Reaction of Aromatic Thiocyanates with Trialkyl Phosphites

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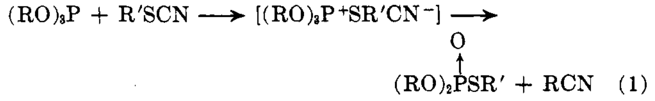
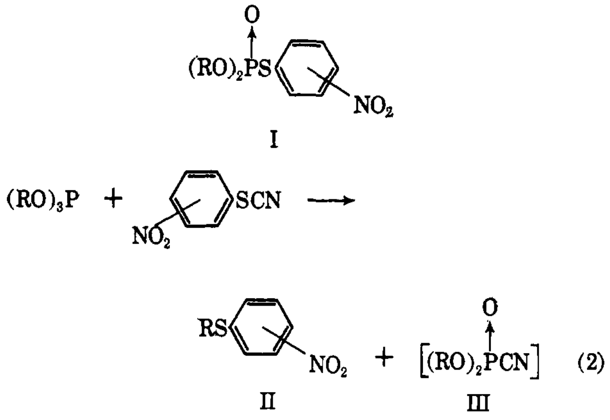
In contrast to aliphatic thiocyanates, which react with trialkyl phosphites exclusively by an Arbuzov mechanism to form phosphorothioates, aromatic thiocyanates, ArSCN, react with trialkyl phosphites, $(RO)_3P$, to give a mixture of phosphorothioate and sulfide, RSAr. The formation of sulfide is favored by substituents (NO_2, etc.) on the aryl ring that can stabilize an anionic species, an observation that suggests a mechanism involving attack of phosphite on the carbon of the thiocyano group followed by alkylation of the resulting thiophenoxide ion by the phosphonium cation. The reactions of trialkyl phosphites with related sulfur compounds, RSX (disulfides, sulfenyl chlorides, sulfenate esters, etc.), are rationalized on the theory that heterolysis of the RS–X bond will occur in the direction RS^+X^- when X^- is the anion of a fairly strong acid.

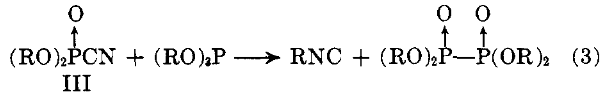
The classical Michaelis–Arbuzov reaction between trivalent phosphorus compounds and alkyl halides has been considerably expanded in scope since its discovery[2] and now embraces as coreactants for the trivalent phosphorus compound a large number of compounds containing displaceable groups other than halogen. Among these coreactants are a substantial number of sulfur compounds such as sulfonyl halides,[3,4] sulfenyl halides,[5] thiosulfonates,[6] symmetrical[7] and unsymmetrical[8] disulfides, and thiocyanates.[9]

Work on the reaction of thiocyanates with trialkyl phosphites has been quite sketchy; one group[9a] investigated the reactions of two trialkyl phosphites with ethyl and benzyl thiocyanate and came to the conclusion that the reactions followed the typical Michaelis–Arbuzov course (eq. 1). Sheppard[9c] postulated the same mechanism independently and, although he extended the reaction to include two aryl thiocyanates, no departure from the expected Arbuzov products was observed. When the reaction was extended by one of us[10] to nitroaryl thiocyanates, however, it was found to take a different course in that the main product containing the nitroaryl moiety was not the phosphorothioate (I) but was instead the alkyl nitroaryl sulfide (II) (eq. 2). The fate of the phosphorus compound (III) was not established with certainty but the detection of isonitrile suggested that at least part of the phosphorocyanidate (III) reacted with excess trialkyl phosphite according to eq. 3.



$$(RO)_3P + R'SCN \longrightarrow [(RO)_3P^+SR'CN^-] \longrightarrow (RO)_2\overset{O}{\overset{\uparrow}{P}}SR' + RCN \quad (1)$$





$$\underset{III}{(RO)_2\overset{O}{\overset{\uparrow}{P}}CN} + (RO)_3P \longrightarrow RNC + (RO)_2\overset{O}{\overset{\uparrow}{P}}-\overset{O}{\overset{\uparrow}{P}}(OR)_2 \quad (3)$$

At first, this apparently anomalous result with nitroaryl thiocyanates was ascribed to the unique electron-withdrawing properties of the nitro group,[10] but it soon became clear from a qualitative study of several halogenated aryl thiocyanates that all of them gave sulfide in varying amounts when allowed to react with trimethyl phosphite. Consequently, in order to gain an insight into the mechanism of this "abnormal" reaction (eq. 2), we have studied the behavior of eleven halogenated aryl thiocyanates in their reaction with trimethyl phosphite. Relative reaction rates have been measured at 60° and the product ratio (*i.e.*, sulfide–phosphorothioate) has been determined, both by gas–liquid chromatographic (g.l.c.) techniques.

