Synthesis and Reaction of α-Chlorostyryl Isocyanates[1]

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The reaction of arylacetonitriles, bearing at least two methyl groups on the 2 and 6 position of the benzene ring, *p*-nitrophenylacetonitrile, and α-chlorophenylacetonitrile with phosgene in the presence of hydrogen chloride was investigated. α-Chlorostyryl isocyanates thus obtained were isolated as urea derivatives in 5–48% yield. The pyrolysis and hydrolysis reaction of the ureas were also studied. On heating α-chloro-2,3,5,6-tetramethylstyryl isocyanate (**2a**) and α-chloro-2,3,4,5,6-pentamethylstyryl isocyanate (**2c**) with hydrogen chloride in acetonitrile at 100–105°, the demethylation reaction occurred to yield 3-chloro-5,6,8-trimethylisocarbostyril and 3-chloro-5,6,7,8-tetramethylisocarbostyril in 70 and 68% yield, respectively. In the reaction of α-chloro-*p*-nitrostyryl isocyanate (**2e**) with acetonitrile in the presence of hydrogen chloride at 55–60°, 6-chloro-2-(*p*-nitrobenzyl)-4(3*H*)-pyrimidone was formed in 22% yield.

In a preceding paper,[2] we reported the facile one-step synthesis of 1,3-dichloroisoquinoline derivatives by reacting arylacetonitriles with phosgene in the presence of hydrogen chloride and also clarified the formation of α-chlorostyryl isocyanate as an intermediate.

α,β-Unsaturated isocyanates have been synthesized by several methods; the Curtius rearrangement of acrylic acid azides,[3] reaction of ketimine with phosgene,[4] dehydrochlorination of polychloroalkyl isocyanates,[5] and elimination of ethanol from *N*-ethoxycarbonyl ketimines.[6] However, they are elaborative and require many steps.

In view of the proposed mechanism for isoquinoline formation,[2] it is speculated that some nitriles may react with phosgene in the presence of hydrogen chloride to give α,β-unsaturated isocyanates exclusively.

This paper deals with the reaction of phosgene with duryl-, isoduryl-, pentamethylphenyl-, and mesitylacetonitrile, which seem to be unable to yield isoquinolines, and then *p*-nitrophenylacetonitrile and α-chlorophenylacetonitrile, which are reluctant to cyclize owing to the presence of the electron-attracting group.[2] The reactions of isocyanates prepared with hydrogen chloride in acetonitrile are also discussed.

Results and Discussion

Synthesis of Isocyanates.—In a sealed glass tube, arylacetonitriles **1a–f** were allowed to react with phosgene in the presence of hydrogen chloride at 105–125° for 6 days. Isocyanates were obtained as isomeric mixtures of cis and trans. Nmr spectra of **2a**, **2c**, **2d**, and **2e** showed two olefinic proton signals (Table I), but assignments of these peaks to the cis and trans isomers were not made.

Isolation of pure isocyanates from reaction mixtures was difficult, because large amounts of unreacted nitriles were present. Thus, all the isocyanates were converted to phenylurea derivatives **3a–f** by reacting with aniline; the isolation yields as ureas were 5–48% (Scheme I).

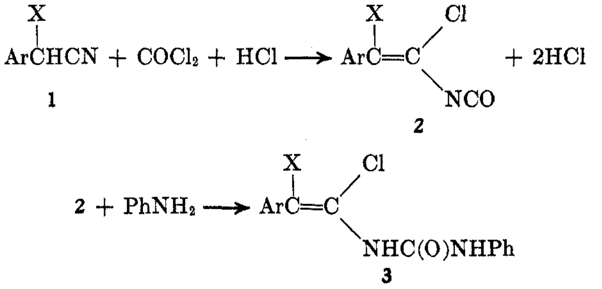
TABLE I

OLEFINIC PROTON SIGNALS OF ISOCYANATES

Compd[a]	Solvent	Chemical shift, τ (area ratio)
2a	CCl_4	3.76, 3.91 (4.7:1)
2c	$CDCl_3$	3.68, 3.84 (3.6:1)
2d	CCl_4	3.82, 3.96 (4.4:1)
2e	$CDCl_3$	3.54, 3.82 (1.1:1)

[a] The mixture of isocyanate and the starting nitrile was examined.

SCHEME I



a, Ar = duryl; X = H
b, Ar = isoduryl; X = H
c, Ar = pentamethylphenyl; X = H
d, Ar = mesityl; X = H
e, Ar = *p*-nitrophenyl; X = H
f, Ar = phenyl; X = Cl

The structure of **3** was determined on the basis of ir spectra and elemental analysis. The results are summarized in Table II.

