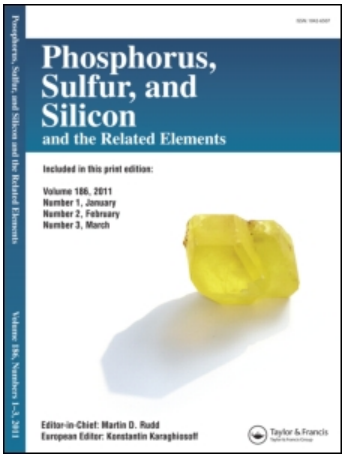


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

NOVEL HALOGENATION OF THIOPHENES WITH BENZENESELENINYL CHLORIDE AND ALUMINUM HALIDE

Nobumasa Kamigata[a]; Takashi Suzuki[a]; Masato[a]; Yoshida[a]
[a] Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Tokyo, Japan

To cite this Article Kamigata, Nobumasa , Suzuki, Takashi , Masato and Yoshida(1990) 'NOVEL HALOGENATION OF THIOPHENES WITH BENZENESELENINYL CHLORIDE AND ALUMINUM HALIDE', Phosphorus, Sulfur, and Silicon and the Related Elements, 53: 1, 29 — 35
To link to this Article: DOI: 10.1080/10426509008038010
URL: http://dx.doi.org/10.1080/10426509008038010

Phosphorus, Sulfur, and Silicon, 1990, Vol. 53, pp. 29–35
Reprints available directly from the publisher
Photocopying permitted by license only

NOVEL HALOGENATION OF THIOPHENES WITH BENZENESELENINYL CHLORIDE AND ALUMINUM HALIDE

NOBUMASA KAMIGATA,† TAKASHI SUZUKI and MASATO YOSHIDA

Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Fukazawa, Setagaya-ku, Tokyo 158, Japan

(Received October 24 1989)

In the presence of aluminum halide, benzeneseleninyl chloride is an efficient regioselective halogenating reagent for heterocyclic compounds such as thiophene, 2-methylthiophene, 3-methylthiophene, 2,5-dimethylthiophene, and furan. In the case of pyrrole, no halogenated product was obtained. A plausible reaction mechanism involving a positive halogen intermediate is proposed.

Key words: Benzeneseleninyl chloride; thiophenes; regioselective halogenation; halonium ion.

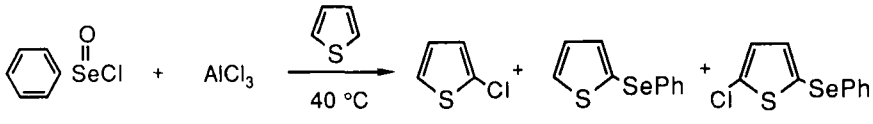
A number of studies on the halogenation of heterocyclic compounds have been reported.[1] 2-Chlorothiophene has been formed in 37% yield when thiophene was treated with 1 equiv. of chlorine in the dark at −30°C.[2] 2-Bromothiophene was formed when molecular bromine was used in an acetic acid-ether mixture or in carbon tetrachloride.[3] 3-Bromothiophene has been prepared by debromination of 2,3,5-tribromothiophene.[4] However, these methods tend to give the monohalogenated compound in lower yields with the concurrent formation of di- or tri-halogenated products. More recently, improved regioselective bromination of thiophene was reported by several authors with various brominating reagents.[4,5,6] However, the regioselective chlorination of thiophene has not been appreciably investigated.

Recently, we reported that benzeneseleninyl chloride in the presence of aluminum halide is an excellent vinylic halogenating reagent of olefins,[7] and is also a para-halogenating reagent for aromatic compounds possessing electron-donating groups such as anisole, phenetole, and *N,N*-dimethylaniline.[8] The reaction proceeds in one step under mild conditions and affords high yields. The high yield and high regioselectivity in the halogenation of aromatic compounds prompted us to study the halogenation of heterocyclic compounds such as thiophenes and furan by this method. We have investigated the halogenation of heterocyclic compounds with benzeneseleninyl chloride in the presence of aluminum halides, and the results are described herein.