Experimental

Preparation of Aromatic Thiocyanates.—All of the thiocyanates used in this study (Table I) were prepared from the corresponding aniline by diazotization followed by treatment with cuprous thiocyanate and potassium thiocyanate.[11]

Relative Reaction Rates.—The apparatus used to determine the relative reaction rates consisted of a four-necked flask equipped with a stirrer, thermometer, condenser, and sampling syringe. The experiments were run under nitrogen. The flask containing trimethyl phosphite (62 ml., 0.525 mole) was immersed to a depth above the reaction level in a water bath at 62°. The thiocyanate (0.025 mole) was added to the phosphite ester and, since the addition of the thiocyanate lowered the temperature of the phosphite by 2°, the bath temperature was also immedi-

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[2] G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950, Chapter 7; P. C. Crofts, *Quart. Rev.* (London), **12**, 341 (1958).

[3] E. E. Gilbert and C. J. McGough, U. S. Patents 2,690,450 and 2,690,451 (1954).

[4] F. W. Hoffmann, T. R. Moore, and B. Kagan, *J. Am. Chem. Soc.*, **78**, 6413 (1956).

[5] D. C. Morrison, *ibid.*, **77**, 181 (1955).

[6] (a) T. C. Myers, S. Preis, and E. V. Jensen, *ibid.*, **76**, 4172 (1954); (b) J. Michalski, T. Modro, and J. Wieczorkowski, *J. Chem. Soc.*, 1665 (1960).

[7] (a) H. I. Jacobson, R. G. Harvey, and E. V. Jensen, *J. Am. Chem. Soc.*, **77**, 6064 (1955); (b) A. C. Poshkus and J. E. Herweh, *ibid.*, **79**, 4245 (1957); (c) J. Michalski and J. Wieczorkowski, *Bull. acad. polon. sci., Classe III*, **5**, 917 (1957); *Chem. Abstr.*, **52**, 6157 (1958); (d) C. Walling and R. Rabinowitz, *J. Am. Chem. Soc.*, **79**, 5326 (1957); **81**, 1243 (1959); (e) A. J. Parker and N. Kharasch, *Chem. Rev.*, **59**, 621 (1959).

[8] R. G. Harvey, H. I. Jacobson, and E. V. Jensen, *J. Am. Chem. Soc.*, **85**, 1618 (1963).

[9] (a) J. Michalski and J. Wieczorkowski, *Bull. acad. polon. sci., Classe III*, **4**, 279 (1956); *Chem. Abstr.*, **51**, 4266 (1957); (b) K. Pilgram, Ph.D. Thesis, Universität Wurzburg, 1959; (c) W. A. Sheppard, *J. Org. Chem.*, **26**, 1460 (1961).

[10] K. Pilgram and F. Korte, *Tetrahedron*, **20**, 177 (1964).

[11] L. Gattermann and W. Hausknecht, *Ber.*, **23**, 738 (1890).

TABLE I

AROMATIC THIOCYANATES

Structure	Formula (mol. wt.)	Yield, %	M.p. or b.p. (mm.), °C.	Nitrogen, % Calcd.	Nitrogen, % Found	Sulfur, % Calcd.	Sulfur, % Found
1-SCN-3,5-$Cl_2C_6H_3$	$C_7H_3Cl_2NS$ (204.0)	16.7	36 109 (0.1)	6.9	6.8	15.7	15.3
1-SCN-3,4-$Cl_2C_6H_3$	$C_7H_3Cl_2NS$ (204.0)	68.8	60	Cl, 34.8	Cl, 35.1	15.7	15.4
1-SCN-2,4-$Cl_2C_6H_3$	$C_7H_3Cl_2NS$ (204.0)	79	72	Cl, 34.8	Cl, 34.7	15.7	15.8
1-SCN-2,5-$Cl_2C_6H_3$	$C_7H_3Cl_2NS$ (204.0)	54	81	Cl, 34.8	Cl, 34.6	15.7	15.3
1-SCN-2-ClC_6H_4[a]	C_7H_4ClNS (169.5)	40	126 (13)	Cl, 20.9	Cl, 20.9	18.9	18.8
1-SCN-3-ClC_6H_4[a]	C_7H_4ClNS (169.5)	65	134 (15)	Cl, 20.9	Cl, 21.2	18.9	18.8
1-SCN-2-FC_6H_4	C_7H_4FNS (153.1)	32.6	74 (0.01)	9.2	8.9	20.9	21.2
1-SCN-3-FC_6H_4	C_7H_4FNS (153.1)	26.5	61 (0.05)	9.2	8.9	20.9	21.2
1-SCN-2-$CF_3C_6H_4$	$C_8H_4F_3NS$ (203.1)	57.3	64 (0.09)	6.9	7.0	15.8	15.6
1-SCN-3-$CF_3C_6H_4$	$C_8H_4F_3NS$ (203.1)	48.8	58 (0.01)	6.9	6.8	15.8	15.6
1-SCN-3-CF_3-4-ClC_6H_3	$C_8H_3ClF_3NS$ (237.6)	21	89 (0.1)	5.9	5.6	13.5	12.8

