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REACTIVITY OF ARYLAZOMETHYLENETRIPHENYLPHOSPHORANES TOWARDS ELECTROPHILES: REACTION WITH CS_2.

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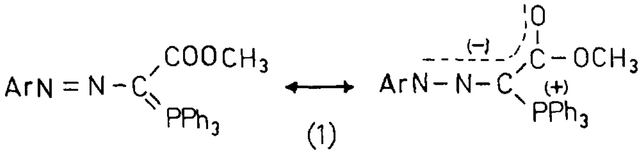
Abstract - The title reaction proceeds via the direct attack of the electrophilic reagent onto the nitrogen atom β to the ylidic carbon of the phosphoranes, followed by ring closure to 4-aryl-1,3,4-thiadiazoline-5-thiones, with elimination of PPh_3.

In spite of the very large amount of literature on phosphoranes, little is known about the reactivity of the terms stabilized by an azo group. We have been investigating the behaviour of the arylazomethylenetriphenylphosphoranes (1)[1,2] for a long time, mainly because the presence of the azo group suggested the possibility of employing them in the synthesis of heterocycles.


(1)

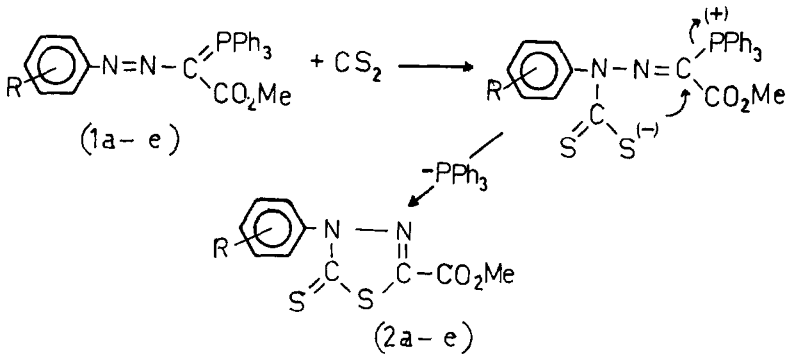
Our previous studies on these compounds were concerned with *inter* and *intra* molecular reactions with double and triple C-C bonds[3] and with *intra* molecular reactions with C=O groups[4,5]. The results showed a new and peculiar kind of reactivity of compounds (1) and were only partially in agreement with the known behaviour of the phosphoranes. We thought it interesting, therefore, to investigate the reactivity of the arylazomethylenephosphoranes toward the common electrophilic reagents. The negative charge in compounds (1), can, in principle, be delocalized on a great portion of the molecule and the electrophilic reagents may attack them, *a priori*, onto different positions. Among these reagents, CS_2 had already shown an interesting type of reactivity toward the ylidic carbon of non stabilized alkylidene phosphoranes[6]. In the case of azophosphoranes (1) an analogous reactivity could have led to the synthesis of 2-aryl-4-alkoxycarbonyl-1,2,3-thiadiazoline-5-thiones.

We wish now to submit the results of our research on the reactions of phosphoranes (1 a-e) (Table 1) with CS_2. The reactions were carried out following two procedures, *i.e.*:

A) Refluxing solutions of the arylazomethylenephosphoranes (1 a-e) in a very large excess of CS_2, which acted also as the solvent.

B) Refluxing solutions in CH_3CN of (1 a-d) and CS_2 in large excess (about 1:10; 1:17 moles).

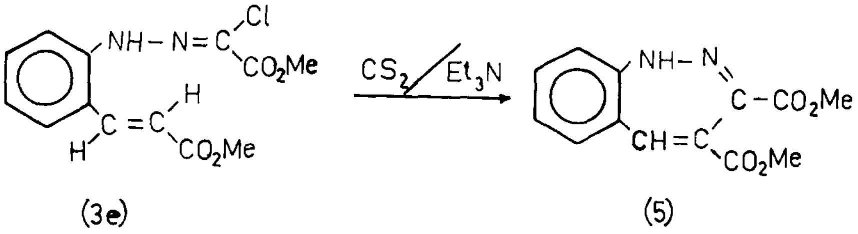
TABLE 1



Reactant	R	Reaction	Reaction time (h)	Product, %yield
(1a)	H	A	20	(2a), 90
		B	6.5	" , 70
(1b)	p. CH_3O	A	30	(2b), 60
		B	6	" , 90
(1c)	p. Cl	A	30	(2c), 70
		B	9	" , 75
(1d)	p. NO_2	A	>> 72	(2d), 10
		B	28	" , 90
(1e)	o. $\overset{H}{C}=\underset{H}{C}-CO_2Me$	A	72	(2e), 90

Reaction procedure, times and results are reported in Table 1.