Raw products of **3a–e** are very unstable and decompose gradually into the nitriles **1**, phenyl isocyanate, and hydrogen chloride at room temperature. After purification, **3a–c** were stable at room temperature, and no change in ir absorption bands was observed. **3d** and **3e**, however, were unstable even after purification. All of the ureas decomposed at their melting points even after purification.

The pyrolysis of **3a**, **3d** and **3e** at 80° for 15 min in acetonitrile indeed gave the nitrile **1**, phenyl isocyanate, and hydrogen chloride (Scheme II). Phenyl isocyanate was isolated as *sym*-diphenylurea in 73, 82, and 66% yield, respectively.

Thermal dissociation of symmetrically disubstituted ureas in aniline, alcohol, and fatty acid has been reported to form amines and isocyanates,[7] which further

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[1] (a) The reaction of nitriles with phosgene series, part VI. (b) Part V: S. Yanagida, M. Yokoe, M. Ohoka, and S. Komori, *Bull. Chem. Soc. Jap.*, **44**, 2182 (1971).

[2] S. Yanagida, M. Ohoka, and S. Komori, *J. Org. Chem.*, **34**, 4127 (1969).

[3] P. A. S. Smith, *Org. React.*, **3**, 337 (1946).

[4] L. I. Samaraj, O. W. Wischnewskij, and G. I. Derkatsch, *Angew. Chem.*, **80**, 620 (1968).

[5] K. H. Koenig and H. Pommer, *Chem. Abstr.*, **59**, 454 (1963).

[6] J. Hoch, *C. R. Acad. Sci.*, **201**, 773 (1935); *Chem. Abstr.*, **30**, 1362 (1936).

[7] (a) T. L. Davis and K. C. Blanchard, *J. Amer. Chem. Soc.*, **45**, 1816 (1923); (b) T. Hoshino, T. Mukaiyama, and H. Hoshino, *ibid.*, **74**, 3094 (1952); (c) T. Hoshino, T. Mukaiyama, and H. Hoshino, *Bull. Chem. Soc. Jap.*, **25**, 392 (1952); (d) T. Mukaiyama, *ibid.*, **28**, 253 (1955); (e) T. Mukaiyama and Y. Fujita, *ibid.*, **29**, 54 (1956).

TABLE II

SYNTHESIS OF α-CHLOROSTYRYL ISOCYANATES AND ISOLATION AS UREA DERIVATIVES

Urea	Amounts of reactants, mmol Nitrile	$COCl_2$	HCl	Aniline	Yield,[a] %	Mp,[b] °C	$\nu_{C=O}$ (Nujol), cm^{-1}	Found, % (calcd, %)
3a[c]	15	94	20	13	48	139	1647	C, 69.65 (69.40) H, 6.08 (6.44) N, 8.66 (8.52)
3b[d]	7.5	45	8	4	36	124–125.5	1643	C, 69.72 (69.40) H, 6.24 (6.44) N, 8.68 (8.52)
3c[e]	7.5	44	8	5	48	134–136	1642	C, 69.79 (70.06) H, 6.66 (6.76) N, 7.85 (8.17)
3d	15	92	19	9	33	101.5[g]	1645	Cl, 11.2[h] (11.26)
3e	15	154	0[f]	9	43	106–108[g]	1645	Cl, 11.5[h] (11.16)
3f[c]	10	88	8	3	5	182–185	1647	C, 58.78 (58.65) H, 4.12 (3.94) N, 9.24 (9.12)

[a] Based on the nitrile used. [b] All of the ureas decomposed at their melting points. [c] Recrystallized from THF–CH_3CN (3:1, v/v). [d] Recrystallized from THF–CH_3CN (1:4, v/v). [e] Recrystallized from THF–CH_3CN (1:1, v/v). [f] MeOH (1 ml) was added to evolve HCl. [g] Melting point of raw product. [h] Raw product was analyzed.

