Phosphorus–Carbon Exchange Promoted by $AlCl_3$: Reactivity of Heterocyclic Systems Containing the S–P–P Unit

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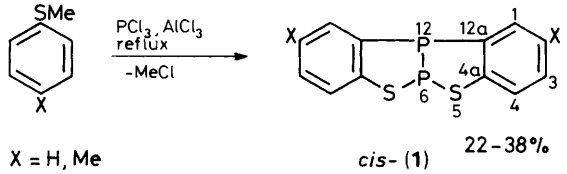
The reaction under mild conditions of fused *cis*-1,2,3-benzothiadiphospholes (**1**) with RCOCl–$AlCl_3$ (R = Me, Et, Pr^i, $CH_2(CH_2)_2CH_2Cl$, hexyl, CH_2Ph) gave fused *cis*-6-R-1,3-benzothiaphospholes (**2**) *via* a phosphorus carbon exchange, in good yields. Use of a variety of acyl chlorides showed that the reaction does not occur when the R group is very bulky. Following the reaction by g.l.c.–m.s., it was noted that, initially, *trans*-(**2**) is formed and this isomerizes to *cis*-(**2**). A mechanism for this unusual phosphorus–carbon exchange is reported.

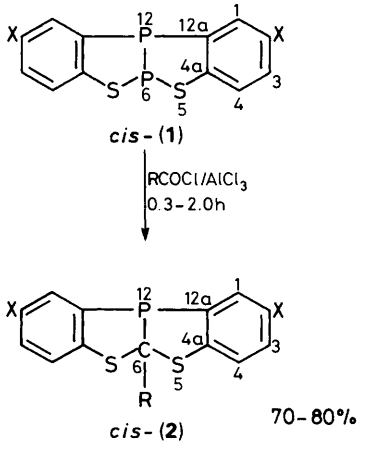
During a study of the use of PCl_3 in the synthesis of new phosphorus and sulphur heterocycles, we prepared *cis*-[1,2,3]benzothiadiphospholo[2,3-*b*][1,2,3]benzothiaphospholes *cis*-(**1**)[1,2] by treating aryl methyl sulphides with PCl_3



Scheme 1.

and $AlCl_3$. This new system was highly unstable to the conditions under which phosphines normally react, *i.e.* formation of phosphonium salts with alkyl halides, oxidation with H_2O_2, reaction with diethyl azodicarboxylate (DEAD)[3]/catechol or with phenyl azide. In such cases, rather than the corresponding salts, oxides, spiro derivatives[4] or phosphazenes[5] of (**1**), decomposition products were obtained, presumably deriving from P–S and P–P bond cleavage.

Exploiting this instability of (**1**) in order to synthesize other phosphorus and sulphur heterocycles, we carried out a Friedel–Crafts acylation with acetyl chloride and $AlCl_3$ and obtained, surprisingly, a highly stereospecific replacement of the phosphorus in the 6-position with the carbonyl carbon atom of acetyl chloride. This phosphorus–carbon exchange occurred under mild conditions in a one-pot reaction, and gave *cis*-6-R-[1,3]benzothiaphospholo[2,3-*b*][1,3]benzothiaphosphole derivatives (**2**) in very good yields. In a previous communication,[6] the first examples of this new heterocyclic system and its *X*-ray crystal structure determination were reported; it was also observed there is the *cis*-configuration between the phosphorus atom and the 6-methyl substituent. We describe here a possible generalization of the reaction with other acyl chlorides and note features involved in this phosphorus–carbon exchange which may lead to an understanding of the mechanism involved.



