

Synthesis of 4-Phosphonyl-1,3-dithioles and 1,3-Dithiolanes via the $\text{Bu}_3\text{P-CS}_2$ Adduct

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ABSTRACT: *New one-pot syntheses of 2-arylidene-4-phosphonyl-1,3-dithioles or 1,3-dithiolanes were realized by reaction of the tributylphosphine-carbon disulfide adduct with phosphonyl alkynes or phosphonyl alkenes and aldehydes in moderate yields.*
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INTRODUCTION

Since the red crystalline adduct formed between a trialkylphosphine (Bu_3P) and carbon disulfide (CS_2) had been established by X-ray crystallography to have a 1,3-dipolar structure [1], the reactivities of this adduct have not been adequately investigated. Although several papers have been reported in the recent literature on cycloaddition of the $\text{Bu}_3\text{P-CS}_2$ adduct with electron-deficient alkynes [2–7], the reactivity of this adduct with double bonds has been examined only for electron-deficient alkenes, such as maleic anhydride [8] and *N*-phenylmaleimide [8], and for an angle-strained alkene, such as norbornene [4,9,10]. However, the $\text{Bu}_3\text{P-CS}_2$ adduct was unreactive towards a wide variety of alkenes, such as styrene, stilbene, cyclohexene, and cyclopentene [9].

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As part of our research on new syntheses of phosphonyl heterocycles, this article will report the synthesis of the title compounds using the $\text{Bu}_3\text{P-CS}_2$ adduct.

RESULTS AND DISCUSSION

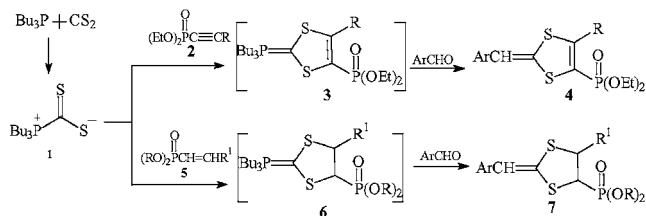
Aldehydes and the phosphonylalkyne **2** or phosphonylalkene **5** are successively added to the preformed $\text{Bu}_3\text{P-CS}_2$ adduct **1** in solution. After several hours, the products **4** or **7** are separated from the reaction mixture, and are characterized by ^1H NMR, ^{31}P NMR spectroscopy and elemental analyses (Tables 1 and 2).

As depicted in Scheme 1, the formation of **4** or **7** might occur via the ylide **3** or **6**, which then reacts further with an aldehyde in the manner expected for the Wittig reaction [11,12]. The NMR spectra indicate that the compound **4** is a mixture of two isomers. To further ascertain the configuration of **4c**, as a typical example, we have performed an X-ray single-crystal diffraction study on this compound, as shown in Fig. 1. Crystallographic analysis has shown that the 2-arylidene-1,3-dithiole ring is located in a plane (Table 3). Depending on the position of the phosphonyl group relative to the aromatic ring, E and Z isomers are easily identified.

The crystal structure depicted in Fig. 1 is assigned to the E configuration because the phosphonyl group and aromatic ring are on opposite sides of the plane. For the E isomer, the NMR spectra reveal that δ_{H} of the vinyl proton (ArCH=) is 6.61, and δ_{P}

TABLE 1 ^1H NMR, ^3P NMR Spectral Data, and Elemental Analysis of Compounds **4**

