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Chlorinolyses of Alkyl (or Aryl) Phthalimidomethyl Sulfoxides with Sulfuryl Chloride, Chlorine and Thionyl Chloride

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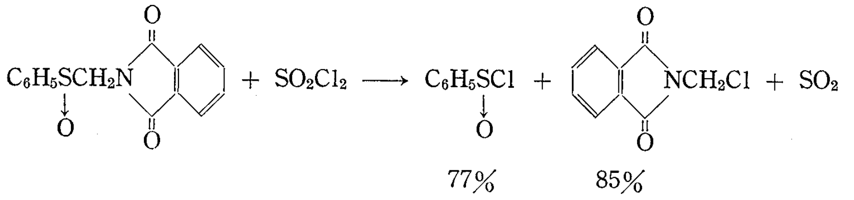
Cleavage of the carbon-sulfur bond of sulfoxide was effected, when a phthalimidomethyl moiety is linked to the sulfur of sulfoxide, by the action of sulfuryl chloride, molecular chlorine or thionyl chloride, affording an organic sulfinyl chloride or sulfenyl chloride. In the presence of alcohol, chlorine also gave the sulfonyl chloride. The preparation of organic sulfinyl chlorides was extensively examined to investigate the generality of these reactions.

Keywords——chlorinolysis; alkyl(or aryl)phthalimidomethyl sulfoxide; alkane(or arene)sulfinyl chloride; arenesulfenyl chloride; arenesulfonyl chloride

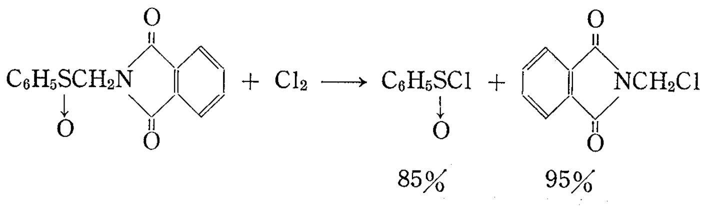
The reactions of sulfoxides with sulfuryl chloride,[2] molecular chlorine[3] and N-halo(bromo and chloro)succinimide[4] generally result in halogenation α to the sulfoxide function and that with thionyl chloride[5] results in the formation of an α-chlorinated sulfide with deoxygenation.

Instead of α-halogenation, cleavage of the carbon-sulfur bond of sulfoxides would occur if such cleavage leads to a relatively stable carbonium ion, as reported previously[6] for the N-halosuccinimide reaction of a sulfoxide carrying *tert*-butyl or α-phenethyl as an alkyl group, giving alkyl halide and alkanesulfinate, when carried out in the presence of alcohol.

We have found that cleavage of the carbon-sulfur bond of sulfoxide is effected, when a phthalimidomethyl moiety is linked to the sulfur of sulfoxide, by the action of sulfuryl chloride, molecular chlorine or thionyl chloride. The reactions of the newly prepared phenyl phthalimidomethyl sulfoxide were found to result in the production of benzenesulfinyl chloride in the runs with sulfuryl chloride and molecular chlorine, and benzenesulfenyl chloride in the run with thionyl chloride, as shown in equations (1), (2) and (3) with side formation of N-(chloromethyl)phthalimide.



(1)



(2)

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1) Location: *2-2-1 Oshika, Shizuoka 422, Japan.*

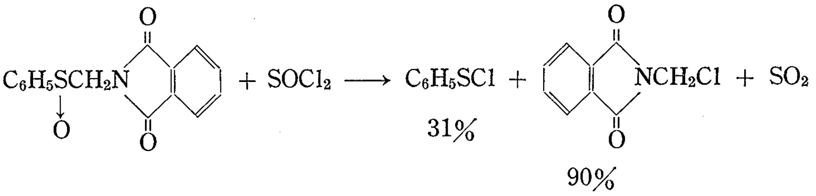
2) *a*) K.C. Tin and T. Durst, *Tetrahedron Lett.*, **1970**, 4643; *b*) G. Tsuchihashi, K. Ogura, S. Iriuchijima, and S. Tomizawa, *Synthesis*, **1971**, 89.

3) G. Tsuchihashi and S. Iriuchijima, *Bull. Chem. Soc. Jap.*, **1970**, 2271.