† Author to whom all correspondence should be addressed.

RESULTS AND DISCUSSION

Benzeneseleninyl chloride (**1**), prepared from benzeneselenenyl chloride treated with ozone in dichloromethane, was allowed to react with thiophene in the presence of aluminum chloride at 40°C. 2-Chlorothiophene (**2**) was obtained in 27% yield, and no formation of 3-chlorothiophene was observed by gas chromatography. In this reaction, besides the formation of **2**, 2-phenylselenothiophene (**3**) and 5-chloro-2-phenylselenothiophene (**4**) were formed in yields of 2%, and 44%, respectively. In order to improve the yield of **2**, the reaction was carried out using chloroform as the solvent instead of dichloromethane. In this case, **2**, **3**, and **4** were obtained in 46, 16, and 0% yield, respectively. The results show that chloroform is the better solvent. It was



1 2 3 4

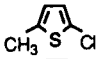
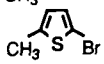
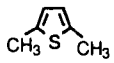
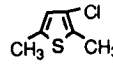
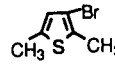
	2	3	4
CH_2Cl_2	27 %	2 %	44 %
$CHCl_3$	46 %	16 %	0 %

therefore decided to carry out reactions of **1** with heterocyclic compounds in the presence of aluminum chloride in chloroform. When **1** was allowed to react with 2-methylthiophene, 3-methylthiophene, and 2,5-dimethylthiophene in chloroform at room temperature, 2-chloro-5-methylthiophene, 2-chloro-3-methylthiophene, and 3-chloro-2,5-dimethylthiophene were formed in high yields, and no regio-isomer was detected by gas chromatography. The results are summarized in Table I. As shown in Table I, thiophene and 2-methylthiophene were regioselectively chlorinated at the 2- and 5-positions, respectively. The chlorination of 3-methylthiophene occurred only at the 2-position to give 2-chloro-3-methylthiophene, although the formation of 5-chloro-3-methylthiophene was expected. On the other hand, the chlorination of 2,5-dimethylthiophene afforded 3-chloro-2,5-dimethylthiophene in high yield. These results show that the chlorination of thiophenes by **1** in the presence of aluminum chloride is highly regioselective. The higher yields were observed in the more methyl-substituted thiophenes than thiophene, and this method is efficient for chlorination of electron rich thiophenes.

The chlorination of thiophenes using **1** and aluminum chloride is presumed an electrophilic substitution and the reaction mechanism is accounted for by Scheme 1 which proposes a chloronium ion intermediate.[5,6] The aluminum chloride interacts with the oxygen atom of **1** to give chloronium trichloro(phenylselenooxy)aluminum intermediate (**5**). The following electrophilic reaction of the chloronium ion toward heterocyclic nucleus affords chlorinated products via the formation of a carbocation intermediate (**6**). The observed high regioselectivity is a consequence of the transfer chlorinations going through a "late" arenium ion like transition state. The phenylselenated products (**3**) and (**4**) may be formed by

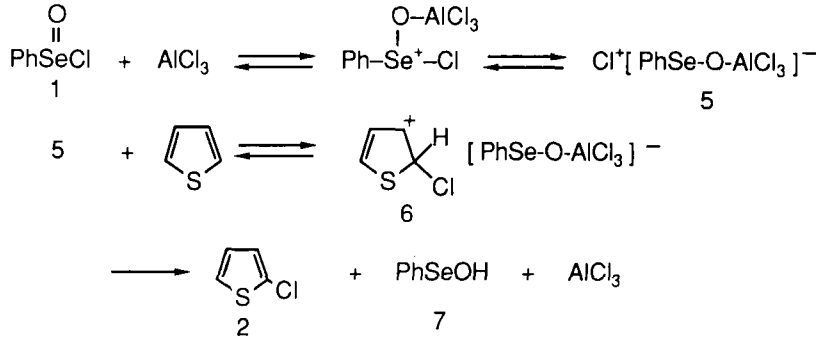
TABLE I

Halogenation of heterocyclic compounds with benzeneseleninyl chloride and aluminum halide

