636. *Cyanamides. Part IV. The Interaction of Arylthioureas and Aromatic Sulphonyl Chlorides.*

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Interaction of aromatic sulphonyl chlorides and arylthioureas in pyridine at moderate temperatures results in rapid removal of sulphur and production of arylcyanamides. Some of the cyanamide reacts further with the excess of sulphonyl chloride, as shown by the isolation of *N*-aryl-*N*-arylsulphonylcyanamides, while part of the sulphonyl chloride is converted into the thiolsulphonate during the reaction.

The results of a number of experiments aimed at the elucidation of the mechanism of this reaction are in agreement with a reaction sequence which involves the intermediate formation of *S*-sulphonylthioureas (I).

INTERACTION of arylureas and aromatic sulphonyl chlorides in pyridine under restrained conditions was recently found to occur with simultaneous dehydration, giving *N*-aryl-*N*-arylsulphonylcyanamides in good yields (cf. Parts I and II, *J.*, 1949, 1034, 3029). Production of the appropriate melamines was also observed in some cases (Part III, *J.*, 1949, 3033). In continuation of this work, the action of sulphonyl chlorides on arylthioureas has been examined. The results have already been briefly outlined (*Nature*, 1950, **165**, 817). The present article supplies the essential details and describes some extensions of this work.

The action of benzenesulphonyl chloride on thiourea in alcoholic solution was first studied by Remsen and Turner (*Amer. Chem. J.*, 1901, **25**, 190) who obtained dithioformamidine dihydrochloride and diphenyl disulphoxide. The production of the former substance had also been observed by McGowan (*J.*, 1886, **49**, 191; 1887, **51**, 666; *J. pr. Chem.*, 1886, **33**, 188) in the reaction between thiourea and methanesulphonyl or trichloromethanesulphonyl chloride. Fromm and Heyder (*Ber.*, 1909, **42**, 3804) attempted to prepare the corresponding aryl-substituted dithioformamidine by the action of sulphonyl chlorides on phenylthiourea: the reaction, however, resulted in ring-closure, yielding " Hector's base " (2 : 3 : 4 : 5-tetrahydro-3 : 5-di-imino-2 : 4-diphenyl-1 : 2 : 4-thiadiazole), a compound that had previously been obtained by the action of various oxidising agents (*e.g.*, hydrogen peroxide, bromine, nitrous acid) on phenylthiourea (Hector, *Ber.*, 1889, **22**, 1176; Hugershoff, *Ber.*, 1901, **34**, 3130; Haager, *Monatsh.*, 1906, **27**, 267). Recent interest in sulphonamides of potential chemotherapeutic value has prompted attempts to synthesise *p*-aminobenzenesulphonylthiourea directly by the interaction of the appropriate sulphonyl chloride and thiourea. Leitch, Baker, and Brickman's experiments (*Canadian J. Res.*, 1945, **23**, *B*, 139) employing *p*-acetamidobenzenesulphonyl chloride under various conditions were unsuccessful, however, since the reaction proceeded in all cases as previously outlined by Remsen and Turner (*loc. cit.*). Moreover, the Canadian workers were unable to confirm Migliardi and Tappi's claims (*Arch. Sci. biol.*, 1941, **27**, 164) of having obtained the desired sulphonylthiourea by a variation of this method.

In the present investigation the interaction of arylthioureas and aromatic sulphonyl chlorides has been examined, using conditions recently employed with arylureas (cf. Parts I and II, *loc. cit.*). The reaction proceeds essentially as with arylureas, since the aromatic thiourea rapidly loses sulphur, giving an arylcyanamide as one of the main products. Thus, treatment of 1 mole of arylthiourea with 2·5—3 moles of sulphonyl chloride in pyridine at moderate temperatures gives a product from which up to 1 mole of arylcyanamide and 1 g.-equivalent of sulphur are obtained. Varying quantities of the cyanamide, depending on the nature of the substituents and on the conditions, react further with the excess of the sulphonyl chloride, as shown by the isolation of *N*-aryl-*N*-arylsulphonylcyanamide. Part of the sulphonyl chloride is converted into the aryl thiolsulphonate during the reaction, and traces of diarylsulphonyl trisulphide are occasionally obtained.

As an example, the reaction between phenylthiourea and toluene-*p*-sulphonyl chloride gave phenylcyanamide (56% yield), sulphur (80%, based on the thiourea), *N*-phenyl-*N*-toluene-*p*-sulphonylcyanamide (20%), and *p*-tolyl toluene-*p*-thiolsulphonate (35%). Similar results were obtained with 1-naphthylthiourea, and *p*-chlorophenylthiourea, although formation of the fully substituted sulphonylcyanamide (VI) predominated in the latter case. *as*-Diphenylthiourea gave excellent yields of the expected diphenylcyanamide, together with smaller quantities of the appropriate thiolsulphonate. The present reaction is of smaller preparative value than the convenient synthesis involving arylureas, since the resulting *N*-aryl-*N*-arylsulphonylcyanamides and thiolsulphonates must be separated by fractional crystallisation, and since, in any case, alternative methods are available to prepare the individual products independently in good yields.

The products of the interaction of arylthioureas and aromatic sulphonyl chlorides can be accounted for by several reaction mechanisms, of which the following appear to merit closer examination.