No.	Solvent ^a	M.P. (°C)	Yield ^b (%)	R	Ar	^1H NMR (ArCH=C) ^c (ppm)			^3P NMR (ppm)			Elemental Analysis ^e		
						E	Z	Ratio (E/Z) ^d	E	Z	Ratio (E/Z) ^d	C	H	N
4a	PE/EA = 3:1 ^f	128–130	64.5	Cl	4-O ₂ NC ₆ H ₄	6.46 (d) ^g	6.52 (s)	1:1	3.09	3.26	1:1	41.06 (41.23)	3.88 (3.71)	3.67 (3.43)
4b	PE/EA = 1:1 ^h	180–182	38.3	Cl	3-O ₂ NC ₆ H ₄	6.56 (d) ^g	6.58 (s)	1:1	6.06	6.30	1:1	41.35 (41.23)	3.65 (3.71)	3.75 (3.43)
4c	PE/EA = 1:1 ^f	180–182	50.7	H	4-O ₂ NC ₆ H ₄	6.61 (s)	6.59 (s)	3:1	5.81	6.00	3:1	44.59 (45.03)	3.89 (4.32)	3.38 (3.75)
4d	PE/EA = 1:1 ^h	180–182	40.6	CH ₃	4-O ₂ NC ₆ H ₄	6.49 (s)	6.48 (s)	3:1	6.43	6.60	3:1	46.29 (46.50)	4.49 (4.68)	3.36 (3.62)

^aPE is petroleum ether; EA is ethyl acetate.^bCalculated on Bu₃P weight.^cOther signals are omitted.^dThe ratio of E- and Z-isomer was estimated on the basis of NMR data.^eCalculated value in parentheses.^fRecrystallization solvent.^g $^5J_{\text{P-H}} = 2.2$ Hz.^hTLC developing solvent.

SCHEME 1

is 5.81. Therefore, another isomer of **4c** is assigned to the Z configuration (δ_{P} 6.00, δ_{H} 6.59). On the analogy of these data, the configuration of **4d** could be ascertained. The observation is in accord with the literature report [13] that the chemical shift of the vinyl proton in the E-unsaturated ester will occur at lower field than that observed for the corresponding Z isomer.

The two isomers of **4a** have been separated by TLC. The NMR spectra show that an isomer of **4a** has the chemical shift δ_{P} 3.26, δ_{H} 6.52; another isomer has δ_{P} 3.09, δ_{H} 6.46 ($^5J_{\text{PH}} = 2.2$ Hz). The latter is assigned to the E configuration in which the chloro atom and the aromatic ring are on opposite sides of the planar dithiole. In other words, the phosphonyl group and vinyl proton are also on opposite sides; hence long-range coupling is observed between the vinyl proton and the phosphorus atom. Thus, the former is assigned the Z configuration. Similarly, the configuration of **4b** could be assigned.

It is interesting to note that the two isomers of **4a** readily establish an equilibration in organic solvents, and in both, the ratio is 1:1. By comparison, the E isomer of **4a** is more rapidly converted to the E/Z mixture than the corresponding Z isomer. The mechanism of interconversion merits further investigation.

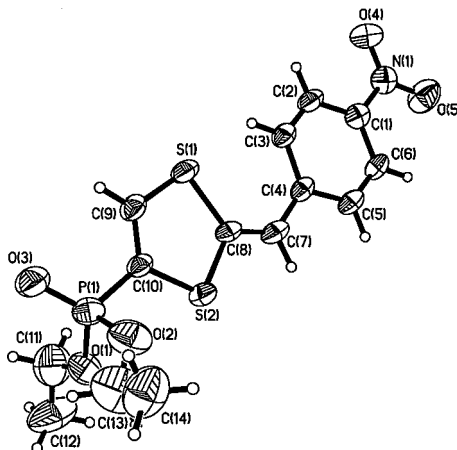
FIGURE 1 Crystal structure of **4c**.

