SYNTHESIS OF 5-DIPHENYLPHOSPHINOYL-2,3-DIHYDROPYRAN-4-ONES

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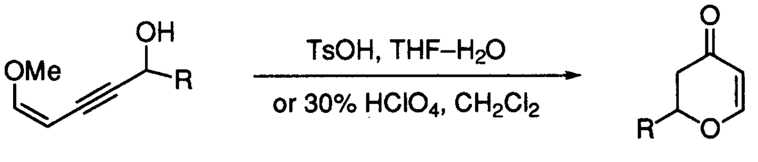
Abstract– 5-Diphenylphosphinoyl-2,3-dihydropyran-4-ones are readily prepared from the corresponding 5-diphenylphosphinoyl-1-buten-3-yne under mild acidic conditions. The phosphorus substituted pyrones are converted to more substituted pyrones *via* 1,4-addition of copper reagents followed by Horner–Wittig reaction.

The tetrahydropyran moiety is found in a large number of natural products, and their syntheses appear a lot in the literatures.[1,2] 2,3-Dihydropyran-4-ones have been widely used for the synthesis of functionalized tetrahydropyrans.[3] There are, thus, many methods for preparation of the dihydropyrones,[3–5] but ones bearing phosphorus substituents at the 5-position are still unknown to our knowledge. 5-Phosphorus-substituted 2,3-dihydropyran-4-ones are expected to be useful substrates, because they would react with nucleophile conjugately and subsequently undergo the Wittig olefination to give functionalized pyrone derivatives. We now report a synthetic method for preparation of 5-diphenylphosphinoyl-2,3-dihydropyran-4-ones.

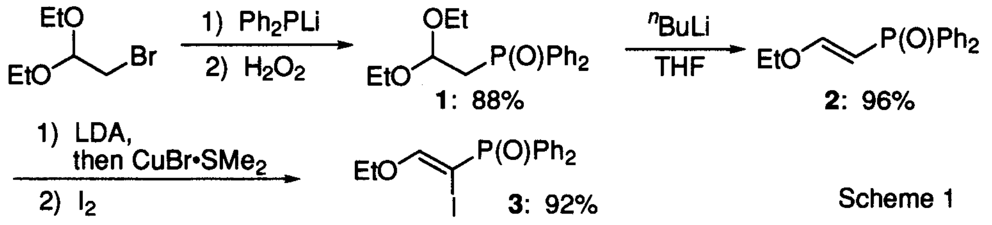
We have recently reported a convenient synthesis of phosphorus substituted 1-ethoxy-1-buten-3-ynes from vinyl halides and alkynes by using palladium-catalyzed coupling.[6] Previously, Crimmins *et al.* have reported that 2,3-dihydropyran-4-ones were readily prepared from 1-methoxy-1-buten-3-yne derivatives under acidic conditions (eq. 1).[5] We applied this method to the synthesis of the pyrone bearing a phosphorus substituent.



(1)

1-Diphenylphosphinyl-1-iodo-2-ethoxyethene (3) was prepared as shown in Scheme 1. Lithium diphenylphosphide was treated with 2-bromo-1,1-diethoxyethane, followed by oxidation of the phosphine with hydrogen peroxide to give the phosphine oxide (**1**). Base treatment of **1** led to β-ethoxy-vinylphosphine oxide (**2**), which was converted to the phosphinoylvinyl halide (**3**) according to the procedure for the preparation of phosphonovinyl halides.[6]

The phosphonovinyl iodide (**3**) was allowed to react with propargyl alcohols (**4a–c**) under conventional palladium-catalyzed cross-coupling conditions. While the coupling reaction of **3** with **4a** was satisfactory, with **4b** and **4c** it led to **5b** and **5c** in moderate yield (eq. 2). The enynes (**5b**,**5c**) or the propargyl alcohols (**4b**,**4c**) probably reacted with the Pd catalyst to form allenylpalladium intermediates, which gave undesired byproducts.

