals. Complete reversal of the reactivities toward reduction was achieved, and control of the reactivity was achieved in dihydroxylation. In addition, a pot-economical one-pot synthesis of a tetrahydrofuran derivative was achieved by using this *in situ* protective dihydroxylation reaction.

## EXPERIMENTAL

### General information

All reagents were purchased from commercial sources. Reactions were performed under a nitrogen atmosphere using purchased anhydrous solvent. All reactions were monitored by thin-layer chromatography using Merck silica gel 60 F254. The products were purified by column chromatography over silica gel Kieselgel 60 (70-230 mesh ASTM) purchased from Merck or Silica Gel 60N (40-50 μm, spherical neutral) purchased from Kanto Chemical. $^{1}$H-NMR and $^{13}$C-NMR spectra were recorded at 25 $^{o}$C on a JEOL JNM-AL300 (at 300 MHz and 75 MHz, respectively), a JEOL JNM-ECS 400 (at 400 MHz

and 100 MHz, respectively) or a JEOL JNM-LA 500 (at 500 MHz and 125 MHz, respectively), and the chemical shifts are reported relative to internal TMS ($^1$H, $\delta$ = 0.00) and $CDCl_3$ ($^{13}$C, $\delta$ = 77.0). Data for $^1$H NMR spectra are reported as follows: chemical shift (d ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra (KBr) were recorded by an SHIMADZU FTIR-8400 or SHIMADZU IRAffinity-1, and are reported in frequency of absorption ($cm^{-1}$). High-resolution mass spectra (MALDI-TOF) were performed by the Elemental Analysis Section of Graduate School of Pharmaceutical Science in Osaka University.

The substrates **1**, **2**, **5**, **6**, **7**, **8**, **10**, **11** are commercially available.

**Experimental details in Scheme 1, eq. 1.**

A solution of **1** (210.0 mg, 1.00 mmol) and **2** (162.1 mg, 1.00 mmol) in $CH_2Cl_2$ (10 mL, 0.1 M) was cooled to –78 °C. DIBAL-H (1.0 M toluene solution, 1.0 mL, 1.0 equiv) was added dropwise to the reaction mixture, and the reaction mixture was stirred for 2 h. After the reaction mixture was quenched with 1*N* HCl, the solvent volume was removed under reduced pressure. The residue left behind was extracted with ethyl acetate (AcOEt) (3 x 30 mL). The organic layer was separated, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/AcOEt = 6/1) to afford the recovered **2** (155.6 mg, 0.96 mmol, 96%) and the reduced product **3** (195.0 mg, 0.92 mmol, 92%), **(*E*)-3-(4-bromophenyl)prop-2-en-1-ol** (**3**)[8]**:** $^1$H-NMR (300 MHz, $CDCl_3$) δ: 7.44 (2H, d, *J* = 8.6 Hz), 7.24 (2H, d, *J* = 8.6 Hz ), 6.56 (1H, d, *J* = 15.9 Hz), 6.35 (1H, dt, *J* = 15.9, 5.6 Hz), 4.32 (2H, d, *J* = 5.6 Hz), 1.59 (1H, brs, OH).

**Experimental details for Scheme 1, eq. 2 and Table 1.**

General procedure for the selective reduction of α,β-unsaturated ester in the presence of enal: To a solution of enal (1.00 mmol, 1.0 equiv), unsaturated ester (1.00 mmol, 1.0 equiv) and $PPh_3$ (393.4 mg, 1.50 mmol, 1.5 equiv) in $CH_2Cl_2$ (10 mL) was added dropwise TMSOTf (272 μL, 1.50 mmol, 1.5 equiv) at 0 °C and the starting enal was consumed.[9] After being stirred for 30 min at 0 °C, the reaction mixture was then cooled to –78 °C. DIBAL-H (2.0 mL, 1.0 M *n*-hexane solution, 2.0 equiv) was added to the reaction mixture. After the starting α,β-unsaturated ester was consumed, suspension of TBAF (1.0 M, 3.0 mL, 3.0 equiv) was added, then the resulting solution was stirred for 30 min. After adding $H_2O$, the mixture was extracted with $CH_2Cl_2$. The extract was dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography to afford the desired products.

**Table 1, Entry 1:** According to the general procedure, **1** (210.0 mg, 1.00 mmol), **2** (162.1 mg, 1.00 mmol), $PPh_3$ (393.4 mg, 1.50 mmol, 1.5 equiv), TMSOTf (272 μL, 1.50 mmol, 1.5 equiv), DIBAL-H (2.0 mL, 1.0 M *n*-hexane solution, 2.0 equiv), and suspension of TBAF (1.0 M, 3.0 mL, 3 equiv) gave recovered **1** (182.7 mg, 0.87 mmol, 87%) and **4** (116.6 mg, 0.87 mmol, 87%) as a colorless oil after purification by flash column chromatography (*n*-hexane/AcOEt = 8/1).