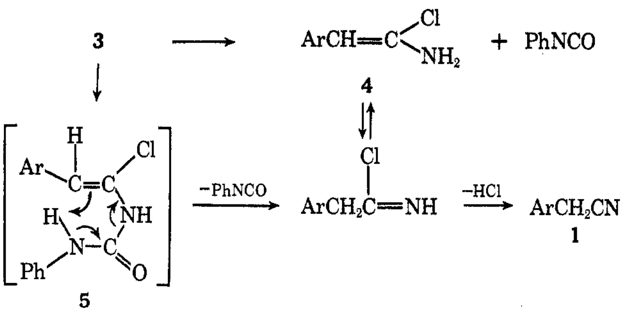
TABLE III

PREPARATION OF ACYLUREAS BY HYDROLYSIS OF **3**

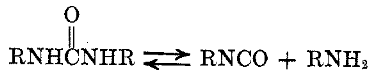
Acylurea	Yield, %	Mp, °C	$\nu_{C=O}$ (KBr), cm^{-1}	Nmr[a] (methylene proton), τ	Found, % (calcd, %)
6a[b]	87	228–230	1715	6.13	C, 73.41 (73.52) H, 7.17 (7.14) N, 9.05 (9.03)
6b[b]	91	196–201	1716[d]	6.19	C, 73.78 (73.52) H, 7.13 (7.14) N, 9.14 (9.03)
6c[b]	94	216–218	1719[d]	6.15	C, 73.73 (74.04) H, 7.39 (7.46) N, 8.88 (8.64)
6d[b]	73	193–196	1715	6.24	C, 72.84 (72.95) H, 6.59 (6.80) N, 9.37 (9.45)
6e[c]	78	219.5–223[e]	1710	6.08	C, 60.14 (60.20) H, 4.11 (4.38) N, 13.97 (14.04)
6f[b]	82	205–211	1702		C, 62.47 (62.40) H, 4.39 (4.54) N, 9.77 (9.70)

[a] DMSO-d_6 was used as solvent. [b] Recrystallized from CH_3CN. [c] Recrystallized from DMSO–CH_3CN (6:1, v/v). [d] Nujol. [e] Mp 235°: S. Basterfield and M. E. Greig, *Can. J. Res.*, **8**, 450 (1933); *Chem. Abstr.*, **27**, 4223 (1933).

SCHEME II



react with the solvents used to give ureas, urethanes, and N-substituted carboxamides, respectively. Based



$$RNH\overset{O}{\overset{\|}{C}}NHR \rightleftharpoons RNCO + RNH_2$$

on this fact, the pyrolysis of **3** is possible to proceed *via* α-chloroenamine **4**. An alternative mechanism including cyclic intermediate **5** is also possible. The cyclic intermediate similar to **5**, for example, has been reported in the pyrolysis of ethyl vinyl ether to ethylene and acetaldehyde.[8]

3a–f were also identified by hydrolyzing them to acylureas **6a–f** in dimethyl sulfoxide at room temperature (Table III).

$$3 \xrightarrow{H_2O\text{–}DMSO} Ar\overset{X}{\overset{|}{C}}H\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}NHPh$$

6

Reaction of Isocyanates.—In this investigation the pyrimidone **7** (R = R′ = Ar), expected to form in view of the previous work,[2,9] was not isolated. We have found that *N*-(α-chlorobenzylidene)carbamoyl chloride (**8**) reacts with alkyl cyanide in the presence of hydro-

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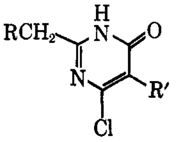
[8] A. T. Blades and G. W. Murphy, *J. Amer. Chem. Soc.*, **74**, 1039 (1952).

[9] (a) S. Yanagida, M. Ohoka, M. Okahara, and S. Komori, *Tetrahedron Lett.*, 2351 (1968); (b) S. Yanagida, M. Ohoka, M. Okahara, and S. Komori, *J. Org. Chem.*, **34**, 2972 (1969).

gen chloride to give the pyrimidone **9** and the pyrimidine **10**.[1b]



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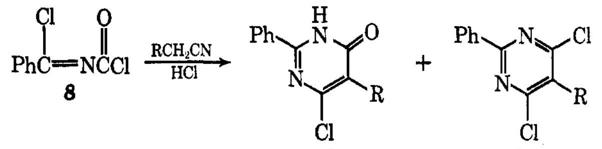
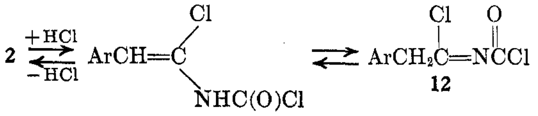


8 **9** **10**

In the presence of hydrogen chloride, the isocyanate **2** is considered to be in equilibrium with **11** and **12**. The structure of **12** is analogous to that of **8**. Thus