The experimental results can be interpreted by a mechanism analogous to that suggested for the interaction of arylureas and aromatic sulphonyl chlorides (cf. Part III, *loc. cit.*). The first stage of the reaction may thus be considered to involve the intermediate formation of the *S*-sulphonylthiourea (I). The great instability of imidosulphonates of type $R'\cdot C(:NH)\cdot O\cdot SO_2\cdot R$ has been demonstrated by Oxley, Peak, and Short (*J.*, 1948, 1514, 1618), who showed that the expected *N*-phenylbenzamidine cannot be obtained from benzamide, benzenesulphonyl chloride, and aniline, as phenyl cyanide is formed instead even at low temperatures. If the analogous behaviour of *S*-sulphonylthioureas (I) may be assumed, the formation of all products observed in the present reaction follows readily: the unstable intermediate (I) decomposes immediately to the thiolsulphonic acid (II) and arylcyanamide (III); the latter reacts further with the excess of sulphonyl chloride, yielding varying quantities of *N*-aryl-*N*-arylsulphonylcyanamide (VI). Aromatic thiolsulphonic acids (II) are stable in the form of their salts only; the free acids decompose spontaneously into sulphur and the corresponding arylsulphinic acids (Blomstrand, *Ber.*, 1870, **3**, 963). The conversion of the latter into aryl arylthiolsulphonates (V) under a variety of conditions is a well-known reaction and can be expected to account for the occurrence of these substances amongst the products of the reaction.

$$\begin{tikzcd}
R\cdot SO_2Cl + NH_2\cdot CS\cdot NHR' \arrow[r] & \underset{\text{(I.)}}{[R\cdot SO_2\cdot S\cdot C(:NH)\cdot NHR']} \arrow[r] & \underset{\text{(II.)}}{R\cdot SO_2\cdot SH} \arrow[dl, "R\cdot SO_2Cl"'] \arrow[d] & + \underset{\text{(III.)}}{R'\cdot NH\cdot CN} \arrow[d] \\
 & \underset{\text{(V.)}}{R\cdot SO_2\cdot SR} & \underset{\text{(IV.)}}{R\cdot SO_2H + S} \arrow[l, "R\cdot SO_2Cl"] & \underset{\text{(VI.)}}{R\cdot SO_2\cdot NR'\cdot CN}
\end{tikzcd}$$

Experiments devised to test the validity of the above explanation have provided indirect evidence in support of a modified form of the suggested reaction sequence.

Attempts were made to examine the decomposition of an arylthiolsulphonic acid under the conditions of the thiourea–sulphonyl chloride interaction by preparing toluene-*p*-thiolsulphonic acid *in situ* from a pyridine solution of its stable sodium salt and pyridine hydrochloride. It was found, however, that sodium toluene-*p*-thiolsulphonate was not decomposed as long as any free pyridine, necessarily present as solvent, remained; indeed an aqueous solution of the thiolsulphonate was unaffected by pyridine hydrochloride and began to deposit sulphur only when an excess of hydrochloric acid was added. It is well known that salts of arylthiolsulphonic acids are readily produced by heating sulphinates with finely divided sulphur (Spring, *Ber.*, 1874, **7**, 1158; Otto, *Ber.*, 1882, **15**, 127). The following observations suggested that this method was applicable to the preparation of fairly stable pyridine solutions of aromatic thiolsulphonic acids: When equivalent quantities of toluene-*p*-sulphinic acid and sulphur were heated in this solvent for short periods and the liquid was poured into water, only traces of sulphur (and thiolsulphonate) were reprecipitated even on prolonged storing. On addition of excess of acid, a colloidal precipitate of the sulphur originally added was obtained. Alternatively, partial evaporation of the acidified liquid gave *p*-tolyl toluene-*p*-thiolsulphonate and ditoluene-*p*-sulphonyl trisulphide; these products are also obtained when acidified solutions of sodium toluene-*p*-thiolsulphonate are similarly evaporated. The original formation of toluene-*p*-thiolsulphonic acid, probably in the form of its pyridinium salt, may therefore be inferred. The above results indicated that the observed formation of thiolsulphonate esters in the arylthiourea–sulphonyl chloride reaction was not caused by a simple thermal decomposition of arylthiolsulphonic acids. Interesting results were obtained, however, in the interaction of sodium toluene-*p*-thiolsulphonate or toluene-*p*-sulphinic acid and sulphur with arylsulphonyl chlorides (see below).

Attention was next directed to the postulated intermediate occurrence of arylsulphinic acids. Experiments showed that the well-known disproportionation of arylsulphinic acids to thiolsulphonates (Otto, *Ber.*, 1876, **9**, 1639; von Braun and Weissbach, *ibid.*, 1930, **63**, 2836) according to equation (1) does not occur under the conditions of the the thiourea–sulphonyl chloride reaction. Thus, toluene-*p*-sulphinic acid, when heated in pyridine solution at 100° for up to 1 hour in the absence or presence of pyridine hydrochloride, gave no thiolsulphonate. However, the sulphinic acid reacted with toluene-*p*-sulphonyl chloride in pyridine, to yield not only the

$$3R{\cdot}SO_2H \longrightarrow R{\cdot}SO_2{\cdot}SR + R{\cdot}SO_3H + H_2O \quad . \; . \; . \; . \; . \; . \quad (1)$$

expected di-*p*-tolyl disulphone, but *p*-tolyl toluene-*p*-thiolsulphonate as well. Moreover, a series of experiments indicated that thiolsulphonate formation became the increasingly predominant and eventually exclusive reaction the more closely the experimental conditions of the thiourea reaction under investigation were approached; the change probably involves oxidation of two molecules of sulphinic to sulphonic acid by the oxygen from a sulphonyl group and may be represented by equation (2):

$$3R{\cdot}SO_2H + R{\cdot}SO_2Cl \longrightarrow R{\cdot}SO_2{\cdot}SR + 2R{\cdot}SO_3H + HCl \quad . \; . \; . \; . \quad (2)$$

Interaction of equimolecular quantities of the reactants in pyridine at 70°, for example, gave near-theoretical yields of thiolsulphonate [calculated on the basis of equation (2)], while disulphone formation occurred to the extent of a few per cent. (3%) only. These conditions are comparable with those previously chosen for the thiourea–sulphonyl chloride reaction, where approximately 1 mol. of sulphonyl chloride is available per mol. of sulphinic acid and the temperature of the reaction mixture rises to approximately 70° within a few seconds. Thiolsulphonate was also produced in excellent yields when the reactants were employed in the molecular proportion expressed by equation 2 (*i.e.*, 3 : 1), but a somewhat higher temperature (95°) was then required.