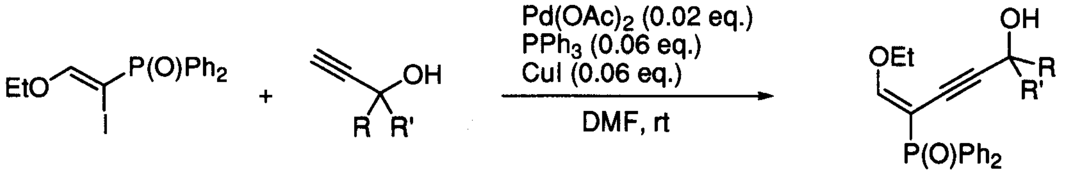


1: 88%

2: 96%

3: 92%

Scheme 1



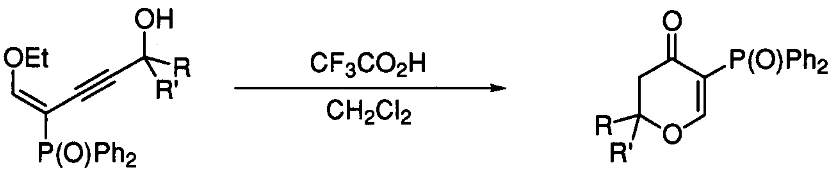
(2)

3

4a (R=R'=Me)
4b (R=Me, R'=H)
4c (R=R'=H)

5a (R=R'=Me)	91%
5b (R=Me, R'=H)	41%
5c (R=R'=H)	51%

Next, we attempted the acid-catalyzed cyclization of **5a** according to Crimmins' procedure($TsOH•H_2O$–THF).[5] The reaction was slow and incomplete even after 24 h at 65 °C to give the phosphinoylpyrone (**6a**) in 59% yield. After screening reaction conditions, we found that treatment of **5** with 2.0 equiv of trifluoroacetic acid in CH_2Cl_2 afforded **6** even at room temperature in good yield (eq. 3). The cyclization of **5c** resulted in a moderate yield because of decomposition of an unstable product (**6c**).

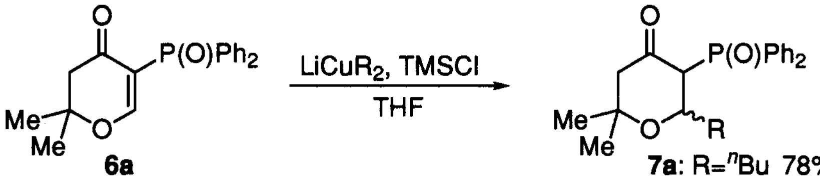


(3)

5a-c

6a (R=R'=Me)	86%
6b (R=Me, R'=H)	88%
6c (R=R'=H)	45%

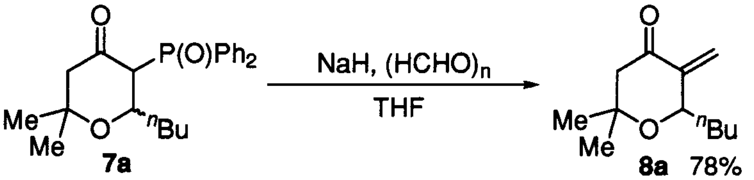
Having accomplished the first synthesis of 5-phosphorus-substituted 2,3-dihydropyran-4-ones (**6**), the application of **6** to the synthesis of substituted pyrone was tried. 1,4-Addition of organocopper reagents to **6a** in the presence of TMSCl furnished substituted pyrone (**7**) containing a β-ketophosphine oxide moiety. The pyrone (**7a**) was allowed to react with paraformaldehyde under the Horner–Wittig reaction conditions to afford 5-methylenetetrahydropyran-4-one (**8a**) (eq. 5).



(4)

6a

7a: R=^{n}Bu	78%
7b: R=Me	78%
7c: R=Ph	80%



(5)

7a

8a 78%

In summary, the first synthesis of 5-diphenylphosphinoyl-2,3-dihydropyran-4-ones using acid-catalyzed cyclization of enynes has been described. The phosphorus substituted pyrone have been demonstrated to be useful substrates for the preparation of more substituted pyrone through 1,4-addition of copper reagents followed by Horner–Wittig reaction.