[a] F. Challenger, C. Higginbottom, and A. Huntington, *J. Chem. Soc.*, 29 (1930).

TABLE II

HALF-LIVES AND HAMMETT σ VALUES FOR THE REACTION OF AROMATIC THIOCYANATES WITH TRIMETHYL PHOSPHITE

Thiocyanate	$t_{1/2}$, min.	σ (Hammett) or σ^* (Taft)
1-SCN-2-$CF_3C_6H_4$	133	...
1-SCN-2-ClC_6H_4	92	0.20
1-SCN-3-FC_6H_4	90	0.34
1-SCN-3-ClC_6H_4	80	0.37
1-SCN-2,4-$Cl_2C_6H_3$	66	0.43
1-SCN-3-$CF_3C_6H_4$	63	0.42
1-SCN-2,5-$Cl_2C_6H_3$	53	0.57
1-SCN-3-CF_3-4-ClC_6H_3	52	0.74
1-SCN-2-FC_6H_4	50	0.24
1-SCN-3,5-$Cl_2C_6H_3$	38	0.75
1-SCN-3,4-$Cl_2C_6H_3$	36	0.60

TABLE III

PRODUCT RATIO FOR THE AROMATIC THIOCYANATE–TRIMETHYL PHOSPHITE REACTION

RSCN R	Temp., 60°		Composition after heating			
	$RSCH_3$, %	$RS\overset{\overset{O}{\uparrow}}{P}(OCH_3)_2$, %	$RSCH_3$, %	$RS\overset{\overset{O}{\uparrow}}{P}(OCH_3)_2$, %	Time, min.	Temp., °C.
2-FC_6H_4–	8.3	91.7	11	89	60	115
3-FC_6H_4–	10.2	89.8	12.3	87.7	30	115
3-$CF_3C_6H_4$–	14.9	85.1	15.2	84.8	10	115
			100	0	120	180
2-$CF_3C_6H_4$–	25.3	74.7	27.9	72.1	10	115
			28.5	71.5	120	115
2-ClC_6H_4–	28	72	27.6	72.4	10	115
3-CF_3-4-ClC_6H_3–	29.3	70.7	37.2	62.8	45	115
3-ClC_6H_4–	32.2	64.8	32.5	67.5	90	115
			47.7	52.3	60	150
3,4-$Cl_2C_6H_3$–	37.3	62.7	51.3	48.7	10	115
			94.5	5.5	30	180
2,4-$Cl_2C_6H_3$–	41.8	58.2	65	35	60	140
3,5-$Cl_2C_6H_3$–	46.7	53.3	80	20	45	180
			100	0	60	180
2,5-$Cl_2C_6H_3$–	65	35	100	0	60	180

ately lowered to 60 ± 0.5° by adding water. (A few experiments were carried out at 50 ± 0.5°.) At fixed time intervals, 0.5-ml. samples of the reaction mixture were withdrawn and analyzed by injecting 40 ml. into a Model 500 linear programmed temperature gas chromatograph (F and M Scientific Corp., Avondale, Pa.). The 2-ft. column was packed with 30–60-mesh Chromosorb P, coated with 20% silcone rubber; the injection port temperature was 200°.

The relative reaction rates (shown in Figures 1–4 and expressed as half-lives in Table II) were determined by following the disappearance of thiocyanate, and the product ratios shown in Table III were determined from the relative peak areas assignable to sulfide and phosphorothioate, respectively. These peaks were usually identified by preparing the sulfide and phosphorothioate independently on a macroscale and analyzing them by g.l.c. under the same conditions. In all cases the order of emergence was sulfide, thiocyanate, and lastly phosphorothioate. In this way the stability of the phosphorothioate to the analytical method was verified.