TABLE 2 ¹H NMR, ³¹P NMR Spectral Data, and Elemental Analysis of Compounds 7

No.	Solvent ^a	M.P. (°C)	Yield ^b (%)	R	R ¹	Ar	¹ H NMR (ArCH=C) ^c (ppm)	³¹ P NMR (ppm)			Elemental Analysis ^d		
								E	Z		C	H	N
7a	EA/PE=1:2 ^e	158–160	74.8	CH ₃	H	4-O ₂ NC ₆ H ₄	6.67 (s)	22.58	22.06	41.48 (41.49)	4.09 (4.06)	4.26 (4.03)	
7b	EA/PE=1:0 ^f		45.3	CH ₃	H	3-O ₂ NC ₆ H ₄	6.65 (s)	22.86	22.39	41.78 (41.49)	4.18 (4.06)	3.99 (4.03)	
7c	EA/PE=1:0 ^f		40.6	CH ₃	H	2-CHOC ₆ H ₄	7.30 (s)	23.01	22.80	47.27 (47.26)	4.58 (4.58)	—	
7d	EA/CH ₂ Cl ₂ =1:15 ^f		30.7	CH ₃	H	C ₆ H ₅	6.63 (s)	23.50	22.95	47.58 (47.67)	4.84 (5.00)	—	
7e	EA/CH ₂ Cl ₂ =1:40 ^f		35.9	CH ₃	H	4-FC ₆ H ₄	6.57 (s)	23.37	22.88	44.92 (44.99)	4.34 (4.41)	—	
7f	EA/PE=11:2 ^f		36.6	CH ₃	H	4-ClC ₆ H ₄	6.55 (s)	23.27	22.74	42.84 (42.79)	4.45 (4.58)	—	
7g	EA/PE=7:1 ^f		31.4	CH ₃	H	3-BrC ₆ H ₄	6.54 (s)	23.18	22.67	38.04 (37.81)	3.75 (3.70)	—	
7h	EA/PE=6:1 ^f		41.2	CH ₃	H	2,4-Cl ₂ C ₆ H ₃	6.78 (s)	22.91	22.56	38.84 (38.82)	3.60 (3.53)	—	
7i	EA/PE=1:1 ^f		43.3	CH ₃	H	2-Furyl	6.49 (s)	23.17	23.01	41.17 (41.09)	4.41 (4.48)	—	
7j	AC/CH ₂ Cl ₂ =1:10 ^f		20.5	CH ₃	CH ₃	4-O ₂ NC ₆ H ₄	6.60 (s), 6.58 (s)	22.54	22.12	43.24 (43.21)	4.48 (4.46)	3.45 (3.88)	
7k	EA/PE=1:2 ^e	86–89	70.9	CH ₂ CH ₃	H	4-O ₂ NC ₆ H ₄	6.65 (s)	20.01	19.48	44.64 (44.79)	4.89 (4.83)	3.30 (3.73)	
7l	EA/PE=1:1 ^f		44.7	CH ₂ CH ₃	H	3-O ₂ NC ₆ H ₄	6.62 (s)	20.13	19.66	44.69 (44.79)	4.64 (4.83)	3.86 (3.73)	
7m	EA/CH ₂ Cl ₂ =1:40 ^f		41.1	CH ₂ CH ₃	H	2-CHOC ₆ H ₄	7.30 (s)	20.27	20.09	49.99 (50.27)	5.38 (5.34)	—	
7n	EA/PE=1:0 ^f		31.0	CH ₂ CH ₃	H	C ₆ H ₅	6.62 (s)	20.76	20.28	50.73 (50.89)	6.08 (5.80)	—	
7o	EA/PE=1:0 ^f		36.4	CH ₂ CH ₃	H	4-FC ₆ H ₄	6.57 (s)	20.66	20.20	48.35 (48.26)	5.16 (5.21)	—	
7p	EA/PE=3:1 ^f		33.7	CH ₂ CH ₃	H	4-ClC ₆ H ₄	6.57 (s)	20.52	20.02	46.18 (46.09)	5.02 (4.97)	—	
7q	EA/PE=6:1 ^f		29.8	CH ₂ CH ₃	H	3-BrC ₆ H ₄	6.52 (s)	20.42	19.98	41.29 (41.08)	4.48 (4.43)	—	
7r	EA/PE=10:1 ^f		40.5	CH ₂ CH ₃	H	2,4-Cl ₂ C ₆ H ₃	6.78 (s)	20.32	19.97	41.92 (42.11)	4.13 (4.29)	—	
7s	EA/PE=12:1 ^f		44.1	CH ₂ CH ₃	H	2-Furyl	6.51 (s)	20.52	20.33	45.18 (44.99)	5.41 (5.35)	—	

^aPE is petroleum ether; EA is ethyl acetate; AC is acetone.^bCalculated on Bu₃P weight.^cOther signals are omitted.^dCalculated value in parentheses.^eRecrystallization solvent.^fTLC developing solvent.