Scheme 2. **a**, R = Me, X = H; **b**, R = Me, X = Me; **c**, R = Et, X = Me; **d**, R = Pr^i, X = Me; **e**, R = Hex, X = Me; **f**, R = $CH_2(CH_2)_2CH_2Cl$, X = Me; **g**; R = CH_2Ph, X = Me

Results and Discussion

The reaction was carried out by adding acetyl chloride and fused 1,2,3-benzothiadiphospholes (**1**) to a solution of $AlCl_3$ in 1,2-dichloroethane at 5—10 °C. The mixture was brought to, and held at, room temperature and the products (**2**) were recovered by filtration of the mixture on a Florisil column. Scheme 2 shows the results obtained using different acyl chlorides. In all the reactions performed, compounds (**2**) were isolated in very good yields. In contrast when we used acyl chlorides with R = Bu^t, Ph, *p*-ClC_6H_4, CCl_3, we observed disappearance of the starting material (**1**) with formation of unidentified products. Only traces of the corresponding fused 1,3-benzothiaphospholes were detected by g.l.c.–m.s. analysis. From these simple results we deduce that this exchange reaction is dependent on the steric factors associated with the acyl chloride. In fact, with a more constrained R group, it is very likely that cleavage of P–S and/or P–P bonds does occur, but the ring closure is disfavoured presumably because of steric congestion.

Products (**2**) were characterized essentially on the basis of ^1H, ^{13}C, and ^{31}P n.m.r. spectral results. Although a downfield shift for the phosphorus resonance with increasing steric crowding at phosphorus (and consequent widening of P bond angles) has been reported for phosphines,[7] in our heterocycles we found the reverse trend. Although at first sight these results seem to be in disagreement, we believe that the same steric effect gives rise to both. Thus an increase in the bulk of the alkyl group (R = Me, Et, Pr^i) in the 6-position of compounds (**2**) leads to a contraction in the C(1)–P–C(8), C(1)–P–C(15), and C(15)–P–C(8) bond angles with a consequent upfield shift of the ^{31}P signals. In Figure 1 the P bond angles of compound (**2b**) are depicted.

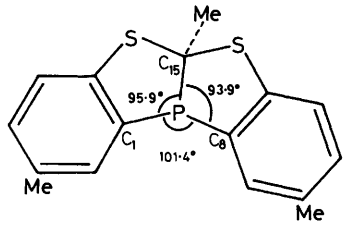


Figure 1.

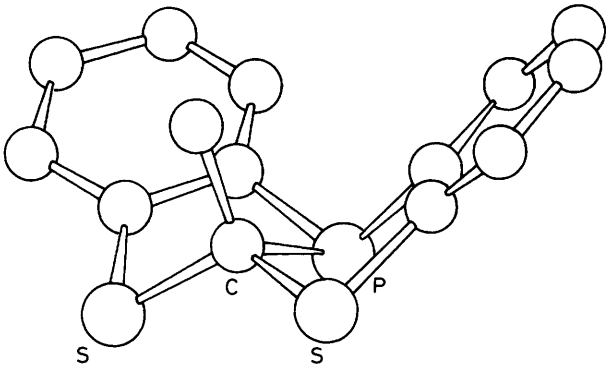
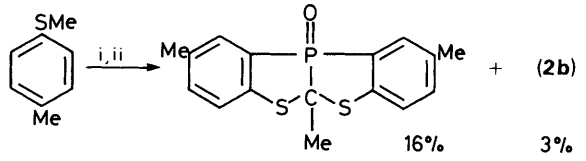
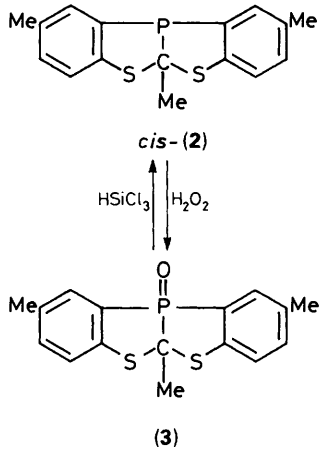


Figure 2. Probable structure of compound *trans*-(**2b**) obtained by PCMODEL program (Serena software[8])



(3)

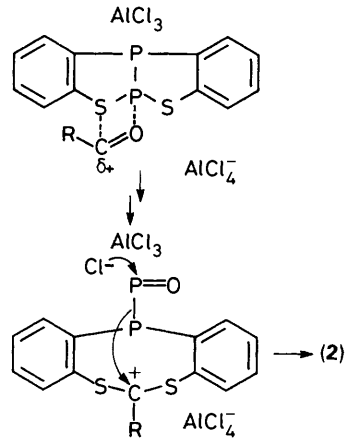
Scheme 3. *Reagents:* i, PCl_3, $AlCl_3$, reflux, 2 h; ii, MeCOCl, $AlCl_3$, r.t., 20 h



(3)

Scheme 4.

