SYNTHESIS OF 8-HYDROSELENOQUINOLINE AND ITS DERIVATIVES

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The methods of synthesis 8-hydroselenoquinoline and its alkyl-, alkyl-oxy- and phenyl- derivatives have been discussed in the present work. The applicability of potassium selenocyanate and selenourea as the selenium-introducing reagent has been studied. The best results are obtained by the use of selenourea as the selenium-introducing agent. Using this reagent it seems to be possible to obtain some derivatives of 8-hydroselenoquinoline that cannot be synthesized by using potassium selenocyanate as selenium-introducing agent. The corresponding 8,8'-diquinolylselenide and methylselenoquinolines synthesized also. The obtained substances characterized by UV-spectra.

Key words: *8-hydroselenoquinoline; 8-hydroselenoquinoline alkyl-derivatives; 8-hydroselenoquinoline alkyloxy derivatives; 8-hydroselenoquinoline phenyl derivatives.*

INTRODUCTION

8-Hydroselenoquinoline represents itself an analog of the widely known analytical reagents – 8-hydroxyquinoline [1] and 8-mercaptoquinoline [2]. These reagents have found wide application in analytical chemistry for photometric, fluorometric, potentiometric and radiometric determination of minute quantities of heavy metals in the natural and industrial objects as well as for their concentration and separation.

From this point of view, 8-hydroselenoquinoline and its derivatives have been investigated insufficiently. The studies of the analogous reagents containing oxygen, sulfur and selenium offer opportunity to evaluate the influence of the mentioned chalcogens on the physicochemical properties of the reagents themselves and their inner complex compounds. The investigations of interaction of 8-hydroxyquinoline and 8-mercaptoquinoline with metal ions have shown that the latter reagent interacts with the smaller number of metals, that is, it is more selective and its internal complexes are more stable and possess more intense colour. The further improvement of the analytical properties in the case of 8-hydroselenoquinoline is expected.

The latest investigations have shown that 8-hydroselenoquinoline as well as its derivatives and internal complexes possess a definite cytotoxic activity towards the cells of malignant tumors [3–5].

EXPERIMENTAL AND RESULTS

In the present, 8-hydroselenoquinoline and its derivatives have been obtained:

Such derivatives as 2,4-dimethyl-, 2,5-dimethyl-, 2,6-dimethyl-, 2,7-dimethyl- and 5,6-dimethyl-8-hydroselenoquinolines have been prepared as well.

8-Hydroselenoquinolines have been prepared using two methods in relation to the method of introducing of selenium atom in the quinoline nucleus. The first method provides the introduction of selenium atom in the quinoline molecule using potassium selenocyanate; the second method provides the use of selenourea.

The first method has been applied by Sekido et al. [6, 7]. 8-Hydroselenoquinoline has been synthesized according to the scheme (Fig. 1).

Fig. 1. Scheme of synthesis 8-hydroselenoquinoline by using potassium selenocyanate.

According to this scheme, 8-aminoquinoline (1) is diazotized and by action of potassium selenocyanate on the diazonium salt (2) 8-selenocyanatoquinoline (3) has been obtained. By the acidic hydrolysis of 8-selenocyanatoquinoline (3), 8-hydroselenoquinoline (4) has been prepared. From 8-hydroselenoquinoline, under the action of hydrogen peroxide, 8,8'-diquinolyl diselenide (5) has been obtained, but under the action of methyl iodide in the alkaline medium 8-methylselenoquinoline (6) has been prepared.

According to this scheme, Sekido and coworkers have synthesized 8-hydroselenoquinoline [6, 7], Bankovsky and coworkers [8] have prepared 2-methyl-

8-hydroselenoquinoline, but Ashaks and coworkers have obtained 6-methyl- [9], 2-phenyl- [10] and 2,4-dimethyl-8-hydroselenoquinoline [11]. Attempts to synthesize 4-methyl-, 7-methyl- and 5-methoxy-8-hydroselenoquinolines in accordance with the above scheme have not been successful, and therefore Ashaks and coworkers have elaborated a new method for the synthesis of 8-hydroselenoquinoline. In this method, selenourea is used as a selenium-introducing reagent instead of potassium selenocyanate. Synthesis of 8-hydroselenoquinoline by this method is represented by the scheme (Fig. 2).

Fig. 2. Scheme of synthesis 8-hydroselenoquinoline by using selenourea.

8-Aminoquinoline (**1**) is diazotized and then by the action of selenourea on the obtained diazonium salt (**2**) quinoline 8-isoselenouronium derivative (**7**) is obtained. At the alkaline hydrolysis of this isoselenouronium derivative, in the presence of hydrogen peroxide 8,8'-diquinolyl diselenide (**5**) has been obtained. The latter compound can be reduced by hypophosphorous acid in hydrochloric acidic medium to give 8-hydroselenoquinoline (**4**) but by the action of methyl iodide on 8-hydroselenoquinoline in the alkaline medium 8-methylselenoquinoline (**6**) has been prepared.

