ISSN 1070-3632, Russian Journal of General Chemistry, 2009, Vol. 79, No. 9, pp. 1934–1935. © Pleiades Publishing, Ltd., 2009.
Original Russian Text © O.I. Kolodyazhnyi, 2009, published in Zhurnal Obshchei Khimii, 2009, Vol. 79, No. 9, pp. 1578–1579.

LETTERS TO THE EDITOR

Method of Ketone Hydrophosphorylation

O. I. Kolodyazhnyi

Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine,
Murmanskaya ul. 1, Kiev, 02094 Ukraine
fax: 38(044)573-2555
e-mail: olegkol321@rambler.ru

Received December 8, 2008

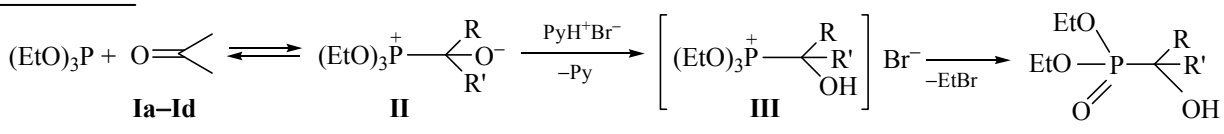
DOI: 10.1134/S1070363209090229

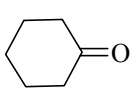
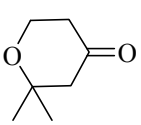
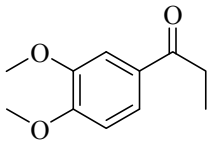
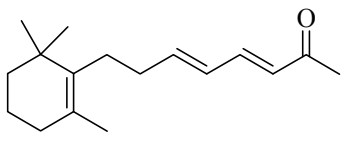
Aldehydes and occasionally activated ketones are readily phosphonylated under the Abramov reaction condition, the most important method of synthesis of hydroxyphosphonates. The reaction with non-activated ketones does not generally proceed [1, 2]. We found a convenient method of ketone hydroxyphosphonylation using trialkylphosphite-pyridinium bromide reaction pair. This method allows a successful hydrophosphonylation in high yields both of the simple ketones **Ia** and ketones of the complex nature like **Ic–Id**.

The reaction was carried out in methylene chloride solution at room temperature or at slight heating. The high activity of the reaction pair is due to the easy deprotonation of the intermediate betaine **II** with pyridinium bromide. Moreover, the bromine ion readily dealkylates the phosphonium group in the intermediate compound **II**. The scheme given below is conform to the generally accepted mechanism of phospho-aldol reaction [2, 3]. Some typical experimental examples demonstrating the efficiency of this method are cited below. The more detailed description of this method and its use for synthesis of analogs of natural compounds will be reported later.

Diethyl 1-hydroxycyclohexylphosphonate (IVa). A solution of 1g of cyclohexanol, 2.25 g of triethylphosphite, and 1.6 g of pyridinium bromide in 3 ml of methylene chloride was stirred for 6 h at 40°C. Then the solvent was removed. The residue was dissolved in 5 ml of ether, filtered off, evaporated, and distilled in a vacuum. Yield 80%, mp 120°C (0.1 mm Hg). Then the product was recrystallized from hexane at 0°C. Prismes, mp 61–63°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.3 t (6H, C*H*$_3$CH$_2$,*J* 7.2 Hz), 1.52 m (2H, CH_2), 1.66 m (4H, CH_2), 1.87 m (4H, CH_2), 3.6 br. (1H, OH), 4.16 d.q (4H, OCH$_2$,*J* 7 Hz, *J* 8 Hz). ^{31}P ($CDCl_3$), δ, ppm: 26.93. Found, %: C 50.62; H 8.91; P 13.09. $C_{10}H_{21}O_4P$. Calculated, %: C 50.84; H 8.96; P 13.11.

