THE CHEMISTRY OF SELENOPHENE

LX. The Direction of Enolization in β-Diketones of the Selenophene Series with a 3-Selenienyl Radical*

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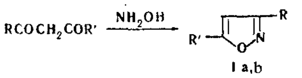
In the present work it has been shown that 3-(2-selenenoylacetyl)-selenophene is enolized at the carboxyl group adjacent to the 2-selenienyl radical and 3-(benzoylacetyl)selenophene at the carboxyl group adjacent to the phenyl radical (judging from the formation of the corresponding isoxazoles by the reaction of these diketones with hydroxylamine). On reduction with lithium aluminum hydride, methyl 3-selenophenecarboxylate has given 3-selenienylmethanol and the nitrile of the same acid has yielded 3-selenophenealdehyde. Several new chalcones and isoxazoles with β-selenienyl radicals have been described.

In our preceding papers [1,2] it was shown that the reaction of β-diketones of the selenophene series with hydroxylamine, taking place with the formation of the corresponding disubstituted isoxazoles, permits a determination of the direction of enolization in β-diketones containing a phenyl or α-thienyl radical in addition to the α-selenienyl radical. It was established that the capacity of these aromatic systems for causing the enolization of a neighboring carbonyl group rises in the sequence $C_6H_5 < \alpha\text{-}C_4H_3Se < \alpha\text{-}C_4H_3S$.

In the present work we have used the same reaction to determine the direction of enolization in β-diketones in which the influence of a β-selenienyl radical and that of an α-selenienyl or a phenyl radical compete.

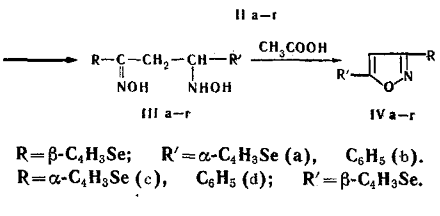
The reaction of 3-(2-selenenoylacetyl)selenophene [3] and 3-(benzoylacetyl) selenophene [3] with hydroxylamine gave 5-(α-selenienyl)-3-(β-selenienyl)isoxazole (yield 94.5%) and 5-phenyl-3-(β-selenienyl)-isoxazole (92.5%), respectively:



I a,b

$R=\beta\text{-}C_4H_3Se$; $R'=\alpha\text{-}C_4H_3Se$(a), C_6H_5(b).

The structure of the isoxazole **Ia** was shown by the independent synthesis of it and the isomeric 3-(α-selenienyl)-5-(β-selenienyl)isoxazole by the reaction of the corresponding chalcones with hydroxylamine and the subsequent cyclization, in the presence of acetic acid, of the hydroxyamino oximes formed:



III a–r IV a–r

$R=\beta\text{-}C_4H_3Se$; $R'=\alpha\text{-}C_4H_3Se$ (a), C_6H_5 (b).
$R=\alpha\text{-}C_4H_3Se$ (c), C_6H_5 (d); $R'=\beta\text{-}C_4H_3Se$.

The initial chalcones [3-(2-selenenylideneacetyl)-selenophene and 2-(selenenylideneacetyl)selenophene] were obtained by the condensation in the presence of alcoholic alkali of 2-selenophenealdehyde with 3-acetylselenophene and of 3-selenophenealdehyde with 2-acetylselenophene, respectively.

The isoxazole **Ia** was identical with the isoxazole **IVa**, judging from the melting point (a mixture gave no depression), the IR and UV spectra, and the results of chromatography in a thin layer of alumina in benzene, but differed from the isoxazole **IVc** in respect to its melting point and UV spectrum.

The results obtained show that 3-(2-selenenoylacetyl)selenophene is enolized at the carbonyl group adjacent to the α-selenienyl radical.

The reaction of 3-(benzoylacetyl)selenophene with hydroxylamine led to the formation of 5-phenyl-3-(β-selenienyl)isoxazole (**Ib**), which was identical with respect to its melting point, IR and UV spectra, and the results of chromatography in a thin layer of alumina in benzene with the isoxazole **IVb** but differed from the isomeric 3-phenyl-5-(β-selenienyl)-isoxazole (**IVd**) with respect to its melting point and UV spectrum.