Since sulphur and a thiolsulphonate (V) are obtained side by side in the thiourea reaction under investigation it appeared necessary, as a next step, to examine the influence of this element on the interaction of arylsulphinic acid and arylsulphonyl chloride. It was found that the thiolsulphonate was produced with equal ease when a mixture of equivalent quantities of sulphinic acid and sulphur (*i.e.*, in effect a solution of thiosulphonic acid) was treated with the acid chloride at temperatures above 70°. Under these conditions the added sulphur did not affect the result of the reaction except in producing small quantities of diarylsulphonyl trisulphide as a by-product; this substance has also sometimes been isolated in the interaction of aromatic thioureas and sulphonyl chlorides. All observations are therefore in agreement with the view that the thiolsulphonates obtained in the thiourea reaction arise from the action of the excess of arylsulphonyl chloride on the intermediate arylsulphinic acids, or directly on the arylthiolsulphonic acids:

$$3R{\cdot}SO_2{\cdot}SH + R{\cdot}SO_2Cl \longrightarrow R{\cdot}SO_2{\cdot}SR + 2R{\cdot}SO_3H + 3S + HCl \quad . \; . \; . \quad (2a)$$

The action of an aromatic sulphonyl chloride on sodium toluene-*p*-thiolsulphonate has also been examined. Under the usual conditions, the reaction afforded *p*-tolyl toluene-*p*-thiolsulphonate together with ditoluene-*p*-sulphonyl trisulphide. The formation of the latter product in a synthesis that would normally be expected to furnish the monosulphide according to equation (3)

$$R{\cdot}SO_2Cl + NaS{\cdot}SO_2R \longrightarrow R{\cdot}SO_2{\cdot}S{\cdot}SO_2R + NaCl \quad . \; . \; . \; . \; . \quad (3)$$

is not surprising, since varying proportions of the trisulphide are invariably obtained whenever the monosulphide or disulphide is synthesised; indeed conversion of the pure dry monosulphide into the trisulphide appears to take place on storage (Otto and Tröger, *Ber.*, 1891, **24**, 1125; Tröger and Hornung, *J. pr. Chem.*, 1899, **60**, 113). Ditoluene-*p*-sulphonyl trisulphide has previously been prepared from alkali toluene-*p*-thiolsulphonate and iodine (Blomstrand, *Ber.*, 1870, **3**, 957; Otto and Tröger, *loc. cit.*) or sulphur dichloride (Tröger and Hornung, *loc. cit.*). The present reaction, which incidentally provides a new method of preparation of aromatic pentathionates, may be thought to proceed in the following stages: the reaction between sodium toluene-*p*-thiolsulphonate and toluene-*p*-sulphonyl chloride produces, in the first place, sulphonyl cations and thiolsulphonate anions, the latter breaking down into sulphur and sulphinate anions (equation 4). Combination of two oppositely charged ions with three sulphur atoms provides the pentathionate (equation 5) leaving equal numbers of sulphonyl and sulphinate ions. Interaction involving three pairs of these ions, such that oxidation of two sulphinate to sulphonate anions occurs at the expense of a third sulphinate, which is itself reduced to sulphide, affords the units required for building up the thiolsulphonate (equations 6 and 7). The sulphonyl cations and sulphonate anions remaining in equal numbers (equivalent to sulphonic anhydride) may form pyridinium compounds with the solvent (equation 8) and eventually give rise to sulphonic acids when the reaction mixture is poured into water. Alternatives to the suggested sequence involving oxidation–reduction processes can be formulated: An alternative mode of oxygen transfer in stage (6), for example, may produce intermediate sulphenyl cations; hypothetical sulphenic acids have often been postulated to explain reactions involving thiolsulphonates and related compounds (cf. Kharasch *et al.*, *Chem. Reviews*, 1946, **39**, 275). The resulting overall equation (9) obtained in each case is in good agreement with the magnitude of the yields observed experimentally.

$$
\begin{array}{rcll}
3\mathrm{R{\cdot}SO_2Cl} + 3\mathrm{R{\cdot}SO_2{\cdot}SNa} & \longrightarrow & 3\mathrm{NaCl} + 3\mathrm{R{\cdot}SO_2}^{\oplus} + 3\mathrm{R{\cdot}SO_2}^{\ominus} + 3\mathrm{S} & (4)\\
 & \longrightarrow & 3\mathrm{NaCl} + (\mathrm{R{\cdot}SO_2})_2\mathrm{S_3} + 2\mathrm{R{\cdot}SO_2}^{\oplus} + 2\mathrm{R{\cdot}SO_2}^{\ominus} & (5)\\
3\mathrm{R{\cdot}SO_2}^{\oplus} + 3\mathrm{R{\cdot}SO_2}^{\ominus} & \longrightarrow & 3\mathrm{R{\cdot}SO_2}^{\oplus} + 2\mathrm{R{\cdot}SO_3}^{\ominus} + \mathrm{R{\cdot}S}^{\ominus} & (6)\\
 & \longrightarrow & \mathrm{R{\cdot}SO_2{\cdot}SR} + 2\mathrm{R{\cdot}SO_2}^{\oplus} + 2\mathrm{R{\cdot}SO_3}^{\ominus} & (7)\\
\mathrm{R{\cdot}SO_2}^{\oplus} + \mathrm{R{\cdot}SO_3}^{\ominus} + \mathrm{C_5H_5N} & \longrightarrow & (\mathrm{C_5H_5N{\cdot}SO_2R})^{\oplus}\mathrm{R{\cdot}SO_3}^{\ominus} & (8)\\
9\mathrm{R{\cdot}SO_2Cl} + 9\mathrm{R{\cdot}SO_2{\cdot}SNa} + 4\mathrm{C_5H_5N} & \longrightarrow & & \\
 & & 3(\mathrm{R{\cdot}SO_2})_2\mathrm{S_3} + 2\mathrm{R{\cdot}SO_2{\cdot}SR} + 9\mathrm{NaCl} + 4(\mathrm{C_5H_5N{\cdot}SO_2R})^{\oplus}\mathrm{R{\cdot}SO_3}^{\ominus} & (9)
\end{array}
$$

It has been shown above that reaction in pyridine above 70° between arylsulphinic acid and sulphur (equivalent to arylthiolsulphonic acid) with sulphonyl chloride produces thiolsulphonate, while sulphur is recovered. At lower temperatures, diarylsulphonyl trisulphide becomes one of the main products and the reaction then proceeds by equation (9) instead of (2*a*).