After all of the thiocyanate had disappeared and the ratio of sulfide to phosphorothioate had remained constant for at least 2 hr., the reaction mixture was heated to reflux (115–120°) for different periods of time and then analyzed for sulfide and phosphorothioate by the same g.l.c. procedure. In some cases, the reaction mixture was then heated from 150–180° and, after all the trimethyl phosphite had been isomerized to dimethyl methylphosphonate, the sulfide–phosphorothioate ratio was again determined by g.l.c. This was done because in our earlier experiments with some of these thiocyanates, a different ratio of products was obtained at higher temperatures than at 60°. The results are listed in Table III.

Because the reaction proceeds to a small extent immediately on mixing at 60° and, because the injection temperature of 200° results in some reaction, none of the curves passes through 100% for thiocyanate or 0% for sulfide or phosphorothioate at zero time. Since all of the thiocyanate–trimethyl phosphite reactions were analyzed by the same procedure, however, it was felt that any error introduced by the analytical method would be small. The extremely good reproducibility of the results (1–2%) tended to confirm this.

Preparation of Methyl α,α,α-Trifluoro-*o*-tolyl Sulfide.—This and the following experiment illustrate a typical macroscale preparation of the two products from the reaction of trimethyl

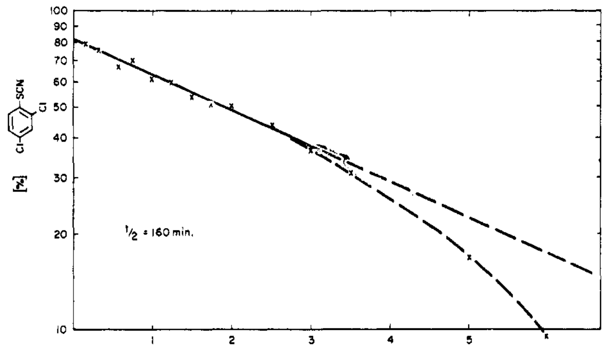


Figure 1.—Reaction of 2,4-dichlorophenyl thiocyanate with trimethyl phosphite; rate of thiocyanate consumption at 50°.

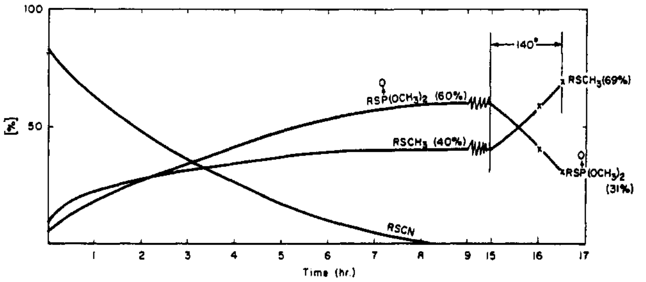


Figure 2.—Reaction of 2,4-dichlorophenyl thiocyanate with trimethyl phosphite at 50°.

phosphite with an aromatic thiocyanate, *i.e.*, the methyl aryl sulfide and the phosphorothioate.

To 33 g. (0.162 mole) of α,α,α-trifluoro-*o*-tolyl thiocyanate in 50 ml. of methanol was added, with stirring, a solution of 30 g. of sodium hydroxide in 150 ml. of methanol. The cold solution (0°) of the resulting mercaptide was treated with 25 g. (0.2 mole) of dimethyl sulfate and stirred for an additional 2 hr. at room temperature. The reaction mixture was diluted with water, extracted with ether, and the dried ethereal extract evaporated at reduced pressure. The pale yellow oil was distilled to give 26 g. (83%) of the sulfide: b.p. 102° (22 mm.), m.p. 12°, $n^{25}D$ 1.5088; lit.[12] m.p. 3.7–5°, b.p. 96° (25 mm.), $n^{25}D$ 1.509.

Anal. Calcd. for $C_8H_7F_3S$: S, 16.65. Found: S, 17.0.

The **sulfone** crystallized from methanol as colorless needles, m.p. 75°.

Anal. Calcd. for $C_8H_7F_3O_2S$: S, 14.28. Found: S, 14.1.

Preparation of O,O-Dimethyl S-α,α,α-Trifluoro-*o*-tolyl Phosphorothioate.—A solution of 30.5 g. (0.15 mole) of α,α,α-trifluoro-*o*-tolyl thiocyanate in 20 g. (0.16 mole) of trimethyl phosphite was heated slowly to 95° at which point a vigorously exothermic reaction ensued and the temperature briefly rose to 200°. The reaction product was distilled *in vacuo* to give 18 g. of a forerun, b.p. <67° (0.5 mm.), which was shown by g.l.c. to be a mixture of the methyl sulfide (see above), dimethyl methylphosphonate, and trimethyl phosphate. The main fraction was 21 g. (49%) of O,O-dimethyl S-α,α,α-trifluoro-*o*-tolyl phosphorothioate, b.p. 116–117° (0.5 mm.), $n^{25}D$ 1.5925.

