# CHEMISTRY OF BENZO[b]SELENOPHENE

## IV.* BROMINATION AND ACETYLATION OF BENZO[b]SELENOPHENE

N. N. Magdesieva and V. A. Vdovin

UDC 547.739.307:543.422.6:541.67

The bromination of benzo[b]selenophene with an equimolecular amount of bromine and its acetylation with acetic anhydride in the presence of boron trichloride etherate proceed to form a mixture of isomeric 2- and 3-substituted derivatives; 2,3-dibromobenzo[b]selenophene is formed on bromination with two equivalents of bromine. Benzo[b]selenophene-2-carboxylic acid, its acid chloride and methyl ester, as well as 2-acetylbenzo[b]selenophene, were synthesized from the lithium derivative of benzo[b]selenophene.

The literature contains only one communication [2] regarding the investigation of electrophilic substitution in the benzo[b]selenophene series. However, the site of entry of the substituents was not proved in this communication, and in analogy with benzo[b]thiophene, it was only assumed that the electrophilic substitution reactions of benzo[b]selenophene proceed unambiguously at the 3 position. In the present paper, we have investigated the bromination and acetylation of benzo[b]selenophene. The sites of entry of the substituents were determined by chemical means on the basis of the PMR spectra [3] and also by gas–liquid chromatography (GLC).

The PMR spectrum of the monobromide isolated from the products of the bromination of benzo[b]-selenophene with an equimolecular amount of bromine at 20°C contains intense singlets with chemical shifts of 7.73 and 7.33 ppm. The assignment of these signals to the $\alpha$- and $\beta$-protons of the selenophene ring was made with allowance for the fact that the chemical shifts of these protons in unsubstituted benzo-[b]selenophene are 7.76 and 7.36 [3], while bromine usually induces a slight shift of the signal of the adjacent proton in aromatic and heterocyclic compounds (from −0.04 to +0.01 ppm) [4-7]. Thus the monobromide isolated under the conditions indicated above is not a pure compound but a mixture of isomeric 2- and 3-bromobenzo[b]selenophenes.

We obtained 2-bromobenzo[b]selenophene by bromination of the 2-lithio derivative of benzo[b]selenophene at −70°. Dibromobenzo[b]selenophene was obtained by bromination of benzo[b]selenophene with two equivalents of bromine, and the debromination of 2,3-dibromobenzo[b]selenophene gave 3-bromobenzo[b]-selenophene.

The PMR spectrum of this dibromide in the region of aromatic protons contains two multiplets characteristic for benzo[b]selenophene derivatives [3] centered at ~7.60 and ~7.15 ppm; the spectrum does not contain singlets from $H_{(\alpha)}$ or $H_{(\beta)}$ protons. The PMR spectrum of 3-bromobenzo[b]selenophene contains an intense singlet with a chemical shift of 7.73 ppm ($\alpha$-proton), while the PMR spectrum of 2-bromobenzo[b]selenophene contains a singlet with a chemical shift of 7.33 ppm ($\beta$-proton) (Figs. 1 and 2).

Judging from the intensity of the singlets at 7.73 and 7.33 ppm, which corresponds to the resonance signals of the 2- and 3-protons of benzo[b]selenophene, it can be assumed that the monobromide obtained in the bromination of benzo[b]selenophene with one equivalent of bromine at 20° is a mixture of approximately equal amounts of 2- and 3-bromobenzoselenophenes. The composition of this mixture of isomeric

*See [1] for communication III.

M. V. Lomonosov Moscow State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 15-19, January, 1972. Original article submitted September 29, 1970.

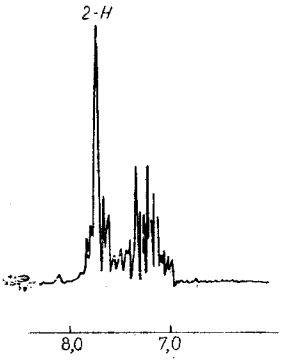



Fig. 1

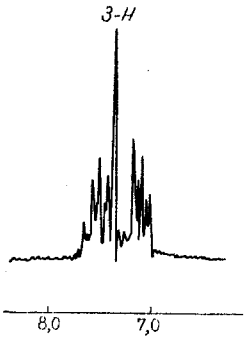



Fig. 2

Fig. 1. PMR spectrum of 3-bromobenzo[b]selenophene (10% solution in $CCl_4$).

