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LETTERS TO THE EDITOR

Functional P-Substituted Hydrophosphoryl Compounds and α-Aminoalkylphosphonates

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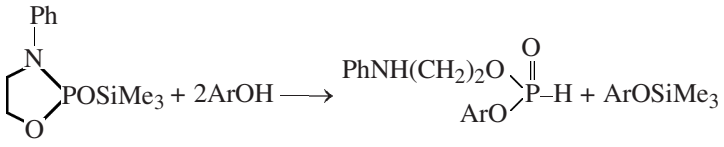
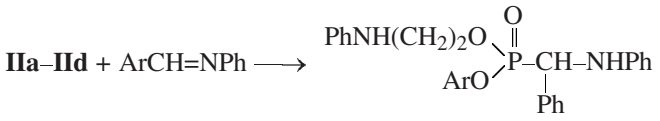
Aminophosphonic acids, being direct analogs of natural aminocarboxylic acids—building blocks of peptides and proteins, exhibit a broad-range biological activity [1]. In this connection α-aminoalkylphosphonate derivatives with structural fragments containing amino groups on the phosphorus atom present indubitable interest. The presence of two amino groups in such compounds opens up new possibilities for their modification and for preparation of various linear and cyclic compounds including the aminophosphonate fragment. α-Aminoalkylphosphonates with the phosphorus atom bearing functional substituents can be synthesized via addition of the corresponding P-substituted phosphorous acids to imines. We have developed a method for synthesis of mixed phosphorous acids involving the aminoalkyl fragment, using the example of the reaction of cyclic silyl phosphoramidites [2] with phenols. The reaction involves ring cleavage and liberation of phenoxysilane.



I **IIa, IIb**

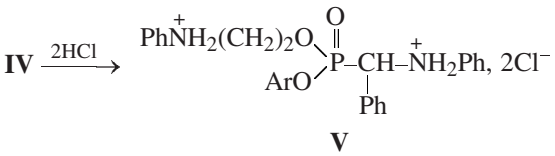
II, Ar = Ph (**a**); Ar = 4-$MeOC_6H_4$ (**b**).

Acid **IIa** readily adds to imine **III** to form P-functional aminoalkylphosphonate **IV**.



III **IV**

The addition reaction forms the second chiral center, and, as a result, compound **IV** is a mixture of diastereomers in a ratio of 76 : 24. The prevailing diastereomer was isolated from the mixture by fractional crystallization; its individuality was confirmed by the observation of a single signal in the ^{31}P NMR spectrum and one doublet proton signal of the PCH group in the ^{1}H NMR spectrum. Bubbling dry HCl through a solution of compound **IV** provides salt **V**.



V

Phenyl 2-(phenylamino)ethyl phosphonate (IIa). A mixture of 3.82 g of silyl phosphite **I** and 2.82 g of phenol was heated at 60°C for 2 h, after which 1.92 g (77%) of phenoxytrimethylsilane was distilled off in a vacuum, bp 67°C (11 mm Hg), n_D^{20} 1.4738 [3].

From the residue, 3.11 g (75%) of compound **IIa** was isolated, mp 44–45°C. IR spectrum (KBr), ν, cm^{-1} 2418 (P–H), 3430 (NH). ^{31}P NMR spectrum, δ_P, ppm: –4.22, J_{PH} 720 Hz. Found, %: C 60.51; H 6.11; N 4.92; P 11.12. $C_{14}H_{16}NO_3P$. Calculated, %: C 60.64; H 5.77; N 5.05; P 11.29.

4-Methoxyphenyl 2-(phenylamino)ethyl phosphonate (IIb) was prepared by the same procedure as compound **IIa** from 2.55 g of silyl phosphite **I** and 2.48 g of 4-methoxyphenol. Yield 2.42 g (79%), viscous liquid. IR spectrum (KBr), ν, cm^{-1}: 2415 (P–H). ^{31}P NMR spectrum, δ_P, ppm: –4.25, J_{PH} 720 Hz. Found, %: C 58.52; H 5.97; N 4.64; P 9.87. $C_{15}H_{18}NO_4P$. Calculated, %: C 58.63; H 5.86; N 4.56; P 10.09.

Phenyl 2-(phenylamino)ethyl [phenyl(phenylamino)metyl]phosphonate (IV). A mixture of 2.77 g of compound **IIa**, 1.81 g of benzalaniline, and a catalytic quantity of sodium phenolate in 20 ml of benzene was heated at 60°C for 4 h to obtain a crystalline product **VI**, yield 80%, mp 138–142°C, as a mixture of two diastereomers (δ_P 19.72 and 19.52 ppm). Fractional crystallization from acetonitrile gave 1.8 g (39%) of a diastereomerically individual compound **IV**, mp 147°C. ^{31}P NMR spectrum, δ_P, ppm: 19.48. ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 3.35 m (2H, CH_2N), 4.32 m (2H, CH_2O), 5.04 d (1H, PCH, $^2J_{HP}$ 15.0), 7.32 m (25H, Ph). Found, %: C 70.78; H 5.97; N 6.14; P 6.61. $C_{27}H_{27}N_2O_3P$. Calculated, %: C 70.74; H 5.89; N 6.11; P 6.76.

Phenyl 2-(phenylammonio)ethyl [phenyl(phenylammonio)methyl]phosphonate dichloride (V). Through a solution of 2.29 g of phosphonate **IV** in 30 ml of benzene, gaseous HCl was bubbled. The precipitate formed was filtered off and washed with two portions of benzene to obtain 76% (2.0 g) of compound **V**, mp 113–115°C. 31P NMR spectrum, δ_P, ppm: 12.87. Found, %: C 61.49; H 5.73; Cl 13.33; N 5.27; P 5.79. $C_{27}H_{29}Cl_2N_2O_3P$. Calculated, %: C 61.01, H 5.46; Cl 13.37; N 5.27; P 5.83.

The IR spectra were recorded on a UR-20 spectrometer in the range of 400–3600 cm^{-1} in mineral oil. The ^1H NMR spectra were registered on a Bruker WM-250 instrument at 250.132 HMz, internal reference TMS. The ^{31}P NMR spectra were measured on a Bruker MSL-400 NMR Fourier spectrometer at 162.0 MHz.

ACKNOWLEDGMENTS

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REFERENCES

1. Kukhar, V.P. and Hudson, H.R., *Aminophosphonic and Aminophosphinic Acids: Chemistry and Biological Activity,* New York: Wiley, 2000, p. 634.
2. Pudovik, M.A., Kibardina, L.K., Medvedeva, M.D., Anoshina, N.P., and Pudovik, A.N., *Zh. Obshch. Khim.,* 1978, vol. 48, no. 12, p. 2648.
3. Speier, J.L., *J. Am. Chem. Soc.,* 1952, vol. 74, no. 5, p. 1003.