

LETTERS
TO THE EDITOR

Dithiophosphorylation of Trimethylsilyl Ethers of Enantiomerically Pure Menthols

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Received September 29, 2014

Keywords: tetraphosphorus decasulfide, menthol, silyl ethers, optical activity, dithiophosphates

DOI: 10.1134/S107036321412????

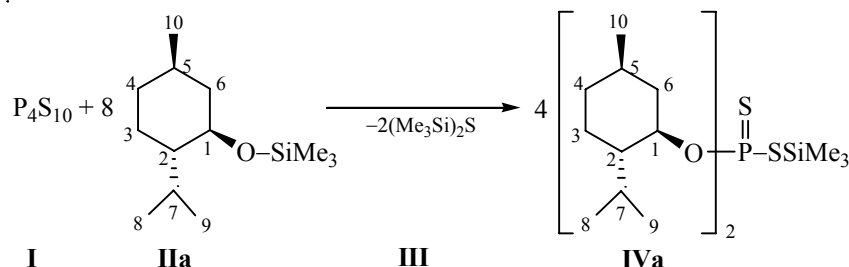
Cyclic terpenoids, contained in galipot, extractives of wood and bark of conifers, are widely used for the production of various bioactive substances, including the application in asymmetric synthesis methods [1]. An example of the creation of bioactive dithiophosphate derivatives of chiral monoterpene alcohols consists in their interaction with tetraphosphorus decasulfide accompanied with the formation of the dithiophosphorylation products with a significant enantiomeric and diastereomeric excess [2, 3]. Recently, we performed reactions with (*S*)-(-) and (*R*)-(+)-menthols giving optically active dithiophosphoric acids [4]. This report presents the results of studying the interaction of silyl ethers of enantiomerically pure menthols with tetraphosphorus decasulfide that leads to the formation of chiral *S*-silyl ethers of phosphorus dithioacids. We believe that the latter may be of interest as intermediates in substitution or addition reactions for introducing chiral terpene synthons into organic molecules.

Previously it was shown that alkoxy-silanes reacted with tetraphosphorus decasulfide **I** to form a *S*-silyl-*O,O*-dialkyl dithiophosphanes [5]. We found that similar reaction of phosphorus sulfide **I** with (-)-*O*-[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-1-yl]trimethylsilane **IIa** proceeded easily in benzene at 50°C for 2 h to give optically active (-)-*S*-trimethylsilyl-*O,O*-bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-1-yl] dithiophosphate **IVa** in 95% yield. The by-product bis-(trimethylsilyl)sulfide **III** can be easily removed from the reaction medium and does not contaminate the product **IVa** (Scheme 1).

The optical rotation angle of *S*-silyl dithiophosphate **IVa** ($[\alpha]_D^{20} -20.8^\circ$, c 1.035, C_6H_6) was much smaller than that of the previously obtained (-)-*O,O*-bis-[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-1-yl] dithiophosphate ($[\alpha]_D^{22} -64.7^\circ$, c 1.0, C_6H_6) [4].

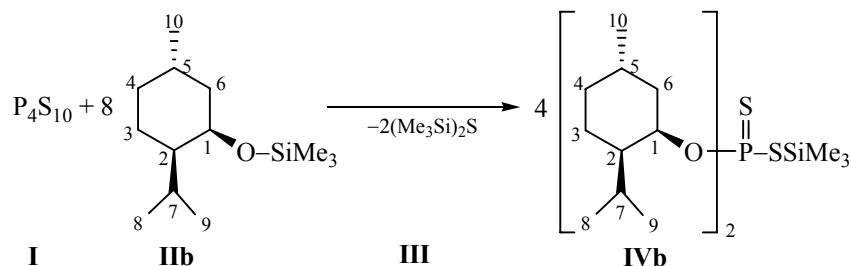
Chemical shift of the phosphorus nucleus in the ³¹P NMR spectrum of ester **IVa** was 81.3 ppm, which is

Scheme 1.



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Scheme 2.



typical of other *S*-silyl dithiophosphates [5, 6], and is virtually identical to that of the corresponding dithiophosphoric acid (δ_p 81.9 ppm) [4]. In the ¹H NMR spectrum of **IVa** the protons of trimethylsilyl group resonated as a singlet at 0.08 ppm. The signal of methine proton POC¹H was shifted downfield (4.46 ppm) compared to the signal of the OC¹H proton of the source silane **IIa** (3.43 ppm).