4) G. Tsuchihashi and K. Ogura, *Bull. Chem. Soc. Jap.*, **1971**, 1726.

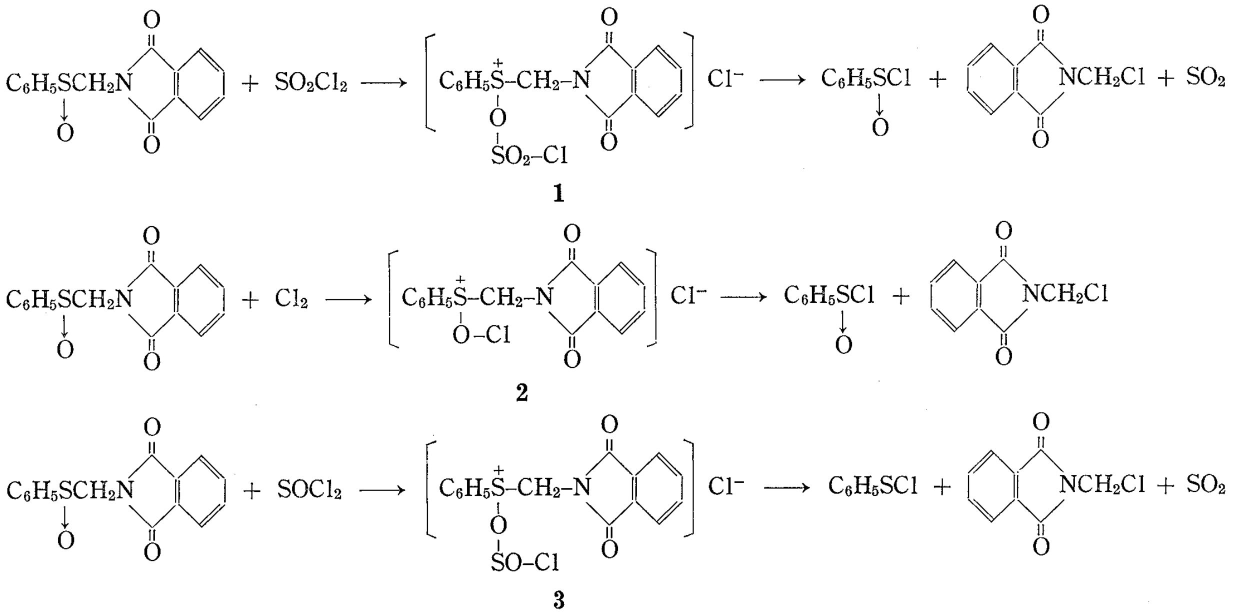
5) F.G. Bordwell and B.M. Pitt, *J. Am. Chem. Soc.*, **77**, 572 (1955).

6) F. Jung and T. Durst, *J. Chem. Soc. Chem. Comm.*, **1973**, 4.



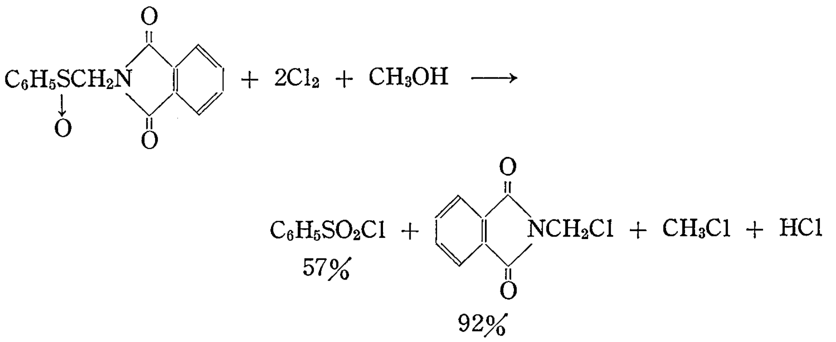
(3)

These reactions proceeded smoothly with stoichiometric amounts of the materials in benzene or carbon tetrachloride. Benzenesulfinyl and benzenesulfenyl chloride were obtained in the indicated yields and were identified by converting them into the corresponding anilide and diethylamide, respectively. Plausible reaction pathways may be written as follows.