Using this method, 8-hydroselenoquinoline [12] and its derivatives: 3-methyl- [13], 4-methyl- [14], 5-methyl- [15], 7-methyl- [14], 3-ethyl- [16], 4-ethyl- [17], 5-methoxy [18], 2,5-dimethyl- [19], 2,6-dimethyl- [12], 2,7-dimethyl- [19] and 5,6-dimethyl-8-hydroselenoquinolines [20] have been synthesized.

8-Hydroselenoquinolines are red crystalline substances (2-phenyl-8-hydroselenoquinoline is a blue substance), they are easily oxidized by the air oxygen, colourless 8,8'-diquinolyl diselenides (7,7'-dimethyl-8,8'-diquinolyl diselenide and 2,2',7,7'-tetramethyl-8,8'-diquinolyl diselenide are yellow) being formed.

8-Hydroselenoquinolines due to their easy oxidability in the air are preserved in the form of the corresponding 8,8'-diquinolyl diselenides, which directly before the use are reduced by hypophosphorous acid in the hydrochloric acid medium during 5–10 min at the ambient temperature.

This yields and melting points of the synthesized compounds are compiled in the Table 1.

Table 1. Yields and melting points of 8,8'-diquinolyl diselenide, 8-methylselenoquinoline and their derivatives

Compound	Method of synthesis	Yield, %	Melting point, °C	Reference
8,8'-Diquinolyl diselenide	1	12	205–206	6
8,8'-Diquinolyl diselenide	1	40	205	7
8,8'-Diquinolyl diselenide	2	38	205	12
2,2'-Dimethyl-8,8'-diquinolyl diselenide	1	11	237–238	8
3,3'-Dimethyl-8,8'-diquinolyl diselenide	2	17	263	13
4,4'-Dimethyl-8,8'-diquinolyl diselenide	2	33	253	14
5,5'-Dimethyl-8,8'-diquinolyl diselenide	2	28	258–260	15
6,6'-Dimethyl-8,8'-diquinolyl diselenide	1	13	231–232	9
7,7'-Dimethyl-8,8'-diquinolyl diselenide	2	17	194	14
3,3'-Diethyl-8,8'-diquinolyl diselenide	2	25	207	16
4,4'-Diethyl-8,8'-diquinolyl diselenide	2	30	235	17
5,5'-Dimethoxy-8,8'-diquinolyl diselenide	2	34	243–244	18
2,2'-Diphenyl-8,8'-diquinolyl diselenide	1	16	247–248	10
2,2',4,4'-Tetramethyl-8,8'-diquinolyl diselenide	1	14	273–274	11
2,2',5,5'-Tetramethyl-8,8'-diquinolyl diselenide	2	27	220	19
2,2',6,6'-Tetramethyl-8,8'-diquinolyl diselenide	2	24	210	12
2,2',7,7'-Tetramethyl-8,8'-diquinolyl diselenide	2	15	212	19
5,5',6,6'-Tetramethyl-8,8'-diquinolyl diselenide	2	27	275–277	20
8-Methylselenoquinoline	1	70	60	6
8-Methylselenoquinoline	2	75	60	12
2-Methyl-8-methylselenoquinoline	1	75	84–85	8
3-Methyl-8-methylselenoquinoline	2	84	92	13
4-Methyl-8-methylselenoquinoline	2	85	70	14
5-Methyl-8-methylselenoquinoline	2	84	60	15
6-Methyl-8-methylselenoquinoline	1	71	74	9
7-Methyl-8-methylselenoquinoline	2	75	Liquid	14
3-Ethyl-8-methylselenoquinoline	2	80	70	16
4-Ethyl-8-methylselenoquinoline	2	85	83	17
5-Methoxy-8-methylselenoquinoline	2	75	116	18
2-Phenyl-8-methylselenoquinoline	1	68	71	10
2,4-Dimethyl-8-methylselenoquinoline	1	78	108	11
2,5-Dimethyl-8-methylselenoquinoline	2	85	52	19
2,6-Dimethyl-8-methylselenoquinoline	2	75	101	12
2,7-Dimethyl-8-methylselenoquinoline	2	70	35	19
5,6-Dimethyl-8-methylselenoquinoline	2	80	71	20

Spectral properties of the obtained compounds in the chloroform solutions are presented in the Table 2.