In the IR spectrum of the product **IVa** strong absorption at 1250 cm⁻¹ corresponded to the symmetrical bending vibrations of CH₃(Si) moiety. The stretching vibrations of the P=S and P-S bonds were observed as medium absorption bands at 666 and 566 cm⁻¹ [7].

Isomeric (-)-*O*-[(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohex-1-yl]trimethylsilane **IIb** reacted with phosphorus sulfide **I** under the same conditions to form (-)-*S*-trimethylsilyl-*O*,*O*-bis[(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohex-1-yl] dithiophosphate **IVb** in 95% yield. Physicochemical characteristics and spectral parameters of isomer **IVb** was identical to those of **IVa** (Scheme 2).

In summary, dithiophosphorylation of silyl ethers of enantiomerically pure menthols with tetraphosphorus decasulfide is a suitable approach towards synthesis of new optically active *S*-silyl ethers of phosphorus dithioacids with potentially a wide spectrum of biological activity.

(-)-*S*-Trimethylsilyl-*O*,*O*-bis[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-1-yl] dithiophosphate (IVa). Phosphorus sulfide **I**, 0.2 g, was added by portions to a solution of 0.8 g of silane **IIa** in 30 mL of anhydrous benzene at 20°C under argon atmosphere. The reaction mixture was stirred at 50°C for 2 h. After cooling, the mixture was filtered. The filtrate was evaporated at 40°C for 1 h at 0.5 mmHg and 1 h at 0.02 mmHg. The resulting oil solidified at standing. Yield 0.8 g (95%), mp 61–63°C. IR spectrum, ν , cm⁻¹: 2954 v.s., 2928 v.s.,

2869 s, 2858 s (CH₃, CH₂), 1450 s [δ_{as} (CH₃)], 1335 m [δ_s (CH₃)], 1250 s { ν_s [CH₃(Si)]}, 1041 s [(P)O–C], 934 c. m (OC–C, O–C), 666 m (P=S), 566 m (P–S). ¹H NMR spectrum, δ , ppm: 0.08 s [9H, (CH₃)₃Si], 0.09 s [9H, (CH₃)₃Si], 0.86 d [6H, C¹⁰H₃CH, ³J_{HH} 6.9 Hz], 0.949 d [12H, (C^{8,9}H₃)₂CH, ³J_{HH} 6.9 Hz], 0.952 d [12H, (C^{9,8}H₃)₂CH, ³J_{HH} 6.4 Hz], 1.15 m (2H, C²H), 1.47 m (2H, CH₃C⁵H), 1.40 m [2H, (CH₃)₂C⁷H], 1.72 m (4H, C⁴H₂), 2.20 m (4H, C³H₂), 2.42 d (2H, C⁶H₂), 4.46 d.d.t (2H, POC¹H, ³J_{HH} 10.9, ³J_{HH} 4.5, ³J_{PH} 10.9). ³¹P–{¹H} NMR spectrum (C₆H₆): δ_p 81.3 ppm. Found, %: C 57.57; H 10.26; P 6.14; S 13.66; Si 5.63. C₂₃H₄₇O₂PS₂Si. Calculated, %: C 57.69; H 9.89; P 6.47; S 13.39; Si 5.87.

(-)-*S*-Trimethylsilyl-*O*,*O*-bis[(1*S*,2*R*,5*S*)-2-isopropyl-5-methylcyclohex-1-yl] dithiophosphate (IVb) was prepared similarly from 1.0 g of silane **IIb** and 0.243 g of phosphorus sulfide **I**. Yield 95%. ³¹P–{¹H} NMR spectrum (C₆H₆): δ_p 81.5 ppm. Parameters of IR and ¹H NMR spectra were identical to those for the isomer **IVa**. Found, %: C 57.88; H 9.78; P 6.67; S 13.78; Si 5.54. C₂₃H₄₇O₂PS₂Si. Calculated, %: C 57.69; H 9.89; P 6.47; S 13.39; Si 5.87.

IR spectra were recorded on a Bruker Vector 22 Fourier spectrometer (400–4000 cm⁻¹) from KBr pellets. ¹H NMR spectra of the solutions in acetone-*d*₆ were taken on a Bruker Avance-600 spectrometer (600 MHz). ³¹P NMR spectra were registered on a Bruker Avance-400 spectrometer (161.98 MHz), external reference 85% H₃PO₄. The angle of optical rotation [α]_D²⁰ was measured on a Perkin Elmer 341 polarimeter (λ 589 nm, sodium halide lamp, quartz cell, *l* 55 mm).

ACKNOWLEDGMENTS

This work was financially supported by the Kazan Federal University in the frame of the project part of the governmental contract.

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