Fig. 2. PMR spectrum of 2-bromobenzo[6]selenophene (10% solution in $CCl_4$).

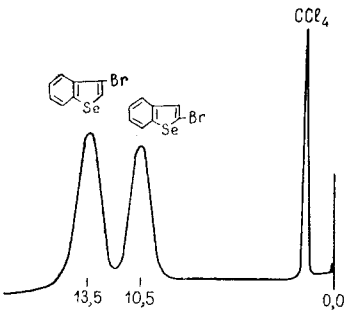



Fig. 3

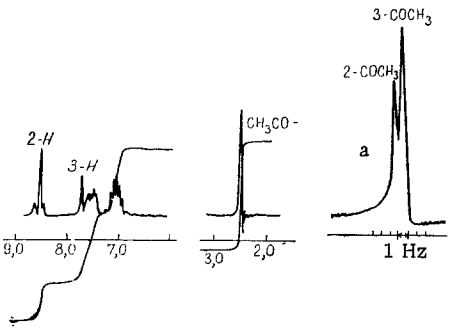



Fig. 4

Fig. 3. Chromatogram of the monobromide isolated from the products of the bromination of benzo[b]selenophene with an equimolecular amount of bromine at 20° in $CCl_4$.

Fig. 4. PMR spectrum of monoacetyl derivatives of benzo[b]selenophene isolated from the products of direct acetylation: a) signals of the methyl protons of the acetyl group.

TABLE 1. Chemical Shifts of the Protons in the Benzo[b]selenophene Derivatives

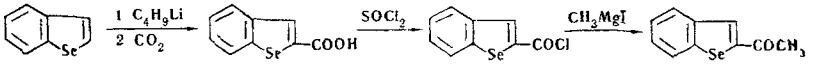
| Substituent | δ, ppm | | Functional group | Intensity ratio |
|---|---|---|---|---|
| | $H_{(2)}$ | $H_{(3)}$ | | |
| 2-COOH | — | 8,32 | 5,75 | 1 : 1 |
| 2-COCl | — | 8,41 | — | — |
| $2\text{-COOCH}_3$ | — | 8,17 | 3,85 | 1 : 3 |
| $2\text{-COCH}_3$ | — | 7,95 | 2,52 | 1 : 3 |
| $COCH_3$* | 8,75 | 7,95 | 2,32; 2,50 | 1 : 1 : 3 |
| H | 7,76 | 7,36 | — | — |
| 2-Br | — | 7,38 | — | — |
| 3-Br | 7,78 | — | — | — |
| $2,3\text{-Br}_2$ | — | — | — | — |
| Br† | 7,78 | 7,38 | — | — |

*Product of the direct acetylation of benzoselenophene.

†Product of direct bromination.

monobromides was also determined by means of GLC. An analysis of the chromatogram (Fig. 3) demonstrated that the mixture consists of 53% 3-bromo- and 47% 2-bromobenzo[b]selenophene. Gas–liquid chromatography also demonstrated that the monobromide isolated from the bromination of benzo[b]selenophene at – 5° in the presence of traces of iodine contains 85% 3-bromo- and 15% 2-bromobenzoselenophene.

The PMR spectra made it possible to demonstrate that the acetylation of benzo[b]selenophene with acetic anhydride in the presence of boron trifluoride at 50-60° also proceeds to form a mixture of isomeric 2- and 3-acetyl derivatives (Fig. 4). Crystallization of this mixture from alcohol yielded the 2-substituted isomer, which proved to be identical to 2-acetylbenzo[b]selenophene obtained by alternative synthesis via the following scheme:



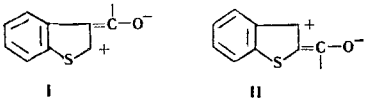
The data from the investigation of the PMR spectra of the benzo[b]selenophene derivatives obtained in this research are presented in Table 1.

The assignment of the singlet with a chemical shift of 8.75 ppm in the PMR spectrum of the monoacetyl derivative of benzo[b]selenophene (Fig. 4) to the signal of the proton in the 2 position was made on the basis of the fact that only the 2- and 3-protons form an MN spectrum [6]; in addition, this sort of signal is absent in the spectrum of 2-acetylbenzo[b]selenophene.

