SYNTHESIS AND STEREOCHEMISTRY OF COMPOUNDS CARRYING TWO CHIRAL ALKYLALKOXYTHIOPHOSPHORYL SUBSTITUENTS ON THE PHOSPHORUS ATOM

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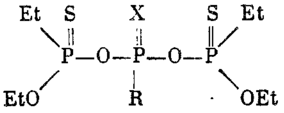
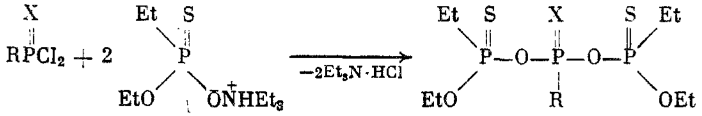
Pseudochirality of the phosphorus atom has been observed in compounds in which the phosphorus carries two identical chiral substituents. Compounds have been reported [1-4] in which the chiral center in these substituents is carbon. The ^{31}P NMR spectrum of 1,2,3-triphenyltrifluorophosphine is given in [5], in which the pseudochirality is due to the presence in the molecule of two identical substituents with chiral phosphorus atoms. However, the 1,2,3-triphenyltriphosphine was not isolated in the pure state, and its spectral data were extrapolated from a complex spectrum of a mixture of several phosphines.

We here report the synthesis and an examination of the stereochemistry of compounds with a pseudochiral phosphorus atom, of general formula:



$R = Ph$, $X =$ lone pair (I), $R = Me$, $X = O$ (II), $R = Ph$, $X = S$ (III).

Bis(ethylethoxythiophosphoryl) phenylphosphonite (I) and bis(ethylethoxythiophosphoryl) methylphosphonate (II) were obtained by reacting phenyldichlorophosphine (I') and methyl dichlorophosphonate (II') with two equivalents of the triethylammonium salt of racemic O-ethylethylthiophosphonic acid:



$R = Ph$, $X =$ lone pair (I') $R = Me$, $X = O$ (II').

(I), (II)

Bis(ethylethoxythiophosphoryl) phenylthiophosphonate (III) was obtained by treating (I) with sulfur.

Compounds (I)-(III) are capable of existing as four stereoisomers. Two of the stereoisomers, in which the chiral phosphorus atoms have identical configurations, are enantiomers with respect to each other, and together comprise the racemic d,*l*-form. The central phosphorus in these isomers is achiral. The other two stereoisomers, in which the chiral phosphorus atoms have antipodal configurations (meso-forms), are diastereoisomers in which the central phosphorus is pseudochiral.

The stereoisomeric composition of the products obtained was examined by NMR. The $^{31}P-\{^1H\}$ NMR spectrum of (I) in benzene showed two groups of signals, one at ~95 ppm (P=S) and one at ~150 ppm (P(III)). Signals for the phosphorus atoms of the two chiral thiophosphoryl groups were seen as two doublets with POP coupling constants of 24.7 and 26.8 Hz. The signals for the three-coordinated phosphorus consist of two triplets A and C, with a multiplet B (doublet of doublets) situated between them. The triplets have POP coupling constants of 25.1 (A) and 29.0 Hz (C), and the multiplet B, 29.5 and 25.9 Hz. The ratio of integral intensities A:B:C is 1.1:2.3:1. It is noteworthy that the centers of the triplets A and C are located at different distances from the center of the multiplet B (1.23 and 1.45 ppm).

Bearing in mind that the enantiomers of the racemic d,*l*-form do not differ in their NMR spectra in achiral media, it may be concluded from the ratio of integral intensities that