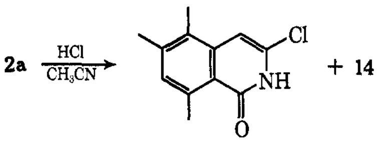


$$2 \underset{-HCl}{\overset{+HCl}{\rightleftarrows}} ArCH{=}C(Cl)NHC(O)Cl \rightleftarrows ArCH_2CCl{=}NC(O)Cl$$

11 **12**

expecting the formation of the pyrimidone **7** (R = Ar; R′ = H), the reaction of **2** with acetonitrile in the presence of hydrogen chloride was attempted. In this investigation, the isocyanates **2** containing the starting nitriles were allowed to react with acetonitrile and hydrogen chloride.

On heating **2a** with acetonitrile and hydrogen chloride in a sealed glass tube at 100–105° for 110 hr, the expected pyrimidone **7** (R = duryl; R′ = H) was not obtained, but unexpectedly the demethylation reaction occurred to give 70% yield of 3-chloro-5,6,8-trimethylisocarbostyril (**13**) and a small amount of 1,3-dichloro-5,6,8-trimethylisoquinoline (**14**) (7%). The structure of **13** was confirmed on the basis of microanalysis and spectral properties, and moreover by converting it to **14**. The reaction at 55–60° for 93 hr gave a 9% yield of **13** and 26% of unreacted **2a** was recovered.



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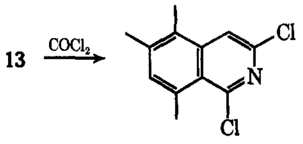

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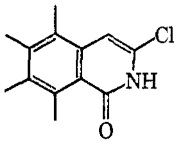
Treatment of **2c** with hydrogen chloride at 100–105° for 70 hr yielded 3-chloro-5,6,7,8-tetramethylisocarbostyril (**15**) (68%) and 1,3-dichloro-5,6,7,8-tetramethylisoquinoline (**16**) (13%).



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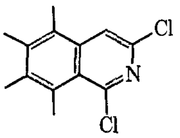

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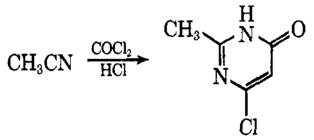
From **2b**, trace amounts of isocarbostyril and 6-chloro-2-methyl-4(3*H*)-pyrimidone (**17**), and moreover dichloroisoquinolines **18** (7.6%) and **19** (0.8%), were isolated.



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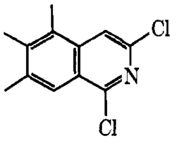

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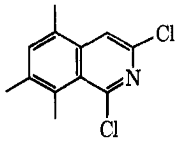

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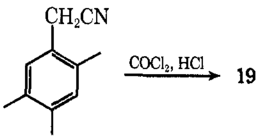
The structure of **19** was confirmed by comparing its ir spectrum with that of an authentic sample, prepared from 2,4,5-trimethylphenylacetonitrile (**20**),[2] and the mixture melting point showed no depression.



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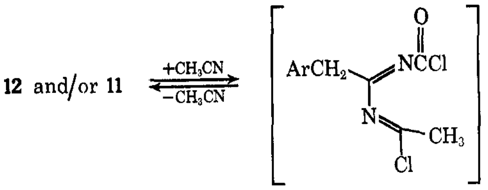
From **2d**, neither pyrimidone **7** (R = mesityl; R′ = H) nor isocarbostyril was isolated, but 1,3-dichloro-5,7-dimethylisoquinoline (**21**) (8%) and a trace amount of **17** were obtained, and **2d** was not recovered.

In view of the previous papers,[9] **17** was evidently formed by the reaction of acetonitrile with hydrogen chloride and phosgene, formed by decomposition of the carbamoyl chloride (**11** and/or **12**).

Dichloroisoquinoline derivatives (**14**, **16**, **18**, **19**, and **21**) were formed by the reaction of phosgene with the corresponding isocarbostyrils; they might be formed in part during the preparation of **2**. In fact, a small amount of **14** (1.4%) was isolated from the filtrate of **3a** by chromatography over alumina.

On heating **2e** with acetonitrile and hydrogen chloride at 100–105° for 140 hr, a trace amount of 3-chloro-7-nitroisocarbostyril was isolated. On the other hand, treatment of **2e** with acetonitrile and hydrogen chloride at 55–60° for 7 days afforded the expected 6-chloro-2-(*p*-nitrobenzyl)-4(3*H*)-pyrimidone (**7**, R = *p*-nitrobenzyl; R′ = H) in 22% yield.

