SYNTHESIS OF BENZO[b]SELENOPHENE AND ITS METHYL HOMOLOGS

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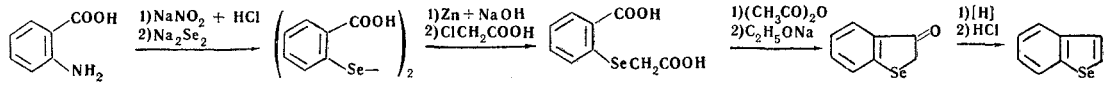
UDC 547.739.3.07:543.422.6:541.67

A method for the synthesis of benzo[b]selenophenes was perfected. 3-Oxo-2,3-dihydrobenzo[b]selenophene and 2-methyl-3-oxo-2,3-dihydrobenzo[b]selenophene exist only in the keto form. 3-Methylbenzo[b]selenophene was obtained by the reaction of 3-oxo-2,3-dihydrobenzo[b]selenophene with methylmagnesium iodide. Metallation of benzo[b]selenophene with butyllithium proceeds at the 2 position of the selenophene ring.

Several methods for obtaining benzo[b]selenophene are known: reaction of selenium dioxide with styrene in the presence of chromic oxide on aluminum oxide [1], reaction of selenophenol with bromoacetaldehyde dimethylacetal [2], and reaction of o-chlorobenzaldehyde with sodium diselenide and chloroacetic acid [3]. However, the synthesis of benzo[b]selenophene from anthranilic acid via the following scheme is still the most convenient method:



In this study we used this method to synthesize benzo[b]selenophene and 2-methylbenzo[b]selenophene. We introduced changes into this method which made it possible to significantly raise the product yields in almost all steps. Thus, we carried out the reaction of diazotized anthranilic acid with sodium diselenide under nitrogen in order to prevent oxidation of sodium diselenide and obtained diselenosalicylic acid in 95% yield. We accomplished the cyclization of o-carboxyphenylselenoacetic acid with subsequent distillation of the acetic anhydride in vacuo and hydrolyzed the 3-acetoxybenzo[b]selenophene formed with alcoholic alkali, again under nitrogen, and monitored the completion of the reaction with thin-layer chromatography. This enabled us to obtain benzo-selenophen-3-one in 80% yield. Finally, we used sodium borohydride to reduce 3-oxo-2,3-dihydrobenzo[b]selenophene and obtained benzo[b]selenophene in 92% yield rather than the 58% yield reported in [4].

Since the literature contains contradictory opinions as to in which of the two tautomeric forms selenoindoxyl exists [5, 6], in this study we have isolated the so-called selenoindoxyl and 2-methylselenoindoxyl and have established their structures by means of physicochemical and chemical methods. Carbonyl absorption bands at 1700 cm^{-1} of completely identical intensity were observed in the IR spectra of 0.1-M solutions of 3-oxo-2,3-dihydrobenzo[b]selenophene and its 2-methyl homolog in both polar (dimethoxyethane) and nonpolar (carbon tetrachloride) solvents (Fig. 1). Consequently, the solvent polarity does not affect the shift in the keto-enol equilibrium and confirms the ketone structure of these compounds. This structure was also confirmed from their NMR spectra (Fig. 2). The NMR spectrum of I has a singlet with a chemical shift of 3.71 ppm relative to hexamethyldisiloxane, which corresponds to the resonance of the methylene protons, and a multiplet from the protons of the benzene ring from 7.13-7.59 ppm (intensity ratio 1:2). The NMR spectrum of II contains a doublet from the protons of the methyl group with a chemical shift of 1.59 ppm (J = 7.5 Hz), a quartet from the proton of the $-CH$ group with a chemical shift of 4.00 ppm (J = 7.5 Hz), and signals from the four protons of the benzene ring at 7.06-7.58 ppm (intensity ratio 3:1:4).

M. V. Lomonosov Moscow State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1475-1480, November, 1970. Original article submitted May 12, 1969.

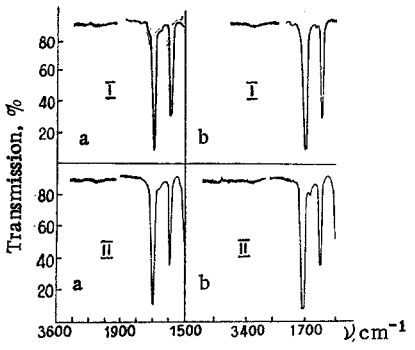


Fig. 1

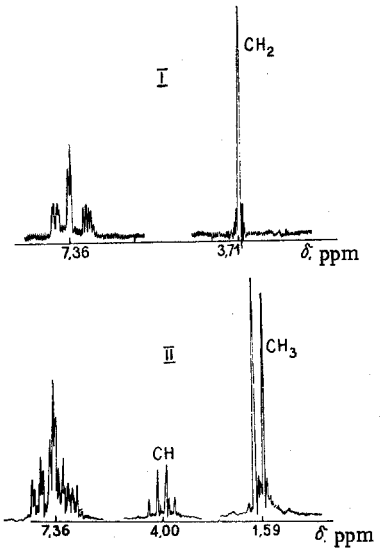
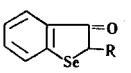


