

111. Urea and Related Compounds. Part II.* The Reaction of Arylureas with Aromatic Sulphinyl and Sulphenyl Chlorides.

By FREDERICK KURZER.

The main products of the interaction of arylureas and aromatic sulphinyl chlorides in pyridine are *N*-aryl-*N'*-arylsulphinyl- and *N*-aryl-*N'*-aryl-sulphenyl-ureas. The latter products are also formed from arylureas and sulphenyl chlorides. The structures of both classes of compounds are established by their oxidative conversion into *N*-aryl-*N'*-arylsulphonylureas. Some properties of sulphinyl- and sulphenyl-ureas, particularly their hydrolysis under various conditions, are described.

THE results obtained in the reactions of aromatic ureas and thioureas with sulphonic and carboxylic acid chlorides suggested that the related reaction between ureas and sulphinyl chlorides might yield either sulphinylcyanamides, $R'SO \cdot NR \cdot CN$, or sulphinylureas (I) (Kurzer, *Chem. Reviews*, 1952, **50**, 1, 13). The synthesis of compounds of this type had apparently not been previously described: the only relevant publication (Geigy, Swiss P. 261,774) refers to a conversion of one sulphinylurea, of undisclosed origin, into another.

Benzene- and toluene-*p*-sulphinyl chlorides (2—2.5 mols.) were found to react with arylureas (1 mol.) in pyridine at moderate temperatures to yield *N*-aryl-*N'*-arylsulphinyl-ureas (25—30%) and *N*-aryl-*N'*-arylsulphenylureas (25—30%) as main products. The appropriate arylsulphonic acid (in amounts approximately equivalent to that of the sulphenylurea), and the aryl arylthiolsulphonate, arising from the excess of the acid halide, were also isolated. The ease, with which disproportionations occur in reactions involving sulphonic acids and their derivatives necessitated very careful control of the experimental conditions in the sulphinyl chloride-urea reaction: the use of slightly higher temperatures, or insufficient amounts of solvent, or the presence of moisture or traces of thionyl chloride caused serious or complete destruction of the reactants. Details concerning this general reaction are summarised in the Table (p. 553).

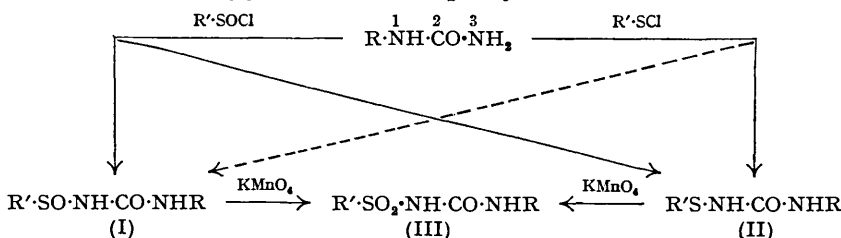
The reaction presents two chief features of interest: first, sulphinyl halides, in their interaction with arylureas, resemble halides of carboxylic acids rather than those of sulphonic acids. Unlike sulphonyl halides, which initially attack at the oxygen atom of the enolic urea configuration, forming unstable intermediate *O*-sulphonylureas, $R \cdot NH \cdot C(:NH) \cdot O \cdot SO_2 R'$, and yielding cyanamides by the immediate elimination of sulphonic acids, $R' \cdot SO_3 H$, sulphinyl halides cause substitution at $N_{(3)}$ directly.

The second point of special interest is the unexpected formation of sulphenyl derivatives. Since the corresponding sulphinylcyanamides would have similar properties, and almost the same ultimate composition (corresponding derivatives differing only by two atoms of hydrogen), the structure of the sulphenylureas (II) was confirmed by their synthesis from the urea and sulphenyl chloride, and by their oxidation to *N*-aryl-*N'*-arylsulphonylureas (see below). The sulphinyl halides, prepared as usual, afforded only sulphinamides with

* The communication, *J.*, 1949, 2292, is regarded as Part I of this series. The present results have been reported in a preliminary summary (*Nature*, 1952, **170**, 167).

amines and were therefore substantially free from sulphenyl chlorides. It is unlikely that the reaction under discussion is preceded by the change of sulphinyl halides into sulphenyl and sulphonyl halides (or their equivalents in pyridine solution), since the latter would convert part of the urea into an *N*-aryl-*N*-arylsulphonylcyanamide (*J.*, 1949, 3029). Finally, sulphinylureas were found to be stable under the prevailing experimental conditions and, once formed, cannot be expected to give rise to sulphenylureas. It is therefore suggested that the simultaneous formation of sulphinyl- and sulphenyl-ureas occurs by a rapid disproportionation, during which a proportion of the sulphinyl residues is converted into equal amounts of sulphenyl and sulphonyl units, a conclusion which is supported by the isolation of an equivalent of sulphonic acid. The precise stage at which the postulated disproportionation occurs cannot be specified, but may well involve arylsulphinyl cations, $R\cdot SO^+$, and their reactivity probably explains the necessity for careful control of the experimental conditions in the urea-sulphinyl chloride reaction. It seems significant that comparable reactions of sulphinyl chlorides with numerous other compounds are not complicated by the parallel production of sulphenyl derivatives (*e.g.*, amines: von Braun and Kaiser, *Ber.*, 1923, 56, 549; Raiford and Hazlet, *J. Amer. Chem. Soc.*, 1935, 57, 2172; esters: Phillips, *J.*, 1925, 127, 2552). Although oxidation-reduction phenomena in syntheses involving arylsulphinic acids are common, the present example appears to be first in which the use of sulphinyl halides introduces sulphenyl radicals into organic structures.

