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

Dithiophosphorylation of Racemic and Enantiomerically Pure Trimethyl-*N*-(1-phenylethyl)silanamine

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Abstract—Trimethylsilyl *P*-aryl-*N*-[(*RS*)-, (*S*)-(–)-, and (*R*)-(+)-(1-phenylethyl)]phosphonamidodithioates were synthesized by reactions of 2,4-diaryl-1,3,2λ^5,4λ^5-dithiadiphosphetane 2,4-disulfides with racemic and and enantiomerically pure trimethyl-*N*-(1-phenylethyl)silanamine.

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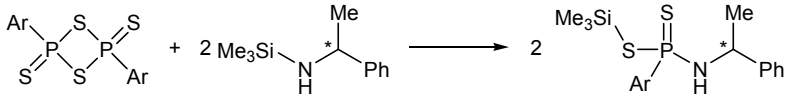
In recent years, structural, chemical, physicochemical, and applied properties of various enantiomeric organophosphorus compounds have attracted increased attention [1–3]. The chiral center in their molecules may be located both on the phosphorus atom and in substituents. Four-coordinate phosphorus dithio acids, their ammonium and metal salts, and *S*-esters occupy a particular place among organophosphorus compounds due to their potential applications as pesticides, corrosion inhibitors, antioxidants, lubricant additives, extractants, and complexing agents. A promising line in the synthesis of phosphorus dithio acids and their derivatives implies introduction of a dithiophosphoryl fragment into molecules of natural compounds, e.g., terpenes possessing chiral centers. By reactions of tetraphosphorus decasulfide and 2,4-diaryl-1,3,2λ^5,4λ^5-dithiadiphosphetane 2,4-disulfides with unsaturated monoterpene hydrocarbons and alcohols [camphene, (*R*)-(+)-limonene, L-(–)-menthol, D-(+)-menthol, (1*S*)-*endo*-(–)-borneol], as well as with (2*S*,3*S*)-(+)-dimethyl tartrate, we previously synthesized a number of new dithiophosphoric and mono- and bis-dithiophosphonic acid derivatives having a chiral center in the *O*-substituents [4–12]. The reaction of racemic 1-phenylethanol with tetraphosphorus decasulfide gave a mixture of isomeric (*R*,*S*)-*O*,*O*-di(1-phenylethyl) dithiophosphates [13].

Reactions of tetraphosphorus decasulfide and 1,3,2λ^5,4λ^5-dithiadiphosphetane 2,4-disulfides with silyl ethers derived from chiral synthetic alcohols and with aminosilanes were not studied. These reactions could provide a synthetic route to new phosphorus dithio acid derivatives with asymmetric centers in the substituents on the oxygen and nitrogen atoms. Reagents containing readily departing groups can be brought into substitution and exchange reactions with organic compounds possessing pharmacophoric groups with a view to obtain new phosphorus dithio acid *S*-esters as potentially physiologically active compounds. Reactions of achiral trimethylalkoxysilanes

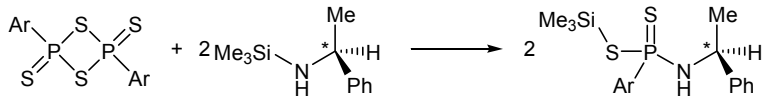
Scheme 1.



Ia, **Ib** (*RS*)-**IIa/IIb** (*RS*)-**IIIa/IIIb**, (*RS*)-**IIIc/IIId**

R = 3,5-di-*tert*-butyl-4-hydroxyphenyl (**a**), 4-phenoxyphenyl (**b**).

Scheme 2.



Ia, **Ib** (*S*)-(–)-**IIa** (*S*)-**IIIa**, (*S*)-**IIIc**

R = 3,5-di-*tert*-butyl-4-hydroxyphenyl (**a**), 4-phenoxyphenyl (**b**).

and *N*,*N*-dialkyl(trimethyl)silanamines with tetraphosphorus decasulfide and 1,3,2λ^5,4λ^5-dithiadiphosphetane 2,4-disulfides were reported previously to produce *S*-trimethylsilyl dithiophosphates, phosphonodithioates, diamidophosphorodithioates amidophosphonodithioates [14–20].

