

LETTERS TO THE EDITOR

Dithiophosphorylation of Trimethylsilyl Ethers of Enantiomerically Pure Menthols

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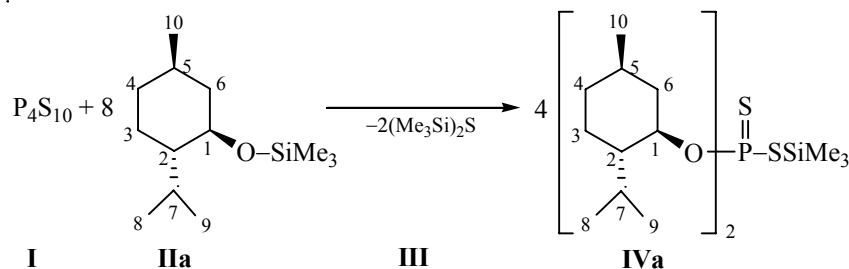
Cyclic terpenoids, contained in galipot, extractives of wood and bark of conifers, are widely used for the production of various bioactive substances, including the application in asymmetric synthesis methods [1]. An example of the creation of bioactive dithiophosphate derivatives of chiral monoterpene 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 esters 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 alkoxysilanes reacted with tetraphosphorus decasulfide **I** to form a *S*-silyl-*O,O*-dialkyl dithiophosphates [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).

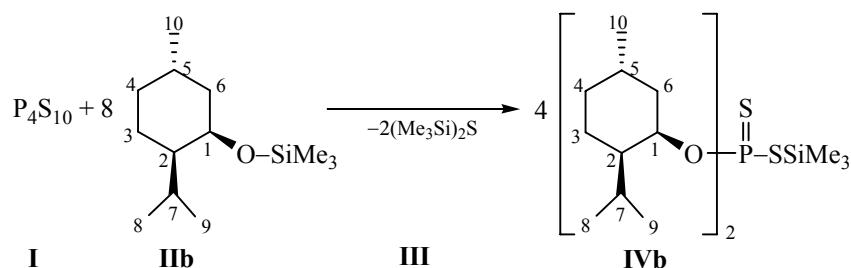
The optical rotation angle of *S*-silyl dithiophosphate **IVa** ($[\alpha]_D^{20} -20.8^\circ$, c 1.035, C₆H₆) was much smaller than that of the previously obtained (-)-*O,O*-bis-[(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohex-1-yl] dithiophosphate ($[\alpha]_D^{22} -64.7^\circ$, c 1.0, C₆H₆) [4].

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

Scheme 1.



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 POC^1H was shifted downfield (4.46 ppm) compared to the signal of the OC^1H 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 $CH_3(Si)$ 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 esters 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 $61\text{--}63^\circ\text{C}$. IR spectrum, ν , cm^{-1} : 2954 v.s., 2928 v.s.,

2869 s, 2858 s (CH_3 , CH_2), 1450 s [$\delta_{as}(CH_3)$], 1335 m [$\delta_s(CH_3)$], 1250 s [$\nu_s[CH_3(Si)]$], 1041 s [$(P)O-C$], 934 s.br ($OC-C$, $O-C$), 666 m ($P=S$), 566 m ($P-S$). 1H NMR spectrum, δ , ppm: 0.08 s [9H, $(CH_3)_3Si$], 0.09 s [9H, $(CH_3)_3Si$], 0.86 d [6H, $C^{10}H_3CH$, $^3J_{HH}$ 6.9 Hz], 0.949 d [12H, $(C^{8,9}H_3)_2CH$, $^3J_{HH}$ 6.9 Hz], 0.952 d [12H, $(C^{9,8}H_3)_2CH$, $^3J_{HH}$ 6.4 Hz], 1.15 m (2H, C^2H), 1.47 m (2H, CH_3C^5H), 1.40 m [2H, $(CH_3)_2C^7H$], 1.72 m (4H, C^4H_2), 2.20 m (4H, C^3H_2), 2.42 d (2H, C^6H_2), 4.46 d.d.t (2H, POC^1H , $^3J_{HH}$ 10.9, $^3J_{HH}$ 4.5, $^3J_{PH}$ 10.9). $^{31}P-\{^1H\}$ NMR spectrum (C_6H_6): δ_P 81.3 ppm. Found, %: C 57.57; H 10.26; P 6.14; S 13.66; Si 5.63. $C_{23}H_{47}O_2P_2S_2Si$. 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%. $^{31}P-\{^1H\}$ NMR spectrum (C_6H_6): 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. $C_{23}H_{47}O_2P_2S_2Si$. 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 ($400\text{--}4000\text{ cm}^{-1}$) from KBr pellets. 1H NMR spectra of the solutions in acetone- d_6 were taken on a Bruker Avance-600 spectrometer (600 MHz). ^{31}P NMR spectra were registered on a Bruker Avance-400 spectrometer (161.98 MHz), external reference 85% H_3PO_4 . The angle of optical rotation $[\alpha]_D^{20}$ was measured on a Perkin Elmer 341 polarimeter (λ 589 nm, sodium halide lamp, quartz cell, l 55 mm).

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