Anal. Calcd. for $C_9H_{10}F_3O_3PS$: P, 10.84; S, 11.19. Found: P, 10.7; S, 11.3.

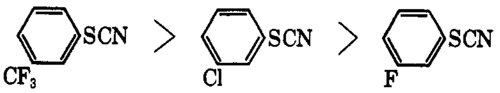
Results and Discussion

The relative reaction rates for eleven aromatic thiocyanates in their reaction with trimethyl phosphite are expressed as half-lives in Table II. The considerable spread in these half-lives (36–133 min.) and their high reproducibility (1–2%) suggest that the differences in reactivity are real and that information concerning structural effects on the reactivity of aryl thiocyanates can reasonably be drawn from these data. The obvious problem in relating these data to mechanism is that the thiocyanate is being consumed in two different reactions: one presumably involves attack on sulfur to form phosphorothioate (eq. 1) and the other presumably (see below) involves attack on carbon to form aryl sulfide (eq. 4). Furthermore, the reactions were

$$(RO)_3P + ArSCN \longrightarrow [(RO)_3P^+CN\ ArS^-] \longrightarrow ArSR + [(RO)_2\overset{\overset{O}{\uparrow}}{P}CN] \quad (4)$$

run pseudo first order, *i.e.*, in the presence of a large excess of trimethyl phosphite. Changes in the composition of the reaction mixture by formation of products and isomerization of trimethyl phosphite caused a tailing off (Figure 1).

In spite of these complications it seems clear from the data in Table II that both reactions are favored by electron-withdrawing groups in the aryl ring. For example, among the *meta*-substituted thiocyanates in Table II the reactivity parallels the Hammett σ values. Similarly, the 2,5-dichloro isomer ($\sigma + \sigma^{*13} =$



$t_{1/2}$, min.	63	80	90
σ	+0.42	+0.37	+0.34

0.57) is more reactive ($t_{1/2}$ = 53 min.) than the 2,4-dichloro isomer ($\sigma + \sigma^*$ = 0.43) whose half-life is 66 min. Since the same steric effects presumably operate in these two isomers it seems safe to conclude that the reactivity in the reaction with trimethyl phosphite parallels the electron-withdrawing properties of the *m*- and *p*-chlorine atoms. The only disubstituted thiocyanate that seems out of line with this general trend is the 3,4-dichloro analog (Table II). It is more reactive toward trimethyl phosphite than one would predict on the basis of Hammett σ values; reasons for this apparent exception are not clear at the present time.

A steric effect is clearly operating in this reaction as evidenced by the very slow reaction of the *o*-trifluoromethyl compound; it is less reactive than the *o*-chloro analog and this in turn is much less reactive than the *o*-fluoro analog (Table II). The *o*-fluoro compounds seems out of place in the over-all reactivity picture but the value of 0.24 for *o*-fluorine (Table II) is a σ* constant and therefore may not be directly comparable to σ values.[13]

The data from some typical kinetic runs are plotted in Figures 2–4. These curves reveal several interesting features of the reaction between aromatic thiocyanates and trimethyl phosphite. Figures 2 and 3 are typical of those thiocyanates that afforded substantial quantities (>40%) of sulfide; invariably sulfide formation was rapid at first but then leveled off and usually fell behind the rate of phosphorothioate formation. Even with 20–30% of the thiocyanate apparently remaining, sulfide formation had ceased for all practical purposes and all of the remaining thiocyanate was apparently converted to phosphorothioate. This behavior was even more striking in the case of those thiocyanates that afforded very little sulfide. For example, in Figure 4 is plotted the data from the reaction between the *m*-trifluoromethyl thiocyanate and trimethyl phosphite. Essentially all of the sulfide (~14%) was formed in the first 20 min. and, although <30% of the thiocyanate

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[12] E. T. McBee and P. J. Graham, *J. Am. Chem. Soc.*, **72**, 4235 (1950).

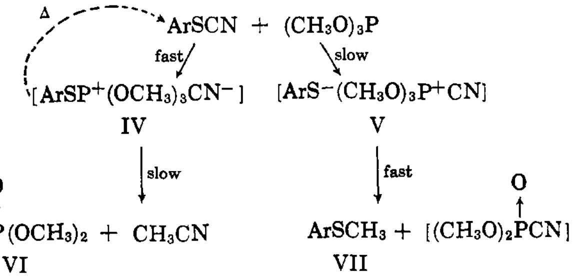
[13] R. W. Taft, *ibid.*, **74**, 3120 (1952); **75**, 4231 (1953).

had reacted at this point, essentially all of the remaining 70% appeared to go to phosphorothioate.

