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LETTERS TO THE EDITOR

Optically Active 2-(1-Phenylethyl)aminoethylphosphonates

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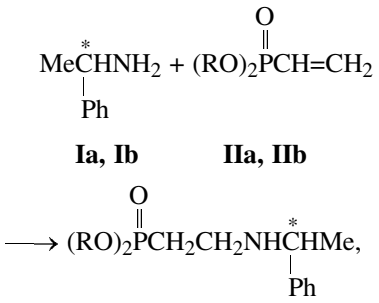
Amino phosphonic acids, which are direct analogs of natural amino acids, show a wide spectrum of biological activity [1]. Suffice it to say, the first amino phosphonic acid found in the nature was 2-aminoethanephosphonic acid [2]. Recently there has been a great deal of interest in the synthesis of the enantiomerically pure organophosphorus compounds because of their possible application as biological active compounds and ligands for preparation of homogeneous and heterogeneous catalysts [1, 3, 4]. It is known that dialkyl vinylphosphonates readily add secondary amines to form β-aminoalkylphosphonates [5]. The related reaction with ammonia occurs only in the presence of sodium ethoxide [6, 7].

We found that racemic amine **Ia** and *R*-(+)-phenylethylamines **Ib** undergo addition to vinylphosphonates **IIa** and **IIb** in the absence of any catalyst with the formation of 2-aminoethylphosphonates **IIIa**–**IIId**:

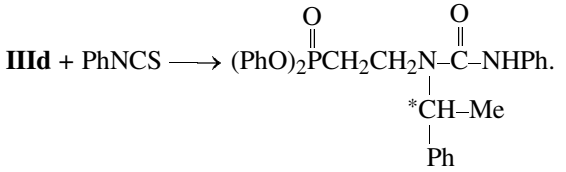


Ia, Ib **IIa, IIb**

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**).

It should be noted that the ease of the reaction is significantly affected by the nature of substituents at the phosphorus atom. Whereas the addition of amines to diphenyl phosphonate **IIb** readily occurs at 20°C, their addition to diethyl phosphonate **IIa** requires heating for several hours. As a result of addition of amino phosphonate **IIId** to phenyl isothiocyanate, enantiomerically pure phosphorus-containing urea **IV** was prepared:



IV

Diethyl 2-(1-phenylethyl)aminoethylphosphonate (IIIa). A mixture of 4.1 g of vinylphosphonate **IIa** and 6.0 g of amine **Ia** was kept at 100°C for 2 h. Then the reaction mixture was distilled, and compound **IIIa** in 3.4 g (47%) yield was obtained, bp 138°C (0.08 mm Hg). IR spectrum (KBr), ν, cm^{-1}: 1226, 1247 (P=O), 3305, 3443 (NH). ^{1}H 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-phenylethyl)aminoethylphosphonate (IIIb) was prepared similarly to **IIIa** from 4.1 g of vinylphosphonate **IIb** and 6.0 g of amine **Ib** in 55% (3.9 g) yield, 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). ^{1}H 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-phenylethyl)aminoethylphosphonate (IIIc). A mixture of 5.2 g of phosphonate **IIb** and 4.8 g of amine **Ia** was allowed to stand at 20°C for 48 h. Excess amine was 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 to **IIIc** 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*-(2-Diphenoxyphosphorylethyl)-*N*-(1-phenylethyl)-*N*^{1}-phenylthiourea (IV).** A mixture of 0.30 g of phosphonate **IIId** and 0.11 g of phenyl isothiocyanate was allowed to stand at 20°C for 20 days. The crystals formed were separated, repeatedly washed with ether, and dried in a vacuum to give 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 spectra were recorded on a UR-20 instrument within the range 400–3600 cm^{-1} in mineral oil. The ^1H NMR spectra were measured on a Bruker WM-250 spectrometer (250.132 MHz), internal reference TMS. The ^{31}P NMR spectra were recorded on a Bruker MSL-400 NMR Fourier spectrometer operating at 100.62 MHz.

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