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LETTERS TO THE EDITOR

Optically Active 2-(1-Phenylethyl)aminoethylphosphonates

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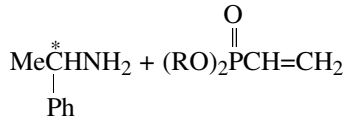
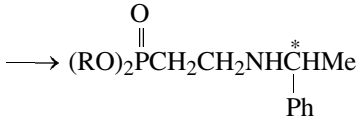
Aminophosphonic acids are direct analogs of natural amino acids constituting building blocks of peptides and proteins, and they demonstrate broad and diverse biological activity [1]. It is enough to mention that the first amino acid found in the nature was 2-aminoethylphosphonic acid [2]. In recent years, considerable attention has been given to the synthesis of enantiopure organophosphorus compounds because of their possible application as biologically active compounds and ligands for homogeneous and heterogeneous catalysts [1, 3, 4]. It is known that secondary amines smoothly add to dialkyl vinylphosphonates to form β-aminoalkylphosphonates [5]. The similar reaction with ammonia proceeds in the presence of sodium ethoxide only [6, 7].

We established that racemic and *R*-(+)-phenylethylamines **Ia**, **Ib** add to vinylphosphonates **IIa**, **IIb** in the absence of catalyst to give 2-aminoethylphosphonates **IIIa**–**IIId**.



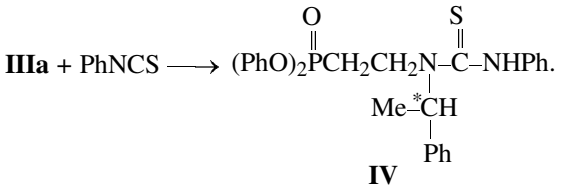
Ia, Ib **IIa, IIb**



IIIa–**IIId**

I, racemic (**a**), *R*-(+) (**b**); **II**, R = Et (**a**), Ph (**b**); **III**, R = Et (**a**); Et, *R*-(+) (**b**), Ph (**c**), Ph, *R*-(+) (**d**).

Note that the facility of the reaction depends on the nature of substituents at the phosphorus atom. Thus, the addition of amines to diphenyl phosphonate **IIb** readily occurs at 20°C, whereas their addition to diethyl phosphonate **IIa** requires a few hours to occur. The addition of aminophosphonate **IIId** to phenyl isothiocyanate results in the preparation of an enantiopure phosphorus-containing urea **IV**.



IV

Diethyl 2-(1-phenylethylamino)ethylphosphonate (IIIa). A mixture of 4.1 g of vinylphosphonate **IIa** and 6.0 g of amine **Ia** was kept for 2 h at 100°C. Distillation of the mixture gave 3.4 g (47%) of compound **IIIa**, bp 138°C (0.08 mm Hg). IR spectrum (KBr), ν, cm^{-1}: 1226, 1247 (P=O), 3305, 3443 (NH). ^1H NMR spectrum ($CDCl_3$), δ, ppm, (*J*, Hz): 1.27 d.t (6H, CH_3CH$_2$, $^3J_{HH}$ 7.0, $^4J_{HP}$ 2.1), 1.40 d (3H, CH_3, $^3J_{HH}$ 7.1), 1.98 m (2H, CH_2P), 2.85 m (2H, CH_2N), 3.82 q (1H, CHN, $^3J_{HH}$ 7.0), 4.06 m (4H, CH_2O), 7.15–7.18 m (5H, Ph). Found, %: N 4.88; P 10.65. $C_{14}H_{24}NO_3P$. Calculated, %: N 4.91; P 10.88.

