$AlCl_3$-Mediated Aromatic Phenylthiation with *N*-Phenylthiophthalimide

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***N*-Phenylthiophthalimide reacts with $AlCl_3$ or $TiCl_4$ in arenes to give phenylthiated arenes alone *via* a phenylsulfenium ion intermediate, modified neglect of diatomic overlap (MNDO) molecular orbital calculations of which revealed that the positive charge preferentially populates the sulfur atom rather than the phenyl group in the phenylsulfenium ion.**

Key words phenylthiation; *N*-phenylthiophthalimide; phenylsulfenium ion; modified neglect of diatomic overlap calculation

N-Alkylthio- and *N*-arylthioimides have been used as sulfur-transfer reagents. They react with thiols,[1)] hydrosulfides,[1a)] alkoxides,[2)] amines,[3)] arenesulfinates,[4)] active methylene compounds,[5)] enamines,[6)] and organometallic compounds[7)] to give the corresponding sulfenylated products. However, reaction of sulfur-transfer reagents with arenes have been little investigated and to our knowledge only two examples are reported: reactions of sulfur-transfer reagents with an unusually reactive pyrrole[8)] and with lithiated arene-tricarbonylchromium complexes.[9)]

In the course of our investigation on the chemistry of electron-deficient heteroatoms, we have shown that *N*-phenoxy- and *N*-phenylamino-phthalimides (**1a**, **b**) reacted with $AlCl_3$ in benzene to generate phenoxenium and phenylnitrenium ions (**2a**, **b**), respectively, which were trapped by benzene to give hydroxybiphenyls from **2a** and aminobiphenyls and diphenylamine from **2b**.[10)] Now, we report the reaction of *N*-phenylthiophthalimide (**1c**) with arenes in the presence of $AlCl_3$. Compound **1c** is a commercially available, easily handled sulfur-transfer reagent.

In our initial experiments, we have undertaken reaction of **1c** with $AlCl_3$ in benzene. Treatment of **1c** with $AlCl_3$ (5 eq) in benzene for 20 min at room temperature gave diphenyl sulfide (**3a**) (94%). The phenylthiation was carried out in this way, and the results are presented in Table 1. For anisole, diphenyl ether and naphthalene, 1.2 eq of the arenes were employed using CH_2Cl_2 as solvent.

The proposed mechanism is as follows: $AlCl_3$ coordinates with imide carbonyl of **1c** and assists in the elimination of the phthalimide group to produce a phenylsulfenium ion which is trapped by arenes to give **3**. In the case of nucleophilic arenes having an oxygen atom (runs 4, 5), $TiCl_4$ works better than $AlCl_3$, probably because $AlCl_3$ coordinates more strongly with the oxygen to reduce the nucleophilicity of the starting arenes. Formation of small amounts of diphenyl disulfide (**4**) was observed in these reactions with moderate yields (runs 4, 5), which suggests that **2c** generated from **1c** did not react completely with the $AlCl_3$ coordinated

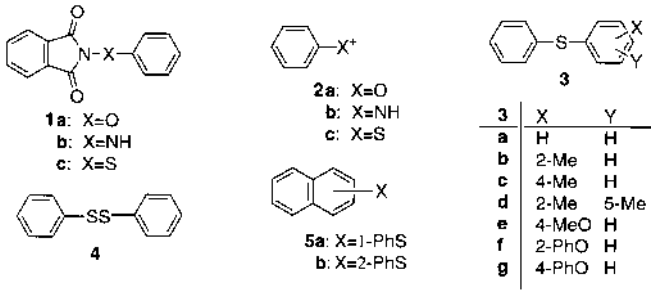

Fig. 1

Table 1. Phenylthiation of Arenes with **1c** using $AlCl_3$

Run	Arene[a)]	Reaction time[b)] (min)	Product	Yield,[c)] (%)
1	Benzene	20	**3a**	94
2	Toluene	30	**3b**	43
			3c	47
3	*p*-Xylene	30	**3d**	92
4	Anisole[d)]	45 (30)	**3e+4**	58 (83)+17 (1)
5	Diphenyl ether[d)]	40 (50)	**3f+4**	10 (2)+18 (5)
			3g	39 (61)
6	Naphthalene[d)]	30	**5a+4**	39[e)]+5
			5b	41[e)]

