Convenient Synthesis of (1-Alkyl-2-hydroxyethyl)diphenylphosphine Oxides

Mitsuji YAMASHITA,* Manabu YAMADA, Kenji TSUNEKAWA, and Saburo INOKAWA†

Department of Chemistry, Faculty of Engineering, Shizuoka University, Hamamatsu 432

† *Department of Chemistry, Faculty of Science, Okayama University, Okayama 700*

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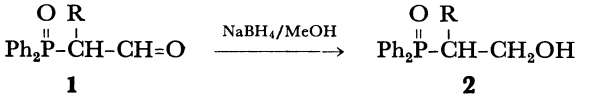
Synopsis. (1 - Alkyl - 2 - hydroxyethyl)diphenylphosphine oxides were synthesized from the corresponding (1-alkyl-2-oxoethyl)diphenylphosphine oxides in excellent yields. The structures of 2-hydroxy derivatives and their acetates were confirmed by elemental and spectral analyses.

We have recently reported the synthesis of diphenylphospine oxide derivatives having a nitro group on the β-carbon atom of phosphorus, *i.e.*, (1-alkyl-2-nitroethyl)diphenylphosphine oxides, and the conversion of the nitro compound into the aldehyde compound by oxidation with ozone/methoxide method.[1,2] The present note deals with a convenient method for the synthesis of (1-alkyl-2-hydroxyethyl)diphenylphosphine oxides,[3,4] which have the partial structure of a phosphorus-sugar derivative, from (1-alkyl-2-oxoethyl)diphenylphosphine oxides by reduction with sodium tetrahydridoborate, and their conversion into the acetates.

Results and Discussion

Aldehydes 1, which were prepared from (1-alkyl-2-nitroethyl)diphenylphosphine oxides,[2] were transformed into 2-hydroxyethyl compounds **2** in excellent yields by treatment with sodium tetrahydridoborate in methanol under reflux as shown in Table 1.[5] Compounds **2** were characterized by microanalysis, IR, ^{1}H NMR, and MS.

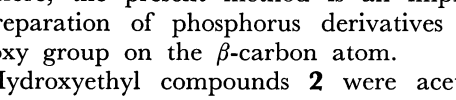


1 **2**

Yields of (2-hydroxyethyl)diphenylphosphine oxide derivatives were 31—81%[3] and 69—85%[4] in the reaction of lithium derivative of methyldiphenylphosphine oxide derivatives with carbonyl compounds such as aldehydes and ketones. 2-Hydroxyethylphosphonates were previously synthesized from vinylphosphonates by hydroboration in 50—65% yields.[6] Therefore, the present method is an improved one in preparation of phosphorus derivatives having a hydroxy group on the β-carbon atom.

2-Hydroxyethyl compounds **2** were acetylated in excellent yield with acetic anhydride in pyridine at room temperature.[7]

The structure of acetates **3** were determined by microanalysis, IR, ^{1}H NMR, and MS. The produced derivatives **3** clearly reconfirmed the structure of compounds **2**.



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The high yield and simple operation in preparation of (1-alkyl-2-hydroxyethyl)diphenylphosphine oxides show that the method provides a convenient preparative way to afford phosphorus compounds possessing a 2-hydroxyethyl group. This procedure will provide a new route to synthesize phosphorus-sugars.

Experimental

Apparatus. IR spectra were measured by a JASCO A-3 spectrophotometer. ^{1}H NMR spectra were run on a Hitachi R-20 (60 MHz) spectrometer. MS spectra were measured by a Hitachi RMU DMG GC-MS spectrometer. Liquid chromatography was carried out using a Toyo Scientific Industry UVICON-540M.

Materials. (1 - Alkyl - 2 - oxoethyl)diphenylphosphine oxides were prepared from (1-alkyl-2-nitroethyl)diphenylphosphine oxides.[2] Pyridine and acetic anhydride were purified before use.