Heterocyclic Compound	Aluminium Halide	Reaction Temp./°C	Reaction Time/h	Product	Yield[a] / %
	$AlCl_3$	40	6		27
	$AlCl_3$ [b]	40	6		46
	$AlBr_3$	r. t.	3.5		76
	$AlCl_3$ [b]	r. t.	3		77
	$AlBr_3$	r. t.	2.5		96
	$AlCl_3$ [b]	r. t.	3		78
	$AlBr_3$	r. t.	3		98
	$AlCl_3$ [b]	r. t.	3		89
	$AlBr_3$	r. t.	2		145

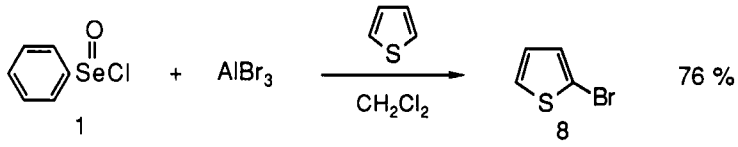
a) The yields are determined by GLC using an internal standared. b) The reaction was carried out in chloroform, others in dichloromethane.

the reaction of benzeneselenenic acid (**7**) once formed with thiophene and **2**, respectively, although **7** was not detected in the reaction mixture.

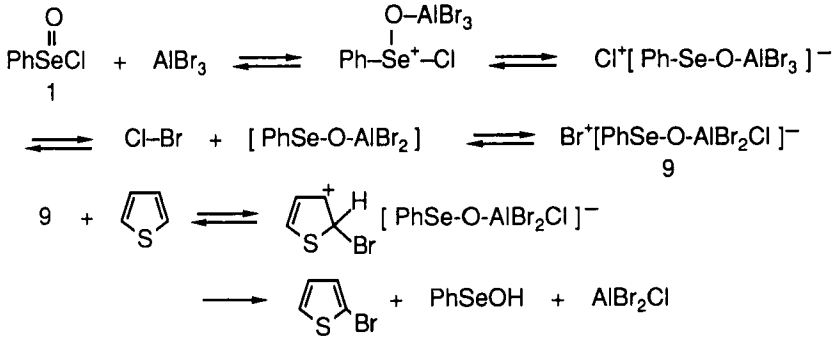


SCHEME 1

When the reaction of **1** with thiophene was carried out in the presence of aluminum bromide instead of aluminum chloride in dichloromethane at room temperature, 2-bromothiophene (**8**) was obtained in 76% yield and no formation of 2-chlorothiophene was observed. The phenylselenated products such as **3** and **4** were in trace quantities. Their formation was observed in the reaction of **1** with



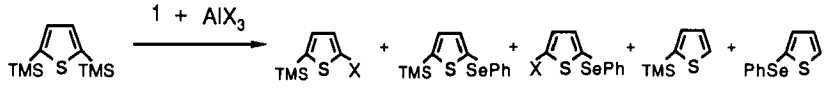
thiophene in the presence of aluminum chloride. Therefore, the bromination of thiophenes was achieved in dichloromethane. The results are shown in Table I. The formation of the bromonium ion is proposed in the reaction of benzeneseleninyl chloride with aluminum bromide as shown in Scheme 2. The data in Table I show that the bromonium intermediate (**9**) acts as an efficient regioselective brominating reagent of heterocyclic compounds.



SCHEME 2

The yield of 3-bromo-2,5-dimethylthiophene in the bromination of 2,5-dimethylthiophene showed 145%, and similar results were obtained by the repeated experiments. The results show that two bromine atoms of aluminum bromide act as the brominating reagent in the reaction of **1** with 2,5-dimethylthiophene although the reaction mechanism is not known.

The reaction between 2,5-bis(trimethylsilyl)thiophene, which was synthetically useful, with **1** and aluminum halide was also studied. However, the expected 3-halo-2,5-bis(trimethylsilyl)thiophene was not formed, and the unexpected products shown below were obtained.