Instead of the 1,2,3-thiadiazoline-5-thiones both A and B procedures gave the isomeric 1,3,4-thiadiazoline-5-thiones (2 a-e) as the only reaction products. The structure of these products was confirmed by elemental analysis, IR, ^{1}H NMR, mass spectra, and by comparison with authentic samples prepared from the corresponding arylhydrazonoyl halides (3 a-e) and xantate[7]. In order to check whether the reaction of our phosphoranes with CS_2 could take place through the intermediate formation of nitrile imine and elimination of PPh_3[3], the nitrile imines bearing the same substituents as the phosphoranes (1 a-e) were generated in situ from the hydrazonoyl halides (3 a-e) with Et_3N, and reacted with CS_2* following procedure A and/or B. The spiro derivatives (4 a-d), however, (Table 2), were the main reaction products from (3 a-d), while (3e) did not react with CS_2 and gave only the 3,4-dimethoxycarbonylbenzo[f]1,2-diazepine (5) by intra molecular cyclization[3]. Moreover, the 4-p.chlorophenyl-2-methoxycarbonyl-1,3,4-thiadiazoline-5-



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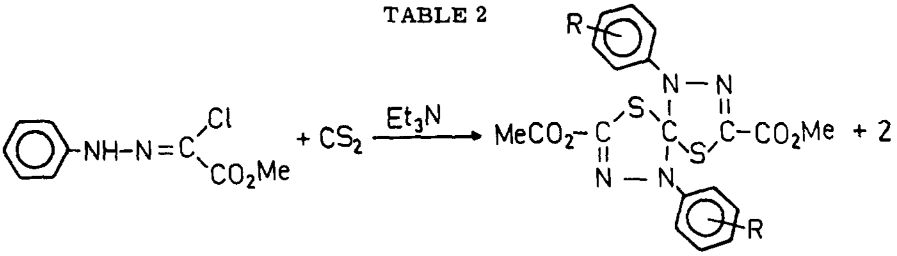
* To our knowledge, only one example of such reaction, leading to the formation of a spiro derivative, has yet been reported[8].

TABLE 2



(3a - d) (4a-d)

Reactant	R	Reaction method	Reaction time(h)	Products	%Yield
(3a)	H	B	4	(4a)	70
(3b)	p.CH_3O	A B	32 6	(4b) (4b)-(2b)	6 32-5
(3c)	p.Cl	A	19	(4c)	50
(3d)	p.NO_2	B	3	(4d)-(2d)	21-9

thione (2c) did not further react with the azophosphorane (1c), even by refluxing it in CH_3CN for 18 h, whereas by reaction with the hydrazonoyl halide (3c) and Et_3N, it gave the spiroderivative (4c). It is demonstrated, therefore, that nitrile imines are not the intermediate in the reaction of (1) to give (2), that CS_2 attacks directly the nitrogen atom β to the ylidic carbon of the arylazophosphoranes (1) and that the ring closure follows with elimination of PPh_3. (Table 1, heading).

The attack of an electrophilic agent onto a site different from the ylidic carbon in the arylazomethylenephosphoranes (1) is in agreement with their ^{13}C NMR spectral data[9]. In compounds (1 a-d), the chemical shift of the ylidic carbon ranges from 90 to 99 ppm; in the simpler phosphoranes, stabilized only by an alkoxycarbonyl function, it ranges from 29 to 33 ppm[10]. This difference in the chemical shift shows that the ylidic carbon in the azomethylenephosphoranes (1) bears less negative charge than in simpler alkoxycarbonyl phosphoranes.

Reaction times, although only qualitatively determined, show that all the described reactions are considerably accelerated by the presence of the polar solvent CH_3CN^*, and that the reaction of the phosphoranes with CS_2 is favoured by the presence on the aryl moiety of electron donors, whereas it is unfavoured by the presence on the same moiety of electron withdrawing groups. This fact should be consistent with the first step of the reaction (electrophilic attack onto the N atom) beeing the rate determining one.

Research on the reactivity of the arylazomethylenephosphoranes (1) towards other electrophilic reagents is in progress.