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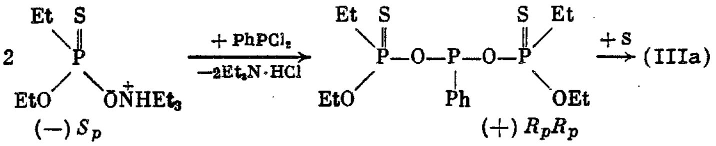
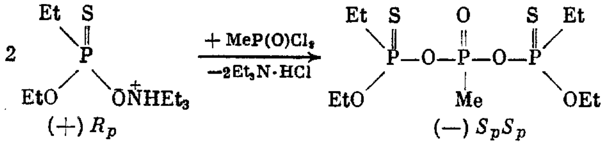
triplets A and C correspond to the two nonequivalent meso-forms, and the multiplet B to the d,*l*-form. In fact, in the spectrum of bis(ethylethoxythiophosphoryl)phenylphosphonite (Ia), obtained from the optically active O-ethylethylthiophosphonic acid with $[\alpha]_D^{20}$ −12.72° (optical purity ~90%), in the ~150 ppm region the intensity of the triplet signals is almost at the noise level. In this instance, the intense multiplet corresponds mainly to one of the enantiomers of the d,*l*-form of (I), namely the enantiomer with the R-configuration of the chiral phosphorus atoms. The levorotatory O-ethylethylthiophosphonic acid is known [6] to have the phosphorus atom in the S-configuration, and the reaction of its triethylammonium salt with phenyldichlorophosphine is known not to affect the chiral centers:



The signals for the three-coordinated phosphorus in the enantiomers of the d,*l*-form consist of a doublet of doublets, indicating that the two chiral phosphorus atoms are nonequivalent. In theory, the signals for the phosphorus atoms of the two P=S groups in (I) should appear as four doublets, since the central phosphorus is characterized by four POP coupling constants. In fact, replacement of the benzene solvent by carbon tetrachloride results in the appearance in the $^{31}P-\{^{1}H\}$ NMR spectrum of (I) at ~95 ppm of four doublets with coupling constants of 29.1, 28.0, 24.2, and 25.0 Hz.

Similar behavior, qualitatively speaking, is seen in the $^{31}P-\{^{1}H\}$ spectrum of (II). The spectrum consists of three triplet signals with an integral intensity ratio A':B':C' of 1:2.1:1.1. The triplets have three different POP coupling constants: 32.9 (A'), 31.9 (B'), and 39.0 Hz (C'). The centers of the triplets A' and C', as in the case of (I), lie at different distances from the center of the triplet B' (0.09 and 0.16 ppm). In the $^{31}P-\{^{1}H\}$ NMR spectrum of bis(ethylethoxythiophosphoryl)methylphosphonate (IIa), obtained from optically active O-ethylethylthiophosphonic acid with $[\alpha]_D^{20}$ +11.98° (optical purity ~85%), only one triplet is seen near 11 ppm. This triplet corresponds to the principal enantiomeric d,*l*-form of (II) in which the chiral phosphorus atoms have the S-configuration.



Hence, triplets A' and C' correspond to the two diastereoisomeric meso-forms, and triplet B' to the racemic d,*l*-form of (II).

In contrast to the spectra of (I) and (II), the $^{31}P-\{^{1}H\}$ NMR spectrum of (III), in the region of the signals for the central phosphorus atom (~91 ppm), there are only two triplets, with an integral intensity ratio of 2.7:1, and POP coupling constants of 41.0 and 39.1 Hz. The distance between the centers of these triplets is 0.25 ppm. As might be expected, the same region in the spectrum of bis(ethylethoxythiophosphoryl) phenylthiophosphonate (IIIa), obtained from optically active O-ethylethylthiophosphonic acid with $[\alpha]_D^{20}$ −12.72° (optical purity ~90%), contains only one triplet, with a coupling constant of 41.0 Hz. In the case of (III), therefore, the spectrum shows overlapping of the triplet (A") of one of the meso-forms with the triplet C", corresponding to the enantiomers of the d,*l*-form.

It is noteworthy that the diastereoisomer ratio in both (I) and (II) is equal to the statistical value, 1:2:1. Compound (III) is obtained from (I) by the addition of sulfur without change in the configuration of the three-coordinated phosphorus atom. The statistical diastereoisomer ratio indicates the absence of stereoselectivity in the formation of these compounds.

