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Reactions of Benzopentathiepin with Trialkyl Phosphites. A New Preparative Method for *S*-Aryl *O,O′*-Dialkyl Thiophosphates

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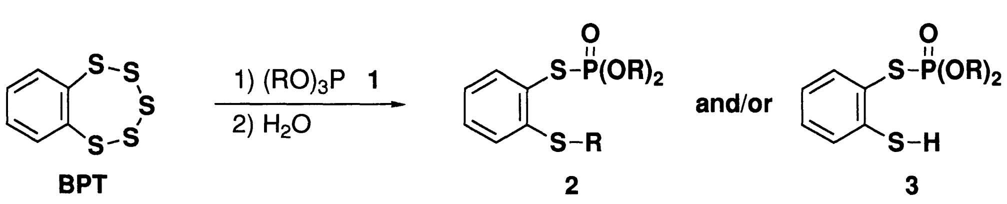
Benzopentathiepin readily reacted with trialkyl phosphites to give *S*-[2-(alkylthio)-phenyl] *O,O′*-dialkyl thiophosphates and/or *O,O′*-dialkyl *S*-(2-mercaptophenyl) thiophosphates. The selectivity for formation of these thiophosphates was dramatically affected by the reaction temperature and the solvent used.

There is considerable current interest on the chemical behavior of various cyclic polysulfides.1) We have reported the syntheses, structures, and reactions of cyclic polysulfides fused to benzene ring such as benzopentathiepin (BPT) and the related compounds.2) However, there have been a few reports on the reactions of cyclic polysulfides with organic phosphorus compounds.3) Now we have found that BPT readily reacted with several trialkyl phosphites **1** to give *S*-[2-(alkylthio)phenyl] *O,O′*-dialkyl thiophosphates **2** and/or *O,O′*-dialkyl *S*-(2-mercaptophenyl) thiophosphates **3** (Scheme 1). In this paper, we report the results of these reactions and discuss the reaction mechanism.

A typical reaction procedure is as follows. To a stirred solution of BPT (118 mg, 0.5 mmol) in CH_2Cl_2 (10 mL) was added dropwise 4 equiv. of trimethyl phosphite (**1a**) (0.24 mL, 2.0 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h under reflux condition and then treated with water. After the usual work-up, crude products were purified by column chromatography (silica gel; eluent, hexane/EtOAc = 3/2) to give **2a**4) in 66% yield together with a quantitative amount (3 equiv.) of trimethyl thiophosphate (Table 1).



Scheme 1.

The intramolecular Arbuzov rearrangement products, *S*-[2-(alkylthio)phenyl] *O,O′*-dialkyl thiophosphates **2a-d**, were obtained in moderate yields in the reactions of BPT with trialkyl phosphites **1a-d** in CH_2Cl_2 under reflux (run 1-4). The same treatment of BPT with triphenyl phosphite (**1e**), however, gave no products due to the low nucleophilicity of **1e**. Surprisingly, the same treatment of BPT with **1a-d** at -15 °C gave the corresponding *O,O′*-dialkyl *S*-(2-mercaptophenyl) thiophosphates **3a-d**5) as sole products in moderate yields (run 6-9). We examined the effects of the temperature and the solvent on the reaction pathways.

When BPT was treated with **1c** at several temperatures in the range from -15 to 40 °C, the ratio of **2c**/**3c** was increased with elevating temperature (Table 2). Furthermore, a remarkable solvent effect was also observed as shown in Table 3 and the ratio of **2c**/**3c** was increased in proportion to the Dimroth-Reichardt parameter [$E_T(30)$] of the solvent used. The isolated yields of the mixture of **2c** and **3c** in Table 2 and 3 were similar to that of run 3 or 8 in Table 1.

Table 1. Reactions of Benzopentathiepin (BPT) with Phosphites

Run	Phosphite **1**		Temp/°C	Time/h	Solvent	Isolated yield/%			
	R					**2**		**3**	
1	Me	**1a**	reflux	2	CH_2Cl_2	66	**2a**	-	-
2	Et	**1b**	reflux	2	CH_2Cl_2	63	**2b**	-	-
3	i-Pr	**1c**	reflux	2	CH_2Cl_2	60	**2c**	-	-
4	Bu	**1d**	reflux	2	CH_2Cl_2	70	**2d**	-	-
5	Ph	**1e**	reflux	2	CH_2Cl_2	-	-	-	-
6	Me	**1a**	-15	4	CH_2Cl_2	-	-	65	**3a**
7	Et	**1b**	-15	4	CH_2Cl_2	-	-	51	**3b**
8	i-Pr	**1c**	-15	4	CH_2Cl_2	-	-	59	**3c**
9	Bu	**1d**	-15	4	CH_2Cl_2	-	-	86	**3d**

Table 2. Reactions of BPT with **1c** in CH_2Cl_2 (Temperature Effect)

Run	Temp/ °C	Product ratio[a)] **2c**/**3c**
1	40	95/5
2	20	71/29
3	-15	0/100

a) The ratios were determined by ^{1}H NMR.