In view of the above results the corresponding reaction involving sulphenyl halides was examined. A sulphenylurea has recently been obtained from 4-nitrobenzenesulphenyl chloride and benzylurea in benzene (Geigy, *loc. cit.*). Under the usual experimental conditions, sulphenyl chlorides and arylureas were found to afford good yields of *N*-aryl-*N'*-arylsulphenylureas (II). Varying quantities of diaryl disulphides, arising from the excess of sulphenyl chlorides employed, appeared as by-products, and small amounts of the corresponding sulphinylureas (I) were also isolated in some experiments. Owing to the absence of the mobile oxygen atom in sulphenyl chlorides, an oxidation-reduction



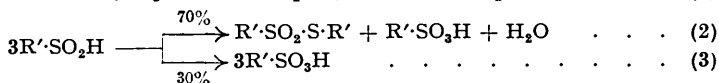
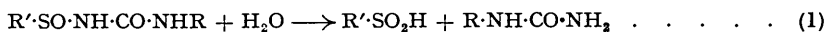
mechanism of the type postulated for the sulphinyl halide reaction cannot account for the formation of sulphinylureas in the present conversion. Since sulphinylureas were never formed in yields exceeding 3%, atmospheric oxidation is probably responsible for their production in these instances. The sulphenyl chloride-urea synthesis proved to be much less sensitive than the corresponding reaction of sulphinyl halides. This observation is explained by the absence of disproportionations in the former case. Various sulphenylureas synthesised by this procedure were identical with samples prepared by the sulphinyl halide method (*cf.* Tables, p. 553).

In contrast to sulphonylureas of analogous structure (*J.*, 1951, 1258), sulphinylureas are generally easily crystallisable, sparingly soluble solids. Owing to the presence of the $-NH\cdot SO-$ grouping, they behave as weak acids and dissolve in alkalis with formation of salts. Aqueous solutions of their sodium or potassium salts are strongly alkaline; the salts are precipitated from their concentrated solutions by addition of an excess of sodium or potassium hydroxide. Fairly consistent results for the molecular weights of sulphinylureas are obtainable by titration with alkali in aqueous acetone, phenolphthalein being used as indicator. Sulphenylureas, on the other hand, are insoluble in alkali hydroxides. This result agrees with the observation that structurally similar sulphenamides display no acid properties: *o*-nitrobenzenesulphenamides, for example, are insoluble in 10% sodium hydroxide solution (Billman and O'Mahony, *J. Amer. Chem. Soc.*, 1939, 61, 2340).

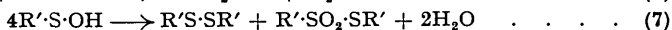
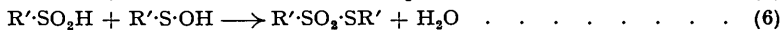
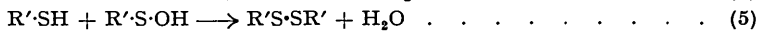
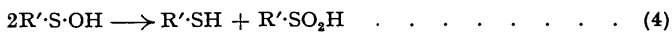
On storage at room temperature, *N*-aryl-*N'*-arylsulphinylureas decomposed slowly

(during 2—8 weeks) into viscous oils, which consisted of arylureas, aryl arylthiolsulphonates, and sulphonic acids. In a dry atmosphere at 0°, however, pure specimens of sulphinyureas remained unchanged indefinitely. The decomposition is probably initiated by slow hydrolysis into arylurea and sulphinic acid (eqn. 1), the latter disproportionating subsequently in the familiar manner (eqn. 2). Since the yields of arylsulphonic acids predominated over those of the aryl arylthiolsulphonates, some direct oxidation of the intermediate sulphinic to sulphonic acids must also occur (eqn. 3) (cf. Experimental section, p. 554). Sulphenylureas, on the other hand, proved to be stable at room temperature. Like the sulphinyl analogues, they decompose at the m. p.

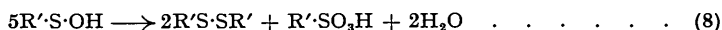
Hydrolysis of sulphinyl- and sulphenyl-ureas under various conditions gave results in agreement with the suggested formulæ. Alkaline hydrolysis of *N*-phenyl-*N'*-toluene-*p*-sulphenylurea gave aniline, ammonia, and toluene-*p*-sulphonic acid, the latter being identified as the benzylthiuronium salt (*J.*, 1952, 3728). Phenylurea was obtained in acid, the sulphinic acid being directly converted into sulphonic acid and thiosulphonate ester (eqn. 2).