The signal of the methyl protons of the acetyl group in the spectrum of a mixture of monoacetyl derivatives of benzo[b]selenophene (Fig. 4) is split into two signals with an intensity ratio of 2:3 on scanning in the 50 Hz range. The same intensity ratio is observed for the signals with chemical shifts of 7.90 and 8.70 ppm, which corresponds to the $\alpha$- and $\beta$-protons of the selenophene ring. This is evidence that the mixture of monoacetyl derivatives of benzoselenophene consists of ~40% 2-acetyl- and ~60% 3-acetylbenzo[b]-selenophene.

The unshielding effect of carbonyl-containing acceptor substituents on the chemical shift of the proton in the 3 position is comparable to the corresponding values for benzo[b]thiophene derivatives [6, 7, 8].

Different shifts to the weak field of the signal of the proton in the 2 position (−0.96 ppm) and of the signal of the proton in the 3 position (−0.59 ppm) under the influence of the adjacent acetyl group are observed for 2-acetyl- and 3-acetylbenzo[b]selenophene. This is in good agreement with the data presented in [8, 9] for 2- and 3-carbonyl-containing derivatives of benzo[b]thiophene. The greater unshielding of the $H_{(2)}$ protons in the 3-substituted benzo[b]thiophene, as compared with the $H_{(3)}$ protons in the corresponding 2-substituted benzo[b]thiophenes, is explained [9] by the greater contribution of resonance structure I as compared with structure II:



I II

## EXPERIMENTAL

The PMR spectra were recorded with a Varian T-60 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard. The chemical shifts (Table 1) are given on the δ scale (obtained by the addition of 0.05 ppm to the chemical shift relative to HMDS).

The composition of the mixture of isomeric monobromides of benzo[b]selenophene was determined with a KhLM-8 chromatograph. A 3.5 meter-long column with a diameter of 4 mm was used for the separation. It was packed with 25% Apiezon Z on Chromosorb W. At a gas (nitrogen)-carrier rate of 50 ml/min and a temperature of 280°, the retention times of 2-bromobenzo[b]selenophene and 3-bromobenzo[b]-selenophene were 10.5 min and 13.5 min, respectively. (The retention time of benzo[b]selenophene under these conditions was 7 min.)

Bromination of Benzo[b]selenophene. A) A solution of 9.06 g (0.05 mole) of benzo[b]selenophene in 50 ml of dry chloroform and 6 g (0.075 mole) of anhydrous sodium acetate were placed in a 250-ml round bottom, three-necked flask equipped with a stirrer, dropping funnel, and reflux condenser. The mixture was stirred, and 2.65 ml (0.05 mole) of bromine in 20 ml of chloroform was added dropwise with stirring in the course of 30 min. The mixture was stirred at 20° for 30 min, and 100 ml of water was added. The chloroform layer was dried with sodium sulfate. The chloroform was removed by distillation, cetyl alcohol was added to the residue, and the mixture was vacuum distilled under nitrogen to give 4 g of the starting benzo[b]selenophene [fraction up to 148° (9 mm), $R_f$ 0.52 on Silufol in heptane], 3 g of monobromo derivatives of benzo[b]selenophene [148-155° fraction (9 mm), $R_f$ 0.58 on Silufol in heptane], and 2.7 g of the

dibromo derivative of benzo[b]selenophene [boiling above 155° (9 mm), mp 58° (from petroleum ether)]. The yield based on the benzo[b]selenophene consumed in the reaction was 40% for the monobromide and 29% for the dibromide of benzo[b]selenophene.

B) An iodine crystal was added to a solution of 4.5 g (0.025 mole) of benzo[b]selenophene in 50 ml of dry chloroform, and the mixture was cooled to − 5°. While maintaining this temperature, 1.35 ml (0.025 mole) of bromine in 20 ml of chloroform was added dropwise with stirring in the course of 1 h, and the mixture was then stirred for 30 min. The mixture was washed with sodium carbonate solution and water and dried with magnesium sulfate. The chloroform was removed by distillation, and the residue was vacuum distilled under nitrogen after the addition of cetyl alcohol to give 4.3 g (66%) of a mixture of monobromides with bp 150-155° (9 mm) and $R_f$ 0.58 on Silufol in heptane. Found: C 36.7; H 2.5%. $C_8H_5BrSe$. Calculated: C 36.9; H 1.9%.