In all these reactions the oxysulfonium ions (**1**, **2** or **3**) formed by attack of the chlorinating agents may act as intermediates. Owing to the positively charged sulfur, the oxysulfonium ions are able to undergo nucleophilic substitution by chloride at the phthalimidomethyl carbon. Hetero-functional groups, *i.e.* chloro, bromo, hydroxy, ethoxy and sulfonyl, linked to a phthalimidomethyl moiety have been reported to suffer nucleophilic substitution readily.[7] This substitution therefore replaces the α-chlorination which has been reported [2-5] with usual sulfoxides.

Furthermore, in the reaction of eq. (2), when methanol is present, the presence of twice the amount of chlorine affected the oxidation to give benzenesulfonyl chloride according to equation (4).



(4)

This reaction may involves oxidation with methyl hypochlorite formed transiently.

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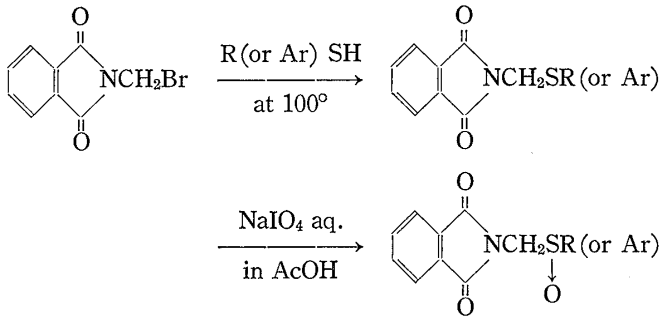
[7] M. Uchino, K. Suzuki, and M. Sekiya, *Chem. Pharm. Bull.* (Tokyo), **26**, 1837 (1978).

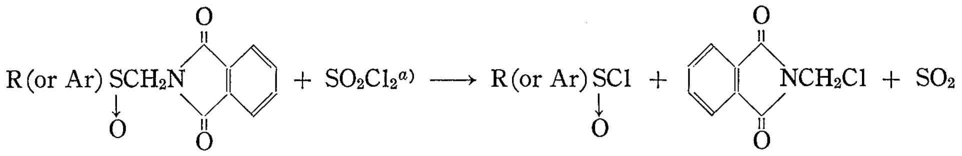
Table I. Syntheses of Alkyl (or Aryl) Phthalimidomethyl Sulfides and Sulfoxides

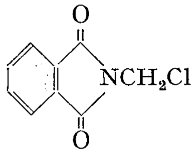


R (or Ar)	Yield (%)	
	Sulfide	Sulfoxide
C_6H_5–	90	74
p-$CH_3C_6H_4$–	80	74
p-ClC_6H_4–	80	70
p-$NO_2C_6H_4$–	76	81
β-$C_{10}H_7$–	82	78
$C_6H_5CH_2$–	—[a]	79[b]
$CH_3(CH_2)_4$–	—[a]	93
$CH_3(CH_2)_{11}$–	—[a]	78
C_6H_{11}–	76	77

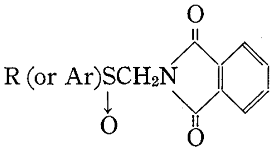
a) Preparation of this sulfide by the same procedure was reported in the preceding paper.[7]
b) Only this sulfoxide was obtained by oxidation with dinitrogen tetroxide.

Table II. Reaction with Sulfuryl Chloride



R (or Ar)	Solvent	Reaction		Yield (%)	
		Temp. (°C)	Time (hr)	$\text{R (or Ar)}\underset{\underset{O}{\downarrow}}{S}Cl$[b]	
C_6H_5–	C_6H_6	60	4	77	85
	CCl_4	60	4	65	92
	$CHCl_3$	60	6	67	82
p-$CH_3C_6H_4$–	C_6H_6	60	1	57	85
p-ClC_6H_4–	C_6H_6	60	1	85	92
p-$NO_2C_6H_4$–	C_6H_6	60	16	53	82
β-$C_{10}H_7$–	C_6H_6	60	1	86	82
$C_6H_5CH_2$–	C_6H_6	r.t.	1	82	99
$CH_3(CH_2)_4$–	C_6H_6	r.t.	0.5	86	99
$CH_3(CH_2)_{11}$–	C_6H_6	r.t.	1	82	97
C_6H_{11}–	C_6H_6	r.t.	1	56	99

a) Molar ratio:



: $SO_2Cl_2 = 1 : 1$.

b) Yield of anilide, to which the sulfinyl chloride was converted.