Following the reaction by g.l.c.–m.s. analysis we observed a very interesting stereochemical feature. In the first few minutes we noted the prevalent formation of an isomer, presumably *trans*-(**2**); successively, complete isomerization to *cis*-(**2**) occurred and the latter was isolated almost exclusively. This behaviour was noted in all cases, the *cis*-configuration being assigned to the final product (**2**) on the basis of ^{31}P n.m.r. spectral results and confirmed by an *X*-ray analysis[6] of (**2b**).



Scheme 5.

Thus the reaction gives, as a final result, a high degree of stereoselectivity. The *trans*-isomer was recovered only in the reaction with (**1b**) as a mixture, the *cis*:*trans* ratio being *ca.* 2:1. ^{31}P N.m.r. signals of the two isomers resonate at quite different fields, *i.e.* $\delta_P = 64$ for *cis*-(**2b**), and $\delta_P = 138$ for *trans*-(**2b**) (see Figure 2).

A change in the isomer ratio in $CDCl_3$ solution failed to occur after several hours and this suggested that isomerization of compounds (**2**) may arise from the formation of fluxional phosphorane adducts in the reaction mixture. The other spectroscopic data (^1H and ^{13}C n.m.r.) of the *trans*-isomer show that the 6-methyl substituent resonates in both the ^1H and ^{13}C spectra upfield with respect to the corresponding *cis* signals and that it has higher coupling constants. The products (**2**) are quite stable and tend to oxidize slowly in the air to give the corresponding oxides such as (**3**). The latter was unexpectedly obtained as the major product by a one-pot two-stage procedure as depicted in Scheme 3.

In this case acetyl chloride was added to the reaction mixture after the formation of fused 1,2,3-benzothiadiphospholes (**1**; X = Me). The reaction was monitored by t.l.c. and g.l.c.–m.s. analyses and showed the gradual disappearance of (**1**) and the concomitant formation of the oxide (**3**) with minor amounts of the *cis*- and *trans*-phosphines (**2b**). That compounds (**2b**) did not form in significant amounts in the initial reaction may be explained in terms of the formation of an adduct of the phosphine (**2b**) with the remaining PCl_3 or with its derivatives, which is oxidized during the work-up or quenching with water. In addition, oxidation of compound (**2b**) with H_2O_2 affords the same oxide (**3**) quantitatively and g.l.c.–m.s. analysis and spectroscopic data show that this oxide is only one of two possible configurational isomers. Subsequent reduction of (**3**) with $HSiCl_3$ gave again *cis*-phosphine (**2b**).

It is generally reported that the oxidation of phosphines with H_2O_2 occurs with complete retention of configuration;[4] therefore, if this is true, we might tentatively assign the *cis* configuration to the oxide (**3**). However it is known that phosphorus stereochemistry is highly dependent on the reaction conditions, on the nature of the substrate and, consequently, on the stability of the intermediate phosphoranes[4] which are involved. For this reason it is not possible to assign *a priori* a general stereochemical pattern of behaviour for every type of reaction.[9] In addition, the ^{31}P n.m.r. spectrum of the oxide (**3**) showed a signal at 64 p.p.m. both very close and downfield to the signal of the *cis*-phosphine (**2**), but largely upfield to that of the corresponding isomer of (**2**). This anomalous data may throw doubt on the previous assignment.

In Scheme 5 a mechanism for the reaction is illustrated: it is

Table 1. Physical and analytical data of *cis*-(**2**)

