On the Selectivity in the Bromination of Selenophene-2-carbonyl Derivatives in the Presence of Aluminum Trichloride

Dmitry N. Antonov and Leonid I. Belen'kii*

Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
Leninsky Prospect 47, 117913 Moscow, Russia

Salo Gronowitz*

Organic Chemistry 1, Chemical Center, University of Lund, P. O. Box 124, S-221 00 Lund, Sweden

Received September 14, 1994

Bromination reactions of 2-selenophenecarbaldehyde and 2-acetylselenophene in the presence of aluminum trichloride have been investigated and the reactivity and positional selectivity compared with those of the analogous thiophene derivatives.

J. Heterocyclic Chem., **32**, 53 (1995).

The dependence of reactivities of five-membered heterocycles on the nature of the heteroatom has attracted special attention. Electrophilic substitution reactions appear to be a good tool to investigate this problem. Quantitative data on reactivity and positional selectivity in the pyrrole, furan and thiophene series as well as quantum chemical calculations on these heterocycles including also selenophene have been discussed in a recent review [1].

The main feature of this data is that the relative reactivities of the heterocycles (N >> O > S) and their positional selectivities (O > S > N) do not correspond to each other, which can be interpreted in terms of stabilities of the respective σ-complexes formed by electrophilic attack at the α- and β-positions [1]. The differences in positional selectivities (α/β-ratios) of the parent heterocycles result in profound differences in their substituted derivatives. In particular regular acyl groups in the the 2-position of the pyrrole ring direct electrophilic attack exclusively or at least preferentially to the 4-position. In order to achieve the same result in the thiophene series a greater increase of the electron-withdrawing ability of the acyl group by complex formation with a proton or Lewis acid is needed. However, in the furan series even such acyl group modifications only result in partial formation of 4-substituted derivatives.

Unfortunately, systematic quantitative studies of reactivity and position selectivity of electrophilic substitution in the selenophene series are absent. There are only data by Marino [2] showing the place of selenophene in the row of reactivities between other congeners (N >> O > Te > Se > S). The conclusion that selenophene should be similar to thiophene in positional selectivity in electrophilic substitutions was until now supported only by scattered data. Thus nitration of selenophene-2-carbaldehyde (**1a**) or 2-acetylselenophene (**1b**) under condition of protonation (with nitric acid/sulfuric acid) resulted in the preferential formation of the 4-nitro-substituted derivatives [3,4]. Upon bromination of **1a** and **1b** in an excess of aluminum trichloride (2.5 equivalents) without any solvent 4-substituted derivatives were isolated, though the formation of minor amounts of the 5-isomers cannot be excluded [5]. It should also be mentioned that quantum chemical calculations (CNDO/2) [6] predicted rather close similarity between selenophene and thiophene in positional selectivities in electrophilic substitution.

In this work quantitative data on positional selectivities of the aldehyde **1a** and the ketone **1b** upon bromination of their complexes with aluminum trichloride (Table 1) have been obtained for the first time. In addition the relative reactivities of complexes of the aldehyde **1a** and 2-thiophenecarbaldehyde (**1c**) have been studied using competitive bromination. The need for the latter study is due to the fact that the reactivity of the **1c**-aluminum trichloride complex is greater than that of the furfural-aluminum trichloride complex, while the reverse is true for the free

Table 1

Compositions of Mixtures (%) Formed on Bromination of Aluminum Trichloride Complexes of Selenophene and Thiophene Compounds

Bromination of Selenophene-2-carbaldehyde (**1a**)

	1a	**2a**	**3a**	**4a**
Glc [a]	19.4	3.2 (4.5)	69.0 (95.5)	8.4
^{1}H nmr	15	5	72	8

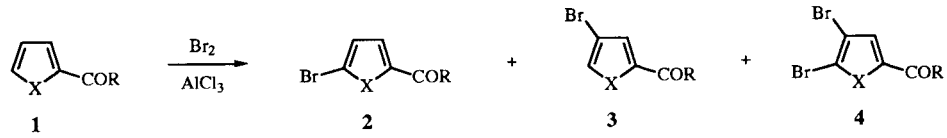
Bromination of 2-Acetylselenophene (**1b**)

Glc	21.0	6.6 (10.3)	58.0 (89.7)	12.0
^{1}H nmr	17	7	57	19

Competitive Bromination of Selenophene-2-carbaldehyde (**1a**) and Thiophene-2-carbaldehyde (**1c**) (3 equivalents of aluminum trichloride)

	1a/1c before the bromination	**1a/1c** after the bromination
Glc	44.2/55.8	26.1/73.9 [b]

[a] The ratio of monobrominated derivatives is given in brackets. [b] According to ^{1}H nmr the ratio is about 20/80.



a R = H, X = Se
b R = Me, X = Se
c R = H, X = S

aldehydes. The ^{1}H nmr and glc analyses were used in this study. The ^{1}H nmr data are given in Table 2; ratios of reagents used in various experiments are collected in Table 3.