2-Bromobenzo[b]selenophene. A solution of 3 ml (0.06 mole) of bromine in 20 ml of absolute ether was added at − 70° to an ether solution of the 2-lithio derivative of benzo[b]selenophene, obtained from 7.2 g (0.04 mole) of benzo[b]selenophene [3]. The mixture was stirred for 1 h, washed with 5% alkali solution and water, and dried with magnesium sulfate. The dried mixture was distilled in vacuo under nitrogen after the addition of cetyl alcohol to give 0.8 g of the starting benzo[b]selenophene [fraction up to 148° (15 mm), $R_f$ 0.52] and 3 g of 2-bromobenzo[b]selenophene [bp 148° (15 mm), $R_f$ 0.58 on Silufol in heptane, mp 58-58.5° (from petroleum ether)]. The yield based on the benzoselenophene consumed in the reaction was 32%. Found: C 37.2; H 2.1%. $C_8H_5BrSe$. Calculated: C 36.9; H 1.9%.

2,3-Dibromobenzo[b]selenophene. A solution of 6.15 ml (0.12 mole) of bromine in 20 ml of chloroform was added dropwise with stirring in the course of 2 h to a solution of 10.86 g (0.06 mole) of benzo[b]-selenophene in 100 ml of dry chloroform and 9.85 g (0.12 mole) of anhydrous sodium acetate. The mixture was washed with 2% sodium thiosulfate solution and water dried with magnesium sulfate. The chloroform was removed by distillation to give 19 g (93%) of 2,3-dibromobenzo[b]selenophene with mp 58° (from petroleum ether). Found: C 28.2; H 1.4%. $C_8H_4Br_2Se$. Calculated: C 28.3; H 1.2%.

3-Bromobenzo[b]selenophene. n-Butyllithium was obtained from 0.84 g (0.12 g-atom) of lithium and 6.5 ml (0.06 mole) of n-butyl bromide in 200 ml of absolute ether in a 500-ml round-bottom, four-necked flask equipped with a stirrer, dropping funnel, a nitrogen inlet tube, and a reflux condenser. A solution of 10.2 g (0.03 mole) of 2,3-dibromobenzo[b]selenophene in 100 ml of absolute ether was added under nitrogen to the cooled (− 70°) solution of butyllithium. The mixture was stirred for 1 h and diluted with 2 N HCl until it was acidic. The ether layer was separated, the ether was removed by distillation, and the residue was steam distilled. The distillate was extracted with ether, and the ether layer was dried with magnesium sulfate. Cetyl alcohol was added, and the mixture was vacuum distilled under nitrogen to give 3 g (38.5%) of 3-bromobenzo[b]selenophene with bp 150-152° (7 mm) and $R_f$ 0.58 on Silufol in petroleum ether. Found: C 37.3; H 2.2%. $C_8H_5BrSe$. Calculated: C 37.0; H 1.9%.

Acetylation of Benzo[b]selenophene. A 5.4 g (0.03 mole) sample of benzo[b]selenophene, 3.5 ml (0.035 mole) of acetic anhydride, and 1.5 ml of boron trifluoride etherate were placed in a 50-ml two-necked, round-bottom flask equipped with a mechanical stirrer and a reflux condenser with a calcium chloride tube. The reaction mixture was stirred at 50-60° for 3 h, washed with water, and extracted with 60 ml of chloroform. The chloroform solution was dried with sodium sulfate, and the reaction product was isolated by chromatography with a column filled with aluminum oxide with elution by chloroform ($R_f$ 0.78). The residue remaining after the chloroform was removed was vacuum distilled under nitrogen to give 5 g (75%) of a mixture of isomers in the form of a light-green liquid that partially crystallized on standing and had bp 165-169° (7 mm). Found: C 54.1; H 3.9%. $C_{10}H_8OSe$. Calculated: C 53.8; H 3.6%.