On the basis of the results obtained, it was established that 3-(benzoylacetyl)selenophene is enolized at the carbonyl group adjacent to the phenyl ring.

Thus, in β-diketones of the selenophene series with a 3-selenienyl radical the capacity of the substituents for causing enolization of an adjacent carbonyl group rises in the sequence β-selenienyl < phenyl < α-selenienyl.

A comparison of the electron-accepting properties of these radicals from the strength of the corresponding monocarboxylic acids enables them to be arranged in an analogous sequence: pK_a in water at 25° C (determined by the potentiometric titration method) is $2.61 \cdot 10^{-5}$ for 3-selenophenecarboxylic acid, $6.46 \cdot 10^{-5}$ for benzoic acid, and $2.63 \cdot 10^{-4}$ for 2-selenophenecarboxylic acid [2]; the same relationship exists for the dissociation constants of the β-diketones containing the same radicals [4, 5].

Consequently, in the cases considered above, the enolization of the β-diketones takes place at the carbonyl group adjacent to the more strongly electron-accepting substituent.

3-Selenophenealdehyde, the starting material for the synthesis of the chalcones **IIc** and **IId**, was obtained by the lithium aluminum hydride reduction of 3-selenophenecarbonitrile (isolated in the form of its simplest derivatives):

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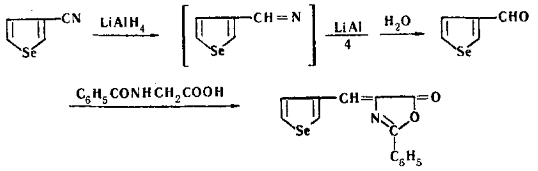
*For part LIX, see [5].

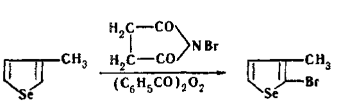
Table 1

Chalcones, RCOCH = CHR'

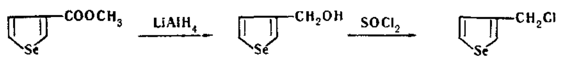
Compound	R	R'	Mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %
					C	H	C	H	
IIa	β-C_4H_3Se	α-C_4H_3Se	89.5—91	$C_{11}H_8OSe_2$	42.17 42.15	2.56 2.77	42.06	2.57	87
IIb	β-C_4H_3Se	C_6H_5	107—108	$C_{13}H_{10}OSe$	60.02 59.82	3.80 4.08	59.78	3.85	87
IIc	α-C_4H_3Se	β-C_4H_3Se	69—69.5	$C_{11}H_8OSe_2$	42.07 42.26	2.40 2.67	42.06	2.57	61.5
IId	C_6H_5	β-C_4H_3Se	88—89	$C_{13}H_{10}OSe$	60.18 60.24	3.87 3.84	59.78	3.85	77



It is known that 3-thiophenealdehyde can easily be obtained by the Sommlet reaction from 3-bromomethylthiophene [6]; however, this reaction could not be carried out in a selenophene series since when 3-methylselenophene was brominated with bromosuccinimide in the presence of benzoyl peroxide only the α-hydrogen of the selenophene ring was replaced by bromine.



Consequently, attempts were made to obtain 3-selenophenealdehyde from 3-chloromethylselenophene by the Sommlet reaction [7]. The lithium aluminum hydride reduction of methyl 3-selenophenecarboxylate with the subsequent replacement of the hydroxyl in the 3-selenienylmethanol formed by chlorine yielded 3-chloromethylselenophene, which was isolated in the form of the thiouronium picrate.



An attempt to obtain 3-selenophenealdehyde by the reaction of 3-bromoselenophene with dimethylformamide was also unsuccessful, although in the thiophene series 3-thiophenealdehyde has been obtained in 70% yield by this reaction [8].

EXPERIMENTAL

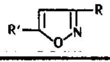
Chalcones with a β-selenienyl radical (IIa-d). Three milliliters of a saturated solution of caustic soda in methanol was added to 35 mmole of 2-selenophenealdehyde and 35 mmole of 3-acetylselenophene in 150 ml of absolute methanol, the mixture was left at 20°C for 48 hr, the solvent was distilled off, and the residue of IIa was washed with water and recrystallized from heptane (Table 1). The other chalcones IIb-d were obtained similarly (Table 1).