**Table 1, Entry 2:** According to the general procedure, **5** (182.2 mg, 1.00 mmol), **2** (162.1 mg, 1.00 mmol), $PPh_3$ (393.4 mg, 1.50 mmol, 1.5 equiv), TMSOTf (272 μL, 1.50 mmol, 1.5 equiv), DIBAL-H (2.0 mL, 1.0 M *n*-hexane solution, 2.0 equiv), and suspension of TBAF (1.0 M, 3.0 mL, 3.0 equiv) gave recovered **5** (160.3 mg, 0.88 mmol, 88%) and **4** (122.0 mg, 0.91 mmol, 91%) as a colorless oil after purification by flash column chromatography (*n*-hexane/AcOEt = 20/1).

**Table 1, Entry 3:** According to the general procedure, **1** (210.0 mg, 1.00 mmol), **6** (156.1 mg, 1.00 mmol), $PPh_3$ (393.4 mg, 1.50 mmol, 1.5 equiv), TMSOTf (272 μL, 1.50 mmol, 1.5 equiv), DIBAL-H (2.0 mL, 1.0 M *n*-hexane solution, 2.0 equiv), and suspension of TBAF (1.0 M, 3.0 mL, 3.0 equiv) gave recovered **1** (186.9 mg, 0.89 mmol, 89%) and **7** (108.9 mg, 0.85 mmol, 85%) as a colorless oil after purification by flash column chromatography (*n*-hexane/AcOEt = 10/1).

**Table 1, Entry 4:** According to the general procedure, **5** (182.2 mg, 1.00 mmol), **6** (156.1 mg, 1.00 mmol), $PPh_3$ (393.4 mg, 1.50 mmol, 1.5 equiv), TMSOTf (272 μL, 1.50 mmol, 1.5 equiv), DIBAL-H (2.0 mL, 1.0 M *n*-hexane solution, 2.0 equiv), and suspension of TBAF (1.0 M, 3.0 mL, 3.0 equiv) gave recovered **5** (133.0 mg, 0.73 mmol, 73%) and **7** (102.5 mg, 0.80 mmol, 80%) as a colorless oil after purification by flash column chromatography (*n*-hexane/AcOEt = 10/1).

**Table 1, Entry 5:** According to the general procedure, **1** (210.0 mg, 1.00 mmol), **8** (146.0 mg, 1.00 mmol), $PPh_3$ (393.4 mg, 1.50 mmol, 1.5 equiv), TMSOTf (272 μL, 1.50 mmol, 1.5 equiv), DIBAL-H (2.0 mL, 1.0 M *n*-hexane solution, 2.0 equiv), and suspension of TBAF (1.0 M, 3.0 mL, 3.0 equiv) gave recovered **1** (184.8 mg, 0.88 mmol, 88%) and **9** (135.1 mg, 0.90 mmol, 90%) as a colorless oil after purification by flash column chromatography (*n*-hexane/AcOEt = 3/1).

**(*E*)-3-Phenylprop-2-en-1-ol (4)**[3e]**:** $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.38 (2H, d, $J$ = 7.3 Hz), 7.31 (2H, t, $J$ = 7.3 Hz), 7.24 (1H, t, $J$ = 7.3 Hz), 6.60 (1H, d, $J$ = 16.0 Hz), 6.35 (1H, dt, $J$ = 16.0, 5.5 Hz), 4.30 (2H, dd, $J$ = 5.5, 1.4 Hz).

**(*Z*)-2-(3-Hydroxyprop-1-en-1-yl)phenol (9)**[10]**:** $^1$H-NMR (500 MHz, $CDCl_3$) δ: 7.07-6.75 (4H, m), 6.51 (1H, d, $J$ = 8.0 Hz), 5.74-5.68 (1H, m), 4.15-4.12 (2H, m).

**Experimental detail in Scheme 2, eq. 1**

To a solution of **10** (132 mg, 1.0 mmol) and **2** (162 mg, 1.0 mmol) in acetone/$H_2O$ (50:1) (10.0 mL, 0.1 M) were added $K_2OsO_4/2H_2O$ (36.8 mg, 10 mol%) and NMO (58.6 mg, 1.5 mmol, 1.5 equiv). The

reaction mixture was stirred at room temperature for 2 h under a $N_2$ balloon. $Na_2SO_3$ was added, then the resulting solution was stirred for 30 min. After filtration throug celite pad, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane /AcOEt =1/3) to afford the recovered **10** (8.3 mg, 0.51 mmol, 51%) and **2** (9.6 mg, 0.59 mmol, 59%) and the oxidized products **11** (8.8 mg, 0.49 mmol, 49%) and **12** (8.0 mg, 0.41 mmol, 41%) as a colorless oil.