Alkaline fission of sulphenylureas (II) gave, in addition to the appropriate urea, an aromatic thiol and a sulphinic acid. With one exception, sulphenic acids are not known in the free state, but rearrange, according to conditions, into a variety of products (Kharasch Potempa, and Wehrmeister, *Chem. Reviews*, 1946, 39, 269). In the presence of alkali, the disproportionation terminates with the formation of the sodium salts of thiols and sulphinic acids. The production of the above compounds thus supports the view that hypothetical sulphenic acids occur as intermediates in this hydrolysis. In the acid fission, the arylsulphenyl residue was isolated as diaryl disulphide and arylthiolsulphonate; these may again be visualised as arising from the primary sulphenic acids (eqns. 4—6), resulting in the overall reaction (7):



With acetic anhydride, containing small quantities of concentrated sulphuric acid, sulphenylureas (II) gave *N*-acetyl-*N'*-arylureas and diaryl disulphides; the formation of the latter from the hypothetical sulphenic acid may again be explained by a disproportionation such as (8). The observed yields of disulphide are in agreement with this view.



The structures of the sulphinyl- (I) and sulphenyl-ureas (II) were confirmed, and the position of the substituents in the molecule demonstrated by oxidation of both series by alkaline potassium permanganate to known *N*-aryl-*N'*-arylsulphonylureas (III). Reaction was rapid at room temperature when the reagent was added to a solution of the sulphinyl-urea in dilute alkali; the alkali-insoluble sulphenylureas were successfully oxidised, though in lower yields, in suspension. Absence of rearrangements under the very mild conditions of the oxidation may reasonably be assumed. Further structural proof, obtained by an unequivocal synthesis of sulphenylureas from sulphenamides, will be detailed later.

The sulphinyl chlorides were prepared by action of a large excess of thionyl chloride on the stable hydrated sodium sulphinates rather than on the free acids. This variation of the standard method (Hilditch and Smiles, *Ber.*, 1908, 41, 4115) avoids the preliminary isolation and troublesome drying of the labile arylsulphonic acids and gives excellent yields of benzene- and toluene-*p*-sulphinyl chlorides. The possible destructive action of the excess of thionyl chloride on the freshly formed sulphinyl chloride (Hilditch, *J.*, 1910, 97, 2579) was not encountered at the lower temperatures used. The present results differ from the report by Knoevenagel and Römer (*Ber.*, 1923, 56, 217) that only benzenesulphonyl chloride and

phenyl benzenethiolsulphonate are formed from sodium benzenesulphinate and thionyl chloride in ether.

EXPERIMENTAL

Analyses are by Drs. Weiler and Strauss, Oxford.

Toluene-p-sulphinyl Chloride.—To thionyl chloride (74.4 g., 0.625 mole), finely powdered sodium toluene-*p*-sulphinyl dihydrate (26.75 g., 0.125 mole) was added in portions during 10 minutes. Reaction occurred with vigorous evolution of hydrogen chloride and sulphur dioxide, but after a slight spontaneous warming on the addition of the first portion of sulphinate the temperature of the reaction mixture fell to 0–5° during the addition of the remainder. The ice-cold mixture was set aside for 1½ hours, during which the suspended white granular material gradually changed into translucent crystals. The excess of thionyl chloride was then distilled off below 45° in a vacuum, and the last traces were removed by twice adding ether (40 ml.; dried over P₂O₅) and repeating the evaporation. The crude toluene-*p*-sulphinyl chloride was readily separated from the suspended sodium chloride by dissolution in ether (80 and 20 ml.) and rapid decantation; removal of the solvent left almost pure sulphinyl chloride as a pale yellow viscous oil (86–92%). Vacuum-distillation gave the product as a deep yellow, mobile oil, b. p. 113–115°/3.5 mm., 99–102°/0.5 mm. (14.4–16.2 g., 66–74%).