In conclusion, an observation providing support for the postulated intermediate formation of thiolsulphonic acids (II) in the arylthiourea–sulphonyl chloride reaction may be reported. When the reaction product from equimolecular quantities of *as*-diphenylthiourea and toluene-*p*-sulphonyl chloride in pyridine was poured into water, the expected diphenylcyanamide, but only traces of sulphur, were precipitated. The aqueous phase gave a precipitate of sulphur with excess of acid, or deposited, after acidification (Congo-red) and heating, considerable quantities of *p*-tolyl toluene-*p*-thiolsulphonate and ditoluene-*p*-sulphonyl trisulphide, thus behaving as a solution of a thiolsulphonate under identical conditions. The presence of toluene-*p*-thiolsulphonic acid, presumably as the pyridinium salt, in the aqueous phase is therefore indicated. Owing to the lack of excess of sulphonyl chloride under the selected conditions of the experiment, the reaction had apparently stopped at the intermediate stage [*i.e.*, formation of (II) and (III)]. *as*-Diphenylthiourea is particularly suitable for the above test, since the changes are simplified by the absence of the side-reaction producing *N*-aryl-*N*-arylsulphonylcyanamides (VI).

In the light of the above discussion the successive steps in the interaction of arylthioureas and aromatic sulphonyl chlorides may be represented by equations (10) and (2), the overall reaction being given by a net equation such as (11). The postulated intermediate formation of an unstable *S*-sulphonyl*iso*thiourea (I) in the present reaction brings its mechanism into line with that previously suggested for the analogous reaction between arylureas and aromatic sulphonyl chlorides (cf. Part III). In fact, the new observations with arylthioureas now recorded provide additional support for the original hypothesis. Thus, while aromatic cyanamides, whose intermediate occurrence was assumed, were never isolated in the arylurea series except in special cases, in the form of their trimers (melamines), arylcyanamides are found amongst the main products in the corresponding reactions involving aromatic thioureas. The occasional isolation of diarylsulphonyl trisulphide also appears to be a strong point in support of the suggested mechanism.

$$
\begin{array}{rcll}
\mathrm{R{\cdot}SO_2Cl} + \mathrm{NH_2{\cdot}CS{\cdot}NHR'} & \begin{array}{c}\nearrow\\ \searrow\end{array} & \begin{array}{l}\mathrm{R{\cdot}SO_2{\cdot}SH} + \mathrm{R'{\cdot}NH{\cdot}CN} + \mathrm{HCl}\\ \mathrm{R{\cdot}SO_2H} + \mathrm{S} + \mathrm{R'{\cdot}NH{\cdot}CN} + \mathrm{HCl}\end{array} & (10a)\\
2\mathrm{R{\cdot}SO_2Cl} + \mathrm{NH_2{\cdot}CS{\cdot}NHR'} & \begin{array}{c}\nearrow\\ \searrow\end{array} & \begin{array}{l}\mathrm{R{\cdot}SO_2{\cdot}SH} + \mathrm{R{\cdot}SO_2{\cdot}NR'{\cdot}CN} + 2\mathrm{HCl}\\ \mathrm{R{\cdot}SO_2H} + \mathrm{S} + \mathrm{R{\cdot}SO_2{\cdot}NR'{\cdot}CN} + 2\mathrm{HCl}\end{array} & (10b)\\
\mathrm{R{\cdot}SO_2Cl} + 3\mathrm{R{\cdot}SO_2H} & \longrightarrow & \mathrm{R{\cdot}SO_2{\cdot}SR} + 2\mathrm{R{\cdot}SO_3H} + \mathrm{HCl} & (2)\\
\mathrm{R{\cdot}SO_2Cl} + 3\mathrm{R{\cdot}SO_2{\cdot}SH} & \longrightarrow & \mathrm{R{\cdot}SO_2{\cdot}SR} + 2\mathrm{R{\cdot}SO_3H} + 3\mathrm{S} + \mathrm{HCl} & (2a)\\
4\mathrm{R{\cdot}SO_2Cl} + 3\mathrm{NH_2{\cdot}CS{\cdot}NHR'} & \longrightarrow & & \\
 & & \mathrm{R{\cdot}SO_2{\cdot}SR} + 2\mathrm{R{\cdot}SO_3H} + 3\mathrm{S} + 3\mathrm{R'NH{\cdot}CN} + 4\mathrm{HCl} & (11a)\\
7\mathrm{R{\cdot}SO_2Cl} + 3\mathrm{NH_2{\cdot}CS{\cdot}NHR'} & \longrightarrow & & \\
 & & \mathrm{R{\cdot}SO_2{\cdot}SR} + 2\mathrm{R{\cdot}SO_3H} + 3\mathrm{S} + 3\mathrm{R{\cdot}SO_2{\cdot}NR'{\cdot}CN} + 7\mathrm{HCl} & (11b)
\end{array}
$$

Of other possible mechanisms for the arylthiourea–sulphonyl chloride reaction, brief reference will be made only to the hypothesis advanced by Remsen and Turner (*loc. cit.*) for the analogous reaction involving thiourea in ethanol. These workers interpreted the production of dithioformamidine and thiolsulphonates by the postulate that two molecules of the thiourea first combine by abstracting chlorine from the sulphonyl chloride (equation 12); the two residual arylsulphonyl radicals then react with more thiourea, being reduced to the thiolsulphonate, while sulphur is deposited (equation 13). Although neither cyanamide nor its polymerisation products were isolated, Remsen presumed that cyanamide was also formed in the reaction.