a) Arenes were used as solvent. *b*) Figures in parentheses indicate reaction times using $TiCl_4$. *c*) Figures in parentheses indicate yields using $TiCl_4$. *d*) 1.2 eq was used in CH_2Cl_2. *e*) Determined by GC analyses.

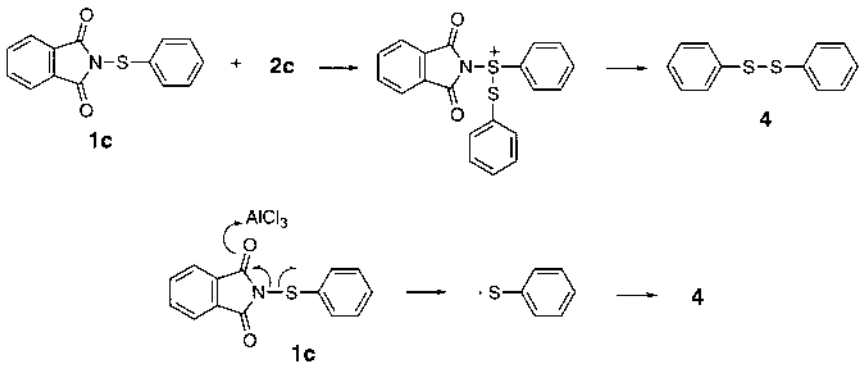

Fig. 2

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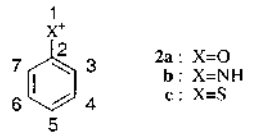
arenes and was trapped by another **1c** to produce **4**, or that $AlCl_3$-mediated homolytic S–N scission occurred to some extent to give a phenylthiyl radical, giving **4** by its dimerization.

It cannot yet be explained now why almost the same amounts of 1- and 2-phenylthionaphthalenes (**5a**, **b**) were obtained (run 6), because usually the 1-position is more reactive to electrophiles and a phenylsulfenium ion generated from *N*-ethyl-*S*-phenylsulfenamide in the presence of strong protonic acids reacted with naphthalene to give **5a** alone in low yield.[11]

It was reported that nucleophilic attack preferentially occurred on the nitrogen atom in **2b** formed from phenyl azide,[12] although a study of modified neglect of diatomic overlap (MNDO) calculations on **2b** indicates that a positive charge preferentially populates the *ortho* and *para* positions rather than the nitrogen atom.[13] We reported that **1a** and **b** reacted with $AlCl_3$ in benzene to give the biphenyl derivatives as major products (*vide supra*).[10] In contrast, **2c** generated from **1c** was trapped by benzene to give **3a** alone under similar reaction conditions and no biphenyl derivatives were detected in the reaction mixture. MNDO calculations on **2a**, **b** and **c** support this difference, that is, in **2c**, the positive charge exclusively populated the sulfur atom, while in **2a** and **b**, the positive charge preferentially populated the *para*- and *ortho*-positions rather than the oxygen and the nitrogen atoms (Table 2).

Table 2. Calculated Atomic Charges[a]



Atom	2a	2b	2c
1	−0.2315	−0.2072	0.4084
		(0.0307)	
2	0.2833	0.0225	−0.3569
3	0.0326	0.0672	0.0722
	(0.2530)	(0.2569)	(0.2748)
4	−0.1481	−0.1481	−0.1231
	(0.0419)	(0.0315)	(0.0556)
5	0.1391	0.1049	0.0859
	(0.3584)	(0.3092)	(0.2882)
6	−0.1480	−0.1572	−0.1216
	(0.0420)	(0.0216)	(0.0572)
7	0.0326	0.1190	0.0705
	(0.2529)	(0.3275)	(0.2728)

a) Values in parentheses show the atomic charges including the charge of connecting hydrogen atoms.