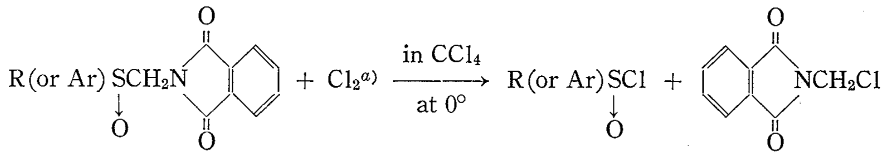
In the above four reactions it is advantageous that the high solubility of the sulfinyl, sulfenyl and sulfonyl chlorides in petroleum ether renders their separation from N-(chloromethyl)phthalimide easy.

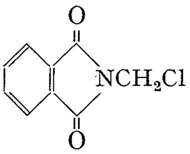
Among these reactions, it seems particularly interesting to explore the generality of reactions (1) and (2) to develop a synthetic method for sulfinyl chlorides.

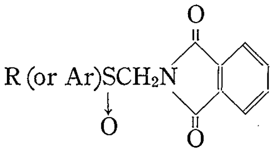
As can be seen in Table I, several new aryl and alkyl phthalimidomethyl sulfoxides were synthesized by oxidation of the corresponding sulfides, prepared as reported previously,[7] with sodium metaperiodate in acetic acid. As an exception, benzyl phthalimidomethyl sulfoxide could be prepared only by oxidation of the corresponding sulfide with dinitrogen tetroxide[8] in chloroform.

The reactions of these sulfoxides were carried out with sulfuryl chloride and with chlorine, yielding alkane- and arenesulfinyl chlorides in generally good yields, as can be seen in Tables II and III. The alkyl sulfoxides are more reactive than the aryl analogs. Thus, these reactions are general and should be applicable as convenient methods for the preparation of organic sulfinyl chlorides.

TABLE III. Reaction with Chlorine



R (or Ar)	Reaction Time (hr)	Yield (%)	
		$\underset{\underset{O}{\downarrow}}{\text{R (or Ar)SCl}}$[b]	
C_6H_5-	2	85	95
p-$CH_3C_6H_4-$	3	74	95
p-ClC_6H_4-	2	62	92
β-$C_{10}H_7-$	2	88	95
$C_6H_5CH_2-$	0.5	85	99
$CH_3(CH_2)_4-$	0.5	76	94
$CH_3(CH_2)_{11}-$	1	89	99
$C_6H_{11}-$	1	69	97

a) Molar ratio:  : Cl_2 = 1 : 1.

b) Yield of anilide, to which the sulfinyl chloride was converted.

Experimental[9]

Alkyl (or Aryl) Phthalimidomethyl Sulfides (Table I)

Alkyl as well as aryl phthalimidomethyl sulfides, as shown in Table I, were prepared from N-(bromomethyl)phthalimide and the corresponding thiol by the method reported previously.[7] Yields and data for the newly obtained products are recorded in Tables I and IV, respectively.

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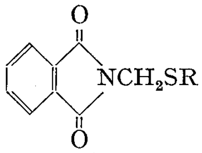
[8] R.D. Whitaker and H.H. Sisler, *J. Org. Chem.*, **25**, 1038 (1960).

[9] All melting points and boiling points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi EPI-G2 spectrophotometer. NMR spectra were taken with a JEOL-C-60-H spectrophotometer (60 MHz). Chemical shift values are given in δ (ppm) relative to tetramethylsilane as an internal standard. The following abbreviations are used: s=singlet, t=triplet, q=quartet, m=multiplet.