Table 3. Reactions of BPT with **1c** at 20 °C (Solvent Effect)

Run	Solvent	ε[a)]	$E_T(30)$	Product ratio[b)] **2c**/**3c**
1	CH_2Cl_2	8.93	41.1	71/29
2	$CHCl_3$	4.81	39.1	59/41
3	THF	7.58	37.4	55/45
4	Et_2O	4.34	34.6	38/62
5	CCl_4	2.24	32.5	25/75

a) Dielectric constant.

b) The ratios were determined by ^{1}H NMR.

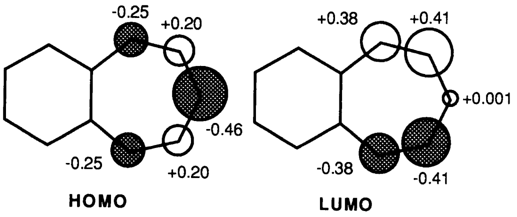
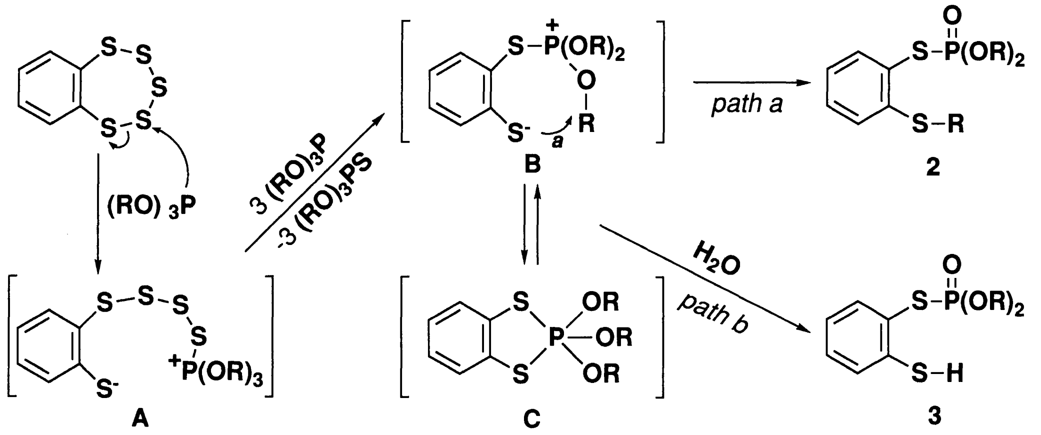


Fig. 1. HOMO and LUMO molecular orbitals of BPT.

A plausible reaction pathway based on the above results is as follows (Scheme 2). In an attempt to understand the initial reaction site of BPT, semiempirical PM3 calculation was carried out.[6,7] The computed HOMO and LUMO of BPT are shown in Figure 1 and the density gradient of virtual LUMO of polysulfide ring suggests a significant favoring of the nucleophilic attack to the sulfur atom at 2-position. Therefore, trialkylphosphite initially attacks the sulfur atom at 2-position to form zwitterionic intermediate **A**. Although the following desulfurization steps are still unclear at this time, on losing sulfur atoms intermediate **A** is transformed into zwitterionic intermediate **B** or phosphorane intermediate **C** accompanying the formation of trialkyl thiophosphates. It can be considered that there is an equilibrium between intermediates **B** and **C**, whereas low temperature ^{1}H, ^{13}C, and ^{31}P NMR spectra of the reaction mixture in CD_2Cl_2 (in the case of trimethyl phosphite **1a**) were attributed to either phosphorane **C** or a mixture of rapid equilibrium between **B** and **C**.[8] On warming to room temperature ^{31}P NMR signal at 1.26 ppm disappeared and it was replaced by that of thiophosphate **2a** (24.0 ppm). An intramolecular Arbuzov rearrangement of intermediate **B** takes place at relatively high temperature according to *path a* to give *S*-[2-(alkylthio)phenyl] *O,O'*-dialkyl thiophosphate **2** . On the other hand, upon treatment with water at -20 °C the signal at 1.26 ppm disappeared at once and it was replaced by that of thiophosphate **3a** (23.5 ppm). At low temperature phosphorane **C** or a mixture of rapid equilibrium between **B** and **C** reacts with water to give *O,O'*-dialkyl *S*-(2-mercaptophenyl) thiophosphate **3** (*path b*).



Scheme 2.

