Supplementary Material (ESI) for Chemical Communications

Electronic Supporting Information

meso-Phbox-Pd(II) Catalyzed Tandem Carbonylative Cyclization of 1-Ethynyl-1-propargyl Acetate

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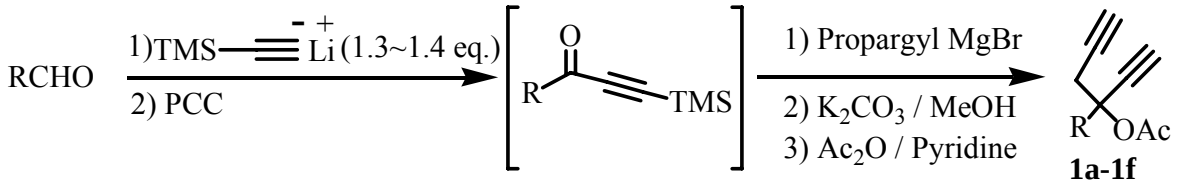
General Information.

All melting points were measured on a Yanaco MP-3S micro melting point apparatus and are uncorrected. ^{1}H, ^{13}C NMR spectra were recorded on JEOL AL 400 and JEOL Lambda 500 spectrometer spectrometers in $CDCl_3$ with Me_4Si as an internal reference. ^{13}C NMR spectra were recorded at 100 MHz. High-resolution mass spectra (HR-MS) and fast atom bombardment mass spectra (FAB MS) were obtained with JEOL GC Mate II, JMS-SX102 and JEOL JMS 600H spectrometer. IR spectra were recorded with JASCO FT/IR-300 spectrometer. All reagents were purchased from commercial sources and used without purification. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed.



R (5 steps) R (5 steps)

1a : $PhCH_2CH_2$: 74% **1d** : *c*-Hexyl : 53 %

1b : Octyl : 81% **1e** : Ph : 87%

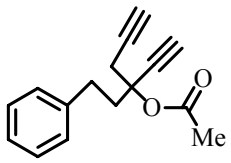
1c : Hexyl : 40%

Typical experimental procedure for the preparation of substrates 1.

To a solution of trimethylsilyl acetylene (1.41g, 14.4 mmol) in THF (20 mL) under an Ar atmosphere was added *n*-BuLi (4.8 mL of 2.6 M in hexane, 12.5 mmol) at -78 ˚C and the mixture was stirred for 0.5 h at 0 ˚C. After the solution was cooled to -78 ˚C, benzaldehyde (1.02 g, 9.6 mmol) in THF (20 mL) was added dropwise slowly. The mixture was stirred for 0.5 h and quenched with water (80 mL) and EtOAc (80 mL). The organic layer was separated, the aqueous layer was extracted with EtOAc (50 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. To a solution of the crude product in CH_2Cl_2 (30 mL) was added PCC (4.14 g, 19.2 mmol) and the mixture was stirred for 1.5 h at room temperature. The solution was passed through a Florisil column and eluted with CH_2Cl_2 to afford the crude product (1.88 g).

The crude product in THF (3 mL) was added to a solution of propargyl Grignard reagent[1] (22 mmol) in THF (20 mL) at -20 ˚C. The solution was stirred at the same temperature for 0.5 h and quenched by addition of H_2O (5 mL). The mixture was filtered on celite, and washed with EtOAc (30 mL × 3). The resulting filtrate was washed with H_2O (50 mL). The organic layer was separated, the aqueous layer was extracted with EtOAc (50 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. To a solution of the crude product in MeOH (20 mL) was added K_2CO_3 (3.58 g, 25.9 mmol) and the mixture was stirred for 0.5 h at room temperature. The mixture was diluted with water (50 mL) and EtOAc (50 mL). The organic layer was separated, the aqueous layer was extracted with EtOAc (50 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo.

To a solution of the crude product in pyridine (8 mL) and Ac_2O (4 mL) was added 4-dimethylaminopyridine (50 mg) and the mixture was stirred for 12 h at room temperature. The mixture was diluted with water (50 mL) and EtOAc (50 mL). The organic layers were separated, the aqueous layer was extracted with EtOAc (50 mL), and the combined organic layers were washed with 10% aq HCl, dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane/ethyl acetate (50:1) afforded **1e** (1.83g, 87%).



1a

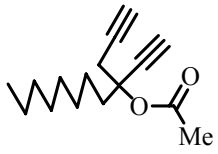
1a : Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 2.06 (3H, s), 2.09 (1H, t, *J* = 2.6 Hz), 2.20-2.27 (1H, m), 2.40-2.48 (1H, m), 2.68 (1H, s), 2.84 (2H, dd, *J* = 7.6, 9.2 Hz), 2.94 (1H, dd, *J* = 2.6, 17.0 Hz), 3.22 (1H, dd, *J* = 2.6, 17.2 Hz), 7.18-7.32 (5H, m).

^{13}C NMR (CDCl3): δ = 21.6, 29.0, 30.3, 40.2, 71.7, 75.1, 75.2, 78.0, 81.6, 126.1 (2C), 128.5 (2C), 128.5, 141.1, 162.3.

IR (neat): 3288, 1741, 1225 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{16}H_{16}O_2$: 240.1150; found 240.1145.



1b

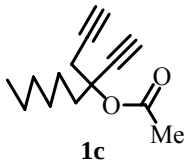
1b : Colorless oil.

^{1}H-NMR ($CDCl_3$): *δ* = 0.87 (3H, t, *J* = 7.0 Hz), 1.25-1.36 (10H, m), 1.42-1.53 (2H, m), 1.90-1.98 (1H, m), 2.05-2.13 (2H, m), 2.07 (3H, s), 2.60 (1H, s), 2.87 (1H, dd, *J* = 2.6, 17.0 Hz), 3.15 (1H, dd, *J* = 2.8, 16.8 Hz),

^{13}C-NMR ($CDCl_3$): *δ* = 14.1, 21.7, 22.7, 23.8, 28.9, 29.2, 29.4, 29.4, 31.9, 38.3, 71.4, 74.6, 75.5, 78.3, 82.0, 169.3.