A possible explanation for these results may be found by examining the various equilibria and reaction intermediates in the thiocyanate–trimethyl phosphite reaction (Scheme I).

SCHEME I

EQUILIBRIA IN THE $ArSCN-(CH_3O)_3P$ REACTION



In the reaction between trimethyl phosphite and a thiocyanate, attack can occur on sulfur to form the intermediate IV or on carbon to form intermediate V. From the work of Michalski[9a] and Sheppard[9c] it can safely be concluded that attack on sulfur is preferred or, stated another way, that the rate of formation of IV is greater than that of V. Both IV and V are formed by reversible reactions, but reversal to starting materials is more prevalent with IV than with V because the further reaction of V (as shown in Scheme I) would be much faster than the further reaction of IV; this follows because ArS^- is more nucleophilic toward carbon than is CN^-.[14] The consequence of these equilibrium considerations is that early in the reaction one would be measuring only the sulfide VII concentration because, on injection at 200° in the g.l.c. apparatus, intermediate IV would be converted, in large part, back to reactants. However, later on in the process, one would be measuring phosphorothioate VI (from the relatively slow reaction IV → VI), sulfide VII, and thiocyanate that had been formed by the reversal of IV. Thus, the apparent presence of much unreacted thiocyanate after sulfide formation had become constant is probably an artefact introduced by the analytical method. This explanation requires as a corollary the assumption that in most cases, attack on sulfur to form IV is preferred to attack on carbon to form V; this is borne out by the observation that in every example except one, the 2,5-dichloro analog, more phosphorothioate than sulfide is obtained. It is hoped in further studies on this reaction to avoid this problem by developing a suitable spectroscopic method of analysis.

So far the discussion has dealt only with substituent effects on the relative reactivities of aromatic thiocyanates in their reaction with trimethyl phosphite. The ratio of products found, *i.e.*, sulfide–phosphorothioate (see Table III), is also revealing, however, as it suggests a plausible mechanism for the formation of the "abnormal" product, the sulfide. For example, if the mechanism proposed for the formation of sulfide (eq. 4, $R = CH_3$) has any merit, there should be a relationship between the amount of sulfide formed and the stability of the corresponding thiophenoxide ion, ArS^-; *i.e.*, those substituents that stabilize an ArS^- ion should give more sulfide than those which are less able to stabilize this anion. The simplest measure of thiophenoxide anion stabilities would be the relative pK_a values of the corresponding thiophenols but, unfortunately, relatively few pK_a values are available in the literature for thiophenols. However, from those that have been measured, along with the pK_a values of the corresponding phenols which are similar in their requirements for anion stabilization, a trend among the data in Table III becomes apparent.

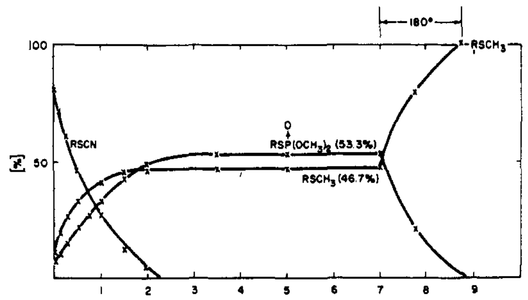


Figure 3.—Reaction of 3,5-dichlorophenyl thiocyanate with trimethyl phosphite at 60°.

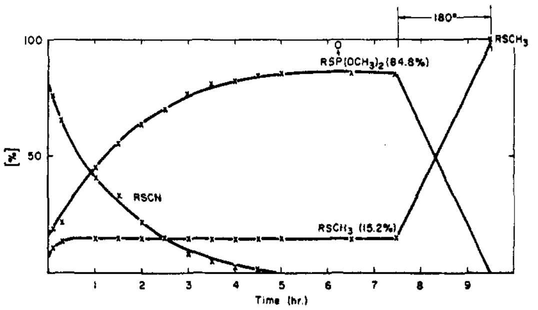
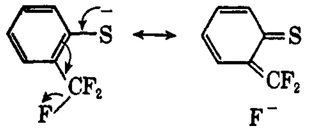


Figure 4.—Reaction of 3-(trifluoromethyl)phenyl thiocyanate with trimethyl phosphite at 60°.