**Experimental details for Scheme 2, eq. 2 and Table 2.**

To a solution of enal (1.0 mmol), α,β-unsaturated ester (1.0 mmol) and $PPh_3$ (262 mg, 1.0 mmol, 1.0 equiv) in acetone, (10 mL, 0.1 M) was added dropwise TMSOTf (181 μL, 1.0 mmol, 1.0 equiv) at 0 °C. After being stirred for 30 min at 0 °C and the starting enal was consumed,[9] $H_2O$ (10 μL), $K_2OsO_4$ (10 mol%), and NMO (0.5 mmol, 5.0 equiv) were added to the mixture. After the starting α,β-unsaturated ester was consumed, $Na_2SO_3$ (0.1mmol, 1.0 equiv) and TBAF (3.0 mL of 1.0 M THF solution, 3.0 mmol) were added to the mixture, then the resulting solution was stirred for 30 min. After adding $H_2O$, the mixture was extracted with AcOEt. The extract was dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography to afford the recovered enal and dihydrated ester.

**Table 2, Entry 1:** According to the general procedure, **10** (132 mg, 0.10 mmol), **2** (162 mg, 0.10 mmol), $PPh_3$ (262 mg, 0.10 mmol), TMSOTf (181 $\mu$L, 0.10 mmol), $K_2OsO_4 \cdot 2H_2O$ (37 mg, 10 mol%), NMO (590 mg, 0.5 mmol, 5.0 equiv), $H_2O$ (0.1 mL), TBAF (1.0 M, 3.0 mL, 3.0 equiv) and $Na_2SO_3$ (104 mg, 1.0 mmol, 1.0 equiv) gave recovered **10** (112 mg, 0.85 mmol, 85%), **12** (175 mg, 0.89 mmol, 89%) as a colorless oil after purification by flash column chromatography (*n*-hexane /AcOEt = 1/2).

**Table 2, Entry 2:** According to the general procedure, **5** (182 mg, 0.10 mmol), **6** (156 mg, 0.10 mmol), $PPh_3$ (262 mg, 0.10 mmol), TMSOTf (181 $\mu$L, 0.10 mmol), $K_2OsO_4 \cdot 2H_2O$ (37 mg, 10 mol%), NMO (590 mg, 0.5 mmol, 5.0 equiv), $H_2O$ (0.1 mL), TBAF (1.0 M, 3.0 mL, 3.0 equiv) and $Na_2SO_3$ (104 mg, 1.0 mmol, 1.0 equiv) gave recovered **5** (131 mg, 0.84 mmol, 84%), **13** (158 mg, 0.83 mmol, 83%) as a colorless oil after purification by flash column chromatography (*n*-hexane/AcOEt = 2/3).

**Methyl 2,3-dihydroxy-3-phenylpropanoate (12)**[3e]**: $^1$H-NMR** (300 MHz, $CDCl_3$) δ: 7.42-7.32 (5H, m), 3.82 (3H, s), 3.35 (1H, d, *J* = 7.5 Hz), 3.18 (1H, d, *J* = 7.5 Hz), 3.13 (1H, brs), 2.77 (1H, brs).

**Methyl 2,3-dihydroxyoctanoate (13)**[3e]**:** $^1$H-NMR (500 MHz, $CDCl_3$) δ: 4.18-4.09 (1H, m), 3.90-3.82 (1H, m), 3.81 (s, 3H), 3.48 (1H, brs), 2.56 (1H, brs), 1.68-1.58 (2H, m), 1.47-1.44 (m, 1H), 1.41-1.25 (m, 5H), 0.87 (3H, t, *J* = 6.8 Hz) .