IR (neat): 3293, 2925, 1745, 1225 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{16}H_{24}O_2$: 248.1776; found 247.1778.



1c

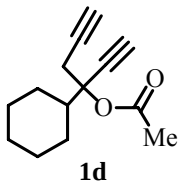
1c : Colorless oil.

^{1}H-NMR ($CDCl_3$): *δ* = 0.90 (3H, t, *J* = 6.8 Hz), 1.24-1.40 (6H, m), 1.41-1.55 (2H, m), 1.90-1.98 (1H, m), 2.05-2.13 (2H, m), 2.07 (3H, s), 2.60 (1H, s), 2.87 (1H, dd, *J* = 2.6, 17.0 Hz), 3.15 (1H, dd, *J* = 2.6, 16.8 Hz),

^{13}C-NMR ($CDCl_3$): *δ* = 14.0, 21.7, 22.5, 23.7, 28.9, 29.1, 31.6, 38.3, 71.3, 74.6, 75.5, 78.3, 82.0, 169.3.

IR (neat): 3292, 2929, 1744, 1223 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{14}H_{20}O_2$: 220.1463; found 220.1472.



1d

1d : Colorless oil.

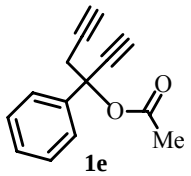
^{1}H-NMR ($CDCl_3$): δ = 1.11-1.35 (5H, m), 1.67-1.84 (4H, m), 1.93-1.98 (1H, m), 2.04 (1H, t, *J* = 2.6 Hz), 2.07 (3H, s), 2.08-2.15 (1H, m), 2.59 (1H, s), 2.93 (1H, dd, *J* = 2.6, 17.4 Hz), 3.33 (1H, dd, *J* = 2.6, 17.4 Hz),

^{13}C-NMR ($CDCl_3$): δ = 21.7, 25.9, 26.1, 26.1, 26.3, 26.8, 26.9, 43.8, 71.2, 75.5, 78.3, 78.7, 80.9, 169.5.

IR (neat): 3290, 2931, 2118, 1741, 1221 cm^{-1}.

LRMS-EI *m/z* : 218 (M^+)

Anal. Calcd for $C_{14}H_{18}O_2$: C,77.03; H, 8.31. Found: C, 76.64 ; H, 8.24.



1e

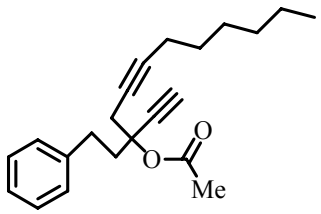
1e : Colorless needles. mp. 58˚C (hexane).

^{1}H-NMR ($CDCl_3$): δ = 2.04 (1H, t, *J* = 2.6 Hz), 2.12 (3H, s), 2.88 (1H, s), 3.05 (2H, t, *J* = 2.6 Hz), 7.30-7.40 (3H, m), 7.56-7.60 (2H, m).

^{13}C-NMR ($CDCl_3$): δ = 21.6, 35.0, 71.8, 76.4, 76.8, 78.0, 81.0, 125.4, 126.1, 128.3 (2C), 128.4 (2C),168.3.

IR (neat): 3286, 1747, 2120, 1219 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{14}H_{12}O_2$: 212.0837; found 212.0839.



1f

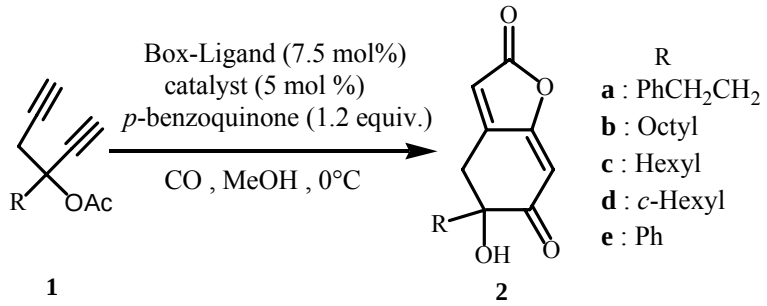
1f : Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 0.89 (3H, t, *J* = 6.8 Hz), 1.24-1.32 (4H, m), 1.36-1.58 (4H, m), 2.03 (3H, s), 2.04-2.06 (1H, m), 2.12-2.27 (3H, m), 2.38-2.46 (1H, m), 2.83 (2H, t, *J* = 8.4 Hz), 2.89 (1H, dd, *J* = 2.4, 17.2 Hz), 3.21 (1H, dd, *J* = 2.4, 17.2 Hz), 7.17-7.31 (5H, m).

^{13}C NMR (CDCl3): δ = 14.0, 18.8, 21.8, 22.6, 28.5 (2C), 29.4, 30.6, 31.3, 40.7, 71.2, 76.0, 78.3, 78.8, 87.9, 125.9, 128.4 (2C), 128.5 (2C), 141.2, 169.3.

IR (neat): 2930, 2242, 1742, 1333 cm^{-1}.

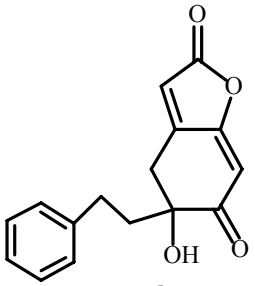
HRMS-EI m/z: [M^+] calcd for $C_{22}H_{28}O_2$: 324.2089; found 224.2089.