TABLE IV. Physical, Spectral and Analytical Data for



R	mp (lit. mp) (°C) Appearance (recryst. solvt.)	IR $\nu_{\max}^{\text{KBr}}$ (cm^{-1}) C=O	NMR (δ in CDCl$_3$)			Analysis (%) Calcd. (Found)		
			Aromatic protons	$\gt$NCH$_2$S–	Alkyl protons (J=Hz)	C	H	N
C_6H_5–	126—127 (127)[a] Needles (MeOH)	1778 1718	7.78—6.92	4.98		66.90 (66.83	4.12 4.18	5.20 5.14)
p-$CH_3C_6H_4$–	98—100 Leaflets (MeOH)	1778 1710	7.95—6.97	4.98	2.28 s	67.82 (67.86	4.62 4.65	5.20 5.14)
p-ClC_6H_4–	99—101 (99—101)[b] Prisms (MeOH)	1776 1712	8.00—7.05	5.01		59.31 (59.01	3.32 3.36	4.61 4.62)
p-$NO_2C_6H_4$–	175—177 Leaflets (benzene)	1770 1716	8.35—7.50	5.23		57.32 (57.28	3.21 3.21	8.91 8.95)
β-$C_{10}H_7$–	120—121 Prisms (MeOH)	1775 1714	8.18—7.10	5.20		71.45 (71.39	4.10 4.10	4.39 4.39)
C_6H_{11}–	67—69 Plates (MeOH)	1778 1714	8.00—7.60	4.73	3.10—0.70 11H, m	65.43 (65.15	6.22 6.18	5.09 5.10)

[a] Ref. 10.
[b] C.P. Lo, *J. Org. Chem.*, **26**, 3591 (1961).

Alkyl (or Aryl) Phthalimidomethyl Sulfoxides (Table I)

General Procedure——Alkyl (or aryl) phthalimidomethyl sulfides listed in Table I, except for benzyl phthalimidomethyl sulfide, were oxidized to the corresponding sulfoxides by sodium metaperiodate.

To a stirred saturated solution of 0.05 mol of alkyl (or aryl) phthalimidomethyl sulfide in acetic acid (130—1000 ml), a saturated aqueous solution of 0.05 mol of sodium metaperiodate was added dropwise at room temperature, and stirring was continued overnight. (In the run with p-nitrophenyl phthalimidomethyl sulfide, the reaction mixture was heated at 70—80° for 2 hr then allowed to cool.) The resulting precipitates of alkyl (or aryl) phthalimidomethyl sulfoxide were collected by filtration, washed with cold water and dried. Removal of the filtrate by evaporation under reduced pressure and washing the resulting solid residue with water gave an additional alkyl (or aryl) phthalimidomethyl sulfoxide. Recrystallization of the products from appropriate solvents (Table V) gave pure crystals.

Benzyl phthalimidomethyl sulfide was well oxidized only by dinitrogen tetroxide.[8] To a stirred solution of 8.5 g (0.03 mol) of benzyl phthalimidomethyl sulfide in 50 ml of chloroform, 4.2 g (0.045 mol) of dinitrogen tetroxide in 50 ml of chloroform was added dropwise at 0°, and stirring was continued for 4 hr. The reaction solution was concentrated under reduced pressure. Recrystallization of the resulting solid residue from EtOH gave benzyl phthalimidomethyl sulfoxide.

Yields of the sulfoxides are shown in Table I and their physical, spectral and analytical data in Table V.

Alkane(or Arene)sulfinyl Chlorides General Procedure

Method A: Reaction with Sulfuryl Chloride——To a suspension of 0.02 mol of alkyl (or aryl) phthalimidomethyl sulfoxide in 50 ml of benzene, 2.7 g (0.02 mol) of sulfuryl chloride was added dropwise. In the runs with alkyl analogs the mixture was stirred at room temperature and in the runs with aryl analogs the reaction was carried out at 60°. In all runs the mixture became homogeneous at the end of the reaction. The reaction solution was concentrated under reduced pressure. Alkane(or arene)sulfinyl chloride was extracted from the resulting residue with several portions of petroleum ether and identified by conversion into the corresponding sulfinyl anilide. Spectral and analytical data of these anilides thus obtained are shown in Table VI. N-(Chloromethyl)phthalimide obtained as a powder insoluble in petroleum ether was recrystallized from AcOEt to give prisms, mp 132—134° (lit.[10] mp 134°).

Method B: Reaction with Chlorine——To a suspension of 0.02 mol of alkyl (or aryl) phthalimidomethyl sulfoxide in 30 ml of carbon tetrachloride, a solution of 1.4 g (0.02 mol) of chlorine dissolved in 6 ml of carbon tetrachloride was added dropwise with stirring at 0°. In all runs the initial heterogeneous reaction mixture became homogeneous in the course of the reaction, then a part of the N-(chloromethyl)phthalimide precipitated and was collected by filtration. Treatment of the filtrate by a procedure similar to those described in method A gave alkane(or arene)sulfinyl chloride and additional N-(chloromethyl)phthalimide. Identification

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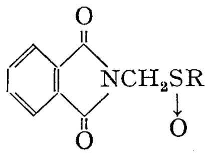
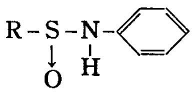
[10] H. Böhme and A. Müller, *Arch. Pharm.*, **296**, 54 (1964).