Oxime of 2-hydroxyamino-1-phenyl-2-(3-selenenoyl)ethane (IIIb). A solution of 18 mmole of 3-(benzylideneacetyl)selenophene and 18 mmole of hydroxylamine hydrochloride in 150 ml of ethanol was treated with 95 ml of 10% aqueous caustic soda, boiled in the water bath for 2 hr, left to stand for 20 hr, poured into 500 ml of water, and extracted with ether, after which the ethereal extract was dried with magnesium sulfate and the ether was distilled off in vacuum to give 4.5 mmole of the oxime IIIb (25%) with mp 186°–187°C (from 60% aqueous ethanol). Found, %: 51.28, 51.20; H 4.36, 4.23. Calculated for $C_{13}H_{14}N_2O_2Se$, %: C 50.49; H 4.56.

Compounds IIIa, c, and d were obtained by the same method in the form of noncrystallizing oils with yields of 31.5, 19, and 30%, respectively.

The isoxazoles Ia and Ib. A mixture of 1 mmole of 3-(2-selenenoylacetyl)selenophene or 3-(benzoylacetyl)selenophene and 3 mmole of hydroxylamine hydrochloride in 2 ml of dry pyridine and 10 ml of anhydrous ethanol was boiled in the water bath for 4 hr and poured into 200 ml of water; the precipitate was filtered off and washed with 50% aqueous ethanol, and the isoxazole was recrystallized from heptane (Table 2).

Table 2

Isoxazoles 

Compound	R	R'	Mp, °C	Empirical formula	Found, %		Calculated, %		UV spectrum		Yield, %
					C	H	C	H	λ_{max}, nm	log	
Ia	β-C_4H_3Se	α-C_4H_3Se	107.5—109	$C_{11}H_7NOSe_2$	40.81 40.69	2.28 2.25	40.39	2.16	270 295	4.30 4.30	94.5
IVa			107.5—109		40.84 40.85	2.14 1.92			270 295	4,30 4,30	91.5
Ib	β-C_4H_3Se	C_6H_5	121—121.5	$C_{13}H_9NOSe$	56.68 57.43	3.47 3.48	56.95	3.31	273	4.48	92.5
IVb			120.5—121.5		56.97 57.20	3.26 3.33			273	4.49	85
IVc	α-C_4H_3Se	β-C_4H_3Se	104.5—106	$C_{11}H_7NOSe_2$	40.44 40.40	2.31 2.22	40.39	2,16	226 278	4.26 4.40	59
IVd	C_6H_5	β-C_4H_3Se	118.5—119	$C_{13}H_9NOSe$	57.36 57.39	3.12 3.27	56.95	3.31	285	4.26	73.5

The isoxazoles IVa-d. A solution of 4 mmole of a hydroxyaminoketone oxime IIIa-d (obtained from the corresponding chalcone) in 20 ml of glacial acetic acid was boiled in the oil bath at 125°C for 2 hr and was poured into 200 ml of water, and the mixture was made alkaline with 2 N aqueous caustic soda solution. The precipitate was filtered off and washed with water, and the isoxazole obtained was recrystallized from heptane (Table 2).

2-Bromo-3-methylselenophene. With stirring and ice cooling, 24 g of N-bromosuccinimide and 0.2 g of benzoyl peroxide were added to 20 g of 3-methylselenophene in 50 ml of absolute benzene containing 0.2 g of benzoyl peroxide. The succinimide was separated off and washed with absolute benzene. After the benzene had been driven off, vacuum distillation of the residue yielded 22.5 g (74%) of the bromide: bp 70°C (10 mm) d_4^{20} 1.9271; n_D^{20} 1.6131. Found, %: C 27.02, 26.94; H 2.35, 2.48; MR_D 40.45. Calculated for $C_5H_5BrSeF_2$, %: C 26.81; H 2.20; MR_D 40.56.