This suggests that at higher temperature the intermediate **22** for pyrimidone formation is unstable. The



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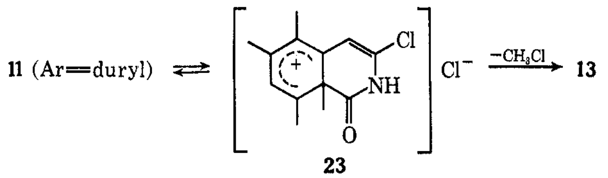
failure of **2a** to form the expected pyrimidone even at 55–60° is probably due to the steric hindrance of two methyl groups on the 2 and 6 position of the benzene ring in the step of forming **22** (Ar = duryl).

As mentioned above, in cases of **2a** and **2c**, the dramatic increase in the yield of isocarbostyrils was observed. This is ascribed to higher electron density at the ortho position in **2a** and **2c** than in **2b**, **2d**, and **2e**.

Isocarbostyrils are probably formed *via* σ complex **23** followed by elimination of methyl chloride, the formation of which was confirmed by glpc analysis of gaseous product.

An analogous σ complex has been suggested by Olah and Kuhn[10] as an intermediate for dealkylating nitration of polyalkylbenzenes. To our knowledge, such a demethylation reaction in the absence of Lewis acid catalyst has not been reported.



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Experimental Section

Melting points were determined on a Yanagimoto micro melting point apparatus and were corrected. The nmr spectra were obtained using a Model JNM-G-60 spectrometer (Japan Electronic Optics Laboratory, Co.) with tetramethylsilane as an internal reference. The ir spectra were recorded with a Japan Electroscopic IR-E spectrophotometer. The mass spectra were recorded with a Hitachi mass spectrometer, Model RMU-6E.

Preparation of Isocyanates 2 and Isolation as Ureas 3. General Procedure.—The amounts of reactants are listed in Table II. The nitrile **1** and chlorobenzene (5 ml) were placed in a 100-ml glass tube, and dry hydrogen chloride was allowed to be absorbed in the mixture. A chlorobenzene–phosgene solution (7 ml of chlorobenzene) was then added and the glass tube was stoppered, cooled in Dry Ice–acetone, and sealed. The sealed glass tube was heated at 105–125° in an oil bath for 6 days. After heating, the sealed glass tube was chilled in Dry Ice–acetone and opened carefully. After purging HCl and phosgene from the reaction mixture, chlorobenzene was removed *in vacuo*. The residue was dissolved in benzene (15 ml) and treated with aniline under cooling to form a white precipitate of **3**, which was filtered, washed with a small portion of benzene, dried *in vacuo*, recrystallized, and analyzed. The results are summarized in Table II. In cases of **1b** and **1c**, the reaction was carried out in a 50-ml sealed glass tube.

In the case of **1e**, instead of dissolving HCl, MeOH (1 ml) was added to the mixture of **1e**, phosgene, and chlorobenzene (12 ml) to evolve HCl, because the solubility of HCl in the nitrile–chlorobenzene mixture was very low.

Hydrolysis of Ureas 3.—A typical procedure is as follows. To a solution of 131 mg (0.34 mmol) of **3a** in DMSO (4 ml) was added 0.4 ml of water. The mixture was allowed to stand for 5 days at room temperature. To the reaction mixture was added 5 ml of water to form a white precipitate, which was filtered and dried *in vacuo* to give 107 mg (87%) of **6a**. The results are summarized in Table III.

Pyrolysis of 3.—A typical procedure is described. The suspension of 92 mg (0.24 mmol) of **3a** in 5 ml of acetonitrile was heated at 80° for 15 min on a water bath. To the resulting solution was added 71 mg (0.76 mmol) of aniline in 0.5 ml of acetonitrile at room temperature and the solvent was evaporated *in vacuo*. The residual solid was suspended in benzene, filtered, washed with water to remove aniline hydrochloride, and dried to give 43 mg (73%) of *sym*-diphenylurea.