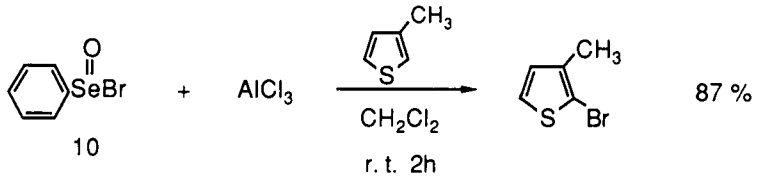


X = Cl	30 %	23 %	47 %	11 %	3 %
X = Br	72	19	9	42	77

The bromination of the other heterocyclic compounds such as furan and pyrrole were also carried out in dichloromethane at room temperature for 3 hours. However, 3-bromofuran was detected in only 14% yield and no bromopyrrole was found by GC analysis.

In order to corroborate the reaction mechanism proposed in Schemes 1 and 2,

the reaction of benzeneseleninyl bromide (**10**) with 3-methylthiophene in the presence of aluminum chloride was carried out in chloroform at room temperature. The regioselective brominated product, 2-bromo-3-methylthiophene, was



formed in 87% yield. The result supports the mechanism shown in Schemes 1 and 2.

In conclusion, it was found that benzeneseleninyl halide in the prsence of aluminum halide is a versatile regioselective mono-halogenating reagent of heterocyclic compounds without the formation of di- and tri-halogenated products.

EXPERIMENTAL

Measurement. Boiling points were uncorrected. The infrared absorption spectra were determined on a Hitachi Model 260–10 spectrometer with samples in the form of neat liquids. The proton magnetic resonance spectra were recorded at 60 MHz on a JEOL JNM-PMX 60 SI spectrometer using Me_4Si as an internal standard in $CDCl_3$. The ^{13}C NMR spectra were recorded on a JEOL JNM-FX 90 Q spectrometer using Me_4Si as an internal standard. Gas chromatography was performed on a Hitachi 263-30 and G-3000 gas chromatographs using SE 30 (10%), 1 m column. The gel-permeation chromatography was performed on a JAI Model LC-08 liquid chromatograph with a JAIGEL-1H column (20 mm × 600 mm × 2) using chloroform as an eluent. Mass spectra were determined using a JEOL JMX-DX 300 mass spectrometer equipped with a JEOL JMA 5000 Mass Data System at an ionizing voltage of 20–70 eV.

Materials. Benzeneselenenyl chloride of Nakarai Chemicals was distilled prior to use; bp 82°C/3 mmHg (120°C/20 mmHg).[9] Benzeneselenenyl bromide obtained from the Aldrich Chemical Company was distilled prior to use; 107°C/15 mmHg (107–108°C/15 mmHg).[10] Benzeneseleninyl chloride was prepared by the ozonization of benzeneselenenyl chloride with stirring in dry dichloromethane at −70°C (or in dry chloroform at −60°C) until the orange-red color faded to a light yellow by introducing ozone prepared by a Nippon Ozone Model 0–3–2 ozonizer. Benzeneseleninyl bromide was prepared by ozonization of benzeneselenenyl bromide under similar conditions until the red-brown color faded to a yellow. The benzeneseleninyl halide was used in the reactions with heterocyclic compounds *in situ* since benzeneseleninyl halide is extremely hygroscopic and care must be taken to avoid moisture. 2,5-Bis(trimethylsilyl)thiophene was prepared as described in the literature.[11,12]

General Procedure for the Reaction of Benzeneseleninyl Halide with Heterocyclic Compounds. To a stirred solution containing benzeneseleninyl halide (1.0 mmol) in 30 ml of dichloromethane or chloroform at ice temperature, under an atmosphere of nitrogen, was added 1.0 mmol of aluminum halide. The mixture was stirred for 1 h at room temperature. Heterocyclic compound (3.0 mmol) was added to the mixture in an ice bath, and the reaction mixture was stirred for 2–6 hours at room temperature or 40°C. Water (30 ml) was added to the reaction mixture, which was then extracted with dichloromethane or chloroform (20 ml × 2). The combined organic extracts were washed with saturated solution of sodium carbonate (20 ml) and water (30 ml), and dried over anhydrous magnesium sulfate. The reaction products were isolated by gel-permeation chromatography, and the structures were identified on the basis of their spectroscopic data. 2-Chlorothiophene, 2-bromothiophene, and 3-bromofuran were identified in comparison with authentic samples by GC analysis.

