

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

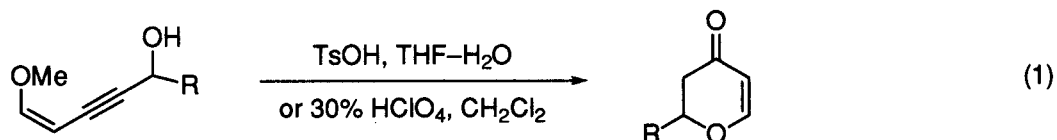
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Abstract– 5-Diphenylphosphinoyl-2,3-dihydropyran-4-ones are readily prepared from the corresponding 5-diphenylphosphinoyl-1-buten-3-yne under mild acidic conditions. The phosphorus substituted pyrones are converted to more substituted pyrones *via*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

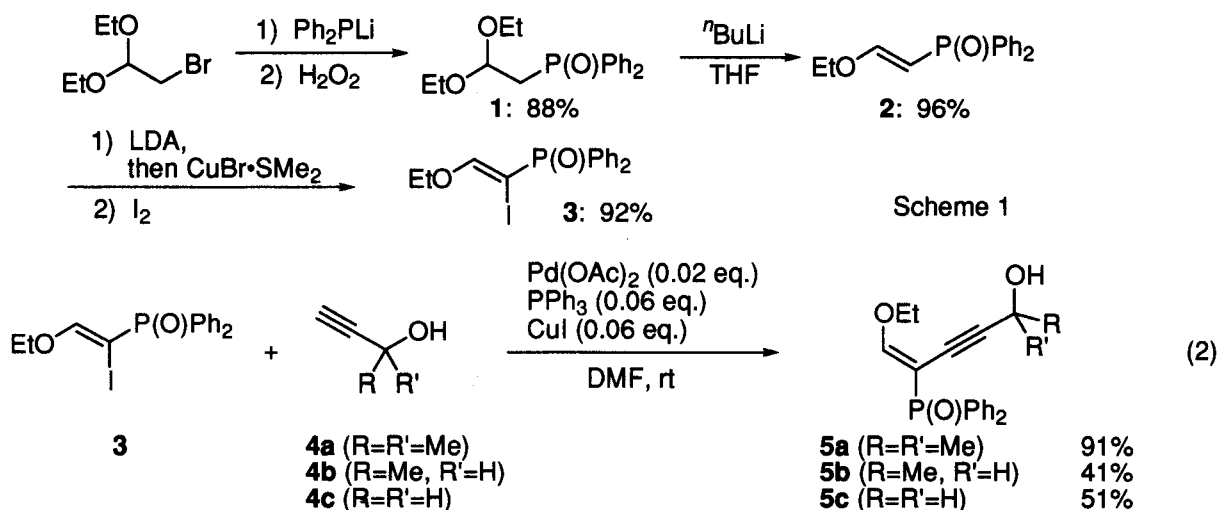
The tetrahydropyran moiety is found in a large number of natural products, and their syntheses appear a lot in the literatures.^{1,2} 2,3-Dihydropyran-4-ones have been widely used for the synthesis of functionalized tetrahydropyrans.³ There are, thus, many methods for preparation of the dihydropyrones,^{3–5} 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-yne 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.

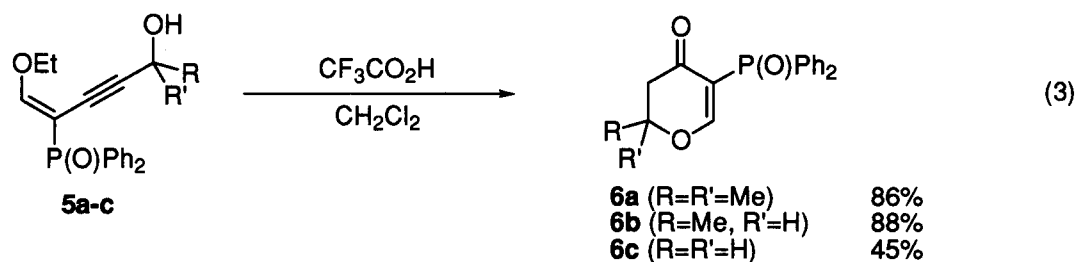


1-Diphenylphosphinyl-1-iodo-2-ethoxyethene (**3**) was prepared as shown in Scheme 1. Lithium diphenylphosphide was treated with 2-bromo-1,1-diethoxyethane, followed by oxidation of the phosphine with hydrogen peroxide to give the phosphine oxide (**1**). Base treatment of **1** led to β -ethoxy-vinylphosphine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