Reaction of 2a with Acetonitrile and HCl at 100–105°.—In a 20-ml sealed glass tube, 0.9 g of the mixture of **2a** and **1a** (the content of **2a** is *ca.* 0.43 g), acetonitrile (3 ml), and HCl (0.65 g) were heated at 100–105° for 110 hr. After purging HCl, the precipitate formed was filtered, washed with a small portion of acetonitrile, and dried *in vacuo* to yield 286 mg (70%) of **13**. Recrystallization from THF-CH_3CN (3:1, v/v) gave colorless fine needles: mp 259–262°; ir (KBr) 1635 cm^{-1} (C=O); nmr (CF_3COOH) τ 2.49 (s, 1 H), 2.59 (s, 1 H), 7.14 (s, 3 H), 7.44 (s, 3 H), and 7.47 (s, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 223 (34, $M^+ + 2$), 221 (100, M^+), 186 (45), 185 (43), 157 (19), 131 (38), and 115 (24).

Anal. Calcd for $C_{12}H_{12}NOCl$: C, 65.01; H, 5.46; N, 6.32. Found: C, 64.96; H, 5.34; N, 6.30.

Acetonitrile was evaporated from the filtrate and the residue was chromatographed over alumina. The elutions with petroleum ether gave 30 mg of **14** (7%), but the expected pyrimidone **7** (R = duryl; R′ = H) was not obtained.

Chlorination of 13 with Phosgene.—**13** (123 mg, 0.56 mmol) and chlorobenzene (3 ml) were placed in a 20-ml glass tube and 1.5 g of phosgene was allowed to be absorbed. After sealing the glass tube, it was heated at 100–105° for 40 hr. The reaction mixture was evaporated to dryness to yield a tan crystalline residue, which was sublimed under reduced pressure to give 101 mg (76%) of **14** as colorless needles: mp 115–117°; ir (KBr) 1560 (ring), 1290, and 838 cm^{-1}; nmr ($CDCl_3$) τ 3.39 (s, 1 H), 2.86 (s, 1 H), 7.14 (s, 3 H), and 7.60 (s, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 241 (66, $M^+ + 2$), 239 (100, M^+), 224 (48, $M^+ - CH_3$) and 158 (36).

Anal. Calcd for $C_{12}H_{11}NCl_2$: C, 60.02; H, 4.62; N, 5.83. Found: C, 60.21; H, 4.84; N, 5.86.

Reaction of 2a with Acetonitrile and HCl at 55–60°.—The mixture of **2a** and **1a** (0.7 g, the content of **2a** is *ca.* 0.33 g), acetonitrile (3 g), and HCl (0.4 g) were heated in a 20-ml sealed glass tube at 55–60° for 93 hr. The precipitate formed was filtered, washed with acetonitrile, and dried to give 27 mg (9%) of **13**. The filtrate was concentrated, and to the residue (CH_3CN solution) was added 0.2 g of aniline to yield a yellow precipitate of **3a** (0.12 g, 26%).

Reaction of 2c with Acetonitrile and HCl.—In a 20-ml sealed glass tube, 1.7 g of the mixture of **2c** and **1c** (the content of **2c** is *ca.* 0.93 g), CH_3CN (3 g), and HCl (0.6 g) were heated at 100–105° for 70 hr. The precipitate formed was filtered, washed with a small portion of CH_3CN, and dried to yield 0.60 g (68%) of **15**, which was sublimed under reduced pressure to give white powder: mp 300–303°; ir (Nujol) 1635 cm^{-1} (C=O); nmr (CF_3COOH) τ 2.46 (s, 1 H), 7.13 (s, 3 H), 7.43 (s, 6 H), and 7.50 (s, 3 H).

Anal. Calcd for $C_{13}H_{14}NOCl$: C, 66.24; H, 5.99; N, 5.94. Found: C, 66.02; H, 5.94; N, 5.85.

The filtrate was concentrated and chromatographed over alumina. The elutions with petroleum ether gave **16** (0.12 g, 13%), which was sublimed under reduced pressure to give colorless needles: mp 117–118.5°; nmr ($CDCl_3$) τ 2.41 (s, 1 H), 7.24 (s, 3 H), 7.55 (s, 3 H), and 7.63 (s, 6 H).

Anal. Calcd for $C_{13}H_{13}NCl_2$: C, 61.43; H, 5.16; N, 5.51. Found: C, 61.42; H, 5.01; N, 5.58.

Reaction of 2b with Acetonitrile and HCl.—In a 20-ml sealed glass tube, 1.65 g of the mixture of **2b** and **1b** (the content of **2b** is *ca.* 0.62 g), CH_3CN (3.5 g), and HCl (0.8 g) were heated at 100–105° for 110 hr. The precipitate formed was filtered, dried, and sublimed under reduced pressure to yield 10 mg of **17**, which was identified by comparing its ir spectrum with that of an authentic sample.[9] The filtrate was concentrated and a small portion of benzene was added, and the benzene-insoluble material was filtered, washed with acetone and water, dried, and sublimed under reduced pressure to give 8 mg of isocarbostyril: mp 280–288°; ir (KBr) 1630 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 223 (36, $M^+ + 2$), 221 (100, M^+), and 186 (28).