In the present article we report on the results of studying the reactions of 2,4-diaryl-1,3,2λ^5,4λ^5-dithiadiphosphetane 2,4-disulfides **Ia** and **Ib** with racemic and enantiomerically pure trimethyl-*N*-(1-phenylethyl)-silanamine. Compounds **Ia** and **Ib** readily reacted with racemic trimethyl-*N*-[(*RS*)-(1-phenylethyl)]silanamine (**IIa**/**IIb**) in benzene at 20–30°C (1–1.5 h) to afford crystalline trimethylsilyl *P*-aryl-*N*-(1-phenylethyl)-phosphonamidodithioates **IIIa**/**IIIb** and **IIIc**/**IIId** (Scheme 1). The ^{31}P NMR spectrum of **IIIa**/**IIIb** contained two signals at δ_P 70.65 and 70.53 ppm at a ratio of 1:1; the corresponding signals (1:1) of stereoisomers **IIIc**/**IIId** were observed in a weaker field (δ_P 76.82, 77.00 ppm). In the ^{1}H NMR spectrum of **IIIa**/**IIIb** protons in the $(CH_3)_3Si$ group resonated as two strong signals at δ 0.453 and 0.457 ppm. Two doublets at δ 7.800 and 7.805 ppm belong to the *ortho*-protons in the 3,5-di-*tert*-butyl-4-hydroxyphenyl substituent in **IIIa** and **IIIb** ($^3J_{PH}$ = 16.0 and 16.4 Hz, respectively). Phosphonamidodithioates **IIIc**/**IIId** showed in the IR spectrum absorption bands at 3631 and 3409 cm^{-1} due to stretching vibrations of the O–H and N–H bonds, respectively.

Enantiomerically pure trimethyl-*N*-[(*S*)-(–)-(1-phenylethyl)]silanamine (*S*-**IIa**) reacted with disulfides **Ia** and **Ib** at 30–50°C (1.5–2 h) to give crystalline trimethylsilyl *P*-aryl-*N*-[(*S*)-(1-phenylethyl)]phosphonamidodithioates (*S*)-**IIIa** and (*S*)-**IIIc**, respectively. The ^{31}P NMR spectrum of **IIIa** contained two signals at δ_P 70.65 and 70.52 ppm (1:1) due to the presence of two diastereoisomers. Likewise, trimethylsilyl ester **IIIc** displayed in the ^{31}P NMR spectrum two signals at δ_P 76.86 and 76.96 ppm. In the electron impact mass spectrum of **IIIa** we observed the molecular ion peak, *m*/*z* 494.0 $[M]^{+\cdot}$. Symmetric bending and rocking vibrations of methyl groups in the Me_3Si fragment of ester **IIIc** gave rise to IR absorption bands at 1242 and 887 cm^{-1}, respectively.

Trimethylsilyl *P*-aryl-*N*-[(*R*)-(1-phenylethyl)]phosphonamidodithioates **IIIb** and **IIId** were formed as mixtures of diastereoisomers in the reaction of trimethyl-*N*-[(*R*)-(+)-(1-phenylethyl)]silanamine (**IIb**) with diphosphetane disulfides **Ia** and **Ib** (30–45°C, 2 h). Compounds **IIIb** and **IIId** were isolated as solid substances. Two signals were present in their ^{31}P NMR spectra at δ_P 70.57 and 70.71 ppm (1:1) for **IIIb** and at δ_P 76.85 and 77.02 ppm (1:0.3) for **IIId**. In the ^{1}H NMR spectrum of **IIId**, protons in the methyl groups on the silicon atom resonated as two strong singlets at δ 0.453 and 0.457 ppm, and two doublets at δ 7.91 ($^3J_{PH}$ = 8.8 Hz) and 7.95 ppm ($^3J_{PH}$ = 9.1 Hz) were assigned to aromatic protons in the *ortho*-positions of the substituted phenyl ring on the phosphorus.