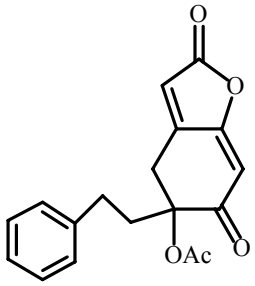
1 **2**

General procedure for the carbonylation of 1.

A 30 mL two-necked round-bottomed flask containing a magnetic stirring bar, $Pd(TFA)_2$ (0.015 mmol), ligand (0.0225 mmol), *p*-benzoquinone (0.36 mmol) and MeOH (3 mL) was fitted with a rubber septum and a three-way stopcock connected to a balloon filled with carbon monoxide. The apparatus was purged with carbon monoxide by pumping-filling via the three-way stopcock. To the stirred solution, the substrate **1** (0.3 mmol) was added dropwise (1 mL × 3) via a syringe at 0 ˚C. After being stirred for a certain period of time at 0 ˚C, the mixture was diluted with CH_2Cl_2 (50 mL), and washed with H_2O (50 mL × 2). The combined aqueous layers were extracted with CH_2Cl_2 (25 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by short column chromatography on silica gel. The fraction eluted with hexane / ethyl acetate (7/1-5/1) afforded a mixture of **2** and acetate **2'**. Pure compounds were obtained by preparative TLC or recrystallization.



2a



2a'

2a : **2a'** = 7 : 1 ((*S*)-Phbox)
2a : **2a'** = 11 : 1 (*meso*-Phbox)

2a : Colorless needles; mp 144˚C (EtOAc/hexane). ((*S)*-Phbox; 2% ee; Chiralpak OD-H, Hexane / EtOH = 5/1, 1.0 mL/min, t_R = 16.9 min, 22.6 min).

^{1}H-NMR (CD_2Cl_2): δ = 1.85-2.00 (2H, m), 2.37-2.45 (1H, m), 2.67-2.74 (1H, m), 2.95 (1H, dd, *J* = 2.4, 17.2 Hz), 3.43 (1H, d, *J* = 17.2 Hz), 4.00 (1H, br-s), 6.04 (1H, d, *J* = 2.0 Hz), 6.24-6.25 (1H, m), 7.11-7.27 (5H, m).

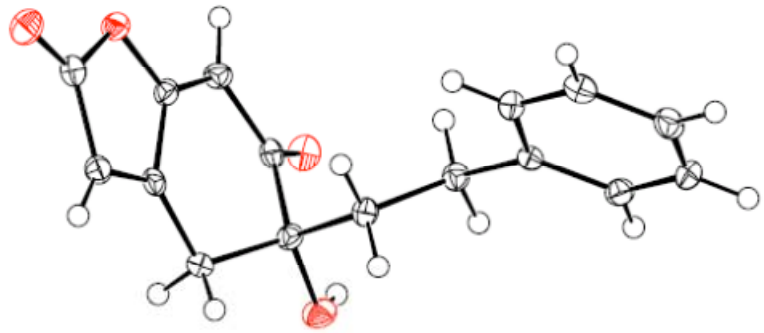
^{13}C-NMR (CD_2Cl_2): δ = 29.9, 36.1, 42.8, 77.4, 104.6, 117.9, 126.5, 128.7 (2C), 128.8 (2C), 141.3, 153.6, 163.4, 167.2, 200.2.

IR (KBr): 3503, 3063, 1794, 1664, 1614 cm^{-1}. LRMS-EI *m/z* : 270 (M^+)

Anal. Calcd for $C_{16}H_{14}O_2$: C,71.10; H, 5.22. Found: C, 71.03 ; H, 5.36.

X-ray crystallographic analysis (Fig. 1): X-ray diffraction data were collected on a Bruker SMART APEX II CCD diffractometer equipped with a graphite crystal and incident beam monochromator using Mo Kα radiation (λ = 0.71073 Å) at 100 K. The structure was solved by direct method.[2] The non-hydrogen atoms were refined anisotropically. Crystallographic parameters: $C_{16}H_{14}O_4$, M_W = 270.27, monoclinic, space group $P2_1/n$, with unit cell a = 6.1176(7) Å, b = 8.1836(9) Å, c = 25.614(3) Å, β = 93.427(2)º and V = 1280.1(2) Å^3. Z = 4, $D_{calcd.}$ = 1.402 gcm^{-3}, $R1(I > 2\sigma(I))$ = 0.0398, $wR2$ = 0.0951, $R1$(all data) = 0.0522, $wR2$ = 0.1028, 3045 independent reflections (R(int) = 0.0238), 182 parameters refined on F^2. Crystallographic data (excluding structure factors) for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 685066.

Fig. 1 X-Ray structure of 2a.



2a' : Colorless needles; mp 139˚C (EtOAc/hexane).

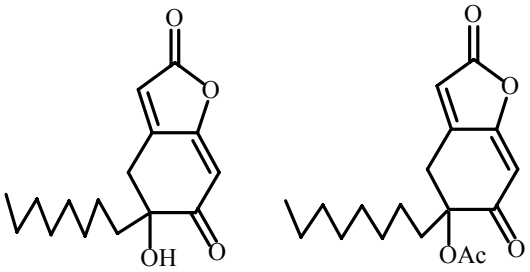
^{1}H-NMR ($CDCl_3$): δ = 2.04-2.09 (2H, m), 2.16 (3H, s), 2.50-2.58 (1H, m), 2.73-2.83 (1H, m), 3.23 (1H, dd, J = 1.0, 17.4 Hz), 3.84 (1H, dd, J = 2.6, 17.4 Hz), 6.06 (1H, d, J = 1.6 Hz), 6.17-6.18 (1H, m), 7.11-7.30 (5H, m).

^{13}C-NMR ($CDCl_3$): δ = 21.2, 29.4, 32.7, 40.6, 81.5, 106.4, 116.8, 126.4, 128.3 (2C), 128.6 (2C), 140.2, 152.6, 161.9, 166.7, 170.2, 192.4.