We have shown that positional selectivities in bromination of **1a** and **1b** are noticeably lower than those of their thiophene analogues for which admixtures of 5-substituted derivatives formed under comparable conditions do not exceed 1% [7]. Upon bromination of compounds **1a** and **1b** in the presence of aluminum trichloride a considerable amount of 4,5-dibromo derivatives **4a** and **4b** were formed in addition to the 5- and 4-monobromo derivatives **2a,b** and **3a,b**, respectively. The orienting effect of the 2-acetyl group is lower than that of the 2-formyl group, as is also the case for the furan and thiophene derivatives. The reactivity of the the **1a**-aluminum trichloride complex is higher than that of the analogous complex of **1c**.

In the absence of aluminum trichloride (entry 1.5, Table 3) the bromination of **1a** occurs exclusively in the 5-position. With an equimolar amount of aluminum trichloride (entry 1.6, Table 3) this bromination practically does not occur at all (the yield of the 5-bromo-2-selenophenecarbaldehyde does not exceed 5%). This may be due to the fact that molecular bromine is not a sufficiently powerful electrophile to substitute a selenophene ring, which is strongly deactivated by the aluminum trichloride-complexed formyl group. A small aluminum trichloride excess (25%, entry 1.7, Table 3) does not apparently suppress the dissociation of the **1a**-aluminum trichloride complex; the ratio of the bromo derivatives **3a** and **2a** is approximately 80:20. A further increase of the aluminum trichloride quantity (1.8, 3.0 and 6.0 mole per mole of the aldehyde) leads to complete binding of the latter as the **1a**-aluminum trichloride complex, which results in practical identical product mixtures with a ratio of 95:5 of the 4- and 5-substituted derivatives, respectively, (entry 1-3, Table 3).

Similar results have been obtained for **1b**, the ratio of 4- and 5-substituted ketones, **3b:2b**, being equal to *ca.* 90:10, which corresponds to the lower electron-withdrawing ability of the substituent acetyl-aluminum trichloride complex compared to that of formyl-aluminum trichloride complex [8].

Thus, selenophene-2-carbaldehyde and 2-acetylselenophene in the form of the respective complexes with aluminum trichloride give upon bromination, like their thiophene analogs, predominantly 4-bromo-substituted derivatives. However, the amounts of the 5-isomers which are formed are considerably larger, which is apparently a con-

Table 2

^{1}H NMR Chemical Shifts (ppm) and Coupling Constants (Hz) for some Selenophene Derivatives in Deuteriochloroform

Compound	COR	H^3	H^4	H^5
1a	9.81 d	8.02 dd	7.47 dd	8.49 ddd
	J = 1.1	J_{34} = 3.9	J_{45} = 5.4	J_{35} = 1.2
2a	9.68	7.70 d	7.41 d	
		J_{34} = 4.2		
3a	9.75 d	7.92 d		8.35 dd
	J = 1.1			J_{35} = 1.4
4a	9.71 s	7.80 s		
1b	2.55 s	7.88 dd	7.36 dd	8.34 dd
		J_{34} = 3.9	J_{45} = 5.4	J_{35} = 1.1
2b	2.49 s	7.55 d	7.30 d	
		J_{34} = 4.3		
3b	2.53 s	7.80 d		8.21 d
				J_{35} = 1.4
4b	2.50 s	7.64 s		

Table 3

Bromination Conditions

Bromination of Selenophene-2-carbaldehyde (**1a**)

Entry	Substrate ml/μmole	Bromine ml/μmole	Aluminum Trichloride mg/μmole
1.1	2.4/221.8	1.7/224.4	53.4/400.5
1.2	2.2/203.3	1.54/203.3	80.0/600.0
1.3	2.2/203.3	1.54/203.3	160.1/1200.7
1.4	2.4/221.8	1.54/203.3	27/202.5
1.5	2.4/221.8	1.54/203.3	—
1.6	2.0/187.4	1.42/187.4	25/187.5
1.7	2.34/215.9	1.64/215.9	36/270.0

Bromination of 2-Acetylselenophene (**1b**)

2.1	1.98/200.8	1.52/200.6	54/405.0
2.2	2.46/249.4	1.89/249.5	80/600.0
2.3	1.98/200.8	1.52/200.6	175/1312.4

Competitive Bromination of Selenophene-2-carbaldehyde (**1a**) and Thiophene-2-carbaldehyde (**1c**)

3.1	2.35/217.1:1.8/217.8	1.65/217.8	145/1087.4
3.2	2.76/255.0:2.1/254.1	1.93/254.8	170/1274.9

sequence of greater positional selectivity (α:β-ratio) of unsubstituted selenophene as compared to thiophene. The formation of considerable amounts of dibromo-substituted derivatives should be mentioned which is reminiscent of the behavior of 2-acylfuran complexes [7].