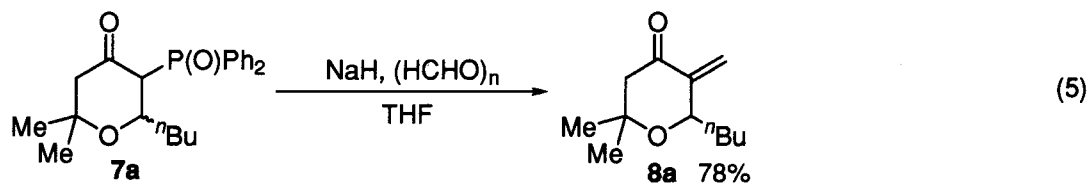
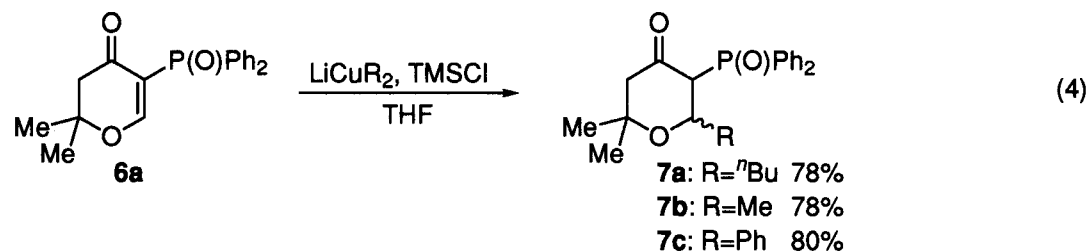
The phosphonovinyl iodide (**3**) was allowed to react with propargyl alcohols (**4a–c**) under conventional palladium-catalyzed cross-coupling conditions. While the coupling reaction of **3** with **4a** was satisfactory, with **4b** and **4c** it led to **5b** and **5c** in moderate yield (eq. 2).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



Next, we attempted the acid-catalyzed cyclization of **5a** according to Crimmins' procedure (TsOH·H₂O–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 CH₂Cl₂ 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**).



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).