TABLE V. Physical, Spectral and Analytical Data for



R	mp (°C) and Appearance (recryst. solvt.)	IR ν_{max}^{KBr} (cm^{-1})		NMR (δ in CDCl$_3$)					Analysis (%) Calcd. (Found)		
					Alkyl protons (J=Hz)						
		C=O	S→O	Aromatic protons	$>NCH_2\overset{\downarrow}{S}$– (S→O)	CH$_3$–	–$\overset{\downarrow}{S}$CH$_2$– (S→O)	Others	C	H	N
C$_6$H$_5$–	173—175 Needles (AcOEt)	1778 1712	1047	8.08—7.10	4.80 q (12)				63.14 (63.20	3.89 3.83	4.91 4.74)
p-CH$_3$C$_6$H$_4$–	168—170 Leaflets (MeOH)	1784 1726	1050	8.00—7.16	4.86 q (12)	2.40 s			64.20 (64.21	4.38 4.37	4.68 4.66)
p-ClC$_6$H$_4$–	168—170 Prisms (EtOH)	1784 1722	1054	8.15—7.24	4.80 q (12)				56.34 (56.25	3.15 3.15	4.38 4.43)
p-NO$_2$C$_6$H$_4$–	191—193 Prisms (AcOH)	1778 1724	1058	8.70—7.66	5.32 s				54.54 (54.28	3.16 3.07	8.43 8.34)
β-C$_{10}$H$_7$–	169—170 Prisms (EtOH)	1780 1724	1046	8.45—7.18	4.84 q (12)				68.04 (67.73	3.91 3.90	4.18 4.14)
C$_6$H$_5$CH$_2$–	173—176 Prisms (EtOH)	1785 1728	1048	8.06—7.20	4.70 s		4.10 s		64.20 (64.02	4.38 4.27	4.68 4.73)
CH$_3$(CH$_2$)$_4$–	90—91 Needles (iso-Pr$_2$O)	1784 1728	1034	8.02—7.46	4.80 s	0.93 t (6)	2.82 t (8)	2.16—1.10 6H, m	60.19 (60.05	6.13 6.11	5.01 4.91)
CH$_3$(CH$_2$)$_{11}$–	114—116 Needles (MeOH)	1777 1728	1036	8.07—7.56	4.78 s	0.88 t (6)	2.85 t (8)	2.26—1.07 20H, m	66.81 (66.86	8.28 8.28	3.71 3.72)
C$_6$H$_{11}$–	150—152 Prisms (MeOH)	1779 1772	1045	8.22—7.52	4.77 s			3.11—0.91 11H, m	61.83 (61.47	5.88 5.86	4.81 4.79)