IR (CCl_4): 2931, 1792, 1729, 1676, 1650, 1619 cm^{-1}. LRMS-EI *m/z* : 312 (M^+)

HRMS-FAB m/z: [M^++H] calcd for $C_{18}H_{17}O_5$: 313.1076; found 313.1040.

Anal. Calcd for $C_{18}H_{16}O_5$: C,69.22; H, 5.16. Found: C, 68.90 ; H, 5.14.



2b **2b'**

2b : **2b'** = 15 : 1

2b : Colorless needles; mp 39˚C (EtOAc/hexane).

^{1}H-NMR ($CDCl_3$): δ = 0.87 (3H, t, J = 7.0 Hz), 1.02-1.12 (1H, m), 1.18-1.41 (11H, m), 1.55-1.68 (2H, m), 2.95 (1H, dd, J = 2.6, 17.4 Hz), 3.41 (1H, d, J = 17.6 Hz), 3.95 (1H, s), 6.05 (1H, d, J = 2.0 Hz), 6.27-6.28 (1H, m).

^{13}C-NMR ($CDCl_3$): δ = 14.1, 22.6, 23.3, 29.1, 29.3, 29.5, 31.8, 35.8, 40.9, 77.2, 104.4, 117.4, 153.5, 162.9, 166.7, 200.0.

IR (CCl_4): 3485, 2925, 2854, 1799, 1676, 1647, 1619 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{16}H_{22}O_4$: 278.1518; found 278.1506.

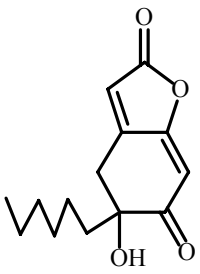
2b' : Colorless needles; mp 47˚C (EtOAc/hexane).

^{1}H-NMR ($CDCl_3$): δ = 0.87 (3H, t, J = 7.0 Hz), 1.17-1.42 (12H, m), 1.72-1.76 (2H, m), 2.13 (3H, s), 3.21 (1H, dd, J = 1.2, 17.6 Hz), 3.77 (1H, dd, J = 2.4, 17.6 Hz), 6.04 (1H, d, J = 2.0 Hz), 6.20-6.22 (1H, m).

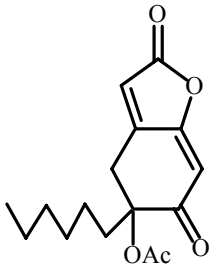
^{13}C-NMR ($CDCl_3$): 14.1, 21.2, 22.6, 23.1, 29.1, 29.3, 29.5, 31.8, 32.6, 39.1, 81.7, 106.7, 116.5, 153.0, 161.9, 166.8, 170.3, 192.9.

IR (CCl_4): 2925, 1802, 1742, 1682, 1650, 1619 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{18}H_{24}O_5$: 320.1624; found 320.1620.



2c



2c'

2c : **2c'** = 17 : 1

2c : Colorless oil.

^{1}H-NMR ($CDCl_3$): δ = 0.86 (3H, t, J = 7.0 Hz), 1.01-1.12 (1H, m), 1.21-1.39 (7H, m), 1.55-1.68 (2H, m), 2.95 (1H, dd, J = 2.4, 17.2 Hz), 3.41 (1H, d, J = 17.2 Hz), 3.95 (1H, s), 6.05 (1H, d, J = 2.0 Hz), 6.27-6.28 (1H, m).

^{13}C-NMR ($CDCl_3$): δ = 14.0, 22.5, 23.3, 29.2, 31.5, 35.8, 40.9, 77.2, 104.4, 117.4, 153.5, 162.9, 166.7, 200.0.

IR (CCl_4): 3482, 2928, 2857, 1795, 1674, 1646, 1618 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{14}H_{18}O_4$: 250.1205; found 250.1206.

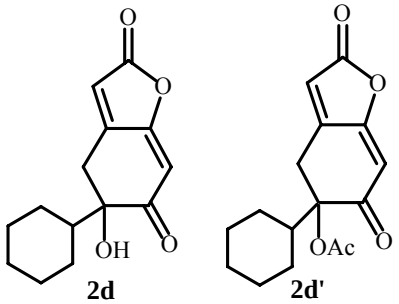
2c' : Colorless oil.

^{1}H-NMR ($CDCl_3$): δ = 0.87 (3H, t, J = 7.0 Hz), 1.14-1.42 (7H, m), 1.55-1.67 (1H, m), 1.73-1.77 (2H, m), 2.13 (3H, s), 3.21 (1H, dd, J = 0.8, 17.6 Hz), 3.77 (1H, dd, J = 2.8, 17.6 Hz), 6.04 (1H, d, J = 1.6 Hz), 6.20-6.21 (1H, m).

^{13}C-NMR ($CDCl_3$): 14.0, 21.2, 22.5, 23.0, 29.2, 31.5, 32.6, 39.2, 81.7, 106.7, 116.5, 153.0, 161.9, 166.8, 170.3, 192.9.

IR (CCl_4): 2928, 1798, 1739, 1680, 1649, 1618 cm^{-1}.

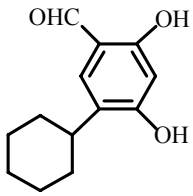
HRMS-EI m/z: [M^+] calcd for $C_{16}H_{20}O_5$: 292.1311; found 292.1314.



2d

2d'

2d : **2d'** = 5 : 1



5

2d : Colorless needles; mp 107˚C (EtOAc/hexane).