Interaction of Phenylurea and Toluene-p-sulphinyl Chloride.—The freshly prepared sulphinyl chloride (not purified by vacuum-distillation, quantities as above) was added, in one portion, at room temperature, to a solution of phenylurea (6.8 g., 0.05 mole) in anhydrous pyridine (80 ml.). The resulting deep orange liquid, the temperature of which rose to 45–48°, was set aside for 4–5 minutes, and was then slowly stirred into a mixture of water (300 ml.), ice (300 g.), and concentrated hydrochloric acid (100 ml.). The separated oil soon solidified and was then filtered off (filtrate B), washed by successive grinding in a mortar with dilute hydrochloric acid and water, and drained (dry weight, 12–15 g.). The material was stirred for half-hour periods with successive portions of sodium hydroxide solution (6% w/v, 80 ml. at 30°; 3% w/v, 60 ml. at 45°; 60 ml. at 65°) (insoluble residue A). The combined filtrates were filtered (charcoal) and gave, on slow acidification with concentrated hydrochloric acid (Congo-red) at 0°, a copious white precipitate (4.5 g., 33%). Two crystallisations, by dissolution in boiling ethanol and dilution with water (30 ml. and 10 ml. respectively, per g.), gave platelets of *N*-phenyl-*N'*-toluene-*p*-sulphinylurea, m. p. 164–167° (decomp.) (2.5 g.) [Found: C, 61.35; H, 5.4; N, 9.9; S, 11.5%; *M* (Rast), 258, 265; *M* (titration in acetone with 0.2*N*-sodium hydroxide; phenolphthalein), 280. C₁₄H₁₄O₂N₂S requires C, 61.3; H, 5.1; N, 10.2; S, 11.7%; *M*, 274]. The mother-liquors gave a second crop of satisfactory purity on rapid evaporation in a vacuum to quarter-bulk at the lowest possible temperature (Total yield: 3.5–4.0 g., 25–30%). The product was soluble in hot acetone, ethanol, and benzene, and in dilute alkalis with formation of salts, and was unchanged by pyridine during 15 minutes at 60°.

The alkali-insoluble residue A (4.5–5.0 g.) was twice heated with water (70 ml.) to 100° to remove any sulphinylurea and traces of unchanged phenylurea. Crystallisation once from aqueous ethanol [ethanol (10 ml.), water (4 ml.) per g.] and twice from ethanol (25 ml. per g.) gave *N*-phenyl-*N'*-toluene-*p*-sulphenylurea, needles, m. p. 171–173° (decomp.) (yield, including material from mother-liquors, 3.2 g., 25%) [Found: C, 65.2; H, 5.8; N, 10.8; S, 12.2%; *M* (Rast), 244, 258. C₁₄H₁₄ON₂S requires C, 65.1; H, 5.4; N, 10.85; S, 12.4%; *M*, 258]. The final mother-liquors contained *p*-tolyl toluene-*p*-thiolsulphonate (0.5–1.1 g.; m. p. 77°).

The aqueous filtrate B was evaporated slowly on the steam-bath to small volume (120 ml.) during 6–8 hours. The small oily deposit (0.2–0.5 g., obtained in some experiments only) was *p*-tolyl toluene-*p*-thiolsulphonate (m. p. 76–77°; from ethanol). The pale yellow syrup was adjusted to pH 8 with alkali, diluted with water (to 250 ml.), and treated with a saturated aqueous solution (60°) of *S*-benzylisothioureia hydrochloride (8 g.). Platelets of benzylthiuronium toluene-*p*-sulphonate (3.6 g., 86% calc. on the amount of sulphenylurea formed), m. p. 182–183° (from aqueous ethanol), were obtained on storage at 0°.

The Table summarises the use of this general method for the preparation of analogous compounds.

Spontaneous Decomposition of N-Aryl-N'-arylsulphinylureas.—Pure *N*-phenyl-*N'*-toluene-*p*-sulphinylurea (1.37 g., 0.005 mole) retained its crystalline form for 4–8 weeks at room temperature in closed vessels, but then had m. p. 100–120° and had become highly soluble in ethanol; on further short storage, conversion into an orange highly viscous oil occurred. Extraction with boiling water (2 × 10 ml.) (extracts A) and crystallisation of the residue from ethanol (8 ml.) (carbon) gave *p*-tolyl toluene-*p*-thiolsulphonate, prisms (0.31 g., 68%), m. p. 77–78° (Found:

N-Aryl-*N'*-arylsulphinylureas, R·SO·NH·CO·NHAr.^a

No.	R	Ar	Temp. of prep. ^b	Yield, % ^c	M. p. (decomp.) ^d	Cryst. solvent
1	Ph	Ph	18—45°	35	162—164°	EtOH
2	Ph	<i>p</i> -C ₆ H ₄ Me	18—45	24	190—191	Aq. EtOH
3	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -C ₆ H ₄ Me	18—42	42	161—163	"
4	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -C ₆ H ₄ Ph	18—50	12	206—207	EtOH
5	<i>p</i> -C ₆ H ₄ Me	<i>a</i> -C ₁₀ H ₇	18—35	36	190—192	COMe ₂ -EtOH
6	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -EtO·C ₆ H ₄	18—50	30	189—191	Aq. EtOH
			5—44	2	191—192	EtOH
7	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -C ₆ H ₄ Cl	18—40	36	166—168	Aq. EtOH