Compound (formula)	M.p. (°C)	Found (required) C, H, P, S	*M* (*m*/*z*) Found (calc.)	Time (h) [yield (%)]	R_F(light petroleum)
a	80—83	61.28 (61.30)	274.0034	0.3	0.13
($C_{14}H_{11}PS_2$)	Pale-yellow	4.02 (4.04)	(274.0040)	[78]	
		11.31 (11.29)			
		23.39 (23.37)			
b	160—163	63.56 (63.55)	302.0353	0.3	0.14
($C_{16}H_{15}PS_2$)	White	5.03 (5.00)	(302.0353)	[79]	
		10.25 (10.25)			
		21.15 (21.19)			
c	93—94	64.52 (64.53)	316.0502	2.0	0.15
($C_{17}H_{17}PS_2$)	White	5.44 (5.42)	(316.0509)	[70]	
		9.82 (9.79)			
		20.22 (20.26)			
d	94—97	65.40 (65.43)	330.0671	1.5	0.17
($C_{18}H_{19}PS_2$)	White	5.82 (5.80)	(330.0666)	[70]	
		9.33 (9.37)			
		19.45 (19.40)			
e	103—106	60.26 (60.23)	378.0441	0.5	0.08
($C_{19}H_{20}ClPS_2$)	White	5.32 (5.32)	(378.0433)	[80]	
		8.15 (8.17)			
		16.93 (16.92)			
		Cl 9.34 (9.36)			
f	98—101	67.75 (67.71)	372.1133	1.0	0.19
($C_{21}H_{25}PS_2$)	White	6.75 (6.76)	(372.1135)	[80]	
		8.33 (8.31)			
		17.16 (17.21)			
g	Glassy solid	69.85 (69.82)	378.0665	1.0	0.08
($C_{22}H_{19}PS_2$)		5.08 (5.06)	(378.0666)	[70]	
		8.16 (8.18)			
		16.91 (16.94)			

Table 2. Selected spectral data in $CDCl_3$ solutions of *cis*-(**2**)

	^{1}H N.m.r.[a] (J_{HH})[c]		^{31}P N.m.r.[b]	^{13}C N.m.r.[a] (J_{CP})[c]			
	1-H	R	P-12	C-1	C-6	C-12a	R
a	7.45bt	2.23d	63.0	130.1d	71.4d	136.7d	27.9d
	(7.0)	(16.4)		(23.8)	(23.6)	(14.1)	(28.7)
b	7.27d	2.21d	63.4	130.7d	71.3d	136.6d	27.8d
	(7.0)	(16.4)		(23.5)	(23.5)	(14.8)	(28.6)
c	7.26bd	2.36—2.56m	60.0	130.4d	78.9d	136.8d	34.6d (26.2)
	(6.6)	1.23t (7.4)		(24.0)	(25.8)	(13.9)	12.5d (12.8)
d	7.24bd	2.68—2.86m	57.0	130.1d	84.5d	137.2d	39.6d (22.8)
	(6.4)	1.19d (6.4)		(24.5)	(28.9)	(12.8)	20.7d (9.8)
e	7.26bd	3.47—3.60m	61.3	130.4d	77.3d	136.4d	40.5d (25.4)
	(6.6)	2.32—2.51m		(22.2)	(25.7)	(13.6)	25.6d (12.6)
		1.76—1.90m					44.3, 32.3
f	7.26bd	2.32—2.48m	61.0	130.4d	77.8d	136.3d	41.3d (24.7)
	(6.6)	1.57—1.75m		(24.0)	(25.7)	(13.6)	28.2d (12.0)
		1.22—1.42m					31.4, 29.1,
		0.81—0.92m					22.3, 13.8
g	7.48bd	3.68d (9.6)	62.3	130.5d	78.0d	136.2d	46.2d (27.4)
	(7.6)	6.94—7.32m		(23.7)	(25.8)	(13.5)	

[a] δ From Me_4Si. [b] δ From H_3PO_4 85%, downfield shifts are positive. [c] Values in parentheses are coupling constants in Hz.

based on the lability of the P–S bond, the affinity of the phosphorus for the oxygen atom, and the observed stereospecificity with inversion of configuration in the initial reaction. As depicted, we believe that initially a concerted breaking of the P–S bonds occurs with formation of C–S and P–O bonds; in the final step we have ring closure, which is favoured when the R group is relatively small; this is in accord with our experimental data. Also, as in the formation of starting material (**1**), we think that $AlCl_3$ is the promoter of most of the processes involved in this synthesis and has, therefore, potential to catalyse other phosphorus–carbon exchange reactions.