^{1}H-NMR ($CDCl_3$): δ = 1.02-1.28 (6H, m), 1.43-1.49 (1H, m), 1.60-1.65 (1H, m), 1.71-1.83 (3H, m), 2.77 (1H, dd, J = 2.6, 17.4 Hz), 3.62 (1H, d, J = 17.6 Hz), 3.84 (1H, s), 6.05 (1H, d, J = 2.0 Hz), 6.24-6.25 (1H, m).

^{13}C-NMR ($CDCl_3$): δ = 25.8, 25.9, 26.0, 26.1, 27.1, 33.1, 45.1, 79.4, 104.7, 116.8, 153.7, 163.0, 166.8, 200.5.

IR (CCl_4): 3452, 2928, 1795, 1674, 1647, 1619 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{14}H_{16}O_4$: 248.1049; found 248.1055.

2d' : Colorless amorphous.

^{1}H-NMR ($CDCl_3$): δ = 1.07-1.28 (5H, m), 1.64-1.82 (6H, m), 2.11 (3H, s), 3.40 (1H, dd, J = 1.0, 18.2 Hz), 3.59 (1H, dd, J = 2.6, 18.2 Hz), 6.08 (1H, d, J = 2.0 Hz), 6.15-6.17 (1H, m).

^{13}C-NMR ($CDCl_3$): δ = 21.2, 25.9, 26.1, 26.1, 26.8, 26.8, 30.2, 46.4, 83.4, 108.0, 115.4, 153.5, 162.2, 167.0, 170.5, 193.3.

IR : 2930, 1799, 1740, 1676, 1651 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{16}H_{18}O_5$: 290.1154; found 290.1150.

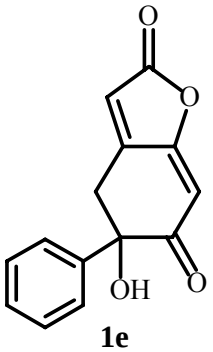
5 : Colorless needles. mp 158˚C (EtOAc/hexane).

^{1}H-NMR ($CDCl_3$): δ = 1.22-1.48 (5H, m), 1.76-1.93 (5H, m), 2.72-2.80 (1H, m), 6.34 (1H, s), 6.48 (1H, s), 7.30 (1H, s), 9.69 (1H, s), 11.26 (1H, s).

^{13}C-NMR ($CDCl_3$): δ = 26.2, 26.9 (2C), 33.2 (2C), 36.4, 102.9, 115.3, 127.4, 132.6, 161.4, 162.2, 194.7.

IR (CCl_4): 3311, 2927, 1644 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{13}H_{16}O_3$: 220.1100; found 220.1094.



1e

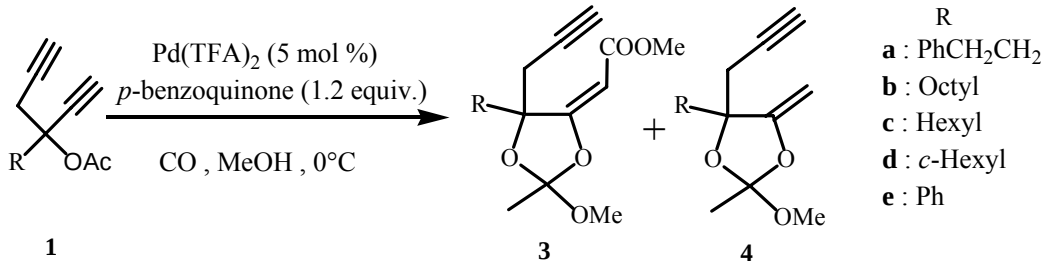
1e : Colorless amorphous. The corresponding acetate was not obtained.

^{1}H-NMR ($CDCl_3$): δ = 3.28 (1H, dd, J = 2.8, 17.6 Hz), 3.93 (1H, dd, J = 0.8, 17.6 Hz), 4.60 (1H, s), 6.12 (1H, d, J = 2.0 Hz), 6.32-6.33 (1H, m), 7.25-7.36 (5H, m).

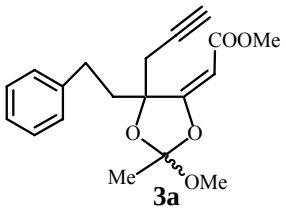
^{13}C-NMR (CD_2Cl_2): δ = 36.3, 77.7, 105.7, 117.3, 125.8 (2C), 128.9, 129.2 (2C), 141.5, 153.5, 163.6, 167.1, 198.0.

IR (CCl_4): 3450, 1793, 1672, 1647, 1617 cm^{-1}.

HRMS-EI m/z: [M^+] calcd for $C_{14}H_{10}O_4$: 242.0579; found 242.0588.



The carbonylation reaction was performed with similar manner that described above without using ligand.

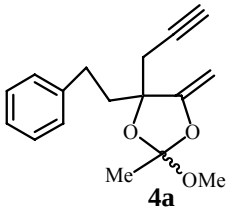


3a

3a : Inseparable mixture of diastereomers (ratio = 1.9 : 1), Colorless oil.

Major diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 1.74 (3H, s), 2.04 (1H, t, J = 2.8 Hz), 2.49-2.83 (4H, m), 3.03 (1H, dd, J = 2.8, 17.0 Hz), 3.37 (1H, dd, J = 2.6, 17.0 Hz), 3.43 (3H, s), 3.68 (3H, s), 5.50 (1H, s), 7.15-7.19 (3H, m), 7.25-7.28 (2H, m). ^{13}C-NMR ($CDCl_3$): δ = 21.8, 27.7, 30.2, 35.9, 51.2, 51.2, 70.8, 79.7, 88.0, 91.4, 123.1, 125.9, 128.4 (2C), 128.5 (2C), 141.3, 166.6, 170.4. IR (neat): 3295, 1712, 1652 cm^{-1}.; HRMS-EI m/z: [M^+] calcd for $C_{19}H_{22}O_5$: 330.1467; found 330.1466.