$$2\text{R}{\cdot}\text{SO}_2\text{Cl} + 2\text{NH}_2{\cdot}\text{CS}{\cdot}\text{NH}_2 \longrightarrow \text{NH}_2{\cdot}\text{C}({:}\text{NH}){\cdot}\text{S}{\cdot}\text{S}{\cdot}\text{C}({:}\text{HN}){\cdot}\text{NH}_2 + 2\text{HCl} + 2\text{R}{\cdot}\text{SO}_2 \quad . \quad (12)$$

$$2\text{R}{\cdot}\text{SO}_2 + 2\text{NH}_2{\cdot}\text{CS}{\cdot}\text{NH}_2 \longrightarrow \text{RSO}_2{\cdot}\text{SR} + 2\text{NH}_2{\cdot}\text{CN} + 2\text{S} + 2\text{H}_2\text{O} \quad . \ . \ . \ . \quad (13)$$

$$\text{NH}_2{\cdot}\text{C}({:}\text{NH}){\cdot}\text{S}{\cdot}\text{S}{\cdot}\text{C}({:}\text{NH}){\cdot}\text{NH}_2 \longrightarrow \text{NH}_2{\cdot}\text{CN} + \text{NH}_2{\cdot}\text{CS}{\cdot}\text{NH}_2 + \text{S} \quad . \ . \ . \ . \ . \ . \ . \quad (14)$$

Diphenyldithioformamidine, derived from phenylthiourea, has apparently not been prepared; a number of methods expected to furnish this compound lead to other products, *e.g.*, substituted benzthiazoles (Hugershoff, *Ber.*, 1901, **34**, 3130; 1903, **36**, 3121). Since dithioformamidine is readily decomposed to thiourea, cyanamide, and sulphur (Claus, *Annalen*, 1875, **179**, 139), a variation of the above mechanism can be applied to the observations now recorded for aromatic thioureas, but suffers from several disadvantages, including, for example, the necessity of assuming simultaneous formation of the arylcyanamide by two different routes. The role of dithioformamidines in the reactions of arylthioureas is being further examined and will be reported in another connexion.

EXPERIMENTAL.

M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford. Unless otherwise stated, yields of thiolsulphonates have been calculated on the basis of equation (11).

*Interaction of Phenylthiourea and Toluene-*p*-sulphonyl Chloride.*—To a solution of phenylthiourea (15·2 g., 0·1 mol.) in pyridine (100 ml.), toluene-*p*-sulphonyl chloride (47·6 g., 0·25 mol.) was added in one portion. The resulting deep-red solution, the temperature of which rose to 80°, was allowed to cool spontaneously to 40—35° during 20—25 minutes and poured into water (600 ml.) acidified with concentrated hydrochloric acid (50 ml.). The yellow highly viscous oil was exhaustively extracted with warm chloroform, and the chloroform solution (300 ml.) extracted first with hydrochloric acid (1 : 1; 3 × 30 ml.) to remove pyridine and then with warm sodium hydroxide solution (10% w./w.; 3 × 35 ml.), and washed with warm water until neutral.

The alkaline extracts were shaken with carbon and filtered, and the pale-yellow filtrate made acid with acetic acid at 0° (addition of ice), a voluminous precipitate of a white crystalline material separating; this was filtered off and washed with ice-water, giving phenylcyanamide (6·6 g., 56%), m. p. 44—46° (Found: C, 71·5; H, 4·95; N, 23·6. Calc. for $\text{C}_7\text{H}_6\text{N}_2$: C, 71·2; H, 5·1; N, 23·7%). Alternatively, the alkaline extracts were shaken with excess of benzoyl chloride (28 g., 0·2 mol.); crystallisation of the crude separated product (11—12 g., 50—55%) from ethanol (80 ml.) gave white lustrous needles of *N*-benzoylphenylcyanamide, m. p. 125—127°.

The final neutral chloroform extracts were evaporated under reduced pressure, the residue (from which a yellow crystalline material had begun to separate already during the distillation) boiled with acetone (20 ml.)–ethanol (20 ml.) then allowed to cool, and the yellow crystalline powder filtered off. Crystallisation from chloroform–benzene (40 and 10 ml. respectively) gave elongated yellow blades of sulphur (Total, 2·53 g.; 80% loss of sulphur from phenylthiourea).

The filtrate (from which further small quantities of sulphur had been filtered off) deposited, on evaporation, a lustrous white solid (m. p. varying between 60° and 70°) which was collected (total, 8—9·5 g.) and fractionated as follows: It was dissolved in ethanol (50 ml.) and decolorised with charcoal; on successive evaporation and filtration, seven fractions (each approx. 1 g.) were isolated. The first three fractions, consisting of opaque white elongated prisms (total weight, 3·3 g.; m. p. between 76° and 79°) were united and gave, on recrystallisation from ethanol (15 ml.), opaque prismatic columns of *p*-tolyl toluene-*p*-thiolsulphonate, m. p. 77—78° (undepressed on admixture with authentic material) (estimated yield: approx. total, 3—3·5 g., 32—38%) (Found: C, 60·1; H, 5·0; N, 0·5; S 22·4. Calc. for $\text{C}_{14}\text{H}_{14}\text{O}_2\text{S}_2$: C, 60·4; H, 5·0; S, 23·0%). The final three fractions consisted mainly of transparent hexagonal plates (3·2 g.; m. p. 85—88°) and crystallised from acetone–ethanol in transparent hexagonal plates of *N*-phenyl-*N*-toluene-*p*-sulphonylcyanamide, m. p. 86—88° (undepressed on admixture with authentic material prepared from phenylurea; mixed m. p. with *p*-tolyl toluene-*p*-thiolsulphonate, 60—64°, *i.e.*, that of the original mixed crystals) (Found: C, 61·5; H, 4·6; N, 10·5; S, 11·6. Calc. for $\text{C}_{14}\text{H}_{12}\text{O}_2\text{N}_2\text{S}$: C, 61·8; H, 4·4; N, 10·3; S, 11·8%). Estimated yield, 17—20%.