TABLE 3 Important Molecular Parameters of Compound **4c**

Bond Lengths ^a (Å)		Angle ^{a,b} (deg)	
P(1)—C(10)	1.747 (6)	O(3)—P(1)—O(2)	118.9 (3)
P(1)—O(1)	1.585 (5)	O(3)—P(1)—O(1)	117.1 (3)
P(1)—O(2)	1.556 (5)	O(2)—P(1)—O(1)	99.3 (3)
P(1)—O(3)	1.431 (4)	O(3)—P(1)—C(10)	113.5 (3)
S(1)—C(8)	1.768 (5)	O(2)—P(1)—C(10)	100.3 (3)
S(1)—C(9)	1.733 (6)	O(1)—P(1)—C(10)	105.2 (2)
S(2)—C(8)	1.734 (6)	C(9)—S(1)—C(8)	95.5 (3)
S(2)—C(10)	1.751 (5)	C(8)—S(2)—C(10)	97.9 (3)
C(4)—C(7)	1.440 (8)	C(8)—C(7)—C(4)	132.0 (5)
C(7)—C(8)	1.343 (7)	C(7)—C(8)—S(2)	120.9 (4)
C(9)—C(10)	1.341 (7)	C(7)—C(8)—S(1)	126.4 (4)
		S(2)—C(8)—S(1)	112.7 (3)
		C(10)—C(9)—S(1)	119.4 (4)
		C(9)—C(10)—P(1)	124.7 (4)
		C(9)—C(10)—S(2)	114.4 (4)
		P(1)—C(10)—S(2)	120.9 (3)

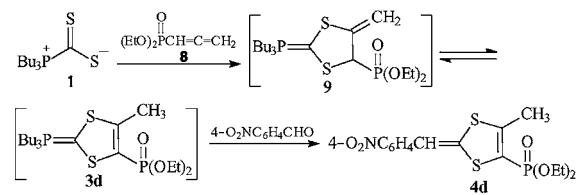
^aNumbers in parentheses in the second and fourth columns are estimated standard deviations in the least significant digits.

^bPlane1 = S(1)—C(9)—C(10)—S(2)—C(8); Plane 2 = C(1)—C(2)—C(3)—C(4)—C(5)—C(6), dihedral angle degrees Plane1—Plane 2 = 5.9°.

The ³¹P NMR spectrum shows that the compound **7** (R=H) has two peaks, and in the ¹H NMR spectrum, it appears that the vinyl proton appears as a single signal. There is general agreement that the 1,3-dipolar cycloaddition reaction is a concerted and stereospecific syn cycloaddition with respect to the dipolarophile [14]. The adduct **1** reacts with dipolarophile **5** (R=H) by syn addition stereoselectively to give the ylide **6**, which reacts with an aldehyde to give a pair of diastereoisomers. Therefore, two ³¹P resonances of the diastereoisomers are observed; the vinyl proton probably has the same chemical shifts in its ¹H NMR spectrum. In the case of **7j** (R = R¹ = CH₃), the adduct **1** reacts with *cis*-**5** and *trans*-**5** (R = R¹ = CH₃) in the same manner as with **5** (R = H) to form two ylides. Because of steric effects, only the ylide formed by *cis*-**5** (R = R¹ = CH₃) predominantly reacts further with an aldehyde to give a pair of diastereoisomers which has two peaks in its ³¹P NMR spectrum and two signals of the vinyl proton in the ¹H NMR spectrum.

We have also obtained interesting results in studying the reaction of adduct **1** with the phosphynylallene **8** (Scheme 2).

The first step of the reaction is cycloaddition of adduct **1** with the phosphynylallene **8** to give **9**, which then undergoes a 1,3-proton shift leading to **3d**. The product **4d** is also prepared by reaction of adduct **1** with the phosphonyl-1-propyne **2d**, as depicted in Scheme 1. Thus, the mixture of compounds **8** and **2d** that are obtained by the following route



SCHEME 2

(Scheme 3) are also used without separation to give **4d** in good yield.