EXPERIMENTAL

Melting points were determined in open capillary with a Buchi-530 melting point apparatus and are uncorrected. NMR spectra were recorded on a JEOL JNM-A500 spectrometer at 500 MHz (^1H NMR), 126 MHz (^{13}C NMR) or on a Bruker Avance 400 spectrometer at 400 MHz (^1H NMR), 101 MHz (^{13}C NMR). Chemical shifts are reported in ppm relative to TMS as internal standard. MS were measured on a JEOL JMS-SX102A system. Infrared spectra were recorded on a JEOL JIR-WINSPEC50 spectrometer. Column chromatography on silica gel was performed with Fuji Silysia BW-127ZH. Preparative TLC was performed on Wakogel B-5F/TLC-cards (20×20×0.7 cm). All reagents were purified before use. Organic solvents were purified and dried by standard procedures.

(2,2-Diethoxyethyl)diphenylphosphine oxide (1). A solution of PPh_3 (14.5 g, 55 mmol) and lithium shavings (0.86 g, 120 mmol) in THF (150 mL) was stirred for 14 h at rt and resulting phenyllithium was destroyed with *tert*-butyl chloride (6.0 mL, 55 mmol). To the solution was added bromoacetaldehyde diethyl acetal (7.5 mL, 50 mmol) below 5 °C. After the addition, the mixture was allowed to be stirred at rt for 2 h. Then H_2O_2 (30% in water, 17 mL, 150 mmol) was added. After being stirred for 1 h, the reaction was quenched by the addition of saturated $Na_2S_2O_3$ solution. After usual workup, the crude product was purified by column chromatography on silica gel (AcOEt/hexane = 1/1) to give **1** (12.2 g, 76%). **1**: white crystal; mp 86–89 °C (AcOEt/hexane); IR (KBr) 2973, 1438, 1184, 1118, 1056, 700, 536 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (6H, t, J = 7.0 Hz), 2.74 (2H, dd, J = 5.6 Hz, ${}^2J_{P-H}$ =11.3 Hz), 3.40–3.46 (2H, m), 3.55-3.92 (2H, m), 5.02 (1H, q, J = 5.4 Hz), 7.42–7.52 (6H, m), 7.74–7.79 (4H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.8, 35.9 (d, ${}^1J_{P-C}$ = 71.2 Hz), 62.5, 98.6, 128.3 (d, ${}^3J_{P-C}$ = 12.0 Hz), 130.8 (d, ${}^2J_{P-C}$ = 9.4 Hz), 131.5 (d, ${}^4J_{P-C}$ = 2.7 Hz), 133.4 (d, ${}^1J_{P-C}$ = 101.1 Hz); MS(FAB/NBA) *m/z* 319 ($M+H^+$); HRMS(FAB/NBA) calcd for $C_{18}H_{24}O_3P$ ($M+H^+$) 319.1463, found 319.1482.

(*E*)-(2-Ethoxyvinyl)diphenylphosphine oxide (2). To a solution of **1** (0.21 g, 0.65 mmol) in THF (6.5 mL) was added dropwise BuLi (0.23 mL, 3.0 M in hexane, 0.71 mmol) at –78 °C. After being stirred at this temperature for 15 min, the reaction was quenched by the addition of phosphate buffer (pH = 7). After usual workup, the crude product was chromatographed on preparative TLC (AcOEt : hexane = 4 : 1) to give **2** (0.17 g, 0.62 mmol, 96%). **2**: colorless crystal; mp 140–141 °C (AcOEt/hexane); IR (KBr) 1608, 1197 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.34 (3H, t, J = 7.0 Hz), 3.95 (2H, q, J = 7.0 Hz), 5.28 (1H, dd, J = 13.7, ${}^2J_{P-H}$ = 14.7 Hz), 7.03 (1H, dd, J = 13.7 Hz, ${}^3J_{P-H}$ = 11.0 Hz), 7.45–7.52 (6H, m), 7.69–7.74 (4H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.5, 66.5, 93.0 (d, ${}^1J_{P-C}$ = 114.8 Hz), 128.5 (d, ${}^3J_{P-C}$ = 12.4 Hz), 131.2 (d, ${}^2J_{P-C}$ = 9.3 Hz), 131.6 (d, ${}^4J_{P-C}$ = 3.0 Hz), 134.0 (d, ${}^1J_{P-C}$ = 107.6 Hz), 162.0 (d, ${}^2J_{P-C}$ = 15.6 Hz). Anal. Calcd for $C_{16}H_{17}O_2P$: C, 70.58; H, 6.29. Found: C, 70.34; H, 6.27.

