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LETTERS TO THE EDITOR

Stereoselective Synthesis of 2,4-Dioxo-5-phenyl-1-phenylethylamino-4-phenoxy-1,3,4-dazaphospholidine

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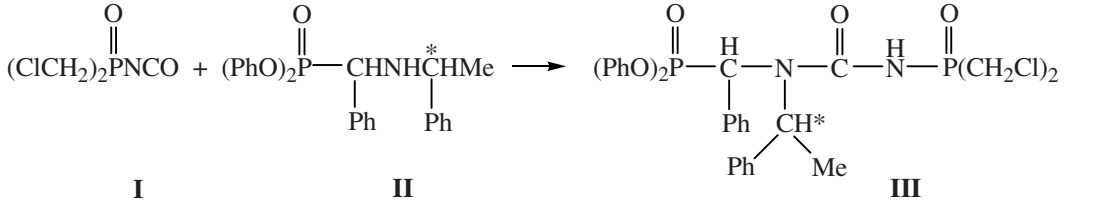
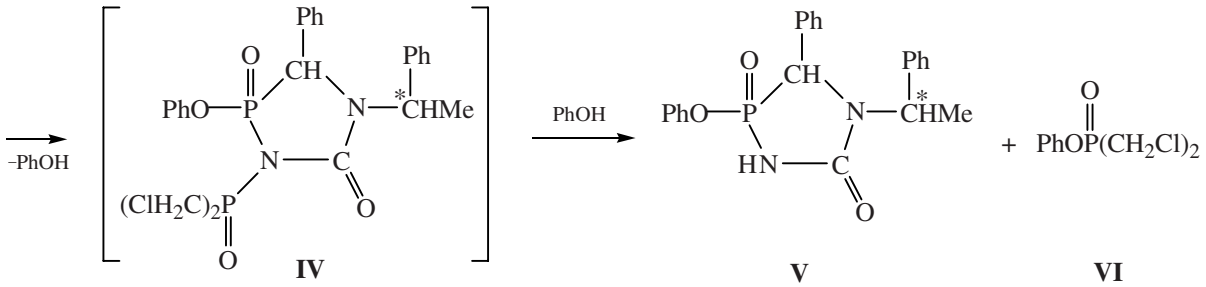
Recently we showed that diphenyl (α-methylamino) benzylphosphonate easily added to phenyl isocyanate or phenyl isothiocyanate in the presence of a catalytic amount of triethylamine affording *N*,*N*′-substituted (thio)ureas; cyclization of the latter led to the formation of 1,3,4-diazaphospholidines [1]. Now we studied reaction of bis(chloromethyl)isocyanatophosphinate (**I**) with optically active diphenyl(α-methylamino)-benzylphosphonate (**II**). Noteworthy that the formation of the latter compound was registered recently in the reaction of catalytic addition of diphenyl hydrogen phosphite to the optically active (*S*)-(–)-benzal(1-phenyl)ethylamine (catalyst BF_3) by ^{31}P NMR spectroscopy as a mixture of stereoisomers which was not separated [2]. We obtained optically active aminophosphonate **II** in the same reaction using sodium phenolate as a catalyst:

II

The reaction mixture contained a mixture of aminophosphonate **II** diastereomers in the ratio 74:26%, with chemical shifts of phosphorus nuclei 16.64 and 16.25 ppm respectively. By fractional crystallization one diastereomer of the phosphonate **II** was isolated in enantiomerically pure form ($[\alpha]_D^{20}$ –53.7). By X-ray structural analysis we established that configurations of two chiral centers in this compounds were the same (S_C1S_C2). Reaction of isocyanate **I** with aminophosphonate **II** proceeds stereoselectively.



I **II** **III**



IV **V** **VI**

In the ^{31}P NMR spectrum of the reaction mixture appeared two signals of phosphorus nuclei, at 21.51 and 22.83 ppm, indicating the formation of diazaphospholidine **V** as a diastereomeric mixture in the ratio 83:17 %, and a signal of phenyl bis(chloromethyl)phosphinate (**VI**) (δ_P 37.5 ppm). By the fractional crystallization we isolated enantiomerically pure 1-phenylethyl-2,4-dioxo-4-phenoxy-5-phenyl-1,3,4-dizaphospholidine (**V**) with $[\alpha]_D^{20}$ +31.0. We suggest that the first step in the addition of aminophosphonate **II** to isocyanate **I** leads to the formation of diasteremerically uniform phpsphorylated urea **III**. The subsequent intramolecular nucleophilic substitution at the tetracoordinated phosphorus atom forms a five-membered cyclic frame with appearance of the third chiral center on the phosphorus atom. Since the cyclisation process proceeds stereoselectively, we obtain final product as a diastereomeric mixture: **Va**, $S_C1S_C2S_P$, and **Vb**, $S_C1S_C2R_P$; the prevailing form **Va** was isolated.

Diphenyl (α-phenylethylamino)benzylphosphonate (II). To a solution of 4.9 g of diphenylphosphite in 20 ml of anhydrous acetonitrile was added at stirring 4.38 g of (*S*)-(–)-benzalphenylethylimoine and 1 drop of sodium phenolate. The reaction mixture was heated for 4.5 h at 80°C, then the solvent was removed and the residue was recrystallized from ether. 0.95 g (10%) of phosphonate **II** was obtained, mp 122–123°C. IR spectrum (KBr), ν, cm^{-1}: 1195, 1220 (P–O–Ph), 1275 (P=O), 1590 (Ph), 3325 (NH). ^1H NMR spectrum [$(CD_3)_2CO$], δ, ppm (*J*, Hz): 1.4 d (3H, MeC, $^3J_{HH}$ 6.3), 3.73 q (1H, NCH, $^3J_{HH}$ 6.7), 4.16 d (1H, PCH, $^2J_{PH}$ 23.6), 7.3 m (20 H, Ph). ^{31}P NMR spectrum, δ_P, ppm: 16.55. $[\alpha]_D$ –53.7. Found, %: C 72.85; H 6.07; N 3.33; P 6.88. $C_{27}H_{26}NO_3P$. Calculated, %: C 73.12; H 5.91; N 3.16; P 6.99.

2,4-Dioxo-5-phenyl-1-phenylethylamino-4-phenoxy-1,3,4-diazaphospholidine (Va). To a solution of 0.5 g of aminophosphonate **II** in 20 ml of anhydrous acetonitrile was added at stirring 0.21 g of bis(chloromethyl)isocyanatophosphinate (**I**). After 45 days a crystalline precipitate separated and was filtered off. After triple recrystallization from acetonitrile 0.2 g (45%) of diastereomer **Va** was obtained, mp 182–183°C. IR spectrum (KBr), ν, cm^{-1}: 1190, 1215 (P–O–Ph), 1255 (P=O), 1595 (Ph), 1695 (C=O), 3070 (NH). ^1H NMR spectrum [$(CD_3)_2CO$], δ, ppm (*J*, Hz): 1.62 d (3H, MeC, $^3J_{HH}$ 4.6), 4.86 q (1H, NCH, $^3J_{HH}$ 5.0), 5.07 d (1H, PCH, $^2J_{PH}$ 13.1), 7.2 m (15H, Ph), 8.54 s (1H, NH). ^{31}P NMR spectrum, δ_P, ppm: 21.60. $[\alpha]_D$ +31.0. Mass spectrum, *m/z*: 392 [M^+]. Found, %: C 67.05; H 5.16; N 6.80; P 7.72. $C_{22}H_{21}N_2O_3P$. Calculated, %: 67.33; H 5.39; N 7.13; P 7.89.

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

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