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[*] In the case of (1 b-d), the solvent effect appears particularly significant also because these compounds are only slightly soluble in CS_2.

TABLE 3

Analytical data of new compounds

Comp.	M.p. (°C) (Cryst. solvent)	Formula	Found %			Required %		
			C	H	N	C	H	N
(1e)	178 (MeOH)	$C_{31}H_{27}N_2O_4P$	70.79	5.21	5.31	71.26	5.17	5.36
(2a)	120 (EtOH)	$C_{10}H_8N_2O_2S_2$	47.23	3.21	10.97	47.61	3.17	11.11
(2b)	148 (MeOH)	$C_{11}H_{10}N_2O_3S_2$	46.36	3.59	9.85	46.80	3.55	9.93
(2c)	180-1 (C_6H_6)	$C_{10}H_7ClN_2O_2S_2$	42.42	2.46	9.86	41.88	2.45	9.76
(2d)	180-1 (BuOH)	$C_{10}H_7N_3O_4S_2$	40.88	2.38	14.31	40.40	2.35	14.14
(2e)	121-2 (C_6H_6-light petroleum)	$C_{14}H_{12}N_2O_4S_2$	49.80	3.61	8.25	49.95	3.57	8.33
(3d)	215-17 (CH_3CN)	$C_9H_8ClN_3O_4$	42.36	3.15	16.24	41.94	3.11	16.31
(3e)	97-9 (MeOH)	$C_{13}H_{13}ClN_2O_4$	52.64	4.45	9.37	52.70	4.49	9.46
(4a)	149 (EtOH)	$C_{19}H_{16}N_4O_4S_2$	53.00	3.77	12.98	53.27	3.73	13.08
(4b)	126 (i.PrOH)	$C_{21}H_{20}N_4O_6S_2$	51.06	4.14	11.32	51.64	4.10	11.47
(4c)	161-3 (MeOH)	$C_{19}H_{14}Cl_2N_4O_4S_2$	46.03	2.78	11.15	45.87	2.82	11.27
(4d)	220 (BuOH)	$C_{19}H_{14}N_6O_8S_2$	43.96	2.75	16.09	44.01	2.70	16.22
(5)	150-2 (MeOH)	$C_{13}H_{12}N_2O_4$	59.96	4.57	10.68	60.00	4.61	10.77

Spectral data of new compounds

Comp.	ν_{max} (cm^{-1}) (nujol)	^1H N.M.R. ($CDCl_3$ unless otherwise stated)
(1e)	1720, 1670, 1630	3.72(3H, s), 3.78(3H, s), 5.9(1H, d, J=16), 6.8-7.8(20 H, m)
(2a)	1750	4.05(3H, s), 7.25-7.78(5H, m)
(2b)	1745	3.9(3H, s), 4.02(3H, s), 6.99(2H, d, J=10), 7.6(2H, d, J=10)
(2c)	1745	4.06(3H, s), 7.52(2H, d, J=9), 7.75(2H, d, J=9)*
(2d)	1745	4.09(3H, s), 8.1(2H, d, J=9), 8.41(2H, d, J=9)
(2e)	1740, 1700	3.83(3H, s), 4.08(3H, s), 6.45(1H, d, J=16), 7.35-7.9(5H, m)
(3d)	3260, 1705	3.92(3H, s), 7.32(2H, d, J=9), 8.25(2H, d, J=9), 11.12(1H, s)**
(3e)	3360, 1730, 1710, 1630	3.87(3H, s), 3.98(3H, s), 6.42(1H, d, J=16), 7-7.77(4H, m), 7.85(1H, d, J=16), 8.57 (1H, s)
(4a)	1740	
(4b)	1740, 1710	
(4c)	1745, 1720	3.9(3H, s), 7.3(4H, s)***
(4d)	1715	4(3H, s), 7.4(2H, d, J=9), 8.2(2H, d, J=9)
(5)	3285, 1720	3.85(6H, s), 6.75(1H, d, J=8), 6.90(1H, s), 7.06-7.4(4H, m), 7.93(1H, s)

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[*] Mass spectrum: m/z 286(M^+)

[**] DMSO

[***] Mass spectrum: m/z 497(M^+)

EXPERIMENTAL

M.p.s were taken by means of a Büchi apparatus and are uncorrected. I.R. and N.M.R. spectra were recorded by Perkin-Elmer 377 and Varian EM-390 spectrometers respectively. Chemical shifts are expressed as δ values ($SiMe_4$ as the internal standard). Coupling constants are given in Hz. Mass spectra were taken with a Varian MAT 311-A mass spectrometer. Silica gel 60 (Merck, 70-230 mesh) was used for column chromatography. T.l.c.s were performed on Merck pre-coated silica gel 60F-254 plates.
Analytical and chemicophysical data of new compounds are reported in Table 3.