(Z)-(2-Ethoxy-1-iodovinyl)diphenylphosphine oxide (3). To a solution of LDA, generated *in situ* from diisopropylamine (1.4 mL, 11 mmol) and BuLi (3.0 M in hexane, 3.2 mL, 9.7 mmol) in THF (50 mL) at –78 °C for 30 min, was added dropwise a solution of **2** (2.2 g, 8.1 mmol) in THF (30 mL) and the mixture was stirred for 30 min at –78 °C. Then copper(I) bromide–dimethyl sulfide complex (0.69 g, 3.4 mmol) was added and the mixture was stirred for 5 min at –78 °C. A solution of I_2 (2.4 g, 9.5 mmol) in THF (30 mL) was added and the mixture was stirred for 2 h at –78 °C. The reaction was quenched by the addition of saturated $Na_2S_2O_3$ solution. After usual workup, the crude product was purified by column chromatography on silica gel (AcOEt/hexane = 4/1) to give **6** (3.0 g, 7.5 mmol, 92%). **3**: colorless crystal; mp 108–109 °C (AcOEt/hexane); IR (KBr) 1598, 1214 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.37 (3H, t, J = 7.0 Hz), 4.18 (2H, q, J = 7.0 Hz), 7.27 (1H, d, ${}^3J_{P-H}$ = 7.3 Hz), 7.46–7.50 (4H, m), 7.54–7.58

(2H, m), 7.78–7.82 (4H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.3, 63.2 (d, $^{1}J_{P-C}$ = 105.4 Hz), 70.7, 128.4 (d $^{3}J_{P-C}$ = 12.4 Hz), 130.9 (d, $^{1}J_{P-C}$ = 111.6 Hz), 132.1 (d, $^{4}J_{P-C}$ = 2.1 Hz), 132.6 (d, $^{2}J_{P-C}$ = 10.3 Hz), 162.7 (d, $^{2}J_{P-C}$ = 21.7 Hz). Anal. Calcd for $C_{16}H_{16}O_2IP$: C, 48.26; H, 4.05. Found: C, 48.39; H, 4.07.

General Procedure for Palladium-catalyzed Cross-coupling Reaction of 3 with Propargyl Alcohol (4). A solution of $Pd(OAc)_2$ (5.0 mg, 0.02 mmol) and PPh_3 (18 mg, 0.07 mmol) in DMF (3 mL) was stirred at rt for 15 min. To the solution were added CuI (13.0 mg, 0.07 mmol) and a solution of vinyl halide (**3**) (1.1 mmol), propargyl alcohol (**4**) (1.3 mmol), and triethylamine (0.24 mL, 1.7 mmol) in 6 mL of DMF. The mixture was stirred at rt for 24 h. The reaction was quenched by the addition of phosphate buffer (pH = 7), and the mixture was filtrated through Celite pad. After usual workup, the crude product was chromatographed on silica gel to give **6**. The coupling products (**6a–c**) had the following physical properties.

(*E*)-5-Diphenylphosphoryl-6-ethoxy-2-methyl-5-hexen-3-yn-2-ol (5a). colorless crystal; mp 120–121 °C (AcOEt/hexane); IR (KBr) 3311, 2217, 1608, 1214 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (3H, t, *J* = 7.2 Hz), 1.36 (6H, s), 4.17 (2H, q, *J* = 7.2 Hz), 7.42 (1H, d, $^{3}J_{P-H}$ = 8.3 Hz), 7.43–7.55 (6H, m), 7.78–7.82 (4H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.3, 31.0, 65.5, 71.2, 75.1 (d, $^{2}J_{P-C}$ = 8.3 Hz), 90.8 (d, $^{1}J_{P-C}$ 116.7 Hz), 102.9 (d, $^{3}J_{P-C}$ = 7.3 Hz), 128.2 (d, $^{3}J_{P-C}$ = 12.4 Hz), 131.9 (d, $^{2}J_{P-C}$ = 4.1 Hz), 131.9 (d, $^{4}J_{P-C}$ = 3.0 Hz), 132.4 (d, $^{1}J_{P-C}$ = 108.6 Hz), 165.0 (d, $^{2}J_{P-C}$ = 17.6 Hz). Anal. Calcd for $C_{21}H_{23}O_3P$: C, 71.18; H, 6.54. Found: C, 71.00; H, 6.57.