For example, it is not surprising to find that *o*- and *m*-fluorophenyl thiocyanates give the least sulfide on reaction with trimethyl phosphite. *o*-Fluorophenol is a weaker acid than *o*-chlorophenol and the acidity of the corresponding thiophenols is probably in the same direction.[15] Because it is the most electronegative of the halogens, fluorine supplies electrons to the benzene ring more effectively than chlorine and this is in the wrong direction for stabilizing an anion. Moreover, the *ortho* effect, which decreases acidities of aromatic acids by hydrogen bonding, is even more pronounced with thiophenols than with phenols. Trifluoromethyl groups are only slightly better than fluorine in this respect; hyperconjugation of the type shown in VIII ↔ VIIIa allows for a small degree of stabilization[16] and is probably responsible for the larger amount of sulfide from the *o*-trifluoromethyl analog than from the *meta* isomer (see Table III) where such resonance interaction is prohibited.



VIII VIIIa

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(14) J. O. Edwards and R. G. Pearson, *J. Am. Chem. Soc.*, **84**, 16 (1962).

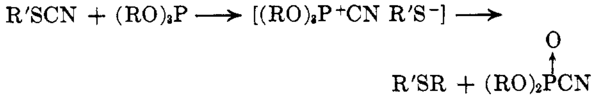
(15) D. H. McDaniel and H. C. Brown, *ibid.*, **77**, 3756 (1955).

(16) J. D. Roberts, R. L. Webb, and E. A. McElhill, *ibid.*, **72**, 408 (1950).

m-Chlorothiophenol is a stronger acid than is *p*-chlorothiophenol[17] and one would consequently predict that 2,5-dichlorothiophenol (a *m*-chlorothiophenol) would be a stronger acid than 2,4-dichlorothiophenol (a *p*-chlorothiophenol), since any steric factors would probably cancel out. The larger amount of sulfide from the 2,5-dichloro analog is in the right direction for these relative acidities. Similarly, 3,5-dichlorothiophenol should be a stronger acid than 3,4-dichlorothiophenol, and the larger amount of sulfide from the former is also in agreement with our basic premise. Clearly, a precise measurement of the relative pK_a values for the thiophenols corresponding to the thiocyanates in Table III would be very informative; this point is under investigation.

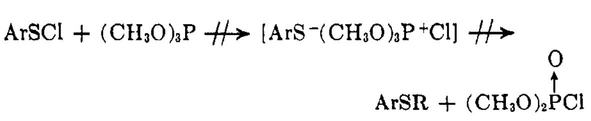
There is also qualitative evidence, from the behavior of nitroaryl thiocyanates, for the postulate that more sulfide will be formed from aromatic thiocyanates that give stable ArS^- species. The *m*-nitro isomer gives the least sulfide of the three nitrophenyl thiocyanates and *m*-nitrothiophenol is a weaker acid than either *o*- or *p*-nitrothiophenol.[17] As a matter of fact, the amount of phosphorothioate obtained from the reaction of *o*- or *p*-nitrophenyl thiocyanate with trimethyl phosphite is so small that it almost escaped detection.[10]

From considerations such as these, it is not surprising that aliphatic thiocyanates react exclusively by the Arbuzov mechanism to give phosphorothioate (eq. 1) rather than by heterolysis of the S–CN bond to give sulfide (eq. 5). Alkyl mercaptans are much weaker acids than are thiophenols[18] so that the formation of $R'S^-$ species (R' = alkyl) requires greater activation energies than the formation of ArS^- ions. Because of this, the alternate pathway is followed, *i.e.*, attack on sulfur to give (eventually) phosphorothioate (eq. 1).



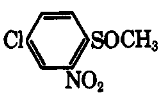
$$R'SCN + (RO)_3P \longrightarrow [(RO)_3P^+CN\ R'S^-] \longrightarrow R'SR + (RO)_2\overset{\overset{\displaystyle O}{\uparrow}}{P}CN \quad (5)$$

Also, it is interesting to note that the related reaction between sulfenyl halides and trialkyl phosphites affords exclusively the Arbuzov product, *i.e.*, phosphorothioate, uncontaminated by sulfide. Even in those instances that afforded very large amounts of sulfide in the aryl thiocyanate reaction, *i.e.*, *o*- and *p*-nitrophenyl thiocyanate, the corresponding nitroaryl sulfenyl halide gave no sulfide on reaction with trimethyl phosphite. This indicates that heterolysis of an ArSCl bond in the direction shown in eq. 6 must be quite unfavorable and, since it is obviously not because of the anion (ArS^-), it must be due to the reluctance of chlorine to give up electrons and become a cation.