Fig. 2

Fig. 1. IR spectra of 0.1-M solutions of 3-oxo-2,3-dihydrobenzo[b]selenophene (I) and 2-methyl-3-oxo-2,3-dihydrobenzo[b]selenophene (II). a) In CCl_4; b) in dimethoxyethane (obtained with a UR-20 spectrophotometer).

Fig. 2. NMR spectra of 3-oxo-2,3-dihydrobenzo[b]selenophene (I) and 2-methyl-3-oxo-2,3-dihydrobenzo[b]selenophene (II) (obtained in CCl_4 with a C-60 HL spectrophotometer at an operating frequency of 60 MHz with hexamethyldisiloxane as the internal standard).

TABLE 1. UV Spectra of 3-Oxo-2,3-dihydrobenzo-[b]selenophenes

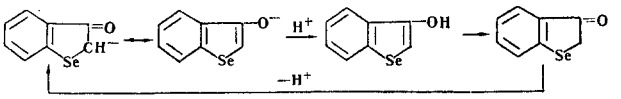


λ_{max}, nm (lg ε)	
R=CH₃	R=H
243 (4,52) 264 (3,72) 312 (2,30) 377 (3,18)	242 (4,54) 262 (3,81) 315 (2,68) 372 (3,39)

The UV spectra of I and II, obtained in ethanol, contain the same absorption maxima of approximately equal intensity and satisfactorily agree with the UV spectrum of selenonaphthen-3-one [6] (see Table 1).

As for the keto-enol equilibrium of the closest sulfur analog of I – thionaphthen-3-one – the ketone form of this compound is contained exclusively in solutions with pH < 8, as was shown [7] during an investigation of the polarographic reduction of solutions of this compound at various pH values. In alkaline media a mesomeric anion is formed, the attack on which by a proton during acidification gives the unstable enol, which is immediately again converted to the keto form. Such keto-enol transformations can apparently occur for I also.

The following facts speak in favor of this conclusion. First, an alkaline solution of I is rapidly oxidized by air oxygen, while the substance is stable in solutions with pH < 8. Second, all attempts to alkylate I with diazomethane were unsuccessful, i.e., the enol form of this compound is absent in solutions with pH < 8.



At the same time, reactions at the carbonyl group proceed in quantitative yields. We obtained the 2,4-dinitrophenylhydrazones of I and II. In addition, the carbonyl group of these ketones is readily reduced with sodium borohydride. Finally, I reacts at the carbonyl group with methylmagnesium iodide to form, after dehydration of the alcohol obtained, 3-methylbenzo[b]selenophene.

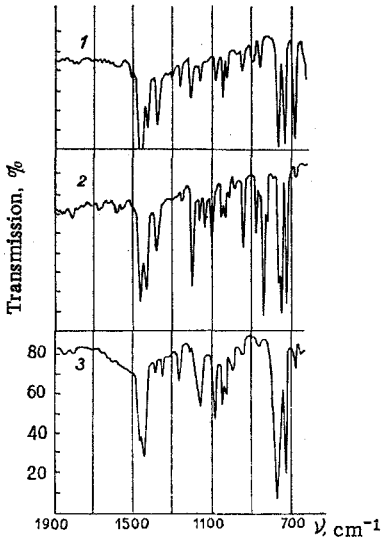


Fig. 3

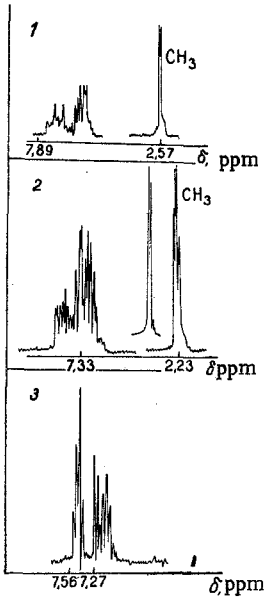
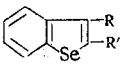


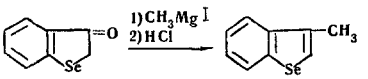
Fig. 4

Fig. 3. IR spectra of: 1) benzo[b]selenophene; 2) 2-methylbenzo[b]selenophene (in mineral oil); 3) 3-methylbenzo[b]selenophene (obtained with a UR-20 spectrophotometer).