(*E*)-5-Diphenylphosphoryl-6-ethoxy-5-hexen-3-yn-2-ol (5b). colorless oil; IR (neat) 3338, 2979, 2219, 1606, 1436, 1220 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (3H, d, *J* = 6.7 Hz), 1.35 (3H, t, *J* = 7.0 Hz), 4.16 (2H, q, *J* = 7.0 Hz), 4.54 (1H, dq, $^{5}J_{P-H}$ = 3.4 Hz, *J* = 6.7 Hz), 7.40 (1H, d, $^{3}J_{P-H}$ = 8.2 Hz), 7.41–7.54 (6H, m), 7.77–7.82 (4H, m); ^{13}C NMR (126 MHz, C_6D_6) δ 15.1, 24.4, 70.8, 77.0 (d, $^{2}J_{P-C}$ = 8.0 Hz), 92.0 (d, $^{1}J_{P-C}$ 116.9 Hz), 101.6 (d, $^{3}J_{P-C}$ = 7.0 Hz), 128.4 (d, $^{3}J_{P-C}$ = 11.4 Hz), 128.4 (d, $^{3}J_{P-C}$ = 12.4 Hz), 131.7, 132.3 (d, $^{2}J_{P-C}$ = 9.0 Hz), 134.0 (d, $^{1}J_{P-C}$ = 107.4 Hz), 134.0 (d, $^{1}J_{P-C}$ = 107.6 Hz), 165.9 (d, $^{2}J_{P-C}$ = 18.6 Hz); MS(EI) *m*/*z* 341 (M^+); HRMS(EI) calcd for $C_{20}H_{22}O_3P$ 341.1307, found 341.1313.

(*E*)-4-Diphenylphosphoryl-5-ethoxy-4-penten-2-yn-1-ol (5c). colorless oil; IR (neat) 3288, 2173, 1604, 1220 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (3H, t, *J* = 7.4 Hz), 4.15 (2H, q, *J* = 7.4 Hz), 4.27 (2H, d, $^{5}J_{P-H}$ = 4.0 Hz), 7.37 (1H, d, $^{3}J_{P-H}$ = 8.3 Hz), 7.42–7.53 (6H, m), 7.76–7.81 (4H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 15.3, 51.5 (d, $^{4}J_{P-C}$ = 2.0 Hz), 71.4, 77.9 (d, $^{2}J_{P-C}$ = 8.2 Hz), 90.9 (d, $^{1}J_{P-C}$ 117.9 Hz), 96.7 (d, $^{3}J_{P-C}$ = 7.3 Hz), 128.3 (d, $^{3}J_{P-C}$ = 12.4 Hz), 131.9 (d, $^{2}J_{P-C}$ = 10.4 Hz), 132.0 (d, $^{4}J_{P-C}$ = 3.1 Hz), 132.1 (d, $^{1}J_{P-C}$ = 108.4 Hz), 165.7 (d, $^{2}J_{P-C}$ = 18.6 Hz); MS(EI) *m*/*z* 326 (M^+); HRMS(EI) calcd for $C_{17}H_{15}O_3P$ 326.1072, found 326.1062.

General Procedure for Acid-catalyzed Cyclization of 5. To a solution of **5** (0.4 mmol) in CH_2Cl_2 (4 mL) was added trifluoroacetic acid (0.06 mL, 0.8 mmol) at 0 °C. After the addition, the mixture was allowed to warm to rt, and stirred for 24 h. The reaction was quenched by the addition of phosphate buffer (pH = 7). After usual workup, the crude product was purified by column chromatography on silica gel (AcOEt/$CHCl_3$ = 1/2). The cyclized products (**6a–c**) have the following physical properties.