When phenylthiourea (1 mol.) was allowed to react with 4 mols. of toluene-*p*-sulphonyl chloride at 70° for 30 minutes, and the reaction mixture was worked up as previously described, no phenylcyanamide was obtained; the yield of *N*-phenyl-*N*-toluene-*p*-sulphonylcyanamide was increased to 86%. In some experiments, small quantities (0·2—0·5 g.) of ditoluene-*p*-sulphonyl trisulphide, m. p. 185—186°, were isolated during the crystallisation of the neutral fraction (most sparingly soluble portion. Found: S, 39·8. Calc. for $\text{C}_{14}\text{H}_{14}\text{O}_4\text{S}_5$: S, 39·4%).

Interaction of p-*Chlorophenylthiourea and Toluene*-p-*sulphonyl Chloride*.—A solution of *p*-chlorophenylthiourea (18·6 g., 0·1 mol.) in pyridine (80 ml.) was treated with toluene-*p*-sulphonyl chloride (47·6 g., 0·25 mol.). The resulting hot (80°) liquid was set aside for 20 minutes and poured into acidified water (600 ml.), an orange-yellow granular solid separating. The product was dissolved in chloroform and the solution extracted with hydrochloric acid and then sodium hydroxide solution, and washed with water as previously described.

The filtered alkaline extracts were divided into two parts: One half gave, on acidification with acetic acid, a white precipitate (0·85 g.) which formed, after two crystallisations from benzene–light petroleum (4 and 8 ml. respectively), silky needles of *p*-chlorophenylcyanamide, m. p. 108—109° [Krall *et al.*, *J. Indian Chem. Soc.*, 1946, **23**, 373, give 97°; Mann *et al.*, *J.*, 1947, 916, give 103°; Ainley, Curd, and Rose, *J.*, 1949, 101, give 106—107° (from water)]. The second half of the alkaline extracts was shaken with excess of benzoyl chloride (10 g.) and gave N-*benzoyl*-p-*chlorophenylcyanamide*, m. p. 133—134° (from ethanol) (Found: C, 65·7; H, 3·5. $C_{14}H_9ON_2Cl$ requires C, 65·5; H, 3·5%) (total yield of *p*-chlorophenylcyanamide, 6—8%).

The neutral chloroform extracts were evaporated in a vacuum, the residue was boiled with acetone–ethanol (20 and 60 ml. respectively), and the separated sulphur (2·8 g., 88%) filtered off. After purification with carbon the material was fractionated from acetone–ethanol, giving on successive filtration and evaporation, the following crops:

(i)	11·80 g.	White compact prisms	m. p. 136—138°	Found, N: 8·9%
(ii)	4·80 g.	Nearly white prisms	m. p. 130—132°	,, 8·4%
(iii)	2·35 g.	Yellowish crystals	m. p. 80— 84° (→ 112°)	,, 0·4%
(iv)	1·20 g.	Yellow prismatic columns	m. p. 77— 79°	,, 0·3%
(v)	3·0 g.	Orange oil	—	—

Crops (i) and (ii) were twice recrystallised from ethanol (100 ml., 80 ml.), and gave lustrous compact prisms of N-p-*chlorophenyl*-N-*toluene*-p-*sulphonylcyanamide*, m. p. 138—139° (Found: C, 54·85; H, 3·7; N, 8·9. $C_{14}H_{11}O_2N_2SCl$ requires C, 54·8; H, 3·6; N, 9·1%) (total yield: approx. 16·6 g., 54%). Further purification of the more soluble fractions (iii) and (iv) from ethanol gave elongated prisms of *p*-tolyl toluene-*p*-thiolsulphonate, m. p. 78—79° (approx. yield, 35%).

Interaction of p-*Chlorophenylthiourea and Benzenesulphonyl Chloride*.—*p*-Chlorophenylthiourea (9·4 g., 0·05 mol.) in pyridine (50 ml.) was treated with benzenesulphonyl chloride (22 g., 0·125 mol.). The hot (75°) orange liquid was poured, after 20 minutes, into acidified water (300 ml.), and the separated oil was taken up in chloroform, which was in turn extracted with hydrochloric acid, sodium hydroxide solution, and water (until neutral). From the alkaline extracts, *p*-chlorophenylcyanamide (0·6 g., 8%), m. p. 108—109°, was obtained. The neutral chloroform solution was evaporated, the sulphur removed, and the residue fractionated from acetone–ethanol, yielding minute white prisms of N-*benzenesulphonyl*-N-p-*chlorophenylcyanamide*, m. p. 93—95° (Found: C, 53·8; H, 2·9. $C_{13}H_9O_2N_2SCl$ requires C, 53·3; H, 3·1; N, 9·6%), in 52% yield, and phenyl benzene-*p*-thiolsulphonate (38%), m. p. 45—46° (Found: C, 57·2; H, 4·1. Calc. for $C_{12}H_{10}O_2S_2$: C, 57·6; H, 4·0%).

Benzenesulphonyl-*p*-chlorophenylcyanamide was also prepared directly by the interaction of *p*-chlorophenylurea (3·7 g., 0·02 mol.) and benzenesulphonyl chloride (10·6 g., 0·06 mol.) in pyridine (20 ml.) in the usual manner (cf. Part II, *J.*, 1949, 3029) and formed colourless prismatic crystals (4·3 g., 73%), m. p. 93—95° (undepressed on admixture with material obtained as above).

N-*p*-Chlorophenyl-*N*-toluene-*p*-sulphonylcyanamide was similarly prepared by the use of toluene-*p*-sulphonyl chloride (11·4 g., 0·06 mol.) and consisted of lustrous prisms, m. p. 138—140° (undepressed on admixture with material obtained from *p*-chlorophenylthiourea).