2-Phenylselenothiophene. IR (neat) 3040, 1565, 1465, 1390 and 720 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 6.85–7.38 (8H, m); ^{13}C NMR ($CDCl_3$) δ = 126.77, 128.34, 129.21, 130.07, 131.97, 133.43 and 136.90; MS *m/z* 240 (^{80}Se, M^+); Found: *m/z* 239.9557. Calcd for $C_{10}H_8SSe$: M, 239.9512.

5-Chloro-2-phenylselenothiophene. IR (neat) 3050, 1570, 1470, 1400, 785 and 725 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 6.79$ and 7.07 (2H, A_2B_2, $J = 3.6$ Hz) and 7.22–7.25 (5H, m); ^{13}C NMR ($CDCl_3$) $\delta = 127.15$, 127.42, 129.37, 130.34 and 136.36; MS m/z 274 (^{35}Cl, ^{80}Se, M^+); Found: m/z 273.9074. Calcd for $C_{10}H_7ClSSe$: M, 273.9122.

2-Chloro-5-methylthiophene [13]. IR (neat) 2900, 1540, 1445 and 780 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 2.36$ (3H, s), 6.42 and 6.58 (2H, A_2B_2, $J = 3.2$ Hz); MS m/z 132 (^{35}Cl, M^+).

2-Bromo-5-methylthiophene [14]. IR (neat) 2900, 1435 and 775 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 2.39$ (3H, s), 6.44 and 6.73 (2H, A_2B_2, $J = 3.6$ Hz); MS m/z 176 (^{79}Br, M^+).

2-Chloro-3-methylthiophene [15]. IR (neat) 2910, 1550, 1405, 1040, 825 and 690 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 2.16$ (3H, s), 6.68 and 6.94 (2H, A_2B_2, $J = 5.4$ Hz); MS m/z 132 (^{35}Cl, M^+).

2-Bromo-3-methylthiophene [14]. IR (neat) 2920, 1545, 1405, 1225, 990, 820 and 695 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 2.16$ (3H, s), 6.66 and 7.05 (2H, A_2B_2, $J = 6.0$ Hz); MS m/z 176 (^{79}Br, M^+).

3-Chloro-2,5-dimethylthiophene [16]. IR (neat) 2910, 1550, 1540, 1320, 1010 and 815 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 2.29$ (3H, s), 2.36 (3H, s) and 6.46 (1H, s); MS m/z 146 (^{35}Cl, M^+).

3-Bromo-2,5-dimethylthiophene [17]. IR (neat) 2910, 1550, 1440, 1000 and 820 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 2.31$ (3H, s), 2.38 (3H, s) and 6.51 (1H, s); MS m/z 190 (^{79}Br, M^+).

2,5-Bis(trimethylsilyl)thiophene. Bp 83–84°C/5 mmHg; IR (neat) 2950, 1490, 1405, 1250, 1010 and 840 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 0.30$ (18H, s) and 7.27 (2H, s); MS m/z 228 (M^+).

2-Trimethylsilylthiophene [18]. IR (neat) 2950, 1405, 1250, 995, 845 and 700 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 0.31$ (9H, s), 7.05–7.23 (2H, m) and 7.47–7.56 (1H, m); ^{13}C NMR $\delta = 0.00$, 128.07, 130.04 and 133.92; MS m/z 156 (M^+).

2-Chloro-5-trimethylsilylthiophene. IR (neat) 2950, 1410, 1250, 835 and 755 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 0.27$ (9H, s) and 6.98–7.85 (2H, m); ^{13}C NMR ($CDCl_3$) $\delta = 0.16$, 127.58, 133.49, 134.73 and 140.47; MS m/z 190 (^{35}Cl, M^+); Found: m/z 191.0056 Calcd for $C_7H_{12}ClSSi$: 191.0118.