Benzo[b]selenophene-2-carboxylic Acid. An ether solution of the 2-lithio derivative of benzo[b]selenophene, obtained from 10.86 g (0.06 mole) of benzo[b]selenophene [3], was poured into a mixture of dry ice and absolute ether. The ether was removed, and the residue was dissolved in sodium carbonate solution. The solution was refluxed with activated charcoal and filtered. The filtrate was acidified to give 11 g (81%) of the 2-carboxylic acid with mp 238° (from benzene) (mp 238° [10]).

Acid Chloride of Benzo[b]selenophene-2-carboxylic Acid. A solution of 3.85 g (0.017 mole) of benzo-[b]selenophen-2-carboxylic acid in 50 ml of benzene containing 5 ml (0.07 mole) of thionyl chloride was refluxed for 2 h in a 100-ml round-bottom flask equipped with a reflux condenser fitted with a calcium chloride tube. The solvent was removed by vacuum distillation under nitrogen to give 3.9 g (67%) of the acid chloride with mp 68° (from petroleum ether). Found: C 44.9; H 2.4%. $C_9H_5ClOSe$. Calculated: C 44.3; H 2.1%.

2-Acetylbenzo[b]selenophene. A solution of methylmagnesium iodide was prepared from 1 g (0.04 g-atom) of magnesium and 2.25 ml (0.036 mole) of methyl iodide in 50 ml of absolute ether in a 100-ml four-necked, round-bottom flask equipped with a stirrer, dropping funnel, and reflux condenser with a calcium chloride tube. Anhydrous cadmium chloride [1.83 g (0.01 mole)] was added, the reflux condenser was fitted for distillation, and the solvent was removed by distillation. Absolute benzene (20 ml) was added, and the mixture was distilled. Another 5 ml of absolute benzene was added. The mixture was then cooled with ice water, 3.6 g (0.015 mole) of the acid chloride of benzo[b]selenophene-2-carboxylic acid in 30 ml of absolute ether was added dropwise, and the mixture was stirred for 2 h. It was then heated on a water bath, and solvent residues were removed by distillation. Ice water was added to the cooled residue, and the resulting precipitate was removed by filtration and dried. The dry residue was chromatographed with a column filled with aluminum oxide with elution by chloroform ($R_f$ 0.78) to give 2.4 g (72%) of 2-acetylbenzo-[b]selenophene as colorless needles with mp 99°. Found: C 54.3; H 4.0%. $C_{10}H_8OSe$. Calculated: C 53.8; H 3.6%. The 2,4-dinitrophenylhydrazone had mp 279° (dec., from dioxane). Found: C 47.9; H 3.3%. $C_{16}H_{12}O_4N_4Se$. Calculated: C 47.6; H 3.0%.

Methyl Benzo[b]selenophene-2-carboxylate. An 11.25 g (0.06 mole) sample of benzo[b]selenophene-2-carboxylic acid in 300 ml of ether was allowed to stand for 2 h at 0° with 200 ml of an ether solution of diazomethane obtained from 20.6 g (0.2 mole) of nitrosomethylurea and 70 ml of 50% potassium hydroxide. The ether was removed by distillation to give 11.65 g (97%) of the methyl ester with mp 65° (from petroleum ether) (mp 65° [10]).

## LITERATURE CITED


1. N. N. Magdesieva and V. A. Vdovin, Khim. Geterotsikl. Soedin., 1640 (1971).
2. G. Komppa and G. A. Nyman, J. prakt. Chem., 139, 229 (1934).
3. N. N. Magdesieva, V. A. Vdovin, and N. M. Sergeev, Khim. Geterotsikl. Soedin., 1382 (1971).
4. J. Emsley, J. Finney, and L. Sutcliffe, High-Resolution Nuclear Magnetic Resonance, Pergamon.
5. A. R. Katritzky (editor), Physical Methods in the Heterocyclic Chemistry, Academic Press (1963).
6. K. Takahashi and T. Kanda, Bull. Chem. Soc. Japan, 38, 508 (1965).
7. B. Caddy, M. Smith, R. Norris, S. Reid, and S. Sternhell, Austral. J. Chem., 21, 1853 (1968).
8. P. Faller, Bull. Soc. Chim. France, 934 (1969).
9. N. Chapman, D. Ewing, R. Schrowston, and R. Westwood, J. Chem. Soc., C, 764 (1968).
10. L. Christians and M. Renson, Bull. Soc. Chim. Belg., 77, 153 (1968).