Anal. Calcd for $C_{12}H_{12}NOCl$: C, 65.01; H, 5.46; N, 6.32. Found: C, 65.03; H, 5.42; N, 6.31.

The benzene-soluble material was chromatographed over alumina. The elutions with petroleum ether gave **19** (7 mg, 0.8%), and further elutions with petroleum ether gave **18** (65 mg, 7.6%). **19** was sublimed under reduced pressure to give colorless needles: mp 146.5–150°; mass spectrum (70 eV) *m/e* (rel intensity) 241 (64, $M^+ + 2$), 239 (100, M^+), and 224 (57).

Anal. Calcd for $C_{12}H_{11}NCl_2$: C, 60.02; H, 4.62; N, 5.83. Found: C, 60.33; H, 4.57; N, 5.71.

18 was recrystallized twice from acetone to give colorless needles: mp 167–175°; nmr ($CDCl_3$) τ 2.20 (s, 1 H), 2.36 (s, 1 H), 7.55 (s, 6 H), and 7.62 (s, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 241 (66, $M^+ + 2$), 239 (100, M^+), and 224 (70).

Anal. Calcd for $C_{12}H_{11}NCl_2$: C, 60.02; H, 4.62; N, 5.83. Found: C, 59.79; H, 4.62; N, 6.06.

Preparation of the Authentic Sample of 19.—In a 150-ml sealed glass tube, the mixture of **20**, HCl (1.0 g), $COCl_2$ (4.2 g), and chlorobenzene (11 ml) was heated at 100–105° for 93 hr. After

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(10) G. A. Olah and S. J. Kuhn, *J. Amer. Chem. Soc.*, **86**, 1067 (1964).

purging unreacted $COCl_2$ and HCl, the reaction mixture was cooled in Dry Ice–acetone, and the precipitate formed was filtered, washed with a small portion of CCl_4, and dried *in vacuo* to give 2.6 g (51%, based on $COCl_2$) of **19**, which was recrystallized twice from acetone to give pale yellow plates: mp 151–153°; nmr ($CDCl_3$) τ 2.44 (s, 1 H), 2.72 (s, 1 H), 7.22 (s, 3 H), 7.52 (s, 3 H), and 7.61 (s, 3 H).

Anal. Calcd for $C_{12}H_{11}NCl_2$: C, 60.02; H, 4.62; N, 5.83. Found: C, 59.88; H, 4.57; N, 5.68.

Reaction of 2d with CH_3CN and HCl.—In a 20-ml sealed glass tube, 0.8 g of the mixture of **2d** and **1d** (the content of **2d** is *ca.* 0.31 g), CH_3CN (3 g), and HCl (0.5 g) were heated at 100–105° for 5 days. The precipitate formed was filtered, washed with CH_3CN, dried *in vacuo*, and sublimed under reduced pressure to give 7 mg of **17**. The filtrate was concentrated and chromatographed over alumina. Petroleum ether eluted 25 mg of **21** (8%): mp 111–117°; mass spectrum (70 eV) *m/e* (rel intensity) 227 (66, $M^+ + 2$), 225 (100, M^+), 210 (43), 190 (36), 154 (32), and 127 (26).

Reaction of 2e with CH_3CN and HCl at 100–105°.—In a 20-ml sealed glass tube 0.5 g of the mixture of **2e** and **1e** (the content of **2e** is *ca.* 0.28 g), CH_3CN (4 g), and HCl (0.4 g) were heated at 100–105° for 140 hr. From the reaction mixture 6 mg of brown powder was isolated by filtration. It was sublimed under reduced pressure to give the yellow powder of 3-chloro-7-nitroisocarbostyril: mp above 300°; ir (KBr) 1675 cm^{-1} (C=O); mass spectrum (70 eV) *m/e* (rel intensity) 226 (29, $M^+ + 2$), 224 (85, M^+), 194 (93), 178 (40), 150 (51), 130 (100), 123 (49), and 114 (65).

