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LETTERS TO THE EDITOR

Chiral Phosphonium Salts

O. O. Kolodyazhnaya and O. I. Kolodyazhnyi

Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine, ul. Murmanskaya 1, Kiev, 02094 Ukraine
e-mail: olegkol321@rambler.ru

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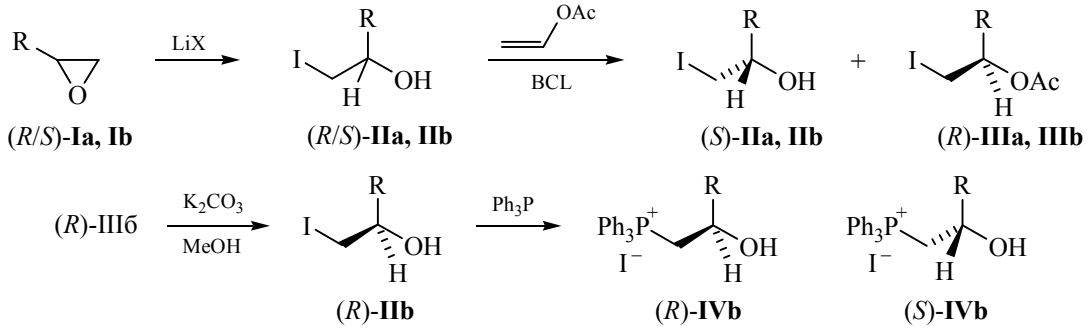
We have synthesized phosphonium salts containing an asymmetric center in the side chain, which are interesting chiral reagents for organic synthesis [1, 2]. Phosphonium salts **IV** were synthesized starting from racemic iodohydrins **II**, whose biocatalytic resolution resulted in two racemates. The racemic iodohydrins **IIa** and **IIb** were prepared by the reaction of epoxides **Ia** and **Ib** with lithium halides in methylene chloride in the presence of wet silica gel [3].

The halohydrins obtained were separated into the enantiomers via the kinetically controlled transesterification with vinyl acetate in the presence of a biocatalyst, *Burkholderia cepacia* lipase (BCL) [4, 5]. The reaction was stopped at 50% conversion.

Under these conditions the alcohols (*S*)-**II** and acetates (*R*)-**III** were obtained with 99% *ee* and the enantioselectivity factor >100. The alcohols and acetates were resolved chromatographically on a silica gel and distilled under vacuum. The hydrolysis of acetate (*R*)-**IIIb** by treating with potassium carbonate in methanol afforded the second enantiomer (*R*)-**IIb**. Optical purity and absolute configuration of the enantiomeric halohydrins (*S*)-**IIa**, **IIb,** and (*R*)-**IIa**, **IIb** were determined using Mosher's acid [6]. The absolute configuration was confirmed by the chemical correlation via the transformation of these compounds into the previously described chiral epoxides **Ia** and **Ib** [7]. Thus, the kinetically controlled biocatalytic esterification of iodohydrins **II** with vinyl acetate proceeds in accordance with the Kazlauskas rule [8].

In the final stage the iodohydrins were heated for several hours in the presence of triphenylphosphine in tetrahydrofuran to obtain the chiral phosphonium salt (*S*)- and (*R*)-**IVb** in high yields. When the reaction was carried out in toluene only triphenylphosphonium diiodide and traces of the phosphonium salt **IV** formed.

(*S*)-(+)-1-Iodopropan-2-ol (*S*)-IIa. To a solution of 2.5 g of racemic 1-iodo-2-propanol [2] in 5 ml of vinyl acetate and 5 ml of toluene was added 0.15 g of lipase. The mixture was stirred at 24°C until the reaction reached 50% conversion (~5 h). Then the lipase was filtered off, the volatiles were evaporated, and the residue was column chromatographed using an ethyl acetate–hexane as eluent. In the first fraction (*R*)-(–)-acetate **III** was obtained and in the second, the alcohol (*S*)-(+)-**IIa**. Yield 50%, bp 80–90°C (10 mm Hg),



R = Me (**a**), Et (**b**).

$[\alpha]_D^{20}$ +20 ($CHCl_3$, *c* 5). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.31 d (3H, *J* 7), 2.2 br. s (1H, OH), 3.23 m and 3.36 m (2H, CH_2I), 3.77 m (1H, CHOH). Found, %: C 19.42; H 3.829. C_3H_7IO. Calculated, %: C 19.37; H 3.79.