Compounds **IIIa**–**IIId** (both racemic and nonracemic) are sensitive to atmospheric moisture, and they undergo fast hydrolysis on exposure to air. When the above reactions were carried out under more severe conditions or without protection from atmospheric moisture and oxygen, complex mixtures of phosphorus-and-sulfur containing compounds were formed (according to the ^{31}P NMR data), which were difficult to identify. Nevertheless, trimethylsilyl phosphonamidodithioates synthesized in the present work may be used as synthons to introduce an S=P–N–C* fragment into organic molecules with a view to obtain biologically active compounds.

EXPERIMENTAL

The IR spectra were recorded in the range from 400 to 4000 cm^{-1} on a Bruker Vector 22 spectrometer with Fourier transform. The ^{1}H NMR spectra were measured on Bruker Avance-400 (400 MHz) and Bruker Avance-600 (600 MHz) spectrometers; the ^{31}P NMR spectra were recorded on a Bruker Avance-400 instrument (161.98 MHz) from solutions in benzene relative to 85% H_3PO_4 (external reference). The electron impact (70 eV) and chemical ionization mass spectra were obtained on a DFS Thermo Electron Corporation GC–MS system. All operations, including spectral measurements, were carried out in a stream of dry argon with thorough protection from air.

Trimethylsilyl *P*-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-*N*-[(*RS*)-(1-phenylethyl)]phosphonamidodithioate (IIIa/IIIb, mixture of stereoisomers**).** Compound **Ia**, 2.3 g (3.8 mmol), was added in portions under stirring in a stream of dry argon to a solution of 1.5 g (7.8 mmol) of racemic aminosilane **IIa**/**IIb** in 20 ml of anhydrous benzene, heated to 50°C. The mixture was stirred for 1 h at 50°C, kept for ~12 h at 20°C, and evacuated for 1 h at 0.5 mm (40°C) and for 1 h at 0.02 mm. Yield 3.5 g (92%), mp 77–78°C. IR spectrum (KBr), ν, cm^{-1}: 3631 s (O–H), 3409 m.br (N–H), 3060 sh, 3030 sh (C–H_{arom}), 2957 s, 2910 v.s, 2875 v.s (C–H_{aliph}), 1584 m, 1494 s (C=C_{arom}), 1428 v.s ($\delta_{as}CH_3$), 1365 m (δ_sCH_3), 1060 s [(P)O–C], 977 s.br, 890 s (O–C, OC–C), 847 v.s [ρCH_3(Si)], 654 m (P=S), 532 m (P–S), 460 m (SPC). ^{1}H NMR spectrum, δ, ppm: 0.453 s and 0.457 s [9H each, $(CH_3)_3$Si], 1.47 s and 1.48 s (18H each, *t*-Bu), 1.64 d (3H, C**H**$_3$CHN, $^3J_{HH}$ = 6.9 Hz), 4.49 d.q (1H, CH_3C**H**N, $^3J_{HH}$ = 6.8 Hz), 7.11–7.36 m (5H, C_6H_5), 7.800 d (2H, *o*-H, $^3J_{PH}$ = 16.0 Hz), 7.805 d (2H, *o*-H, $^3J_{PH}$ = 16.4 Hz), 8.20 m (1H, NH). Found, %: C 61.06; H 8.36; N 2.91; P 5.92; S 13.29; Si 5.34. $C_{25}H_{40}NOPS_2Si$. Calculated, %: C 60.81; H 8.17; N 2.84; P 6.27; S 12.99; Si 5.59.

Compounds **IIIc**/**IIId** (mixture of isomers), **IIIa**, **IIIb**, **IIIc**, and **IIId** were synthesized in a similar way.

Trimethylsilyl *N*-[(*RS*)-(1-phenylethyl)]-*P*-(4-phenoxyphenyl)phosphonamidodithioate (IIIc/IIId, mixture of stereoisomers**).** Yield 52%, mp 80–82°C. ^{1}H NMR spectrum, δ, ppm: 0.453 s and 0.457 s [9H each, $(CH_3)_3$Si], 1.69 d (3H, C**H**$_3$CHN, $^3J_{HH}$ = 5.0 Hz), 4.40 m (1H, CH_3C**H**N), 7.00–7.44 m (12H, C_6H_5, *m*-H), 7.49 d (2H, *o*-H, $^3J_{PH}$ = 6.3 Hz), 8.71 m (1H, NH). Found, %: C 60.55; H 6.33; N 3.14; P 6.50; S 14.08; Si 6.26. $C_{23}H_{28}NOPS_2Si$. Calculated, %: C 60.36; H 6.17; N 3.06; P 6.77; S 14.01; Si 6.14.