Experimental

^{1}H and ^{13}C n.m.r. spectra were recorded at 200.00, 50.30 MHz respectively with a Gemini 200 instrument and $\{^1H\}$P n.m.r. spectra were recorded at 32.20 MHz with a Varian FT80A instrument. ^{1}H and ^{13}C N.m.r. chemical shifts are given in p.p.m. from Me_4Si and ^{31}P n.m.r. chemical shifts are given in p.p.m. from 85% H_3PO_4 (external standard) in $CDCl_3$ solutions. Mass spectra were recorded with a VG 7070 spectrometer or with an HP 59970 workstation formed by an HP-5890 gas chromatograph equipped with a methyl silicone capillary column and by an HP-5970 mass detector. I.r. spectra

were recorded on a Perkin-Elmer 983 spectrophotometer. M.p.s are uncorrected and were determined with a Buchi apparatus. Commercial acyl chlorides and aluminium chloride were used without purification. 1,2-Dichloroethane was dried over molecular sieves 4A before use. Yields of (**2**) and (**3**) are reported for isolated products from starting *cis*-[1,2,3]benzothiadiphospholo[2,3-*b*][1,2,3]benzothiadiphosphole derivatives (**1**) and methyl *p*-tolyl sulphide respectively.

Reaction of cis-2,10-X-[1,2,3]*benzothiadiphospholo*[2,3b][1,2,3]*benzothiadiphosphole* (**1**) *with* RCOCl *and* $AlCl_3$: *General Procedure*.—To a stirred slurry of anhydrous $AlCl_3$ (16.8 mmol) in 1,2-dichloroethane (15 ml) was added dropwise RCOCl [R = Me, Et, Pr^i, $CH_2(CH_2)_2CH_2Cl$, hexyl, CH_2Ph] (10 mmol) the temperature being kept at 5—10 °C. *cis*-2,10-X-[1,2,3]Benzothiadiphospholo[2,3-*b*][1,2,3]benzothiadiphosphole (**1**; X = H, Me) (7.2 mmol) was then added similarly over *ca.* 10 min. The mixture was brought to, and held at, 25 °C with stirring for *ca.* 0.3—2.0 h. The reaction was monitored by t.l.c. (light petroleum as eluant) and g.l.c.–mass spectrometry. The products *cis*-(**2a**—**g**) were separated by filtration of the mixture on a Florisil column with cyclohexane–CH_2Cl_2 (90:10) as eluant. Compounds *cis*-(**2a**—**g**) were obtained in 70—80% yields. Physical, analytical, and spectroscopic data of *cis*-(**2**) are reported in Tables 1 and 2. Isomers *trans*-(**2**) were noted by g.l.c.–m.s. in the initial reaction. Only during the separation of compound (**2b**), was it possible to obtain a chromatographic fraction containing *trans*-(**2b**) from a mixture *cis*:*trans* (2:1). Some data for this isomer are reported. Compound *trans*-(**2b**), R_F 0.13 (light petroleum): selected $\delta_H(CDCl_3)$ 1.66 (d, 3 H, Me, J_{HP} 20.4 Hz) and 2.33 (s, 6 H, Me); selected $\delta_C(CDCl_3)$ 21.0 (Me), 22.0 (d, Me, J_{CP} 32.8 Hz), 126.4 (d, C-1, J_{CP} 42.0 Hz), and 129.2 (C-3); ^{31}P-$\{^1H\}$ n.m.r. ($CDCl_3$) 138.9; *m*/*z* 302.0353 (base-peak, M^+, calc. for $C_{16}H_{15}PS_2$ 302.0353), 287, 272, 239, 206, 179, 136, 115, and 63.