EXPERIMENTAL

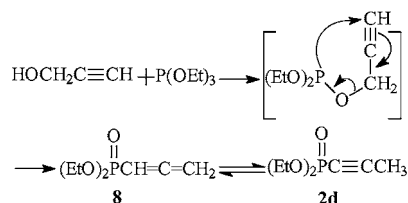
¹H and ³¹P NMR spectra were taken on a Bruker AC-P200 spectrometer with CDCl₃ as solvent. Elemental analyses were run on a Yana MT-3 instrument. (C₂H₅O)₂P(O)C≡CCl [15], (C₂H₅O)₂P(O)C≡CH [16, 17], (C₂H₅O)₂P(O)C≡CCH₃ [18], (C₂H₅O)₂P(O)CH=C=CH₂ [18], (CH₃O)₂P(O)CH=CH₂ [19], (C₂H₅O)₂P(O)CH=CH₂ [20], and (CH₃O)₂P(O)CH=CHCH₃ [21, 22] were prepared according to published procedures.

Preparation of Phosphynylallene **8** and Phosphonyl-1-propyne **2d**

A solution of propargyl alcohol (5.6 g, 0.10 mol), triethyl phosphite (8.3 g, 0.05 mol), *p*-toluenesulfonic acid (0.43 g) in DMF (15 ml) was stirred for 20 h at room temperature. The mixture solution was concentrated under a vacuum to give the crude products. Distillation gave 5.1 g of colorless liquid, b.p. 68–74°C/7.5 Pa, which is the mixture of compounds **8** and **2d**. The mixture can be used directly in the preparation of **4d**. Compounds **8** and **2d** can also be separated by TLC. The developing solvent was petroleum ether:ethyl acetate (1:2).

General Procedure for Preparation of Compounds **4**

A solution of Bu₃P (95%, 0.63 g, 3.0 mmol) and CS₂ (0.25 g, 3.3 mmol) in dry ether (7 ml) and THF (3 ml) was stirred at room temperature for 10 min. Then, the aldehyde (3.0 mmol) and phosphonyl alkyne **2**



SCHEME 3

(3.0 mmol) were successively added. The reaction mixture was stirred at room temperature for 12 h, until the red color of the Bu₃P-CS₂ adduct almost disappeared. The reaction mixture was concentrated in a vacuum to give crude products **4**. Compounds **4a** and **4c** were solids which could be purified by recrystallization. Compounds **4b** and **4d** were viscous liquids and could be purified by TLC.

Procedure for Preparation of Compound 4d from 8

The procedure was the same as that for **4** from **2**.

Procedure for Preparation of Compound 4d from the Mixture of Compounds 2d and 8

The procedure was the same as that for **4** from **2**. The product had the same spectroscopy data as that prepared from **8**, yield 42.1%.

General Procedure for Preparation of Compounds 7

A solution of Bu₃P (95%, 0.63 g, 3.0 mmol) and CS₂ (0.25 g, 3.3 mmol) in anhydrous solvent was stirred at room temperature for 10 min, and the solvent was varied along with the aldehyde that was added in the following process. Then, the aldehyde (3.0 mmol) and phosphonyl alkene (3.0 mmol) were successively added. The reaction mixture was stirred at room temperature for 12–72 h, until the red color of the Bu₃P-CS₂ adduct had almost disappeared. The reaction mixture was concentrated under a vacuum to give crude products **7**. Compounds **7a** and **7k** were solids and could be purified by recrystallization. Compounds **7b–j** and **7l–s** were viscous liquids and could be purified by TLC. The products **7a**, **7b**, **7j**, **7k**, and **7l** were synthesized in dry dichloromethane (10 ml) or anhydrous ether (7 ml) and anhydrous THF (3 ml). The products **7c–i** and **7m–s** were obtained by reactions carried out in anhydrous acetonitrile (10 ml).

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