Minor diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 1.82 (3H, s), 2.00 (1H, t, J = 2.8 Hz), 2.89 (1H, dd, J = 2.8, 17.0 Hz), 3.46 (1H, dd, J = 3.0, 17.0 Hz), 3.66 (3H, s), 5.48 (1H, s). ^{13}C-NMR ($CDCl_3$): δ = 22.0, 26.4, 30.1, 37.9, 50.9, 51.1, 70.5, 80.2, 89.0, 90.5, 123.8, 126.0, 128.4 (2C), 128.6 (2C), 141.5, 166.9, 171.0.

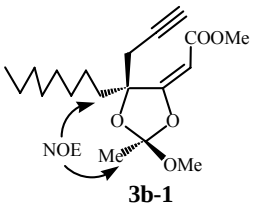


4a

4a : Inseparable mixture of diastereomers (ratio = 1.8 : 1); Colorless oil.

Major diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 1.68 (3H, s), 1.91-1.99 (1H, m), 2.08 (1H, t, J = 2.8 Hz), 2.33-2.41 (1H, m), 2.60-2.89 (4H, m), 3.36 (3H, m), 4.13 (1H, d, J = 2.8 Hz), 4.48 (1H, d, J = 2.8 Hz), 7.17-7.31 (5H, m). ^{13}C-NMR ($CDCl_3$) δ = 21.6, 29.9, 30.5, 39.8, 50.7, 71.0, 79.6, 80.6, 83.7, 121.9, 125.9, 128.4 (2C), 128.5 (2C), 141.6, 160.5. IR (neat): 3291, 1685, 1387 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{17}H_{20}O_3$: 272.1413; found 272.1412.

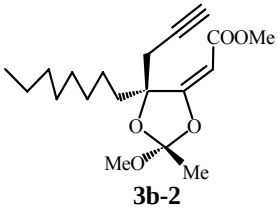
Minor diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 1.69 (3H, s), 2.08 (1H, t, J = 2.8 Hz), 3.34 (3H, m), 4.08 (1H, d, J = 2.8 Hz), 4.44 (1H, d, J = 2.8 Hz). ^{13}C-NMR ($CDCl_3$): δ = 23.6, 29.6, 30.2, 40.1, 50.0, 70.9, 79.4, 80.2, 83.8, 122.1, 126.0, 128.3 (2C), 128.5 (2C), 141.6, 160.9.



3b-1

3b-1 : The stereochemistry was determined by NOE experiment.

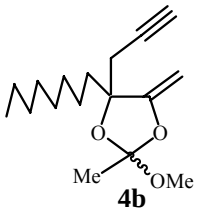
Major diastereomer (more polar); Colorless oil. : ^{1}H-NMR ($CDCl_3$): δ = 0.87 (3H, t, J = 6.8 Hz), 1.19-1.36 (12H, m), 1.70 (3H, s), 2.04 (1H, t, J = 2.6 Hz), 2.12-2.20 (1H, m), 2.27-2.34 (1H, m), 2.99 (1H, dd, J = 2.6, 17.2 Hz), 3.33 (1H, dd, J = 2.6, 17.0 Hz), 3.41 (3H, s), 3.67 (3H, s), 5.45 (1H, s). ^{13}C-NMR ($CDCl_3$): δ = 14.1, 21.3, 22.7, 23.6, 27.6, 29.2, 29.4, 29.4, 31.8, 34.1, 51.1, 51.1, 70.6, 80.0, 88.4, 90.9, 123.0, 166.7, 171.0. IR (neat): 2926, 1714, 1653 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{19}H_{30}O_5$: 338.2093; found 338.2096.



3b-2

3b-2 : Minor diastereomer (less polar); Colorless oil. : ^{1}H-NMR ($CDCl_3$): δ = 0.87 (3H, t, J = 6.8 Hz), 1.10-1.34 (12H, m), 1.78 (3H, s), 1.94-2.02 (1H, m), 1.97 (1H, t, J = 2.6 Hz), 2.26-2.34 (1H, m), 2.82 (1H, dd, J = 2.6, 17.2 Hz), 3.37 (3H, s), 3.40 (1H, dd, J = 2.8, 17.2 Hz), 3.67 (3H, s), 5.46 (1H, s). ^{13}C-NMR ($CDCl_3$): δ = 14.1, 22.1, 22.7, 23.4, 26.0, 29.2, 29.4, 29.7, 31.8, 36.0, 50.7, 51.1, 70.3, 80.5, 89.4,

90.1, 123.7, 166.9, 171.7. IR (neat): 2926, 1713, 1652 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{19}H_{30}O_5$: 338.2093; found 338.2097.

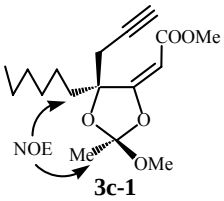


4b

4b : Inseparable mixture of diastereomers (ratio = 1.9 : 1); Colorless oil.

Major diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 0.88 (3H, t, J = 6.8 Hz), 1.23-1.50 (13H, m), 1.63 (3H, s), 1.97-2.05 (1H, m), 2.04 (1H, t, J = 2.6 Hz), 2.63 (1H, dd, J = 2.6, 16.8 Hz), 2.80 (1H, dd, J = 2.6, 16.8 Hz), 3.33 (3H, s), 4.03 (1H, d, J = 2.8 Hz), 4.40 (1H, d, J = 2.8 Hz). ^{13}C-NMR ($CDCl_3$) δ = 14.1, 21.7, 22.7, 23.3, 29.2, 29.4, 29.6, 30.4, 31.9, 37.8, 50.5, 70.7, 79.9, 80.2, 84.0, 121.8, 160.9. IR (neat): 2925, 1685, 1386 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{17}H_{28}O_3$: 280.2039; found 280.2034.