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 $\text{Na}_2\text{S}_2\text{O}_3$ solution. After usual workup, the crude product was purified by column chromatography on silica gel ($\text{AcOEt}/\text{hexane} = 1/1$) to give **1** (12.2 g, 76%). **1**: white crystal; mp 86–89 °C ($\text{AcOEt}/\text{hexane}$); 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, $^2J_{\text{P-H}} = 11.3$ 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, $^1J_{\text{P-C}} = 71.2$ Hz), 62.5, 98.6, 128.3 (d, $^3J_{\text{P-C}} = 12.0$ Hz), 130.8 (d, $^2J_{\text{P-C}} = 9.4$ Hz), 131.5 (d, $^4J_{\text{P-C}} = 2.7$ Hz), 133.4 (d, $^1J_{\text{P-C}} = 101.1$ Hz); MS(FAB/NBA) m/z 319 ($\text{M}+\text{H}^+$); HRMS(FAB/NBA) calcd for $\text{C}_{18}\text{H}_{24}\text{O}_3\text{P}$ ($\text{M}+\text{H}^+$) 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 ($\text{AcOEt} : \text{hexane} = 4 : 1$) to give **2** (0.17 g, 0.62 mmol, 96%). **2**: colorless crystal; mp 140–141 °C ($\text{AcOEt}/\text{hexane}$); 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, $J = 13.7$, $^2J_{\text{P-H}} = 14.7$ Hz), 7.03 (1H, dd, $J = 13.7$ Hz, $^3J_{\text{P-H}} = 11.0$ 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, $^1J_{\text{P-C}} = 114.8$ Hz), 128.5 (d, $^3J_{\text{P-C}} = 12.4$ Hz), 131.2 (d, $^2J_{\text{P-C}} = 9.3$ Hz), 131.6 (d, $^4J_{\text{P-C}} = 3.0$ Hz), 134.0 (d, $^1J_{\text{P-C}} = 107.6$ Hz), 162.0 (d, $^2J_{\text{P-C}} = 15.6$ Hz). Anal. Calcd for $\text{C}_{16}\text{H}_{17}\text{O}_2\text{P}$: 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 $\text{Na}_2\text{S}_2\text{O}_3$ solution. After usual workup, the crude product was purified by column chromatography on silica gel ($\text{AcOEt}/\text{hexane} = 4/1$) to give **6** (3.0 g, 7.5 mmol, 92%). **3**: colorless crystal; mp 108–109 °C ($\text{AcOEt}/\text{hexane}$); 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, $^3J_{\text{P-H}} = 7.3$ 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, $^1J_{\text{P-C}} = 105.4$ Hz), 70.7, 128.4 (d $^3J_{\text{P-C}} = 12.4$ Hz), 130.9 (d, $^1J_{\text{P-C}} = 111.6$ Hz), 132.1 (d, $^4J_{\text{P-C}} = 2.1$ Hz), 132.6 (d, $^2J_{\text{P-C}} = 10.3$ Hz), 162.7 (d, $^2J_{\text{P-C}} = 21.7$ Hz). Anal. Calcd for $\text{C}_{16}\text{H}_{16}\text{O}_2\text{IP}$: 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 $\text{Pd}(\text{OAc})_2$ (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} ; ^1H 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, $^3J_{\text{P-H}} = 8.3$ 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, $^2J_{\text{P-C}} = 8.3$ Hz), 90.8 (d, $^1J_{\text{P-C}} = 116.7$ Hz), 102.9 (d, $^3J_{\text{P-C}} = 7.3$ Hz), 128.2 (d, $^3J_{\text{P-C}} = 12.4$ Hz), 131.9 (d, $^2J_{\text{P-C}} = 4.1$ Hz), 131.9 (d, $^4J_{\text{P-C}} = 3.0$ Hz), 132.4 (d, $^1J_{\text{P-C}} = 108.6$ Hz), 165.0 (d, $^2J_{\text{P-C}} = 17.6$ Hz). Anal. Calcd for $\text{C}_{21}\text{H}_{23}\text{O}_3\text{P}$: 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} ; ^1H 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, $^5J_{\text{P-H}} = 3.4$ Hz, $J = 6.7$ Hz), 7.40 (1H, d, $^3J_{\text{P-H}} = 8.2$ 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, $^2J_{\text{P-C}} = 8.0$ Hz), 92.0 (d, $^1J_{\text{P-C}} = 116.9$ Hz), 101.6 (d, $^3J_{\text{P-C}} = 7.0$ Hz), 128.4 (d, $^3J_{\text{P-C}} = 11.4$ Hz), 128.4 (d, $^3J_{\text{P-C}} = 12.4$ Hz), 131.7, 132.3 (d, $^2J_{\text{P-C}} = 9.0$ Hz), 134.0 (d, $^1J_{\text{P-C}} = 107.4$ Hz), 134.0 (d, $^1J_{\text{P-C}} = 107.6$ Hz), 165.9 (d, $^2J_{\text{P-C}} = 18.6$ Hz); MS(EI) m/z 341 (M^+); HRMS(EI) calcd for $\text{C}_{20}\text{H}_{22}\text{O}_3\text{P}$ 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} ; ^1H 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, $^5J_{\text{P-H}} = 4.0$ Hz), 7.37 (1H, d, $^3J_{\text{P-H}} = 8.3$ 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, $^4J_{\text{P-C}} = 2.0$ Hz), 71.4, 77.9 (d, $^2J_{\text{P-C}} = 8.2$ Hz), 90.9 (d, $^1J_{\text{P-C}} = 117.9$ Hz), 96.7 (d, $^3J_{\text{P-C}} = 7.3$ Hz), 128.3 (d, $^3J_{\text{P-C}} = 12.4$ Hz), 131.9 (d, $^2J_{\text{P-C}} = 10.4$ Hz), 132.0 (d, $^4J_{\text{P-C}} = 3.1$ Hz), 132.1 (d, $^1J_{\text{P-C}} = 108.4$ Hz), 165.7 (d, $^2J_{\text{P-C}} = 18.6$ Hz); MS(EI) m/z 326 (M^+); HRMS(EI) calcd for $\text{C}_{17}\text{H}_{15}\text{O}_3\text{P}$ 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/ $\text{CHCl}_3 = 1/2$). The cyclized products (6a–c) have the following physical properties.