N-Aryl-*N'*-arylsulphenylureas, RS·NH·CO·NHAr.^a

8	Ph	Ph	18—45°	32	180—182°	EtOH
9	Ph	<i>p</i> -C ₆ H ₄ Me	18—45	36	196—197	"
10	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -C ₆ H ₄ Me	18—42	30	192—193	"
11	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -C ₆ H ₄ Ph	20—40	20	204—205	Aq. EtOH
12	<i>p</i> -C ₆ H ₄ Me	<i>a</i> -C ₁₀ H ₇	18—35	34	214—215	EtOH or COMe ₂ -EtOH
13	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -MeO·C ₆ H ₄	12—40	33	201—202	EtOH
14	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -EtO·C ₆ H ₄	5—40	42	202—204	"
			5—44	68	202—203	"
15	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -C ₆ H ₄ Cl	5—35	40	177—178	COMe ₂ -EtOH
16	<i>p</i> -C ₆ H ₄ Me	<i>p</i> -C ₆ H ₄ Br	18—45	42	199—200	EtOH

N-Aryl-*N'*-arylsulphinylureas, R·SO·NH·CO·NHAr.^a

No.	Formula	Found, %				Required, %			
		C	H	N	S	C	H	N	S
1	C ₁₃ H ₁₅ O ₂ N ₂ S	60.0	4.6	10.5	11.95	60.0	4.6	10.8	12.3
2	C ₁₄ H ₁₄ O ₂ N ₂ S	61.0	5.3	9.95	11.8	61.3	5.1	10.2	11.7
3	C ₁₅ H ₁₆ O ₂ N ₂ S ^f	62.4	5.2	9.7	11.1	62.5	5.6	9.7	11.1
4	C ₂₀ H ₁₆ O ₂ N ₂ S	69.1	5.4	8.5	8.8	68.6	5.1	8.0	9.1
5	C ₁₈ H ₁₆ O ₂ N ₂ S	67.0	4.9	—	—	66.7	4.9	—	—
6	C ₁₆ H ₁₈ O ₃ N ₂ S ^g	60.35	5.8	—	—	60.4	5.7	—	—
		60.2	5.6	—	—	—	—	—	—
7	C ₁₄ H ₁₃ O ₂ N ₂ SCI	54.7	4.1	8.7	10.3	54.5	4.2	9.0	10.4

N-Aryl-*N'*-arylsulphenylureas, R·S·NH·CO·NHAr.^a

8	C ₁₃ H ₁₅ ON ₂ S	63.6	5.0	11.1	12.7	63.9	4.9	11.5	13.1
9	C ₁₄ H ₁₄ ON ₂ S	65.0	5.3	—	—	65.1	5.4	—	—
10	C ₁₅ H ₁₆ ON ₂ S ^h	65.7	5.6	10.3	11.9	66.2	5.9	10.3	11.8
11	C ₂₀ H ₁₆ ON ₂ S	71.8	5.4	9.0	9.7	71.8	5.4	8.4	9.6
12	C ₁₈ H ₁₆ ON ₂ S	69.7	5.3	—	—	70.1	5.2	—	—
13	C ₁₅ H ₁₆ O ₂ N ₂ S	62.8	5.4	—	—	62.5	5.55	—	—
14	C ₁₆ H ₁₈ O ₂ N ₂ S ⁱ	63.3	6.05	9.8	10.9	63.6	6.0	9.3	10.6
		63.7	6.2	—	—	—	—	—	—
15	C ₁₄ H ₁₃ ON ₂ SCI ^j	57.5	4.4	9.3	—	57.4	4.4	9.6	—
16	C ₁₄ H ₁₃ ON ₂ SBr ^k	50.0	3.8	—	—	49.9	3.9	—	—

^a Obtained from arylureas and sulphinyl chlorides, except for nos. 13 and 16 which were prepared by means of the sulphenyl chlorides. Nos. 6 and 14 were obtained by both methods. ^b *Sulphinyl chlorides*. When the stated reaction time and temperature were exceeded (e.g., 20 min.; 56—60°), the addition of the resulting deep orange liquid to ice-water gave orange oils which failed to solidify on prolonged storage at 0°. The expected products were still obtained but in low yield, with a greater proportion of *p*-tolyl toluene-*p*-thiolsulphonate, by dissolving the oil in benzene, extracting the sulphinylurea with alkali, and isolating the sulphenylurea from the washed neutral benzene layer. Temperatures of 60—80° (owing to incomplete removal of thionyl chloride, use of an insufficient volume of solvent, or too high an initial temperature) gave intractable oils of pungent odour. *Sulphenyl chloride*. The spontaneous temperature rise was less pronounced, and failure of experiments due to this cause was not observed. In some instances, the reaction mixture had to be warmed to the required temperature. ^c Average of 2—3 expts. ^d Variable, depending on the rate of heating, width of m. p. tube, etc. Therefore the specimen was inserted into the apparatus about 30—40° below the approx. m. p., and the temp. raised at approx. 20°/min. M. p.s of sulphenylureas were reproduced without difficulty. On fusion, sulphinylureas generally gave a deep violet to black mass, while sulphenylureas decomposed to a deep orange-red melt. ^e Sulphinylureas, platelets; sulphenylureas, generally needles. Both series were, as a rule, first crystallised by diluting their boiling saturated ethanolic solution with 0.25—0.33 vol. of water, which resulted in a satisfactory recovery of nearly pure products. All the compounds were fairly sparingly soluble, requiring generally 60—100 ml. (but some members up to 200 ml.) of boiling ethanol per g. The substances were finally purified from the solvents stated. ^f Found: *M* (titration), 294. Required: 288. ^g Found: *M* (titration), 310. Required: 318. ^h Found: *M* (Rast), 245. Required: 272. ⁱ Found: *M* (Rast), 280. Required: 302. ^j Found: Cl, 12.35. Required: 12.1%. ^k Found: Br, 23.5. Required: 23.7%.