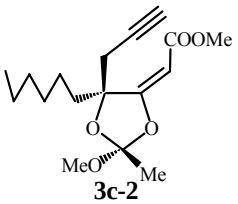
Minor diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 0.88 (3H, t, J = 6.8 Hz), 1.66 (3H, s), 2.01 (1H, t, J = 2.6 Hz), 3.30 (3H, s), 4.02 (1H, d, J = 2.8 Hz), 4.39 (1H, d, J = 2.8 Hz). ^{13}C-NMR ($CDCl_3$) δ = 14.1, 23.7, 38.1, 49.9, 70.5, 79.7, 79.8, 84.2, 121.9, 161.4.



3c-1

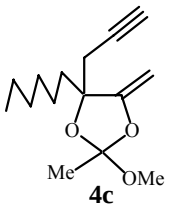
3c-1 : The stereochemistry was determined by NOE experiment.

Major diastereomer (more polar); Colorless oil. : ^{1}H-NMR ($CDCl_3$): δ = 0.87 (3H, t, J = 6.6 Hz), 1.17-1.40 (8H, m), 1.70 (3H, s), 2.04 (1H, t, J = 2.6 Hz), 2.12-2.20 (1H, m), 2.27-2.35 (1H, m), 3.00 (1H, dd, J = 2.6, 17.0 Hz), 3.33 (1H, dd, J = 2.6, 17.0 Hz), 3.41 (3H, s), 3.67 (3H, s), 5.45 (1H, s). ^{13}C-NMR ($CDCl_3$): δ = 14.1, 21.3, 22.6, 23.5, 27.6, 29.1, 31.6, 34.1, 51.1, 51.1, 70.6, 80.0, 88.3, 90.9, 123.0, 166.7, 171.0. IR (neat): 2930, 1714, 1654 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{17}H_{26}O_5$: 310.1780; found 310.1775.



3c-2

3c-2: Minor diastereomer (less polar); Colorless oil. : ^{1}H-NMR ($CDCl_3$): δ = 0.87 (3H, t, J = 6.0 Hz), 1.20-1.48 (8H, m), 1.78 (3H, s), 1.95-2.02 (1H, m), 1.97 (1H, t, J = 2.6 Hz), 2.26-2.34 (1H, m), 2.82 (1H, dd, J = 2.6, 17.2 Hz), 3.34 (3H, s), 3.40 (1H, dd, J = 2.6, 17.2 Hz), 3.48 (3H, s), 5.46 (1H, s). ^{13}C-NMR ($CDCl_3$): δ = 14.0, 22.1, 22.6, 23.4, 26.0, 29.4, 31.7, 36.0, 50.7, 51.1, 70.3, 80.5, 89.3, 90.1, 123.7, 166.9, 171.7. IR (neat): 2929, 1712, 1651 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{17}H_{26}O_5$: 310.1780; found 310.1780.

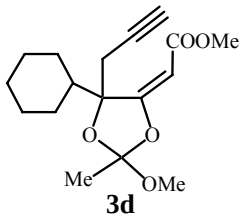


4c

4c : Inseparable mixture of diastereomers (ratio = 2.3 : 1); Colorless oil.

Major diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 0.88 (3H, t, J = 6.8 Hz), 1.25-1.36 (8H, m), 1.63 (3H, s), 1.75-2.04 (2H, m), 2.06 (1H, t, J = 2.6 Hz), 2.63 (1H, dd, J = 2.6, 16.8 Hz), 2.80 (1H, dd, J = 2.6, 16.8 Hz), 3.33 (3H, s), 4.03 (1H, d, J = 2.4 Hz), 4.40 (1H, d, J = 2.4 Hz). ^{13}C-NMR ($CDCl_3$): δ = 14.1, 21.7, 22.6, 23.3, 29.3, 30.5, 31.7, 37.8, 50.5, 70.7, 79.8, 80.2, 84.0, 121.8, 160.9. IR (neat): 2928, 1685, 1466 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{15}H_{24}O_3$: 252.1726; found 252.1735.

Minor diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 0.89 (3H, t, J = 6.8 Hz), 1.65 (3H, s), 2.03 (1H, t, J = 2.6 Hz), 3.30 (3H, s), 4.02 (1H, d, J = 2.8 Hz), 4.39 (1H, d, J = 2.4 Hz). ^{13}C-NMR ($CDCl_3$): δ = 14.1, 22.6, 23.6, 23.7, 29.4, 29.5, 31.6, 38.1, 49.9, 70.5, 79.7, 79.9, 84.2, 121.9, 161.4.

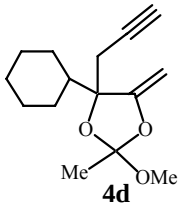


3d

3d : Inseparable mixture of diastereomers (ratio = 3.1 : 1); Colorless oil.

Major diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 1.06-1.38 (5H, m), 1.54-1.85 (4H, m), 1.71 (3H, s), 1.99-2.05 (1H, m), 2.02 (1H, t, J = 2.8 Hz), 2.30-2.43 (1H, m), 3.16 (1H, dd, J = 2.8, 17.3 Hz), 3.21 (1H, dd, J = 2.8, 17.3 Hz), 3.39 (3H, s), 3.67 (3H, s), 5.48 (1H, s). ^{13}C-NMR ($CDCl_3$) δ = 20.6, 26.2, 26.2, 26.3, 26.4, 26.6, 28.1, 43.7, 51.0, 51.1, 70.7, 80.5, 90.7, 91.1, 123.0, 166.7, 171.3. IR (neat): 2931, 1712, 1651 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{17}H_{24}O_5$: 308.1624; found 308.1628.