EXPERIMENTAL

The ^1H nmr spectra were recorded on a Varian XL-300 instrument. Glc analyses were carried out on a Varian 3300 chromatograph using OV-17 (3% on Chromosorb) as stationary phase.

General Procedure for the Brominations.

Standard solutions of 2-selenophene carbaldehyde (734.4 mg in 50 ml, 92.4 μmoles/ml), 2-acetylselenophene (877.8 mg in 50 ml, 101.4 μmoles/ml), 2-thiophene carbaldehyde (345.5 mg in 25 ml, 121 μmoles/ml and bromine (1.054 mg in 50 ml, 132 μmoles/ml) in anhydrous methylene chloride were prepared. Sublimed aluminum trichloride was weighed under nitrogen in a glovebox. Then solutions of substrate (or substrates) were added kept for half an hour with stirring and a portion of the bromine solution was added to the reaction mixture according to Table 3.

The mixtures were stirred for 24 hours at room temperature, then poured into 10 ml of water and extracted with three 15 ml portions of chloroform. The organic phases were dried over magnesium sulfate filtered and evaporated.

Samples were dissolved in deuteriochloroform for nmr and glc measurements. For qualitative and quantitative glc anlysis of the products formed, samples of 5-bromo-2-selenophene carbaldehyde [9], 2-acetyl-5-bromoselenophene [10], 4-bromo-2-selonophene carbaldehyde [5] and 2-acetyl-4-bromoselenophene [5] were prepared according to literature.

4,5-Dibromo-2-selenophenecarbaldehyde and 2-Acetyl-4,5-dibromoselenophene.

One g of the 2-selenophenecarbonyl derivatives **1a** or **1b** was dissolved in 10 ml of anhydrous methylene chloride, mixed with three equivalents of aluminum trichloride with stirring for 20 minutes. Two equivalents of bromine were then added to the mixture. After stirring at room temperature for 24 hours the reaction mixture was poured into 20 ml of water and extracted with three 15 ml portions of chloroform. The combined organic phases were dried over magnesium sulfate filtered and evaporated. The solid residue was recrystallized from hexane.

4,5-Dibromo-2-selenophenecarbaldehyde.

This compound was obtained as gray needles, mp 81.5-82.5° (61%), lit mp 83° [11].

2-Acetyl-4,5-dibromoselenophene.

This compound was obtained as yellow-green prisms, mp 72-73° (54%).

Anal. Calcd. for $C_6H_4Br_2OSe$: C, 21.78; H, 1.22. Founds: C, 21.65; H, 1.30.

Acknowledgement.

The stay in Lund of D. M. A. was made possible by a grant from the Royal Swedish Academy of Sciences. We are grateful to Mrs. K. Petterson for the preparation of 2-acetylselenophene and 2-selenophenecarbaldehyde.

REFERENCES AND NOTES

[1] L. I. Belen'kii, *Heterocycles*, **37**, 2029 (1994).

[2] G. Marino, *Chem. Heterocyclic Comp. (USSR)*, 537 (1973).

[3] Yu. K. Yur'ev and E. L. Zaitseva, *J. Gen. Chem. (USSR)*, **30**, 873 (1960).

[4] Yu. K. Yur'ev and E. L. Zaitseva, *J. Gen. Chem. (USSR)*, **28**, 2203 (1958).

[5] V. I. Dulenko and N. N. Alekseev, *Chem. Heterocyclic Comp. (USSR)*, 845 (1973).

[6] L. I. Belen'kii and I. A. Abronin, *J. Org. Chem. (USSR)*, **17**, 997 (1981).

[7] L. I. Belen'kii, Ya. L. Gol'dfarb and G. P. Gromova, *Bull. Acad. Sci. (USSR), Chem. Ser.*, **22**, 2666 (1973).

[8] L. I. Belen'kii, V. S. Bogdanov and I. B. Karmanova, *Bull. Acad. Sci. (USSR), Chem. Ser.*, **28**, 1599 (1979).

[9] Yu. K. Yur'ev, N. N. Mezentseva and A. T. Monakhova, *J. Gen. Chem. (USSR)*, **30**, 2706 (1960).

[10] O. Karlsson, *Synth. Commun.*, **11**, 29 (1981).

[11] C. Paulmier, J. Morel, P. Pastour and D. Semard, *Bull. Soc. Chim. France*, 2511 (1969).