Interaction of α-*Naphthylthiourea and Toluene*-p-*sulphonyl Chloride*.—Addition of toluene-*p*-sulphonyl chloride (19·1 g., 0·1 mol.) to freshly recrystallised α-naphthylthiourea (10·1 g., 0·05 mol.) in pyridine gave a bluish-black liquid, which produced a dark violet oil on dilution with water. Separation into the constituents in the usual way gave α-naphthylcyanamide, m. p. 130—131° (32%), sulphur (68%), *N*-α-naphthyl-*N*-toluene-*p*-sulphonylcyanamide, m. p. 155—157° (28%), and smaller quantities of *p*-tolyl toluene-*p*-thiolsulphonate.

as-*Diphenylthiourea*.—To a saturated solution of hydrogen sulphide in ethanol at 0° (150 ml.; *i.e.*, approx. 4·2 g. of H_2S, 0·125 mol.) contained in a thick-walled flask of 250-ml. capacity, diphenylcyanamide (19·4 g., 0·1 mol.) was added, followed by concentrated ammonia solution (5 ml.; *d* 0·88). The closed vessel was slowly heated to 105° (brine-bath) and maintained at this temperature for 6 hours. On cooling, the product separated as well-defined white needles (21·0 g., 92%). Crystallisation of the powdered material by dissolving it in boiling chloroform (400 ml.), distilling the filtered liquid to ⅓ bulk, and diluting the residue with ethanol (100 ml.) gave white needles of diphenylthiourea, which melted at 224—226° when slowly heated (giving a green melt), or at 214—216° when kept at this temperature for 1 minute (the m. p. has variously been recorded between 198° and 214°).

Interaction of as-*Diphenylthiourea and Toluene*-p-*sulphonyl Chloride*.—A solution of *as*-diphenylthiourea (2·28 g., 0·01 mol.) in pyridine (30 ml.) was treated with toluene-*p*-sulphonyl chloride (3·8 g., 0·02 mol.), and the cold liquid heated on the steam-bath for 2 hours. When the dark orange reaction mixture was poured into water (250 ml.) a viscid oil separated, and the mixture was acidified with hydrochloric acid (to Congo-red). The material solidified overnight, was filtered off (dry wt., 3·1 g.), and boiled with ethanol (20 ml.), and the residual sulphur filtered off with suction (dry wt., 0·27 g., 84% based on the thiourea). The ethanolic filtrate was purified by boiling it with carbon, and the resulting white crystalline product was separated by fractional crystallisation, yielding white plates of diphenylcyanamide, m. p. 70—72° (1·71 g., 88%), and glass-like prisms of tolyl toluene-*p*-thiolsulphonate, m. p. 77—78°.

Attempted Conversion of Toluene-p-*sulphinic Acid into Tolyl Toluene*-p-*thiolsulphonate in Pyridine.*—A solution of toluene-*p*-sulphinic acid (4·7 g., 0·03 mol.) in pyridine (30 ml.) was heated at 70° for 15 minutes and poured into water (150 ml.), giving a yellow liquid which remained clear on prolonged storage. The presence of the unchanged sulphinic acid was shown by slowly evaporating the strongly acidified (40 ml. of concentrated hydrochloric acid) solution on the steam-bath and heating the liquid for 8 hours, whereupon tolyl toluene-*p*-thiolsulphonate separated gradually [1·85 g., 67% calc. on the basis of equation (1)]. The same results were obtained when the acid was heated for up to 1 hour at 100°, in the presence of pyridine hydrochloride (7 g., 0·06 mol.).

Interaction of Sodium Toluene-p-*thiolsulphonate and Toluene*-p-*sulphonyl Chloride.*—To a solution of sodium toluene-*p*-thiolsulphonate (8·4 g., 0·04 mol.) in pyridine (120 ml.) at 60°, toluene-*p*-sulphonyl chloride (22·9 g., 0·12 mol.) was added. The temperature of the clear orange liquid rose momentarily to 70° and was kept at 60—65° for 20 minutes. The clear liquid was poured into water (500 ml.), yielding an oil, which soon solidified and was filtered off, ground, and washed. The crude product (dry wt., 6·0 g.) was boiled with ethanol (60 ml.); after 6 hours, the alcohol-insoluble, nearly white powder (3·15—3·7 g., 60—70%) was collected and rinsed with cold ethanol (filtrates : A). Two crystallisations from benzene–ethanol (20 and 3 ml., respectively, per g.) gave white microcrystalline prisms of ditoluene-*p*-sulphonyl trisulphide, m. p. 185—186° (slight sintering at 160°) undepressed on admixture with authentic material prepared by the interaction of sodium *p*-toluenethiolsulphonate and sulphur dichloride [Tröger and Hornung, *J. pr. Chem.*, 1899, **60**, 113, 131, report m. p. 180° (from glacial acetic acid). Cf. Christiansen (*Z. Electrochem.*, 1928, **34**, 638), who reports forms of m. p. 160° and 183°, the former passing into the latter on keeping] [Found : C, 41·4; H, 3·6; S, 40·1; *M* (Rast), 360, 365. Calc. for $C_{14}H_{14}O_4S_5$: C, 41·4; H, 3·4; S, 39·4%; *M*, 406].

Filtrates A were evaporated in a vacuum, and the residual orange oil was dissolved in warm ethanol (10 ml.). The orange crystals separating on storage gave, on further recrystallisation from ethanol with addition of carbon, colourless lustrous prisms of *p*-tolyl toluene-*p*-thiolsulphonate (1·9 g., 75%), m. p. 78—79°, undepressed on admixture with authentic material obtained from toluene-*p*-sulphinic acid (Found : C, 59·95; H, 5·0. Calc. for $C_{14}H_{14}O_2S_2$: C, 60·4; H, 5·0%) (yields calculated according to equation 9).

Interaction of Toluene-p-*sulphinic Acid and Toluene*-p-*sulphonyl Chloride in Pyridine.*—(*a*) A solution of toluene-*p*-sulphinic acid (4·7 g., 0·03 mol.) in pyridine (30 ml.) at 50° was treated with toluene-*p*-sulphonyl chloride (5·7 g., 0·03 mol.). The orange liquid, the temperature of which rose to 85—90°, was allowed to cool spontaneously for 15 minutes, and then stirred into water (150 ml.). The oil soon solidified and was filtered off (filtrate : A) and powdered (dry wt. 2·8 g.). The product was separated into its constituents by brief boiling with ethanol (15 ml.), when most of it dissolved. The small crystalline white residue [m. p. 220° (decomp.); 0·25 g., 3%] gave, on recrystallisation from benzene–ethanol, minute prisms of di-*p*-tolyl disulphone, m. p. 222—224° (decomp.). The ethanolic filtrates were diluted with water (2 ml.) and deposited lustrous elongated prisms of *p*-tolyl toluene-*p*-thiolsulphonate, m. p. 77—79° (undepressed on admixture with authentic material) (total yield, including material from the mother-liquors : 2·1 g., 75% calculated on the basis of equation 2). The aqueous filtrate A was acidified (to Congo-red) with concentrated hydrochloric acid, slowly evaporated to small bulk on the steam-bath, heating at 100° being continued for 10 hours; very little thiolsulphonate separated, showing the absence of appreciable quantities of toluene-*p*-sulphinic acid in the original filtrate.