Minor diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 1.80 (3H, s), 1.96 (1H, t, J = 2.6 Hz), 2.90 (1H, dd, J = 2.8, 16.9 Hz), 3.40 (3H, s), 3.67 (3H, s), 5.49 (1H, s). ^{13}C-NMR ($CDCl_3$) δ = 21.0, 26.0, 26.3, 26.9, 27.9, 42.0, 51.0, 51.6, 70.3, 81.1, 90.4, 93.1, 123.6, 166.9, 170.5.



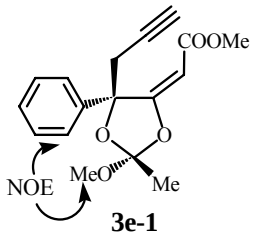
4d

4d : Inseparable mixture of diastereomers (ratio = 6.6 : 1); Colorless oil.

Major diastereomer : ^{1}H-NMR ($CDCl_3$): δ = 1.00-1.31 (6H, m), 1.58-1.92 (5H, m), 1.63 (3H, s), 2.03 (1H, t, J = 2.8 Hz), 2.72 (1H, dd, J = 2.8, 17.2 Hz), 2.81 (1H, dd, J = 2.8, 17.2 Hz), 3.32 (3H, s), 4.13

(1H, d, J = 2.6 Hz), 4.43 (1H, d, J = 2.6 Hz). ^{13}C-NMR ($CDCl_3$): δ = 20.1, 26.2, 26.3, 26.4, 26.4, 26.6, 28.3, 43.1, 51.0, 70.3, 79.8, 81.3, 86.2, 121.5, 160.2. IR (neat): 2930, 1685 cm^{-1}. HRMS-EI m/z: [M$^+$] calcd for $C_{15}H_{22}O_3$: 250.1569; found 250.1576.

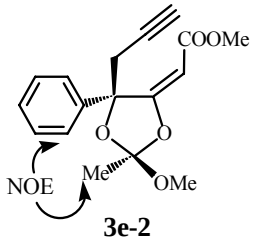
Minor diastereomer : ^{1}H-NMR ($CDCl_3$): δ = 1.67 (3H, s), 2.01 (1H, t, J = 2.8 Hz), 2.54 (1H, dd, J = 2.8, 17.2 Hz), 2.65 (1H, dd, J = 2.8, 16.4 Hz), 3.35 (3H, s), 3.99 (1H, d, J = 2.8 Hz), 4.46 (1H, d, J = 2.8 Hz).



3e-1

3e-1 : The stereochemistry was determined by NOE experiment.

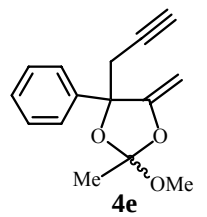
More polar diastereomer; Colorless oil. : ^{1}H-NMR ($CDCl_3$): δ = 1.82 (3H, s), 2.06 (1H, t, J = 2.6 Hz), 2.88 (3H, s), 3.28 (1H, dd, J = 2.6, 17.2 Hz), 3.58 (3H, s), 3.83 (1H, dd, J = 2.6, 17.2 Hz), 5.79 (1H, s), 7.27-7.36 (3H, m), 7.47-7.52 (2H, m). ^{13}C-NMR ($CDCl_3$) δ = 22.6, 28.5, 50.6, 51.2, 70.7, 80.4, 90.0, 92.9, 124.1, 126.2 (2C), 128.2 (2C), 128.4, 138.5, 166.3, 168.2. IR (neat): 1717, 1654 cm^{-1}. FABMS *m/z*: 303 [M+H]. Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.56; H, 6.08.



3e-2

3e-2 : The stereochemistry was determined by NOE experiment.

Less polar diastereomer; Colorless oil. : ^{1}H-NMR ($CDCl_3$): δ = 1.33 (3H, s), 2.02 (1H, t, J = 2.6 Hz), 3.44 (1H, dd, J = 2.6, 17.6 Hz), 3.52 (3H, s), 3.64 (3H, s), 3.65 (1H, dd, J = 2.8, 17.6 Hz), 5.73 (1H, s), 7.29-7.38 (3H, m), 7.451-7.54 (2H, m). ^{13}C-NMR ($CDCl_3$): δ = 23.8, 28.4, 50.3, 51.2, 71.0, 80.2, 88.5, 92.5, 123.0, 126.3 (2C), 128.2 (2C), 128.6, 138.9, 166.4, 167.6. IR (neat): 1716, 1654 cm^{-1}. FABMS *m/z*: 303 [M+H]. Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54; H, 6.00. Found: C, 67.73; H, 6.27.



4e

4e : Inseparable mixture of diastereomers (ratio = 2.1 : 1); Colorless oil.

Major diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 1.41 (3H, s), 1.96 (1H, t, J = 2.8 Hz), 2.93-3.06 (2H, m), 3.45 (3H, s), 4.33 (1H, d, J = 2.8 Hz), 4.65 (1H, d, J = 2.8 Hz), 7.28-7.39 (3H, m), 7.59-7.65 (2H, m). ^{13}C-NMR ($CDCl_3$) δ = 24.0, 32.0, 49.6, 71.3, 79.1, 82.3, 84.7, 122.1, 125.7 (2C), 128.2 (2C), 128.2,

140.7, 159.2. IR (neat): 3292, 1684, 1385 cm^{-1}. HRMS-EI m/z: [M^+] calcd for $C_{15}H_{16}O_3$: 244.1100; found 244.1100.

Minor diastereomer : ^{1}H-NMR ($CDCl_3$) δ = 1.77 (3H, s), 2.00 (1H, t, J = 2.6 Hz), 2.94 (3H, s), 4.31 (1H, d, J = 2.8 Hz), 4.76 (1H, d, J = 2.8 Hz). ^{13}C-NMR ($CDCl_3$) δ = 23.8, 33.7, 50.2, 70.8, 79.6, 83.5, 85.5, 122.6, 125.7 (2C), 128.1, 128.2 (2C), 140.7, 158.6.

References

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