**Ethyl (2*E*,6*E*)-8-oxoocta-2,6-dienoate (14)**

To a solution of succinaldehyde (13.0 g, 151 mmol) in $CH_2Cl_2$ (302 mL, 0.5 M) was slowly added ethyl

(triphenylphosphoranylidene)acetate (63.1 g, 181 mmol, 1.2 equiv) at rt. After being stirred 5 h at rt, the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/AcOEt = 7/1) to afford **ethyl (*E*)-6-oxohex-2-enoate** (**16**)[11] (20.3 g, 130 mmol, 86%) as a colorless oil. **16**: $^1$H-NMR (500 MHz, $CDCl_3$) $\delta$: 9.81 (1H, s), 6.94 (1H, dt, $J$ = 16.1, 6.3 Hz), 5.85 (1H, d, $J$ = 16.1 Hz), 4.18 (2H, q, $J$ = 7.5 Hz), 2.65 (2H, t, $J$ = 7.5 Hz), 2.53 (2H, dt, $J$ = 6.3, 7.5 Hz) 1.29 (3H, t, $J$ = 7.5 Hz). To a solution of **16** (14.0 g, 89.7 mmol) in toluene (90 mL, 1.0 M) was added (triphenylphosphoranylidene)acetaldehyde (32.8 g, 108 mmol, 1.2 equiv) at rt. After being stirred overnight at 80 °C, the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/AcOEt = 5/1) to afford **14** (15.2 g, 83.4 mmol, 93%) as a colorless oil. **14**: IR (neat) 1782, 1702 cm$^{-1}$. $^1$H-NMR (500 MHz, $CDCl_3$) $\delta$: 9.52 (1H, d, $J$ = 4.0 Hz), 6.95 (1H, dt, $J$ = 16.3, 6.3 Hz), 6.84 (1H, dt, $J$ = 16.3, 6.3 Hz), 6.16 (1H, d, $J$ = 16.3 Hz), 5.85 (1H, m), 4.19 (2H, q, $J$ = 7.4 Hz), 2.54 (2H, m), 2.45 (2H, m), 1.28 (3H, t, $J$ = 7.4 Hz). $^{13}$C-NMR (125 MHz, $CDCl_3$) $\delta$: 193.6, 166.1, 156.0, 146.2, 133.4, 122.5, 60.2, 30.7, 30.0, 14.1. HRMS (MALDI-TOF) Calcd for $C_{10}H_{14}NaO_3$ $[M+Na]^+$: 208.0835, found 208.0831.

**Ethyl 2-hydroxy-2-[5-(2-oxoethyl)tetrahydrofuran-2-yl]acetate** (**15**)

To a solution of **14** (100 mg, 0.65 mmol) and $PPh_3$ (170 mg, 0.65 mmol, 1.0 equiv) in MeOH (2.6 mL, 0.25 M) was added dropwise TMSOTf (0.12 mL, 0.65 mmol, 1.0 equiv) at 0 °C. After the starting material was consumed (TLC analysis was conducted after quenching a small amount of the reaction mixture with a drop of TBAF (1.0 M in THF)), the solvent was evapolated. *t*-BuOH/$H_2O$/ (1:1), (2.6 mL, 0.25 M), $K_2OsO_4$ (12 mg, 5 mol%), and NMO (228 mg, 1.95 mmol, 3.0 equiv) were added to the mixture at 0 °C. After the material was consumed (TLC analysis was conducted after quenching a small amount of the reaction mixture with a drop of TBAF (1.0 M in THF)), the solvent was evapolated, and 1,4-dioxane (6.5 mL, 0.1 M) and *t*-BuOK (0.37 g, 3.3 mmol, 5.0 equiv) were added to the residue at rt, and the resulting solution was stirred under reflux. After the material was consumed, the reaction was quenched by sat. $NH_4Cl$ aq. and the mixture was extracted with AcOEt (50 mL × 3). The extract was dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane : AcOEt = 3 : 1 ) to afford the desired product **15** (99 mg, 0.46 mmol, 70%) as a colorless oil. **15**: $^1$H-NMR (500 MHz, $C_6D_6$) $\delta$: 9.41 (1H, t, $J$ = 2.5 Hz), 4.33 (1H, m) 4.22 (1H, m), 4.01 (1H, d, $J$ = 4.5 Hz), 3 .98 (2H, q, $J$ = 7.3 Hz), 2.21-2.16 (1H, ddd, $J$ = 15.0, 10.0, 5.0 Hz), 1.96-1.91 (1H, ddd, $J$ = 15.0, 10.0, 5.0 Hz), 1.81-1.73 (2H, m), 1.63-1.61 (2H, m), 0.96 (3H, t, $J$ = 7.3 Hz ).$^{13}$C-NMR (125 MHz, $CDCl_3$) $\delta$: 199.6, 171.6, 80.8, 75.4, 61.0, 49.8, 32.6, 27.7, 18.9, 14.6. HRMS (MALDI-TOF) Calcd for $C_{10}H_{16}NaO_5$ $[M+Na]^+$: 239.0890, found 239.0898.

## ACKNOWLEDGEMENTS

This work was supported by Grant-in-Aid for Scientific Research (C) (18K06576) from JSPS and Grant-in-Aid for JSPS Research Fellow Grant Number 18J12815.

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