C, 60.4; H, 4.9. Calc. for $C_{14}H_{14}O_2S_2$: C, 60.4; H, 5.0%). The extracts A, on cooling and partial spontaneous evaporation, deposited phenylurea (0.49 g., 72%), m. p. and mixed m. p. 148° (from aqueous ethanol). The aqueous filtrates, treated with hot saturated aqueous *S*-benzylisothioureahydrochloride (2.0 g.) and cooled to 0°, deposited benzylthiuronium toluene-*p*-sulphonate, m. p. 182—183° (from aqueous ethanol) (0.90 g.; 0.40 g. thereof corresponds to the 68% yield of *p*-tolyl toluene-*p*-thiolsulphonate, formed according to eqn. 2; the rest is formed by direct oxidation of the primarily produced sulphinic to sulphonic acid, to the extent of 29%).

When stored in open vessels, sulphinylureas decomposed more rapidly (1—2 weeks), as did specimens that had only been purified by reprecipitation from alkaline solution. In a dry atmosphere at 0°, crystalline sulphinylureas remained unchanged for at least 12—18 months, though their m. p.s had sometimes dropped by several degrees.

Alkaline Hydrolysis of N-Phenyl-N'-toluene-p-sulphinylurea.—The sulphinylurea (1.65 g., 0.006 mole) in aqueous sodium hydroxide (6% w/w; 60 ml.) was boiled under reflux for 2 hours. Ammonia was evolved and drops of oil appeared. The solution was then subjected to slow downward distillation, the volume of the residual liquid being kept constant by the simultaneous dropwise addition of water (residual liquid A). The distillate, the first few ml. of which contained oil, was made strongly alkaline and exhaustively extracted with ether, and the isolated aniline collected as the acetyl derivative (m. p. 113—114°; 0.72 g., 89%).

The residual liquid (A) contained toluene-*p*-sulphonic acid (iron and copper salt tests). It was strongly acidified with concentrated hydrochloric acid (15 ml.) and slowly evaporated twice on the steam-bath nearly to dryness during 4 hours, and the residue was stirred with water (30 ml.). The separated oil solidified and, crystallised from aqueous ethanol, gave *p*-tolyl toluene-*p*-thiolsulphonate, m. p. and mixed m. p. 76° (0.48 g., 86%). The aqueous filtrate from the solidified oil gave benzylthiuronium toluene-*p*-sulphonate, m. p. 181—182° (0.59 g., 88%). Alternatively, toluene-*p*-sulphonic acid was directly obtained as the benzylthiuronium salt, m. p. and mixed m. p. 167—168°, in 82% yield (Kurzer and Powell, *J.*, 1952, 3728). A control experiment showed that sodium toluene-*p*-sulphinat is not decomposed during 2 hours' boiling with 6% aqueous sodium hydroxide.

Acid Hydrolysis of N-Phenyl-N'-toluene-p-sulphinylurea.—The sulphinylurea (1.37 g., 0.005 mole) in absolute ethanol (50 ml.)—hydrochloric acid (12 ml.) was refluxed for 2 hours, most of the solvent removed in a vacuum, and the residual liquid diluted with water (20 ml.). The solidified oil was filtered off (filtrate A) and extracted with boiling water (10 ml.) (extracts B). The residue was crystallised from ethanol, giving *p*-tolyl toluene-*p*-thiolsulphonate, m. p. 76—77° (0.29 g., 62%). On cooling and partial evaporation, the extracts B deposited phenylurea, m. p. 147° (0.20 g., 30%). The filtrate A contained aniline hydrochloride, which was isolated by partial evaporation and identified as acetanilide (0.39 g., 58%; *i.e.*, total recovery of the *N*-aryl part of the molecule, 88%).

Interaction of Phenylurea and Toluene-p-sulphenyl Chloride.—Phenylurea (6.8 g., 0.05 mole) in pyridine (100 ml.) at 10° was rapidly treated with toluene-*p*-sulphenyl chloride (15.85 g., 0.1 mole) (Lecher *et al.*, *Ber.*, 1924, 57, 755; 1925, 58, 409). The red colour of the chloride was momentarily discharged but reappeared as the temperature of the liquid rose to 40—45°. After 5 minutes, the solution was slowly stirred into water (250 ml.)—ice (250 g.)—concentrated hydrochloric acid (100 ml.), and after several hours the aqueous phase was decanted from the coagulated orange viscous resin-like material. The latter was vigorously stirred with aqueous sodium hydroxide (100 ml., 5% w/v) for 15 minutes. The soft resin changed into friable pale-yellow fragments which were filtered off (alkaline extracts A) and several crystallisations from ethanol gave *N*-phenyl-*N'*-toluene-*p*-sulphenylurea (6.45—7.1 g.; 50—55%), m. p. and mixed m. p. 171—173° (decomp.) (Found: C, 64.8; H, 5.0. Calc. for $C_{14}H_{14}ON_2S$: C, 65.1; H, 5.4%). The final mother-liquors deposited, on slow evaporation, varying quantities (2—3 g.) of di-*p*-tolyl disulphide, m. p. 46—47° (from ethanol).