3-Selenienylmethanol. To 4.8 g of lithium aluminum hydride in 200 ml of absolute ether was added 22.2 g of methyl 3-selenophenecarboxylate, bp 95°C (12 mm)[3], in 150 ml of absolute ether at such a rate that the ether boiled gently; it was heated at 40°C for another 1 hr and left at 20°C for 20 hr and was then decomposed with 200 ml of 20% Rochelle salt solution. The ethereal layer was separated off and the aqueous layer was extracted with ether in a liquid extractor for 30 hr. The ethereal solutions were dried with magnesium sulfate, the solvent was evaporated off, and the residue was distilled in vacuum. This gave 19 g (90%) of a substance with bp 110°C (10 mm); d_4^{20} 1.6250; n_D^{20} 1.6027. Found, %: C 37.82, 37.83; H 3.77, 3.48; MR_D 34.05. Calculated for $C_5H_6OSeF_2$, %: C 37.29; H 3.78; MR_D 34.29 **Phenylurethane,** yield 92%, mp 60.5-61.5°C (from petroleum ether). Found %: C 52.00, 51.82; H 3.96, 4.07. Calculated for $C_{12}H_{11}NO_2Se$, %: C 51.44; H 3.96.

3-Chloromethylselenophene. With stirring at -10°C, 8.4 ml of thionyl chloride in 200 ml of chloroform was added dropwise to 14 g of 3-selenienylmethanol in 30 ml of dry chloroform and 18 ml of dry pyridine and the mixture was stirred at -15°C for 1 hr and was poured onto ice; the organic layer was separated off and washed with dilute (1:10) hydrochloric acid and then with 3% caustic soda solution and was dried with potassium carbonate; the solvent was driven off in vacuum in a current of nitrogen and the residue was distilled, also in a current of nitrogen. This gave 2.5 g (16%, very pronounced resinification during distillation) of a substance with bp 69°-71.5°C (5mm). Chromatography on an alumina plate in chloroform gave two spots (R_f 0.1 — 3-selenienylmethanol— and R_f 0.85 — 3-chloromethylselenophene). **Thiouronium picrate**—yield 54%, mp 160-161°C (from aqueous ethanol). Found, %: C 32.59, 32.28; H 2.69, 2.72. Calculated for $C_{12}H_{11}N_5O_7SSe$, %: C 32.15; H 2.47.

3-Selenophenealdehyde. Lithium aluminum hydride (0.76 g in 100 ml of absolute ether) was added to a boiling solution of 10 g of 3-selenophenecarbonitrile, bp 90°-91°C (10 mm) [9] in 20 ml of absolute ether, and the mixture was heated at 40°C for 1 hr, left at 20°C for 20 hr, and decomposed with 7 ml of water; the ethereal layer was separated off and the residue was repeatedly washed with ether; the ethereal extract was dried with magnesium sulfate and the ether was driven off. The aldehyde was extracted from the residue with petroleum ether, the solvent was driven off in a current of nitrogen, and the residue was vacuum-distilled in a current of nitrogen. This gave 4 g of the aldehyde (39%); bp 81.5-82.5°C (4 mm). Chromatography on a plate of hydrated silica in benzene gave two spots (R_f 0.25 and 0.8). It was impossible to purify the aldehyde via the bisulfite derivative. **2,4-Dinitrophenylhydrazone**—yield 87%, mp 231-232°C (from ethyl acetate). Found %: C 38.95, 38.70; H 2.53, 2.55. Calculated for $C_{11}H_8N_4O_4Se$, %: C 38.91; H 2.38. **Semicarbazone**—yield 68%, mp 218-219°C (from aqueous ethanol). Found, %: C 34.63, 34.49; H 3.70, 3.57; Calculated for $C_6H_7N_3OSe$, %: C 34.97; H 3.43. **Thiosemicarbazone**—yield 84%, mp 157-158.5° C(from aqueous ethanol). Found, %: C 31.46, 31.38; H 3.23, 2.90. Calculated for $C_6H_5N_3SSe$, %: C 31.03; H 3.04.

2-Phenyl-5-(3-selenenylidene)-4-oxazolone. A mixture of 0.4 g of 3-selenophenealdehyde, 0.45 g of hippuric acid, and 0.2 g of anhydrous potassium acetate in 2.4 ml of acetic anhydride was heated in the water bath at 60°-70°C for 1 hr. This gave 0.45 g (59%) of a product with mp 187°-188°C (from benzene). Found, %: C 55.53, 55.67; H 3.14, 3.06. Calculated for $C_{14}H_9NO_2Se$, %: C 55.64; H 3.00.

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