Since it has been well known that such types of thiophosphates **2** and **3** frequently show biological activities such as pesticidal effect, some procedures for the synthesis of these compounds have been developed.[9] Our present method will provide a new preparative route for *S*-aryl *O,O'*-dialkyl thiophosphates.

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4) Compound **2a**: mp 61 °C; IR (KBr) 2950, 1440, 1245, 1010, and 795 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ=7.57 (ddd, J=7.8, 1.8 Hz, $^4J_{PH}$=1.8 Hz, 1H, 6-ArH), 7.38 (td, J=7.8, 1.8 Hz, 1H, 4-ArH), 7.20 (d, J=7.8 Hz, 1H, 3-ArH), 7.13 (t, J=7.8 Hz, 1H, 5-ArH), 3.82 (d, $^3J_{PH}$=12.7 Hz, 6H, OCH_3), 2.48 (s, 3H, SCH_3); $^{13}C\{^1H\}$ NMR (125 MHz, CD_2Cl_2) δ=145.1 (d), 137.0 (d), 130.4 (d), 125.4 (d), 125.3 (d), 123.9 (d), 54.9 (d), 15.9 (s); ^{31}P NMR (109 MHz, CD_2Cl_2) δ=24.0; MS m/z 264 (M^+). Found: C, 40.71; H, 4.90%. Calcd for $C_9H_{13}O_3PS_2$: C, 40.90; H, 4.96%. Compounds **2b**-**d** were also identified by IR and NMR spectroscopy and elemental analysis.

5) Compound **3a**: colorless oil; IR (neat) 2950, 2480, 1430, 1240, 1010, and 760 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ=7.59 (ddd, J=7.8, 1.7 Hz, $^4J_{PH}$=1.7 Hz, 1H, 6-ArH), 7.39 (d, J=7.7 Hz, 1H, 3-ArH), 7.25 (td, J=7.8, 1.8 Hz, 1H, 4-ArH), 7.14 (t, J=7.7 Hz, 1H, 5-ArH), 4.24 (s, 1H, SH), 3.62 (d, $^3J_{PH}$=12.8 Hz, 6H, CH_3); $^{13}C\{^1H\}$ NMR (125 MHz, CD_2Cl_2) δ=139.8 (d), 137.6 (d), 130.5 (d), 130.0 (d), 126.6 (d), 125.3 (d), 55.0 (d); ^{31}P NMR (109 MHz, CD_2Cl_2) δ=23.5; Found: m/z 249.9892. Calcd for $C_8H_{11}O_3PS_2$: M, 249.9886. Compounds **3b**-**d** were also identified by IR and NMR spectroscopy and elemental analysis.

6) PM3 calculations of BPT were carried out on a HITAC M680/160E computer by the MOPAC Ver. 6.02 [(QCPE No. P015), J. J. P. Stewart, *QCPE Bull.*, **9**, 10 (1989); Revised as Ver. 6.01 by T. Hirano, University of Tokyo, for HITAC and UNIX machines, *JCPE Newsletter,* **1**, 10 (1989); Revised as Ver. 6.02 by present authors]. The structure of BPT was optimized by Allinger's MM2(77) molecular mechanics force field.[7)]

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8) NMR Spectra of the reaction mixture at -20 °C (R=CH_3) suggest the formation of the pentacoordinated phosphorane; ^{31}P NMR (109 MHz, CD_2Cl_2) δ=1.26; ^1H NMR (270MHz, CD_2Cl_2) δ=7.45-7.35 (m, 2H, ArH), 7.05-6.90 (m, 2H, ArH), 3.63 (d, $^3J_{PH}$=16.2 Hz, 9H, CH_3); $^{13}C\{^1H\}$ NMR (68 MHz, CD_2Cl_2) δ=134.1 (d), 124.3 (d), 122.3 (d), 56.3 (d). The relatively down-field shift of ^{31}P NMR for the phosphorane has previously been observed for phosphoranes bound to two sulfur and three oxygen atoms. For example, see, B. C. Burros, N. J. De'Ath, D. B. Denny, D. Z. Denny, and I. J. Kipnis, *J. Am. Chem. Soc.*, **100**, 7300 (1978); Y. Kimura, T. Kokura, and T. Saegusa, *J. Org. Chem.*, **48**, 3815 (1983); K. C. K. Swamy, J. M. Holmes, R. O. Day, and R. R. Holmes, *J. Am. Chem. Soc.*, **112**, 6092 (1990); J. Hans, R. O. Day, L. Howe, and R. R. Holmes, *Inorg. Chem.*, **30**, 3132 (1991). Variable temperature NMR studies from -90 to -20 °C showed no significant change in the spectra. Therefore, it can not be ruled out that these NMR signals show the coalescence ones of rapid equilibrium between phosphorane and zwitterionic compound at this stage.

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