Russian Journal of General Chemistry, Vol. 74, No. 6, 2004, pp. 965–966. Translated from Zhurnal Obshchei Khimii, Vol. 74, No. 6, 2004, pp. 1045–1046.

LETTERS TO THE EDITOR

Asymmetric Synthesis of (1*S*,2*R*)-(1,2,3-Trihydroxypropyl)diphenylphosphine Oxide

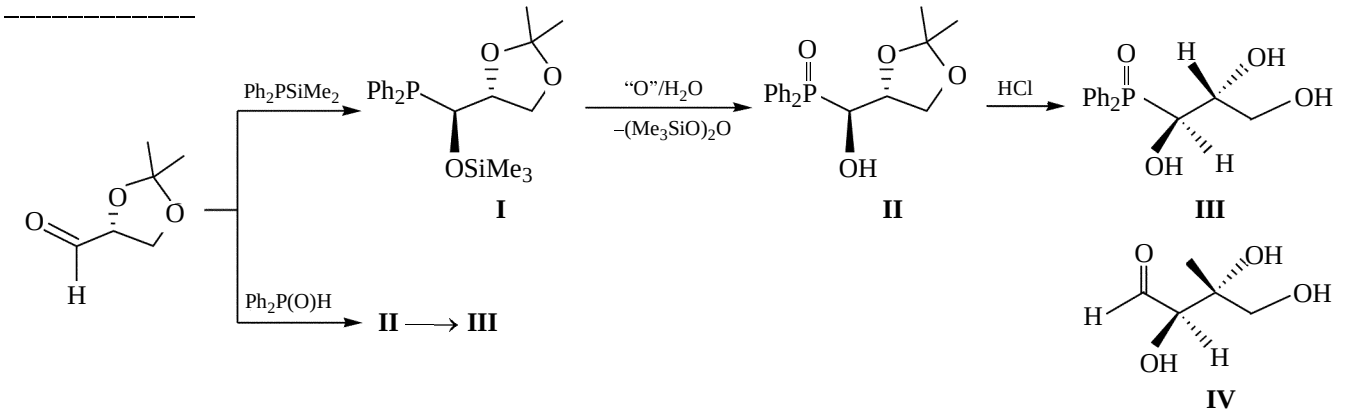
A. O. Kolodyazhnaya, V. P. Kukhar', and O. I. Kolodyazhnyi

Institute of Bioorganic and Oil Chemistry, National Academy of Sciences of Ukraine, Kiev, Ukraine

Received October 21, 2003

Hydroxyphosphonic acids and organophosphorus structural analogs of carbohydrates attract great interest as potentially biologically active compounds [1]. In the present work we have performed an asymmetric synthesis of (1*S*,2*R*)-(1,2,3-trihydroxypropyl)-diphenylphosphine oxide (**III**), a structural analog of the linear form of erythrose **IV**.

Addition of diphenyl(trimethylsilyl)phosphine to acetonide of (*R*)-glyceraldehyde proceeds stereoselectively to form a diastereomerically enriched [1-hydroxy-2,3-(isopropylidenedioxy)propyl]diphenylphosphine (**II**) in high yield. Subsequent removal of the acetonide group with hydrochloric acid in dioxane gave (1,2,3-trihydroxypropyl)diphenylphosphine oxide (**III**).



Phosphaldol addition (Abramov reaction) of diphenylphosphine oxide to acetonide of (*R*)-glyceraldehyde, too, leads to formation of compound **II**, but the stereoselectivity of this reaction is lower and depends on the solvent, temperature, and base catalyst [2, 3]. The highest stereoselectivity was achieved by performing the reaction in THF in the presence of a catalytic amount of alkali (potassium hydroxide, 2–3 mol%) (de ~75%). If 1,8-diazabicyclo[5.4.0]undec-7-ene was used as catalyst (~3 mol%) the stereoselectivity was 60% in toluene, 50% in benzene, 40% in diethyl ether, and 30% in methylene chloride.

The optical purity of diastereomers **I**–**III** was established by means of the $^{31}P–\{^1H\}$ NMR spectra. The *anti* configuration of the major phosphaldol diastereomer **II** was assessed by NMR: The high $^3J_{HH}$ and low $^2J_{HP}$ constants point to an *anti* conformation of the H–C^1–C^2–H and O=P–C^1–H bonds. The *anti* diastereomer [proposed absolute configuration (1*S*,2*R*)] was purified by crystallization from toluene and isolated optically pure. The *syn* diastereomer was characterized spectroscopically.