Diethyl 4-hydroxy(tetrahydro-2,2-dimethyl-2*H*-pyran-4-yl)phosphonate (IVc). A mixture of 0.9 g of ketone **Ib**, 1.2 g of triethylphosphite, and 1.2 g of pyridinium bromide was heated at 50–60°C (temperature of oil bath) overnight. Then the volatile products were evaporated and the residue was distilled in a vacuum and recrystallized from cooled (0°C) hexane. Yield 80%, bp 130–135°C (0.08 mm Hg), mp 72–75°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.19 s



RR'C=O =  (**a**),  (**b**),  (**c**),  (**d**).

(3H, $[(CH_3)_2C]$, 1.43 s (3H, $[CH_3)_2C]$, 1.64-19 m (4H, CH_2), 3.65 m (2H CH_2O), 3.95 br. (1H, OH), 3.65 m (1H, CH_2), 4.05 m (1H, CH_2), 4.15 d. q (4H, CH_3CH_2O, *J* 7 Hz, *J* 8 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ, ppm: +23.6. Found, %: P 11.63. $C_{11}H_{23}O_5P$. Calculated, %: P 11.63.

Diethyl [1-(3,4-dimethoxyphenyl)-1-hydroxypropyl]phosphonate (IVd) was prepared similarly. The product was purified by column chromatography, eluent ethyl acetate-hexane (1:1). Yield 60%, R_f 0.33. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.77 t (3H, CH_3, *J* 7.2 Hz); 1.15 t (3H, CH_3CH_2O, *J* 7.2 Hz), 1.27 t (3H, CH_3CH_2O, *J* 7.2 Hz); 2.13 d. q (1H, *J* 7 Hz, *J* 8 Hz), 2.24 d.q (1H, *J* 7 Hz, *J* 8 Hz), 3.87 s and 3.89 s (3H, CH_3O), 4.1 m (4H, CH_2O), 6.9–7.5 m (3H, C_6H_3). ^{31}P NMR spectrum ($CDCl_3$), δ_P, ppm: +24.3. Found, %: P 9.32. $C_{15}H_{25}O_6P$. Calculated, %: P 9.32.

Diethyl [(2*E*,4*E*)-1-hydroxy-1,5-dimethyl-7-(2,6,6-trimethyl-1-cyclohexyl)-2,4-heptadienyl]phosphonate (IVe) was prepared similarly. The product was purified by column chromatography, eluent ethyl acetate-hexane (1:1). R_f 0.3. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.8 m (3H, CH_3), 0.9 m (3H, CH_3), 1.32 t (6H, CH_3CH_2), 1.5 s (3H, CH_3), 1.6 s (3H, CH_3), 1.4–1.9 m (13H, CH_2), 2.25 d (3H, CH_3), 4,17 d.q (4H, CH_2O, *J* 8 Hz, *J* 8 Hz), 5.7 d. d (1H, *J* 4.5 Hz, *J* 16 Hz), 5.9 d. d (1H, CH=C, *J* 10.5Hz, *J* 13.5 Hz), 6.65 d. d. d (1H, CH=C, *J* 4.5 Hz, *J* 10.5 Hz, *J* 15 Hz). ^{31}P NMR spectrum ($CDCl_3$), δ, ppm: +24.5. Found, %: C 66.00; H 9.55; P 7.41. $C_{22}H_{39}O_4P$. Calculated, %: C 66.30; H 9.86; P 7.77.

The NMR spectra were registered on a Varian-300 device, internal reference TMS (^1H and ^{13}C),external reference 85% H_3PO_4 in D_2O (^{31}P).

REFERENCES

1. Abramov, V.S., *Khimiya i primeneniye fosfororganicheskikh soedinenii* (Chemistry and Application of Organophosphorus Compounds), Moscow, 1957, p. 218.
2. Engel, R., *Phosphorus Addition at sp^2 Carbon. Organic Reactions*, New York: Wiley, 1988, vol. 50, p. 176.
3. Kolodyazhnyi, O.I., *Usp. Khim*., 2006, vol. 75, no. 3, p. 254.