*Synthesis of (2-Hydroxy-1-methylethyl)diphenylphosphine Oxide (**2a**, R=Me).* To a solution of (2-oxo-1-methylethyl)-diphenylphosphine oxide (**1a**, R=Me; 0.415 g, 1.6 mmol) in anhydrous methanol (25 ml) was added sodium tetrahydridoborate (0.612 g, 16 mmol) at room temperature, then the solution was refluxed for 16 h. A small amount of water was added to the reaction mixture and then it was refluxed for further 30 min. After the solution was neutralized with acetic acid, the solvent was removed off by a rotary evaporator and the residue was taken up into chloroform (40 ml). The chloroform solution was washed with water (20 ml×2) and dried over anhydrous sodium sulfate. Evaporation of the solvent *in vacuo* and recrystallization of the product from chloroform–cyclohexane gave (2-hydroxy-1-methylethyl)diphenylphosphine oxide (**2a**, 0.418 g) in 82% yield, mp 141—142 °C. ^{1}H NMR ($CDCl_3$) δ 1.22 (dd, J_{HH}=7.0 Hz, J_{HP}=16.0 Hz, CH_3), 2.4—3.0 (m, 1H, CH), 3.83 (dd, 2H, J_{HH}=5.0 Hz, J_{HP}=13.0 Hz, CH_2), 4.46 (s, 1H, OH), and 7.3—8.0 (m, 10H, Ph); IR ν_{max}^{KBr} 3200 cm^{-1} (OH); MS *m/e* 260 (M^+). Found: C, 68.96; H, 6.34%. Calcd for $C_{15}H_{17}O_2P$: C, 69.22; H, 6.58%. Found: *m/e* 260.0970. Calcd for $C_{15}H_{17}O_2P$: 260.0966.

*Synthesis of [1-(Hydroxymethyl)propyl]diphenylphosphine Oxide (**2b**, R=Et).* Treatment of a solution of **1b** (R=Et, 0.738 g, 2.71 mmol) in anhydrous methanol (25 ml) with sodium tetrahydridoborate (1.03 g, 27.1 mmol) followed by work-up and recrystallization from chloroform–cyclohexane gave product **2b** (0.660 g) in 89% yield, mp 105—106 °C. ^{1}H NMR ($CDCl_3$) δ 0.97 (t, 3H, J_{HH}=7.0 Hz, CH_3), 1.4—2.0 (m, 2H, J_{HH}=7.0 Hz, $CH_3C\underline{H}_2$), 2.1—2.7 (m, 1H, CH), 3.94 (dd, 2H, J_{HH}=5.0 Hz, J_{HP}=18.0 Hz, $C\underline{H}_2OH$), 5.77 (s, 1H, OH), and 7.4—8.1 (m, 10H, Ph); IR ν_{max}^{KBr} 3300 cm^{-1} (OH); MS *m/e* 274 (M^+). Found: C, 70.02; H, 6.93%. Calcd for $C_{16}H_{19}O_2P$: C, 70.06; H, 6.98%. Found: *m/e* 274.1138. Calcd for $C_{16}H_{19}O_2P$: 274.1123.

[1 - (Hydroxymethyl) - 2 - methylpropyl]diphenylphosphine oxide (**2c**, R=*i*-Pr) and (2-hydroxy-1-phenylethyl)diphenylphosphine oxide (**2d**, R=Ph) were synthesized by an analogous method mentioned above in 92 and 63% yields, respectively.

Table 1. Compounds **2** and **3** prepared

Product[a]	Yield/%	Mp θ_m/°C	MS *m/e*	IR ν_{max}^{KBr}/cm^{-1}	^{1}H NMR ($CDCl_3$) (δ)
2a; R=Me	82	141—142	260 (M^+)	3200 (OH) 1440 (P-Ph) 1160 (P=O) 720 (C-P)	1.22 (dd, 3H, J_{HH}=7.0 Hz, J_{HP}=16.0 Hz, CH_3), 2.4—3.0 (m, 1H, CH), 3.83 (dd, 2H, J_{HH}=5.0 Hz, J_{HP}=13.0 Hz, CH_2), 4.46 (s, 1H, OH), 7.3—8.0 (m, 10H, Ph)
2b; R=Et	89	105—106	274 (M^+)	3300 (OH) 1440 (P-Ph) 1170 (P=O) 720 (C-P)	0.97 (t, 3H, J_{HH}=7.0 Hz, CH_3), 1.4—2.0 (m, 2H, J_{HH}=7.0 Hz, $CH_3C\underline{H}_2$), 2.1—2.7 (m, 1H, CH), 3.94 (dd, 2H, J_{HH}=5.0 Hz, J_{HP}=18.0 Hz, $C\underline{H}_2OH$), 5.77 (s, 1H, OH), 7.4—8.1 (m, 10H, Ph)
2c; R=*i*-Pr	92	148	288 (M^+)	3350 (OH) 1440 (P-Ph) 1170 (P=O) 720 (C-P)	1.00 (d, 6H, J_{HH}=7.0 Hz, CH_3), 1.8—2.2 (m, 1H, $Me_2C\underline{H}$), 2.2—2.7 (m, 1H, P-CH), 3.99 (dd, 2H, J_{HH}=5.0 Hz, J_{HP}=16.0 Hz, CH_2), 4.60 (s, 1H, OH), 7.3—8.1 (m, 10H, Ph)
2d; R=Ph	63	168—170	322 (M^+)	3400 (OH) 1440 (P-Ph) 1170 (P=O) 720 (C-P)	3.14 (s, 1H, OH), 3.6—4.4 (m, 3H, $C\underline{H}C\underline{H}_2$), 7.0—8.1 (m, 15H, Ph)
3a; R=Me	99	133—134	302 (M^+)	1740 (C=O) 1440 (P-Ph) 1180 (P=O) 720 (C-P)	1.20 (dd, 3H, J_{HH}=7.0 Hz, J_{HP}=16.0 Hz, CH_3), 1.79 (s, 3H, CH_3CO), 2.7—3.2 (m, 1H, J_{HH}= 7.0 Hz, CH), 4.1—4.52 (m, 2H, CH_2), 7.3—8.1 (m, 10H, Ph)
3b; R=Et	80	108—109	316 (M^+)	1738 (C=O) 1440 (P-Ph) 1180 (P=O) 720 (C-P)	0.99 (t, 3H, J_{HH}=7.0 Hz, CH_3), 1.1—1.9 (m, 2H, $CH_3C\underline{H}_2$), 1.72 (s, 3H, CH_3CO), 2.4—3.0 (m, 1H, CH), 4.43 (dd, 2H, J_{HH}=7.0 Hz, J_{HP}= 13.0 Hz, CH_2O), 7.2—8.1 (m, 10H, Ph)
3c; R=*i*-Pr	99	157—158	330 (M^+)	1740 (C=O) 1440 (P-Ph) 1178 (P=O) 720 (C-P)	1.09 (d, 6H, J_{HH}=7.0 Hz, CH_3), 1.69 (s, 3H, CH_3CO), 2.0—2.4 (m, 1H, $Me_2C\underline{H}$), 2.5—3.0 (m, 1H, P-CH), 4.48 (dd, 2H, J_{HH}=7.0 Hz, J_{HP}=13.0 Hz, CH_2), 7.3—8.1 (m, 10H, Ph)