Diethyl *R*-(+)-2-(1-phenylethylamino)ethylphosphonate (IIIb) was prepared similarly from 4.1 g of vinylphosphonate **IIb** and 6.0 g of amine **Ib**, yield 3.9 g (55%), bp 143°C (0.08 mm Hg), n_D^{20} 1.4877, $[\alpha]_D^{20}$ +35.1 (*c* 0.429, CH_2Cl_2). IR spectrum (KBr), ν, cm^{-1}: 1228, 1249 (P=O), 3305, 3443 (NH). ^1H NMR spectrum ($CDCl_3$), δ, ppm, (*J*, Hz): 1.25 d.t (6H, CH_3CH$_2$ $^3J_{HH}$ 7.0, $^4J_{HP}$ 2.1), 1.32 d (3H, CH_3, $^3J_{HH}$ 7.0), 1.94 m (2H, CH_2P), 2.08 br.s (1H, NH), 2.71 m (2H, CH_2N), 3.84 q (1H, CHN, $^3J_{HH}$ 7.0),

4.03 m (4H, CH_2O), 7.19–7.28 m (5H, Ph). ^{31}P NMR spectrum, δ_P, ppm: 30.41.

Diphenyl 2-(1-phenylethylamino)ethylphosphonate (IIIc). A mixture of 5.2 g of phosphonate **IIb** and 4.8 g of amine **Ia** was kept for 48 h at 20°C. Excess amine was then removed in a vacuum, and the residue was distilled in a vacuum to obtain 4.8 g (63%) of compound **IIIc**, bp 180–185°C (0.1 mm Hg). ^1H NMR spectrum ($CDCl_3$), δ, ppm, (*J*, Hz): 1.39 d (3H, CH_3, $^3J_{HH}$ 7.0), 2.31 m (2H, CH_2P), 2.97 m (2H, CH_2N), 3.83 q (1H, CHN, $^3J_{HH}$ 7.0), 7.17 m (5H, Ph), 7.38 m (10H, Ph). ^{31}P NMR spectrum, δ_P, ppm: 23.99. Found, %: N 3.61; P 7.97. $C_{22}H_{24}NO_3P$. Calculated, %: N 3.67; P 8.14.

Diphenyl *R*-(+)-2-(1-phenylethylamino)ethylphosphonate (IIId) was prepared similarly from 2.0 g of phosphonate **IIb** and 1.8 g of amine **Ib**, yield 1.7 g (61%), bp 183–188°C (0.1 mm Hg), $[\alpha]_D^{20}$ +21.3 (*c* 0.939, CH_2Cl_2). ^1H NMR spectrum ($CDCl_3$), δ, ppm, (*J*, Hz): 1.39 d (3H, CH_3, $^3J_{HH}$ 7.0), 2.31 m (2H, CH_2P), 2.97 m (2H, CH_2N), 3.82 q (1H, CHN, $^3J_{HH}$ 7.0), 7.17 m (5H, Ph), 7.38 m (10H, Ph). ^{31}P NMR spectrum, δ_P, ppm: 22.25. Found, %: N 3.59; P 8.19. $C_{22}H_{24}NO_3P$. Calculated, %: N 3.67; P 8.14.

***N*-(Diphenoxyphosphinoylethyl)-*N*-(1-phenylethyl)-*N*^{1}-phenylthiourea (IV).** A mixture of 0.30 g of phosphonate **IIId** and 0.11 g of phenyl isothiocyanate was kept for 20 days at 20°C. Crystals formed and were separated, repeatedly washed with ether, and dried in a vacuum to obtain 0.22 g (53.6%) of compound **IV**, mp 120–123°C, $[\alpha]_D^{20}$ +65.0 (*c* 0.185, CH_2Cl_2). IR spectrum (KBr), ν, cm^{-1}: 3327 (NH). ^{31}P NMR spectrum, δ_P, ppm: 30.41. Found, %: C 67.96; H 5.68; N 5.76; P 6.20; S 6.26. $C_{22}H_{24}NO_3P$. Calculated, %: C 67.44; H 5.62; N 5.43; P 6.01; S 6.20.

The IR spectrum was registered on a UR-20 spectrometer within the range 400–3600 cm^{-1} in Vaseline. The ^1H NMR spectra were obtained on a Bruker WM-250 instrument (250.132 MHz) against internal TMS. The ^{31}P NMR spectra were recorded on a Bruker MSL-400 NMR Fourier spectrometer operated at 100.62 MHz.

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