Experimental

General Methods All the melting points were determined with a Yanagimoto hot-stage melting point apparatus and are uncorrected. ^{1}H-NMR spectra were measured at 270 MHz on a JEOL JNM-EX270 spectrometer or at 500 MHz on a JEOL JNM-A500 spectrometer with tetramethylsilane (Me_4Si) as an internal reference and $CDCl_3$ as the solvent, unless otherwise noted. ^{1}H-NMR spectral data are reported in parts per million (δ) relative to Me_4Si. IR spectra were recorded on a JASCO IR 810 spectrophotometer. Mass spectra were obtained with a JEOL JMS-700 spectrometer with a direct inlet system at 70 eV. Gas chromatography was performed on a Shimadzu GC-14A equipped with a flame ionization detector (FID) using a glass column (2.1 m×3.2 mm i.d.) packed with 10% OV-1 on Chromosorb W (60—80 mesh). Elemental analyses were performed in the Microanalytical Laboratory of this University.

Materials Compounds (**1c**, **3a**, **4**), benzene, toluene, *p*-xylene, anisole, diphenyl ether and naphthalene were purchased from Tokyo Kasei Kogyo Co. Compound **3f**: mp 51—52 °C (lit.[14] mp 46—47 °C) (spectral data, see Table 3).

Procedure for MNDO Method The structure of each compound (**2a**, **b** or **c**) is generated by molecular modeling program SYBYL and optimized by semiempirical molecular orbital program MOPAC 93 using the MNDO method. Mulliken charges are calculated by the *ab initio* molecular orbital program GAUSSIAN 94 with the 6-311G** basis set.

To evaluate the accuracy of MNDO calculations, compounds **2a**—**c** are also optimized by GAUSSIAN 94 with STO-3G basis set and its Mullicken charges are calculated with the 6-311G** basis set. We compared the result of this calculation with the results of calculations of compounds **2a**—**c** described above and confirmed that they gave almost the same results.

Synthesis of Diphenylsulfide (3a); Typical Procedure To a solution of **1c** (200 mg, 0.783 mmol) and benzene (10 ml) was added $AlCl_3$ (522 mg, 3.92 mmol) under cooling in an ice-bath. After stirring the reaction mixture for 20 min at room temperature, H_2O (10 ml) was added under cooling in an ice-bath; 5 min later 10% NaOH (20 ml) was added under the same conditions. The aqueous layer was extracted with AcOEt (25 ml×2), and the combined organic layers were washed with brine (30 ml), dried over Na_2SO_4, and concentrated. The crude product was chromatographed on a column of silica gel with hexane as the eluent to give **3a** (137 mg, 94%). **3a** was identical with commercially available authentic sample.