Reaction of 2e with CH_3CN and HCl at 55–60°.—In a 20-ml sealed glass tube 0.67 g of the mixture of **2e** and **1e** (the content of **2e** is *ca.* 0.37 g), CH_3CN (4 g), and HCl (0.5 g) were heated at 55–60° for 7 days. The precipitate formed was filtered, washed with CH_3CN, and dried *in vacuo* to give brown powder of 6-chloro-2-(*p*-nitrobenzyl)-4(3*H*)-pyrimidone (81 mg, 22%), which was recrystallized from CH_3CN to give yellow plates: mp 250–259° dec; ir (KBr) 1675 cm^{-1} (C=O); nmr (CF_3COOH) τ doublets centered at 1.65 (2 H) and 2.35 (2 H, A_2B_2 system), 3.10 (s, 1 H), and 5.47 (s, 2 H); mass spectrum (70 eV) *m/e* (rel intensity) 267 (26, $M^+ + 2$), 265 (70, M^+), 264 (100), 116 (68), 106 (50), 89 (92), 68 (78), and 63 (50).

Anal. Calcd for $C_{11}H_8N_3O_3Cl$: C, 49.73; H, 3.04; N, 15.82. Found: C, 49.79; H, 2.77; N, 16.01.

Registry No.—**2a**, 31579-10-9; **2c**, 31579-11-0; **2d**, 31579-12-1; **2e**, 31579-13-2; **3a**, 31579-14-3; **3b**, 31579-15-4; **3c**, 31579-16-5; **3d**, 31579-17-6; **3e**, 31579-18-7; **3f**, 31579-19-8; **6a**, 31579-20-1; **6b**, 31579-21-2; **6c**, 31579-22-3; **6d**, 31579-23-4; **6e**, 31579-24-5; **6f**, 31579-25-6; **13**, 31579-26-7; **14**, 31579-27-8; **15**, 31579-28-9; **16**, 31579-29-0; **18**, 31579-30-3; **19**, 31579-31-4; **21**, 31579-32-5; isocarbostyryl, 31579-33-6; 3-chloro-7-nitroisocarbostyryl, 24633-93-0; 6-chloro-2-(*p*-nitrobenzyl)-4(3*H*)-pyrimidone, 31579-35-8.

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A Novel Reaction of Acetylsulfenyl Chloride with Activated Aromatic Compounds

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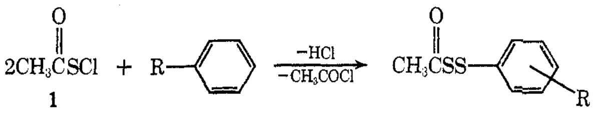
A novel aromatic sulfuration reaction is described. The reaction of acetylsulfenyl chloride with activated aromatic compounds such as anisole, *m*-xylene, toluene, and phenol yields acetyl aryl disulfides. A mechanism involving a tetravalent sulfur intermediate is proposed.

Preceding papers on aromatic sulfurations have shown that a catalytic amount of iron powder promotes the reaction of aromatics with the compounds containing bivalent sulfur-chlorine bonds. The reactions with sulfur chlorides[1] and sulfenyl chlorides[2] yield symmetric sulfides and asymmetric sulfides, respectively. On the other hand, benzenethiosulfenyl chlorides give disulfide or monosulfide depending on whether or not they have an ortho group.[3]

With a view to extending the scope of the aromatic sulfuration reaction, our attention was attracted to acetylsulfenyl chloride (**1**) which also has a sulfur-chlorine bond. **1** was first synthesized by Böhme and Clement,[4] and since then there have been several reports on the chemical behavior of **1**. However, previous works have dealt almost entirely with the reaction between **1** and such functional groups as active hydrogen[4–6] and olefinic double bonds.[7,8] The only example involving the reaction of **1** with aromatic compounds is the one with phenols[9] (*vide infra*).

In the present paper a novel reaction of **1** with activated aromatic compounds is described, which results in the formation of acetyl aryl disulfide (**2**). To



2a, R = 4-CH_3O
b, R = 2,4-di-CH_3
c, R = 2-CH_3
d, R = 4-CH_3
e, R = 4-HO

our knowledge this is the first example of asymmetric disulfide formation in aromatic sulfuration with sulfenyl halides.

A methylene chloride solution of a 1:1 mixture of acetylsulfenyl chloride (**1**) and anisole was stirred for 40 hr at room temperature and then refluxed for 2 hr. The main product was acetyl *p*-anisyl disulfide (**2a**) instead of acetyl *p*-anisyl sulfide, the product expected on the basis of analogy with previous studies. Confirmation of structure **2a** was obtained from ele-

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