5-Diphenylphosphoryl-2,2-dimethyl-2,3-dihydro-4*H*-pyran-4-one (6a). colorless crystal; mp 143–145 °C (AcOEt/hexane); IR (KBr) 1672, 1562, 1288 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (6H, s), 2.55 (2H, s), 7.42–7.53 (6H, m), 7.75–7.80 (4H, m), 8.18 (1H, d, $^{3}J_{P-H}$ = 8.8 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 26.2, 47.9 (d, $^{3}J_{P-C}$ = 6.2 Hz), 83.7, 108.3 (d, $^{1}J_{P-C}$ = 118.0 Hz), 128.3 (d, $^{3}J_{P-C}$ = 12.4 Hz), 131.7 (d, $^{2}J_{P-C}$ = 10.4 Hz), 131.9 (d, $^{4}J_{P-C}$ = 3.1 Hz), 132.6 (d, $^{1}J_{P-C}$ =109.7 Hz), 171.4

(d, $^2J_{P-C}$ = 14.5 Hz), 190.1 (d, $^2J_{P-C}$ = 4.2 Hz). Anal. Calcd for $C_{19}H_{19}O_3P$: C, 69.93; H, 5.87. Found: C, 69.82; H, 5.92.

5-Diphenylphosphoryl-2-methyl-2,3-dihydro-4*H*-pyran-4-one (6b). colorless oil; IR (neat) 2929, 1675, 1560, 1436, 1276, 1174 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (3H, d, *J* = 6.4 Hz), 2.47–2.58 (2H, m), 4.68–4.76 (1H, m), 7.27–7.55 (6H, m), 7.70–7.86 (4H, m), 8.26 (1H, d, $^3J_{P-H}$ = 8.5 Hz); ^{13}C NMR (101 MHz, acetone-d_6) δ 19.3, 42.6 (d, $^3J_{P-C}$ = 5.6 Hz), 77.3, 110.1 (d, $^1J_{P-C}$ = 104.5 Hz), 128.0 (d, $^3J_{P-C}$ = 12.4 Hz), 128.1 (d, $^3J_{P-C}$ = 12.5 Hz), 131.4 (d, $^2J_{P-C}$ = 10.7 Hz), 131.4 (d, $^4J_{P-C}$ = 2.6 Hz), 131.4 (d, $^4J_{P-C}$ = 2.6 Hz), 131.5 (d, $^4J_{P-C}$ = 2.9 Hz), 131.6 (d, $^2J_{P-C}$ =10.7 Hz), 133.7 (d, $^1J_{P-C}$ =108.2 Hz), 133.7 (d, $^1J_{P-C}$ =109.0 Hz), 172.5 (d, $^2J_{P-C}$ = 15.0 Hz), 190.0 (d, $^2J_{P-C}$ = 3.7 Hz); MS(EI) *m/z* 312 (M^+); HRMS(EI) calcd for $C_{18}H_{17}O_3P$ 312.0916, found 312.0905.

5-Diphenylphosphoryl-2,3-dihydro-4*H*-pyran-4-one (6c). colorless oil; IR (neat) 1672, 1565, 1284, 1178 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.64 (2H, t, *J* = 6.7 Hz), 4.65 (2H, t, *J* = 6.7 Hz), 7.45–7.54 (6H, m), 7.77–7.81 (4H, m), 8.28 (1H, d, $^3J_{P-H}$ = 8.6 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 36.2 (d, $^3J_{P-C}$ = 6.2 Hz), 68.9, 110.7 (d, $^1J_{P-C}$ = 103.3 Hz), 128.3 (d, $^3J_{P-C}$ = 12.4 Hz), 131.7 (d, $^2J_{P-C}$ = 11.3 Hz), 132.0 (d, $^4J_{P-C}$ = 2.1 Hz), 132.2 (d, $^1J_{P-C}$ = 108.6 Hz), 173.0 (d, $^2J_{P-C}$ = 14.4 Hz), 189.4 (d, $^2J_{P-C}$ = 3.1 Hz); MS(EI) *m/z* 298 (M^+); HRMS(EI) calcd for $C_{17}H_{15}O_3P$ 298.0759, found 298.0756.