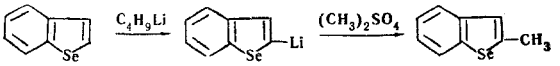
Fig. 4. NMR spectra of: 1) benzo[b]selenophene; 2) 3-methylbenzo[b]selenophene; 3) 2-methylbenzo[b]selenophene (C-60 HL spectrometer, CCl_4 solutions, hexamethyldisiloxane internal standard).

TABLE 2. UV Spectra of Benzo[b]selenophenes 

λ_{max}, nm (lg ε)		
R=CH₃; R′=H	R=R′=H	R=H; R′=CH₃
304 (3,30)	305 (3,80)	306 (3,79)
295 (3,08)	296 (3,63)	297 (3,64)
261 (3,45)	261 (3,74)	262 (3,63)
237 (4,05)	236 (4,41)	237 (4,52)



In this study we obtained 2-methylbenzo[b[selenophene via two routes – reduction of II with sodium borohydride with subsequent dehydration of the alcohol formed with hydrochloric acid, and by alkylation of the lithium derivative of benzo[b]selenophene with dimethyl sulfate.



The preparations were identical (absence of a depression of the melting point of a mixed sample and complete identity of their IR and NMR spectra). Thus, we were able to show that metallation of benzo[b]-selenophene with butyllithium occurs at the 2 position of the selenophene ring.

It should be noted that benzo[b]selenophene and its 2- and 3-methyl homologs have the same chromatographic mobility in a thin layer of aluminum oxide. Thus, in hexane the R_f values are 0.68, compared with 0.92 in benzene.

No substantial difference in the electron transitions was observed in the UV spectra of benzo[b]-selenophene and its homologs (Table 2).

The IR spectra of all of the benzo[b]selenophenes that we synthesized contain intense absorption bands at 720-740 cm^{-1} (Fig. 3), which were assigned [8] to in-plane deformation vibrations of the C−H bonds of the selenophene ring. This involves the absorption band at 736 cm^{-1} for benzo[b]selenophene, 725 cm^{-1} for 2-methylbenzo[b]selenophene, and 723 cm^{-1} for 3-methylbenzo[b]selenophene. In analogy with the assignments of the γ-CH vibrations of thionaphthene and alkylthionaphthenes [9], the following absorption bands should most likely be assigned to the deformation vibrations of the remaining C−H bonds: 680, 762, 855, 890, and 945 cm^{-1} for benzo[b]selenophene; 762, 840, 873, and 941 cm^{-1} for 2-methylbenzo-[b]selenophene; and 768, 855, 860, and 941 cm^{-1} for 3-methylbenzo[b]selenophene. Benzo[b]selenophene and benzo[b]thiophene [9] have the same absorption bands in their IR spectra over a broad range of frequencies: 1045, 1080, 1160, 1207, 1260, 1313, 1380, 1430, and 1460 cm^{-1} (Fig. 3). A similar correspondence can be noted for 3-methylbenzo[b]selenophene (1030, 1045, 1082, 1155, 1265, 1352, 1385, 1450, and 1455 cm^{-1}) and 2-methylbenzo[b]selenophene (1015, 1025, 1140, 1160, 1200, 1255, 1300, 1380, 1438, and 1460 cm^{-1}) and their sulfur analogs [10, 11].

The NMR spectra (Fig. 4) of the methyl homologs of benzo[b]selenophene that we synthesized contain doublets from the methyl protons with chemical shifts of 2.57 ppm relative to hexamethyldisiloxane (J = 1.3 Hz) for 2-methylbenzo[b]selenophene and 2.25 ppm (J = 1.2 Hz) for 3-methylbenzo[b]selenophene. The regularity noted for the chemical shifts of the methyl protons of the corresponding sulfur- and oxygen-containing isologs [12] is also observed here.