Trimethylsilyl *P*-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-*N*-[(*S*)-(1-phenylethyl)]phosphonamidodithioate (IIIa). Yield 56%, mp 75–77°C. ^{1}H NMR spectrum, δ, ppm: 0.30 s and 0.45 s [9H each, $(CH_3)_3$Si], 1.40 s (36H, *t*-Bu), 1.45 d (3H, C**H**$_3$CH, $^3J_{HH}$ = 6.6 Hz), 4.45 m (1H, CH_3C**H**N), 7.37 m and 7.48 m (5H, C_6H_5), 7.74 d (2H, *o*-H, $^3J_{PH}$ = 15.6 Hz). Mass spectrum (EI), *m*/*z* (I_{rel}, %): 494.0 (1) $[M]^{+\cdot}$, 462.04 (3) $[M - S]^{+\cdot}$. Found, %: C 61.11; H 7.94; N 2.89; P 5.89; S 13.14; Si 5.62. $C_{25}H_{40}NOPS_2Si$. Calculated, %: C 60.81; H 8.17; N 2.84; P 6.27; S 12.99; Si 5.59. *M* 493.78.

Trimethylsilyl *P*-(4-phenoxyphenyl)-*N*-[(*S*)-(1-phenylethyl)]phosphonamidodithioate (IIIc). Yield 58%, mp 85–87°C. IR spectrum (mineral oil), ν, cm^{-1}: 3619 m (N–H), 1583 m (C–H_{arom}), 1431 m ($\delta_{as}CH_3$), 1323 m (δ_sCH_3), 1242 m [δ_sCH_3(Si)], 1023 m [(P)O–C], 965 s.br (O–C, OC–C), 887 s [ρCH_3(Si)], 675 s (P=S), 531 m (P–S), 436 m (δSPC). ^{1}H NMR spectrum, δ, ppm: 0.44 s [9H, $(CH_3)_3$Si], 1.67 d (3H, C**H**$_3$CHN, $^3J_{HH}$ = 6.8 Hz), 4.43 m (1H, CH_3C**H**N), 7.33–7.85 m (12H, C_6H_5, *m*-H), 7.93 d (2H, *o*-H, $^3J_{PH}$ = 9.2 Hz), 7.97 d (2H, *o*-H, $^3J_{PH}$ = 8.7 Hz), 8.68 m (1H, NH). Found, %: C 60.02; H 6.19; N 3.27; P 6.57; S 14.01; Si 5.88. $C_{23}H_{28}NOPS_2Si$. Calculated, %: C 60.36; H 6.17; N 3.06; P 6.77; S 14.01; Si 6.14.

Trimethylsilyl *P*-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-*N*-[(*R*)-(1-phenylethyl)]phosphonamidodithioate (IIIb). Yield 80%. Found, %: C 61.19; H 8.00; N 2.70; P 6.22; S 13.34; Si 5.50. $C_{25}H_{40}NOPS_2Si$. Calculated, %: C 60.81; H 8.17; N 2.84; P 6.27; S 12.99; Si 5.59.

Trimethylsilyl *N*-[(*R*)-(1-phenylethyl)]-*P*-(4-phenoxyphenyl)phosphonamidodithioate (IIId). Yield 93%, mp 88–89°C. Mass spectrum (EI), *m*/*z* (I_{rel}, %): 442.96 (1) $[M - Me]^{+\cdot}$, 428.96 (1) $[M - 2Me]^{+\cdot}$, 413.01 (1) $[M - 3Me]^{+\cdot}$, 381.00 $[M - Ph]^{+\cdot}$. Found, %: C 60.35; H 6.39; N 3.21; P 6.47; S 14.35; Si 5.93. $C_{23}H_{28}NOPS_2Si$. Calculated, %: C 60.36; H 6.17; N 3.06; P 6.77; S 14.01; Si 6.14. *M* 457.68.

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