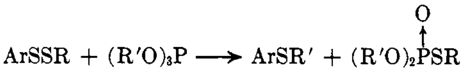


$$ArSCl + (CH_3O)_3P \not\longrightarrow [ArS^-(CH_3O)_3P^+Cl] \not\longrightarrow ArSR + (CH_3O)_2\overset{\overset{\displaystyle O}{\uparrow}}{P}Cl \quad (6)$$

Another observation related to the reactions of these aromatic sulfur compounds with trialkyl phosphites is the failure of methyl 4-chloro-2-nitrobenzenesulfenate (IX) to react with trimethyl phosphite even at reflux (120°). The related unsymmetrical disulfides, ArSSR, react exothermally with trialkyl phosphites[8] to give sulfide and phosphorothioate (eq. 7). Once again, heterolysis of the $ArSOCH_3$ bond in the direction $ArS^+\ OCH_3^-$ must be highly unfavorable.



IX



$$ArSSR + (R'O)_3P \longrightarrow ArSR' + (R'O)_2\overset{\overset{\displaystyle O}{\uparrow}}{P}SR \quad (7)$$

All of these results become more understandable when rationalized in the following manner. If the organosulfur compounds, RSX or ArSX, are arranged in decreasing order of their ability to react with trialkyl phosphites by heterolysis of the RS–X bond (to give phosphorothioates), then there is a direct parallel between the tendency to react in the direction shown (Table IV) and the pK_a of the corresponding hydrogen acid, HX. For example, sulfenyl halides, ArSCl, react with trialkyl phosphites exclusively by heterolysis in the direction shown in Table IV; mixed disulfides, RSSAr, also react exclusively in this direction[8]; aryl thiocyanates, ArSCN, react partly in the direction shown and partly by heterolysis in the opposite direction (this work); mixed disulfides, ArSSR, react exclusively in the opposite direction[8]; and alkyl sulfenate esters, $ArSOCH_3$, fail to react at all.

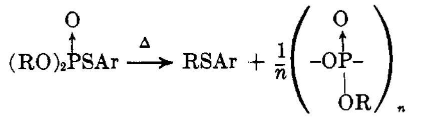
TABLE IV

SULFUR COMPOUNDS AND THEIR HYPOTHETICAL HETEROLYSIS PRODUCTS

ArSX	ArS^+Cl^-	$RS^+\ ^-SC_6H_5$	ArS^+CN^-	$ArS^+\ ^-SEt$	$ArS^+\ ^-OCH_3$
Hydrogen acid	HCL	HSC_6H_5	HCN	HSEt	$HOCH_3$
pK_a	> -7[a]	7.76[b]	9.32[c]	12.0[d]	17[e]

[a] T. G. McCoubert, *Trans. Faraday Soc.*, **51**, 743 (1955). [b] F. G. Bordwell and H. M. Anderson, *J. Am. Chem. Soc.*, **75**, 6019 (1953). [c] H. T. S. Britton and R. A. Robinson, *Trans. Faraday Soc.*, **28**, 531 (1932). [d] J. Maurin and R. A. Paris, *Compt. rend.*, **232**, 2428 (1951). [e] N. Bjerrum, A. Ungemach, and L. Zechmeister, *Kgl. Danske Videnskab. Selskab. Overs. Selskab. Virksomhed*, **5**, 1 (1924).

A final observation from Figures 2–4 and Table III pertains to the dramatic change in composition that occurs when the mixture of sulfide and phosphorothioate is heated to 140–180°. In all cases the sulfide concentration increases at the expense of the phosphorothioate; the extreme may be seen in Figures 3 and 4 where 2 hr. of heating at 180° has converted all of the phosphorothioate to sulfide. We regard this reaction as a thermal alkylation (eq. 8) which is not directly related to the thiocyanate–trialkyl phosphite reaction because it occurs at a measureable rate only at elevated temperatures. Structural effects on the ease of this reaction have been reported in a separate communication.[19]



$$(RO)_2\overset{\overset{\displaystyle O}{\uparrow}}{P}SAr \xrightarrow{\Delta} RSAr + \frac{1}{n}\left(-O\overset{\overset{\displaystyle O}{\uparrow}}{\underset{\underset{\displaystyle OR}{|}}{P}}-\right)_n \quad (8)$$

Acknowledgment.—The authors are grateful to Dr. C. H. Tieman, of this laboratory, for helpful discussions.

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[17] F. G. Bordwell and H. M. Anderson, *J. Am. Chem. Soc.*, **75**, 6019 (1953).

[18] J. Maurin and R. A. Paris, *Compt. rend.*, **232**, 2428 (1951).

[19] K. Pilgram and F. Korte, *Tetrahedron*, **21**, 203 (1965).