SELECTIVE REDUCTION AND DIHYDROXYLATION OF
$\alpha,\beta$-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
$\alpha,\beta$-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 $\alpha,\beta$-unsaturated carbonyl groups, enones and $\alpha,\beta$-unsaturated esters,
are of interest because bidirectional discriminative transformations of $\alpha,\beta$-unsaturated esters, conversion
of the ester moiety and electrophilic addition to the olefin moiety, are possible in the presence of enone.3c
This time, we applied our in situ protection method to the combination of enals ($\alpha,\beta$-unsaturated
aldehydes) and $\alpha,\beta$-unsaturated esters.

†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$_2$Cl$_2$ at −78 °C. As a result, allyl 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.

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$_2$Cl$_2$ 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 and their relative reactivities were completely reversed.

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

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. 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/H2O (50:1) was dihydroxylated (10 mol% of K2OsO4, 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 PPh3 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/H₂O (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 ii⁶ 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/H₂O (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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrates</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>enal</td>
<td>recovered enal</td>
</tr>
<tr>
<td></td>
<td>α,β-unsaturated ester</td>
<td></td>
</tr>
<tr>
<td>1⁻</td>
<td>10</td>
<td>10 (85%)</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>5 (84%)</td>
</tr>
</tbody>
</table>

* 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-disubstituted 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\textsuperscript{7} in one-pot with 70% yield.

Scheme 3. One-pot synthesis of trans-2,5-disubstituted 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 °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\(_2\)Cl\(_2\) (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 1N HCl, the solvent volume was removed under reduced pressure. The residue left behind was extracted with ethyl acetate (Ac OEt) (3 x 30 mL). The organic layer was separated, dried over Na\(_2\)SO\(_4\), 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\(_3\)) \(\delta\): 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 \(\alpha,\beta\)-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\(_2\)Cl\(_2\) (10 mL) was added dropwise TMSOTf (272 \(\mu\)L, 1.50 mmol, 1.5 equiv) at 0 °C and the starting enal was consumed.\(^{2}\) 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 \(\alpha,\beta\)-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\(_2\)O, the mixture was extracted with CH\(_2\)Cl\(_2\). The extract was dried over Na\(_2\)SO\(_4\), 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), PPh3 (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), PPh3 (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 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), PPh3 (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 (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), PPh3 (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 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), PPh3 (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 (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): 1H-NMR (400 MHz, CDCl3) 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): 1H-NMR (500 MHz, CDCl3) 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 aceton/H2O (50:1) (10.0 mL, 0.1 M) were added K2OsO4/2H2O (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 N₂ balloon. Na₂SO₃ was added, then the resulting solution was stirred for 30 min. After filtration through 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 PPh₃ (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, H₂O (10 μL), K₂OsO₄ (10 mol%), and NMO (0.5 mmol, 5.0 equiv) were added to the mixture. After the starting α,β-unsaturated ester was consumed, Na₂SO₃ (0.1 mmol, 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 H₂O, the mixture was extracted with AcOEt. The extract was dried over Na₂SO₄, 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), PPh₃ (262 mg, 0.10 mmol), TMSOTf (181 μL, 0.10 mmol), K₂OsO₄ • 2H₂O (37 mg, 10 mol%), NMO (590 mg, 0.5 mmol, 5.0 equiv), H₂O (0.1 mL), TBAF (1.0 M, 3.0 mL, 3.0 equiv) and Na₂SO₃ (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), PPh₃ (262 mg, 0.10 mmol), TMSOTf (181 μL, 0.10 mmol), K₂OsO₄ • 2H₂O (37 mg, 10 mol%), NMO (590 mg, 0.5 mmol, 5.0 equiv), H₂O (0.1 mL), TBAF (1.0 M, 3.0 mL, 3.0 equiv) and Na₂SO₃ (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): ¹H-NMR (300 MHz, CDCl₃) 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): ¹H-NMR (500 MHz, CDCl₃) 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 (2E,6E)-8-oxooct-2,6-dienoate (14)

To a solution of succinaldehyde (13.0 g, 151 mmol) in CH₂Cl₂ (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) (20.3 g, 130 mmol, 86%) as a colorless oil.  

16: \[ \text{H-NMR} (500 MHz, CDCl}_3 \] \( \delta \): 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\(^{-1}\). \[ \text{H-NMR} (500 MHz, CDCl}_3 \] \( \delta \): 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). 13C-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 evaporated.\( t\)-BuOH/H\(_2\)O/ (1:1), (2.6 mL, 0.25 M), \( K_2\)OsO\(_4\) (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 evaporated, 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\(_4\)Cl aq. and the mixture was extracted with AcOEt (50 mL \( \times 3 \)). The extract was dried over Na\(_2\)SO\(_4\), 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: \[ \text{H-NMR} (500 MHz, C\(_6\)D\(_6\) \] \( \delta \): 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 ). 13C-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
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REFERENCES AND NOTES


5. For example, aldol reaction of α,β-unsaturated ester was performed after the protection of enal. See: R. T. Larson, R. P. Pemberton, J. M. Franke, D. J. Tantillo, and J. T. Regan, *J. Am. Chem. Soc.*, 2015, **137**, 11197.

6. We have already established the formation of two-type phosphonium salts, phosphonium silyl enol...
ether in aprotic solvent such as CH₂Cl₂ and 3-oxophosphonium salt in protic solvent such as MeOH or acetone/H₂O. See ref. 3e.

7. Stereochemistry of compound 15 was deduced to be 2,5-trans, because the relative 2,5-disubstituted THF derivatives in ref. 3e showed 2,5-trans stereochemistry.


9. High polar compound appeared after disappearance of the enal on TLC. At the time, α,β-unsaturated ester remained.