a) Satisfactory micro and milimass analyses were obtained.

*Synthesis of (2-Acetoxy-1-methylethyl)diphenylphosphine Oxide (**3a**, R=Me).* To a solution of **2a** (0.290 g, 1.1 mmol) in anhydrous pyridine (5 ml) was added acetic anhydride (3 ml), and the solution was stood for 24 h at room temperature. The reaction mixture was taken up into chloroform (40 ml). The extract was washed with water (20 ml × 2) and was dried over anhydrous sodium sulfate. Evaporation of the solvent *in vacuo* and recrystallization of the product from carbon tetrachloride–cyclohexane gave **3a** (0.335 g) in 99% yield, mp 133—134 °C. ^{1}H NMR ($CDCl_3$) δ 1.22 (dd, 3H, J_{HH}=7.0 Hz, J_{HP}=16.0 Hz, CH_3), 1.79 (s, 3H, CH_3CO), 2.7—3.2 (m, 1H, J_{HH}=7.0 Hz, CH), 4.1—4.52 (m, 2H, CH_2), and 7.3—8.1 (m, 10H, Ph); IR ν_{max}^{KBr} 1740 cm^{-1} (CO); MS *m/e* 302 (M^+). Found: C, 67.47; H, 6.17%. Calcd for $C_{17}H_{19}O_3P$: C, 67.54; H, 6.33%. Found: *m/e* 302.1091. Calcd for $C_{17}H_{19}O_3P$: 302.1110.

*Synthesis of [1-(Acetoxymethyl)propyl]diphenylphosphine Oxide (**3b**, R=Et).* Treatment of **2b** (0.280 g, 1.02 mmol) in pyridine (5 ml) with acetic anhydride (3 ml) followed by work-up and recrystallization from carbon tetrachloride–cyclohexane gave product **3b** (0.256 g) in 80% yield, mp 108—109 °C. ^{1}H NMR ($CDCl_3$) δ 0.99 (t, 3H, J_{HH}=7.0 Hz, CH_3), 1.1—1.9 (m, 2H, $CH_3C\underline{H}_2$), 1.72 (s, 3H, CH_3CO), 2.4—3.0 (m, 1H, CH), 4.43 (dd, 2H, J_{HH}=7.0 Hz, J_{HP}= 13.0 Hz, CH_2O), and 7.2—8.1 (m, 10H, Ph); IR ν_{max}^{KBr} 1738 cm^{-1} (CO); MS *m/e* 316 (M^+). Found: C, 68.33; H, 6.50%. Calcd for $C_{18}H_{21}O_3P$: C, 68.34; H, 6.69%. Found: *m/e* 316.1259. Calcd for $C_{18}H_{21}O_3P$: 316.1228.

[1-(Acetoxymethyl)-2-methylpropyl]diphenylphosphine oxide (**3c**, R=*i*-Pr) was synthesized by an analorous method mentioned above in 99% yield.

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