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SHORT COMMUNICATIONS

Dedicated to the 100th Anniversary of Corresponding Member of the Russian Academy of Sciences A.A. Petrov

Synthesis of (*S*)-2-[(Dioctylphosphoryl)methylamino]propionic Acid from Trimethylsilyl 2-(Trimethylsilylamino)propanoate

R. A. Cherkasov, A. R. Garifzyanov, and S. A. Koshkin

Kazan (Volga Region) Federal University, ul. Kremlevskaya 18, Kazan, 420008 Tatarstan, Russia
e-mail: rafael.cherkasov@ksu.ru

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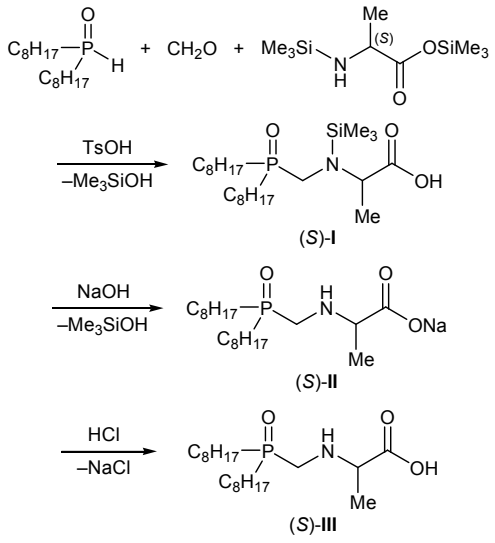
We previously showed [1] that the Kabachnik–Fields reaction in the system dioctylphosphine oxide–paraformaldehyde–amino acid leads to the formation of the corresponding *N*-(dioctylphosphorylmethyl)-substituted amino acid derivatives. In particular, *N*-phosphorylmethyl derivatives of glycine, β-alanine, and *N*-butylglycine were synthesized in this way. Because of poor solubility of amino acids in organic solvents, the reactions were carried out in acetonitrile in the presence of the corresponding amino acid hydrochloride. We made an attempt to perform phosphorylation of (*S*)-α-alanine under similar conditions. However, the reaction in heterogeneous medium gave a mixture of mono- and bisphosphorylation products. With a view to improve the selectivity, the Kabachnik–Fields reaction was carried out with dioctylphosphine oxide, paraformaldehyde, and trimethylsilyl (*S*)-2-(trimethylsilylamino)propanoate prepared by heating of (*S*)-α-alanine with excess hexamethyldisilazane over a period of 72 h under reflux. Heating of the reactants in boiling toluene in the presence of *p*-toluenesulfonic acid (reaction time 3 h) afforded 96% (according to the $^{31}P–\{^1H\}$ NMR data) of silylated aminomethylphosphine oxide **I**. Silylamine **I** was treated with a hot 15% aqueous solution of sodium hydroxide, and the subsequent neutralization of sodium salt **II** with 10% aqueous HCl gave target acid **III**.



(*S*)-**I** (*S*)-**II** (*S*)-**III**

(*S*)-2-{[(Dioctylphosphoryl)methyl](trimethylsilyl)amino}propionic acid (I). White amorphous substance. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.21 s [9H, $Si(CH_3)_3$], 0.86 d (3H, CH_3, $^3J_{HH}$ = 9 Hz), 1.25–1.90 m (34H, C_8H_{17}), 2.88 d.d (2H, CH_2P, $^2J_{HH}$ = 4, $^2J_{PH}$ = 18 Hz), 3.27 q (1H, CH, $^3J_{HH}$ = 9 Hz). $^{31}P–\{^1H\}$ NMR spectrum (PhMe): δ_P 51.2 ppm, s.

(*S*)-2-[(Dioctylphosphoryl)methylamino]propionic acid (III). White crystalline substance, mp 132°C. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 d (3H, CH_3, $^3J_{HH}$ = 9 Hz), 1.25–1.90 m (34H, C_8H_{17}), 2.89 d.d (2H, CH_2P, $^2J_{HH}$ = 4, $^2J_{PH}$ = 18 Hz), 3.27 q (1H, CH, $^3J_{HH}$ = 9 Hz). $^{31}P–\{^1H\}$ NMR spectrum (CH_2Cl_2): δ_P 52.4 ppm, s.

The ^1H and $^{31}P–\{^1H\}$ NMR spectra were recorded on a Varian XL-300 spectrometer at 300 and 122.4 MHz, respectively.

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