(*R*)-(–)-2-Iodo-1-methylethylacetate (*R*)-IIIa. Yield 50%, bp 75–80°C (10 mm Hg). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.31 d (3H, CH_3, *J* 7), 2.20 br.s (3H, OH), 3.4 m and 3.36 m (2H, CH_2I), 3.6 m (1H, CHOH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm (*J*, Hz): 10.50 (CH_3), 20.60 (CH_2I), 21.56 ($\underline{C}H_3CO$), 27.07 ($\underline{C}H_2CH_3$), 71.43 (CHOH), 171.37 (C=O). Found, %: C 26.42; H 4.01. $C_5H_9IO_2$. Calculated, %: C 26.34; H 3.98.

(*R*)-(–)-1-Iodopropan-2-ol (*R*)-IIa. Yield 50%, bp 90°C (10 mm Hg), $[\alpha]_D^{20}$ –19 (*c* 5, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.31 д (3H, *J* 7), 2.2 br.s (1H, OH), 3.23 m and 3.36 m (2H, CH_2I), 3.77 m (1H, CHOH). Found, % C 19.17; H 3.78. C_3H_7IO. Calculated, %: C 19.37; H 3.79.

(*S*)-(+)-1-Iodobutan-2-ol (*S*)-IIb. Yield 50%, bp 90–95°C (10 mm Hg), $[\alpha]_D^{20}$ +24 (*c* 8, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.00 t (3H, CH_3, *J* 7.5), 1.60 m (2H, CH_2), 2.15 br.s (1H, OH), 3.24 m and 3.33 m (2H, CH_2I), 3.42 m (1H, CHOH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.9 (CH_3), 15.9 (CH_2I), 29.5 ($\underline{C}H_2CH_3$), 72.2 (CHOH). Found, %: C 24.09; H 4.65. C_4H_9IO. Calculated, %: C 24.02; H 4.54.

(*R*)-(–)-1-(Iodomethyl)propyl acetate (*R*)-IIIb. Yield 50%, bp 85–90°C (10 mm Hg). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 7.67 (CH_3), 9.35 (CH_2I), 21.06 (CH_2), 27.07 (CH_3CO), 73.33 (CHOH), 170.37 (C=O). Found, % C 29.77; H 4.58. $C_6H_{11}IO_2$. Calculated, %: C 29.77; H 4.58.

(*R*)-(–)-1-Iodobutan-2-ol (*R*)-IIb. Yield 50%, bp 90–95°C (10 mm Hg), $[\alpha]_D^{20}$ –22 (*c* 8, $CHCl_3$). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.98 t (3H, CH_3, *J* 7.5), 1.60 m (2H, CH_2), 2.10 br.s (1H, OH), 3.27 d and 3.41 d (2H, CH_2I, *J* 6.6), 3.50 m (1H, CHOH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 9.95 (CH_3), 15.92 (CH_2I), 29.50 (CH_2CH_3), 72.25 (CHOH). Found, %: C 23.92; H 4.59. C_4H_9IO. Calculated, %: C 24.02; H 4.54.

Triphenyl-[(*R*)-2-hydroxybutyl]phosphonium iodide (*R*)-IVa. A solution of iodohydrin (2 g, 10 mmol) and triphenylphosphine (6 g, 20 mmol) in anhydrous THF (20 ml) was refluxed for 90 h. Then the phosphonium salt was filtered off. Yield 3.1 g (70%), mp > 200°C, $[\alpha]_D^{20}$ –50 (*c* 2, MeOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 0.99 t (3H, CH_3, *J* 7.5), 1.90 m and 2.00 m (2H, CH_2), 3.9 m (1H, CHOH), 4.00 m (1H, PCH_2), 7.60–7.70 m and 7.75–7.9 m (15H, C_6H_5). ^{31}P NMR spectrum ($CDCl_3$): δ_P 24.5 ppm. Found, %: C 57.19; H 59.48. $C_{22}H_{24}IOP$. Calculated, %: C 57.16; H 5.23.

Triphenyl-[(*S*)-2-hydroxybutyl]phosphonium iodide (*S*)-IVb was obtained analogously. Yield 70%, $[\alpha]_D^{20}$ +52 (*c* 2, MeOH). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.00 t (3H, CH_3, *J* 7.5), 1.99 m and 2.10 m (2H, CH_2), 3.90 m (1H, CHOH), 4.10 m (1H, PCH_2), 7.65 m (6H) and 7.8 m (9H, C_6H_5). ^{31}P NMR spectrum ($CDCl_3$): δ_P 24.5 ppm. Found, %: C 57.19; H 5.45. $C_{22}H_{24}IOP$. Calculated, %: C 57.16; H 5.23.

The NMR spectra were recorded on a Varian-300 spectrometer relative to internal TMS (^1H and ^{13}C) and external 85% H_3PO_4 (^{31}P).

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