The extracts A gave a white solid [m. p. 180° (decomp.); 0.42 g.] on acidification; crystallisation from ethanol yielded *N*-phenyl-*N'*-toluene-*p*-sulphinylurea, m. p. 165—166° (decomp.) (Found: C, 61.7; H, 5.3. Calc. for $C_{14}H_{14}O_2N_2S$: C, 61.3; H, 5.1%).

The Table records the similar preparation of four analogues.

Alkaline Hydrolysis of N-p-Ethoxyphenyl-N'-toluene-p-sulphenylurea.—To a solution of the sulphenylurea (3.02 g., 0.01 mole) in ethanol (75 ml.), potassium hydroxide (4.5 g.) in water (6 ml.) was added. The clear liquid obtained after 20 minutes' refluxing was partially neutralised by concentrated hydrochloric acid (5 ml.), most of the ethanol removed in a vacuum, and the residue treated with water (50 ml.). The resulting suspension was cooled to 0° and the separated

p-ethoxyphenylurea (1.55 g., 86%; m. p. 174—175° from ethanol) filtered off. The filtrate was made strongly acid and steam-distilled. The oil which separated from the distillate (100 ml.) and solidified consisted of thio-*p*-cresol (0.29 g., 47%; m. p. 43—44°; benzoyl derivative, m. p. 75—76°). The acid residual liquid from the thio-*p*-cresol on slow evaporation gave *p*-tolyl toluene-*p*-thiolsulphonate (0.32 g., 70%), m. p. 77° (from ethanol).

Acid Hydrolysis of N-Toluene-p-sulphenyl-N'-p-tolylurea.—The sulphenylurea (2.72 g., 0.01 mole), suspended in absolute ethanol (60 ml.), dissolved instantly on addition of hydrochloric acid (15 ml.). The clear liquid was refluxed for 2 hours, the solvent removed nearly completely in a vacuum, and the residue stirred with cold water (30 ml.). The separated solidified oil (2.8 g.) was filtered off (filtrate A), and extracted with boiling water (3 × 15 ml.) (aqueous extracts B). The water-insoluble residual dark oil was dissolved in ethanol (20 ml.), and the solution filtered (charcoal), and allowed to evaporate spontaneously; white feathery crystals and massive prisms separated. Mechanical separation and recrystallisation gave di-*p*-tolyl disulphide, m. p. 45—46° (0.42 g., 68%), and *p*-tolyl toluene-*p*-thiolsulphonate, m. p. 76° (0.35 g., 50%) (both yields calc. according to eqn. 7). The extracts B gave, on partial evaporation *in vacuo* and recrystallisation from boiling water, *p*-tolylurea, m. p. 180—181° (0.80 g., 53%) (Found: N, 18.7. Calc. for C₈H₁₀ON₂: N, 18.7%). The filtrate A contained the hydrochloride of *p*-toluidine, which was isolated from the basified solution with ether and identified as the acetyl derivative, m. p. 148° (0.12 g.).

Hydrolysis of Sulphenylureas by Acetic Anhydride-Sulphuric Acid.—(a) *N-p*-Chlorophenyl-*N'*-toluene-*p*-sulphenylurea (0.87 g., 0.003 mole) was added to acetic anhydride (8 ml.) and concentrated sulphuric acid (1 drop), and the resulting solution boiled for 3 minutes. Its initial deep violet colour faded rapidly; the orange-red liquid obtained was kept at 100° for another 4 minutes and then cooled to room temperature. The white needles which separated were filtered off (filtrate A), washed with a little acetic acid (yield, 0.38 g., 60%; m. p. 228—232°), and crystallised from ethanol (20 ml.), giving *N*-acetyl-*N'*-*p*-chlorophenylurea, needles, m. p. 231—232° (undepressed in admixture with material prepared as detailed below) (Found: C, 50.45; H, 4.4; N, 13.3. C₉H₉O₂N₂Cl requires C, 50.8; H, 4.2; N, 13.2%). Filtrate A was poured into water (100 ml.), and the separated solid (0.40 g.) was fractionated, by means of ethanol, into the above acetylurea (0.13 g., hence total yield 80%), and the very soluble di-*p*-tolyl disulphide (0.21 g., 71% calc. according to eqn. 8), m. p. and mixed m. p. 46—47° (Found: C, 67.9; H, 5.5. Calc. for C₁₄H₁₄S₂: C, 68.3; H, 5.7%). The sulphenylurea was almost completely recovered after 5 minutes' treatment with the above reagent at 50°; more prolonged refluxing (20 minutes) caused complete decomposition.