Formation of 2,6,10-*Trimethyl*[1,3]*benzothiaphospholo*[2,3-b][1,3]*benzothiaphosphole* 3-*Oxide* (**3**).—Methyl *p*-tolyl sulphide (1 g, 7.25 mmol), PCl_3 (1.88 ml, 21.7 mmol), and $AlCl_3$ (0.73 g, 5.44 mmol) were allowed to reflux for *ca.* 2 h under a nitrogen atmosphere. 1,2-Dichloroethane (5 ml), acetyl chloride (0.5 ml, 3.62 mmol), and $AlCl_3$ (0.96 g, 7.25 mmol) were added to the reaction mixture after the formation of the fused 1,2,3-benzothiadiphospholes (**1b**) at 5—10 °C. The stirred mixture was brought to, and held at, 25 °C for *ca.* 20 h. The reaction was monitored by t.l.c. and g.l.c.–m.s. analyses, the gradual disappearance of (**1b**) and the formation of the oxide (**3**) with minor amounts of the *cis*- and *trans*-(**2b**) being observed. After evaporation under reduced pressure of the excess of PCl_3 and 1,2-dichloroethane, the phosphines *cis*- and *trans*-(**2b**) (0.033 g, 0.11 mmol), compound (**1b**) (0.09 g, 0.3 mmol), and compound (**3**) (0.184 g, 0.58 mmol) were recovered by filtration through a Florisil column eluting with cyclohexane–CH_2Cl_2 (9:1) [for the products (**1b**) and (**2b**)] and 30:70 in 3, 8, and 16% yields respectively. Compound (**3**), R_F 0.30 (Et_2O); m.p. 165—168 °C; $\delta_H(CDCl_3)$ 2.13 (d, 3 H, Me, J_{HP} 12.0 Hz), 2.37 (s, 6 H, Me), 7.12 (dd, 2 H, ArH, $J_{HH'}$ 8.2 Hz, J_{HP} 3.8 Hz), 7.27 (d, 2 H, ArH, $J_{HH'}$ 8.2 Hz), and 7.63 (d, 2 H, 1-H, J_{HP} 10.2 Hz); $\delta_C(CDCl_3)$ 21.1 (d, Me, J_{CP} 39.9 Hz), 21.5 (Me), 60.1 (d, C-6, J_{CP} 63.8 Hz), 123.9 (d, C-4, J_{CP} 9.8 Hz), 131.3 (d, C-1, J_{CP} 10.2 Hz), 134.5 (C-3), 136.6 (d, C-2, J_{CP} 10.8 Hz), 141.0 (d, C-12a, J_{CP} 19.8 Hz), and 142.2 (C-4a); ^{31}P-$\{^1H\}$ n.m.r. ($CDCl_3$) 64.6; $\nu_{max.}(CS_2)$ 1 208 and 1 229 cm^{-1} (P=O); *m*/*z* 318.0294 (base-peak, M^+. Calc. for $C_{16}H_{15}OPS_2$: 318.0302), 275, 243, 259, 227, 211, 181, 121, 63, and 59 (Found: H, 4.8; C, 60.35; P, 9.7; S, 20.1. $C_{16}H_{15}OPS_2$ requires H, 4.75; C, 60.36; P, 9.73; S, 20.14%).

Oxidation of cis-2,6,10-*Trimethyl*[1,3]*benzothiaphospholo*-[2,3-b][1,3]*benzothiaphosphole* (**2b**) *with* H_2O_2.—To *cis*-(**2b**) (1.5 g, 5 mmol) dissolved in acetone (20 ml) an equimolar amount of 35% hydrogen peroxide was added dropwise; the temperature was kept below 20 °C by ice-bath cooling for a few minutes. After evaporation of the reaction mixture 2,6,10-trimethyl[1,3]benzothiaphospholo[2,3-*b*][1,3]benzothiaphosphole 3-oxide (**3**) was recovered in quantitative yield.

Trichlorosilane Reduction of 2,6,10-*Trimethyl*[1,3]*benzothiaphospholo*[2,3-*b*][1,3]*benzothiaphosphole* 3-*Oxide* (**3**).—To (**3**) (1.6 g, 5 mmol) in dry benzene (10 ml) dry triethylamine (0.7 ml, 5 mmol) was added under a nitrogen atmosphere, and after cooling of the solution in an ice bath, trichlorosilane (0.5 ml, 5 mmol) was dropped in slowly. The mixture was brought to reflux and maintained there for *ca.* 1 h. It was then cooled and poured into aqueous $NaHSO_4$; the organic layers were separated, washed with water, and dried (Na_2SO_4). G.l.c.–m.s. analysis showed the presence of *cis*-(**2b**), which was recovered in 72% yield by filtration of the crude product on a Florisil column eluting with cyclohexane–Et_2O (9:1).

Acknowledgements

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