Table 2. Absorbtion maxima (λ , nm) and molar extinction coefficients (ϵ) of 8,8'-diquinolyldiselenide, 8-methylselenoquinoline and their derivatives in chloroform solutions

Compound	λ_1 , nm	λ_2 , nm	ϵ_1	ϵ_2	Reference
8,8'-Diquinolyldiselenide	251	335	38000	9600	12
2,2'-Dimethyl-8,8'-diquinolyldiselenide	254	340	44000	10400	8
3,3'-Dimethyl-8,8'-diquinolyldiselenide	250	325	36000	11200	13
4,4'-Dimethyl-8,8'-diquinolyldiselenide	247	334	32000	12000	14
5,5'-Dimethyl-8,8'-diquinolyldiselenide	256	347	36000	10200	15
6,6'-Dimethyl-8,8'-diquinolyldiselenide	253	348	44000	10800	9
7,7'-Dimethyl-8,8'-diquinolyldiselenide	245	312	28000	11800	14
3,3'-Diethyl-8,8'-diquinolyldiselenide	250	327	36800	11200	16
4,4'-Diethyl-8,8'-diquinolyldiselenide	247	335	40000	12000	17
5,5'-Dimethoxy-8,8'-diquinolyldiselenide	260	359	34000	9200	18
2,2'-Diphenyl-8,8'-diquinolyldiselenide	282	347	72000	17800	10
2,2',4,4'-Tetramethyl-8,8'-diquinolyldiselenide	253	330	42000	13200	11
2,2',5,5'-Tetramethyl-8,8'-diquinolyldiselenide	260	345	44000	10800	19
2,2',6,6'-Tetramethyl-8,8'-diquinolyldiselenide	255	341	48400	10400	12
2,2',7,7'-Tetramethyl-8,8'-diquinolyldiselenide	315	328	12400	11600	19
5,5',6,6'-Tetramethyl-8,8'-diquinolyldiselenide	257	350	45000	10800	20
8-Methylselenoquinoline	259	345	16800	4600	12
2-Methyl-8-methylselenoquinoline	260	342	19600	4400	8
3-Methyl-8-methylselenoquinoline	262	343	17200	5000	13
4-Methyl-8-methylselenoquinoline	258	345	16000	6000	14
5-Methyl-8-methylselenoquinoline	263	358	17000	5000	15
6-Methyl-8-methylselenoquinoline	260	347	20000	5000	9
7-Methyl-8-methylselenoquinoline	258	323	14000	4000	14
3-Ethyl-8-methylselenoquinoline	264	345	17600	5000	16
4-Ethyl-8-methylselenoquinoline	258	345	16000	6200	17
5-Methoxy-8-methylselenoquinoline	265	365	15600	4300	18
2-Phenyl-8-methylselenoquinoline	287	347	33600	4800	10
2,4-Dimethyl-8-methylselenoquinoline	262	342	19000	5800	11
2,5-Dimethyl-8-methylselenoquinoline	265	353	20800	5000	19
2,6-Dimethyl-8-methylselenoquinoline	262	345	22600	4500	12
2,7-Dimethyl-8-methylselenoquinoline	257	325	12800	4400	19
5,6-Dimethyl-8-methylselenoquinoline	262	357	20000	5000	20

CONCLUSIONS

1. The methods of synthesis of 8-hydroselenoquinoline and its derivatives have been discussed in the present work. The applicability of potassium selenocyanate and selenourea as the selenium-introducing reagents has been studied.

2. The best results are obtained by the use of selenourea as the selenium-introducing agent. Using this reagent, it seems to be possible to obtain some derivatives of 8-hydroselenoquinoline that cannot be synthesized using potassium selenocyanate as the selenium-introducing agent.

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8-SELENOLHINOLĪNA UN TĀ ATVASINĀJUMU SINTĒZE

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K O P S A V I L K U M S

Darbā apskatītas 8-selenolhinolīna un tā atvasinājumu sintēzes metodes, kā selēnu ievadošu reaģentu izmantojot kālija selenocianātu un selēnurīnvielu. Selēnurīnvielas pielietošana dod labākus rezultātus. Izmantojot šo reaģentu, izdodas iegūt dažus 8-selenolhinolīna atvasinājumus, kurus ar kālija selenocianāta palīdzību nevar iegūt.

СИНТЕЗ 8-СЕЛЕНОЛХИНОЛИНА И ЕГО ПРОИЗВОДНЫХ

Я. Ашакс, Э. Силинь, Д. Зарума

Р Е З Ю М Е

В работе рассмотрены методы синтеза 8-селенолхинолина и его производных. Исследовано применение селеноцианата калия и селеномочевины в качестве селеновводящих реагентов. Применение селеномочевины дает лучшие результаты. Применяя этот реагент, удалось получить некоторые производные 8-селенолхинолина, которые с помощью селеноцианата калия синтезировать не удалось.