6-Butyl-5-diphenylphosphoryl-2,2-dimethyl-2,3,5,6-tetrahydropyran-4-one (7a). To a suspension of copper(I) bromide–dimethyl sulfide complex (68 mg, 0.33 mmol) in THF (1 mL) was added BuLi (1.6 M in hexane, 0.4 mL, 0.67 mmol) slowly at –78 °C. The mixture was stirred at –45 °C for 30 min, then cooled to –78 °C. A solution of **6a** (51 mg, 0.16 mmol) and TMSCl (0.03 mL, 0.16 mmol) in THF (1.3 mL) was added dropwise. The reaction mixture was allowed to warm at –45 °C and stirred for 3 h. The reaction was quenched by the addition of phosphate buffer (pH = 7), and the mixture was filtrated through Celite pad. After usual workup, the crude product was purified with preparative TLC on silica gel (AcOEt/$CHCl_3$ = 1/10) to give **7** (47 mg, 78%). **7**: colorless crystal; mp 139–141 °C (AcOEt/hexane); IR (KBr) 2921, 1718, 1436, 1180, 705 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.70 (3H, t, *J* = 7.2 Hz), 1.02-1.41 (6H, m), 1.13 (3H, s), 1.31 (3H, s), 2.19 (1H, dd, *J* = 13.0 Hz, $^3J_{P-H}$ = 1.1 Hz), 2.80 (1H, d, *J* = 13.0 Hz), 3.45 (1H, dd, *J* = 9.6 Hz, $^4J_{P-H}$ = 9.6 Hz), 4.60 (1H, m), 7.44–7.51 (6H, m), 7.77–7.82 (4H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 13.8, 22.1, 26.7, 27.7, 30.0, 35.5, 51.9, 59.9 (d, $^1J_{P-C}$ = 53.5 Hz), 70.6, 75.1, 128.4 (d, $^3J_{P-C}$ = 12.2 Hz), 128.7 (d, $^3J_{P-C}$ = 12.3 Hz), 130.7 (d, $^1J_{P-C}$ = 101.2 Hz), 131.0 (d, $^2J_{P-C}$ = 9.8 Hz), 131.4 (d, $^2J_{P-C}$ = 9.3 Hz), 132.1 (d, $^4J_{P-C}$ = 2.4 Hz), 132.1 (d, $^4J_{P-C}$ = 2.4 Hz), 132.2 (d, $^1J_{P-C}$ = 100.1 Hz), 204.3 (d, $^2J_{P-C}$ = 4.4 Hz); MS(EI) *m/z* 384 (M^+); HRMS(EI) calcd for $C_{23}H_{29}O_3P$ 384.1856, found 384.1852.

5-Diphenylphosphoryl-2,2,6-trimethyl-2,3,5,6-tetrahydropyran-4-one (7b). Using the procedure similar to that described above. **7b** (78% yield): colorless crystal; mp 183–185 °C (AcOEt/hexane); IR (KBr) 2975, 1718, 1436, 1180, 551 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.06 (3H, d, *J* = 6.1 Hz), 1.19 (3H, s), 1.33 (3H, s), 2.23 (1H, dd, *J* = 13.1 Hz, $^4J_{P-H}$ = 1.2 Hz), 2.74 (1H, d, *J* = 13.1 Hz), 3.43–3.47 (1H, m), 4.71–4.76 (1H, m), 7.46–7.56 (6H, m), 7.79–7.89 (4H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.5, 26.8, 30.0, 51.8, 61.3 (d, $^1J_{P-C}$ = 54.8 Hz), 67.1, 75.3, 128.4 (d, $^3J_{P-C}$ = 12.4 Hz), 128.8 (d, $^3J_{P-C}$ = 12.4 Hz), 130.6 (d, $^1J_{P-C}$ = 101.4 Hz), 131.0 (d, $^2J_{P-C}$ = 9.3 Hz), 131.5 (d, $^2J_{P-C}$ = 9.3 Hz), 132.1 (d, $^4J_{P-C}$ = 4.1 Hz), 132.2 (d, $^4J_{P-C}$ = 3.1 Hz), 132.2 (d, $^1J_{P-C}$ =100.3 Hz), 204.2 (d, $^2J_{P-C}$ = 4.1 Hz); MS(EI) *m/z* 342 (M^+); HRMS(EI) calcd for $C_{20}H_{23}O_3P$ 342.1386, found 342.1378.