Phenylthiation of Naphthalene with 1c; Typical Procedure To a solu-

Table 3. Spectral Data of Products

Compound	^{1}H-NMR ($CDCl_3$/Me_4Si) δ, J (Hz)	IR (neat) ν (cm^{-1})	MS *m/z*
3b	2.38 (3H, s, CH_3), 7.13 (1H, t, J=7.6, Ar-H), 7.17—7.28 (7H, m, Ar-H), 7.29 (1H, d, J=7.6, Ar-H)	1580, 1480, 740	200 (M^+, 100)
3c	2.33 (3H, s, CH_3), 7.13 (2H, d, J=7.9, Ar-H), 7.16—7.27 (5H, m, Ar-H), 7.30 (2H, d, J=8.2, Ar-H)	1580, 1480, 740	200 (M^+, 100)
3d	2.26 (3H, s, CH_3), 2.33 (3H, s, CH_3), 7.04 (1H, d, J=7.6, Ar-H), 7.14—7.18 (5H, m, Ar-H), 7.25 (2H, t, J=7.3, Ar-H)	1580, 1480, 740	214 (M^+, 100)
3e	3.82 (3H, s, CH_3O), 6.90 (2H, d, J=9.2, Ar-H), 7.12—7.26 (5H, m, Ar-H), 7.42 (2H, d, J=9.2, Ar-H)	1500, 1250, 740	216 (M^+, 100)
3f[a]	6.89—6.96 (3H, m, Ar-H), 7.02 (1H, t, J=7.3, Ar-H), 7.09 (1H, t, J=7.3, Ar-H), 7.15—7.43 (9H, m, Ar-H)	1490, 1250, 740	278 (M^+, 100)
3g	6.96 (2H, d, J=8.8, Ar-H), 7.04 (2H, d, J=8.8, Ar-H), 7.11—7.29 (6H, m, Ar-H), 7.36 (2H, t, J=8.2, Ar-H), 7.38 (2H, d, J=8.8, Ar-H)	1490, 1250, 700	278 (M^+, 100)
5a	7.12—7.25 (5H, m, Ar-H), 7.43 (1H, t, J=7.3, Ar-H), 7.49—7.55 (2H, m, Ar-H), 7.67 (1H, dd, J=7.3, 1.1, Ar-H), 7.85—7.90 (2H, m, Ar-H), 8.36—8.40 (1H, m, Ar-H)	1590, 1480, 740	236 (M^+, 100)
5b	7.23—7.42 (6H, m, Ar-H), 7.43—7.50 (2H, m, Ar-H), 7.72—7.82 (3H, m, Ar-H), 7.84 (1H, d, J=1.5, Ar-H)	1580, 1480, 740	236 (M^+, 100)

a) KBr.

tion of **1c** (200 mg, 0.783 mmol), naphthalene (120 mg, 0.940 mmol) and CH_2Cl_2 (5 ml) was added $AlCl_3$ (522 mg, 3.92 mmol) under cooling in an ice-bath. After the reaction mixture was stirred for 30 min at room temperature, H_2O (10 ml) was added under cooling in an ice-bath; 5 min later 10% NaOH (20 ml) was added under the same conditions. The aqueous layer was extracted with CH_2Cl_2 (25 ml×2), and the combined organic layers were washed with brine (30 ml), dried over Na_2SO_4, and concentrated. The crude products were chromatographed on a column of silica gel with hexane as the eluent to give a mixture of **5a** and **b** (148 mg, 80%) along with **4** (5%). Yields of **5a** (39%) and **b** (41%) were determined by gas chromatographic analyses. The authentic samples were prepared by the literature method.[15] Gas chromatographic conditions: glass column (2.1 m×3.2 mm i.d.); 10% OV-1 on Chromosorb W (60—80 mesh); temperature, 210 °C; carrier gas, N_2; flow rate, 45 ml/min; **5a**, t_R 16.8 min, **5b**, t_R 20.1 min.

Phenylthiation of Anisole with $TiCl_4$; Typical Procedure To a solution of **1c** (200 mg, 0.783 mmol), anisole (102 mg, 0.940 mmol) and CH_2Cl_2 (5 ml) was added dropwise 1.0 M solution (in CH_2Cl_2) of $TiCl_4$ (3.9 ml, 3.92 mmol) under cooling in an ice-bath. After stirring the reaction mixture for 30 min at room temperature, H_2O (20 ml) was added under cooling in an ice-bath, and 5 min later 10% NaOH (20 ml) was added under the same conditions. The aqueous layer was extracted with CH_2Cl_2 (25 ml×2), and the combined organic layers were washed with brine (30 ml), dried over Na_2SO_4, and concentrated. The crude products were chromatographed on a column of silica gel with hexane–benzene (20 : 1) as the eluent to give **3e** (144 mg, 83%) along with **4** (1%).

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