(b) Analogous treatment of *N*-phenyl-*N'*-toluene-*p*-sulphenylurea (but pouring the entire reaction mixture into water, since direct crystallisation from acetic anhydride did not occur) gave *N*-acetyl-*N'*-phenylurea, m. p. 182—183°, and di-*p*-tolyl disulphide, in similar yields. N.B. Because of the closeness of the m. p.s of *N*-acetyl-*N'*-*p*-chlorophenylurea and *p*-chlorophenylacetylurea (m. p. 228—230°; Spielmann, Geisler, and Close, *J. Amer. Chem. Soc.*, 1948, **70**, 4189) this additional hydrolysis was performed. The formation of the acetylated urea of known formula under identical conditions confirms the structure of *N*-acetyl-*N'*-*p*-chlorophenylurea.

N-Acetyl-*N'*-*p*-chlorophenylurea.—(a) A solution of *p*-chlorophenylurea (1.7 g., 0.01 mole) in acetic anhydride (18 ml.), treated with concentrated sulphuric acid (4 drops), was kept at 100° for 20 minutes, boiled briefly, kept at 100° for a further 20 minutes, and slowly added to water (120 ml.). The separated solid (m. p. 220—224°; 1.35 g., 64%) gave, after two crystallisations from boiling ethanol (60 ml.), *N*-acetyl-*N'*-*p*-chlorophenylurea, m. p. 231—232° (Found: N, 13.4%).

Heating *p*-chlorophenylurea (0.01 mole) with acetic anhydride (8 ml.) in pyridine (15 ml.) at 100° for $\frac{1}{2}$ —1 hour gave 3—5% of the acetyl derivative, most of the starting material being recovered, while longer treatment (4 hr.) resulted mainly in *p*-chloroacetanilide, m. p. 178—179°.

(b) *p*-Chlorophenylcyanamide (1.53 g., 0.01 mole) was added to acetic anhydride (15 ml.) and concentrated sulphuric acid (4 drops) at room temperature. The resulting hot solution deposited white needles of the product immediately. After 3 minutes' boiling, the liquid was poured into water (120 ml.) and the separated white solid (0.95 g., 45%) (filtrate A) crystallised from ethanol, yielding *N*-acetyl-*N'*-*p*-chlorophenylurea, m. p. 231—232°. The aqueous filtrates A were made alkaline with sodium hydroxide; the precipitate (0.45 g., 27%) was *p*-chloroacetanilide, m. p. 178—179° (from ethanol).

p-Tolylcyanamide gave 21% of *N*-acetyl-*N'*-*p*-tolylurea and 60% of *N*-acetyl-*p*-toluidine.

N-Phenyl-*N'*-toluene-*p*-sulphonylurea.—(a) To a solution of *N*-phenyl-*N'*-toluene-*p*-sulphonylurea (1.37 g., 0.005 mole) in 1.5% (w/v) aqueous sodium hydroxide (27 ml., 0.01 mole),

aqueous potassium permanganate (20 ml., 5% w/v) was rapidly added at room temperature. The excess of the oxidising agent was consumed with sodium sulphite, and the manganese dioxide filtered off. Acidification at 0° (microcrystalline precipitate, m. p. 164—170°; 1.35 g., *i.e.* 93%), and two recrystallisations from acetone–benzene–light petroleum (4 ml. each) gave *N*-phenyl-*N'*-toluene-*p*-sulphonylurea, m. p. 171—173° (undepressed by authentic material; *J.*, 1951, 1258) (Found: C, 58.3; H, 4.65. Calc. for C₁₄H₁₄O₃N₂S: C, 57.9; H, 4.8%).

(b) To a suspension of finely divided *N*-phenyl-*N'*-toluene-*p*-sulphenylurea (2.60 g., 0.01 mole) in aqueous sodium hydroxide (3% w/v; 40 ml.), potassium permanganate solution (5% w/v; 125 ml., 0.02 g.-atom of O) was added with shaking during 10 minutes, in 10 portions, at room temperature. The dark green liquid was set aside for 10 minutes, then treated with excess of sodium sulphite, and the precipitated manganese dioxide removed by filtration. Acidification of the filtrate gave a white flocculent solid (1.8 g., 62%). In order to oxidize any small quantity of sulphonylurea, this was redissolved in alkali and re-oxidized (15 ml.; 5% w/v). The product, isolated as before and crystallised from benzene, was *N*-phenyl-*N'*-toluene-*p*-sulphonylurea, m. p. and mixed m. p. 170—171° (Found: C, 58.2; H, 4.95%). Use of a large excess of oxidising agent causes oxidation of the sulphonylurea.

The author gratefully acknowledges a grant from the Research Fund of the Chemical Society.

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE,
(UNIVERSITY OF LONDON), W.C.1.

[Received, September 1st, 1952.]