5-Diphenylphosphoryl-2,2-dimethyl-6-phenyl-2,3,5,6-tetrahydropyran-4-one (7c). Using the procedure similar to that described above. **7c** (80% yield): colorless crystal; mp 192–195 °C (decomp) (AcOEt/hexane); IR (KBr) 2971, 1712, 1436, 1186, 748, 698, 522 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (3H, s), 1.51 (3H, s), 2.43 (1H, d, J = 12.8 Hz), 3.32 (1H, d, J = 12.8 Hz), 3.92 (1H, dd, J = 9.6 Hz, $^{2}J_{P\text{-}H}$ = 8.8 Hz), 5.63 (1H, dd, J = 9.6 Hz, $^{3}J_{P\text{-}H}$ = 8.2 Hz), 6.98–7.12 (7H, m), 7.23–7.48 (6H, m), 7.71–7.76 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.2, 29.9, 52.0, 61.3 (d, $^{1}J_{P\text{-}C}$ = 53.8 Hz), 73.5, 75.9, 127.2, 128.0, 128.2 (d, $^{3}J_{P\text{–}C}$ = 12.4 Hz), 128.2, 128.4 (d, $^{3}J_{P\text{–}C}$ = 12.4 Hz), 130.4 (d, $^{1}J_{P\text{–}C}$ = 100.4 Hz), 130.6 (d, $^{2}J_{P\text{–}C}$ = 9.3 Hz), 130.9 (d, $^{2}J_{P\text{–}C}$ = 9.3 Hz), 131.2 (d, $^{1}J_{P\text{–}C}$ =103.5 Hz), 131.4 (d, $^{4}J_{P\text{–}C}$ = 3.1 Hz), 131.9 (d, $^{4}J_{P\text{–}C}$ = 2.1 Hz), 140.0, 203.5 (d, $^{2}J_{P\text{-}C}$ = 5.2 Hz); MS(EI) *m/z* 404 (M^+); HRMS(EI) calcd for $C_{25}H_{25}O_3P$ 404.1543, found 404.1577.

6-Butyl-5-methylene-2,2-dimethyl-2,3,5,6-tetrahydropyran-4-one (8a). To a suspension of NaH (2.7 mg, 0.11 mmol) in THF (0.2 mL) was added a solution of **7** (44 mg, 0.11 mmol) in THF (1.0 mL) at –20 °C. After being stirred at this temperature for 5 min, paraformaldehide (17 mg, 0.57 mmol) was added to the reaction mixture. After the addition, the mixture was allowed to warm to room temperature during 30 min, and stirred for 1 h. The reaction was quenched by the addition of phosphate buffer (pH = 7). After usual workup, the crude product was purified by column chromatography on silica gel (AcOEt/hexane = 1/30) to give **8a** (17 mg, 75%). **8a**: colorless oil; IR (neat) 2958, 2859, 1700, 1604, 1382, 1083, 946 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ 0.59 (3H, t, J = 7.4 Hz), 0.65 (3H, s), 0.76 (3H, s), 0.92-1.28 (6H, m), 1.92 (1H, d, J = 16.5 Hz), 1.96 (1H, d, J = 16.5 Hz), 3.93–3.96 (1H, m), 4.57–4.58 (1H, m), 5.91–5.92 (1H, m); ^{13}C NMR (101 MHz, C_6D_6) δ 14.8, 23.5, 25.5, 28.0, 31.1, 35.4, 51.4, 72.2, 72.6, 119.0, 146.2, 196.5; MS(CI/Isobutane) *m/z* 197 ($M+H^+$); HRMS(CI/Isobutane) calcd for $C_{12}H_{21}O_2$ ($M+H^+$) 197.1542, found 197.1519.

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