2-Bromo-5-trimethylsilylthiophene [19]. IR (neat) 2960, 1410, 1250 and 840 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 0.28$ (9H, s), 6.89 and 7.00 (2H, A_2B_2, $J = 3.4$ Hz); ^{13}C NMR ($CDCl_3$) $\delta = 0.00$, 116.75, 131.16, 134.35 and 143.35; MS m/z 234 (^{79}Br, M^+).

2-Phenylseleno-5-trimethylsilylthiophene. IR (neat) 3050, 2950, 1480, 1400, 1250 and 840 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 0.30$ (9H, s) and 7.11–7.35 (7H, m); ^{13}C NMR ($CDCl_3$) $\delta = 0.16$, 127.04, 129.42, 130.67, 133.54, 135.17, 137.77 and 148.55; MS m/z 312 (^{80}Se, M^+); Found: m/z 311.9908 Calcd for $C_{13}H_{16}SSeSi$: M, 311.9907.

2-Bromo-5-phenylselenothiophene. IR (neat) 3060, 1580, 1470, 1400, 725 and 680 cm^{-1}; ^1H NMR ($CDCl_3$) $\delta = 6.95$ and 7.08 (2H, A_2B_2, J = 3.8 Hz) and 7.20–7.42 (5H, m); MS m/z 318 (^{79}Br, ^{80}Se, M^+); Found: m/z 317.8590 Calcd for $C_{10}H_7BrSSe$: M, 317.8617.

REFERENCES

1. A. R. Katritzky and C. W. Rees, "Comprehensive heterocyclic chemistry", vol 4, P 213, 604, and 765 (1984).
2. H. D. Hartough, *Chem. Heterocycl. Compd.*, **3,** 179 (1952).
3. S. Gronowitz, *Adv. Heterocycl. Chem.*, **1,** 1 (1963).
4. A. Hallberg, S. Liljefors and P. Pedaja, *Synth. Commun.*, **11,** 25 (1981).
5. S. Kato and M. Ishizaki, *Jpn. Kokai Tokkyo Koho JP* **62,** 148, 480 [87, 148, 480]; *Chem. Abst.*, **108,** 150299s (1988).
6. B. Fuch, Y. Belsky, E. Tartakovsky, J. Zizuashvili, and S. Wienman, *J. Chem. Soc., Chem. Commun.*, 778 (1982).
7. N. Kamigata, T. Satoh, and M. Yoshida, *Bull. Chem. Soc. Jpn.*, **61,** 449 (1988).
8. N. Kamigata, T. Satoh, M. Yoshida, H. Matsuyama and M. Kameyama, *ibid.*, **61,** 2226 (1988).

9. O. Behaghel and H. Seibert, *Ber.*, **66,** 708 (1933).
10. O. Behaghel and H. Seibert, *ibid.*, **65B,** 812 (1932).
11. D. J. Chadwic and C. Willbe, *J. Chem. Soc., Perkin Trans.*, **1,** 887 (1977).
12. P. A. Konstantinov and R. I. Shupik, *Zh. Obshch. Khim.*, **33,** 2151 (1963).
13. W. J. King and F. F. Nord, *J. Org. Chem.*, **14,** 638 (1949).
14. K. Dittmer, R. P. Martin, W. Herz and S. J. Cristol, *J. Am. Chem. Soc.*, **71,** 1201 (1949).
15. E. Campaigne and W. M. LeSuer, *ibid.*, **70,** 415 (1948).
16. A. Kergomard and S. Vincent, *Bull. Soc. Chim. Fr.*, **6,** 2197 (1967) (Fr).
17. J. Lecocq and B. Hoi, *Comp. rend.*, **224,** 658 (1947).
18. R. A. Benkeser and R. B. Currie, *J. Am. Chem. Soc.*, **70,** 1780 (1948).
19. R. A. Benkeser and A. Torkelson, *ibid.*, **76,** 1252 (1954).