5-Diphenylphosphoryl-2,2-dimethyl-2,3-dihydro-4H-pyran-4-one (6a). colorless crystal; mp 143–145 °C (AcOEt/hexane); IR (KBr) 1672, 1562, 1288 cm^{-1} ; ^1H 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, $^3J_{\text{P-H}} = 8.8$ Hz); ^{13}C NMR (126 MHz, CDCl_3) δ 26.2, 47.9 (d, $^3J_{\text{P-C}} = 6.2$ Hz), 83.7, 108.3 (d, $^1J_{\text{P-C}} = 118.0$ Hz), 128.3 (d, $^3J_{\text{P-C}} = 12.4$ Hz), 131.7 (d, $^2J_{\text{P-C}} = 10.4$ Hz), 131.9 (d, $^4J_{\text{P-C}} = 3.1$ Hz), 132.6 (d, $^1J_{\text{P-C}} = 109.7$ 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-4H-pyran-4-one (6b). colorless oil; IR (neat) 2929, 1675, 1560, 1436, 1276, 1174 cm^{-1} ; 1H 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-4H-pyran-4-one (6c). colorless oil; IR (neat) 1672, 1565, 1284, 1178 cm^{-1} ; 1H 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 $-78^\circ C$. The mixture was stirred at $-45^\circ C$ for 30 min, then cooled to $-78^\circ C$. 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 $-45^\circ C$ 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 $^\circ C$ (AcOEt/hexane); IR (KBr) 2921, 1718, 1436, 1180, 705 cm^{-1} ; 1H 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 $^\circ C$ (AcOEt/hexane); IR (KBr) 2975, 1718, 1436, 1180, 551 cm^{-1} ; 1H 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; ¹H NMR (400 MHz, CDCl₃) 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-H} = 8.8 Hz), 5.63 (1H, dd, *J* = 9.6 Hz, ³*J*_{P-H} = 8.2 Hz), 6.98–7.12 (7H, m), 7.23–7.48 (6H, m), 7.71–7.76 (2H, m); ¹³C NMR (126 MHz, CDCl₃) δ 27.2, 29.9, 52.0, 61.3 (d, ¹*J*_{P-C} = 53.8 Hz), 73.5, 75.9, 127.2, 128.0, 128.2 (d, ³*J*_{P-C} = 12.4 Hz), 128.2, 128.4 (d, ³*J*_{P-C} = 12.4 Hz), 130.4 (d, ¹*J*_{P-C} = 100.4 Hz), 130.6 (d, ²*J*_{P-C} = 9.3 Hz), 130.9 (d, ²*J*_{P-C} = 9.3 Hz), 131.2 (d, ¹*J*_{P-C} = 103.5 Hz), 131.4 (d, ⁴*J*_{P-C} = 3.1 Hz), 131.9 (d, ⁴*J*_{P-C} = 2.1 Hz), 140.0, 203.5 (d, ²*J*_{P-C} = 5.2 Hz); MS(EI) *m/z* 404 (M⁺); HRMS(EI) calcd for C₂₅H₂₅O₃P 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, paraformaldehyde (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; ¹H NMR (500 MHz, C₆D₆) 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); ¹³C NMR (101 MHz, C₆D₆) 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 C₁₂H₂₁O₂ (M+H⁺) 197.1542, found 197.1519.

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