Starting materials

Arylazomethylenetriphenylphosphoranes. (1 a-d) had already been described[1,2b]. (1e) was prepared from o.aminobenzaldehyde by diazotization and reaction with two moles of Ph_3P=CH-COOMe under the same conditions employed by Märkl[1].
Arylchlorohydrazones. (3 a-e) were prepared by a known method[11]. (3 a-c) had already been described[2b,12]. Data for (3 d,e) are reported in Table 3.

Reactions of arylazomethylenetriphenylphosphoranes (1) with CS_2

Procedure A

Arylazomethylenetriphenylphosphoranes (1 a-e) (2.13 . 10^{-3} moles) were refluxed in CS_2 (25 cm^3). The reaction course was monitored by t.l.c. (eluent: C_6H_6-EtOAc 1:1). At the end of the reaction (see times in Table 1) the excess of CS_2 was evaporated underreduced pressure and the residue was crystallized from light petroleum, in the case of (1a). In the other cases it was extracted with hot light petroleum, and then crystallized from the appropriate solvent. Reaction times and yields are given in Table 1.

Procedure B

Arylazomethylenephosphoranes (1 a-d) (1.06 . 10^{-3} moles) and CS_2 (1.7 . 10^{-2} moles) were refluxed in CH_3CN (15 cm^3). The reaction course was monitored by t.l.c. (eluent: C_6H_6-EtOAc 1:1). After complete conversion, the work up was performed as described under procedure A. Reaction times and yields are reported in Table 1.

Reactions of arylchlorohydrazones (3) with Et_3N and CS_2

Procedure A

Arylchlorohydrazones (3 b, c) (8.26 . 10^{-3} moles) and Et_3N (9.75 . 10^{-3} moles, 1.4 cm^3) were refluxed in CS_2 (75 cm^3). The reaction course was monitored by t.l.c. (eluent: Et_2O when starting from (3b), C_6H_6-EtOAc 9:1 when starting from (3c)). After complete conversion of the halohydrazones, the solutions were extracted with water and dried over Na_2SO_4. The excess of CS_2 was evaporated under reduced pressure and the residue was crystallized to give the spiro derivatives (4 b, c). Reaction times and yields are reported in Table 2.
(3e), reacted as above for 1 h, gave the 3,4-dimethoxycarbonyl-benzo[f]1,2-diazepine (5) with a 98 % yield.

Procedure B

Arylchlorohydrazones (3 a, b, d) (8.13 . 10^{-3} moles), CS_2 (8.13 . 10^{-2} moles) and Et_3N (9.75 . 10^{-3} moles, 1.4 cm^2) were refluxed in CH_3CN (30 cm^3). The reaction course was monitored by t.l.c. (eluent:$CHCl_3$ when starting from (3a), Et_2O when starting from (3b), C_6H_6 when starting from (3d)). The work up was performed by evaporating the solvent and the excess of CS_2 and Et_3N under reduced pressure, taking up the residue in water and extracting with $CHCl_3$. (4a) was recovered by evaporating the solvent and crystallizing the residue. From (3b) and (3d) rather complex mixture were obtained, which were separated by column chromatography (eluent: $CHCl_3$ starting from (3b), C_6H_6 starting from (3d)). Reaction times and yields are reported in Table 2.

Reaction of 2-methoxycarbonyl-4-p.chlorophenyl-1,3,4-thiadiazoline-5-thione (2c) with hydrazonoyl chloride (3c) and Et_3N

To a mixture of (2c) ($1.4 \cdot 10^{-3}$ moles) and (3c) ($1.4 \cdot 10^{-3}$ moles) in CH_3CN (30 cm^3) Et_3N ($2.14 \cdot 10^{-3}$ moles, 0.3 cm^3) was added. After 19 h (complete conversion: t.l.c.: eluent C_6H_6) the mixture was poured into water (100 cm^3). The precipitate, filtered, washed with water and dried, was practically pure (4c), m.p. 157-161°C. Yield 90%.

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