Results obtained under other conditions are briefly recorded below (0·03 mol. of $R·SO_2H$ in all cases):

$R·SO_2Cl$ (mol.).	Initial temp.	$R·SO_2·SR$, yield, %.[a]	$R·SO_2·SO_2·R$, yield, %.	$R·SO_2H$, recovery from A.[b]
0·01	95°	80	0	0
0·01	50	17	0	48
0·02	50	40	3	12
0·03	50	75	3	6
0·045	50	57	8	18
0·06	50	46	20	10
0·03	70	83	4	0

[a] Yields are calc. on the basis of equation (2). [b] Determined by conversion into the thiolsulphonate by prolonged evaporation; yields are calc. according to equation (1).

(*b*) *In the presence of sulphur.* The experiment was carried out as above, but an equivalent quantity of sulphur (0·96 g., 0·3 equiv.) was previously dissolved in the pyridine. Addition of the sulphonyl chloride at 75° caused a rise in temperature to 90°. The crude product (4·2 g.) obtained was twice boiled with ethanol (2 × 20 ml.) and the mixture allowed to cool to room temperature before decantation of the extracts. From the granular residue (1·1 g.) ditoluene-*p*-sulphonyl trisulphide, m. p. 185—186° (0·3 g.), was isolated, the rest being unchanged sulphur. The ethanolic extracts gave, on partial evaporation and filtration with carbon, *p*-tolyl toluene-*p*-thiolsulphonate, m. p. 76—77° [2·2 g., 80% calc. on the basis of equation (2)]. At 40—45°, 50—55°, and 60—65° yields of trisulphide were 3·6, 3·2, and 2·5 g., and of thiolsulphonate 0·2, 0·7, and 1·1 g., respectively.

Attempted Decomposition of Toluene-p-*thiolsulphonic Acid in Pyridine.*—(*a*) A solution of sodium toluene-*p*-thiolsulphonate (4·2 g., 0·02 mol.) in pyridine (40 ml.) was treated with pyridine hydrochloride (7·0 g., 0·06 mol.; or larger excess) and kept at 60° for ½ hour. Pouring the liquid into water gave a clear solution from which no precipitate formed on prolonged storage. The presence of unchanged starting material was shown by heating the partly evaporated acidified solution for several hours: the thiolsulphonate, sulphonyl trisulphide, and traces of sulphonyl sulphide, m. p. 134—135°, being isolated.

(*b*) A solution of toluene-*p*-sulphinic acid (4·7 g., 0·03 mol.) in pyridine (30 ml.) at 70° was treated with sulphur (0·96 g., 0·03 equiv.). The temperature rose spontaneously to 80° and was kept at this point for 15 minutes. The liquid was poured into water (150 ml.); the resulting slightly turbid liquid deposited, in 48 hours, 0·20 g. of sulphur and *p*-tolyl toluene-*p*-thiolsulphonate. The clear filtrate therefrom was made acid (to Congo-red) and slowly evaporated (4 hours) on the steam-bath. The separated oily material, which solidified overnight (dry wt. 4·0 g.) was boiled with two successive portions of ethanol (30 and 10 ml.) and yielded the very sparingly soluble ditoluene-*p*-sulphonyl trisulphide (1·95 g.) and the soluble *p*-tolyl toluene-*p*-thiolsulphonate (1·08 g.). In a control experiment a solution of sulphur (0·96 g.) in pyridine (30 ml.), when poured into water (150 ml.), gave a colloidal system, which deposited the solute almost completely as a granular yellow precipitate after 48 hours.

*Intermediate Formation of Toluene-*p*-thiolsulphonic Acid in the Arylthiourea–Sulphonyl Chloride Reaction.*—A solution of *as*-diphenylthiourea (3·4 g., 0·015 mol.) in pyridine (20 ml.), treated with toluene-*p*-sulphonyl chloride (2·9 g., 0·015 mol.), was heated on the steam-bath for 20 minutes, poured into ice-water (180 ml.), and made just acid (to Congo-red) with concentrated hydrochloric acid. The separated oil solidified immediately and was filtered off after ½ hour's standing at 0° (filtrate : A). The solid (3·1 g.) was boiled with ethanol (12 ml.), and the solution decanted from a trace of undissolved sulphur (0·04 g.). The solvent was removed in a vacuum and the white crystalline residue separated by cold acetone, followed by crystallisation, into unchanged *as*-diphenylthiourea, m. p. 224—226° (0·35 g.), and diphenylcyanamide, m. p. 70—72° (2·1 g.).

The clear filtrate A (250 ml.) was evaporated to small bulk and heated on the steam-bath for 3 hours, The separated oily material solidified on cooling (dry wt. 1·55 g.) and was fractionated as previously described, into ditoluene-*p*-sulphonyl trisulphide, m. p. 184—186° (0·45 g.), and *p*-tolyl toluene-*p*-thiolsulphonate, m. p. 77—78° (0·72 g.) (identities checked by mixed m. p. determinations).

In a control experiment a solution of sodium toluene-*p*-thiolsulphonate (3·15 g., 0·015 mol.) in water (100 ml.) and pyridine (20 ml.), on acidification (to Congo-red) and heating as above deposited an orange oil, which solidified on cooling and was separated into the trisulphide (0·72 g.) and thiolsulphonate (0·80 g.).

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