[1-Hydroxy-2,3-(isopropylidenedioxy)propyl]diphenylphosphine (I). Acetonide of (*R*-glyceraldehyde (0.01 mol) was added at 0°C to 0.01 mol of diphenyl(trimethylsilyl)phosphine, and the mixture was left to stand for 1–2 h at this temperature. A colorless liquid easily oxidized in air was obtained. Yield 80%, $[\alpha]_D^{20}$

1070-3632/04/7406-0965

–7 (*c* 4, toluene). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: –0.02 s (CH_3Si), 1.33 s (CH_3), 4.49 m (OCH_2CH), 4.72 m (CH_2CHO), 4.99 m (PCH), 7.5 m, 7.9 m (C_6H_5). ^{31}P NMR spectrum ($CHCl_3$), δ_P: –7.69; –10.62 ppm (11 : 1 ratio).

[1-Hydroxy-2,3-(isopropylidenedioxy)propyl]diphenylphosphine oxide (II). *a*. Compound **I** was left for 12 h in air for oxidation. The crystalline product that formed was crystallized from toluene. Yield 65%, mp 165–167°C, $[\alpha]_D^{20}$ +11 ($CHCl_3$, *c* 1.5).

b. Diphenylphosphine oxide, 0.01 mol, was dissolved in 5 ml of toluene, and 0.011 mol of acetonide of (*R*)-glyceraldehyde was added. The resulting mixture was cooled to 0°C and treated with several drops of 1,8-diazabicyclo[4,5,0]-undec-7-ene. After keeping for 12 h at 0°C, the solvent was removed in a vacuum, and the residue was crystallized from toluene.

***anti* Diastereomer.** Yield 60%. mp 167°C, $[\alpha]_D^{20}$ +11 ($CHCl_3$, *c* 2). ^{1}H NMR spectrum ($CDCl_3$). δ, ppm (*J*, Hz): 1.17 s (Me_2C^a), 1.20 s (Me_2C^b), 3.88 d (C^aH_2, J 2), 3.90 d (C^bH_2, J 1.5), 4.39 d.t ($OCHCH_2$, *J* 6.5, *J* 2), 4.59 d.d (PCH, *J* 5, *J* 0.9), 4.4 m (OH), 7.8 m (4H), 7.49 m (6H), ^{31}P NMR spectrum ($CHCl_3$): δ_P 30.87 ppm.

***cis* Diastereomer.** ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.14 s [$(CH_3)_2C^a$], 1.23 s [$(CH_3)_2C^b$], 3.99 s, 3.90 s (CH_2), 4.39 d.t ($OCHCH_2$, *J* 6.5, *J* 2), 4.4 br. (OH), 4.59 d.d (PCH, *J* 5, J_{HP} 5), 7.8 m (4H), 7.49 m (6H). ^{31}P NMR spectrum ($CHCl_3$), δ_P 29.45 ppm. Found, %: P 9.55. $C_{18}H_{21}O_4P$. Calculated, %: P 9.32.

(1,2,3-Trihydroxypropyl)diphenylphosphine oxide (III). Compound **II**, 0.5 g, was dissolved in 4–5 ml of dioxane, and 2 ml of concentrated hydrochloric acid was added to the obtained solution. The mixture was left overnight at room temperature. The solvent was then removed, and the residue was crystallized from chloroform or chloroform–hexane. Yield 50%, mp 151°C. $[\alpha]_D^{20}$ +5 (*c* 2, $CHCl_3$). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 3.61 d (2H, $CHCH_2OH$, J_{HH} 1), 3.77 br (1H, $CHCH_2$), 4.48 d (1H, PCH, J_{HP} 7.5), 4.62 br (3H, OH), 7.48 m (6H, C_6H_5, 7.84 m (4H, C_6H_5). ^{31}P NMR spectrum ($CHCl_3$): δ_P 35 ppm. Found, %: P 10.50. $C_{15}H_{17}O_4P$. Calculated, %: P 10.60.

The experimental conditions are identical to those described in [3].

The NMR spectra were recorded on a Varian-300 spectrometer against internal TMS (^{1}H, ^{13}C) and 85% phosphoric acid in D_2O (^{31}P). The optical rotations were measured on a Perkin–Elmer polarimeter.

REFERENCES

1. Hilderbrand, R.L., *The Role of Phosphonates in Living Systems*, Boca Raton: CRS, 1983.

2. Kolodiazhnyi, O.I., *Tetrahedron: Asymmetry*, 1998, vol. 9, no. 8, p. 1279.

3. Kolodiazhnyi, O.I., Grishkun, E.V., and Sheiko, S., *Heteroatom. Chem.*, 2000, vol. 11, p. 138.