EXPERIMENTAL

2-Methyl-3-oxo-2,3-dihydrobenzo[b]selenophene. A mixture of 10 g (0.037 mole) of α-(o-carboxyphenyl)selenopropionic acid, obtained by condensation of sodium α-bromopropionate with sodium o-carboxyselenophenoxide, and 10 g of anhydrous sodium acetate was refluxed in 80 ml of acetic anhydride for 1 h. The acetic anhydride was then removed in vacuo under nitrogen. An alcoholic alkali solution was added to the residue until an alkaline medium was obtained, and the mixture was heated under nitrogen for 30 min. The completion of the hydrolysis was monitored with thin-layer chromatography on aluminum oxide* using benzene as the solvent. The disappearance of the spot with R_f 0.7, characteristic for 3-acetoxy-2-methylbenzo[b]selenophene, indicated the completion of hydrolysis. The solution was cooled to 0°, acidified with 2-N hydrochloric acid, and extracted with ether. The ether extracts were dried with sodium sulfate, the ether was removed, and the residue was distilled in vacuo under nitrogen to give 4 g (52%) of a light-green liquid with a characteristic odor, bp 134-135° (7 mm), and n_D^{20} 1.6550. The liquid was rapidly oxidized in air. Found %: C 51.5; H 3.7. C_9H_8OSe. Calculated %: C 51.2; H 3.8. The 2,4-dinitrophenylhydrazone was prepared by dissolving 1.2 g (0.006 mole) of 2,4-dinitrophenylhydrazine in 50 ml of 30% perchloric acid and 100 ml of water and adding to it, with stirring, a solution of 0.63 g (0.003 mole) of 2-methyl-3-oxo-2,3-dihydrobenzo[b]selenophene in 10 ml of methanol. The yield was quantitative (1.1 g) and the product had mp 235° (decomp., from ethyl acetate). Found %: C 46.2; H 3.2. $C_{15}H_{12}N_4O_4Se$. Calculated %: C 46.0; H 3.1.

3-Oxo-2,3-dihydrobenzo[b]selenophene. This was similarly obtained in 80% yield. It was purified by steam distillation to give a substance with mp 70° [6] (from hexane) and R_f 0.53 (benzene).

Benzo[b]selenophene. Pulverized sodium borohydride [6.5 g (0.17 mole)] was added to a solution of 34 g (0.17 mole) of 3-oxo-2,3-dihydrobenzo[b]selenophene in 0.5 liter of ethanol. The completeness of the reduction was monitored chromatographically. Concentrated hydrochloric acid (100 ml) was then added with stirring, and the mixture was refluxed for 30 min. The mixture was cooled to −15°, and the residue was filtered by suction and washed with water to give 27 g of product. Another 1.6 g of product was precipitated with water from the alcohol filtrate to give an overall yield of 92% of product with mp 50° [6] (after recrystallization from alcohol and vacuum sublimation).

2-Methylbenzo[b]selenophene. A. This compound [3.2 g (78%)] was obtained from 4.22 g of 2-methyl-3-oxo-2,3-dihydrobenzo[b]selenophene via the method described for the preparation of benzo[b]selenophene and had mp 62° (recrystallization from alcohol and vacuum sublimation) (mp 63° [13]).

*Activity II aluminum oxide was used.

B. A solution of 3.6 g (0.02 mole) of benzo[b]selenophene in 20 ml of absolute ether was added with stirring under nitrogen to a solution of butyllithium [from 0.56 g (0.08 g-atom) of Li and 4.3 ml (0.04 mole) of n-butyl bromide] in 30 ml of absolute ether. The mixture was refluxed for 30 min, cooled to 0°, and a solution of 2.52 g (0.02 mole) of dimethyl sulfate in 10 ml of absolute ether was added to it with stirring. The mixture was stirred until the temperature of the reaction mixture exceeded 20°, after which it was refluxed for 30 min. The mixture was drenched with 100 ml of water, and the ether layer was separated and dried with sodium sulfate. The residue after removal of ether was distilled in vacuo to give 3.1 g (79%) of a product with bp 122° (8 mm) and mp 62° (from alcohol and vacuum sublimation).

A mixed sample of 2-methylbenzo[b]selenophene obtained by both paths did not display a melting-point depression.

3-Methylbenzo[b]selenophene. A solution of 19.7 g (0.1 mole) of 3-oxo-2,3-dihydrobenzo[b]selenophene in 0.3 liter of absolute ether was added to a solution of methylmagnesium iodide [from 10.2 g (0.4 g-atom) of magnesium and 27.2 ml (0.4 mole) of methyl iodide] in 0.5 liter of absolute ether. The mixture was heated and stirred on a water bath for 2 h. Concentrated hydrochloric acid [150 ml (sp. gr. 1.19)] was added, and the mixture was refluxed for 30 min. Water (300 ml) was added, and the ether layer was separated and dried with sodium sulfate. The ether was removed, and the precipitated starting ketone (2 g) was filtered. 3-Methylbenzo[b]selenophene was isolated from the filtrate by column chromatography with aluminum oxide and hexane eluent. After removal of the hexane the residue was distilled in vacuo to give 6.85 g (40%) of a product with bp 115° (7 mm) and n_D^{20} 1.6572. Found %: C 55.3; H 4.0. C_9H_8Se. Calculated %: C 55.3; H 4.1.

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