TABLE VI. Physical, Spectral and Analytical Data for



$R-\underset{\downarrow \atop O}{S}-\underset{| \atop H}{N}-C_6H_5$

R	mp (lit. mp) (°C) Appearance (recryst. solvt.)	IR ν_{max}^{KBr} (cm^{-1})		NMR (δ in CDCl$_3$)					Analysis (%) Calcd. (Found)		
						Alkyl protons (J=Hz)					
		>N-H	S→O	Aromatic protons	-N-H	CH$_3$-	-SCH$_2$-→O	Others	C	H	N
C_6H_5-	102—104(112—114)[a] Plates (benzene)	3175	1054	7.90—6.70	9.20				66.33 (66.13	5.10 5.14	6.45 6.39)
p-$CH_3C_6H_4$-	130—131(138)[b] Plates (benzene)	3175	1054	7.85—6.85	6.58	2.38 s			67.50 (67.55	5.66 5.62	6.06 6.07)
p-ClC_6H_4-	132(134—135)[c] Prisms (benzene)	3175	1054	8.05—6.45	9.38				57.26 (57.37	4.00 4.14	5.56 5.98)
p-$NO_2C_6H_4$-	127—128 Prisms (benzene)	3175	1052	8.60—6.70	9.60				54.95 (55.08	3.84 3.88	10.68 10.38)
β-$C_{10}H_7$-	145—147 Prisms (EtOH)	3100	1042	8.50—6.70	9.27				71.88 (71.62	4.90 4.98	5.24 5.09)
$C_6H_5CH_2$-	138—141(144—145)[a] Prisms (benzene)	3130	1042	7.45—6.54	7.90		4.18 q (14)		67.75 (67.68	5.66 5.57	6.06 6.25)
$CH_3(CH_2)_4$-	84—85 Prisms (MeOH)	3170	1043	7.40—6.85	7.78	0.92 t (5)	3.00 t (8)	2.03—1.08 6H, m	62.52 (62.92	8.11 8.47	6.63 6.73)
$CH_3(CH_2)_{11}$-	78—80 Plates (MeOH)	3170	1040	7.40—6.85	7.35	0.88 t (6)	3.00 t (8)	1.92—1.05 20H, m	69.85 (69.75	10.10 10.13	4.53 4.48)
C_6H_{11}-	110—112(115—116)[d] Plates (MeOH)	3100	1037	7.38—6.85				3.20—0.70 11H, m	64.54 (64.35	7.67 7.69	6.23 6.25)

a) A. Sonn and E. Schmidt, *Chem. Ber.*, **57**, 1355 (1924).
b) J. von Braun and W. Kaiser, *Chem. Ber.*, **56**, 549 (1923).
c) K. Mori and Y. Ueda, *Yakugaku Zasshi*, **91**, 940 (1971).
d) D. Klamann, C. Sass and M. Zelenka, *Chem. Ber.*, **92**, 1913 (1959).

of the sulfinyl chlorides was carried out as described in method A. Reaction times and yields of the products are shown in Table III.

Benzenesulfenyl Chloride

To a suspension of 5.7 g (0.02 mol) of phenyl phthalimidomethyl sulfoxide in 50 ml of benzene, 3.6 g (0.03 mol) of thionyl chloride was added dropwise with stirring at 60°, and stirring was continued for 6 hr. The mixture became homogeneous at the end of the reaction. The reaction solution was concentrated under reduced pressure, and the resulting residue was extracted with petroleum ether. A crystalline solid insoluble in petroleum ether was assigned as N-(chloromethyl)phthalimide. After removal of petroleum ether, distillation of the resulting residue under reduced pressure gave 0.9 g (31%) of benzenesulfenyl chloride, bp 80—84° (9 mmHg) [lit.[11] bp 73—75° (9 mmHg)], which was identified by converting it into the corresponding sulfenyl diethylamide, bp 79—80° (1 mmHg) [lit.[11] bp 90° (3.5 mmHg)], by treatment with diethylamine. *Anal.* Calcd. for $C_{10}H_{15}NS$: C, 66.30; H, 8.29; N, 7.73. Found: C, 66.18; H, 8.31; N, 7.69.

Benzenesulfonyl Chloride

To a mixture of 5.7 g (0.02 mol) of phenyl phthalimidomethyl sulfoxide and 0.7 g (0.02 mol) of methanol in 30 ml of carbon tetrachloride, a solution of 2.8 g (0.04 mol) of chlorine dissolved in 12 ml of carbon tetrachloride was added dropwise with stirring at 0°. The mixture became homogeneous, and then a part of the N-(chloromethyl)phthalimide gradually precipitated. After filtration, the filtrate was concentrated under reduced pressure. The resulting residue was extracted with petroleum ether. Additional N-(chloromethyl)-phthalimide was obtained as a petroleum ether insoluble powder. After removal of petroleum ether, distillation of the resulting residue under reduced pressure gave 2.0 g (57%) of benzenesulfonyl chloride, bp 91° (0.1 mmHg) [lit.[12] bp 134° (20 mmHg)], which was identified by comparison of its IR spectrum with that of an authentic specimen.

Acknowledgement We wish to thank Mr. K. Narita and other staff of the Analysis Center of this college for microanalyses.

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[11] H. Lecher and F. Holschneider, *Chem. Ber.*, **57**, 755 (1924).

[12] J.W. Howard and C.G. Derick, *J. Am. Chem. Soc.*, **46**, 166 (1924).