EXPERIMENTAL

$^{31}P-\{^{1}H\}$ NMR spectra were obtained on a Bruker WM-250 spectrometer at a frequency of 101.27 MHz, with 85% H_3PO_4 as external standard. The concentration of solute was 0.4 mole/liter, and the temperature of the solution 308 K. Optical rotations were measured on an automatic Polamat polarometer (Carl Zeiss, Jena).

Bis(ethylethoxythiophosphoryl)Phenylphosphonite (I). To a mixture of 4.15 g (0.027 mole) of O-ethylethylthiophosphoric acid and 2.8 g (0.028 mole) of triethylamine in 100 ml of ether was added dropwise at −45°C with stirring under argon over 30 min a solution of 2.41 g (0.013 mole) of phenyldichlorophosphine in 15 ml of ether. After stirring for 30 min at −45°C and a further 1 h at 20°C, the solid which separated was filtered off and the filtrate evaporated under reduced pressure to give 5.45 g (97.8%) of (I) as a clear liquid, n_D^{20} 1.5354. Found, %: P 22.03; S 15.93. $C_{14}H_{25}O_4P_3S_2$. Calculated, %: P 22.46; S 15.46. Similarly, from 4 g (0.026 mole) of O-ethylethylthiophosphonic acid with $[\alpha]_D^{20}$ −12.72° (pure compound), 2.8 g (0.028 mole) of triethylamine and 2.32 g (0.013 mole) of phenyldichlorophosphine there was obtained 5.3 g (98.5%) of (Ia), n_D^{20} 1.5343, $[\alpha]_D^{20}$ +18.86° (c 10.4, C_6H_6). Found, %: P 21.87; S 15.76.

Bis(ethylethoxythiophosphoryl)Methylphosphonate (II). As for (I), from 3 g (0.019 mole) of O-ethylethylthiophosphoric acid, 2.1 g (0.021 mole) of triethylamine, and 1.3 g (0.0097 mole) of methyl dichlorophosphonate there was obtained 3.5 g (97.2%) of (II), n_D^{20} 1.4978. Found, %: P 24.92; S 17.63. $C_9H_{23}O_5P_3S_2$. Calculated, %: P 25.27; S 17.39. Similarly, from 1.5 g (0.0097 mole) of O-ethylethylthiophosphonic acid with $[\alpha]_D^{20}$ +11.98° (pure compound), 1 g (0.01 mole) of triethylamine, and 0.65 g (0.0049 mole) of methyl dichlorophosphonate there was obtained 1.76 g (98.3%) of (IIa), n_D^{20} 1.4970, $[\alpha]_D^{20}$ −33.45° (c 9.1, C_6H_6). Found, %: P 25.55; S 16.90.

Bis(ethylethoxythiophosphoryl)Phenylthiophosphonate (III). To a solution of 4 g (0.0097 mole) of (I) in 15 ml of benzene was added 0.32 g (0.01 mole) of powdered sulfur, and the mixture boiled for 15 min. Removal of the solvent under reduced pressure gave 4.3 g (99.8%) of a colorless liquid, n_D^{20} 1.5430. Found, %: P 29.41; S 22.01. $C_{14}H_{25}O_4P_3S_3$. Found %: P 29.85; S 21.52. Similarly, from 4.3 g (0.01 mole) of (Ia) and 0.5 g (0.011 mole) of sulfur was obtained 4.55 g (98.9%) of (IIIa), n_D^{20} 1.5443, $[\alpha]_D^{20}$ +40.02 (c 10.3, C_6H_6). Found, %: P 29.62; S 21.93.

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CONCLUSIONS

1. Compounds containing a pseudochiral phosphorus atom have been prepared (bis(ethylethoxythiophosphoryl) phenylphosphinite, bis(ethylethoxythiophosphoryl) methylphosphonate, and bis(ethylethoxythiophosphoryl) phenylthiophosphonate). Their optically active stereoisomers have been obtained.

2. $^{31}P-\{^1H\}$ NMR spectroscopy has been used to show that the compounds obtained from racemic O-ethylethylthiophosphonic acid are a mixture of the three diastereoisomers (two meso-forms and the racemic d,*l*-form) in the statistical ratio, 1:2:1.

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